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REVIEWING FDA'S IMPLEMENTATION OF FDASIA

FRIDAY, NOVEMBER 11, 2013

House of Representatives,

Subcommittee on Health,

Committee on Energy and Commerce,

Washington, D.C.

The subcommittee met, pursuant to call, at 10:00 a.m., in Room 2322, Rayburn House Office Building, Hon. Joseph R. Pitts [chairman of the subcommittee] presiding.

Present: Representatives Pitts, Burgess, Whitfield, Shimkus, Rogers, Murphy, Blackburn, Gingrey, Lance, Guthrie, Griffith, Bilirakis, Upton (ex officio), Pallone, Dingell, Engel, Capps, Green, Butterfield, Barrow, Castor, Sarbanes, and Waxman (ex officio).

Staff Present: Clay Alspach, Chief Counsel, Health; Sean Bonyun, Communications Director; Noelle Clemente, Press Secretary;

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Brad Grantz, Policy Director, O&I; Sydne Harwick, Legislative Clerk; Robert Horne, Professional Staff Member, Health; Carly McWilliams, Professional Staff Member, Health; Andrew Powaleny, Deputy Press Secretary; Chris Sarley, Policy Coordinator, Environment & Economy; John Stone, Counsel, Oversight; Ziky Ababiya, Minority Staff Assistant; Eric Flamm, Minority FDA Detailee; Karen Nelson, Minority Deputy Committee Staff Director for Health; Rachel Sher, Minority Senior Counsel; and Ryan Skukowski, Minority Staff Assistant.

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Mr. Pitts. The subcommittee will come to order. The chair will recognize himself for an opening statement.

The Food and Drug Administration Safety and Innovation Act, FDASIA, was signed into law on July 9th, 2012. The purpose of the bill was to bring predictability, consistency, and transparency to FDA's regulation of drugs and devices. To that end, FDASIA reauthorized two successful user fee programs, the Prescription Drug User Fee Act, PDUFA, and the Medical Device User Fee Act, MDUFA, scheduled to expire at the end of fiscal year 2013. It also authorized two new user fee programs, for generic drugs, GDUFA, and biosimilars, BSUFA. In each case the industry negotiated a level of user fees to be paid to FDA in return for the agency meeting agreed-upon performance and accountability metrics.

Additionally, FDASIA permanently reauthorized the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act; reformed both the drug and medical device regulatory processes; addressed drug supply chain and drug shortage issues; and incentivized the development of new antibiotic drugs, among other provisions. The bill represents a bipartisan success not only for our committee, but for Congress as a whole. It passed the House by a voice vote and passed the Senate by a vote of 92-4.

Now, over a year later, we are here to examine whether the law

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has been a success for the American people, resulting in safer drugs and devices, faster approval times, and more consistency and predictability in the process. There is great congressional interest, not only in the overall implementation of FDASIA, but also in the day-to-day operational challenges and successes. And I would like to congratulate Dr. Woodcock for what I understand is significant progress in the Center for Drug Evaluation and Research.

I would like to welcome both Dr. Janet Woodcock and Dr. Jeffrey Shuren to the subcommittee. I look forward to hearing their testimony. And I yield 1 minute to Dr. Gingrey.

[The prepared statement of Mr. Pitts follows:]

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Dr. Gingrey. Mr. Chairman, thank you very much for yielding. I, too, am pleased to see Dr. Woodcock and Dr. Shuren again today. FDASIA looked to address the crisis of antibiotic resistance with Title VIII, the GAIN Act, which I wrote with my colleagues Mr. Green, Mr. Shimkus, Ms. DeGette, Mr. Whitfield, and Ms. Eshoo.

By focusing on incentives to bring new drugs to market we have seen renewed focus on the development of cutting-edge drugs, antibiotic. However, even with the early success of this program, I do believe that we do need to do more.

And so, Mr. Chairman, CDC had a September report, CDC in my great capital center of Atlanta, Georgia, on antimicrobial resistance, highlights 18 known resistance threats. It is estimated that across the country more than 2 million people are sickened every year with antibiotic-resistance infections resulting in at least 23,000 deaths -- 23,000 deaths.

I look forward to continuing to work with the FDA to create innovative pathways and processes. We must make sure that the agency and drug developers have as many tools as possible to navigate this emerging public health problem.

And I yield back.

Mr. Pitts. The chair thanks the gentleman.

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[The prepared statement of Dr. Gingrey follows:]

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Mr. Pitts. And now yields the balance of time to Mr. Lance.

Mr. Lance. Thank you, Mr. Chairman.

Today's hearing serves as a helpful pulse check of the FDA's implementation of the user fee agreements for the prescription drug medical device, generic, and biosimilars industry signed into law last year. In New Jersey alone the life sciences support over 300,000 direct and indirect jobs and contributes more than \$25 billion to the State's economy.

Historically the user fee agreements have improved the times of drug and devices, and today's hearing will help this committee gain further insight on how the FDA is carrying out these congressionally mandated responsibilities. It is important that regardless of the challenges the agency face it remain committed to bringing innovative treatments to market and in the hands of patients who need them the most.

Thank you, Mr. Chairman. I look forward to hearing from our distinguished witnesses, Dr. Woodcock and Dr. Shuren, on these issues. And I yield back to you, sir.

Mr. Pitts. The chair thanks the gentleman.

[The prepared statement of Mr. Lance follows:]

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Mr. Pitts. Now yields 5 minutes to the ranking member, Mr. Pallone, for an opening statement.

Mr. Pallone. Thank you, Chairman Pitts.

And thank you to our witnesses for being here today. I am eager to hear your testimony about FDA's progress in implementing the Food and Drug Administration's Safety Innovation Act, or FDASIA.

Over 1 year ago, FDASIA was signed into law, and among other things designed to promote timely FDA review of drugs, medical devices, generic drugs, and biosimilar biological products through the collection of user fees. It both renewed existing FDA user fee programs for pharmaceutical and medical device manufacturers and established new user fee programs for generic drugs and for lower cost versions of biotech drugs.

The user fees are an essential component of FDA's funding. They help to ensure a predictable and efficient review process so that the American public has access to safe and effective healthcare products.

For generics, at the time of enactment there was a backlog of over 2,500 applications for new generic drugs and a median review time of 31 months. These essential products typically cost 50 to 70 percent less than their brand name counterparts and have provided an estimated \$1 trillion in savings to the Nation's healthcare system over the past decade. It is important that American consumers have access to these

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safe, effective, and low cost alternatives more quickly, which is why the provisions in the generic drug user fee agreement were so important, because it gave FDA the resources they need to make sure that happens. So I am interested to hear in that progress today.

FDASIA also gives FDA additional tools to ensure the safety of the global drug supply chain, such as requiring registration with the unique facility identifier for foreign and domestic drug establishments, administrative detention for adulterated or misbranded drugs, and increased penalties for counterfeit drugs. The additional authorities in FDASIA allow FDA to strengthen cooperation with foreign regulators as well.

These provisions were based on the ideas and proposals contained in the Drug Safety Enhancement Act, which I introduced with Mr. Dingell, Mr. Waxman, and Ms. DeGette. We worked hard with our Republican colleagues during consideration of this law to help FDA keep our medicines safer in this complex and ever-growing global supply chain.

We also included provisions in FDASIA to address drug shortages. FDASIA enhances early notification of supply interruptions for certain medically important drugs and directs FDA to establish a task force and submit a strategic plan on drug shortage mitigation, which FDA submitted to Congress last month. Early notification started as a result of an executive order in 2011 and was codified into law by FDASIA,

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and it has helped FDA to prevent shortages and to decrease the number of new shortages.

I will close by saying that FDASIA is the product of strong bipartisan collaboration and compromise that strengthens FDA's ability to safeguard the public health. What I outlined here today was only a snapshot of the promising provisions of the law. We strengthened both the agency and the public health by its passage while allowing companies to innovate in the process. And I am proud of the work we did in passing FDASIA, and I look forward to hearing about FDA's progress so far in implementing this law.

So I would like to yield the remainder of my time to Mr. Dingell.

[The prepared statement of Mr. Pallone follows:]

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Mr. Dingell. I thank my good friend for that.

This legislation is a fine example of the great work this committee can do when we put politics aside and work together in a bipartisan manner. I hope the committee will return to this spirit when considering a lot of other issues that will lie before us today and in following times.

One year ago President Obama signed the Food & Drug Administration Safety Innovation Act into law, the law [audio gap] user fee programs FAD. Big bold steps to improve supply chain safety, amongst other things. FDA now needs new innovative tools to deal with increasingly globalized supply chain [audio gap] succeed in their mission keeping the American people safe from harm from food, drugs, cosmetics, and other things.

I look forward to hearing from our witnesses today about the progress made by FDA and I commend you for having this hearing, and look forward to hearing from Food and Drug about what it is they are doing, how the matter is proceeding and how much more this committee must do to see to it that they are able to carry out their responsibilities.

Dr. Woodcock, welcome.

I yield back to my good friend Mr. Pallone the time that he so graciously yielded to me.

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[The prepared statement of Mr. Dingell follows:]

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Mr. Pallone. I yield back the balance of my time.

Mr. Pitts. The chair thanks the gentleman.

Now recognize the chair of the full committee, Mr. Upton, 5 minutes for an opening statement.

The Chairman. Well, thank you again, Mr. Chairman. And I appreciate this morning's hearing on the implementation of the FDA Safety and Innovation Act.

You know, as many of us know, this was one of the committee's most significant bipartisan achievements in the last Congress, it really was. I particularly want to thank Dr. Woodcock, who is with us, and Dr. Shuren for coming today to provide an update on that implementation, something that we said we would do when it passed.

Last Congress this committee held at least 10 hearings on subjects related to the legislation, and at these hearings we focused on improving the predictability, consistency, and transparency of FDA's regulations of drugs and medical devices. Improving FDA regs is essential to fostering innovation which brings life-saving and life-improving drugs and medical devices to American patients and boosts job creation across the country, including southwest Michigan, most importantly.

I was very proud of the bipartisan work that we did in the last Congress, and I am pleased to hear that initial reports on

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implementation, especially at the Drug Center, are promising. Today is an opportunity to get an update on whether the FDA is meeting its commitments related to the various user fees that we authorized, as well as the independent assessment of the device center.

