

**AGRICULTURE, RURAL DEVELOPMENT, FOOD
AND DRUG ADMINISTRATION, AND RE-
LATED AGENCIES APPROPRIATIONS FOR
FISCAL YEAR 2018**

TUESDAY, JUNE 20, 2017

U.S. SENATE,
SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met, pursuant to notice, at 10:35 a.m., in room SD-192, Dirksen Senate Office Building, Hon. John Hoeven (chairman) presiding.

Present: Senators Hoeven, Collins, Rubio, Merkley, Leahy, and Tester.

U.S. FOOD AND DRUG ADMINISTRATION

**STATEMENT OF SCOTT GOTTLIEB, M.D., COMMISSIONER, FOOD AND
DRUG ADMINISTRATION**

OPENING STATEMENT OF SENATOR JOHN HOEVEN

Senator HOEVEN. The hearing will come to order. I would like to thank the members for being here, Ranking Member Merkley.

And I certainly want to welcome FDA Commissioner Gottlieb. Thank you for being here this morning. We appreciate it.

Today's hearing will focus on the Food and Drug Administration's fiscal year 2018 budget request. Thank you again for being here, Dr. Gottlieb. Obviously, this is a good opportunity to talk about FDA's priorities for the upcoming year.

Congratulations on your confirmation. We certainly want to welcome you in your first appearance before the subcommittee, and we look forward to working with you.

The agency you head has authority over approximately \$0.20 of every dollar spent in America. Americans expect that the food they eat and the drugs they take will be safe and effective.

FDA's reach is vast. The agency has authority over more than 300,000 foreign establishments and 185,000 domestic establishments, ranging from food processing plants to facilities that manufacture lifesaving medications. In addition to facilities themselves, FDA is tasked with the regulatory responsibility of individual products.

In delivering these regulatory responsibilities, your private sector partners expect transparency and certainty from the FDA.

When I speak to small businesses and AG producers in North Dakota, their overwhelming concerns are that often overly burdensome regulations coming out of Washington, D.C., can stifle innovation and hinder their ability to create jobs. While we all support the FDA's mission, we must also be mindful of these concerns.

I believe that FDA must avoid the trappings of one-size-fits-all solutions, and urge you and your staff to take a common-sense approach.

In regard to the budget request itself, I am concerned that this request relies on a significant increase in user fees that is not feasible and unlikely to gain congressional approval. I am concerned that the proposed cuts to budget authority may negatively impact food safety programs and slow the agency's important work on drugs and medical devices.

That being said, Dr. Gottlieb, I also recognize that these decisions were made before you were confirmed, so I hope you will pledge to work with Congress to ensure that FDA has the resources necessary to meet its critical mission.

We have many other issues to cover this morning, so at this point, I will turn to Senator Merkley for his opening comments.

Senator Merkley.

OPENING STATEMENT OF SENATOR JEFF MERKLEY

Senator MERKLEY. Thank you. I am going to keep this very brief, because we are hoping to hear your testimony and have a round of questions before we go to the vote at 11.

The department you head covers products that constitute 20 percent of what consumers spend both in food and drugs. It makes that work very important, and this budget before us very important on everything from scientific research, support for State and local health organizations, blood safety work, medical devices, post-market surveillance, medical product exams, and so much more.

And so I look forward to hearing your thoughts on the budget and getting to our inquiries.

Thank you and congratulations.

Senator HOEVEN. I would suggest, at this point, we go right to Dr. Gottlieb's statement, so that we can come right back for questions and then any opening statements as well that other members may have.

All right, Dr. Gottlieb.

SUMMARY STATEMENT DR. SCOTT GOTTLIEB

Dr. GOTTLIEB. Thank you. Mr. Chairman, Mr. Ranking Member, and Members of the Subcommittee, I appreciate the opportunity to testify today regarding the President's budget.

I have talked to you in the past about the steps that FDA is taking on the generic drug side to try to bring more low-cost opportunities to patients when it comes to new drugs and improved access. I want to just briefly touch on some of the things we are going to be doing on the new drug side. The most tangible way we are going to reduce health care costs is by finding better treatments for a lot of costly diseases.

BREAKTHROUGH DRUGS

Toward these ends, we will be announcing soon a medical innovation development plan that will include a broad range of steps we will take to make sure that our own regulatory tools and poli-

cies are modern and risk-based, and designed to facilitate the development of potentially breakthrough new treatments.

One area of focus of this new plan is going to be on targeted drugs, especially those that affect rare diseases or diseases for which there is no effective therapy. Among other things, FDA will be updating various guidance documents on the kinds of drug development techniques that help facilitate the discovery and development of targeted therapies. This includes guidance on clinical trial enrichment strategies to improve efficiency and adaptive trial designs so we can modernize the statistical tools we use to evaluate safety and effectiveness. We will also be taking a fresh look at policies that support innovation to allow drugs to be targeted only to those patients who are most likely to benefit from medicine. We will also be taking a broad range of new steps.

Among these new actions, we will be issuing a new guidance document within the next 6 months on the clinical evaluation of targeted therapies for rare disease subsets. This new policy will address targeted drugs and how we can simplify the development of drugs targeted to rare disorders that are driven by genetic variations and where diseases all have a similar genetic fingerprint, even if they have a slightly different clinical expression.

One example is a cancer, where a drug targets a particular molecular subset of cancer, regardless of where the tumor arises. We will clarify when we can give a broad approval to a drug in multiple different kinds of molecularly similar cancers, which are not particular to the tumor being in one specific tissue or organ. In other cases, rare subsets may be grouped by lab testing, so they can be studied in a single clinical trial.

This sort of genetically driven medicine is more common as we understand the genetic basis of disease. Now, our new policy will describe when we will approach drug review less by how a disease is expressed and more by how it is driven by a common set of genetically driven factors.

Many of these targeted drugs are aimed at rare and orphan diseases. But right now, we have a backlog of about 200 orphan drug designation requests where we have not responded to sponsors on whether the drugs will receive an orphan drug designation from FDA. As part of our new plan, we are committing today that, in 90 days, we will completely eliminate this backlog of requests and provide an answer back to the sponsors.

To help eliminate the backlog, we have created a special orphan designation SWAT team. Moreover, we will never again develop a backlog. Going forward, we are committing today that every orphan drug application will receive a response from FDA within 90 days of the request. To enable more efficient reviews and timely responses to sponsors, we are also implementing a new streamlined orphan designation review template.

These are just some of the things we are working on. I look forward to discussing with you how FDA's budget and this committee can support all of the agency's key priorities, including food safety, and enable consumers to improve their lives.

Thanks a lot.

[The statement follows:]

PREPARED STATEMENT OF DR. SCOTT GOTTLIEB, M.D.

Good morning Chairman Hoeven, Ranking Member Merkley, and Members of the Subcommittee, I am Dr. Scott Gottlieb, Commissioner of the Food and Drug Administration (FDA). Thank you for the opportunity to appear before you today to discuss the President's fiscal year 2018 Budget request for FDA.

First of all, I would like to thank you all for your continued support of FDA. FDA has received strong bipartisan support throughout the appropriations process in recent years. This funding is critical to the agency fulfilling its mission. Without your support, we could not meet the critical public health challenges confronting the nation.

I am honored to have been chosen by the President and confirmed by Congress to lead FDA. As a physician, an entrepreneur, a cancer survivor, and a father, I know personally the importance of FDA's role in improving and protecting the lives of all Americans. Every person in this country is affected in one way or another by the decisions made by FDA. For this reason, I am honored and humbled to serve as FDA's Commissioner.

FDA's fiscal year 2018 Budget requests \$5.1 billion—a nearly 10 percent (\$456 million) increase over the fiscal year 2017 Continuing Resolution (CR) funding level. Mindful of the larger pressures on the Federal budget, FDA has focused our request on the most urgent needs. The fiscal year 2018 Budget aims to protect the public health by wisely investing taxpayer dollars, requiring industries that benefit from the FDA's review process to pay their share, and advancing regulatory and administrative efficiencies.

FDA PLAYS A CRITICAL ROLE IN AMERICA'S PUBLIC HEALTH SYSTEM

As a science-based regulatory agency, FDA's broad mission is to promote and protect the nation's public health and touches the lives of all Americans. Over \$2.4 trillion annually, roughly 20 cents of every dollar, is spent by consumers on a product that FDA regulates. These products include human and animal drugs, medical devices, biologics, such as vaccines and blood, dietary supplements, and cosmetics. Tobacco is another product within FDA's purview—the agency protects the public health of future generations by reducing tobacco use by America's children.

FDA's regulation of food is another critical part of FDA's mission. FDA works to assure that the nation's food supply is safe, sanitary, wholesome, and appropriately labeled. FDA has made great strides in promoting the safety of the foods we eat as envisioned by Congress in the FDA Food Safety Modernization Act (FSMA). Thanks to the support of this Committee and your colleagues in the House, we have been working closely with our state partners, to educate and assist industry during the implementation of FSMA's provisions. These include preventive controls for manufactured human and animal foods, sanitary transportation of our food, and as of May 30, verification that our high food safety standards have been met by foreign suppliers. FDA remains committed to working with industry to facilitate innovation to make safe and healthy food choices available to consumers.

FDA HAS A PROVEN TRACK RECORD OF SUCCESS, BUT THERE'S MORE WORK TO DO

In the last year, FDA has helped bring new treatments, including several life-saving cures, onto the market. FDA's Center for Drug Evaluation and Research approved 22 novel drugs in 2016; approvals included the first treatment for patients with spinal muscular atrophy, a new drug to treat patients with a rare chronic liver disease known as primary biliary cirrhosis, and two new treatments for patients with hepatitis C. Additionally, 2016 marked the highest number of generic drug approvals and tentative approvals in the history of the FDA's generic drug program—more than 800 in total. In September 2016, FDA approved the first “artificial pancreas,” a medical device that automatically monitors blood sugar and provides insulin doses when needed. This device has the potential to improve the lives of roughly 1.5 million Americans living with Type-1 diabetes.

As highlighted by the above examples, FDA's collaboration with innovators brings products to the market that make a difference in the lives of all Americans. Since the creation of the first user fees in 1992, user fees have been instrumental in allowing FDA to build capacity and improve the timeliness of the medical product review process without compromising the agency's high standards. The user fee programs provide FDA with the critical and stable funding we need to hire and train the highly-qualified reviewers needed to keep pace with innovation.

However, the medical products field is ever-changing and advancing, and to ensure the agency has the critical resources needed to keep pace with this field, the Fiscal year 2018 Budget recalibrates how the agency finances our medical product

review work. Calling for an increase of \$1.2 billion in user fees, the fiscal year 2018 Budget includes a total program level of \$3.2 billion for medical product safety investments, which is \$505 million above the fiscal year 2017 CR level. The Budget finances the full cost of FDA pre-market review through user fees. These resources will dramatically increase the agency's capacity for pre-market review, and bring more new products to market faster than ever before.

CURES IMPLEMENTATION

The fiscal year 2018 Budget's focus on medical products complements Congress' direction last December in passing the 21st Century Cures Act (Cures). Cures provided a dual directive to FDA—to support innovation while maintaining the evidentiary standards that provide assurance to the American public about the safety and efficacy of medical products. This includes advancing patient-focused drug development and using real-world evidence in modern clinical trial design. As a result, Cures will help FDA facilitate more patient-centered, efficient, and less costly medical product development, ultimately leading to more timely patient access to important medical products. The fiscal year 2018 Budget requests a total of \$60 million to support this critical work, and we look forward to working with Congress, and this Committee, as FDA continues its work on implementing Cures.

PROMOTING INNOVATION BY PRIORITIZING REGULATORY EFFICIENCY

As FDA's Commissioner, part of my job is to ensure the Agency has the policies and processes in place needed to address the important public health issues of our day, as well as emerging threats of tomorrow. We must hold true to our consumer protection mission, while not hampering innovation.

The Administration is committed to the goal of reducing barriers to innovation and spurring innovation on behalf of patients. At FDA, we understand the impact our regulations have on industry and the public—which is why we have, and will continue to engage in robust dialogue with outside stakeholders to ensure our actions strike the right regulatory balance while maintaining our gold standard.

The fiscal year 2018 Budget includes proposals designed to make sure we are taking a risk-based approach to our work and make the process for developing safe and effective medical products more efficient. By leveraging FDA's statutory mandates, including recent enhancements made by Cures, the agency is working to reduce review times by improving processes and gaining efficiencies to the greatest extent possible. These proposals will help reduce uncertainty in medical product development by increasing engagement and early interactions with manufacturers. Improved regulatory science and policies will not only lead to more efficient approvals and increased competition that can help reduce costs to consumers, but more importantly, they will improve patient outcomes. By streamlining clinical trials, integrating patient voice throughout the regulatory process, and promoting greater preparedness for novel and emerging public health threats, Americans will get better products, faster.

PRIORITIZING ADMINISTRATIVE EFFICIENCIES

In addition to regulatory efficiencies, FDA is taking a close look at all of our programs, policies, and procedures to ensure that every dollar dedicated to administrative costs is spent wisely. The fiscal year 2018 Budget proposes the establishment of a Working Capital Fund (WCF) to support agency-wide business services. A WCF will allow FDA to operate in a more efficient and transparent business environment. Over time, this WCF will also allow FDA to recapitalize resources to support IT infrastructure, reduce cost redundancy and improve service delivery for mission critical needs.

Dollar for dollar, FDA remains one of the smartest investments made by the American taxpayer. The fiscal year 2018 Budget also identifies targeted reductions and program changes totaling \$127 million in budget authority while preserving core mission activities. These reductions in budget authority are targeted to certain areas where better tools and policies will allow us to do more with less, and will be coupled with policy efforts to improve the efficiency of the programs that see reductions, to make sure that we are improving our effectiveness and taking a risk-based approach to our consumer protection mission.

