

REAUTHORIZATION OF ANIMAL DRUG USER FEES:
ADUFA AND AGDUFA

HEARING
BEFORE THE
SUBCOMMITTEE ON HEALTH
OF THE
COMMITTEE ON ENERGY AND
COMMERCE
HOUSE OF REPRESENTATIVES
ONE HUNDRED FIFTEENTH CONGRESS
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REAUTHORIZATION OF ANIMAL DRUG USER FEES: ADUFA AND AGDUFA

WEDNESDAY, MARCH 14, 2018

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON HEALTH,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 10:18 a.m., in room 2322, Rayburn House Office Building, Hon. Michael C. Burgess (chairman of the subcommittee) presiding.

Members present: Representatives Burgess, Guthrie, Upton, Shimkus, Blackburn, Latta, Lance, Griffith, Bilirakis, Bucshon, Brooks, Mullin, Hudson, Collins, Carter, Walden (ex officio), Green, Schakowsky, Butterfield, Schrader, Eshoo, DeGette, and Pallone (ex officio).

Staff present: Zack Dareshori, Legislative Clerk, Health; Margaret Tucker Fogarty, Staff Assistant; Ed Kim, Policy Coordinator, Health; Milly Lothian, Press Assistant and Digital Coordinator; Jennifer Sherman, Press Secretary; Danielle Steele, Counsel, Health; Austin Stonebraker, Press Assistant; Hamlin Wade, Special Advisor for External Affairs; Jacquelyn Bolen, Minority Professional Staff Member; Jeff Carroll, Minority Staff Director; Samantha Satchell, Minority Policy Analyst; Andrew Souvall, Minority Director of Communications; Kimberlee Trzeciak, Minority Senior Health Policy Advisor; and C.J. Young, Minority Press Secretary.

OPENING STATEMENT OF HON. MICHAEL C. BURGESS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS

Mr. BURGESS. I now call the subcommittee to order and recognize myself 5 minutes for the purpose of an opening statement.

And the Chair would note that today's hearing marks the Health Subcommittee's fourth hearing to consider reauthorization of vital user fee programs at the United States Food and Drug Administration.

While the bulk of these programs were reauthorized last year through the FDA Reauthorization Act, our focus today on reauthorizing the Animal Drug User Fee Act and the Animal Generic Drug User Fee Act is equally important for the millions of American families and businesses that rely on the critical function of the Food and Drug Administration's Center for Veterinary Medicine.

With this in mind, I expect us to reach a shared commitment to complete our work while reauthorizing these last set of user fees

and get them to the House floor well in advance of the expiration date of September 30 of this year.

We did so last year with the FDA user fee reauthorization, and there is no reason we cannot do so again here.

This morning, we will have two panels of witnesses before the subcommittee. First, I do want to welcome Dr. Steven Solomon, the Director for the Center of Veterinary Medicine at the Food and Drug Administration.

Next, representatives from the Animal Health Institute, the Generic Animal Drug Alliance, and American Veterinary Medical Association will share their insights on the current state of the United States animal drug market and the significance of reauthorizing the Animal Drug User Fee Agreement and the Animal Generic Drug User Fee Agreement.

Last month, the Committee on Energy and Commerce and the Senate Health, Education, Labor, and Pensions Committee released the Animal Drug User Fee Reauthorization Act of 2018, a bipartisan discussion draft to renew the FDA's authority to collect user fees from the manufacturers of brand-name and generic animal drugs for another 5 years.

Among other things, these user fees help the Food and Drug Administration's Center for Veterinary Medicine in their timely review of animal drug applications, market surveillance of animal drug safety and efficacy, and the quality assurance measures for animal food as well as food products derived from animals.

From pet owners and veterinarians to farmers and animal food producers, updating these user fee agreements is essential in ensuring that animal drugs are safe and effective for farm animals and our pets, while keeping our food supply safe.

Reauthorizing these agreements also includes the new commitment between the FDA and industry on performance goals and procedures.