It also is a chance to hear about how the FDA is implementing provisions related to rare diseases, drug shortages, an important provision that we wrote in, prescription drug abuse, and drug imports. These were provisions important to Republicans and Democrats, Americans across the country, and we look forward to working with the FDA on these issues. Our drug and device makers are global leaders in innovation and job growth, and we will continue working to ensure that they remain on top.

And I am prepared to yield to any of my Republican colleagues. Seeing none, I yield back the balance of my time.

Mr. Pitts. The chair thanks the gentleman.

[The prepared statement of The Chairman follows:]

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Mr. Pitts. Now recognize the ranking member of the full committee, Mr. Waxman, 5 minutes for an opening statement.

Mr. Waxman. Thank you, Mr. Chairman. I am pleased we are holding this oversight hearing on the legislation that we passed last year on a bipartisan basis, bipartisan, bicameral, and with the close working relationship with the Food and Drug Administration.

The bill had a number of important provisions. It reauthorized FDA's drug and medical device user fees programs, providing resources to enable the efficient review of applications and give patients access rapidly to new therapies. It reauthorized two pediatric programs which foster the development and safe use of prescription for children. Established two new user fee programs to help FDA speed up the review of new generics and biosimilars. It gave FDA new authorities to address a wide array of issues with respect to drugs and devices, new incentives for the development of antibiotics to treat serious and life-threatening infections. This was designed to ensure that the drugs we most need to protect us from dangerous resistant pathogens are the ones that are developed as quickly as possible.

This law also includes provisions to modernize FDA's authorities with respect to our increasingly globalized drug supply chain. Today 80 percent of the active ingredients in bulk chemicals used in U.S. drugs come from abroad and 40 percent of finished drugs are

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manufactured abroad. This law gave FDA new and improved tools to police today's dramatically different marketplace. The legislation addressed the crisis of drug shortages that has caused many problems for access to medicines in our country.

There are provisions relating to medical devices. I had some concerns about many of the device proposals, but we worked together to address these concerns with the goal of assuring that nothing in the House-passed bill took us backwards in terms of patient safety. And I hope Dr. Shuren will tell us today whether we succeeded in that goal or if there have been unintended and detrimental facts of this legislation.

Mr. Chairman, I thank you for holding this hearing. It is an important part of the job of Congress not just to work together to pass legislation, but to continue our review and oversight. I hope FDA will share with us whether there are any refinements or improvements to any of the law's provisions that we need to pass through the Congress. Our goal was and still is to ensure that the American public benefits from this legislation by getting access to safe and effective drugs and medical devices at the earliest possible time. I look forward to the testimony.

I do notice that I do have a couple of minutes left and if any member on our side of the aisle wants that time I would be happy to

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yield to them. And if not, I will offer the time to anybody on the other side of the aisle who wants to make any further comments. If not, I yield back the time.

Mr. Pitts. The gentleman yields back. Chair thanks the gentleman.

[The prepared statement of Mr. Waxman follows:]

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Mr. Pitts. That concludes the opening statements.

On our panel today we have two witnesses from the U.S. U.S. Food and Drug Administration, Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research, and Dr. Jeffrey Shuren, Director of the Center for Devices and Radiological Health.

Thank you for coming. Your written testimony will be made a part of the record. We ask that you summarize your opening statements to 5 minutes. And at this time the chair recognizes Dr. Woodcock for 5 minutes for an opening statement.

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STATEMENTS OF JANET WOODCOCK, M.D., DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION; AND JEFFREY E. SHUREN, M.D., J.D., DIRECTOR, CENTER FOR DEVICES AND RADIOLOGICAL HEALTH, FOOD AND DRUG ADMINISTRATION

STATEMENT OF JANET WOODCOCK

Dr. Woodcock. Thank you and good morning. I am Janet Woodcock, head of the center for drugs at FDA.

The FDASIA legislation was really landmark legislation for drug regulation. It authorized two new user fee programs, one of which was critically needed to fix a problem, the problem of the backlog of generic drugs, a program that had become burdened by its own success and the massive filing of new generic drug applications that we had. And another one, which is more or less preventive, the biosimilars user fee program, hopefully will help us promptly review biosimilar drugs and get them on the market as we receive applications.

It also made two pediatric pieces of legislation permanent. And I am happy to say we passed a landmark of 500 labels that have been revised and updated with pediatric information because of this legislation. So 500 drug labels have information now for children that

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didn't before.

Additional pressing problems that were addressed included the lack of new pipeline for antibiotics, particularly for drug-resistant organisms, the drug shortage problem, and the supply chain safety issues. In addition, the legislation included a breakthrough designation program that has been very enthusiastically taken up, both by the industry and by the FDA, and many other provisions of course.

Congress laid out a very ambitious agenda and timeframe for our accomplishment of all of this, and we have been working hard, we have been very successful in implementing provisions. However, I brought our spreadsheet. This is two-sided, okay, tracking of all the obligations that we have under this legislation. And this isn't all of them, but it is certainly the ones that have hard deadlines. So we are trying to work against all these deadlines and make all of our timeframes and so forth.

I am happy to discuss this year's progress with you, and I look forward to working with the committee. Thank you.

Mr. Pitts. The chair thanks the gentlelady.

[The prepared joint statement of Dr. Woodcock and Dr. Shuren follows:]

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Mr. Pitts. Dr. Shuren, you are recognized 5 minutes for an opening statement.

STATEMENT OF JEFFREY E. SHUREN

Dr. Shuren. Thank you. Mr. Chairman and members of the subcommittee, I am Dr. Jeff Shuren, Director, Center for Devices and Radiological Health, or CDRH, at the Food and Drug Administration.

FDASIA includes a third authorization of the Medical Device User Fee Act, or MDUFA III. Reauthorization of the medical device user fee program has helped to speed innovative new products to market without compromising safety and effectiveness. It did so by establishing new policies, procedures, and performance goals, and by boosting review capacity. It represents our commitment to increase the predictability, consistency, and clarity of our regulatory processes.

In exchange for the additional user fees, we work with stakeholders to develop much enhanced performance goals. We are committed to meeting those goals, and preliminary data indicates that we are on track to meet or exceed all of our fiscal year 2013 performance goals, and that includes a new shared goal with industry of average time to decision.

Since the early 2000s, CDRH's performance on several key measures

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had been steadily declining each year, reaching its lowest point in 2010. In 2010 we conducted an extensive assessment of our premarket programs, identified the problems, proposed solutions, sought extensive public input, and then issued a plan of action in January 2011, with some corrective action starting in 2010. Since 2010, due to the reforms we put in place in MDUFA III, we have seen improvement in these key measures. For example, our backlogs of 510(k) submissions and PMA applications are each down by about one-third. Our average total time to decision of PMA applications is down 37 percent. The percent of 510(k)s cleared and percent of PMAs approved are back up, in the case of PMAs back to where it was about a decade ago.

To provide greater transparency we are would providing substantially more detailed reporting on our progress in implementing performance goals. These reports are publicly available online and are discussed at quarterly meetings with industry.

FDASIA also includes provisions to streamline the de novo pathway for novel devices of low to moderate risk. Since passage of FDASIA, we have seen the number of de novo requests roughly double. We have also implemented process improvements and are seeing our review times for de novos trending downward as a result. As part of our MDUFA III commitments we agreed to implement our benefit-risk determination guidance we issued in March 2012. For the very first time and with

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public input we described the factors we would use in determining whether or not the benefits of the device outweigh its risk.

The framework we developed is flexible and patient-centric. For example, one factor we may take into account is patients' tolerance for risk and perspectives on benefits. Because patient viewpoints matter and to further implementation of the framework, earlier this year we launched our Patient Preferences Initiative. The initiative seeks to identify and validate tools for assessing patient preferences, establish an approach when incorporating those preferences into our device approval decisions, and then communicating that information publicly so that patients and practitioners can make better-informed decisions.

CDRH implemented the FDASIA provisions relating to investigational device exemptions, or IDEs. We have trained our staff and modified our decision letters to align them with FDASIA's requirement that FDA may not disapprove the clinical investigation on the basis that it would not support approving the device.

We have also taken several steps to facilitate first-in-human studies in the U.S. and to streamline our clinical trials program. As a result, the mean time for giving approval for manufactures to proceed with clinical studies of their devices has been cut almost in half.

We also recently announced a final rule for unique device

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identification, or UDI system, which will provide a standardized way to identify medical devices. The UDI reflects substantial input from the clinical community and from the device industry during all phases of its development. Once fully implemented the UDI system will provide improved visibility for devices as they move through the distribution change to the point of patient use, greatly enhancing our post-market surveillance capabilities and offering a way of documenting device use in electronic health records. We have also made good progress on classifying the remaining pre-amendment devices. Since passage of FDASIA we have issued 13 proposed orders.

Implementing the device-related provisions of FDASIA is a massive undertaking, but we are committed to doing it in a way that provides lasting improvement to public health. Mr. Chairman, I commend the subcommittee's efforts and am pleased to answer any questions.

Mr. Pitts. The chair thanks the gentleman. That concludes the opening statements. We will now begin questioning. I will recognize myself 5 minutes.

Before I begin, Dr. Woodcock, would you submit that spreadsheet for the record? The spreadsheet.

Dr. Woodcock. I will confer with my folks and see what I can send you. We definitely will give you something.

[The information follows:]

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Mr. Pitts. All right. And I have a number of questions for both of you that I will submit for the record. Would appreciate that you respond promptly.

[The information follows:]

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Mr. Pitts. Dr. Woodcock, we enacted FDASIA in order to bring greater predictability, consistency, and transparency to FDA's regulation of medical devices and drugs. FDASIA included some significant changes to the review process on the device and drug side. How have you translated the FDASIA policy changes into the regulatory review process? And how have you communicated these changes to your staff? How are you ensuring that your staff implements the law correctly?

Dr. Woodcock, you want to begin?

Dr. Woodcock. Well, some of the primary changes that we received, we negotiated with the industry under the PDUFA agreements for a new review program for new molecular entities. They are the most innovative drugs. We are now having midcycle meetings during the review process. So this mainly changes how we run the review process, allows for more communication between industry and the review staff during the review process. And it is hoped we can clear up any confusion, answer questions and so forth, and get to a complete response that includes all the issues at the end of the day.