CONCLUSION

Today, we are at an inflection point in public health. Cures for diseases we once believed were incurable are now within our reach. The fiscal year 2018 Budget will protect and advance the health and well-being of every American, while providing

American taxpayers the assurance that we are requiring industries that benefit from the FDA's review process to pay their share. I look forward to answering your questions today and to working with all of you going forward.

Senator HOEVEN. Thank you, Doctor. We will start with questions.

FISCAL YEAR 2018 RESOURCES

As I noted in my opening comments, I have concerns with the administration's proposal to essentially double user fees. It does not appear that the HELP Committee will move forward with that proposal. Instead, Congress will likely pass the previously negotiated user fees.

So my question is, based on the fiscal year 2017 appropriation, are you confident that you are going to be able to meet the program needs, based on your current appropriated level for fiscal year 2017?

Dr. GOTTLIEB. Senator, thanks for your question.

The bottom line is, we can always do more with more when it comes to the resources that the agency has. I am confident that we have been able to be efficient in everything we do.

I think there are still places that we can look within the agency to try to improve our operational efficiency. We recently made an announcement with respect to a realignment when it comes to the field activities. We are going to continue to look for places to improve our operational efficiency.

We appreciate very much, though, the resources that we have gotten from this committee, in particular, the resources on the food safety side and the resources that we have gotten under FSMA. That that has dramatically improved the stature and the base of resources for food safety. It is a very different agency today than the one that I left 10 years ago, in that regard.

HIRING FREEZE

Senator HOEVEN. You have about 1,000 vacancies. The hiring freeze has been lifted for your agency. Are you moving forward? And where are you in that process of filling positions?

Dr. GOTTLIEB. Thanks for the question. That is right. We negotiated the lifting of the hiring freeze about 2 weeks ago, I believe, and we are starting to move forward with filling those vacancies. I put out a notification recently to the Office of the Commissioner, as well as the different centers, in terms of the process of moving forward. But there is already activity with filling some of those existing open slots.

OPIOID CRISIS

Senator HOEVEN. What is the FDA's role in addressing the opioid crisis? And what are you doing?

Dr. GOTTLIEB. Well, it is multifaceted. This is, in my view, the biggest challenge facing the agency, and I think one of the biggest public health crises facing this country.

There are a lot of different components where the FDA is going to play a role. You look at medically assisted therapy where the agency plays an important role trying to address the current addic-

tion problem, and trying to get better opioids on the market that are more tamper-resistant.

I think where we can play a particularly important role, however, is on the new addiction aspects of this crisis. We know that most people who are going to become addicted to opioids are first exposed to opioid drugs in the clinical setting through legitimate prescription. A certain percentage of patients who are exposed to opioids in the clinical setting will go on to develop an addiction.

So I think it is incumbent upon all of us to make sure that only properly indicated patients are being prescribed opioids. And when they are prescribed opioids, they are prescribed opioids for a duration that comports with the clinical circumstance for which the prescription was written in the first place.

There are things that FDA can do to try to address these aspects of the problem. So that is going to be a particular area of focus of ours. We recently developed a steering committee made up of all the center leadership and senior clinicians within the agency to look at trying to see how we can think differently about this problem.

The other place where I have tried to focus some policymaking attention is looking at the risk in the illicit setting. We traditionally have looked at the risk of illicit use as a component of how we evaluate the risk and benefit of opioids overall. But I want to make sure we have a proper framework in place for doing this, and we are looking not just at the risks associated with these drugs in their labeled indication but also the risks associated with how they might be abused and misused and diverted and used illicitly. And we have recently taken an action that factored into it consideration of how the drug was being used in the illicit setting.

Senator HOEVEN. What about approval of drugs that actually help wean people off some of the opioids? I know there is development in this area.

Dr. GOTTLIEB. Right. This is the medically assisted therapy. We need to continue to develop good drugs in this area.

One of the challenges, though, has been reimbursement. While it is outside my mandate, getting these drugs to patients is an important step as well. So we are looking at things we can do to help facilitate the development of clinical trials that move these drugs into different clinical settings to see how we might better study them in real-world settings. Hopefully, we will have more to say on that soon.

NUTRITION FACTS PANEL

Senator HOEVEN. Last week, the FDA announced a delay, for compliance to the Nutrition Facts Panel regulations. I know you are limited on what you can say until it is published in the Federal Register. But given my comment regarding one-size-fits-all solutions, will FDA use a common-sense approach toward those nutrition regulations?

Dr. GOTTLIEB. Thanks a lot.

I am confident we will, Senator. We announced the delay, in part, to provide additional guidance to sponsors on how to interpret aspects of the new Nutrition Facts label.

This is a time limited delay. This is not a suspension of the regulation. We are not reopening the regulation. We are just using this time to develop additional guidance documents that we will be issuing to help inform how people can comply with the new labeling.

Senator HOEVEN. Senator Merkley.

Senator MERKLEY. Thank you, Mr. Chairman.

And welcome, Dr. Gottlieb.

RESPONSE TO MINORITY REQUESTS

The first question I have for you is, a number of news reports have discussed the administration's directive to Federal agencies not to respond to requests from minority Members of the Senate.

That is completely contrary to the very long and positive bipartisan history both on this subcommittee and our dealings with the FDA under both Republicans and Democrats. I think a dialogue with the executive branch for all Members results in stronger bills more likely to have support, and it clearly benefits the FDA and the American public to have that dialogue.

Can we count on you to be engaged in that dialogue and respond to inquiries and requests from the majority and the minority?

Dr. GOTTLIEB. Absolutely, Senator. I responded to all the requests for new information that I got during my confirmation process from the minority. I am prioritizing timely responses equally from both the majority and the minority. We have reached out to many offices, including your own. I had the pleasure to meet with you twice.

So we will not pick sides in how we provide information to Congress. I respect Congress, and we are going to make sure we are providing you the information you need.

Senator MERKLEY. Thank you very much. Your outreach has been appreciated, and I appreciate your commitment to continuing on that course.

OPIOID ADDICTION

During your confirmation process, you described the staggering human consequences of opioid addiction and characterized that epidemic as the biggest crisis facing the agency.

Now we have a prediction that the CDC, engaged with various other experts, that the Trumpcare bill coming out of the House, we do not know what version we will see in the Senate yet, would cut billions of dollars from treatment for mental health and substance abuse disorders, and also that millions of people will lose their insurance, which makes it very unlikely that they will be seeking medical care in the first place.

We are concerned that this budget would damage the ability to take on opioid addiction, with its enormous daily toll on lives. As someone who is leading the charge on this epidemic, who has presented it as a top priority, do you have concerns about the loss of access to health care by millions of Americans, if this bill is enacted?

Dr. GOTTLIEB. Senator, I am very focused on what we are doing at FDA right now to address this crisis, as I know you can appreciate. And you are going to continue to see a series of activity out

of the agency to address this crisis in different ways that hopefully start moving us to a posture where we are getting ahead of the problem, instead of always being one step behind.

I have not focused a lot of attention on the various legislation moving through, with respect to the Affordable Care Act. I am very focused on what I am doing at FDA right now, which is more than a full-time job, as I know you can appreciate, and I will continue to talk to you about those priorities.

Senator MERKLEY. There are 13 Senators who are holding a series of closed meetings to work to prepare a version of the bill that will come before the Senate, probably next week. Have those individuals, or as a group, brought you in to get your consultation and insights on the opioid epidemic?

Dr. GOTTLIEB. I do not know what group you are talking about, but I have had conversations with individual Members about the opioid epidemic. I met with probably 60 Members in the run-up to my confirmation process. I would say that this issue came up in most of those meetings. Since I have been in this position, we have taken a lot of additional meetings with both Democratic and Republican Members in the House and the Senate, and this issue comes up a lot.

So I have consulted widely on this issue, including with you, Senator, and I appreciate all the dialogue I have had with Congress.

Senator MERKLEY. The group that I am referring to are the 13 Republican Senators who have been delegated the authority to prepare a bill to be brought to the floor, one that will have no public input. That is the group. Has that group asked you to come and share your expertise on this?

Dr. GOTTLIEB. I have had no dialogue with any group working on legislation as a group, no.

Senator MERKLEY. Well, I imagine, just knowing your background, that you probably share my concerns that such issues get the insight from experts and also that the public has a chance to weigh in, so that we get, in this “We the People” Republic, a full opportunity to make sure we get kind of policy right, if you will, when it has an impact on so many people.

Dr. GOTTLIEB. Thank you, Senator.

Senator MERKLEY. Thank you.

Senator HOEVEN. Senator Collins.

Senator COLLINS. Thank you, Mr. Chairman.

Mr. Chairman, I have an opening statement that I would request be submitted for the record.

Senator HOEVEN. Without objection.

[The statement follows:]

OPENING STATEMENT OF SENATOR SUSAN M. COLLINS

Thank you Chairman Hoeven and Ranking Member Merkley for holding this important hearing to talk about the fiscal year 2018 Budget request for the Food and Drug Administration. And thank you, Commissioner Gottlieb, for testifying before the Subcommittee today.

The volume and complexity of the FDA’s work have grown considerably in recent years. Charged with assuring the safety and efficacy of human and animal drugs, biologics, and medical devices—FDA must work to strike the appropriate balance between encouraging innovation and timely access while protecting the public’s health and safety. FDA also regulates cosmetics, tobacco, and products that emit ra-

diation. And, it is responsible for ensuring the safety and security of our nation's food supply.

FDA's core mission is critical to the lives of American families and seniors, and I will plan to touch on two issues during questions that are particularly top of mind—the opioids crisis and eliminating barriers that unduly prevent generic drug competition.

With such an extremely broad mandate, I look forward to hearing from the Commissioner about the agency's priorities.

Senator COLLINS. Thank you.

HEALTHCARE PROVIDER EDUCATION—OPIOID PRESCRIPTION

Doctor, we have previously discussed the need for improved health care provider education with regard to the prescribing of opioids. Medicaid beneficiaries are prescribed pain relievers at a higher rate than those with other sources of insurance. And they also, not surprisingly, given that higher rate, have a higher risk of overdose from prescription opioids, heroin, and fentanyl.

What opportunities do you see for greater collaboration among the FDA, CMS, State Medicaid directors, medical societies, and other parties, in order to address this problem of appropriate prescribing of opioids?

Dr. GOTTLIEB. I appreciate the question, Senator. I would also add the DEA (Drug Enforcement Agency) to that, because there might be things we can do in conjunction with our partners at the Justice Department.

As part of the steering committee that we have set up, we are currently having discussions about what steps we can take to improve provider education, and maybe take a look at packaging as well, as a way to help make sure prescriptions are more appropriately matched to the clinical circumstances for which they are being written.

I do not want to get too far ahead of that process, other than to say that this is something that is at the top of the list of things that we are looking at right now. This includes what additional steps we can do under our current authorities, both through the risk management plans that we currently promulgate in conjunction with opioids, the approval of opioids and other narcotics on the schedule of drugs, as well as in partnership potentially with the DEA. DEA obviously has authority to potentially look at certain requirements as part of the process for giving a DEA license to individual practitioners.

Senator COLLINS. Thank you.

DRUG PRICES

As you know from our numerous discussions, the Senate Aging Committee last year undertook a major investigation examining the explosion in prices of off-patent prescription drugs for which there is no generic equivalent. In one case, a drug was purchased by a company that played absolutely no role in developing the medicine, and then raised its price by 5,000 percent overnight.

One of the problems that we found is that these companies ward off competition from generic companies by putting their drugs in closed distribution systems or in specialty pharmacies. The intent in doing so was to delay access or even block access to a suffi-

cient quantity of the brand name drug to do the bioequivalence studies that the FDA requires.

These abuses are serious and contribute to the cost increases that we are seeing. By one estimate, in 2014, such abuses resulted in increased costs to consumers of \$5.4 billion per year.

I have had extensive conversations in hearings and privately with Dr. Janet Woodcock about this problem. She has testified that FDA has done 150 referrals to the Federal Trade Commission (FTC) to take a look at this anticompetitive process without any success. She suggested that there needs to be a law change in order for the Risk Evaluation and Mitigation Strategies (REMS) system not to be abused.

I know that you have testified before the House Appropriations Subcommittee and noted your concern about this type of anti-competitive behavior. Should Congress revise the REMS law, as suggested by Dr. Woodcock, since there is only so much that FDA can do now about the problem?

Dr. GOTTLIEB. Well, I appreciate the question, Senator.

I know there is some legislation that Congress is currently contemplating in this regard. We would be happy to provide technical assistance on that. I think we already have. I believe there are things we can do within the scope of our current authorities through administrative action to address this challenge.

There are two different challenges here. One is the REMS, which is sometimes misused as a way to block the ability of generic companies to get access to the samples they need in order to develop a generic drug. It takes between 1,500 to 3,000 actual doses in order to develop a generic equivalent.

The other issue is things are sometimes embedded in the contracts with the distributors or the specialty pharma companies that make it hard for the distributors or the specialty pharma companies to sell the drugs to the generic companies when they try to purchase them at fair market value in the marketplace.

So there are two different issues. Some we can solve, or address within the scope of FDA, and some might require us, if we want to try to address it administratively, to partner with Medicare, where there might be opportunities to do that.

We can identify, to your point, the situations, the circumstances, where we believe the generic companies are not able to get the access to the doses and make referrals. We cannot fully address some of the commercial restrictions that prevent them from getting access to those doses. But we could, in partnership with other agencies.

Senator COLLINS. Thank you.

Senator HOEVEN. Senator Tester, I understand that you are deferring to Senator Leahy. Is that correct?