This will be the fourth authorization for the Animal Drug User Fee Agreement since its launch in 2004, and we have seen it reviewed several times.

Under the proposed agreement, funding for the program will increase by approximately \$6 million annually. All submissions must be electronic. The Center for Veterinary Medicine is required to begin implementation of the U.S.-E.U. Good Manufacturing Practice Mutual Recognition Agreement for inspections of pharmaceutical manufacturing facilities, and review time for drug combinations for use in feed is shortened to 60 days if no additional data is required.

The Animal Generic Drug User Fee Agreement is going through its third authorization since 2008. The Center for Veterinary Medicine has met or exceeded nearly all of the performance goals in each 5-year authorization.

In addition to increasing funding by approximately \$10 million annually, the proposed agreement would shorten the review time for abbreviated new animal drug applications to 60 days and require all approved drugs to include these applications on the labeling.

Finally, I would like to commend our fellow Health Subcommittee member, Representative Mark Mullin from Oklahoma,

for championing the House Animal Drug User Fee Agreement and Animal Generic Drug User Fee Agreement reauthorizations. Thank you for your hard work on this important measure.

[The prepared statement of Mr. Burgess follows:]

PREPARED STATEMENT OF HON. MICHAEL C. BURGESS

Today's hearing marks the Health Subcommittee's fourth hearing to consider the reauthorization of vital user fee programs at the U.S. Food and Drug Administration (FDA). While the bulk of these programs were reauthorized last year through the FDA Reauthorization Act of 2017, our focus today on reauthorizing the Animal Drug User Fee Act (ADUFA) and the Animal Generic Drug User Fee Act (AGDUFA) is equally important for the millions of American families and businesses that rely on the critical functions of FDA's Center for Veterinary Medicine. With this in mind, I expect us to reach a shared commitment to complete our work reauthorizing these last set of user fees and get them to the House floor well in advance of their expiration on September 30, 2018. We did it last year, so there is no reason we cannot do it again here.

This morning, we have two panels of witnesses before our subcommittee. First, I would like to welcome Dr. Steven Solomon, Director of the Center for Veterinary Medicine at FDA. Next, representatives from the Animal Health Institute, Generic Animal Drug Alliance, and American Veterinary Medical Association will share their insights on the current state of U.S. animal drug market and the significance of reauthorizing ADUFA and AGDUFA.

Last month, the Committee on Energy and Commerce and the Senate Health, Education, Labor, and Pensions Committee released the Animal Drug User Fee Reauthorization Act of 2018, a bipartisan discussion draft to renew FDA's authority to collect user fees from the manufacturers of brand-name and generic animal drugs for another 5 years. Among other things, these user fees help fund FDA's Center for Veterinary Medicine's timely review of animal drug applications, market surveillance of animal drugs' safety and efficacy, and quality assurance measures for animal food as well as food products derived from animals. From pet owners and veterinarians to farmers and animal food producers, updating these user fee agreements are essential in ensuring animal drugs are safe and effective for farm animals and our pets, while keeping our food supply safe. Reauthorizing these agreements also includes the new commitments between FDA and industry on performance goals and procedures.

This will be ADUFA's fourth authorization, and since its launch in 2004, we have seen review times reduced significantly. Under the proposed agreement, funding for the program would increase by approximately \$6 million annually, all submissions must be electronic, the Center for Veterinary Medicine is required to begin implementation of the U.S.-E.U. good manufacturing practice Mutual Recognition Agreement for inspections of pharmaceutical manufacturing facilities, and review time for drug combinations for use in feed is shortened to 60 days when no additional data is required.

AGDUFA is going through its third authorization since 2008. The Center for Veterinary Medicine has met or exceeded nearly all performance goals in each 5-year authorization period. In addition to increasing funding by approximately \$10 million annually, the proposed agreement would shorten the review time for abbreviated new animal drug applications to 60 days and require all approved drugs to include these applications on the labeling.