So we are running that as a pilot. We are going have an independent assessment of that. We have had a number of new molecular entities that have been approved. I believe six have been approved that have gone through that program. So it is in its early stages,

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though, because we are going to run several years of the program and then evaluate its success.

And the other major change, of course, has been the breakthrough designation program, and I could talk about that if you want. So we have received almost up to 100 applications for designation under this program. We have designated more than 25 different products for a range of different diseases as potential breakthrough products. And we have just approved two, one last week and one on Wednesday. On Wednesday we approved a drug for mantle cell lymphoma, which is a rare kind of immune system or blood tumor.

So we feel this program has been fairly successful so far in bringing greater attention to drugs that are potential game changers for people with serious diseases.

Mr. Pitts. All right. Thank you.

Dr. Shuren, under MDUFA III industry and the FDA agreed to have an independent two-phase assessment and program evaluation to objectively assess the FDA's premarket review process. Can you explain how FDA was involved in setting the parameters of this assessment?

Dr. Shuren. Certainly. We have put out calls for an independent contractor to perform the work, and that was assigned to -- oh, my apologies.

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We have put out a call to have an independent contractor perform the assessment, and Booz Allen Hamilton is that contractor. We worked on a draft statement of work which we put out to the public for comment. We had discussions with industry on what should go into that statement of work.

And then finally we have been overseeing the process for the contractor. We get updates on the progress they make. But it is independent, so we don't know what they are actually going to report to us. Our understanding is they have gone out, they have had conversations with stakeholders, particularly industry, they have conducted focus groups. And we are expecting to get their first report very soon, and we have a public commitment to make that available to the public in December, which we will do. And that first phase includes their at this point preliminary findings, a lot of their more of the low-hanging fruit. Six months thereafter, so in May, they will have the second phase, where we will get all of their recommendations. At that point, too, we have a public commitment to issue our plan for implementation of the recommendations.

Mr. Pitts. Would you agree to submit a detailed accounting of the agency's involvement with the contractor relating to the review and any recommendations or directions you provided them?

Dr. Shuren. Yes, we can provide you with information.

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Mr. Pitts. And would you agree to submit a compiled list of recommendations in its entirety to the committee upon its completion?

Dr. Shuren. We are going to make it available to the entire public.

Mr. Pitts. Okay.

Dr. Shuren. But we will include you on that, too.

[The information follows:]

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Mr. Pitts. All right.

Dr. Woodcock, the President's Council of Advisors on Science and Technology September 12th report included specific recommendations on how the Federal Government might propel innovation in drug discovery and development. PCAST expressly recommended, quote, "It could be valuable for the Congress to establish that encouraging innovation and drug development is a clear component of the FDA mission," end quote.

Do you agree with the President's advisors that including innovation in the mission statement would be valuable?

Dr. Woodcock. Well, I think it is a double-edged sword. We don't encourage innovation for innovation's sake. Okay? Innovation can end up being bad as well as being good, right? But innovation is essential to treat current unmet medical needs. So absolutely we should foster innovation and be open to it and allow new methods of both treating patients and manufacturing drugs to have progress. So I think it is really how you state that support for innovation that is important.

Mr. Pitts. All right. My time has expired.

The chair recognize the ranking member, Mr. Pallone, 5 minutes for questions.

Mr. Pallone. Thank you, Mr. Chairman.

My questions of Dr. Woodcock -- first, welcome back. I can guess

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you have had quite a busy year. And I wanted to start today talking about the new Office of Generic Drugs. I was glad to see the decision FDA made last year to elevate the Office of Generic Drugs to a super office on equal footing with the Office of New Drugs within the agency. And as you know, I introduced a bill last year that included a provision to do just that and I have long been an advocate for the structural change within FDA to enhance the role of the Office of Generic Drugs.

I would like to ask you, Dr. Woodcock, whether the Office of Generic Drugs has officially been set up in its new elevated position? And how is it structured? What kinds of changes have been made? And when do you expect the change to be finalized?

Dr. Woodcock. The organizational change has been not finalized. We are in the final stages of that, and I hope it would occur very soon. What it will do is recognize the fact that generic medicines treat most people in the United States. Eighty-four percent of dispensed prescriptions are for generic drugs. And so the new generic drug office will have a much more clinical focus. We will have more doctors there, more clinical staff, very much focused on therapeutic equivalents, the adverse event reporting, making sure those generic drug labels are up to date and so forth.

So as a super office it is proposed to have a bioequivalence office, a research office, because under GDUFA we negotiated and

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received money so that we can do research to get new categories of drugs like inhalers to become generics, right? So they have a research office and then an office that will run the operations, including a clinical safety staff.

Now, as part of this, what we are proposing, though, is that quality regulation, drug quality regulation be reorganized and that we centralize that, and that is a plan that I am working very intimately on. And this would ensure that generic drugs, new drugs, over-the-counter drugs, any kind of drug we regulate have the exact same quality expectations across the industry.

Mr. Pallone. Okay. Then I wanted to speak about the FDA's progress in implementing GDUFA. I commend the FDA on meeting its GDUFA hiring goals for the fiscal year and as I know the difficulties associated with implementing a brand new program. But how many FTEs have you hired to date and how many do you plan to hire in the first two quarters of next year? And given the backlog of pending ANDAs, can you give the committee an estimate on how many of these new hires will be dedicated to ANDA review? I have others, but let's start with that.

Dr. Woodcock. Okay. We have hired upward of 300 people. I mean, that number changes every day. We are aggressively hiring. And we exceeded our GDUFA goal, which was 25 percent of the total number

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of people that were to be hired. Okay?

We have acted on 900, I think, of ANDAs in the backlog in different ways, so we have reduced that pending backlog, but it is still formidable. I wouldn't diminish that. And we have done a lot of things to try and aggressively address this backlog. So your other question?

Mr. Pallone. Well, I was going to ask you if the government shutdown affected the progress for those 2 or 3 weeks?

Dr. Woodcock. Well, the major effect on our review programs, because we were able to continue to operate under the user fees. However, the inspections stopped for those several weeks. So the inspectional programs were not operating. And of course that is one of the things that we really need to ramp up under GDUFA, is to increase the number of facility inspections that we do if we are going to tackle this backlog and get into a steady state.

Mr. Pallone. And the last thing, it is my understanding that FDA recently advised sponsors that it has restricted communications with sponsors during the ANDA process. Specifically, rather than providing ongoing status updates, the FDA has a new policy of only providing approval answers. Can you explain the reasoning behind this, why you feel the need to have less communications than before, given that we have the user fee funds available?

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Dr. Woodcock. We have upward of 8,000 items pending in the generic drug review program. The previous practice was companies would call all over the place to try to find their status. If every chemist and bioequivalence reviewer is answering questions from 8,000 different sites asking them what is the status, we are never going to get done.

So we are trying to bring order to this process, like we have for PDUFA, and what we want to do is have predictable deadlines so that every company knows their application is on track and going to get out of the agency and they are going to get a complete response within the timeframe that has been established under GDUFA.

So I think some of this is a transition issue where we are going from one state to another and we are going to have to get through this period. We are doing everything we can and we are considering additional steps to notify industry as their application approaches an action so that they can prepare, say, for launch or whatever they need to prepare for. We understand that need. However, we can't have companies' thousands of calls to reviewers or we are not going to get this program done.

Mr. Pallone. All right, thanks a lot.

Mr. Pitts. The chair thanks the gentleman.

We are presently voting on the floor. We will try to get through

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a couple more members. The chair recognize Mr. Whitfield for 5 minutes for questions.

Mr. Whitfield. Well, thank you very much, and thank you all for joining us this morning.

Last April I attended a meeting with a group of dermatologists and they were talking about the approval process for over-the-counter in general and sunscreen in particular. And they had indicated that there were, like, eight sunscreen applications that had been at FDA waiting for a decision for, like, 10 years. Some of these have been used in Europe.

We all are very much aware that you all have a very heavy workload and you have limited resources. And I know in conversations with Congressman Dingell, and I know on the Senate side Senator Reid and Isakson have been discussing this issue, and Congressman Dingell and I have draft legislation to try to expedite the process and we had submitted to you all for technical assistance. And I was going to ask, one, are you, with the multitude of issues you deal with, are you even aware of legislation that we have submitted? And if you are, could you give us any idea of maybe when we could expect a response from you?

Dr. Woodcock. We hope you would get a prompt response.

Mr. Whitfield. Okay.

Dr. Woodcock. This is a very intractable problem. I think, if

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possible, we are more frustrated than the manufacturers and you all are about this situation. We have to do regulations to get these ingredients into the monographs. That is the problem. And they are backlogged and they are slow to get through, and we have to do a proposed regulation, sometimes we have to do advanced notice of proposed regulation, then do a proposed rule, and then do a final rule, which can take 6 to 8 years. And we have multiple categories of these over-the-counter products that we have to handle. But the sunscreens, there is a public health issue here.

Mr. Whitfield. Right. And who on your staff specifically can we be in contact with on the technical assistance?

Dr. Woodcock. Well, I think that our lead in this is Dr. Sandra Kweder, who is acting head right now of the office that oversees this, but, of course, work through our legislative staff and we will provide any assistance needed.

Mr. Whitfield. Okay.

Mr. Dingell. Would the gentleman yield?

Mr. Whitfield. I would be happy to yield.

Mr. Dingell. Briefly. First of all, I want to thank the gentleman. Second of all, I want to commend him. And third of all, I want to note that this is important. This matter has been dawdling by prodigious overlong delay, and it has simply got to come to a halt.

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Your assistance would be extremely important. I want to work with my good friend. And I urge you to resolve this problem. It is a significant problem that does do the Food and Drug Administration no credit whatsoever.

Mr. Whitfield. I yield back the balance of my time.

Mr. Pitts. The chair thanks the gentleman.

I think we can get one more in. We will reconvene shortly after the second vote. There are two votes. That will be about 11 o'clock. The chair recognize the gentleman, Mr. Dingell, 5 minutes for questions.

Mr. Dingell. Mr. Chairman, I would like to defer. I move rather slowly.

Mr. Pitts. All right. Then we will at this point recess the committee until after the second vote, and hope you will be patient with us. We will get back as soon as we can. Thank you. The committee is in recess.

[Recess.]

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RPTS JOHNSON

DCMN CRYSTAL

[11:09 a.m.]

Mr. Pitts. The time for our recess having expired, the subcommittee will reconvene. And the chair recognize the gentleman from Texas, Mr. Green, for 5 minutes for questions.

