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IMPROVING ANIMAL HEALTH: REAUTHORIZATION OF FDA ANIMAL DRUG USER FEES

HEARING

OF THE

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS

UNITED STATES SENATE

ONE HUNDRED FIFTEENTH CONGRESS

SECOND SESSION

ON

EXAMINING IMPROVING ANIMAL HEALTH, FOCUSING ON REAUTHORIZATION OF FOOD AND DRUG ADMINISTRATION ANIMAL DRUG USER FEES

FEBRUARY 13, 2018

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IMPROVING ANIMAL HEALTH: REAUTHORIZATION OF FDA ANIMAL DRUG USER FEES

Tuesday, February 13, 2018

U.S. SENATE,
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,
Washington, DC.

The Committee met, pursuant to notice, at 10:05 a.m. in room SD–430, Dirksen Senate Office Building, Hon. Lamar Alexander, presiding.

Present: Senators Alexander [presiding], Isakson, Paul, Young, Roberts, Murkowski, Murray, Casey, Bennet, Murphy, Warren, Hassan, Smith, and Jones.

OPENING STATEMENT OF SENATOR ALEXANDER

The CHAIRMAN. The Senate Committee on Health, Education, Labor, and Pensions will please come to order.

Today, we are holding a hearing on updating the Animal Drug and Generic Animal Drug User Fee Agreements. Senator Murray and I will each have an opening statement, then we will introduce the witness. After the testimony, Senators will each have 5 minutes of questions.

Farmers and families in Tennessee want to have access to the drugs that keep their animals and their pets healthy.

For example, I know an East Tennessee farmer who raises calves. He checks on them several times a day, and when he notices one is not feeling well, he pulls him aside and gives him a drug. This farmer wants to ensure the drug he gives the sick calf is safe for the calf and for our food supply.

We know that the human medical products we use are safe because the Food and Drug Administration has approved them.

The way any farmer knows the drug he has given to his calf is safe is the same: the FDA has approved it.

Similar to the User Fee Agreements this Committee reauthorized last year for human medical products, this year we need to reauthorize the Animal Drug and Generic Drug User Fee Agreements.

These are agreements between the FDA and the animal drug industry to pay user fees to help speed the approval of new drugs for farmers and ranchers, families, and veterinarians to keep their animals and pets safe and healthy.

These agreements are much smaller than the human drug user fee agreements. The revenue FDA receives from the Animal Drug User Fees is only about 3 percent of the revenue FDA receives from

the human drug program. However, they are still critical to keeping our animals healthy and preventing outbreaks of disease.

There are two agreements, one for new brand animal drugs, which the FDA calls pioneer drugs, and one for generic new animal drugs.

Last year, the FDA received 780 applications for new pioneer animal drugs and 240 applications for generic new animal drugs for review. While animal drugs are used to treat almost every animal species, much of the drug development focuses on the seven major species: horses, cattle, pigs, dogs, cats, chickens, and turkeys.

I was telling Senator Murray while coming in about the book, "Guns, Germs, and Steel: The Fates of Human Society," that I read a few years ago by Jared Diamond, Ph.D. One of the main things I took away from it was how few domesticated species there are; maybe 14, 15, 16, something like that.

But these seven major species include both animals that are common family pets, as well as the livestock that is our food supply.

On average, the animal drug industry spends over $30 million a year to develop new products for farm animals, and over $22 million a year for new treatments for our pets. And according to the animal drug industry, it can take up to 8 years for a drug intended for use in farm animals to be available for veterinarians and farmers, and over 6 years for new pet medicines.

These agreements help bring these new medicines to the veterinarians who write prescriptions for families to care for their pets and treat diseases, such as cancer or heartworm disease.

While these agreements are important to our family pets, we also want to ensure the farmers and ranchers raising our food supply are able to treat their animals with the safe drugs they need. Farmers often use animal drugs to prevent outbreaks of infectious diseases, to treat pain, or prevent swelling of joints in animals.

Having safe and effective animal drugs is important to both the consumer—that food-producing animals are safe to eat—and the farmer or rancher that he has a product to treat his animals and prevent outbreaks.

According to the Tennessee Department of Agriculture, the cattle and calves industry and the poultry industry are two of our State's largest agriculture sectors. Since the last reauthorization of these agreements, the number of cattlemen in Tennessee who have been Beef Quality Assurance Certified—meaning they have proper training to administer animal drug products—has increased from about 17,000 cattlemen to 23,000.

It is important that farmers and ranchers continue to have access to new medicines to keep their animals healthy and prevent infectious disease outbreaks.

These updated agreements have been carefully worked out between the Food and Drug Administration and animal drug industry with input from farmers and ranchers, food and feed producers, veterinarians, and other stakeholders.

The FDA and the manufacturers of animal drugs held eight meetings to discuss the pioneer drug agreement and six meetings on the generic drug agreement.

Our Committee has held eight bipartisan staff briefings over the last few months in preparation for reauthorizing these agreements.

Today, we are going to hear from Dr. Steven Solomon, a veterinarian and the Director for the Center for Veterinary Medicine at the FDA about the agreements. One of the important goals in the updated Animal Drug User Fee Agreements is for the FDA to reduce approval times in certain areas.

These user fees are a critical funding source for the FDA to do its job to expedite the review of safe and effective treatments for animals.

If Congress does not do its job to reauthorize these critical programs, more than 115 people, who work on reviewing these drugs, will lose their jobs. This will lead to delays in approving new animal drugs and bringing new treatments to farmers, ranchers, veterinarians, and families. We have to do this by August 1, 2018.

We hope to mark up these two important agreements by the end of this month so we can move them to the floor, and this Committee can continue our work on other important issues.

These agreements are essential to ensure the animal drugs on the market are safe and effective, and keep farm animals and pets healthy, and help keep our food supply safe.

I look forward to quickly reauthorizing them.

Senator Murray.

OPENING STATEMENT OF SENATOR MURRAY

Senator MURRAY. Well, thank you very much, Mr. Chairman.

Thank you, Dr. Solomon, for joining us today.

As we begin to work to reauthorize the Food and Drug Administration's Animal Drug and Animal Generic Drug User Fees, I am optimistic that we can do this with the same bipartisan spirit we brought to this important issue the last time the Animal Drug User Fee, or ADUFA, were up for reauthorization.

The same bipartisan spirit we brought to this issue last year when we passed the FDA Reauthorization Act and reauthorized the user fees for prescription drugs, medical devices, generic drugs, and biosimilars.

The FDA has a critical role in protecting public health and ensuring the safety of food, drugs, and devices that families in my home State of Washington and across the country depend on.

Part of that role is to ensure that our Nation's animal population is healthy. But the development of drugs for animals presents a unique set of challenges and considerations.

One challenge is the sheer set of different health needs we might use drugs for, from treating illnesses that might harm people or the animal to preventing them.

Another is the sheer number of different animals we care for from those that are commonly pets, like dogs, cats, and horses, to animals we commonly rely on for our food supply like chickens, and cows, and turkeys, and pigs.

To minor species that are not common, but are so important to their owners, or may be critically important to protecting public health.

Finally, we have to make sure the drugs approved are not only safe for the animals, but also safe for the people who may consume their meat and the environment around them.

The Animal Drug User Fee Agreements help the FDA maintain needed resources and manages this important task which affects our lives and our families in many ways.

Some of the ways are obvious and personal. When we go to the vet with a furry family member who has an injured paw or a runny nose, we want to know they are getting treatment that is safe and effective.

Some are less obvious, but no less important. We want our farmers and livestock producers to know that the products they use are humane for their animals and safe for consumers. We want to know how the drugs we give animals impact the larger environment, so that we are not creating dangerous and unintended negative consequences.

An important example of this is the work the FDA does to ensure antibiotics are being used judiciously in animals to avoid creating new resistant strains of bacteria that can harm our families.

I am pleased the FDA continues to collect antibiotic sales data and has taken valuable steps to drive down use of antibiotics in our food and animals.

I hope to hear more from you, Dr. Solomon, about how we can continue to better understand how antibiotics are being used in our food supply chain through collaboration with the Department of Agriculture.

As we work to reauthorize this important legislation, I am optimistic the new agreements can bring more collaboration and communication to the drug development process by bringing regulators and sponsors together earlier to clarify expectations.

Congress has historically reauthorized ADUFA with bipartisan support, and I believe this Committee can build on that track record if we keep our focus on ensuring the health and safety of our families and animals.