Finally, I would like to commend our fellow Health Subcommittee member, Representative Mullin, for championing the House ADUFA/AGDUFA Reauthorization bill. Thank you for all your hard work on this important measure.

I again want to welcome all of our witnesses and thank you for being here. I look forward to your testimony.

I yield the balance of my time to Ms. Blackburn of Tennessee, for a statement.

Mr. BURGESS. I again want to welcome all of our witnesses for being here and look forward to your testimony, and I'll yield to Mrs. Blackburn of Tennessee.

Mrs. BLACKBURN. Thank you, Mr. Chairman, and to our witnesses on each panel, thank you so much for being here. And I am so grateful for the chairman's leadership and the fact that we are approaching this in a bipartisan, bicameral manner.

We know that what you do is important. We are pleased to see the amount of progress that is made in animal drugs, whether they are for our pets or for livestock that are in the food supply chain.

We are wanting to focus and get some attention on the innovation side and how we speed the approval process. So we will look forward to addressing those issues with you today.

I yield back.

Mr. BURGESS. Gentelady yields back. Chair thanks the gentelady.

The Chair recognizes the gentleman from North Carolina as the substitute ranking member of the subcommittee, and you're recognized for 5 minutes for the purpose of an opening statement.

OPENING STATEMENT OF HON. G.K. BUTTERFIELD, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NORTH CAROLINA

Mr. BUTTERFIELD. Thank you, Mr. Chairman. I'll take it any way I can get it this morning.

[Laughter.]

Thank you, Mr. Chairman. To the vice chair, Mrs. Blackburn, thank you so very much for your opening comments.

You're right, I am standing in for the ranking member this morning, Gene Green, who will be here momentarily, I am told.

Thank you to the Director for your willingness to come forward and to share your testimony with us today. This hearing, Mr. Chairman, is so very important and so I associate my comments with the gentelady from Tennessee that this is bipartisan, bicameral, and these are two pieces of legislation that we must move and do it very quickly.

The Animal Drug User Fee Act is very important. The Animal Generic Drug User Fee Act is very important to all of us on this committee.

These user fee agreements are important to millions of Americans, including those in my home State of North Carolina who live with companion animals every day.

They are also important to the agriculture community. We have many stakeholders in this legislation. Some of you may not be aware that North Carolina, my State, is the second largest pork producer, the second largest turkey producer, and the third largest poultry producer in the entire country.

Our agriculture community and family farms are essential to feeding our Nation, and they depend on medicines to keep their animals very healthy.

Mr. Chairman, I support reauthorization of these programs. I look forward to hearing about the innovation that's taking place in the animal drugs and how we can support the health of animals and human beings, as well.

Thank you for the time. I yield back.

Mr. BURGESS. Gentleman yields back. The Chair thanks the gentleman.

Chair would now like to recognize the gentleman from Oregon, chairman of the full committee, Mr. Walden, 5 minutes.

OPENING STATEMENT OF HON. GREG WALDEN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF OREGON

Mr. WALDEN. Thank you very much, Mr. Chairman. Thanks for holding this hearing and good morning to everyone. We look forward to yet another “UFA” hearing.

We have a history of producing bipartisan user fee reauthorizations, most recently as last year, and so I look forward to continuing in those efforts with this one.

Whether it be livestock or house pets, the owners of these animals rely on the Food and Drug Administration to ensure the availability of safe and effective medical products to keep their animals healthy.

Through the Center for Veterinary Medicine, FDA evaluates new drugs to determine if the safety and efficacy of those treatments work for their stated use.

In the case of livestock, CVM must also ensure the drug will not impact the food supply and not harm the environment or the health of the livestock producer who administers it.

But the hard work of developing and manufacturing these drugs is done by the animal drug industry, and these companies face unique challenges that need to be considered, including R&D processes that involve developing and manufacturing drugs for different species of animals with different physiologies.