Mr. Green. Thank you, Mr. Chairman, for holding the hearing.

And, Dr. Woodcock and Dr. Shuren, thank you for taking time to be here today.

One of my top priorities is fostering a regulatory environment that would promote the development of the new antibiotic drugs to address the growing public health threat of drug-resistant bacteria. I am proud to have worked with leaders on this committee, Dr. Gingrey and a coalition of other members, to advance the GAIN Act last year. We have always said that this was a good first step, but more must be done. And I know from your testimony today that is true. Thank you for your leadership on the GAIN Act, Dr. Woodcock, and also promoting the new antibiotic development.

In April, CDC released a report on drug-resistant bacteria. In that report, CDC states that antimicrobial resistance is one of the most serious health threats to our country. Dr. Woodcock, does the

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FDA agree with the CDC on the nature of this threat?

Dr. Woodcock. Absolutely. We are very concerned about this.

Mr. Green. In this report, the CDC highlights a handful of strategies to address this threat. One of the main methods they suggested was to develop new antibiotics. As I understand it, part of the challenge of the new developing antibiotics is that drug resistance oftentimes begins in limited populations and approving a drug through the FDA for use in a limited population can be difficult.

Dr. Woodcock, on June 4th of this year you were quoted by the National Public Radio as saying that you hope Congress would pass legislation soon to make it easier for FDA to approve new antibiotics. What type of legislation were you referring to when you made those statements on NPR?

Dr. Woodcock. Well, there have been discussions, and the PCAST report referred to earlier -- I am sorry. There have been discussions, and the PCAST report referred to earlier have talked about a program for limited use that is specifically directed where there is subpopulation of broader population. Because one of the problems we have with the antibiotics, as you well know, is overuse. And what we are concerned about if we approve an antibiotic for a limited use, just for drug-resistant organisms, that there would be temptation to use it more broadly and thus lose its effectiveness. And so we feel that

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it should be explored that Congress could make some kind of program that would really send a signal about limited use and then good antibiotic stewardship.

Mr. Green. Well, I am working on legislation with my colleague Dr. Gingrey, and meant to be the next step from GAIN, focused primarily on promoting antibiotics meant to be used in limited populations. Is there anything that you believe we should keep in mind as we draft this legislation?

Dr. Woodcock. Well, I feel that a strong signal from Congress to the healthcare community about stewardship would be extremely important. FDA frequently approves drugs for limited populations, but usually there isn't that sort of, let's say, an orphan population, there isn't that sort of temptation or ability to use it broadly in a much broader population.

So one of the main things is a signal from Congress that it is fine to do limited populations out of a broader disease with a very small development program, but then there should be that stewardship by the healthcare community to not use it more broadly.

Mr. Green. Well, and I know if you deal with any of the infectious disease specialties, they talk about that. And can we statutorily, because I know in medical practice a doctor can make that decision on their own, and that may be part of the problem. But you can't limit

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it to just, for example, people who deal with infectious diseases, I guess.

Dr. Woodcock. We feel that there shouldn't be an overt limitation like that, because it is not feasible. Patients come in, they have infections, there is a resistant strain circulating in the community, doctors should have the discretion to use appropriate antibiotics. However, I think a signal of prudence and stewardship would be a mechanism I think would be very effective.

Mr. Green. And I am almost out of time, but the other issue on that is we need to make sure we keep this, because what may be successful a year from now or 10 years from now, we will still have people who develop those resistance, so we need to keep that pipeline going for these new levels of antibiotics and other ways to treat these terrible illnesses.

As health care gets more advanced and threats to our health get more complicated, it is important that both Congress and the FDA be responsive to this changing world. Many of the processes at FDA are decades old. Drug resistance, medical software, and personalized medicine are going to strain the limits of the outdated statute. I hope we can work together and have FDA as an active partner when we are drafting this and protect not only public health, but foster that innovation we need for that long term.

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So, Mr. Chairman, thank you for your time.

Mr. Pitts. The chair thanks the gentleman.

Now recognize the vice chair of the committee, Dr. Burgess, for 5 minutes for questions.

Dr. Burgess. Thank you, Mr. Chairman. I apologize I wasn't here earlier. I had some obligations on the House floor.

I do want to take this opportunity just to recognize the fact that this subcommittee, and in fact the Energy and Commerce Committee as a full committee, did its work in what was sometimes a very difficult election year of 2012. Food and Drug Administration reauthorization of user fee agreements was going to expire. All of the people who write in the important papers around town said we couldn't do it. And you and Mr. Upton did it. The bill went through regular order, passed the subcommittee, passed the full committee, went over to the Senate, conference with the Senate, and the President signed it into law on July 9th of 2012. No one knows that because there was no signing ceremony and there was no press present. But Congress, when pressed, can actually function in a very reasonable way.

Dr. Woodcock, as you will recall, during the reauthorization discussion, actually I worked with Ranking Member Pallone on the concept of the advisory committees to make certain that they were staffed with the very best experts to serve patients well, serve you

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and your agency well, and reduce backlogs and save resources. And so it looks to me like the initial thing, reports I am getting are good. Do you have any updates for the committee today?

Dr. Woodcock. Yes. We have been able to remove several steps that were very time consuming within the vetting of the advisory committee process for members for a specific committee. That has helped us streamline that program. Of course, all advisory committee members are still subject to the broad Federal conflict of interest requirements, and that is, you know, fairly stringent as well. But the additional steps have been removed, and that has been helpful.

Dr. Burgess. And sometimes it is helpful to have someone on an advisory committee who actually has some knowledge of the pathophysiology that might be involved in the disease under which we are contemplating treatment? Would that be a fair statement?

Dr. Woodcock. I would say it is essential.

Dr. Burgess. I think so, too.

Now, there is going to be a rare disease meeting in January of this year. Is that correct?

Dr. Woodcock. I believe so.

Dr. Burgess. And looking forward to improving the regulatory process for approving drugs for rare diseases. You held a similar meeting in 2010 and issued a report with recommendations. Can you kind

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of update us as to the implementations of those recommendations made 3 years ago in advance of this next meeting in January?

Dr. Woodcock. Well, I think we are doing extremely well on rare diseases. We have established a rare disease staff. We are tracking all the rare diseases. In 2013 we approved a large number of products for rare diseases. Every one of them was approved based on a surrogate in fiscal year 2013. That is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 were products for rare diseases. And then one was approved on an animal rule without human efficacy testing. So we do have a robust program, and we are going to try to take it to the next level as we have more meetings, public meetings.

Dr. Burgess. Dr. Shuren, as you know, for some time I have been interested in the research use only application. And there is recent guidance put out by your department that only products that could significantly restrict patient access and restricting sales of these products. Is there any evidence out there of patients being harmed by research use only products?

Dr. Shuren. Well, we do have evidence of companies who are putting those products out for research use only, but actually promoting them for clinical diagnosis in cases where those research use only, because they are research use only, haven't been shown necessarily to be accurate. And in times where we have taken action,

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it is predominantly where there is an already available approved or cleared test that would be there as an alternative.

We have recognized some of the concerns, I will tell you, with the guidance. And one of the things in there was about putting on the makers of research use only that they should reasonably know about the people they are selling it to and their intentions. That is something we heard loud and clear. I want to tell you we have heard those comments. That will come out of the final guidance. And that final guidance will come out probably by the end of this month, and we will get you a copy of that, too.

[The information follows:]

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Dr. Burgess. And I appreciate that. But specifically, do you have evidence that patients have been harmed by using the research use only designation?

Dr. Shuren. I am not aware of a specific patient for one of those. I don't know. We can look a little bit further.

Dr. Burgess. Thank you. And I would appreciate your further investigation of that.

[The information follows:]

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Dr. Burgess. Finally, Dr. Woodcock, I just have to ask a question. January 1st of 2012 I lost access to a low-cost over-the-counter asthma inhaler. When am I going to get it back?

Dr. Woodcock. Well, I can't talk, as you know, publicly about applications that might be pending and so forth. But certainly that monograph status remains. And we certainly heard your concern.

Dr. Burgess. Thank you.

Mr. Pitts. The chair thanks the gentleman.

And now recognize the gentlelady, Ms. Castor, for 5 minutes for questions.

Ms. Castor. Well, thank you, Mr. Chairman.

And welcome. Dr. Woodcock, in September, in Tampa we had the BioFlorida Conference with researchers and device manufacturers and folks that are developing drugs come from all across the State. And FDA was kind enough to send Dr. Richard --

Dr. Woodcock. Moscicki.

Ms. Castor. -- Moscicki, thank you, from the Center for Drug Evaluation and Research. And I want to thank you very much, because it is, I know, the budgets are very tight, but to have folks that are leaders at FDA be able to interact directly with the folks in my State was greatly appreciated. So thank you. And the conference focused a lot on the future of drug approvals.

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So we are pleased that the Federal laws are working well. I think the number one fear of everyone, the topic of this conference turned to sequestration, because people are rather surprised that even though FDA relies a lot on user fees, the user fees are subject to sequestration. This is not smart.

Some of the analysis I have seen, and tell me if these numbers are right, that to your budget, I don't know if this is the entire FDA budget or just your section, that in fiscal year 2013 you were subject to sequestration of \$209 million. And on top of that, \$85 million in private funding, the user fees, were sequestered at the same time. And then in fiscal year 2014, if the sequester is not replaced, you are looking at a cut of \$319 million. And \$112 million of that, or you can explain that, on top of that or as part of that is the private funding user fees.

I mean, this has got to have a harsh impact on development of new therapies, on review of devices, on review of innovative drugs. Tell us what you are facing now in your shop.

Dr. Woodcock. Well, the sequestration has been very difficult. Of course, it cuts the appropriated support for these programs as well as where there are use fees, some of the user fee programs have been subject. My understanding is that total for user fees has been \$79 million in the last fiscal year. But, frankly, how these are

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calculated is above my pay grade, all right? But what certainly has happened, there are user fees that we are not able to access, across the device and the PDUFA program, and that would continue.

And what happened with PDUFA, we negotiated and the bill was passed. It recognized the new agreements on rare diseases, patient-focused drug development, and these other programs. And then the sequester removed practically the whole amount that was negotiated for these new programs, these patient-focused programs, and other programs.