I am confident the insight from our witness today, and the stakeholders offering comments to our bipartisan discussion draft released last week, will help us do that.

Thank you, Dr. Solomon. Again, I am looking forward to your testimony.

The CHAIRMAN. Thank you, Senator Murray.

I want to thank Senator Murray and her staff, as well as the majority staff, for working so well together over the last couple of years on our user fee agreements.

They are complicated, and we were able to come to a consensus about them last August, and I look forward to the same kind of process here.

I am pleased to welcome Dr. Steven Solomon. He will have to up to 5 minutes to give his testimony. He was appointed Director of the Food and Drug Administration's Center for Veterinary Medicine in January 2017.

Before he was appointed as Director of that Center, Dr. Solomon served in various policy and leadership roles at the FDA for almost 30 years.

He was Deputy Associate Commissioner for Regulatory Affairs, the Assistant Commissioner for Compliance Policy, and is a veterinary medical officer in the Center for Veterinary Medicine.

Welcome, Dr. Solomon. Thank you for being here. We look forward to your testimony. If you can summarize in 5 minutes, we will then go to questions.

STATEMENT OF STEVEN SOLOMON, DVM, MPH, DIRECTOR, CENTER FOR VETERINARY MEDICINE, U.S. FOOD AND DRUG ADMINISTRATION, ROCKVILLE, MARYLAND

Dr. SOLOMON. Good morning, Chairman Alexander, Ranking Member Murray, and Members of the Committee.

I am Dr. Steven Solomon, Director of the Center for Veterinary Medicine at the Food and Drug Administration.

Thank you for the opportunity to discuss the FDA's proposals for reauthorization of the Animal Drug User Fee Act and the Animal Generic Drug User Fee Act.

As you mentioned, I recently returned to CVM as the Director after working extensively in other roles in the FDA. This is a very good time to be at CVM for a number of reasons, including the fact that we are seeking the development of significant and innovative new animal products. New animal drugs offer the promise of longer and healthier life for our pets and other companion animals.

For example, FDA has approved new oncology treatments for dogs targeting canine-specific tumors. These drugs represent a significant advance for veterinary medicine, which traditionally relies on human oncology treatments.

In recent years, the FDA has improved innovative therapy options that target bone changes in horses to treat a common cause of performance-ending lameness.

New stem cell therapies offer great promise for future veterinary treatments and cures. Meanwhile, approval of the first generic version of a vital heartworm treatment has alleviated a shortage of a critically important treatment for dogs and provided an alternative for pet owners.

The FDA plays a vital role in animal agriculture by reviewing safety and efficiency of new drugs for food-producing animals such as cattle, pigs, and chickens.

For Food-producing animals, we also evaluate whether products derived from treated animals are safe for human consumption.

Awareness of the public health challenge created by antimicrobial resistance has led to important changes in animal agriculture.

For example, as an alternative to antimicrobials, the FDA approved a new treatment to prevent mastitis in dairy cows. At the same time, animal welfare awareness has grown and we have approved the first drug to reduce pain in food producing animals.

The FDA considers timely review of new animal drug safety and effectiveness to be central to the agency's missions to protect and promote human and animal health.

ADUFA and AGDUFA are highly successful programs that enhance the availability of approved drugs for food producing and companion animals. Before their enactment, the FDA CVM had a large backlog of overdue submissions and sponsors had to wait, on average, 500 to 700 days for drug review. However, thanks to ADUFA and AGDUFA user fees, CVM eliminated the backlog in applications and dramatically reduced review times.

Both programs enable the FDA to maintain an outstanding scientific and technical workforce, improve timely communication with drug sponsors, and achieve other efficiencies in the drug approval process while maintaining scientific standards for drug safety and efficiency.

However, without reauthorization, both programs will sunset on October 1, 2018. Timely reauthorization is needed to assure the FDA's ability to deliver continued high levels of performance and ensure there are no disruptions to these important programs.

The ADUFA IV proposal is built on the success of prior ADUFA achievements and proposes changes to current performance goals to further enhance review. In it, the FDA agrees to maintain current performance goals for most applications and submissions, and to add four new performance goals to enhance the exchange of scientific information.

The FDA would slash the timeframe for reviewing categorical exclusion and animal drug availability and combination medicated feed requests by two-thirds. We also established new goals for presubmission conferences and tissue residue method demonstrations.

ADUFA IV also includes an FDA commitment to work on implementing the U.S.-European Union Good Manufacturing Practice Inspection Mutual Recognition Agreement for animal drug facilities.

The AGDUFA III agreement includes a significant additional financial commitment from the animal generic drug industry that reflects its growth. These resources would help significantly decrease review times for multiple generic submissions and provide greater review predictability.

Both the ADUFA and the AGDUFA recommendations require 100 percent electronic submission starting next year to facilitate efficient review. Additionally, both programs include financial recommendations to bolster the program's stability.

The ADUFA IV and AGDUFA III agreements produced with considerable input from the FDA, industry, and other important stakeholders build on the achievements of these highly successful programs. They will ensure the FDA has the resources needed to conduct timely reviews and assist drug sponsors in fostering innovation, enhancing access to safe and effective therapies for food-producing and companion animals.

The FDA looks forward to working with the Committee to achieve a timely reauthorization of these important human and animal health programs.

Thank you for the opportunity to discuss the ADUFA and AGDUFA program.

I would be happy to answer any questions.

[The prepared statement of Dr. Solomon follows:]

PREPARED STATEMENT OF STEVEN SOLOMON

Good afternoon, Chairman Alexander, Ranking Member Murray, and Members of the Committee. I am Dr. Steven Solomon, Director of the Center for Veterinary Medicine (CVM) at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). Thank you for the opportunity to discuss FDA's proposals for the reauthorization of the Animal Drug User Fee Act and the Animal Generic Drug User Fee Act for an additional 5 years (ADUFA IV and AGDUFA III).

I recently returned to CVM as the Director after more than 20 years serving in other roles in FDA. This is a very exciting time for veterinary therapeutics nec-

essary to protect both animal and human health. Advances in biotechnology are leading to the development of innovative, new animal drug products and approaches that offer the promise of a safer and healthier future for the people and animals we serve.

According to the American Veterinary Medical Association, more than half of American households include pets, most of whom are viewed as part of their families. Overall, this includes approximately 70 million dogs, 74 million cats—and a diverse assortment of birds, fish, and other animals. Our companion animals are living longer as promising new products are being developed to treat chronic and insidious diseases. In recent years, FDA has approved innovative treatment options, including two treatments for navicular disease in horses, one of the most common causes of lameness. The drugs, for the first time, target bone changes commonly caused by the disease. FDA has also approved new oncology treatments for dogs targeting canine-specific tumors. The drugs represent a significant advance for veterinary medicine which traditionally relies on oncology treatments approved for humans to treat cancer in animals. These approved animal drugs contain canine-specific dosing instructions and safety information. Stem cell therapies offer great promise for future veterinary treatments and cures. Meanwhile, approval of the first generic version of a vital heartworm treatment has alleviated a shortage of this critically important treatment for dogs—and provided a safe, effective, and more affordable alternative for pet owners.

FDA plays a vital role in animal agriculture by reviewing the safety and efficacy of new drugs for food producing animals, such as cattle, pigs, and chickens. When reviewing new animal drugs indicated for food producing animals, FDA also evaluates whether edible products derived from treated animals (e.g., meat, milk and eggs) are safe for human consumption. Awareness of the public health crisis created by antimicrobial resistance has led to important changes in animal agriculture—and innovative new products. For example, as an alternative to antimicrobials, FDA approved a new treatment to prevent mastitis in dairy cows. Another innovative new approval was the first drug to reduce pain in food producing animals.

FDA considers timely review of the safety and effectiveness of new animal drug applications (NADAs) to be central to the Agency's mission to protect and promote human and animal health. ADUFA and AGDUFA are highly successful programs that facilitate the availability of approved products for food-producing and other animals and foster a flexible, risk-based review framework to accommodate innovative approaches to drug development. Prior to initiating these user fee programs, FDA's CVM had a large backlog of overdue submissions, and sponsors had to wait on average 500 days for pioneer drug review responses and 700 days for generic drug review responses. As a result of ADUFA and AGDUFA user fees, CVM eliminated the backlog in applications and has dramatically reduced the time needed to review animal drug applications and other submissions. Both programs help FDA to maintain a stable scientific and technical workforce, improve timely communications with drug sponsors, and achieve other efficiencies in the drug approval process while maintaining science-based regulatory standards for drug safety and efficacy.