So, given the success of the human drug user fee programs in expediting approval of treatments by bolstering resources for the agency, the FDA and the animal drug industry came together to propose the animal drug user fee programs.

These programs have succeeded in dramatically reducing review times by providing the FDA with much-needed additional resources. So it is a win-win scenario where everyone benefits, including farmers, pet owners, and veterinarians.

Today, we are considering the reauthorization of those programs—the Animal Drug User Fee Act and the Animal Generic Drug User Fee Act—both of which will expire at the end of the fiscal year.

So it is critical that these programs are passed and signed into law well before the end of September. Before each reauthorization, as set forward in statute, FDA meets with the animal drug industry to reevaluate specific goals for review time lines, solicits comments from stakeholders and members of the public to consider additional enhancements, then the final agreement is delivered to Congress for the program to be reauthorized.

So for this cycle, that process began in May of 2016, and after numerous public meetings, the final negotiated recommendations were sent to Congress in January of this year. This year’s agreements include increased collections from industry as well as more aggressive performance goals for the FDA. They also include several process improvements and other enhancements. We look forward to hearing more about these agreements from our witnesses today.

Encouraging innovation is a top priority of this committee, and we want to take this opportunity to examine the animal drug approval process to ensure the incentives are in place to encourage

innovative treatments to be developed and for generic animal drugs to be made available.

And we don't often think of the FDA when it comes to animal drugs, sadly, but these programs are critical and are important to pet owners of America and our farmers and ranchers that we rely on to produce food.

And so we appreciate the witness today. We are actually going to get the wisdom of Solomon today, apparently. So we do appreciate that.

[The prepared statement of Mr. Walden follows:]

PREPARED STATEMENT OF HON. GREG WALDEN

Good morning, everyone, and thank you for joining us for yet another "UFA" hearing! We have a history of producing bipartisan user fee reauthorizations, most recently as last year, and I look forward to continuing those efforts today.

Whether it be livestock or house pets, the owners of these animals rely on the Food and Drug Administration (FDA) to ensure the availability of safe and effective medical products to keep their animals healthy. Through the Center for Veterinary Medicine, FDA evaluates new drugs to determine the safety and efficacy of those treatments for their stated use. In the case of livestock, CVM must also ensure that the drug will not impact the food supply and not harm the environment or the health of the livestock producer who administers it.

But the hard work of developing and manufacturing these drugs is done by the animal drug industry. And these companies face unique challenges that need to be considered-including an R&D process that involves developing and manufacturing drugs for different species of animals with different physiologies.

Given the success of the human drug user fee programs in expediting approval of treatments by bolstering resources for the agency, the FDA and the animal drug industry came together to propose the animal drug user fee programs. These programs have succeeded in dramatically reducing review times by providing FDA with much needed additional resources. It's a win-win scenario where everyone benefits-including farmers, pet owners, and veterinarians.

Today we are considering the reauthorization of those programs-the Animal Drug User Fee Act and the Animal Generic Drug User Fee Act-both of which expire at the end of this fiscal year. It is critically important that these programs are passed and signed into law well before the end of September.

Before each reauthorization, as set forward in statute, FDA meets with the animal drug industry to reevaluate specific goals for review timelines and solicits comments from stakeholders and members of the public to consider additional enhancements. Then the final agreement is delivered to Congress for the program to be re-authorized.

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Encouraging innovation is a top priority of this committee, and we want to take this opportunity to examine the animal drug approval process to ensure the incentives are in place to encourage innovative treatments to be developed and for generic animal drugs to be made available.

We don't often think of the FDA when it comes to animal drugs, but these programs are critically important to the pet owners of America and our farmers that we rely on to produce the food that feeds our country.

This is important must-pass legislation and we are committed to getting it done on time before these user fee programs expire in September. I'd like to thank our witnesses for being here with us today, and Mr. Mullin for leading this legislative effort for our committee.