Now, we have put on the patient-focused drug development meetings regardless, but our implementation of our rare disease staff has been delayed because of the sequester, and similarly with a number of the other programs that we agreed to.

Ms. Castor. So that is not good news for families across the country, families with rare diseases that rely on your agency. It seems like we have taken a step forward with the Federal laws that have given you certain authorities and expanded user fees, but then it seems like on the other hand sequestration, brought by the Congress, is going to handicap you. I mean, this is a bad time to shortchange FDA. Can you characterize what it means, where you are very concerned? And I would assume you would recommend that sequestration be replaced going forward.

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Dr. Woodcock. Well, as I said, the whole financial issues are above my pay grade. That is really up to Congress. However, we are in a threshold, and I think with devices, too, of a revolution in biomedicine, and we are starting to see the benefits of that. And we need to have the programs that can respond to that, and also programs that can get for those older drugs, get low cost, affordable generics out on the market promptly, and at the same time, shepherd those innovations, both devices and drugs, that are going to make a difference for people who are still suffering from untreatable diseases.

And we really, I passionately feel we have to deliver this to the public. We have to make sure our regulatory programs are up to the task of dealing with drug-resistant organisms, of dealing with the new science that is coming forward.

And we are always close to the bone, as you know, in FDA. We have to shepherd our resources very carefully. More is at stake here than just having our staff. What is at stake is are we going to translate these innovations into benefit for the public.

Ms. Castor. Thank you.

Mr. Pitts. The chair thanks the gentlelady.

Now recognize the gentleman from Illinois, Mr. Shimkus, 5 minutes for questions.

Mr. Shimkus. Thank you, Mr. Chairman. I am glad to follow my

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colleague from Florida, because obviously history, it is interesting in that this was the President's proposal to go into sequestration. It was passed by the House. I voted for it. And the real way to solve sequestration is understand debt, deficits, and our entitlement programs, and get those reforms.

My fear for any agency, that without that the expansion of our entitlement programs is going to squeeze out the discretionary budget, whether that is the military, whether that is your agency. And the sooner we as a Nation own up to that, then we wouldn't be having this debate.

One of the great things I love about the job of being a Member of Congress is working with our constituents. So right during votes I had one of my constituents go, and we measured the Ohio clock, because I have a constituent who is building a replica. So we were tape measuring and stuff. So that is an example of kind of the things that we do.

And it is just lucky that you are testifying when I was approached by a constituent, a member of my church. And so I am going to get a privacy release statement and we are going to follow up with the FDA, but he was supposed to be in clinical trials in September. They have not been called. He has asked me to ask why. So if you all would just be prepared for when we get involved with that, I would appreciate that

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on behalf of my constituent.

So having said that, really my questions are to Dr. Shuren on the 510(k), some issues revolving with that, which I have been trying to follow closely. Many companies are providing us feedback that they are experiencing a significant shift in requirements for various 510(k)s. Particular concerns have arisen about new requirements being communicated by the FDA during the 510(k) review that go beyond previously sufficient data requirements.

If true, this concerns me because in many instances FDA has not issued any new guidance on public communication regarding policy changes. So the question is, has the FDA changed its data requirements for submission types without issuing updated guidance documents? And if so, can you tell me why the change in consistency?

Dr. Shuren. Well, first of all, I will say that oftentimes if we are asking a company for additional data, sometimes it is in response to the data they provided to us, that there may have been issues in what was submitted.

One thing I will ask you is, if you have companies who believe that something has been changed and changed inappropriately, you are very welcome to send them to me directly, and I promise you I will look into it.

Mr. Shimkus. Thank you.

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At hearings in this committee prior to the enactment of FDASIA you acknowledged that in some cases the CDRH reviewers were asking for data to support product applications that they should not be asking for. You also indicated in an October 2011 document that you planned to work on training reviewers to avoid these sorts of data requests. Can you give us an update on this and what steps have you taken to address this?

Dr. Shuren. So we have taken a variety of steps to assure that the questions that we ask are need to know rather than nice to know. And I will tell you even from our own analysis it is not common, but it happens, and it concerns us.

So one of the things we have done is we have been reorganizing in our premarket review offices, and thanks to MDUFA III we have been bringing in additional managers for more oversight of the process. We have changed policies and procedures to put more checks into the system.

Under MDUFA III, we have also put in a back check. So with our high-risk devices, we actually have a dedicated staff who will review any and all major deficiency letters that go out for accuracy and appropriateness. We have biweekly premarket review rounds, where if issues get raised we are dealing with them with the reviewers and the managers at that point. And of course we have done training for everyone for starters.

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Mr. Shimkus. And I will end up on this. What, if any, consequences are there for reviewers who ask questions beyond what is appropriate? And are those annotated on their performance review evaluation so that if it happens numerous times? Many of us have been managers of personnel. And, you know, the reality is you have got to document, document, document, especially on a Federal employee who may not be responding to the proper directions.

Dr. Shuren. Well, I will first say, and I am going to put this in because my folks get sometimes a hard rap, they are a great group of people. They are very smart, they are dedicated, and they have been working exceptionally hard to implement FDASIA and to make changes. And I think it is reflected, quite frankly, in our premarket review numbers. The bottom line is our performance is getting better, and it is getting better for the first time in a decade of worsening, and that is a lot of credit to them.

Making changes is hard when it is a large organization, and there are going to be blips along the way. And it is our responsibility to keep good oversight in the center. And when things do arise, we do engage with the individual. We try to educate and work with them and keep on top of it.

Mr. Shimkus. If the chairman would for just a follow-up, of course, annotating if there is numerous examples and writing it down

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is part of a good personnel status. So I hope you would consider and do that.

Dr. Shuren. Yes. And I will say for anyone who is not performing appropriately, and that goes for anything, then appropriate documentation in the file, and also discussions with the employee, because you always want to, if an employee isn't doing well, to try to help them to get back on par with performance.

Mr. Pitts. The chair thanks the gentleman.

And now recognize the gentlelady from California, Ms. Capps, for 5 minutes for questions.

Mrs. Capps. Thank you, Mr. Chairman.

And thank you to our witnesses for being here today. I am so pleased that we were able to reschedule what I consider to be a very important hearing. And I am very pleased that FDASIA included parts of my Sentinel Assurance for Effective Devices Act, also known as the SAFE Act, in its final form.

One section of that bill was to ensure swift release of the UDI, the unique device identifier rule, for public comment to improve device tracking and aid in any potential recalls. So, Dr. Shuren, I want to commend you for getting the final rule out on UDI. And I know it has been a long time coming, and I am glad that you finalized it so things can finally move forward.

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One concern we have heard from consumer groups has been that the final UDI, unique device identifier -- I want to make sure people know what I am talking about -- rule does not require the identifier to actually be on the individual product itself. Can you explain the decision to not require the UDI to be on each one of these products?

Dr. Shuren. One of the principal drivers was cost, cost to the companies. And we want to make sure that in implementing and putting forward this important regulation that we keep in mind what the burdens may be for companies to try to comply. So that was the major reason.

We do still keep in marking the devices in really one exception, and that is if you make a device that is going to be used more than once and it is going to be reprocessed. Because in that case, the labeling that came along with the product that had the UDI got thrown away, now it is moving over to someone else, and you wouldn't know what that device is unless you marked those devices. And that is a requirement in the rule.

Mrs. Capps. Okay. Okay. That is good to know.

My SAFE Act also built upon the existing Sentinel program at FDA, a program that enables FDA to actively query automated healthcare data to evaluate possible drug safety issues quickly and securely. The SAFE Act, and section 615 of FDASIA, both broadened that usage to the medical device space, which will benefit producers and consumers alike by

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catching problems early and ensuring that data, not conjecture, but data determine our device safety policies.

Unfortunately, the rollout of Sentinel on the drug side has taken many years, more than many in the field think is necessary. So I hope that expansion to the device side will not be plagued with the same delays. And can you each give me a brief update on where the agency is with Sentinel? I would appreciate a longer update for the record.

[The information follows:]

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Mrs. Capps. But just quickly, can you explain for us how UDI fits into FDA's postmarket surveillance of medical devices? Will it be good for patients and for providers and for manufacturers?

Dr. Shuren. So the UDI is absolutely essential. It is a condition precedent for having Sentinel for medical devices. And the reason is right now it is very hard to link a device with a patient's experience with that device in electronic health information, electronic health records. Unlike drugs, which had a new drug code that they could use right away, we didn't have anything for devices. So the UDI we need to have in place. And that is going to take a few years.

But in the interim, what we are also doing is the following. We are identifying, helping to develop new and validating tools for active surveillance, being able to go through information to find out what are better understanding of benefits, risks, and problems with devices, And we are working with our conflicts in CDER on that.

Also, Sentinel will be part of a broader National Medical Device Postmarket Surveillance System. So electronic health information and registries will be the backbone. And we view this not so much as an FDA system, but truly a national system to meet the needs of industry, healthcare providers, insurers, FDA.

So moving forward, the Brookings Institution is very soon going

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to call for the creation of a multistakeholder planning board to start to lay out the governance structure, policies, and procedures for such a surveillance system, which we think is important not only for identifying problems, but being able to use postmarket information to help lower burden and better inform decisions on premarket approval, help products get to market, help doctors and patients make better-informed decisions.

Mrs. Capps. Thank you very much.

And finally and briefly, another piece of FDASIA was a key component of my HEART for Women Act, bipartisan legislation that focused on doing all we can to address women's heart health and address health disparities. Section 907 of the FDASIA required an examination of the extent to which data on how approved medical products affect women, minorities, and ethnic groups be collected, analyzed, and publicly reported. This is an important step, but concerns persist I know, and I will be submitting many questions for the record, and I appreciate your team's attention to this matter.

[The information follows:]

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Mrs. Capps. And I don't think there is much time for you to respond. I just wanted to put that out. We will follow up with you. Thank you.

Mr. Pitts. The chair thanks the gentlelady.

And now recognize the gentleman from Pennsylvania, Dr. Murphy, 5 minutes for questions.

Mr. Murphy. Thank you, Dr. Shuren and Dr. Woodcock. I appreciate you for being here today.

I would like to take just a moment to ask you about an important medical device issue, although it was not part of FDASIA. The FDA has regulations about proper maintenance of complex medical devices such as radiation therapy and imaging equipment, and manufacturers are required to recommend maintenance standards to hospitals and physicians and collect data on how that equipment is kept and serviced.