Senator TESTER. I was not going to, but go ahead.

[Laughter.]

Senator LEAHY. There has to be some advantage of being vice chairman of this committee.

Senator HOEVEN. Senator Leahy.

Senator LEAHY. Thank you. I will be brief. I will put my full statement in the record.

[The statement follows:]

PREPARED STATEMENT OF SENATOR PATRICK LEAHY

Thank you, Chairman Hoeven and Ranking Member Merkley, for holding this hearing today to examine the President's fiscal year 2018 budget proposal for the Food and Drug Administration. And thank you, Commissioner Gottlieb [got-LEEB], for joining us here today. I thank the Chair and Ranking Member for giving me the opportunity to offer a few opening remarks.

The Food and Drug Administration has an enormous responsibility to ensure the safety of all Americans. From our food supply, to pharmaceuticals and cosmetic products, the FDA must have the resources it needs to effectively review these products. That is why I was so disappointed and alarmed to see the woefully inadequate budget submission from the FDA, which, when excluding the user fee proposal and the mandatory funding through the 21st Century Cures Act, includes a 34 percent cut. The cuts include \$119 million from monitoring food safety and a \$55 million reduction in medical product safety. In my many years in the Senate, I have heard repeatedly that the FDA needs more, not less, resources to adequately fulfill the agency's mission. Commissioner Gottlieb, I am curious to hear from you about your justification for how these proposed reductions will not adversely impact Americans' health and safety, and help bolster consumer confidence in our Nation's food supply.

The FDA also has a responsibility to approve new drugs, including generic alternatives. With the price of prescription drugs on the rise, crippling households and seniors on a fixed income, I will also want to discuss with you ways to help ensure more competition in the pharmaceutical market. Commissioner Gottlieb, as a physician and someone who has worked in the industry for many years, I am interested in hearing your thoughts.

Finally, Dr. Gottlieb, I would be remiss if I did not make one thing very clear: President Trump's abysmal budget assumes savings from the repeal of the Affordable Care Act, and deep cuts to the Medicaid program. As we talk today about how to increase access to safe, affordable—life-saving—prescription drugs, we cannot forget the millions of Americans that would be left without health insurance if the Affordable Care Act is repealed. Whatever Senate Republicans are crafting behind closed doors, we cannot—and should not—accept any proposal that strips essential and affordable healthcare from millions of Americans.

As I have said in other Appropriations hearings, as Vice Chairman of this Committee, I will work to craft a budget that truly puts Americans first. I look forward to working with the other members of this Committee, on both sides of the aisle, who I believe also want to fulfill that goal.

Senator LEAHY. Commissioner, I am glad you are here today. I appreciate you being here.

FDA'S FISCAL YEAR 2018 BUDGET SUBMISSION

I was disappointed to see I think a woefully inadequate budget submission from the FDA. When you exclude the user fee proposal and mandatory funding to the 21st Century Cures Act that is about a 34 percent cut, \$119 million is cut from monitoring food safety, \$55 million reduction in medical product safety.

I have been here for over 40 years. I have heard repeatedly the FDA needs more money, not less. This is the first time I have seen such a huge cut, especially with the price of prescription drugs on the rise, crippling opioids, and so forth.

So I think the budget that the President has submitted is abysmal. It assumes deep cuts of the Medicaid program. It assumes repeal from the Affordable Care Act. It is kind of saying the check is in the mail. But I would really like to have a budget that puts Americans first, not political slogans first.

DRUG PRICES AND CREATES ACT

But I want to follow up on something Senator Collins was saying about drug prices and the Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act. We care, all of us, I do not care whether you are Republicans or Democrats, about the high

cost of prescription drugs. I know that some of the pharmaceutical companies have used inappropriate delay tactics to limit the ability of generic competitors to enter the market. Some will not give the generics the samples needed for testing.

I proposed a bill joined by Republicans and Democrats both here in the Senate and in the House, the CREATES Act, which would deter pharmaceutical companies from blocking cheaper generic alternatives.

So can you explain again the role access to these samples plays in market competition?

Dr. GOTTLIEB. Thanks for the question.

The bottom line is that there is no question there are places where companies do take advantage of rules meant for one purpose as a way to gain commercial advantage. What I want to do is make sure we have a framework in place that makes it hard to do that. I think that when we put in place rules for, in this case, a risk management plan trying to address drug safety questions, we do not want to see those rules misused as a way to try to forestall access to generic competition that Congress intended under the laws that exist right now.

So I do not want to be playing whack-a-mole with companies either. I want to have in place a consistent framework and a consistent set of rules that prevent these kinds of abuses.

I think we can achieve that. I would be happy to work with Congress on the legislation that you are contemplating. But I also think that there are things that we can do administratively through our current authorities. That is where I am going to be focusing my attention.

Now the REMS is not the only place where this kind of potentially anticompetitive behavior goes on. We are going to be looking across all those places. We are going to be announcing a public meeting very soon to solicit input from the public on where other people believe there are practices that could be forestalling access to generic competition, where branded companies might be taking advantage of certain rules that we could potentially address through our existing authorities.

But this is an important focus of mine.

Senator LEAHY. You commented recently the FDA is evaluating whether to waive the law's existing preference for brands and generics for REMS. And Janet Woodcock, as mentioned already, testified that a statutory change might be needed.

Which is better for you, statutory, or can you do it from regulatory?

Dr. GOTTLIEB. Well, I have been in the job for about 6 weeks now, and I have spent a lot of my time looking at what I can do, and starting to put those actions in motion. So I have spent far less time looking at potential statutory solutions.

I think you just referred to the single, shared REMS, where branded companies and generic companies are obligated to try to negotiate a single REMS to try to reduce burdens on providers. And the question there becomes, at what point do we step in and say, "You know what? The negotiations have gone on for long enough, and we are going to allow the generics to move forward with their own REMS program."

That is a decision we could make. We have to develop the administrative record to do that. That is something where we, through our current policy, can help address a potential stall tactic.

I think if we put in place a policy signifying that we were willing to step in and say, "You know what? These negotiations have gone on long enough. We are going to allow the generic company to move on their own," I think maybe companies might reach agreement quicker than they are today.

Senator LEAHY. Thank you.

Thank you, Mr. Chairman. I think you are going to find both Republicans and Democrats are going to be interested in working with you to do that, because these prices are getting out of control.

Senator HOEVEN. Senator Rubio.

Senator RUBIO. Thank you.

Thank you, Dr. Gottlieb, for being here.

PREMIUM CIGARS

As you know, as we discussed for your confirmation, there are a number of small businesses in Florida that have been making premium hand-rolled cigars for generations. The industry is at stake.

Last year, under the previous administration, they finalized a rule that would require premium cigars, not the stuff you get from behind the counter, but the premium ones, to regulate the manufacture, import, packaging, labeling, advertising, promotion, sale, and distribution, at the premium cigar level.

So it is already illegal to sell tobacco products to anyone under the age of 18, which I think addresses the underage smoking issue. Plus, the premium cigar market really is not marketed toward that. It is a different market altogether.

Are there any plans to reevaluate the inclusion of premium hand-rolled cigars from this rule, as was proposed under the preliminary rule?

Dr. GOTTLIEB. Thanks for the question.

We are currently looking at aspects of the rule. As you know, there was a 3-month delay in implementation of certain compliance dates announced before I arrived at FDA. We are coming up on the end of that delay.

Whatever we do in this regard is going to need to be science-based, of course. But we are cognizant of the challenges faced by small businesses. I also understand that there are a number of legislative measures to exempt premium cigars. If Congress were to act, we would be happy to work with legislators to mitigate any unintended consequences of these measures.

I do not want to comment too specifically, given that there is pending litigation right now around this issue, other than to say that I understand the concerns. You and I have had the opportunity to talk about them on a few occasions now. I do understand the concerns of the small businesses that make premium cigars, Senator.

Senator RUBIO. Yes. And just for those who might be watching, we are talking about the premium cigars, or what the name implies, a premium cigar.

Dr. GOTTLIEB. That is right.

Senator RUBIO. I mean, it is an expensive product marketed toward a very specific audience. If it is science-based, I think it will show, as we have seen repeatedly, that it is really not a product that it is marketed to people under age, or the like.

PEDIATRIC CANCER TREATMENTS

Real quick, I really appreciate the assistance FDA has provided to me and to Senator Bennet on our legislation, RACE for Children, to close the gap on cancer treatments that exist between adults and children. I was just wondering if you could provide some background as to why the FDA initially requested legislation to close this loophole after years of trying to encourage development of pediatric cancer treatments only through the Best Pharmaceuticals for Children Act?

Dr. GOTTLIEB. Well, I know the legislation, Senator. I assure you, we want to do everything we can to try to make products available to pediatric patients, particularly pediatric patients who have rare diseases where current available therapy might not fully address their clinical needs. I know that we have provided technical assistance with respect to this legislation and have worked with your office and will continue to do that.

Senator RUBIO. Just again, as an aside, what Senator Bennet and I are aiming at is, right now it is basically on an incentive system, where we are trying to incentivize companies, in every one of their trials, to have a pediatric component. Unfortunately, it is not working.

They are not doing that enough because sometimes the target audience is not big enough for them, or the target potential patient mix is not large enough for them to be encouraged to do that.

So our hope is to be able to drive more of that. I think everyone has been impacted in their own families by pediatric cancer, and it is critically important that we develop new treatment options at that level, because when it strikes a family, it is devastating.

So again, we thank you for your cooperation and look forward to continuing to interact with you.

Thank you, Mr. Chairman.

Senator HOEVEN. Senator Tester.

TOBACCO PRODUCTS

Senator TESTER. Thank you, Mr. Chairman. I am glad I stuck around for Marco's questions, because the fact is, I think he is absolutely right on the premium cigars. I would tell you, on the other side, there are companies that are marketing their tobacco products to kids, and, hopefully, you can do something about that, too, because it is ridiculous. It smells bad.

You do not need to comment on that. I just hope you would pursue that.

GENERIC DRUGS

Would you agree that expediting the review of high-need generic drugs should be a priority for the FDA?

Dr. GOTTLIEB. We currently do expedite various categories of what I think you and I might agree are high-need generic drugs.

In fact, we just announced we are going to be prioritizing the review of drugs that do not face any competition. There are 180 generic drugs right now, or drugs that are off-patent.

FISCAL YEAR 2018 BUDGET

Senator TESTER. And the chairman talked about 1,000 vacancies. CBO has estimated that, if we are going to do this, it could be as many as 500 additional employees over the next 5 years. At \$60,000 a year a pop, that is a fair amount of money.

I think it is the right thing to do. I think it is an important thing to do. But how, under this budget, are you going to be able to accomplish that?

Dr. GOTTLIEB. Well, look, as the chairman noted, I was not involved in the formulation of the budget.

Senator TESTER. I got it.

Dr. GOTTLIEB. I would have to, obviously, make it work, if the budget were to pass as it was proposed.

These are challenging budgetary times. We are going to have to figure out ways to do more with less. We have tried to target the cuts that this budget does distribute. This budget is an overall increase, but there will be certain cuts distributed under the budget, because of the way the money is allocated with the emphasis towards the user fees.

We will have to try to, and we have tried to allocate the reductions to places of lower priority. But in an agency where there is an important mission, and a lot of what we do is important, sometimes it is challenging to find those areas. We have tried to do the best we can to identify them.

Senator TESTER. I think this is really important. I think, as many of the people on this committee have talked about, prescription drugs is a huge driver in health care costs. They are huge. We need to make sure they are safe. But the backlog, whether it is with generics or orphan drugs, as you talked about in your opening statement, is critically important.

I love to do more with less, but we have to do a lot more with a third less, and I just do not see how that works. You do not have to justify this, because I have heard the "more with less" from a lot of different folks.

But the truth is, in the end, if we are going to be able to hold you accountable and you come back in and say, "You know what? I just did not have the manpower to do it," that is our job here, to make sure you have the manpower to do it. And your recommendations are really important when it comes to manpower.

And I get it. There is fat in every agency. And there are priorities in every agency. So I would hope that you would be honest with us and say, "You know what? This is a big issue." Because I think the generic drug thing is a huge issue. And to get these high-need generics out I think is something we should all try to achieve. But you also need to be realistic on the manpower and the budget that it takes, because it is important.

Dr. GOTTLIEB. Well, Senator, as you are trying to think through what you think are the appropriate allocations to help support the agency's mission, you can rest assured I would be happy to work with you to provide you any advice you need.

Senator TESTER. Not only me but this entire subcommittee on your budget. I would love to get your recommendations. Because, like I said, I think this is an incredible driver in health care, and we need to figure out ways to do reduce costs.

GENERIC DRUGS

I think generics have been one of the bright lights over the last 15, 20 years, however long they have been around. And so when we see hedge fund folks buying up prescription drug companies, doing the kinds of things Senator Collins talked about, we have to figure out ways to block that, whether it is through your agency or some other agency.

Dr. GOTTLIEB. Right. We are also going to contemplate this very issue in the GDUFA reauthorization that is before Congress right now.

Senator TESTER. All right. Thank you.

IMPORTATION OF PRESCRIPTION DRUGS

Now I want to talk about importation of prescription drugs. There have been all sorts of efforts over the last 20 years that I know of, from Montana hauling busloads of folks up into Canada to buy prescription drugs. There have been bills put forth here for reimportation, some of them good, some of them not so good.

Do you think Americans should be allowed to import drugs from other countries?

Dr. GOTTLIEB. Well, this question has been put to FDA Commissioners across both Republican and Democratic administrations, and there is a certification. It is currently legal to have drug reimportation, as long as the Secretary of Health and Human Services can certify the safety of the drugs that are coming in. That legislation has existed through both Republican and Democratic administrations.