In my testimony today, I will provide the status of FDA's reauthorization activities. I will also provide some information about each program, our achievements to date, and our proposed changes.

Status of FDA's Reauthorization Activities

The ADUFA III and AGDUFA II provisions of the Federal Food, Drug, and Cosmetic (FD&C) Act will sunset on October 1, 2018. Timely reauthorization is needed to ensure FDA's ability to deliver continued high levels of performance and help ensure there are no disruptions to these important programs. FDA began the reauthorization process on May 16, 2016, with public meetings for both programs. These meetings included presentations by FDA and presentations and public comment by representatives of different stakeholder groups, including regulated industry, veterinary professionals, scientific and academic experts, and representatives of consumer advocacy groups. Transcripts and webcast recordings are available on FDA's website at *https://www.fda.gov/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/ucm042891.htm* for ADUFA and *https://www.fda.gov/ForIndustry/UserFees/AnimalGenericDrugUserFeeActAGDUFA/ucm270232.htm* for AGDUFA.

Based on comments to a public docket and the Agency's own analysis of program challenges, FDA developed a set of potential proposed enhancements for ADUFA IV and AGDUFA III and began negotiations with industry. AGDUFA III negotiations took place between August 2016 and January 2017; ADUFA IV negotiations took place between October 2016 and April 2017. Discussions with a broader group of stakeholders also occurred throughout this process.

Negotiated recommendations were published in the *Federal Register* in October for public comment.[1] Final public meetings were held on November 2, 2017, to discuss the ADUFA IV and AGDUFA III recommendations and solicit input from stakeholders. The final recommendations were transmitted to Congress in early January, and include, for each program, the goals letter outlining performance metrics, proposed legislative language, and a summary of public comments.

ADUFA Background

The 5-year reauthorization cycles for ADUFA—and AGDUFA—have supported continuous program innovation, evaluation, and improvement. Through successive reauthorizations, program enhancements have evolved and expanded to include extensive communication and consultation between drug sponsors and FDA throughout drug development. ADUFA I enabled FDA to increase the number of staff dedicated to animal drug review by approximately 30 percent. ADUFA II included important measures to enhance communications with industry, develop and implement electronic submission capability for applications and submissions, and added pre-approval foreign inspection goals. It also supported 10 public workshops on mutually agreed upon topics.

ADUFA III added review flexibility to shorten second-cycle review and included extensive information technology enhancements. The early information process has fostered drug product innovation and increased the availability of safe and effective products. Early information leverages existing data and informs the scope of animal studies required to demonstrate the new animal drug's safety and effectiveness, which helps move the project more quickly into clinical trials.

Under ADUFA III, FDA has made multiple enhancements to the chemistry, manufacturing, and controls (CMC) technical section of the NADA—one of the most complex components of the new animal drug submission—which have reduced overall review time. The Agency now permits the submission and review of early completed CMC information, permits comparability protocols to be submitted as protocols without substantial data in an investigational new animal drug (an INAD) file, and permits certain prior approval manufacturing supplements to be resubmitted as Supplements—Changes Being Effected in 30 Days (CBE–30's).

FDA continues to improve communications, timeliness, and predictability of foreign pre-approval inspections. As a result of ADUFA III, sponsors may voluntarily submit a list of foreign manufacturing facilities they anticipate including in their applications subject to pre-approval inspections for the following fiscal year. Six sponsors voluntarily submitted such lists in FY 2016, allowing better planning for all parties involved and timely execution of good manufacturing practice (GMP) inspections by FDA.

Also as part of ADUFA III, FDA agreed to two long-term goals. First, we agreed to explore the possibility of pursuing statutory changes to expand the use of conditional approval. FDA is continuing work on the goal of exploring the feasibility of statutory revisions to expand the use of conditional approvals to other appropriate categories of new animal drug applications beyond the current FD&C Act authority provided under the Minor Use and Minor Species Animal Health Act of 2004 (MUMS Act). CVM formed a Conditional Approval Working Group that has conducted preliminary activities to evaluate the feasibility, practicality, criteria, and potential requirements for expanding the use of conditional approval to certain major uses in major species. FDA is committed to continuing to explore through a public and transparent process the expanded use of conditional approval consistent with the Agency's mission to protect and promote public health. In our second long-term goal, FDA agreed under ADUFA III to explore the feasibility of statutory revisions that may modify the current requirement that the use of multiple new animal drugs in the same medicated feed each be subject to a separate approved application. The Agency held a public meeting on March 16, 2015, to discuss this issue with stakeholders. In FY 2016, CVM fulfilled its commitment as outlined in the ADUFA III goals letter and provided written recommendations concerning the use of multiple new animal drugs in the same medicated feed for consideration through the *Federal*

[1] FDA, "Animal Drug User Fee Act; Recommendations; Request for Comments; Extension of Comment Period," Docket No. FDA—2011—N—0656, October 25, 2017, 82 FR 49380–82, available at *https://www.gpo.gov/fdsys/pkg/FR-2017-10-25/pdf/2017-23172.pdf*; FDA, "Animal Generic Drug User Fee Act; Recommendations; Request for Comments; Extension of Comment Period," Docket No. FDA–2011-N–0655, October 25, 2017, 82 FR 49377–79, available at *https://www.gpo.gov/fdsys/pkg/FR-2017-10-25/pdf/2017-23173.pdf.*

Register on May 2, 2016.[2] This proposal formed the basis for process changes being recommended in ADUFA IV.

ADUFA Performance

FDA continues to deliver predictable high levels of performance against ADUFA goal commitments for timely review, as shown in Table 1. Final FY 2016 performance data show FDA exceeded the 90 percent review performance level for all seven submission types. In preliminary FY 2017 performance, FDA is currently exceeding the review-time goal for all seven submission types.

Table 1: FDA Review Performance—ADUFA FY 2016: Percent of Submissions Acted on by Goal Date

Application/Submission Type	Filed	Goal: Act on 90 Percent Within	On Time	Overdue	Percent on Time
Original NADAs and Reactivations	15	180 days	14	1	93
Administrative NADAs	18	60 days	18	0	100
Non-manufacturing Supplemental NADAs and Reactivations	0	180 days	0	0	——
Manufacturing Supplemental NADAs and Reactivations	324	120 days	322	2	99
Qualifying Labeling Supplements	6	60 days	6	0	100
INAD Studies	181	180 days	181	0	100
INAD Study Protocols	277	50 days	275	2	99

NADA = New Animal Drug Application; INAD = Investigational New Animal Drug

Proposal for ADUFA IV

ADUFA IV builds on the success of prior ADUFA achievements. The negotiated recommendations propose changes to current performance goals to further enhance review.

FDA agrees to maintain the ADUFA III performance goals regarding review of most original and administrative NADAs, investigational new animal drug studies, non-manufacturing supplemental NADAs, and reactivations. To enhance the exchange of scientific information, the Agency and industry have agreed on four new performance goals in ADUFA IV: reducing the timeframe for reviewing Categorical Exclusion requests from 180 to 60 days for certain qualifying submissions; shortening the review timeframe for combination medicated feed applications requiring no data; scheduling pre-submission conferences within 60 days upon FDA's receiving a complete agenda request; and for a product requiring a tissue residue method trial, scheduling the method demonstration within 120 days of receiving a complete request. The ADUFA IV recommendations also include a provision requiring 100 percent electronic submission starting in FY 2019 and a commitment by FDA to

[2] FDA, "Recommendations on the Regulation of Combination Drug Medicated Feeds; Availability; Reopening of Comment Period; Request for Comments," Docket No. FDA–2014-N–1050, April 29, 2016, 81 FR 25677–78, available at *https://www.regulations.gov/document'D=FDA–2014-N-1050-0002;* and FDA, "Recommendations on the Regulation of Combination Drug Medicated Feeds," May 2, 2016, available at *https://www.regulations.gov/docket?D=FDA-2014-N-1050.*

work on implementing the U.S.-European Union GMP Inspection Mutual Recognition Agreement for animal drug facilities.