My understanding is that the Center for Medicare and Medicaid Services may issue guidance telling hospitals they are free to vary from the manufacturer's maintenance recommendation on these types of devices. But we are not dealing with an automobile or refrigerator here. These are highly specialized pieces of equipment. And when a medical device is improperly serviced, the consequences can be pretty deadly, as you know.

When a New York Times series in 2010 raised concerns about patient

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deaths from improperly calibrated diagnostic and therapeutic equipment, this committee held hearings in the matter. I am concerned that weakening of equipment maintenance standards could have some severe consequences for patient safety, and the party responsible for that device is the manufacturer. If something goes wrong, it is that company's name on the label, even though they are not the ones that made the maintenance changes. I believe the FDA has weighed in on this possible action by CMS. Is that true, Dr. Shuren?

Dr. Shuren. Yes, that is true.

Mr. Murphy. Can you discuss the FDA's position on this and you concerned about anything there?

Dr. Shuren. Our concern is that the maintenance schedule is really part of assuring that that device remains safe and effective. And we work with the companies on what is the appropriate maintenance schedule to assure just that. And as you mentioned, these are technologies that may be emitting radiation, and we want to make sure not only are you getting accurate images of patients, you want to make sure they are also getting the right amount of radiation, not too much. And so a good maintenance schedule is essential. And that is why we had raised certain concerns and shared those with our colleagues at CMS.

Mr. Murphy. Okay. Let me ask another issue here. And I will

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gave you a little briefing material on this a little bit ago, but I want to make sure we have it in the record. We are all concerned about hospital-borne infections. E. coli, MRSA, and other infections which spread in hospitals are particular risks for people in hospitals, particularly in an ICU, or people who are immuno-compromised, et cetera, in transplant patients, et cetera, and that people use substances that are put into paints and plastics and clothing to try and reduce infections. But there also is the element of copper, which in research I understand has shown that basically E. coli, MRSA, and some other diseases are killed in minutes, whereas those same diseases can last for weeks on plastics and stainless steel.

The EPA has said that any sort of regulation on this is in the FDA's hands and they are not going to do anything about it, even though they have other jurisdiction over copper. I wonder how this will work at the FDA in terms of expediting this. I mean, it is obviously not a new element. It has been around for billions of years. And it seems to me it ought to be something we can use, copper itself, or copper-nickel alloys and other alloys which we know that can be on handles, on trays, on other equipment and supplies where these diseases can be killed right away.

Can you comment on the procedures you could take on this? And could anything be sped up on this process?

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Dr. Shuren. So we are happy to look into it. If it is a medical device and it has copper on it, if it has an anti-infective, that is something that my center would generally take care of. If it is not on the medical device, so it is just the anti-infective, it tends to work by a chemical action, becomes a drug issue. And that is why if there is a company or companies dealing with it, it is important that we connect so we figure out exactly what we are trying to do and help them as best we can.

Mr. Murphy. Just help me understand this, because I want to make sure we handle it in the right way. So if it is a door handle or a touch plate entering an ICU, if it is a switch plate in a hospital room, would those be medical devices or would they be --

Dr. Shuren. So a lot of those basics oftentimes are not.

Mr. Murphy. What category would they be in?

Dr. Shuren. If you are talking about surgical instruments, you are now getting into --

Mr. Murphy. I understand that. I understand that. So what category would they be in? Because the EPA is saying that FDA has to approve them.

Dr. Woodcock, do you have --

Dr. Woodcock. They would only be considered a drug if they actually had a disease claim in humans. And we don't usually regulate door knobs

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as drugs, all right. I think we are talking about some jurisdictional, like, murkiness here that we would need to sort out.

Mr. Murphy. Well, I would just hope. Let's put that on the record. We will get you the information on it. But I hope that is something that you and the EPA can discuss fairly quickly. Obviously, the 50,000 people who die every year from hospital-borne infections and the hundred billion dollars we spend, if this can be reduced by several, then we ought to work together.

Thank you so much. I appreciate it.

Mr. Pitts. The chair thanks the gentlemen.

Now recognize the gentleman from New York, Mr. Engel, 5 minutes for questions.

Mr. Engel. Well, thank you very much. And welcome to both of you. Followed both of your work. And thank you for your service.

I believe that the good work done by this committee on the Food and Drug Administration Safety and Innovation Act was likely the best healthcare-related legislating done by Congress last year. A little more than a year after its passage, I am pleased that this hearing is taking place so we can continue to monitor the implementation of this important bipartisan law.

I have always fought for those with rare and orphan diseases. I am the author of the ALS Registry Act, and both the Paul D. Wellstone

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Muscular Dystrophy Community Assistance Research and Education Amendments of 2008 and 2013, which I have done with Congressman Burgess. I am particularly interested in the development and approval of drugs for rare diseases.

Therefore, one of the aspects of FDASIA I am most interested in is the improvements made to the accelerated approval pathway as part of the law. To me, diseases like muscular dystrophy are why the accelerated approval pathway is so important. Duchenne muscular dystrophy is the most common lethal genetic disorder of children worldwide, affecting one in every 3,500 live male births. There is no cure. It is always fatal. And the best hope for those with Duchenne is to treat the symptoms and delay its progression. I have a group of people in my district that called this disease to my attention.

However, in recent years the Duchenne research pipeline has held much promise, as potentially life-saving therapies appear on the horizon, making elements of FDASIA particularly relevant to this research community. Earlier this week, the FDA informed Sarepta Therapeutics that its experimental drug for Duchenne muscular dystrophy was not a candidate for the accelerated approval pathway at this time. I recognize that since Sarepta has not filed its new drug application most of the discussions between Sarepta and the FDA are confidential. But I hope that Sarepta will continue to pursue their

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treatment for Duchenne muscular dystrophy, and I hope that the FDA will continue to provide clear feedback to the company as they move through their various clinical trials.

So, Dr. Woodcock, can you elaborate on how you envision the enhanced accelerated approval pathway working?

Dr. Woodcock. Certainly. As I said, in fiscal year 2013 we approved a large number of rare diseases, and all of them were based on surrogate end points, which is the foundation for accelerated approval. However, we granted a number of them full approval because we felt enough information had been provided that a confirmatory trial would not be necessary.

So we certainly are using the accelerated approval in rare diseases. And what the FDASIA instructed us to do was to really consider additional end points, including intermediate clinical end points, in other words clinical end points that are reasonably likely to predict clinical benefit, and we intend to do that.

Mr. Engel. Thank you. Let me ask you another question. Recognizing the challenges in developing therapies within the rare disease space, how is the FDA working with companies to ensure proper parameters for success and failure are being established through the clinical trial process in order for experimental medications to possibly be considered under the accelerated approval pathway?

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Dr. Woodcock. We try to work one by one, because of course each one of these diseases is different. One of the most important things that can be done by the patient communities is to establish a natural history of the disease through data so that we understand and can predict what will happen. If there is an intervention, you can calculate how many patients you need in your trial and so forth.

And this hasn't been done before. And so we have really been pressing on that, and I think we have seen a lot of progress. But we work with the companies one by one to help them design their trial. And as I said, we have set up a rare disease staff, although that has been inhibited because some of that money has been influenced by the sequester.

Mr. Engel. Well, thank you. And let me talk about the sequester and building on what Ms. Castor asked. I didn't vote for the Budget Control Act of 2011, thankfully, which created this huge sequestration mess. I am very frustrated that the user fees paid as part of agreements reached in FDASIA are being sequestered. So why don't I ask Dr. Shuren, can you talk about how sequestration impacts the ability of the FDA to meet goals agreed upon as part of FDASIA?

Dr. Shuren. It is making it challenging. I mean, we are meeting the goals now. But in 2013, we saw about an 8 percent cut. Critical funding for training of our staff, of our review staff who we want to

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be on top of cutting-edge technology. Saw a 15 percent cut in our ability to recognize national and international standards, which provides predictability for industry. We had a 50 percent cut in our investment in regulatory science to have better tools for assessing medical devices faster and at lower cost, which is a big deal for industry. And I had to shift 50 percent of my operating dollars into payroll in order to hire the people I committed to hire under MDUFA III.

So most of my extra money, if you will, beyond paying for employees, is to pay for the rent, keep on the lights, put money in the photocopier. I have very little to actually put in to really improve a program that still needs a lot of help. And if we go into 2014 and this continues, I am not going to have the money to be able to hire and maintain the people we committed to hire and maintain under MDUFA III. It is a big deal for us.

And sequestration, it is important on user fees. Most of our program is still funded by appropriated dollars. And those cuts, they are killing us. And we are a program, like drugs, where years before trying to actually turn the program around, and this is making it very challenging for us to do that.

Mr. Pitts. The gentleman's time has expired.

Mr. Engel. Thank you.

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Mr. Pitts. The chair recognize the gentleman from Virginia, Mr. Griffith, 5 minutes for questions.

Mr. Griffith. Thank you very much, Mr. Chairman.

Dr. Woodcock, greatly appreciate the passion you showed earlier in your testimony. I would agree with you on that passion, particularly about bringing innovative treatments for rare and terminal diseases. I have a little bill that would allow folks to get early access or early approval to those drugs in order to help them, and what we believe will actually lower the costs of some of that experimentation. We will talk about that another time.

I do want to talk about a bill, I know what we are doing here today is important, but I do want to talk a little about a bill we have waiting over in the Senate. The House passed the Drug Quality and Security Act. It was a bipartisan, bicameral compromise to prevent another fungal meningitis outbreak like the one associated with NECC's tainted sterile products, where we had 64 Americans unfortunately died as a result of that situation.

I am proud of the legislation that I worked on with Congressmen Gene Green and Diana DeGette. Ultimately, although we had a different package originally, we came to a compromise with our Senate colleagues and with your agency, and I look forward to the Senate getting around to it. It is held up for other reasons, but I look forward to the Senate

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passing the bill and it being signed into law.

And I am committed to engage in oversight to make sure that patient safety is being properly protected. I also look forward to the agency developing the notification system that Congressman Green, Congresswoman DeGette, and I authored to ensure that the FDA works more closely with those State boards of pharmacy to prevent another public health crisis.