Mr. WALDEN. And with that, I would yield the remainder of my time to Mr. Mullin, I believe, who is seeking time and has been a real leader on this effort.

So Mark, I'll turn it over to you.

Mr. MULLIN. Thank you, Mr. Chairman.

I want to thank you and Chairman Burgess for holding this hearing. I am proud to be the sponsor of the legislation to reauthorize the Animal Drug User Fee Act and its generic version.

ADUFA and AGDUFA will reauthorize user fee agreements between the FDA and the animal drug industry to help speed the approval of new and generic drugs for farmers, ranchers, families, and veterinarians so they can keep their animals and pets safe and healthy.

In the last reauthorization, the FDA committed to working with industry to complete recommendations for expanding conditional approval. I want to reaffirm my commitment to working with the FDA and to industry to come to a consensus as early as possible so we can continue to drive innovation.

Thank you to our witnesses for being here today. I look forward to hearing your testimony regarding the importance of a clean reauthorization for our farming and ranching communities, and I yield back.

Thank you.

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

The Chair recognizes the gentleman from New Jersey, the ranking member of the full committee, Mr. Pallone, 5 minutes for an opening statement, please.

OPENING STATEMENT OF HON. FRANK PALLONE, JR., A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Mr. PALLONE. Thank you, Mr. Chairman. Today we will be examining the FDA's animal drug user fee program and the animal generic drug user fee program, and these critical user fee agreements have helped to accelerate the development of animal drugs, reduce application review times at FDA, and create a more predictable and streamlined process for getting animal drugs to market to help improve the health of our pets and food-producing animals.

Last month, this committee, along with the HELP Committee in the Senate, released a bipartisan discussion draft that reauthorizes FDA's authority to collect user fees from the animal drug and generic animal drug industries for an additional 5 years, as the current authorization for these programs will expire on September 30th.

The discussion draft reflects bipartisan agreement and the recommendations negotiated between FDA and the animal drug industry with input from farmers and ranchers, veterinarians, food and feed producers, and other public health stakeholders.

And these agreements are critically important to pet owners, veterinarians, and farmers so they have access to safe, effective, and affordable medications for their animals. And we want our pets to have the best as possible, and we must ensure that we keep our food supply safe. The animal drug user fee program furthers both of these goals.

I expect we will hear also testimony today on FDA's work to address antimicrobial resistance from the use of antimicrobials in food-producing animals.

I am very interested in what the Center for Veterinary Medicine is doing to ensure the continued effectiveness of antibiotics and how we can protect both animals and humans from the growing threat of antimicrobial resistance.

And I look forward to helping to move these agreements through Congress in a timely fashion so the Center for Veterinary Medicine at FDA can continue its important work.

I don't think anyone else wants my time, and if they don't, I will yield back.

Thank you, Mr. Chairman.

[The prepared statement of Mr. Pallone follows:]

PREPARED STATEMENT OF HON. FRANK PALLONE, JR.

Today we will be examining the FDA's Animal Drug User Fee program and the Animal Generic Drug User Fee program. These critical user fee agreements have helped to accelerate the development of animal drugs, reduce application review times at FDA, and create a more predictable and streamlined process for getting animal drugs to market to help improve the health of our pets and food-producing animals.

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The discussion draft reflects bipartisan agreement and recommendations negotiated between FDA and the animal drug industry with input from farmers and ranchers, veterinarians, food and feed producers, and other public health stakeholders.

These agreements are critically important to pet owners, veterinarians, and farmers so they have access to safe, effective, and affordable medications for their animals. We want our pets to have the best care possible, and we must ensure that we keep our food supply safe. The animal drug user fee programs further both of these goals.

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I look forward to helping to move these agreements through Congress in a timely fashion so the Center for Veterinary Medicine at FDA can continue its important work.

I yield back.

Mr. BURGESS. Chair thanks the gentleman. Gentleman yields back.

This concludes the Member opening statements. The Chair would remind Members, pursuant to committee rules, all Members' opening statements will be made part of the record.