Additionally, ADUFA IV offers the following recommendations:

- Eliminating the Offset Provision, which will allow any excess collections to be more readily available for use by FDA for the process for the review of animal drug applications.
- In conjunction with eliminating the Offset Provision, for any fiscal year the Workload Adjuster is invoked in which FDA had excess collections in the second preceding fiscal year, provide for FDA to reduce the workload-based fee increase by the amount of excess collections. If FDA did not have excess collections in the second preceding fiscal year, FDA will collect the full amount of the workload-adjusted fee revenue.
- Continuing to authorize recovery of collection shortfalls; however, provide for any fee increase to recover shortfalls to be reduced by the amount of remaining prior year excess collections not already applied for purposes of reducing workload-based fee increases.
- Modifying the Workload Adjuster base years from ADUFA II (FY 2009 through FY 2013) to ADUFA III (FY 2014 through FY 2018) to ensure the adjuster adequately captures changes in FDA's workload during ADUFA IV.

The ADUFA IV recommendations submitted to Congress include total fee revenue estimates for FY 2019 of $30,300,000, which includes one-time information technology funding in the amount of $400,000. The proposed statutory language specifies base annual fee revenue of $29,900,000 for each of FY 2020 through FY 2023; however, this amount is subject to possible adjustments, including for inflation, workload, and collections shortfall.

AGDUFA Background

AGDUFA I authorized FDA's first-ever generic animal drug user fee program, launched in FY 2009, to provide livestock and poultry producers and pet owners with greater access to safe, effective, and more affordable generic animal drugs. Under AGDUFA I, FDA increased the number of staff dedicated to generic new animal drug application review by approximately 45 percent enabling the Agency to accelerate review, eliminate a backlog of 680 applications, and create a more predictable, streamlined process, including electronic submission capability. Electronic submissions have grown from approximately 3 percent of submissions in FY 2011 to 58 percent in FY 2017.

AGDUFA II included further enhancements. FDA added flexibility with a second-cycle shortened review process for key submission types, such as protocols, data submissions, and applications that significantly impact the generic new animal drug approval timeline.

Qualifying submissions receive a significantly reduced second-cycle review to shorten approval timelines. FDA also made multiple enhancements to the CMC technical section, similar to the ADUFA changes noted above.

AGDUFA II added a pre-approval foreign inspection goal to improve communications, timeliness, and predictability of these inspections. FDA also developed question-based review (QbR) for bioequivalence submissions, and deployed a QbR for blood-level bioequivalence protocol submissions. Additional templates to further enhance the review of bioequivalence submissions are currently under development.

AGDUFA Performance

FDA continues to review sponsor submissions and deliver predictably high levels of performance against AGDUFA goal commitments for timely review, as shown in Table 2. Final FY 2016 performance data show FDA exceeded the 90 percent on-time goal for all five submission types. Based on preliminary analysis of FY 2017 performance, FDA is again on track to exceed the review-time goals for all five submission types.

Table 2: FDA Review Performance—FY 2016: Percent of Submissions Acted on by Goal Date

Submission Type	Filed	Performance Goal: Act on 90 Percent within	On Time	Overdue	Percent on Time
Original ANADAs and Reactivations	16	270 days	16	0	100
Administrative ANADAs	1	100 days	1	0	100
Manufacturing Supplemental ANADAs and Re-activations	156	270 days	153	3	98
JINAD Studies	63	270 days	61	2	97
JINAD Protocols	22	100 days	22	0	100

ANADA = Abbreviated New Animal Drug Application; JINAD = Generic Investigational New Animal Drug

Proposal for AGDUFA III

The AGDUFA III negotiated agreement includes a significant, additional financial commitment from the animal generic drug industry that reflects the program's growth. The agreement is designed to slash review times for generic submissions and increase the predictability of FDA's review process by providing CVM resources sufficient to keep pace with actual costs. Review times for the following submission types will be cut as indicated in Table 3 below: ANADAs (originals, reactivations, and administrative); prior approval supplements; and JINAD data submissions and protocols. Like the ADUFA IV recommendation, AGDUFA III also would require 100 percent electronic submission starting in FY 2019.

Table 3: AGDUFA III Performance Goal Review Times (Complete 90 percent within the following number of days)

Application Type	Current Goal	AGDUFA III Proposal
Administrative Abbreviated New Animal Drug Application (ANADA)	100	60
ANADA originals/reactivations	270	240 (180 day review + 60 day admin)
ANADA reactivations (shortened review)	190	120 (60 day review + 60 day admin)
Prior Approval supplements (Chemistry, Manufacturing, and Controls)	270	180
Generic Investigational New Animal Drug (JINAD) data submissions	270	180
JINAD data submissions (shortened review)	90	60
JINAD protocols	100	75

Additionally, AGDUFA III offers the following recommendations:

- Eliminating the Offset Provision, which will allow any excess collections to be more readily available for use by FDA for the process for the review of generic new animal drug applications.
- In conjunction with eliminating the offset provision, for any fiscal year the Workload Adjuster is invoked in which FDA had excess collections in the second preceding fiscal year, provide for FDA to reduce the workload-based fee increase by the amount of excess collections. If FDA did not

have excess collections in the second preceding fiscal year, FDA will collect the full amount of the workload-adjusted fee revenue.

- Modifying the Inflation Adjuster from a fixed 4 percent in AGDUFA II to a variable inflation adjuster in AGDUFA III, matching the inflation adjuster used for the ADUFA program.
- Modifying the Workload Adjuster base years from AGDUFA I (FY 2009 through FY 2013) to AGDUFA II (FY 2014 through FY 2018) to ensure the adjuster adequately captures changes in FDA's workload during AGDUFA III.

The AGDUFA III recommendations submitted to Congress include total fee revenue estimates for FY 2019 of $18,300,000; in FY 2020 through FY 2023, this amount is subject to possible adjustments, including for inflation and workload.

Conclusion

The ADUFA IV and AGDUFA III agreements, produced with considerable input from FDA, industry, and other important stakeholders, build on the achievements of these highly successful programs. They will help ensure FDA has the resources needed to conduct timely reviews and assist drug sponsors in bringing more animal drugs to the market. They also will foster innovation and provide enhanced access to safe and effective animal therapies. FDA looks forward to working with the Committee to achieve a timely reauthorization of these important human and animal health programs.

Thank you for the opportunity to discuss the ADUFA and AGDUFA programs. I would be happy to answer any questions.

The CHAIRMAN. Thank you, Dr. Solomon, and thank you for being here.

We will now go a 5 minute round of questions and we will start with Senator Isakson.

Senator ISAKSON. Thank you, Mr. Chairman.

Thank you for being here today. I have a couple of questions, one on the Center for Veterinary Medicine's Draft Guidance for Industry on No. 187.

It is my understanding that you have issued a policy that will consider gene-edited animals as animal drugs regardless of how minor or complex the edit is.

Is that correct?

Dr. SOLOMON. The regulatory framework under 187 is that they are new animal drugs. However, many of these products, we would be able to use enforcement discretion to and therefore, not have to go through a review process.

For example, things like genetically altered fish that are these little glow fish that you see, we did an evaluation of those and found that they pose no human safety, no target animal safety problems, and no environmental concerns. Therefore, we used enforcement discretion and did not apply those standards.

Similar, we apply other standards for animal models of disease and other laboratory animals under that framework.

Senator ISAKSON. Again, I am not a scientific or a medical person, so I want to make sure I understand.

If you approve a gene edit treatment for one type of animal, it is approved for all animals.

Is that what you are saying?

Dr. SOLOMON. We base on the risk associated with the type of animal and the gene editing it is. If it is associated with a food-producing animal, then there is more review and we use the regulatory framework of getting the data for a new animal drug.

If we find no concerns on safety, then we are able to use enforcement discretion and allow those to go to market without a review process.

Senator ISAKSON. Has it ever come up as a trade issue with the Europeans, or the Koreans, or others because it is like a GMO, like a genetic modification?

Dr. SOLOMON. There are very few of these animals on the market, so it has not been a trade issue, although, we certainly understand there is great sensitivity on these issues.

Senator ISAKSON. Are you issuing any conditional modifications or conditional approvals at the Center?

Dr. SOLOMON. Conditional approvals were authorized by Congress under the Minor Use and Minor Species Act of 2004 and therefore, other than the species that Senator Alexander mentioned before as the major species.

We have had four products get conditional approval. One has gone through full approval process. It is on the market. It is a product for fish. There is another one that is still under review and two of the products could not make it through the conditional approval process, which requires full efficacy review at the end of 5 years.

Senator ISAKSON. I know rabies is controlled, to a certain extent, by the disbursement of rabies medicine in the wild, hoping it will be consumed by raccoons and other types of animals that could carry rabies.

Do you have the same approval authority on those types of drugs as you would any that is given to an animal?