That being said, there were some areas that we thought we might be able to get fixed that we didn't in that bill that have raised some concerns. And I would like to ask you about those in regard to that Drug Quality and Security Act. In its previous draft guidance the FDA recognized the importance of maintaining an office stock of compounded drugs that doctors can readily access and administer to patients in their offices. Can we rely on the agency to continue to allow doctors and hospitals to order and keep compounded drugs on hand for office use?

Dr. Woodcock. Well, we are going to have to see what is in the final bill, if it is enacted. And then as I understand it, it really removed the court disparity, which I didn't fully understand, but was a problem. And so it leaves the previous statute more or less intact, and we can implement it aggressively. And obviously, that is one of the considerations in there, is what are the four walls of what is

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Federal, what is State, and what is permitted.

Mr. Griffith. And we didn't change anything in regard to office use, and so there is some concern that maybe we should have put it in. It was compromised that we would just leave it silent. And I hope that we can count on the FDA. I know you maybe can't answer that today. But I would hope that we can count on the FDA to leave that part of it that was working very well, which the FDA had previously done, leave that intact, because I don't think there was any intention, certainly not on our side, that that be changed in any way.

Likewise, repackaging of sterile drug products has typically been regulated by the agency in the same fashion as compounded drugs. Repackaged sterile drugs are vital for many patients, especially those in ophthalmologic health issues. Likewise, can we rely on the FDA not to go in and create chaos, and to preserve the access to these repackaged sterile drugs and limit the impact of burdensome regulations on that practice?

Dr. Woodcock. Well, our intent certainly is not to create chaos.

Mr. Griffith. Yes, ma'am.

Dr. Woodcock. All right? I think one of the goals, mutual goals, is to prevent contaminated drugs. And that is really our goal, and your goal as well, I believe.

Mr. Griffith. It is. There were some clarifications that

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everybody decided to let go and hope that it works out. And so I am just worried about those areas.

The last of the three that I have is the nuclear pharmacists. They compound drug products that have a short radioactive half life and must be quickly delivered to a healthcare entity for administration to a patient. Sometimes this must be done in advance of a patient-specific prescription. Can we rely as well on the FDA to continue to try to monitor that in the same fashion that they did before this bill was passed? And I know that the Senate is either going to pass it today or next week. But anticipating that, since it was a compromise worked out between the two bodies and the FDA, what are your thoughts on that?

Dr. Woodcock. Well, the nuclear pharmacies have not represented a problem here. We have a scheme with them. We have been very successful in implementing a regulation of positron emission tomography facilities, and that has gone very well. And so I think we should continue along that path.

Mr. Griffith. And I appreciate that greatly. And I would be remiss, you know, it is good to see a witness with passion and your dedication. We may not always agree on how to get there, but I always appreciate the fact that you come in with honest answers and a willingness to try to work things out, and I appreciate that.

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Dr. Woodcock. Thank you.

Mr. Griffith. With that, Mr. Chairman, I yield back.

Mr. Pitts. The chair thanks the gentleman.

And recognize the gentleman from Maryland, Mr. Sarbanes,
5 minutes for questions.

Mr. Sarbanes. Thank you, Mr. Chairman.

I just want to pick up on the end of those comments, and thank you, Dr. Woodcock, for being here, and say you are one of the most professional and knowledgeable witnesses we have the pleasure to bring before this committee from time to time. I thank you for your testimony, and yours as well, Dr. Shuren.

And I want to thank the chairman for convening this panel today and the committee hearing so we can get a sense of how things are progressing. These days, sort of bipartisan legislation that we all get behind is hard to come by, so it is nice to have the opportunity to hear that good things are already resulting from the passage of this reform, and we appreciate your testimony in that respect.

I was going to ask as well about how the kind of user fee resource has gotten caught in the switches of sequester, which I think you have answered that. It is particularly jarring I think to the industry, the notion that they are putting forward through the user fees resources from the industry, and even that gets implicated by the sequestration

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that has been put in place. And hopefully, we can address that for all the reasons that you have raised.

I don't have a lot of questions necessarily on the topics you have been covering because I think you have done a good job addressing them. I did want to ask something slightly off topic, which is, as a result of redistricting in Maryland, I now have the privilege of representing some portion of the White Oak facility and had the opportunity to get a tour recently and see the tremendous facilities that are provided there. And I wondered if you could just speak to the benefits of now being able to collocate so many of the FDA personnel and have the labs there near each other and what that represents in terms of the ability of the agency to function.

Dr. Woodcock. Well, we really appreciate this, because CDER, when I took over CDER, first it was in 14 different locations scattered around the metropolitan area here. We expect a move this summer that will move the generic drug program to the White Oak campus, and also move the biologic therapeutics regulation, which has been located on the NIH campus, with their associated laboratories, to White Oak. And also our colleagues in the biologic center, with whom we work on policy very closely.

So for the drug center, this is a tremendous advance, will allow us both to have our new generic office on campus, as well as build our

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quality regulation organization, which I spoke about earlier, where we are going to have the same unit regulate pharmaceutical quality across all different types of drugs.

And also it will enable us to work with our colleagues at CBER very closely. And the benefits of having the device center right near us are tremendous, because there are many combination products with this new technology that is coming about that combine device elements and drug elements. So this has been a tremendous advance for us.

Dr. Shuren. It has been a big deal for us as well. I would also put a plug in on personalized medicine. So much of it depends upon having the right diagnostics tied up with the therapeutics, and we work very closely with our colleagues in CDER. Having them down the hallway is essential.

And having the lab facilities to do absolutely critical work. And that is work that also helps companies. Getting product to market is so important. And one of the challenges we face in the current budget climate is we are getting to the point, getting very close to the point of starting to turn off lights in some of those labs.

Mr. Sarbanes. Thank you very much. I yield back.

Mr. Pitts. The chair thanks the gentleman.

Now recognize Mr. Guthrie 5 minutes.

Mr. Guthrie. Thank you. Thank you for coming. And this is a

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good hearing. And it is one of those things that when you run for Congress you don't think about these kind of issues. You have other things that you more readily read about. But when you get here, you realize they are vitally important to your constituents. We have people come continuously, and they are looking for devices, they are looking for approvals. And I think Mr. Shimkus talked about one specifically that is in a desperate situation. So it is important that we work together.

And I have a couple of questions. One is on the custom devices. And, Dr. Shuren, this would be for you. Those that are made by manufacturers for specific patients upon request by their physician are critically important for patient care, but are not viewed by many as efficient or lucrative. And so therefore, in section 16 of the FDASIA, we established that manufacturers could modify an existing device for which data already existed instead of making an entirely new device.

The FDASIA language limits the manufacture or production of five units per year of a particular device type. And some in the industry have expressed concerns that the FDA may interpret this to say it can only be for five patients per year versus just five devices -- only five patients who needed a custom device. And I think that might render that kind of ineffective. And so I just wonder how

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you interpret that provision.

Dr. Shuren. No, we are not putting such a strict limitation on it. In the next few weeks we are going to put out draft guidance to try to better clarify implementation of that provision, which we think are very important provisions. And we support custom devices, and we think it is so helpful that Congress actually put in a much more clear standard for what is a custom device. And we are going to provide that clarity then in terms of interpreting it.

I would also add that companies do not need to come to us in order to go out with a custom device. There is no premarket review on it. They simply report to us annually. So hopefully in the next few weeks we will have out that guidance so we can have a fuller discussion with industry about it.

I will also say in those cases where they don't meet the statutory definition of a custom device, there are other mechanisms we have in place to help assure that patients who need a device that isn't otherwise approved on the market can get it. So many of those cases, even if the law doesn't allow a custom device, could be for compassionate use and still get it to the patient.

Mr. Guthrie. I know in the reporting that it makes it quicker and better for the patient. I guess there was some concern it might just be five patients. So in a couple weeks you are going to have that

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guidance, and if you could keep us informed, that would be fantastic.

I do want to point out that, I know we talked about sequestration, and we are dealing with budget issues here, and the budget conference committee is meeting as we speak through December, but the FDA has experienced a dramatic increase in appropriations over the past decade. And since the beginning of MDUFA, CDRH has gone from approximately 1,000 MDUFA full-time equivalents to over 1,400. And since 2004, CDRH has doubled its budget from 179 to 385. That is from 2004 to fiscal year 2011. And during this time PMA and 510(k) submissions have decreased.

However, studies have shown, and that is the CHI/BCG report we are all aware of, that review times have gotten 43 percent slower in the past few years and PMA 75 percent longer. So sequestration does have an effect, I am not saying that it doesn't, but there has been some substantial increase in the budget at the FDA as well.

So, Dr. Woodcock, one of the central tenets of the Prescription Drug User Fee program is to provide more certainty and predictability on the timeline for FDA to make decisions to approve a drug. And why is it important for companies in terms of continued innovation and patient access to new medicines for companies to have predictability on the FDA and when it will make decisions on application?

Dr. Woodcock. Well, because these companies invest up to a billion dollars in a development program, and then they need to launch,

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and they have to do a lot of activities to get ready for launch. They have to get their facility all ready, distribution chain, all sorts of things. And so just knowing what the sequence of events is going to be and when that time on to market will be is extremely important to keep this enterprise afloat.

Mr. Guthrie. I agree with you. And then do companies receive patent term restoration based off the time it takes for a company to go through the FDA process?

Dr. Woodcock. Well, I don't understand this very well. They get restoration at the time of approval. So they get that. But there can be things eating away at their patent in the interim.

Mr. Guthrie. Okay. And it is important, because our investment in research is second to none in the world. And I know, we talked in my office, Dr. Shuren, on some of the device companies that are going to other countries for better opportunities to get approval of their processes. And I appreciate the work that you have done on that, because we don't want to lose our industry and our leadership in research, and certainly not because of slow and unpredictable processes. So thanks for working to make that better.

And I yield back.

Dr. Shuren. Thank you. If you may, Mr. Chairman.

Mr. Guthrie. I have three seconds. Go ahead.

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Dr. Shuren. And we are starting to see some changes. I just got called this week by a company who said we were actually going to conduct our first-in-human study overseas, and given the changes at the FDA they were going to start it in the U.S. And we are hearing that from other companies as well.

The numbers you gave in terms of our performance, they are from a report from 2010. And that is actually what I would say was the high point, the watershed mark for the program after about a decade of worsening. And since that time those numbers are actually down a fair bit. They are improving in review.