I have not taken a fresh look at this question. I have not been asked to. I am happy to look at it. But I would remind the committee that FDA Commissioners dating back to when I was last at the agency about 15 years ago have not been able to make that certification.

Senator TESTER. Have not been able to make the certification of safety, of it being a safe product reimported?

Dr. GOTTLIEB. Of the ability to put in place the proper regulatory architecture that, if you have reimportation of drugs, to make sure that the chain of custody can be guaranteed, that you are actually getting a drug that was manufactured by legitimate—

Senator TESTER. Right. I think that is a legitimate concern. I think there is also a legitimate concern of Americans being gouged for their prescription drugs. I am almost to the point where I think we may be subsidizing other countries for their cheaper prescription drugs.

I do not know that to be a fact. But the truth is that when I go into Montana, and I think the same can be said for North Dakota or Oregon, we hear about this issue a lot.

Dr. GOTTLIEB. And I am trying to take steps to address it, Senator, as you know, through what we are doing to try to bring more competition onto the market.

I think you are absolutely right. I do not think it is a debatable proposition. We are subsidizing drugs for other countries through the high prices we pay here to support the research and development, and we need to address that, too. I am not the trade representative, obviously, but I am trying to do all I can through within the context of my agency.

Senator TESTER. Thank you for your answers.

Thank you, Mr. Chairman, for allowing me to go over time.

Senator HOEVEN. Absolutely, Senator.

ADDITIONAL COMMITTEE QUESTIONS

We have votes that have been called, so at this point, we are going to adjourn the hearing.

I do want to thank you, Dr. Gottlieb, for being here today. I appreciate you not only being here but your good work.

For members of the committee, any questions that you want to submit for the hearing record should be turned into subcommittee staff within 1 week, which is Tuesday, June 27th. We would appreciate if we could have a response back from you, Doctor, within 4 weeks from that point.

QUESTIONS SUBMITTED BY SENATOR JOHN HOEVEN

ALZHEIMER'S

Question. Alzheimer's disease is a major public health threat to our country. Patients and providers currently have few impactful therapeutic options when fighting Alzheimer's disease. Costs associated with Alzheimer's disease have been estimated to be \$236 billion, per year. And unless we get new medicines to slow the progression of the disease, cure it, and even one day prevent its onset, those annual costs are projected to top \$1 trillion by 2050. In no uncertain terms, we urgently need new FDA-approved drugs for Alzheimer's disease. To achieve this important goal, FDA must ensure that the right regulatory policies and processes are in place to encourage and facilitate innovation. The status quo with regard to Alzheimer's disease must change.

What is the FDA's policy of requiring clinical trials for new Alzheimer's medicines to meet two endpoints, or co-primary endpoints—one related to cognition and one related to function?

Answer. As stated in FDA's 2013 draft guidance on Alzheimer's disease (AD), clinical trials in the dementia stage of AD should use a co-primary outcome measure approach in which a drug demonstrates efficacy on both a cognitive and a functional or global assessment scale. The measures of neuropsychological performance are sensitive, and on their own, these measures may not be clinically meaningful. Thus, co-primary endpoints are intended to ensure that the drug's observed effect on cognition is clinically meaningful. Before the onset of overt dementia, however, milder functional and/or global impairments are more challenging to assess accurately, especially for patients early in the spectrum of the illness. Accordingly, as expressed, in FDA's 2013 draft guidance on AD, openness to the use of a single primary endpoint, such as the Clinical Dementia Rating—Sum of Boxes score, that integrates both cognition and function in a single assessment. Additional assessments may also be appropriate for use in clinical trials, and FDA is open to considering other assessments that integrate both cognition and function.

Question. From your new position as FDA Commissioner, do you believe the co-primary endpoint standard is appropriate? Have you asked, or will you ask your staff to look into this issue?

Answer. As noted in response to Question #1, and as stated in FDA's 2013 draft guidance on Alzheimer's disease, clinical trials in the dementia stage of AD should use a co-primary outcome measure approach in which a drug demonstrates efficacy on both a cognitive and a functional or global assessment scale. The measures of neuropsychological performance are sensitive, and on their own, these measures may not be clinically meaningful. Thus, co-primary endpoints are intended to ensure that the drug's observed effect on cognition is clinically meaningful. Before the onset of overt dementia, however, milder functional and/or global impairments are more

challenging to assess accurately, especially for patients early in the spectrum of the illness.

Accordingly, as expressed, in FDA's 2013 draft guidance on Alzheimer's disease, openness to the use of a single primary endpoint, such as the Clinical Dementia Rating—Sum of Boxes score, that integrates both cognition and function in a single assessment. Additional assessments may also be appropriate for use in clinical trials, and FDA is open to considering other assessments that integrate both cognition and function. The Agency is prepared to approve new treatments for Alzheimer's disease that are supported by substantial evidence of effectiveness on clinically meaningful outcomes. FDA works closely with drug sponsors to help them develop this evidence.

OPIOIDS

Question. The opioid epidemic continues to plague this country. Both the CDC and World Health Organization recommend treatment for pain starting with non-opioids prescription medication before using opioids. What is FDA doing to ensure non-opioid prescriptions receive a prioritized and timely review?

Answer. FDA's prescription drug efforts are part of a larger, coordinated Departmental strategy around addressing the opioid crisis. HHS strategy includes five priority areas:

- Improving access to prevention, treatment, and recovery services, including the full range of medication-assisted treatments;
- Targeting availability and distribution of overdose-reversing drugs;
- Strengthening our understanding of the crisis through better public health data and reporting;
- Providing support for cutting edge research on pain and addiction; and
- Advancing better practices for pain management.

The FDA continues to support efforts to better understand the treatment of pain, especially as it relates to balancing the need to effectively treat pain with the public health crisis related to opioid use disorder and overdose. Currently, there are FDA-approved drug treatment options, opioids and non-opioids, available for the management of pain.

FDA has a number of programs, such as Fast Track and Breakthrough Designation, which are intended to facilitate the development and expedite the review of products that, for example, meet unmet medical needs. Novel non-opioid medications with the potential to provide pain relief in situations in which opioids often are used could be appropriate candidates for such programs. FDA is also working with the National Institute on Drug Abuse to encourage the development of non-addictive pain medication.

Question. How many non-opioid treatments are currently under review by FDA and are scheduled for review in the next 12–24 months?

Answer. Although FDA is unable to discuss the substance of any matters that may be pending before the Agency, FDA can assure you that the Agency understands the value in and supports the development of new treatment options for pain. In fact, there are a number of novel non-opioid products under development.

Question. What if anything can be done by FDA to ensure more prescription non-opioid medications are available to treat pain?

Answer. Currently, both opioid and non-opioid FDA-approved drugs are available for the management of pain. There are also medical devices indicated to treat specific types of pain. FDA understands the value in new treatment options for pain, and continues to work with the medical device and drug industries to explore new options for patients in pain, especially options that have improved safety profiles and are less likely to result in addiction or abuse. FDA has a number of programs, such as Fast Track and Breakthrough Designation, which are intended to facilitate the development and expedite the review of products that, for example, meet unmet medical needs. Novel non-opioid medications with the potential to provide effective pain relief in situations in which opioids often are used could be appropriate candidates for such programs.

FDA is also working with the National Institutes of Health's (NIH) National Institute on Drug Abuse to encourage the development of non-opioid pain medications, and has been involved in discussions with NIH in a series of meetings to facilitate development of non-addictive pain treatment. In addition, FDA looks forward to a future in which substantially all opioid medications are less susceptible to abuse than the conventional formulations that dominate the market today.

ANTIBIOTIC RESISTANCE

Question. I'm concerned about superbugs—the reports coming out of Asia and other countries is that much of their food-producing livestock is ridden with multi-drug resistant bacteria. FDA and our farmers have eliminated high-value antibiotics from our farm systems, but others haven't done much at all. There's a lot we can do to deter the development of antibacterial resistance, but it seems the cat is out of the bag and we really need a strong and ongoing pipeline of new drugs.

What can we do to develop the next generation of antibiotics?

Answer. Antimicrobial resistance (AMR) is one of the most serious threats to global health in this century. FDA has taken a leading role in addressing this critical threat by working with key stakeholders to identify new approaches to stimulate antibacterial research and development, including by streamlining clinical trial designs; enhancing surveillance through systems such as the National Antimicrobial Resistance Monitoring System; and actively participating in global efforts to reduce resistance.

Recent FDA efforts include administering the incentives available to sponsors under the Generating Antibiotic Incentives Now (GAIN) Act. FDA has granted 136 Qualified Infectious Disease Product (QIDP) designations, including approximately 71 designations for novel drugs. FDA has approved ten drug products with QIDP designation. Moreover, FDA has written, reviewed and revised a number of guidance documents to provide clarity and predictability on recommended trial designs and development pathways. The Agency has also engaged the scientific community through public meetings, partnerships, and regulatory science research.

Efforts to strengthen the antibacterial drug pipeline must also address significant economic and scientific challenges. The President's Advisory Council on Combatting Antibiotic-Resistant Bacteria (PACCARB) recently finalized their report with recommendations addressed to Secretary Price for incentivizing the development of vaccines, diagnostics, and therapeutics/anti-infectives for both human and animal health to address the issues surrounding antibiotic resistance. HHS' Biomedical Advanced Research and Development Authority (BARDA) and the National Institute of Allergy and Infectious Diseases (NIAID) have helped to launch important, new efforts in this space, such as the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), a public-private partnership that provides funding to accelerate the preclinical discovery and development of antibacterial drugs.

As you noted, FDA has been actively working with various stakeholders, in the animal drug context, to implement judicious use policies to promote antimicrobial stewardship. Such efforts include working with animal drug sponsors to transition medically important antimicrobials used in the feed or water of food-producing animals to a marketing status requiring veterinary oversight, and eliminating the use of these products for production (such as growth promotion) purposes. Implementation of this transition process was completed in January 2017 marking an important step forward in promoting antimicrobial stewardship in animal agriculture.

In addition, strengthening the pipeline for antimicrobials or alternatives to antimicrobials intended for use in food-producing animals by developing appropriate incentives (including public-private partnerships) to spur drug and vaccine development is also important to ensure antimicrobial therapy is available to meet the current and future needs of these animals and to provide a safe, wholesome food supply.

FOREIGN HIGH RISK INSPECTIONS

Question. Over the past several years the Committee has provided FDA with additional resources to develop a targeted, risk-based, and efficient inspection model for high-risk establishments for onsite verifications.

Given the challenges of expanded geography, constantly expanding inventory of foreign exporters, and finite budgetary resources, how will FDA leverage third party site verification services to complement FDA foreign site planning and inspection activities?

Answer. In fiscal year 2016, FDA spent the bulk of the money provided to Office of Global Regulatory Operations and Policy (GO) on commercial foreign onsite verification reviews in support of expanding global coverage. FDA contracted with Dun & Bradstreet (D&B) to provide site verification information on specific facilities. D&B performed site verifications across all of the regulated commodities. With respect to medical products, the remaining funds were used in support of the pharmaceutical GMP mutual recognition initiative and enhancing the Center for Drug Evaluation and Research (CDER) site selection model. Regarding foods, the remain-

ing funds were used to enhance the process and consolidate the responsibilities of foreign food inspection planning in the Office of Regulatory Affairs.

In fiscal year 2017, Office of Global Regulatory Operations and Policy, (GO) expanded the number of foreign onsite verifications and facility data delivered through D&B for foreign medical device and food establishments. These specific commodities were chosen due to the value and impact that commercial onsite verifications provide these programs. For the pharmaceutical program, GO has worked with CDER to issue grants for analysis that will support the development of quality scorecards for pharmaceutical facilities and products. A quantitative characterization of the state of quality can enhance oversight by improving the site selection model's identification of high-risk foreign facilities.

As part of the reauthorization of the Generic Drug User Fee Amendments (GDUFA) in the FDA Reauthorization Act (FDARA), FDA committed to working on a guidance explaining the risk-based site selection model as well as outreach activities to better inform foreign regulatory counterparts about our model.

QUESTIONS SUBMITTED BY SENATOR MITCH MCCONNELL

OPIOIDS

Question. Given your public statements, it seems that the FDA and Congress agree that combating the opioid epidemic remains a top priority. How do you plan to coordinate FDA's prescription drug abuse efforts with other agencies? Specifically, how will the FDA work with the NIH to accelerate innovative cures and non-opioid pain therapies to the market faster?

Answer. FDA understands the value in and supports the development of new treatment options for pain, and is committed to continue working with our colleagues at the National Institutes of Health, including the National Institute on Drug Abuse, and other government agencies to explore new options for patients in pain, especially options that are not addictive. Since June 2017, FDA has collaborated with NIH via a series of three meetings to facilitate development of non-addictive pain treatment and treatment for opioid addiction and overdose prevention/reversal. Also, in May 2017, FDA hosted a public meeting on pain management with participation from many Federal agencies to discuss, among other things, non-addictive pain treatment options. FDA notes that the Agency's prescription drug efforts are part of a larger, coordinated Departmental strategy around addressing the opioid crisis.

Question. The FDA Opioid Action plan issued in February 2016 included a commitment to collaborate with advisory committees. FDA stated that after considering advisory committee recommendations and reviewing existing requirements, the agency was inviting affected opioid manufacturers to a meeting to inform them of the agency's intention to require a Risk Evaluation and Mitigation Strategy (REMS) for immediate-release (IR) opioids. This meeting was held on January 25, 2017. Where is the agency in the process of expanding REMS to include IR opioids? What steps has the agency been taking to consult and work with stakeholders on the expansion of the REMS?