Dr. SOLOMON. For veterinary biologics, like a rabies vaccine, they are actually approved by Center for Veterinary Biologics. That is part of the USDA, not the FDA for biologics.

That differs from where we are on human biologics, which are approved by our Center for Biologics within the FDA.

Senator ISAKSON. Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Senator Isakson.

Senator Murray.

Senator MURRAY. Thank you.

Dr. Solomon, animal drugs face additional development challenges compared to human drugs. They can only be used for their approved indications. They have to be assessed for their impact on the environment, and they may need to be evaluated for how they impact meat or other food products.

In addition, since animal drugs are approved for a given species, there are often fewer subjects available for clinical trials.

During the recent reauthorization of the human Drug User Fees, Congress, FDA, and the industry worked to ensure the agency is considering all scientific tools to demonstrate a drug meets the gold standard of safety and efficacy like using real world evidence and embracing alternative clinical trial designs to overcome challenges in the human drug development.

I wanted to ask you, what has the agency learned from previous animal and human drug user fee cycles that can help address innovation and development challenges for animal drugs under the FDA's current legal authorities?

Dr. SOLOMON. Thank you for that question.

We do work closely with our human counterparts on different models of disease, and we have used many of those processes to develop innovative drugs.

For example, the drug that we first produced for pain relief in animals, you cannot ask an animal, "What is your pain score?" as we typically do in humans.

We actually worked with the sponsors that the pain was associated with a disease called infectious pododermatitis, it is a disease called foot rot, where animals do not want to put weight on it.

We developed weight mats to evaluate how much weight the animal puts on this mat because if they are more pain free, they are going to be able to be less lame and put weight on it.

Similarly, for diseases like Addison's disease, which is a decreased level of cortisol, rather than trying to do measurements of cortisol, which are very challenging, we use surrogate points to look at the ratios of sodium and potassium.

We have many examples of how we use alternatives, including using a lot of information from other countries. We recently approved a drug for noise aversion in dogs. Once again, dogs that go through thunderstorms, they can get high anxiety. They can get very concerned. There are field trials in Europe of animals getting the drug where there are fireworks, and we used that data so we did not have to do those studies in the United States.

Senator MURRAY. Very good.

The CDC estimates that over 400,000 people are sickened each year by food that is contaminated with antibiotic resistant bacteria. Bacteria exposed to suboptimal doses or long durations of antibiotics are prone to develop resistance, whether they are in a person or an animal. Everyone wants to keep our animals healthy. But inappropriate, overuse of antibiotics in food-producing animals can fuel resistance, which can then hurt our families.

Now, the FDA has begun to bring down the inappropriate use of antibiotics in food animals by eliminating nonmedical uses on drug labels and bringing the use of antibiotics and feed under veterinary supervision.

In November, the FDA reported that animal antibiotic sales from 2015 to 2016 went down 14 percent. That is good progress, but the threat of antibiotic resistance demands ongoing vigilance.

I wanted to ask you, how is the FDA using its current authorities to continue to reduce non-judicious use?

Dr. SOLOMON. It is a major public health challenge on antibiotic, antimicrobial resistance. It needs judicious use both on the veterinary side and on the human side.

As you mentioned, we did reduce all the products that had growth promotion claims. They now have therapeutic claims. They are also under use by veterinary oversight, which was critical.

The American Veterinary Medical Association just recently issued some new definitions of antibiotic, antimicrobial stewardship and good principles. We were very pleased to see that come out there.

The American Association of Veterinary Medical Colleges has created a curriculum that veterinary students can better understand judicious use principles. We continue to look at engaging the data that we need to better measure how we slow the resistance

of antimicrobial resistance by working with the USDA and CDC. It is a very challenging issue to try and measure. We need to look at trends over time; a critical public health issue.

Senator MURRAY. Thank you very much. Appreciate it.

The CHAIRMAN. Before we go to Senator Paul, I wonder if Senator Isakson wants to reclaim his remaining time to ask about his dog Gracie's separation anxiety.

[Laughter.]

Senator ISAKSON. I wondered if he had any free samples of that medicine, because I have a dog that needs it bad.

[Laughter.]

Dr. SOLOMON. I understand completely.

Senator ISAKSON. It would help my marriage a lot.

[Laughter.]

The CHAIRMAN. Senator Paul.

Senator PAUL. We have become more interested in some of the food additives, and how they become approved, and how long it takes, because we have some companies that are interested in it in Kentucky that sell algae that is high in omega–3 to feed to cows to try to have more omega–3 in the milk, and the same with chickens, and things like that.

This process and this algae are for sale in Canada and Europe. They tell this company here, "You need to do some preapproval study that will cost half a million before you can even get started." It is like, I do not know, it just seems to take a long time.

I think some are estimating three to 5 years, but two and 3 years in the European Union. It is like, if it has already been approved in the European Union, we are talking about feeding salad to a cow. I mean, we are talking about feeding algae to a cow, something that is naturally occurring.

Should it really take 5 years to figure this out and a couple of extra years to have pre-study done? Is there something we can do better? Can we look at foreign data more? Are we looking at foreign data?

Dr. SOLOMON. Thank you for the question.

The approval process has several mechanisms for food additives. Once again, it is important to recognize that for our animals, that often the food that we give them is the sole food that they consume, versus the varied diet that we humans eat. And therefore, it is important to assure the safety for the animals and also the human food safety associated with it.

We do have processes for food additive petitions, generally recognized as safe notifications for food ingredients.

We do use foreign data when it is appropriate to the type of growing conditions and for the type of feed stuffs we use in the United States.

Senator PAUL. Yes, but it seems to me if it is approved in Canada and Europe, you could just look at their studies. A committee could meet and over half the time, you could just approve it. I mean, that is never happening. It still takes you years and years and years.

They are being asked for even a protocol study before they even do their study, and they are not even assured of even getting to the

study, because you are requiring that, and it is already approved and being used all over the world.

I do not really think you are using the foreign studies the way they ought to be used. I think you really ought to review them and there is a good chance, I would say, a very good chance you ought to be able to just look at them and approve them.

Are you ever looking at foreign studies of things we are doing in Europe or Canada, and just approving them without making them do all the studies again?

Dr. SOLOMON. We do use data from other countries, as I mentioned before, on the drug side of the house.

Senator PAUL. Have you ever approved any food additive without making them repeat all of the studies that are repeat studies in our country?

Dr. SOLOMON. We need to assess the validity of the data collected in another country and see how applicable it is to the United States.

Senator PAUL. We do not ever approve them just from the foreign studies. We make them repeat the studies again. So, I mean, that is a question.

For example, we are growing hemp now and hemp is, I think, naturally high in omega–3.

If I want to feed the roots of a hemp plant to a cow, do I have to go to the FDA to ask for permission to do that?

Dr. SOLOMON. Once again, if it is a new feed ingredient that has not been evaluated for safety.

Senator PAUL. It seems kind of crazy if it is not drug, if it is just something that grows in the ground and we are going to feed it to our cows, and somehow, I have to go through a 5-year process to ask your permission to do it. I do not know.

I would think we ought to be able to do this better, Mr. Chairman. We talk about ways to fix this. There has to be a way to get them to look at foreign studies. They say they are going to do it, but then they do not. Or they do it, and they still make our companies repeat all of these studies.

There has to be a way we can speed this up. It puts us at a competitive disadvantage. Really, we are talking about feeding algae. We are talking about feeding something naturally growing to animals as a supplement. And I think we have to figure out a way to make the process better.

Do you have any suggestions or do you think we are doing a good job doing this? I mean, three to 5 years seems like a long time. It is longer than the rest of the world and you are making a company, that has already gone through this process in another part of the world, go through it again.

Really, if they have done 2 years in Canada or 3 years in Europe, now we are doing three to 5 years on top of what they have already done in other countries, and they are having to repeat all of the same studies again.

I just think for something that is being ingested by animals, it might be excessive.

Dr. SOLOMON. We continue to look at efficiencies in the program. There has been a 150 percent increase in food added petitions over

the past several years. There has been a threefold increase in generally recognized as safe petitions.

We want to use the foreign animal data, data used in other countries when it is applicable to conditions in the United States.

Senator PAUL. Is the current process too long or is the current process just fine?

Dr. SOLOMON. I think there are always opportunities for improvement and we will continue to look at those.

Senator PAUL. Thanks.

The CHAIRMAN. Thank you, Senator Paul.