Again, we want to thank all of our witnesses for being here today and taking the time to testify before the subcommittee. Each witness will have an opportunity to give an opening statement followed by questions from Members.

Our first panel today is Dr. Steven Solomon, the Director of the Center for Veterinary Medicine, the United States Food and Drug Administration.

We certainly appreciate you being here this morning, Dr. Solomon. You are now recognized for 5 minutes to give a summary of your opening statement, please.

STATEMENT OF STEVEN SOLOMON, D.V.M., DIRECTOR, CENTER FOR VETERINARY MEDICINE, FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. SOLOMON. Good morning, Chairman Burgess, the acting ranking member, Chairman Walden, and Ranking Member Pallone. I am Dr. Steve Solomon, Director for the Center for Veterinary Medicine at the Food and Drug Administration.

I 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.

I recently returned to CVM as the Director after working extensively in other roles in FDA. This is a very good time to be at CVM for a number of reasons, including the fact that we are seeing 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.

The drugs represent a significant advance for veterinary medicine, which traditionally relies on human oncology treatments. In recent years, FDA has approved innovative therapy options that target bone changes to treat a common cause of performance-ending lameness in horses.

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 this critically important treatment for dogs and provides an alternative to pet owners.

FDA plays a vital role in animal agriculture by reviewing the safety and efficacy of new animal 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, 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.

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

ADUFA and AGDUFA are highly successful programs that enhance the availability of food products for food-producing and companion animals.

Before their enactment, FDA CVM had a large backlog of overdue submissions, and sponsors had to wait an average 500 to 700 days for drug review. However, thanks to ADUFA and AGDUFA user fees, CVM eliminated the backlog in applications and has dramatically reduced review times.

Both programs enable FDA to maintain an outstanding scientific and technical workforce, improve timely communication with drug sponsors, and achieve other efficiencies in the drug approval proc-

ess while maintaining scientific standards for drug safety and efficacy.

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

The ADUFA IV proposal built on the success of prior ADUFA achievements and proposes changes to current performance goals to enhance the review. In it, 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.

FDA would slash the timeframe for reviewing categorical exclusion and Animal Drug Availability Act combination medicated feed requests by two-thirds.

We also establish new goals for presubmission conferences and tissue residue method demonstrations. ADUFA IV also includes an FDA commitment to work on the implementation of the U.S.-European Union Good Manufacturing Practice Inspection Mutual Recognition Agreement for animal drug facilities.

The AGDUFA III agreement includes significant additional financial commitments from the animal generic drug industry that reflect its growth. These resources will help significantly decrease review time for multiple generic submissions and provide greater review predictability.

Both the ADUFA and 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 FDA, industry, and other important stakeholders, build on the achievements of these highly successful programs.

They will ensure 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.

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, and I'd be happy to answer any questions.

[The prepared statement of Dr. Solomon follows:]

**STATEMENT
OF
STEVEN SOLOMON, D.V.M., MPH
DIRECTOR, CENTER FOR VETERINARY MEDICINE
FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**BEFORE THE
SUBCOMMITTEE ON HEALTH
COMMITTEE ON ENERGY AND COMMERCE
UNITED STATES HOUSE OF REPRESENTATIVES**

“REAUTHORIZATION OF ANIMAL DRUG USER FEES: ADUFA AND AGDUFA”

MARCH 14, 2018

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Introduction

Good morning, Chairman Burgess, Ranking Member Green, and Members of the Subcommittee. 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 five 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 necessary 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 five-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

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>.

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 Effectuated in 30 Days (CBE-30s).

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 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.

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>.

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 time frame for reviewing Categorical Exclusion requests from 180 to 60 days for certain qualifying submissions; shortening the review time frame 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 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 Reactivations	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% 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.

Mr. BURGESS. Chair thanks the gentleman, and I do want to thank you for taking time to give us testimony this morning.