Answer. On July 10, 2017, FDA announced that it intends to update and modify the existing Risk Evaluation and Mitigation Strategy (REMS) for extended-release/long-acting (ER/LA) opioid analgesics, and for the first time, to include immediate-release (IR) opioid analgesic products in the modified REMS program. FDA expects this action to take place in the coming weeks. The modified REMS is expected to include revisions to the existing FDA Blueprint for prescriber education which describes the content that must be covered in an educational program for it to be considered REMS-compliant.

FDA sought input from relevant stakeholders in a variety of settings on a number of issues related to the ER/LA Opioid Analgesic REMS, including at an Advisory Committee meeting in May 2016, during a public workshop in May 2017, and through establishment of a docket announced in a Federal Register notice in May 2017.

On May 3 and 4, 2016, FDA convened a joint meeting of the Drug Safety and Risk Management (DSaRM) Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC) to discuss whether the ER/LA Opioid Analgesics REMS assures safe use, whether it is unduly burdensome to patient access to the drugs, and whether it (to the extent practicable) minimizes the burden to the healthcare delivery system. FDA also sought input on possible modifications to the ER/LA Opioid Analgesic REMS, including expansion of the scope and content of pre-

scriber training and expansion of the REMS program to include immediate-release (IR) opioid analgesics.

On May 9 and 10, 2017, FDA held a public workshop to seek input on how to best support prescriber and other healthcare provider education on appropriate pain management and opioid analgesic prescribing. This meeting convened government experts and representatives from state licensing boards, professional associations, healthcare systems, patient groups, and other stakeholder groups involved in the challenges of improving pain management while addressing the opioid epidemic.

In addition to the panel discussions at the meeting, FDA is also considering comments submitted to two public dockets which closed on July 10, 2017. The first docket asked for public comment on how to best support prescriber and other Health Care Provider education on appropriate pain management and opioid analgesic prescribing. FDA has received more than 250 comments to the docket. The second docket under review considers modifications to the existing FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics in light of recommendations from the May 2016 Advisory Committee meeting. The draft revisions to the Blueprint would broaden the Blueprint to incorporate information on pain management, including the principles of acute and chronic pain management, non-pharmacologic treatments for pain, and pharmacologic treatments for pain (both non-opioid analgesic and opioid analgesic). More than 680 comments were submitted to this docket.

Question. Also included in the action plan was the commitment to expand access to abuse deterrent formulations (ADF) to discourage abuse. Beyond the FDA's guidance issued in April 2015 related to the types of studies to assess abuse deterrence efficacy and suggested labeling, what other actions has the FDA taken to expand access to ADF or assist manufacturers in the development and subsequent approval process for bringing these formulations to market?

Answer. FDA's support of opioid products with abuse-deterrent formulations (ADF) is one of a number of steps to which FDA has committed which is focused on policies aimed at reversing the opioid epidemic while still providing patients in pain access to effective relief. To date, the Agency has approved ten opioids with labeling describing properties expected to deter (though not completely prevent) one or more routes of abuse. The 2015 final guidance for industry, Abuse-Deterrent Opioids—Evaluation and Labeling, provides information on abuse-deterrent formulations for applicants seeking such approval.

Given the lower cost, on average, of generic products, the availability of generic ADFs is an important step toward balancing the need to reduce opioid abuse with helping to ensure access to appropriate treatment for patients in pain. To that end, in March 2016, FDA issued draft guidance entitled General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products. The draft guidance, when finalized, will provide recommendations regarding studies that should be conducted to show that a generic opioid is no less abuse-deterrent than a brand name opioid with abuse-deterrent labeling with respect to all potential routes of abuse.

FDA continues to engage advisory committees, as appropriate, to provide advice on novel or challenging issues that arise in connection with the development and evaluation of abuse-deterrent opioids. In July 2017, FDA held a public workshop with expert panel members and interested stakeholders about the challenges in using currently available data and methods for assessing the impact of opioid formulations with properties designed to deter abuse on opioid misuse, abuse, addiction, overdose, and death in the post-market setting.

FDA remains committed to working with sponsors and other stakeholders to support the development of and access to opioid formulations with properties that could lead to a meaningful reduction in prescription opioids misuse and abuse compared to the conventional formulations.

Question. FDA requires manufacturers of extended release (ER/LA) opioids to make available REMS-compliant training for prescribers of ER/LA opioid analgesics, yet physician participation in these training programs is voluntary. At the same time, FDA is holding manufacturers of ER/LA opioids accountable to industry-negotiated performance goals that manufacturers are struggling to meet. As part of the REMS, the ER/LA opioid manufacturers agreed to specific performance goals amounting to 160,000 active prescriber participants in the voluntary REMS-compliant training programs by March 2016. However, the most recent report showed that only 66,000 prescribers completed training, meaning the participation rate amounted to 41 percent of their goal. Beyond updating the ER/LA opioid analgesics REMS, how will the FDA encourage prescribers of these drugs to participate in the training?

Answer. Under the current ER/LA REMS, companies are required to make training available to healthcare providers that prescribe extended-release/long-acting (ER/LA) opioid analgesics. The companies may meet this requirement by working with accredited continuing education providers who offer training to prescribers; however, prescribers are not currently required to complete this training in order to prescribe ER/LA opioid analgesics.

The Agency has been carefully evaluating existing requirements and assessments of the ER/LA Opioid Analgesic REMS, specifically how prescribers are trained on the use of opioids and management of pain. To make sure providers are properly informed about suitable prescribing and the risks and benefits associated with opioid drugs, FDA intends to update the existing REMS on ER/LA opioid analgesics, and for the first time, extend these same regulatory requirements to the manufacturers of immediate release (IR) opioid analgesic products. The new training will be aimed at making sure providers who write prescriptions for the IR opioids are doing so for properly indicated patients, and under appropriate clinical circumstances. In addition to expanding the training to include more healthcare providers, the training will also include expanded information on pain, broad principles of acute and chronic pain management, pharmacologic treatments other than opioids, and the use of other therapies for pain that do not involve medication.

FDA agrees that all healthcare providers involved in the management of pain should be educated about the safe use of opioids. Based on the feedback the Agency has received from two public meetings over the past year, FDA is actively exploring the question of whether, in the future, there should be mandatory provider education and how to operationalize such a requirement. As part of the Opioid Policy Steering Committee's responsibilities, FDA will be reviewing the data necessary to understand the most effective way to move forward.

Question. In 2011, FDA issued an Advisory to Drug Manufacturers regarding glass contamination of injectable drugs and recommended specific actions the industry could voluntarily take to address the problem. Does the current administration have plans to update the Advisory?

Answer. FDA has met with manufacturers who are working to develop glass medical products to address quality issues with respect to glass product design and manufacturing for glass products intended for injectable drugs. The Agency has also initiated a study comparing various types of glass products intended for use in injectable drug products and expects to begin analyzing the results of that study by the end of the year. Additionally, industry experts have initiated studies of new types of glass products to determine superiority to current products and suitability with actual drug product formulations. FDA will use the analysis of its own study, as well as discussions with industry and any other appropriate available data, when considering whether to update the 2011 advisory.

ELECTRONIC DISTRIBUTION OF PRESCRIBING INFORMATION

Question. Congress has prevented the implementation of the 2014 Obama administration proposed rule titled the "Electronic Distribution of Prescribing Information for Human Prescription Drugs Including Biological Products." Given Congress's explicit concerns, does the current administration have plans to revise or withdraw this rule?

Answer. FDA is continuing to review its options with regard to the above rule-making in light of Sec. 734 of Division A, Title VII, of the Consolidated Appropriations Act, 2017, which states:

SEC. 734. None of the funds made available by this Act may be used to propose, promulgate, or implement any rule, or take any other action with respect to, allowing or requiring information intended for a prescribing healthcare professional, in the case of a drug or biological product subject to section 503(b)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 353(b)(1)), to be distributed to such professional electronically (in lieu of in paper form) unless and until a Federal law is enacted to allow or require such distribution.

QUESTIONS SUBMITTED BY SENATOR ROY BLUNT

DRUG REVIEW TIME

Question. It has come to my attention that the FDA median new drug application (NDA) review times vary widely—from 175 days for oncology and anti-viral drugs to 375 and 400 days for neurology and psychiatry drugs. In fact, most NDAs have

a median review time of more than 300 days. Patient needs are not being met with such long review times. Could you please provide me the following:

Compare each division's interpretation and implementation of authority under the Food and Drug Administration Safety and Innovation Act to exercise flexibility in meeting the approval standard regarding unmet medical need, including under the accelerated approval pathway.

Answer. CDER has a longstanding commitment to regulatory flexibility regarding the evidence required to demonstrate that the approval standard has been met for products that are intended to treat serious or life-threatening diseases, especially where no satisfactory alternative therapy exists. This regulatory flexibility extends throughout the Center and is stated in FDA's regulations at 21 CFR 312.80—Subpart E.

FDA instituted its Accelerated Approval Program—one of the Agency's expedited programs—to allow for earlier approval of drugs that treat serious conditions and that would provide a meaningful advantage over available therapies. Provisions of the Food and Drug Administration Safety and Innovation Act of 2012 facilitate somewhat broader use of accelerated approval to expedite patients' access to important treatments for serious conditions.

Divisions across CDER exercise flexibility in determining whether drugs meet approval standards (full or accelerated) based on whether available data indicate that a drug's benefits outweigh the risks for its intended use(s). Medical need, available alternatives, nature of the disease, and patient input are among the factors considered in assessing benefit and risk. Average review times depend on multiple factors such as the amount and quality of data provided by the applicant to CDER, available data (including from natural history studies, if applicable) about the disease or condition to be treated, and the number of applications under review at the time. Depending on the drug under consideration, review teams may work across divisions, leveraging CDER resources to promote collaboration and innovation in the regulatory process.

Question. Identify policies, practices and procedures, staffing and resource issues, division culture and precedents, and other factors which cause or contribute to the differences in review times among divisions for both priority review and standard review New Drug Applications.

Answer. Differences in review and approval times between CDER divisions can be the result of many factors such as the quality of available data (which depends in part on the rigor of study design) provided to support an application, complexity of the disease, whether other effective therapies are available, and the amount and quality of epidemiologic and natural history data about the disease. All divisions within CDER are fully focused on our mission of protecting and promoting public health by helping to ensure that human drugs are safe and effective, meet established quality standards, and are available to patients. As such, division culture places these goals as paramount when reviewing applications, including those being considered under the Agency's expedited review programs.

Question. Make recommendations for actions that could be taken to materially reduce differences in New Drug Application review times among Food and Drug Administration divisions for both priority reviews and standard reviews and shall include recommendations concerning New Drug Applications reviewed under the accelerated approval pathway.

Answer. By leveraging FDA's statutory mandates, the Agency is working to reduce review times by improving processes and gaining efficiencies to the greatest extent possible. This includes helping to reduce uncertainty in drug development by encouraging sponsors to contact the Agency early and often, especially for those products being developed under expedited review programs. Streamlining clinical trials, integrating patient voice throughout the regulatory process based on successful models of participation, and promoting greater preparedness by establishing nimble approaches to address novel and emerging public health threats will help Americans get better products, faster.

FDA is embarking on PDUFA VI, which provides resources for the highly successful, and resource-intensive, breakthrough therapy program and streamlines the review of drug/device or biologic/device combination products. As a result, the Agency suggests that applicants with products designated as "breakthrough therapies" engage in early, frequent, and meaningful communications with the Agency to better enable promising safe and effective products to reach patients faster. Further, PDUFA VI emphasizes patient-focused drug development efforts through a more systematic, science-based approach to collecting meaningful patient input. Review times across CDER divisions are likely to be enhanced by advancing drug development tools, including biomarker qualification, and increasing understanding of how "real-world evidence" can be generated and used in regulatory decisionmaking. Pilot

programs to explore novel approaches to the design of complex clinical trials and the application of advanced modeling techniques to preclinical and clinical data are also important options to consider for reducing review times.

FDA REVIEW TIME

Question. I am concerned about the cost to the healthcare system and confusion to consumers and physicians due to Polyethylene Glycol (Rx PEG) 3350 Abbreviated New Drug Applications remaining on the market when there is a proven over-the-counter drug available. My understanding is that the FDA has been looking into this issue for more than 10 years to confirm that this is a contravention of the Durham Humphrey Amendments to the Food, Drug, and Cosmetic Act.

Can you explain to me why this review has taken so long and appears to be ongoing without resolution?

Answer. The distinction between prescription and OTC drugs was codified by the Durham-Humphrey Amendments, which were enacted in order to address the marketplace confusion that arose from the simultaneous marketing of identical or nearly identical drugs on a prescription and OTC basis for identical or equivalent uses (Public Law 82-215, 65 Stat. 648 (1951). See, e.g., H.R. Rep. No. 82-700, at 5 (1951). The Agency's detailed rationale for this action is set forth in the Notice of Opportunity for Hearing published at 73 F.R. 63491 (Oct 24, 2008).

The sponsors of the abbreviated new drug applications (ANDAs) for prescription PEG 3350 products refused the FDA's request that they withdraw these products voluntarily. As a result, the Notice of Opportunity for Hearing was issued, which was followed in May of 2014 by a Draft Proposed Order. Following issuance of the Draft Proposed Order, several ANDA holders for prescription PEG 3350 drugs submitted responses asserting that there is a genuine and substantial issue of material fact that necessitates a hearing.

Consistent with 21 CFR Part 12 and 314.200, the Office of the Commissioner must review the requests for hearing, the Draft Proposed Order, and the ANDA holder's objections to the proposed order, and must determine whether to grant a hearing or enter a final order withdrawing approval of the ANDAs. The timeframe will depend in part on whether a hearing is granted or denied. The Office of the Commissioner is actively considering the matter at this time. The docket for this matter is available at regulations.gov, Docket No. FDA-2008-N-0549.