Dr. Solomon, Senator Paul has raised this issue before, and I have talked to him about working with our staff and with you to see if we can appropriately address it in this legislation.

Would you be willing to work with Senator Paul and our staff to see if there are improvements that we can make in the area?

Dr. SOLOMON. We would be delighted to work with them.

The CHAIRMAN. Thank you very much.

Senator Paul, we will look forward to continuing the discussion.

Senator Hassan.

Senator HASSAN. Well, thank you, Mr. Chairman, and Ranking Member Murray, for this hearing.

Dr. Solomon, good morning, and thank you for being here.

Dr. SOLOMON. Good morning.

Senator HASSAN. Thank you for your work.

We often hear that the animal drug market and the human drug market have many differences. For example, the animal drug market is much smaller than the human drug market. And unlike the human drug market, there are not really third party payers in the animal drug market with probably a couple of small exceptions here and there.

But as we consider reauthorizing the user fees, I think we should also remain mindful of the unique considerations related to animal drugs.

It would be helpful to me for context if you could walk us through the main differences between these two markets, the animal drug market and the human drug market, and explain why it is important to understand these differences.

Dr. SOLOMON. Thank you.

As you put out, there is a significant difference in both the payers for the market and the economics of the veterinary pharmaceutical industry in developing these products.

We are very conscious of that need, so we work closely with the sponsors very early in the developmental process to try and get drugs that have unmet needs, and can help the food animal populations and companion animals get to the market.

You also gave us incentives under the Minor Use and Minor Species Act to try and bring many of those drugs where the economics are even more challenging and bring you those.

We actually do work in the minor species area with the USDA and other ones to actually have the studies done by academics or other research centers, so that the sponsor does not bear all the cost of trying to bring those products to market. So, that helps a little bit in the minor use and minor species.

We also give a number of incentives such as the conditional approval that we talked about, that allows up to 5 years to demonstrate the efficacy of the product.

Senator HASSAN. Right.

Dr. SOLOMON. We have a process to work closely with the sponsors early in the process, make sure that they have a clear understanding of the types of studies, trying and use different approaches recognizing the difference in species and the difference in production conditions, to try and develop the work and get these products to market, which we share with the industry.

Senator HASSAN. Well, thank you very much. That is very helpful.

I also wanted to touch on something you raised in your testimony. You point out how electronic animal drug review submissions have grown in recent years. I know that both the Animal Drug User Fee Agreement and the Animal Generic Drug User Fee Agreement that have been agreed on by the FDA and industry require now 100 percent electronic submissions starting in Fiscal Year 2019.

Can you walk us through why electronic submissions are important and how the FDA will facilitate this requirement?

Dr. SOLOMON. I step back to, as I said, I have recently returned to CVM. When I was originally there, there used to be large trucks backing up with volumes and stacks of paper to try and deliver the new animal drug applications.

We would have to take those applications apart, give them to the target animal safety, the people looking at efficiency, looking at the human food safety.

By getting the electronic submissions, the data is all available to all the technical submission sections. It becomes a far more efficient process for reviewing the data.

Senator HASSAN. That is really helpful to know. Thank you and congratulations to you and everybody at CVM for making that process move forward.

I want to finally just to touch on and follow-up on Senator Murray's question about the interplay of antibiotic use with animals and the impact on humans as well.

I am pleased with the work CVM has done to help policymakers and other stakeholders better understand the sale and use of antibiotics in animal agriculture, and particularly CVM's collection and reporting of antibiotic sales and distribution data for food producing animals by species.

A provision in the second reauthorization of ADUFA has been instrumental in helping us better understand the role of antibiotics in production agriculture. And your continuing efforts to inform policymakers by ensuring that drug sponsors also report estimates according to food producing species is a natural and appropriate extension of the charge Congress gave you when it enacted this provision.

Can you tell us more about what role this data, this specific to food-producing species plays in helping the FDA assess progress in instituting judicious antibiotic use practices in veterinary settings?

Dr. SOLOMON. Trying to determine the progression and trying to decrease the development of resistance is a challenging scientific

area. This is one data point is the sales data. That does not equate to the actual usage data. We are working with the USDA and others to try and get the actual data for what people are actually using.

It also combines with information from our national antibiotic resistance monitoring system where we measure resistance that is happening both in people, through the CDC, through the USDA with retail meat samples, and through animals. We try and look at resistance patterns and changes.

These data points all need to come together to sort of measure continued progress doing it. I think we are looking at not single data points. We are looking at trends over time to measure the impact of the actions we are taking.

Senator HASSAN. Well, thank you very much.

Thank you, Mr. Chair.

The CHAIRMAN. Thank you, Senator Hassan.

Senator Smith.

Senator SMITH. Thank you very much, Chairman Alexander and Ranking Member Murray.

Thank you, Dr. Solomon, for being here today.

I wanted to talk with you a little bit about the One Health approach, which I understand is something that your daughter in veterinary school is interested in, which is very, very cool.

Dr. SOLOMON. Very much.

Senator SMITH. In 2015, when I was Lieutenant Governor, Minnesota poultry growers were hit really hard by the avian flu epidemic, and 9 million birds were affected, around 100 farms across the State. It was really devastating.

Now thankfully, this particular disease did not move from animals to humans, but it did really raise the specter of that and the concern for that.

I have, as I mentioned before we started, I have had an opportunity to work with Senator Young on legislation that would promote this One Health approach.

Could you talk a little bit about how you see that strategy and how you are working on that as you think about this reauthorization?

Dr. SOLOMON. I cannot speak to specific legislation, but the concepts of One Health are really being ingrained.

If you just look at how we review animal drugs, we are looking at target animal safety. We are looking at animal health. We are looking at human food safety or human user safety, so we are looking at the human aspects. And we have to do environmental impacts; so all three of them are sort of incorporated in One Health.

We have also designated a person within CVM to be the monitor working on One Health because there are lots of initiatives going throughout the country that are better integrating human health, animal health, and environmental impacts.

Senator SMITH. I think sometimes it is difficult for us to figure out how to do this kind of holistic approach.

What are some of the barriers you have to overcome to make that happen?

Dr. SOLOMON. I think there has been a real change in people's thinking about how they approach and tackle problems like you described.

There is not simply an answer of, "I am just going to give a vaccine." Or, "I am going to try and give an antimicrobial to deal with it." There is recognition that there are a lot of conditions that need to really tackle these complex issues.

By bringing the different scientific disciplines together, bringing people together, I think it really creates an integration and a holistic approach to better tackle these problems.

Senator SMITH. Thank you.

I would like to ask you a little bit about generic animal drugs. You mentioned this briefly in your testimony.

As you noted in your testimony, more than half of American households include pets, including both of my children's. And spending on pets has doubled over the last 12 years, I understand, with Americans paying nearly $10 billion for pet medications and health-related pet products.

However, compared to the human drug arena, there have been relatively few animal drugs that have generic substitutes. And so, that means that American families and Minnesota families are paying so much more for care for their pets.

Could you tell us a little bit about how you see this, and what the FDA could do to help incentivize more generics?

Dr. SOLOMON. The generic animal drug industry is a relatively new industry. It is really growing.

Over the past authorization, there was an increase in work that was really positive. So, one of our measures is a workload adjustment and it was tremendous. It was the highest of any of the user fee agreements. We had over 50 percent increase in workload, very positive signs that more generics are coming to the market.

The current reauthorization significantly reduces timeframes for getting these products to the market. So that was something the generic drug industry and the FDA sat down, negotiated, reduces timeframes so we can get more generic animal drugs to the market.

Senator SMITH. Great. Thank you.

Thank you very much, Mr. Chair.

The CHAIRMAN. Thank you, Senator Smith.

Senator Murkowski.

Senator MURKOWSKI. Thank you, Mr. Chairman.

Mr. Chairman, I feel a little bit like a fish out of water here in the HELP Committee talking about animal health and the Center for Veterinary Medicine. We do not have a vet school in Alaska. We wish we had one.

But I do have an issue that I would like to raise. I think many on this Committee have actually heard me raise the issue of genetically engineered salmon, whether in the HELP Committee or certainly on the Appropriations Committee.

But as I look to what the CVM does—protect human and animal health by ensuring the safety and effectiveness of animal drugs, and then review new animal drugs—it really does cause me to, once again, raise an issue that I feel very, very strongly about, and I think it is fair to say most Alaskans share the concern that we have.