Mr. Guthrie. I understand. And I hope I didn't insinuate that. But I was just saying the funding has doubled since 2004. So there has been increased funding even though you are under sequestration now. So I just want to make that point.

Mr. Pitts. All right. The gentleman's time has expired. That concludes the first round of questionings. We will go to one follow-up per side.

Dr. Burgess, you are recognized for 5 minutes for a follow-up.

Dr. Burgess. Thank you, Mr. Chairman.

Dr. Woodcock, can I just ask you briefly about the decision by the FDA to reschedule hydrocodone? Is there any update you can provide us on that?

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Dr. Woodcock. Well, let me explain the process. What we do, we were asked, along with NIH, the National Institute for Drug Abuse, to provide a recommendation to HHS, who then provides a recommendation to DEA, who then go through a formal notification and comment process. And DEA actually does upscheduling. So what we announced was simply the fact that we intended to recommend that the combination products be upscheduled.

Dr. Burgess. Now, is there a report pending from FDA that we have not yet seen or has not yet been made public?

Dr. Woodcock. Correct. What we need to do to actually any scheduling action, we send something called an eight factor analysis, which is stipulated under the Controlled Substance Act, and findings based on that. And we write that up and send that to HHS, who then will evaluate it and then send recommendations to DEA. And that process, we should be moving that process along fairly soon. We expect to.

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[12:05 p.m.]

Dr. Burgess. So we will have access to that report?

Dr. Woodcock. I don't know what point it becomes public. We can get back to you on that part of it.

[The information follows:]

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Dr. Burgess. Okay. Thank you. Well, you know, and it is a concern, there being practicing physicians all over the country who -- sure, there are some things that require -- State law requires triplicate prescription in Texas, those things can't be called in over the telephone in the middle of the night. But someone who has run out of a postoperative medication and still needs help, the doctor has the ability to get that help to that patient without an emergency room visit. So it is important, and it is something I don't want to see us lose.

We had a hearing here on, I guess it was on putting the EpiPen over the counter, an over-the-counter Epinephrine treatment for bee stings. And I don't remember now, quite honestly, who was here from the Food and Drug Administration that day, but I asked the question was there any thought to putting Narcan over the counter, Naloxone, so people would have the availability for that if they got into trouble abusing drugs that either they got legitimately or illegitimately. And then that was a feature of a story on Sanjay Gupta on CCN not too terribly long ago.

So where are we in that process? We have gone to great lengths to make levonorgestrel not just over the counter, but down there with the Snickers bars in the front of the pharmacy. Is there ever going to be any effort to make Narcan over the counter?

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Dr. Woodcock. We are certainly encouraging development of forms of Naloxone. As you know, now it is compounded as nasal sprays and so forth and used by paramedics. So we are certainly encouraging development of sort of dosage forms that can be used out in the field under emergency situations. And then we would certainly consider whether over-the-counter access would meet the criteria for over the counter and then would improve emergency treatment of overdoses by friends and relatives, for example.

Dr. Burgess. Well, thank you. Again, it was a pretty startling film clip that Dr. Gupta showed on that series, and again made me think again about the possibility that -- again, no one wants to condone the use of illicit drugs, but on the other hand you hear about it where you lose -- usually it is a teenager in our community and it is a terrible tragedy when it happens. And if there were another option maybe that would be a good thing.

Dr. Woodcock. We totally agree with you, and if lives could be saved that way then that is something we should really drive toward, and we are very aggressively pursuing this.

Dr. Burgess. Don't misunderstand me, Mr. Chairman, it would be better if they never abused the compounds in the first place, but as a matter of first aid perhaps that is something should be considered. Thank you for the recognition. I will yield back.

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Mr. Pitts. The chair thanks the gentleman.

And now for follow-up, Mr. Sarbanes for 5 minutes.

Mr. Sarbanes. Thank you, Mr. Chairman.

Dr. Shuren, I know when last year we were debating the various proposals around this reform one of the issues was where to draw the line, what the proper balance should be in terms of regulating medical devices. We wanted to make sure that, you know, on the one hand we had sufficient regulation in place and you had sufficient authority at the FDA to ensure that these devices are safe and effective and so forth. At the same time not have so much regulation that it becomes burdensome on industry to a point of sort of quashing innovation and investment.

And I would be curious generally for your thoughts on how industry has responded to where we kind of put that line where we struck the balance. And in particular I would be curious to hear you talk about the new, more streamlined process you have with respect to classification of devices from class 1 up to class 3, where I gather now you can use a kind of administrative process that doesn't necessarily involve full-blown rulemaking and comment, so forth, in every instance. And maybe you can give some examples of how you have used that authority in an effective way.

Dr. Shuren. So, I mean, to answer the first part, I think after

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much discussion that occurred last time around FDASIA there was, I will say, general support for the U.S. standard of reasonable assurance of safety and effectiveness. And the question then becomes, what does that actually look like for particular kinds of devices?

What we have done is put in place this new benefit-risk strength work that is much more flexible and patient-centric to try to set the needle, if you will, in the right place.

One of the things that we are going to be following up in the coming months is to start talking about those circumstances under which data we might otherwise collect premarket can be shifted to the postmarket setting and not compromise patients, but do an appropriate reduction of burden on companies and address some of those cases in the postmarket setting. And that will include some new pathways for high-risk devices as well, and I think that is important.

Regarding classification, FDASIA provided some important changes to the process. One is the fact that we can now issue an order rather than a regulation. So in some respects it has gotten a little easier, and it has been helpful.

But let me tell you one wrinkle we have, and that is where if we do want to in fact reduce burdens on companies, appropriately so because with more experience we realize we should lower the classification, we should go from class 3 to class 2, or class 2 to class 1, we actually

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now have more steps to go through. We must hold an advisory committee meeting where before we didn't have to do that. And that is actually making it more challenging for us under appropriate circumstances to reduce regulatory burden on companies.

Mr. Sarbanes. Thanks very much.

Mr. Pitts. The chair thanks the gentleman.

We have had a couple of members detained on the floor and missed the first round, so I will ask unanimous consent to recognize them as they come in for 5 minutes.

Dr. Gingrey, you are recognized for 5 minutes.

Dr. Gingrey. Mr. Chairman, thank you for that courtesy.

Dr. Shuren, the Office of Combination was created to deal with products that combine drugs, devices, or biologic products. For instance, some companies are toying with the idea of combining drugs and devices into solutions for antibiotic infections, something that I care about personally, as you know. However, the current approval method forcing companies with a mainly device product to go through a drug pathway because it induces a chemical reaction may discourage companies from investing in new and breakthrough technologies because the pathway is not best suited to what their product is.

The drug and device pathways were originally created decades ago when the reality of combination products were not yet realized. What

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steps is the FDA taking in light of its current 1970s framework to work directly with these companies who present the agency with 21st century technology like these combination products?

Dr. Shuren. So the agency in setting up the Office of Combination Products, which sits in the Office of the Commissioner, is there to try to help determine what is the appropriate pathway for those combination products to go through. And they have been more recently trying to provide clarification for when the primary pathway would be device or drug.

But when it is a combination product there are needs that would be met for both, let's say, if it is a device and a drug, for the device side and for the drug side. So even if it is a product that we have primary responsibility for, if it has a biologic component, we go to our Center for Biologics for a consult. If it has a drug component we go to our Center for Drugs.

This is a very challenging area, I have to tell you this, because given the way the law is we have been able to try to minimize duplicative burden, if you will, and challenges on the postmarket side for reporting, or on good manufacturing processes, but when it comes to the standard for approving products the law right now is very challenging for combination product makers.

Dr. Gingrey. Dr. Shuren, thanks you very much.

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Dr. Woodcock, the bipartisan GAIN Act took important steps to encourage the new development of antibiotics by focusing on incentives to new companies to keep companies in the marketplace. At this time can you provide me the number of qualified infectious disease products that have been designated since the law was passed last year, what, last year?

Dr. Woodcock. Certainly. We have designated, as far as I know, 27 products with 16 distinct active modalities. And that number will continue probably to increase.

Dr. Gingrey. Well, I really have to commend the FDA on that and realizing the desire and need for new antibiotics and acting quickly to implement the program. I have received plenty of positive feedback from companies, not just in my district, who have been able to achieve benefits through the GAIN Act.

I think you would agree with me that more needs to be done to combat resistance. One issue that needs attention involves susceptibility tests, interpretive criteria or breakpoints. Now, as you know, Dr. Woodcock, a breakpoint is criteria used to determine a particular infection's susceptibility or resistance to a specific antibiotic, and they are used by physicians in clinical decision making.

With the growing public health threat of antibiotic resistance, it is increasingly important to ensure that physicians have these tools

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they need to prescribe the right dose, of the right antibiotic, for the right patient, in the right situation.

Given what we know about the science behind breakpoints and our failure to keep pace with regulatory science in Europe, are U.S. patients receiving the best medical care, using the most up-to-date science, if the breakpoints for antibiotics are not accurate?

Dr. Woodcock. Well, they would not be. We have updated these criteria for about 121 of the 200 main antibiotic labels that exist. However, we feel that it would remain more up to date if we would not have this information remaining in the drug labels but rather would be able to point to a Web page and possibly to standard development organizations who are actually out there on the ground in the communities and are getting the information on an ongoing basis.

Even when we approve an antibiotic, we only look at a few organisms. As you well know, physicians have to use diagnostic criteria in the devices, the test for susceptibility, for a wide range of organisms, many of which may not be in any drug label. So we think we need a more dynamic and effective process that reflects the ongoing experience in the community.

Dr. Gingrey. Dr. Woodcock, I have about 2 seconds. I want to ask you to commit to me today to work with my office to fix the breakpoint issue, as well as look toward other ideas to address the epidemic of

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antibiotic resistance, one of the chief threats to public health today.

Dr. Woodcock. We would be delighted to do that.

Dr. Gingrey. Thanks, Dr. Woodcock.

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

Mr. Pitts. The chair thanks the gentleman.

That concludes the questions for the members. I am sure members will have follow-up questions. We would ask you to please respond promptly once you get them.

[The information follows:]

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Mr. Pitts. I remind members that they have 10 business days to submit questions for the record, and that means they should submit their questions by close of business on Tuesday, December 3rd.

A very informative hearing. Thank you very much, and thank you for your patience.

Without objection, the subcommittee is adjourned.

[Whereupon, at 12:18 p.m., the subcommittee was adjourned.]