Question. How much time is needed until FDA can come to a conclusion on this issue?

Answer. The sponsors of the abbreviated new drug applications (ANDAs) for prescription PEG 3350 products refused the FDA's request that they withdraw these products voluntarily. As a result, a Notice of Opportunity for Hearing was issued, which was followed in May of 2014 by a Draft Proposed Order. Following issuance of the Draft Proposed Order, several ANDA holders for prescription PEG 3350 drugs submitted responses asserting that there is a genuine and substantial issue of material fact that necessitates a hearing.

Consistent with 21 CFR Part 12 and 314.200, the Office of the Commissioner must review the requests for hearing, the Draft Proposed Order, and the ANDA holder's objections to the proposed order, and must determine whether to grant a hearing or enter a final order withdrawing approval of the ANDAs. The timeframe will depend in part on whether a hearing is granted or denied. The Office of the Commissioner is actively considering the matter at this time. The docket for this matter is available at regulations.gov, Docket No. FDA-2008-N-0549.

QUESTIONS SUBMITTED BY SENATOR DIANNE FEINSTEIN

ANTIBIOTICS

Question. I was encouraged that the FDA recently announced the full implementation of Guidance for Industry #213. This is an important step in maintaining the effectiveness of antibiotics by ensuring the judicious use of antibiotics in food-producing animals and limiting the use of antibiotics to situations that are necessary to protect animal health.

However, I remain concerned by the significant number of antibiotic labels that lack defined durations of use, defined dosages, or that could allow usage under the previous label of "growth promotion".

I understand the FDA has collected comments through the Federal Register on this issue, but what is the timeline as well as the specific policy actions the FDA plans on taking regarding these problematic labels?

Answer. FDA agrees that the full implementation of Guidance for Industry #213 in January 2017 is a critical and important step forward to foster the judicious use of antimicrobial drugs and curb antimicrobial resistance. FDA has and continues to express its appreciation for the cooperation of the animal pharmaceutical industry for meeting its commitment to fully align all affected products with the GFI #213 recommendations. FDA recognizes that additional work is needed to ensure that the labeled use conditions of all medically important antimicrobial drug products are aligned with the principles of judicious use. As you noted, one issue of concern is the fact that some medically important antimicrobial drug products approved for use in animal feed or water have at least one therapeutic indication without a defined duration of use.

While this remains a concern, it is important to note that as of January 2017 it is no longer legal to use such feed or water antimicrobial products for production (such as growth promotion) purposes and their use must be under the authorization of a licensed veterinarian. FDA believes that veterinarian oversight plays a critical role in ensuring that medically important antimicrobials are used judiciously.

In September 2016, FDA published a Federal Register notice requesting comment from the public on this duration of use issue. A key objective in seeking public comment is to optimize the use of medically important antimicrobials by using a dosage strategy that maximizes drug effectiveness, minimizes target animal toxicity, and has an appropriately targeted duration of use. FDA received numerous substantive comments on this issue and is still in the process of analyzing these comments. Once FDA has finished analyzing the comments, the Agency will develop a timeline with proposed actions for addressing this issue. It remains an Agency priority to foster stewardship of medically important antimicrobial drugs in food-producing animals and help preserve the effectiveness of these antimicrobials in animal and human medicine.

Question. How will the FDA continue to improve its collection of data related to antibiotic use on farms and large production facilities?

Answer. Having access to better data on antimicrobial use and resistance is critical for assessing the impact of actions already implemented and for guiding additional steps for fostering judicious antimicrobial use in veterinary settings. FDA is currently working closely with the U.S. Department of Agriculture (USDA) to coordinate data-collection activities across agencies. FDA experts are working with experts at the USDA/Animal and Plant Health Inspection Service (APHIS) Center for Epidemiology and Animal Health on strategies for collecting, analyzing, and reporting data on antimicrobial use. FDA has taken a number of additional actions to enhance data on antimicrobial use and resistance. For example, in September 2015, FDA, in collaboration with the USDA and the Centers for Disease Control and Prevention (CDC), held a public meeting to obtain input on strategies for enhancing the collection of antimicrobial drug use and resistance data. Moreover, in May 2016, FDA issued a final rule revising the annual reporting requirements for antimicrobials sold or distributed for use in food-producing animals to require species-specific estimates of antimicrobial sales or distribution data for major food animal species.

In August 2016, FDA funded two cooperative agreements with university researchers to develop and pilot methodologies to collect detailed information on antibiotic use practices in cattle, swine, chickens, and turkeys. These ongoing projects are expected to provide important information on data collection methodologies and will help support ongoing efforts at USDA to optimize long-term strategies for collecting and reporting such data. In August 2017, FDA published a proposed approach for using a biomass denominator to adjust annual data on the amount of antimicrobials sold or distributed for use in food-producing animals in the U.S. to take into account the size of animal populations. This adjusted estimate will provide insight into broad shifts in the amount of antimicrobials sold for use in food-producing animals. FDA is inviting comment on the methodology and utility of this type of data analysis.

Question. Will the FDA continue to enhance coordination with the Department of Agriculture for on-farm data collection?

Answer. Given the many challenges associated with collecting nationally representative on-farm data on antimicrobial use across the various food animal production sectors, FDA believes it is essential to continue to work in close collaboration with USDA on this issue. FDA is currently working closely with USDA to coordinate data collection activities across agencies. FDA experts are working with experts at the USDA/APHIS Center for Epidemiology and Animal Health on strategies for collecting, analyzing, and reporting data on antimicrobial use. Specifically, USDA/APHIS's National Animal Health Monitoring System provides essential data collection infrastructure for antibiotic-use practices in livestock and poultry oper-

ations and zoonotic pathogen infection in U.S. food-producing animals via its established survey cycle and in-plant biological survey capability. Having access to better data on antimicrobial use and resistance is critical for assessing the impact of actions already implemented and for guiding additional steps for fostering judicious antimicrobial use in veterinary settings. In support of FDA's ongoing work with USDA on this issue, FDA has taken a number of additional actions to enhance data on antimicrobial use and resistance. For example, in September 2015, FDA, in collaboration with the USDA and CDC, held a public meeting to obtain input on strategies for enhancing the collection of antimicrobial drug use and resistance data.

In August 2016, FDA funded two cooperative agreements with university researchers to develop and pilot methodologies to collect detailed information on antibiotic drug use in cattle, swine, chickens, and turkeys. These ongoing projects are expected to provide important information on data collection methodologies and will help support ongoing efforts at USDA to optimize long-term strategies for collecting and reporting such data. Moreover, in August 2017, FDA published a proposed approach for using a biomass denominator to adjust annual data on the amount of antimicrobials sold or distributed for use in food-producing animals in the U.S. to take into account the size of animal populations. FDA's methodology relies on USDA data to estimate the number of animals in a particular U.S. livestock population, including annual totals of animals slaughtered and annual totals of livestock imported into or exported from the U.S. This adjusted estimate will provide insight into broad shifts in the amount of antimicrobials sold for use in food-producing animals. FDA is inviting comment on the methodology and utility of this type of data analysis.

Question. Please provide an update on the progress of collecting species-specific data for the end-of-year use summary.

Answer. In May 2016, FDA issued a final rule revising the annual reporting requirements for drug sponsors of antimicrobials sold or distributed for use in food-producing animals to obtain estimates of sales by major food-producing species (cattle, swine, chickens, and turkeys). The additional data will improve our understanding of how antimicrobials are sold or distributed for use in major food-producing species and help further target efforts to ensure judicious use of medically important antimicrobials.

Section 105 of the Animal Drug User Fee Amendments of 2008 (ADUFA 105) requires antimicrobial drug sponsors to annually report to FDA the amount of all antimicrobial drugs they sell and distribute for use in food-producing animals. ADUFA 105 also requires that FDA issue annual summary reports of these sales and distribution data collected from sponsors. The law further requires that these data be reported out by antimicrobial drug class. To report summary data in a manner protective of both national security and confidential business information, only those antimicrobial drug classes and other categories with three or more distinct sponsors of approved and actively marketed animal drug products are independently reported.

FDA is currently reviewing the sales and distribution data submitted for the 2016 reporting year. The first annual summary report containing estimated species information is expected to publish by December 31, 2017.

Question. Please provide an update on the National Action Plan for Combating Antibiotic-Resistant Bacteria.

Answer. Along with their Federal partners, FDA continues to implement the National Action Plan for Combating Antibiotic-Resistant Bacteria and to support the ongoing work of the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB). An assessment of progress being made under the National Action Plan was published by the PACCARB in March 2016. The full report is available at <https://www.hhs.gov/sites/default/files/paccarb-final-report-03312016.pdf>. More recently, FDA, along with partner agencies, provided an update to their Year 2 milestones and accomplishments in the National Action Plan to the council members at the PACCARB's September 13–14 public meeting.

FDA is committed to advancing efforts to foster the judicious use of antimicrobial drugs in animals. The Agency has issued a number of important guidance documents and regulations to support its judicious use strategy and has actively engaged in outreach efforts to support effective implementation.

DIVERSITY IN CLINICAL TRIALS

Question. Section 907 of the 2012 Food and Drug Administration Safety and Innovation Act directed FDA to take a closer look at the inclusion and analysis of demographic subgroups in applications for drugs, biologics, and devices—including by sex, race and ethnicity, and age—and issue a report on findings.

The report that was issued was followed by an “Action Plan to Enhance the Collection and Availability of Subgroup Data”, which included 27 responsive and pragmatic actions, which fall under three overarching priorities: improving the completeness and quality of demographic subgroup data collection, reporting and analysis; identifying barriers to subgroup enrollment in clinical trials and employing strategies to encourage greater participation; and making demographic subgroup data more available and transparent.

Please provide an update on the implementation of this Action Plan.

Answer. In February 2016, FDA hosted the public meeting “Enhancing the Collection, Analysis, and Availability of Demographic Subgroup Data,” to provide a public update on implementation of the Action Plan (AP). FDA has completed implementation on 26 of 27 action items in the AP. Highlights are as follows:

To address priority I, data quality, FDA authored two guidance documents: “Collection of Race and Ethnicity Data in Clinical Trials” and “Evaluation and Reporting of Age, Race, and Ethnicity Data in Medical Device Clinical Studies.” Both provide clear and detailed guidance for regulated industry on clinical trial inclusion data matters. FDA has updated its MedWatch forms for adverse events reporting to include fields for race and ethnicity. FDA released its “Women’s Health Research Roadmap” to better coordinate women’s health research across the Agency.

To address priority II, participation, FDA declared 2016 the “Year of Diversity in Clinical Trials” to make a strong push to promote representation of diverse groups in clinical trials. Activities like the Minorities in Clinical Trials Campaign and the Diverse Women in Clinical Trials Initiative included public service announcements, educational materials, webinars, and print/digital outreach. Two public stakeholder meetings were held:

In April 2015, the Institute of Medicine and FDA hosted a joint meeting titled “Strategies for Ensuring Diversity, Inclusion, and Meaningful Participation in Clinical Trials: A Workshop.” 100+ participants attended and a publication detailing the proceedings was released in April 2016. In December 2015, FDA and Johns Hopkins held a joint workshop titled “Assessing Safety and Efficacy for a Diverse Population” to advance understanding of the importance of clinical trial diversity.

To address priority III, data transparency, FDA launched Drug Trials Snapshots (DTS). DTS publishes in clear, consumer-friendly plain language demographic data from clinical trials that supported FDA approval of new molecular entities and original biologics. 100+ DTSs have been published.

SAFETY OF IMPORTED FOOD

Question. The United States imports food products from more than 200 countries and territories through over 300 U.S. ports. Food imports have more than doubled in the past decade. As the volume of imports grows, so does the potential for foodborne illness resulting from imported food.

FDA has bilateral and multilateral food safety-related arrangements and agreements with numerous countries to ensure the safety of imported food, and I understand that FDA is also exploring other ways to leverage the work of the food safety authorities in other countries, in accordance with section 305 of the 2011 FDA Food Safety Modernization Act (FSMA). One approach that FDA has been testing as part of this effort is referred to as “systems recognition,” under which FDA would review certain other countries’ food safety systems to ensure that those systems are comparable to that of the United States.

How do FDA’s agreements with other countries ensure that those countries will effectively address U.S. food safety requirements and respond in a timely manner to problems that are identified?

Answer. FDA recognizes that food safety issues and outbreaks can arise in all countries and Systems Recognition accounts for this reality. Systems Recognition focuses not only on the ability of food safety systems to help ensure safe food, but also on the ability of food safety authorities in foreign countries to identify, address, and contain food safety issues and outbreaks that may arise, learn from past events, and strengthen their system over time.

Systems Recognition describes whether: (1) a country’s food safety system provides a similar, though not necessarily identical, system of protections as the U.S. food safety system, and (2) the country’s food safety authority or authorities provide similar oversight and monitoring activities for food produced under its jurisdiction. Systems Recognition is based on the premise that food safety systems with similar elements and similar levels of oversight lead to similar food safety outcomes.

FDA conducts assessments of foreign food safety systems through the application of ten standards, outlined in the International Comparability Assessment Tool (ICAT). These core elements of a food safety system are important to ensure effective

tive food safety outcomes. For example, FDA evaluates a system's capacity for responding to identified problems through surveillance, investigation, response, and subsequent review of alleged food-related incidents and emergencies that can reduce the incidence of illness, injury, and outbreaks. FDA also examines the food safety authority's strategies, procedures, and actions to enforce and achieve compliance with food safety laws and regulations and to evaluate the effectiveness of its compliance and enforcement program. If FDA determines that a country's food safety system meets the ICAT criteria, FDA implements a Systems Recognition Arrangement with monitoring and periodic reevaluation by FDA through the duration of the arrangement.