Our FDA, that has approved, what I have called "frankenfish," this genetically engineered salmon, but they have approved it through the new animal drug pathway. Now, there were millions—millions—of Americans who wrote-in to oppose this approval, wrote into the FDA.

But effectively what we are talking about is the first ever—the first ever—genetically engineered species of animal that is approved for human consumption, and it was approved through the animal drug route, which just does not make sense to me.

I actually left my office, and I had to move my way through about a dozen Alaskans who were back to visit me. They are the Alaska longliners. They fish for a living. They are part of a very important industry.

The seafood industry, in Alaska creates about $14.6 billion in economic output and nearly 112,000 jobs nationally. In Alaska, more than 63,000 direct jobs, over $4.6 billion comes from the seafood industry. The Ranking Member here knows full well the value of strong fisheries.

But when I came to say that I was going to be speaking on the fact that you have the first-ever genetically engineered species of animal approved for human consumption, approved through an animal drug route, the fishermen said to me, "Do they not understand that you have animals, and you have humans?"

I said, "Well, apparently there is a distinction within the FDA that somehow or other thinks that you can use the animal drug pathway to signoff on, again, a genetically engineered species that is designed for human consumption." You can tell I have a real issue, a real problem with this.

I have insisted—and I have spoken recently with the head of the FDA, that if, in fact, the FDA is going to continue down, what I believe is, a wrong-headed approach—at a bare, bare minimum these species should be labeled as genetically engineered salmon. And they should further require a third party scientific review for the approval process for this fish, and for any other future fish that might go through this type of an approval process.

I think most are saying that, at a bare minimum, that is what they would understand to be appropriate.

I have had conversations with colleagues who say, "Well, wait a minute. How is this issue of a G.E. salmon any different than a genetically engineered crop?" bringing in the broader GMO debate.

What I would remind people is that genetically engineered animals are not crops. A fish is not a piece of corn. And recognizing that what we are doing here, or proposing to do, is to introduce a new species into our markets, into our homes, and quite possibly, contrary to what any environmental assessment claims, into our ecosystems.

This is a significant issue. I believe a significant problem and it is one, Mr. Chairman, that I will continue to raise. I appreciate the opportunity to raise it in the context with Mr. Solomon here today, as we are talking about reauthorization of the FDA Animal Drug User Fees.

Thank you very much.

The CHAIRMAN. Thank you, Senator Murkowski.

Senator Jones.

Senator JONES. Thank you, Mr. Chairman, Ranking Member Murray.

Dr. Solomon, thank you for being here.

Let me just kind of piggyback on what Senator Isakson said. As somebody here who is new, I have two British Labs who are having serious problems about daddy not being home for the last 6 weeks. But my wife will tell you I am having more problems than they are, probably, with that.

I also want to thank you for your work on behalf, on a personal note, for a son whose life's work has been working with zoo animals. He is about to get a degree in zoo and aquarium management, and he has done it ever since he was 5 years old. So, thank you for your work on that.

Most of my questions about user fees have all have been answered. What I would like to just get from you a little bit is as regard the budget and the funding for your department.

We just went through a budget process here in which we finally came together in a bipartisan way to come up with a budget, and hopefully may end the kind of high stakes budgeting process that we have seen.

Could you just kind of give me a rundown on the priorities for your department for the Center for Veterinary Medicine in the coming year through the FDA funding?

Dr. SOLOMON. In the recently released President's budget is some additional funding, $9.7 million proposed, to be able to support the process of the ADUFA and AGDUFA. Part of that comes from user fees. Some of it comes from budget authority.

It is critical, with the increased workload, that we keep up with it. So, we were delighted to see that in there. That is a critical component of it.

Senator JONES. Right.

Dr. SOLOMON. We also recognized that the evaluation of drugs goes through the whole lifecycle.

We do a certain amount of studies that are based on limited clinical data and the number of animals. We do a fairly thorough review, but we also find—and it is not unusual in human medicine—when you put the products on the market, there may be increased opportunities to evaluate the safety of it.

We are continuing to look for opportunities to look at the whole lifecycle, post marketing area in addition to the preapproval area. We are also looking for opportunities in the areas previously mentioned to improve our review of animal feed ingredients because of the same concerns about the safety of those products and getting them on the market.

Senator JONES. All right. Well, that is great.

That is really all I have, Mr. Chairman. Thank you.

Thank you, Dr. Solomon.

Dr. SOLOMON. Thank you.

The CHAIRMAN. Thank you, Senator Jones.

Senator Murray, do you have any other questions or comments?

Senator MURRAY. I do not have any additional comments, except that I would say that I am really pleased with this hearing and our work on moving this forward.

I also want to thank you on the progress we are making on the cosmetics reform proposal too as well, which is critical to moving forward.

The CHAIRMAN. Yes, Senator Feinstein, Senator Collins, and you have all been working on that. Thank you for saying that.

Dr. Solomon, Senator Murray and I are operating under the assumption that we need to get our work down and to the President by August 1.

What happens if we do not?

Dr. SOLOMON. Failure to reauthorize would be very disruptive. The industry is counting on this. There are constant reviews. We get over 6,000 submissions a year to review it.

Failure to reauthorize would have an impact on the 115 people that you talked about previously. We would have to give notices 60 days prior to those folks if they were no longer going to be able to have the funds to be able to support their activities.

Failure to reauthorize has a tremendous effect on folks, both the industry and how disruptive it would be. But trying to recruit talented staff that we have there, they want to know that there is a process and a stable work environment within the Center for Veterinary Medicine.

The CHAIRMAN. Thank you.

You mentioned there are seven major species. Just out of curiosity, how many domesticated species are there?

Dr. SOLOMON. I will have to get back to you on that one.

The CHAIRMAN. There are not many, right?

Dr. SOLOMON. There are a few. I have the same book you do. I will have to go back and review it.

The CHAIRMAN. I would be interested.

Senator Warren, we are about to wrap up. Let me say the closing words and then, if it is all right with you, I am going to leave the final question and 5 minutes to you. Would you be good enough to close the hearing?

Senator WARREN. I plan to, thank you, if the witness feels safe under those circumstances.

The CHAIRMAN. The hearing record—subject to Senator Warren's 5 minutes of questions, and I appreciate her willingness to do that—the hearing record will remain open for 10 days. Members may submit additional information for the record within the time, if they would like.

Thank you for being here today.

The Committee will stand adjourned following Senator Warren's questions. Thank you for doing that, Senator Warren.

Senator WARREN. Thank you.

The CHAIRMAN. Senator Murray, thank you.

Dr. Solomon, thank you for coming today.

Dr. SOLOMON. Thank you.

Senator WARREN. Thank you, Mr. Chairman, I appreciate it, and I appreciate this opportunity to ask a question.

I wanted to go back to the question about antibiotic drugs.

The FDA's job is to protect public health, and a big part of that is making sure that drugs are safe, that they work. We have been talking today about how the FDA does this work for drugs that are

used in animals. I want to focus on how the drugs used in animals can also affect human health, and this is about antibiotics.

Antibiotics are obviously extremely important for treating bacterial infections, but as we know, they are becoming less and less effective. Today, resistance has been seen in almost antibiotics that have been developed.

The CDC estimates that 2 million people in the U.S. develop antibiotic resistant infections every year that results in about 23,000 deaths and adds about $20 billion in healthcare costs to our already overburdened system.

Antibiotic resistance, we know, comes from the overuse of antibiotics, and not just overuse in humans, but overuse in animals.

Dr. Solomon, can you just get me started here by saying a word about how the use of antibiotics in food animals can lead to antibiotic resistance in humans?

Dr. SOLOMON. Thank you for the question.

The process is giving antibiotics to animals may cause certain resistance in those animals in the gut of those animals.

If, on the process of those animals being slaughtered, that resistant bacteria gets on the meat, and then people consume that, and it is undercooked, they may be able to get that resistant microbe. Or, simply people that are handling the animals——

Senator WARREN. Wait, on someone's hands?

Dr. SOLOMON. Hands.

Senator WARREN. Yes.

Dr. SOLOMON. I mean, we see problems. We have a current problem with people feeding raw pet food to their animals, and unfortunately, two children got very sick because that raw pet food, as many raw products, had salmonella in it, and they got very ill. So, handling raw products like that can get them exposed.

Senator WARREN. Okay. So, it matters if animals become antibiotic resistant or have antibiotic resistant bacteria, and that that then moves over into humans and threatens humans.

Now, I know that the FDA has taken a lot of steps to address this issue, including requiring veterinarians to supervise all antibiotic use in animals. This was meant to make sure that food animal producers use antibiotics only when it is medically necessary, like when the animal is sick or there is a risk of disease, and not use antibiotics just to grow the animals faster.

The 2008 ADUFA reauthorization also required the FDA to collect data from drug manufacturers on the amount of antibiotics they sold for use in animals.

Dr. Solomon, these data tell us how many antibiotics go out the door from the drug company to the farm. But do these data tell us how and when those drugs are actually used on animals?

Dr. SOLOMON. They do not. Right now, this is sales data and how that equates to actual usage data, is data that we are still trying to collect.

We are working with the USDA and doing some of our own contract work to try and better understand the actual usage data, and making sure that everyone is following judicious use principles.

Senator WARREN. Good. So, I am glad to hear that you are trying to get better data.

In March 2017, the Governmental Accountability Office made several specific recommendations for ways to improve this kind of data collection by the FDA.

The GAO also recommended that the FDA work on establishing duration limits on drug labels for certain antibiotics used in animals. In other words, limits on how much of an antibiotic can be used in an animal and for what specified time.

Along with Senator Feinstein and Gillibrand, and colleagues in the House, I followed up with a letter to then Secretary Price about the department's work to implement those recommendations. I never received a response to that.

Dr. Solomon, I would like to follow-up directly with you and submit some written questions for the record after this hearing about your progress on the GAO's recommendations.

Will you commit to answering those questions?

Dr. SOLOMON. Yes, we would be delighted to work with you and get answers to those questions.

Senator WARREN. Good. I do appreciate it.

I look forward to hearing more from you about how you are responding to the GAO's recommendations and in trying to track your progress on this issue.

With 2 million people in the United States developing antibiotic resistant infections every year, it is clear that more work needs to be done and I look forward to continuing to work with the FDA to build on its earlier policies to collect better data and to make sure that we have more careful use of antibiotics.

Thank you.

Dr. SOLOMON. Thank you.

Senator WARREN. Thank you, Madam Chair.

Senator MURRAY. [presiding]. Thank you.

I believe Senator Roberts is on his way. Is that correct or not? How far out is he? A couple of minutes.

What I will do on behalf of the Chairman is to recess for 2 minutes until Senator Roberts comes. If you would not mind waiting, Dr. Solomon, we will let him reconvene and ask his questions and close out the Committee hearing.

I apologize. Thank you.

[Hearing recessed at 11:01 a.m.]

[Hearing resumed at 11:04 a.m.]

Senator ROBERTS. [presiding]. The HELP Committee now resumes its session.

Dr. Solomon, thank you for coming. I appreciate it very much. It is not often that we have a coup like this, but every once in a while, something like this takes place.

In the last user fee agreement, sir, the FDA agreed to explore the expansion of conditional approvals and develop some recommendations by September 2015.

The FDA missed that deadline and in the new user fee agreement, there is no commitment or extension of this timeline to continue working on this issue.

However, it is my understanding there was supposed to be a meeting last week to lay out a process to move forward on this issue.

Can you share some insight on what happened at this meeting? Was there a new timeline agreed to? And if not, what would be a reasonable timeline for the agency to publish recommendations and issue guidance?

Dr. SOLOMON. Thank you for the question.

Senator ROBERTS. I am suggesting 1 year or 2 years at least.

Dr. SOLOMON. Just to step back. The conditional approval was authorized under the Minor Use and Minor Species Act, which allows products to demonstrate efficacy, not at the time that the original safety evaluation takes place, but up to 5 years later, and then the product has to come in.

There was a proposal from industry to expand that from conditional approval for minor species to conditional approval for major species.

We worked with industry on that proposal. We had a series of meetings associated with it. We reached a lot of common understanding, but there were still some areas of disagreement.

Unfortunately, we got caught up in the new authorization process. When I came in, which was January of last year, and found out that we had not finalized that work, I met with the animal health industry, gave my commitment to work on that issue because I think it had some opportunity for us to be able to treat some significant health conditions and some areas of drugs that had difficult efficaciousness.

We held a meeting last week to outline proposals. I reconfirmed my commitment with them. They asked for us to work on this expeditiously. We agreed to work on it, so we are appointing a committee, both within CVM and the animal health industry to work on it.

We need to revisit where we were before and make sure we still have a common understanding of that process, and then we need to work on areas that we still have some challenges, which include the issues of can a product, an animal drug product have both an approved indication and a conditional indication on the same label.

We are committed to expeditiously work with this issue and bring back recommendations to the Committee, and work with the Committee on that area.

Senator ROBERTS. Dr. Solomon, every once in a while, I am asked, "When are we going to get a farm bill?" since I have the privilege of being the Chairman of the Senate Agriculture Committee.

My answer, rather than a specific date, I do not go beyond that in terms of years, but I say, "Sooner than later."

Can I at least elicit that kind of a response from you?

Dr. SOLOMON. We are committed to work on it and it will be sooner rather than later.

Senator ROBERTS. All right. Thank you, sir.

Recently, Commissioner Gottlieb told this Committee, we should consider how to create incentives for the development of animal drugs including a breakthrough therapy designation. This is something that has been successful on the human side and was recently expanded to devices under the 21st Century Cures Act.

Given the numerous expedited pathways for human drugs, do you agree with Commissioner Gottlieb that this is something we should explore also on the animal side?

Dr. SOLOMON. There are a large number of unmet animal health needs that need to be worked at. There are significant conditions on there, and I think it is important that we explore any opportunities to try and address the significant animal and public health issues, and drugs that can help fill those needs appropriately.

Senator ROBERTS. Let me just say that I can speak for virtually every member of the Senate Agriculture Committee in our eagerness to working with you and my colleagues on this Committee, of course, to see if this is something we could move forward with these agreements.

The growing use of guidance documents for government wide has been a concern to me for quite a while. Now, I recognize that the FDA has long used guidance documents and that they are integral to providing, certainly, to the industries that the FDA regulates, especially when good guidance practices are followed.

Currently, CVM has a couple of very old draft guidances on adverse event reporting from 2001 and 2006. The regulations referenced in these documents were written prior to the electronic reporting of adverse events. And as a result, the companies are being told to continue managing disharmonized systems for adverse event collection and reporting. The technology and systems have evolved over the past decades. The regulations and guidance need to follow.

Will you work to withdraw or update and reissue these items?

Dr. SOLOMON. There are a number of outdated items. Under the regulatory reform, we collected a number of ideas from industry and also going internally to look at older guidances and regulations that may no longer be needed. So, we hope to be able to update those.

Senator ROBERTS. I want to talk for just a moment about applicant burden reduction. The FDA's drug center on the human side, CDER, does not routinely require the submission of all raw data of new drug applications.

However, the Center for Veterinary Medicine has expanded their data collection requirements over the years to include nearly all raw data associated with the study.

This requirement seems overly burdensome, not only for innovators, but also for the agency to review. It also appears contrary to the agency's effort to expand electronic submission.

What, if any, efforts have you considered to streamline and standardize the process of submitting study reports as a risk-based approach to audit specific studies been considered?

Dr. SOLOMON. Thank you.

We did understand that under our regulatory reform, we got some input from the industry about the use of raw data. We have a workgroup that is evaluating this and try and make the appropriate decisions on what data is valuable and critical to determine the safety, human food safety and the environmental impact of products, and where we do not need all the data.

Senator ROBERTS. I want to talk just a moment about electronic submissions.

The new agreement requires 100 percent of applications to be submitted electronically by October. You mentioned in your testimony that last year, the electronic submissions for generic applications were at 58 percent.

My question is: is this a realistic goal? How is the agency going to assist applications with this process?

Dr. SOLOMON. We negotiated this agreement with the generic animal drug industry recognizing that they had a far longer way to go than the pioneer industry.

We have committed to also assist them with this process to help facilitate and give them any assistance. We also got some funding to help facilitate the electronic entry of these.

We will continue to work with the industry on this area, but it makes a far more efficient review process.

Senator ROBERTS. Dr. Solomon, I want to thank you for the work that you do. As I look over the rest of these questions, I do not see any reason why we cannot submit then for the record and simply adjourn the Committee, and let you go about your business.

Dr. SOLOMON. Thank you.

Senator ROBERTS. Thank you, sir.

The hearing record will remain open for 10 days. Members may submit additional information for the record within the time, if they would like.

Senator ROBERTS. The Committee stands adjourned.

[Whereupon, at 11:13 a.m., the hearing was adjourned.]

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