Question. To what extent has FDA evaluated the effectiveness of these agreements in keeping the U.S. food supply safe?

Answer. FDA is continuing with efforts to assess potential Systems Recognition partners to determine whether additional partnerships can be achieved. At the same time, the Agency is engaged in a program of monitoring and evaluation for currently recognized partners. To date, Systems Recognition arrangements have been put into place with New Zealand, Canada, and Australia. The latter two arrangements were completed within the past 15 months.

Food safety outcomes typically are judged by microbiological or chemical levels, incidence of foodborne disease, or some other quantitative food safety performance measure. Beyond these case-level measures, FDA is currently exploring additional correlations between food safety performance measures and the elements making up food safety systems as a way to measure a food safety system's overall regulatory performance, in keeping with FSMA's mandate to approach food safety from a systems perspective.

Before determining whether to enter into a Systems Recognition Arrangement with another country, FDA uses a tool called the International Comparability Assessment Tool (ICAT) to assess the country's food safety system, including the laws, regulations, programs, and policies upon which a foreign food safety authority relies to help ensure the safety of food. Based on FDA's experience with the oversight of domestic state programs and the Manufactured Food Regulatory Program Standards (MFRPS), from which the ICAT was derived, FDA believes that the standards reviewed through the ICAT assessments correspond to comparable food safety outcomes associated with the food safety system.

To ensure that Systems Recognition Arrangements remain relevant and effective, each arrangement and corresponding foreign competent authority undergoes a periodic review and will be reassessed every 5 years. This schedule allows the parties to monitor and modify terms of the arrangement as needed to account for developments in either party's food safety regulatory system.

Question. Please provide an update on the results of the systems recognition pilots with New Zealand and Canada.

Answer. After establishing Systems Recognition Arrangements with New Zealand in 2012 and Canada in 2016, the countries moved to the implementation phases for both countries.

Under the arrangements, FDA and each systems-recognized country are engaged in regular discussions to promote consumer protection throughout implementation. FDA and the foreign competent authority continue, through ongoing bilateral communication and periodic reviews, to examine the performance of each country's regulatory system to help ensure that the arrangements continue to provide the appropriate level of public health protection. In addition, the bilateral arrangements are reviewed periodically, including when the level of food safety assurance required under domestic law or achieved by one of the parties significantly changes. For example, FDA has updated its assessment tool to incorporate new FDA Food Safety Modernization Act standards, and Canada's Safe Foods for Canadians Act will prompt a re-review of the bilateral terms next year. In addition, all Systems Recognition Arrangements include full reassessment at five-year intervals.

Ongoing monitoring of the New Zealand and Canada system-recognized countries has proved useful in assuring FDA that appropriate public health outcomes have been achieved under these Systems Recognition Arrangements.

Question. How, if at all, does FDA plan to use the "systems recognition" approach and integrate it with its broader efforts to ensure the safety of imported?

Answer. The FDA Food Safety Modernization Act (FSMA) provides FDA with a variety of new authorities to help ensure the safety of imported foods and takes into account the capability of the regulatory system of the exporting country to assure compliance with U.S. food safety standards for a given food. FSMA also directs FDA to consider bilateral and multilateral arrangements and agreements to leverage the work done by foreign competent authorities to help ensure the safety of imported

foods. Both Systems Recognition and commodity-specific arrangements achieve this directive.

FDA uses Systems Recognition when the Agency determines it can rely on another food safety authority's implementation of a science-based food safety system. This level of regulatory partnership and leveraging requires a rigorous assessment process to support a determination that FDA is justified in recognizing a foreign food safety system and using the work of a foreign government to inform FDA's regulatory decisionmaking process.

Because Systems Recognition takes into account the role of the food safety system of an exporting country, it informs FDA's risk-based decisionmaking and resource allocation regarding inspections, monitoring, admissibility, and follow-up when food safety incidents occur. Leveraging the regulatory oversight of comparable food safety systems allows FDA to enhance its risk-based targeting of resources with respect to import controls, foreign facility inspections, and foodborne outbreaks. These arrangements with foreign competent authorities complement FDA's upcoming implementation of the FSMA import tools, such as the Foreign Supplier Verification Program (FSVP) regulation, Third-Party Certification, and the Voluntary Qualified Importer Program. The FSVP regulation incorporates Systems Recognition by establishing modified requirements for importers of certain types of food imported from foreign suppliers in good compliance standing with the food safety authority for a country whose food safety system FDA has determined to be comparable to the U.S. system under the Systems Recognition initiative.

FOOD SAFETY MODERNIZATION ACT

Question. In September 2016, FDA extended the compliance dates for many regulated facilities under the Food Safety Modernization Act (FSMA), especially small and very small businesses that fell under the main core regulations including Preventive Controls for Human and Animal Food, Produce Safety Standards, and the Foreign Supplier Verification Program (FSVP) for food imports. Please provide an update on the implementation of these regulations.

Answer. In 2016, FDA finalized the last of seven foundational rules to implement FSMA and is now focusing on implementation of the regulations. FDA extended certain compliance dates in August 2016 for very specific activities required in four of the FSMA rules, but these extensions did not affect the majority of the provisions contained in the seven rules. FDA is working to address the issues for which the Agency extended the compliance dates as we proceed with implementation of the rules. FDA's implementation activities include industry education, training, outreach, and technical assistance; developing inspection protocols and strategies to achieve compliance; training for FDA and state regulators; establishing necessary information technology systems to support industry, FDA, and states; and coordinating with our partner organizations.

KEY HIGHLIGHTS OF FDA'S IMPLEMENTATION EFFORTS:

Question. FDA initiated inspections to evaluate compliance with two of the regulations—Preventive Controls for Human Food, and Foreign Supplier Verification Programs. Rollout of additional inspection programs are planned for this year.

FDA established a Technical Assistance Network to provide technical assistance to stakeholders for interpretation of the regulations.

FDA is in the third year of a five-year cooperative agreement with the National Association of State Departments of Agriculture, NASDA, to bring together a range of state partners to collaboratively plan implementation of the Produce Safety regulation and Preventive Controls for Animal Food regulation, including facilitating outreach and education and delivery of training to state regulators.

Recently, FDA announced the second round of funding to 43 states for nearly \$31 million to develop produce safety regulatory programs. In 2016, FDA awarded nearly \$22 million to 42 states. The cooperative agreement is renewable for 5 years, provided availability of funds and successful performance by states. Given the states' local presence, knowledge, and relationships with the farm community, FDA believes the states are very important in helping to provide oversight and direct technical assistance.

In June 2017, FDA began accepting applications from accreditation bodies in support of the accredited third-party certification program. FDA posted the Strategy for FSMA training, which outlines the work FDA is doing to prepare its staff, state partners, and industry to implement the regulations. As part of the training strategy, FDA engaged with the Food Safety Preventive Controls Alliance, the Sprout Safety Alliance, and the Produce Safety Alliance to develop industry training on the regulations.

Since October 2016, FDA has released 13 FSMA-related draft or final guidance documents for industry. In 2017, FDA announced its intention to consider how it might simplify the agricultural water standards and to extend compliance dates for those standards (for produce other than sprouts). FDA also recently announced its intention to continue to focus on Current Good Manufacturing Practice requirements during routine animal food facility inspections, but not to begin routine inspections for Preventive Controls requirements until the fall of 2018.

What steps is FDA taking to ensure that small businesses and producers understand and are able to comply with the FSMA requirements?

Answer. FDA is engaging in and sponsoring a great deal of outreach and technical assistance to help small and very small farms and processors in understanding and complying with the provisions of the FSMA regulations.

Beginning with the enactment of FSMA in 2011, FDA has been committed to providing tools to the food industry, particularly small businesses and producers, in meeting the requirements of the law. FDA recognizes that small and very small businesses and farmers face unique circumstances and challenges in implementing FSMA. FDA established phased-in compliance dates to provide small and very small businesses as well as producers additional time to comply with the preventive controls regulations (human and animal food), produce safety regulation, and foreign supplier verification program regulation. FDA also began operating a Technical Assistance Network (TAN), which is a web portal to which questions concerning application of and compliance with the FSMA regulations can be submitted for an individual response.

FDA continues to engage in a number of activities intended to assist small and very small businesses as well as producers in advance of their FSMA compliance dates. To help ensure that our assistance is targeted to meet their needs, FDA partners with groups involved with specific communities to facilitate delivery of training and informational resources to achieve compliance with the FSMA regulations. For example, in 2016 FDA awarded a cooperative agreement to the National Farmers Union Foundation to develop and provide science-based, culturally specific food safety training, education, and outreach for local food producers and processors.

FDA established a Produce Safety Alliance (PSA) to develop and deliver training on the produce safety regulation requirements that would be of particular assistance to small and very small farms, with training courses available since fall 2016. FDA also established the Food Safety Preventive Controls Alliance to develop and deliver training that will help small and very small facilities understand the preventive controls and foreign supplier verification program regulations requirements.

In 2016, FDA awarded almost \$22 million in cooperative agreements to 42 States to develop produce safety infrastructure which included outreach and technical assistance to farms in those states. In July 2017, FDA announced an additional nearly \$31 million in cooperative agreements to 43 States to begin and continue development of these State activities. FDA has also created a Produce Safety Network (PSN), which is a regionally-located staff of produce specialists whose primary focus is to develop relationships with the local farming community and assist in the implementation of the produce safety regulation.

In addition, FDA has issued small entity compliance guides for the current good manufacturing practice (CGMP) and hazard analysis and risk based preventive controls regulations for both human and animal feed, intended to inform small and very small domestic and foreign human and animal food facilities about the CGMP and preventive controls regulations and enable them to better understand the requirements of the regulations.

These guidances should be helpful to small and very small farms that also engage in on-farm manufacturing and processing. FDA also has issued a small entity compliance guide for the Mitigation Strategies to Protect Food Against Intentional Adulteration rule. FDA also intends to issue small entity compliance guides for the produce safety regulation and the other FSMA regulations.

COSMETICS

Question. Virtually every American uses personal care products daily, yet the safety laws for cosmetics and personal care products haven't been modernized since created in 1938. There is support among the industry- both large and small companies- as well as consumer and health groups to take significant steps to update oversight in this area. I have worked with Senator Collins to introduce a bipartisan bill to do just that.

Will you commit to working with us to make meaningful updates, including evaluating the safety of ingredients in these prod?

Answer. FDA shares your interest in the safety of cosmetics marketed to American consumers and commits to continuing dialogue on cosmetics issues.

QUESTIONS SUBMITTED BY SENATOR TOM UDALL

Question. Last year, FDA issued a long overdue rule, known as the deeming rule, to enable the agency to begin to oversee e-cigarettes, cigars, and other previously unregulated tobacco products. FDA was responding, in part, to the thousands of flavored e-cigarettes that have flooded the marketplace in recent years—flavors such as cotton candy, gummy bear, root beer float, and banana split. While youth use of e-cigarettes dipped last year, youth use of e-cigarettes exceeds use of regular cigarettes. As the Surgeon General reported last year, use of e-cigarettes by youth is a public health concern and use of any product containing nicotine by youth, including e-cigarettes, is unsafe.

DEEMING

I am concerned that FDA announced in May a three-month delay in enforcement of future deeming rule compliance dates and that the Administration has delayed filing legal briefs defending the deeming rule from industry challenges. While there is debate about whether e-cigarettes could help some adult smokers to quit regular cigarettes, we should all be able to agree that FDA oversight is needed to protect kids and public health. FDA should be aggressively addressing the flavors and marketing practices that are increasing e-cigarettes' appeal to youth.

During the Subcommittee's hearing, you indicated that FDA was looking at aspects of the deeming rule. Which aspects of the deeming rule you are examining?

Answer. On July 28, 2017, FDA announced a comprehensive approach to the regulation of nicotine which includes the Agency's plan to begin a public dialogue about lowering nicotine levels in combustible cigarettes to non-addictive levels through achievable product standards. The Agency intends to issue an Advance Notice of Proposed Rulemaking (ANPRM) to seek input on the potential public health benefits and any possible adverse effects of lowering nicotine in cigarettes. The comprehensive approach also includes, among other things, a reconsideration of aspects of the implementation of the final deeming rule with an eye towards fostering innovation where innovation could truly make a public health difference, and making sure FDA has the foundational regulations it needs in place to make the entire program transparent, predictable, and sustainable for the long run.

FDA shares the concerns about youth use of e-cigarettes. On August 8, 2017, FDA announced it would pursue a strategic, new public health education campaign aimed at discouraging the use of e-cigarettes and other electronic nicotine delivery systems (ENDS) by kids. The Agency plans to expand its "The Real Cost" public education campaign this fall to include messaging to teens about the dangers of using these products while developing a full-scale campaign that will launch in 2018. The campaign is just one component of the Agency's efforts to restrict youth access, limit youth appeal, and reduce youth exposure to toxic chemicals from all tobacco products. FDA continues to enforce existing regulations specifically aimed at addressing youth access to ENDS and other newly-regulated products, including banning the sale of tobacco products to those under age 18, requiring age verification by photo ID, and prohibiting free samples. Since August 2016, FDA has issued over 6,400 warning letters to brick and mortar and online retailers for selling newly-regulated tobacco products such as e-cigarettes to minors.

On August 4, 2017, FDA issued a guidance that extended the deadlines for the submission of marketing applications for those products that became newly-regulated by last year's deeming rule and were on the market as of August 8, 2016. Applications for newly-regulated combusted products—such as most cigars, pipe tobacco, and hookah tobacco—would be submitted by August 8, 2021. Applications for newly-regulated non-combusted products—such as most e-cigarettes—would be submitted by August 8, 2022. For newly regulated products on the market as of August 8, 2016, FDA anticipates that manufacturers will be able to continue marketing products while FDA reviews product applications submitted by the revised filing dates.

With this additional time, FDA intends to issue other foundational rules and guidances—addressing topics such as the type of information FDA expects to be included in marketing applications—that will help make the product review process more efficient, predictable, and transparent, while still upholding the FDA's public health mission.

This additional time will not only help manufacturers develop higher quality and more complete applications, but also allows FDA additional time to explore clear and meaningful measures to make tobacco products less toxic, appealing, and ad-

dictive, with an intense focus on youth. In particular, the Agency is pursuing product standards for ENDS that would address known risks. This could include measures on battery safety and child-resistant packaging, and product labeling to prevent accidental child exposure to liquid nicotine. The FDA also intends to issue an Advance Notice of Proposed Rulemaking (ANPRM) to seek public comment on the role that flavors—including menthol—in tobacco products play in attracting youth. The FDA also intends to issue an ANPRM to request information on how “premium cigars” should be defined, the health effects of these products, and their patterns of use. Additionally, the Agency plans to explore additional restrictions on the sale and promotion of ENDS, including restrictions on how products may be sold and advertised, to further reduce youth exposure and access to these products.

Question. Will you commit to not delay enforcement of the deeming rule beyond the current three-month delay?

Answer. On July 28, 2017, FDA announced a comprehensive approach to the regulation of nicotine which includes the Agency’s plan to begin a public dialogue about lowering nicotine levels in combustible cigarettes to non-addictive levels through achievable product standards. The Agency intends to issue an Advance Notice of Proposed Rulemaking (ANPRM) to seek input on the potential public health benefits and any possible adverse effects of lowering nicotine in cigarettes. The comprehensive approach also includes, among other things, a reconsideration of aspects of the implementation of the final deeming rule with an eye towards fostering innovation where innovation could truly make a public health difference, and making sure FDA has the foundational regulations it needs in place to make the entire program transparent, predictable, and sustainable for the long run.

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Importantly, the compliance policy described above does not affect any current requirements from the deeming rule that have already gone into effect. For example, the deeming rule provisions regarding mandatory age and photo-ID checks to prevent illegal sales to minors remain in effect and are subject to enforcement by FDA. It also will not affect future deadlines for other provisions of the rule, including, but not limited to, required warning statements, ingredient listing, health document submissions, harmful and potentially harmful constituent reports, and the removal of modified risk claims, such as “light,” “low,” or “mild,” or similar descriptors.

QUESTIONS SUBMITTED BY SENATOR PATRICK LEAHY

HELPING FARMERS COMPLY WITH FOOD SAFETY REGULATIONS

Question. The FDA is still in the long drawn-out process of implementing new regulations under the Food Safety Modernization Act (FSMA). This is something that our farmers and food companies in Vermont have been watching very closely, especially for produce farmers who will be covered under the new regulations and have compliance dates that begin in 2018. However, there has already been significant market pressure for farms of all sizes to demonstrate food safety compliance now,

regardless of whether they are fully subject to the new requirements. It is critical that the FDA and USDA both provide support to farmers in order to build the needed capacity to adapt to this changing food safety regulatory landscape. In addition, food safety training and technical assistance should not be one-size-fits-all, but rather tailored to meet the needs of agricultural operations across the country that vary in types and farm size.

I have heard reports from farmers in Vermont that they feel there is a shortage of information flowing from the FDA, and a growing need for trainings that are tailored to the unique needs of small- and mid-scale diversified farms and local food processors.

The FDA has stated that it will provide additional guidance for trainers to use in assessing the equivalency of their training programs, and it has provided some funding to support the development of training programs tailored toward local food producers. However, at this point very little information has been provided regarding the timelines and processes for these much needed equivalent and alternative trainings, yet compliance starts in 2018. It is imperative that the FDA provide sufficient resources in order to offer a diverse array of farmer food safety capacity-building efforts to help American produce farms of all sizes and stages of development in order to face these new Federal food safety requirements, access markets, and promote public health.

What are the specific processes and timelines that the agency will follow in issuing alternate training and equivalency criteria for farmers as quickly as possible?

Answer. FDA recognizes that this is the first FDA regulation specific to produce farms, which can make implementation challenging for farmers. FDA is actively engaged in activities to ensure that farmers have the training, guidance, and other technical assistance targeted to meet their needs and delivered in a timely manner based on the phased in compliance dates in the final rule. FDA has also announced its intention to extend the compliance dates for agricultural water provisions in the rule (other than for sprouts).

Specifically, FDA is actively engaged in activities that will assist with ensuring that training is and continues to be available to farmers. FDA established a Produce Safety Alliance (PSA) to develop and deliver training on the produce safety requirements that would be of particular assistance to farmers. PSA training courses have been available since fall 2016. In August 2016, FDA announced a partnership with the National Farmers Union, through a Cooperative Agreement, to develop and provide science-based, culturally specific food safety training, education and outreach, for local food producers and processors. The emphasis is on those involved in diversified, sustainable, organic, and identity-preserved agricultural operations; beginning and socially disadvantaged farmers; value-added farm businesses and small-size processors; and direct and intermediate supply chain participants.

In August 2016, FDA announced a partnership with the University of Arkansas at Fayetteville, through a Cooperative Agreement. The partnership is to develop and implement food safety training, education, outreach, and identification of technical assistance resources for key tribal stakeholders, including farmers, packers, and manufacturers/processors that grow, harvest, pack, manufacture/process, or hold food covered by FSMA. Moreover, FDA partnered with the U.S. Department of Agriculture's National Institute of Food and Agriculture to provide a National Coordination Center and four Regional Centers to provide training opportunities for owners and operators of farms, small food processors, and small fruit and vegetable wholesalers. These Regional Centers are also responsible for providing technical assistance to farms and offer yet another mechanism for delivering training in a form and manner that meets farms' needs. One of the four Regional Centers is based at the University of Vermont.

In 2016 and 2017, FDA awarded a combined nearly \$53 million in cooperative agreements to 43 States to develop produce safety infrastructure, which included outreach and technical assistance to farms in those states. FDA has also created a Produce Safety Network, regionally-located staff consisting of produce specialists whose primary focus is to develop relationships with the local farming community and assist in the implementation of the produce safety regulation. The FSMA Collaborative Training Forum is co-led by FDA and USDA and involves all public and private entities engaged in FSMA training, especially those serving small and very small businesses. The members of the Forum are actively working to identify and address any information gaps in the various training materials and help ensure that training programs meet farms' needs.

ADDED-SUGAR NUTRITIONAL LABELING FOR MAPLE AND HONEY:

Question. I understand that the FDA is setting a new compliance date for the updated nutrition facts label. I am a strong supporter of transparency and giving consumers information about what is in the foods they buy. However, I believe consumers should not be misled into thinking that sugar has been added to products like maple syrup and honey, which by their nature are pure single ingredient products.

Have you looked into this issue related to the labeling of sugars in honey and maple syrup? Will you commit to work on this issue to find solutions in order to avoid consumer confusion for these single ingredient pure foods like maple syrup and honey so that we do not adversely impact farmers and producers?

Answer. FDA announced on June 13, 2017, its intention to extend the compliance dates for the Nutrition Facts label final rule. After careful consideration, FDA determined that additional time would provide manufacturers covered by the rule with guidance from FDA, and would help them be able to complete and print updated Nutrition Facts labels for their products before they are expected to be in compliance. FDA will provide details of the extension through a Federal Register notice.

The Nutrition Facts label final rule defines “added sugars,” in part, to include sugars that are either added during the processing of foods, or are packaged as such, which includes packages of sugar or containers of honey. The Agency has heard concerns from the honey industry about declaring added sugars on a jar of honey since no sugar is added to the product. The Agency has also heard similar concerns from the maple syrup industry. Providing industry more information about the labeling of “added sugars” on pure honey, maple syrup, and other single ingredient sugar products—is an Agency priority, and FDA is working to address the complex issues related to this labeling concern. FDA plans to invite further comment in the near future and intends to follow up with the maple syrup and honey industries and other stakeholders at a later date.

MAPLE NUTRITIONAL LABELS AND DECEPTIVE MARKETING

Question. We also must crack down on food manufacturers that use the word “maple” on their labels or utilize maple related graphics on their packaging, when there is not any maple syrup in their products. I am concerned that consumers are being misled into thinking that these manufactured food products contain maple syrup, because to most consumers “maple” is not viewed merely as a characterizing flavor as is the case with a grape or orange soda. Instead, “maple” is synonymous with the ingredient maple syrup. This must be addressed by the FDA because these foods that are masquerading as maple syrup-flavored only serve to deceive and mislead consumers, and can cause economic harm to American maple syrup producers and food producers using real pure maple syrup.

Maple syrup as a premium ingredient has a material bearing on the price and consumer acceptance of food products that contain it, which is why it is frequently an ingredient named in the foods or displayed on its packaging. What steps will the FDA take to exercise its legal authority to investigate and take action against misbranded “maple” products in interstate commerce that give consumers the erroneous impression that such maple syrup is present in the foods they are purchasing?

Answer. FDA’s regulations address labeling requirements for characterizing ingredients and flavors. Those regulations provide a basis to allow firms to include statements that are truthful and not misleading on their labels. In addition, they provide a framework for identifying maple ingredients or maple flavors in products, whether involving the use of real maple syrup, or maple flavors derived from maple sources, or the use of maple flavor that is derived from other natural or artificial components. If maple flavor is derived from maple sources other than maple syrup, such as maple sugar or maple extract, FDA would not object to that product being represented as containing natural maple flavor. However, if the characterizing flavor is derived from a non-maple source, such as fenugreek or an artificial flavor, the food must be labeled as “artificially flavored” in accordance with 21 CFR 101.22(i)(1)(ii) and 101.22(i)(2).

Under FDA’s regulations, the term “maple” is not synonymous with “maple syrup.” Such a reading would require, among other things, evidence that consumers perceive the terms to be synonymous and a change in FDA’s regulations. The process for requesting FDA to issue, amend, or revoke a regulation is described in 21 CFR 10.30 (Citizen petition).

FDA shares your concern for the truthful labeling of food products, and FDA intends to continue to monitor the marketplace for potentially false and misleading labeling. If a food does not contain the ingredient maple syrup, the label cannot include the term “maple syrup” in the ingredient statement or as a part of the state-

ment of identity. FDA will consider taking action, as appropriate, consistent with our food safety priorities and resources, against products that are misbranded.

Further, FDA shares your desire to avoid consumer confusion. In September 2016, FDA developed an FDA Consumer Update to help educate consumers about the differences in the ways that ingredients and flavors are declared on product labels, including “maple” and “maple syrup.” The Update is available at: <https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm521518.htm>. FDA may develop additional educational materials if further needs are identified. Furthermore, FDA has worked with the maple syrup industry and would be willing to meet with them to discuss available data and other industry information on consumer perceptions regarding maple and maple syrup.

FIGHTING THE OPIOID EPIDEMIC

Question. Addiction to opioids has ravaged the nation in recent years. According to the National Institutes of Health (NIH), more than two million Americans suffer from opioid addiction today, with the number of prescriptions written for opioids having tripled in the past 20 years. Overdose deaths from heroin and opioids has also more than tripled in the past two decades.

This epidemic has had devastating consequences. I watched with interest the recent announcement by the FDA on its intention to take steps to address the crisis by exploring new opioid formulations designed to deter abuse, and by engaging stakeholders to evaluate the impact of opioid addiction on addicts, their families, and communities nationwide.

In addition to the FDA’s recent announcement, what other ways can the agency continue to take steps to address the nationwide opioid epidemic?

Answer. The FDA Commissioner has made reducing the scope of the epidemic of opioid addiction his highest initial priority. As a first major step in combatting this crisis, FDA recently created an Opioid Policy Steering Committee which is considering what more the Agency can do to confront the challenges of opioid addiction and opioid-related overdoses and deaths.

Bringing together some of the Agency’s senior leaders and members, the Committee has begun by exploring three questions: whether mandatory education for healthcare professionals who have the capability to prescribe opioids is needed; whether extra risk management steps for opioid prescription need to be taken; and whether a change to the current FDA framework used to assess the risk of abuse and misuse during the drug review process is needed.

While the Committee has begun with these core questions, it has a broad mandate to consider whatever additional questions FDA should be seeking to answer. The Committee will solicit input, and engage the public. FDA is committed to looking at all facets of this complex issue and collaborating on various approaches. To pursue these policies, FDA plans to continue to have public dialogue through various forums and to share additional steps and information FDA is considering in addressing these challenges. FDA continues to collaborate with fellow HHS agencies as part of a coordinated Departmental strategy around addressing the opioid crisis.

Question. Regarding the FDA’s recent announcement to explore new opioid formulations designed to deter abuse, has the agency also considered exploring opioid-alternatives to treat and manage pain?

Answer. FDA continues to support efforts to better understand the treatment of pain, especially as it relates to balancing the need to effectively treat pain with the public health crisis related to opioid use disorder and overdose. Currently, there are both opioid and non-opioid drugs approved by FDA for the management of pain.

FDA has a number of programs, such as Fast Track and Breakthrough Designation, which are intended to facilitate the development and expedite the review of products that are intended to treat a serious condition for which there is an unmet medical need. Novel non-opioid medications with the potential to provide effective pain relief may be appropriate designations, but it will be a product-specific determination.

SUBCOMMITTEE RECESS

Senator HOEVEN. Again, I want to thank everyone for coming today, most of all the Commissioner. Again, we look forward to working with you.

Dr. GOTTLIEB. Thanks a lot.

Senator HOEVEN. We are adjourned.

[Whereupon, at 11:15 a.m., Tuesday, June 20, the subcommittee was recessed, to reconvene subject to the call of the Chair.]