We will move into the portion of the hearing where Members' questions are heard. I will begin by recognizing myself for 5 minutes.

And Dr. Solomon, you referenced the implementation of the U.S.-European Union Good Manufacturing Process Inspection. What are some of the particular challenges that you face with that?

Has that been more straightforward or more difficult than you would have anticipated?

Dr. SOLOMON. So thank you for that question.

We are still in the early stages of doing that. The E.U. GMP Inspection Mutual Recognition Agreement started on the human side, and it then will move over to the veterinary side later on.

So on the human side, it's been making good progress. Once again, lots of countries in the E.U., they need to be assessed. What we've discovered is that not all the authorities in the E.U. have the same authorities on the human side as they do on the animal drug side.

So, as we progress through it and looking at the animal drug side, we are going to utilize the information that the human side has collected as part of their agreement. But as we move into it we are going to need to look at the countries and conduct assessments of them that has separate authorities in the E.U. countries for the animal side.

Mr. BURGESS. So there is an increase in funding in the proposed legislation that Mr. Mullin has given us. How do you propose that the Food and Drug Administration is going to utilize the additional resources, and perhaps how is that going to help us improve the review process?

Dr. SOLOMON. So we are going to be hiring additional reviewers on both sides to meet the new performance commitments. There will be approximately 20 new reviewers in different disciplines on the animal drug user fee side and around 30 new people hired on the generic drug user fee side, and some of those resources will be able to be used for implementation of the E.U. agreement where we need to go over to the E.U. and get the assessments of the other countries' regulatory authorities and oversight over GMP animal facilities.

Mr. BURGESS. Just for a point of reference, how large is the workforce, currently?

Dr. SOLOMON. So the current user fees represent around 35 percent of the staff on the animal drug review side and around 60 percent on the generic drug user fee side. Those are covered by user fees.

Mr. BURGESS. OK. So there are more aggressive approval goals that are laid out in this—in this reauthorization. You have already alluded to it somewhat, but, again, could you just briefly delineate the steps the FDA will be taking to meet these goals?

Dr. SOLOMON. Certainly. So we've already been doing planning in anticipation of getting this. Part of the process is going to be earlier communication.

We have a phase review process in CVM where we really interact with the industry very early in the process, where they're still in developmental stage process.

We want to enhance that early communication. Before the industry is developing a drug, let's meet with them early and make sure we understand what the data requirements—what type of clinical studies are going to need to be done so that we can very quickly decide what those are.

We are also reducing timeframes for some unique aspects of the categorical exclusion in some of our environment findings.

On the generic drug side, we are dramatically reducing the timeframes to be able to get generic animal drugs to the market sooner.

Mr. BURGESS. So, on the issue of the electronic submissions that I believe are going to be required in this reauthorization, obviously, there are going to be benefits to electronic submission. Would you care to share those with us?

Dr. SOLOMON. Thank you.

So electronic submission is a big step in trying to do it. When I first started at CVM 28 years ago, there used to be trucks backing up with these volumes and volumes of paper that needed to be reviewed.

Trying to then take those and give them to the different disciplines was quite a challenge. The electronic review process makes the review much more efficient.

Everyone and all the different scientists have access to the data in a much more expedient way and makes it a much more efficient process of review.

Mr. BURGESS. Well, again, I thank you for being here this morning. Thank you for your testimony and taking our questions.

I would now like to recognize Mr. Butterfield from North Carolina for your questions, please.

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

Dr. Solomon, thank you for your testimony today. Dr. Solomon, I've heard from some of my colleagues and some of my constituents about expanding the use of what is called conditional approval, and it's my understanding that the FDA believes that it needs legislation to provide authority to allow this conditional approval to be used for major uses in major species.

Am I right or wrong about that?

Dr. SOLOMON. You are correct.

So Congress gave us statutory authority back in 2004 for use of conditional approval in minor species or minor use in major species.

What that does is, the applicants' sponsors still need to prove the safety, the environmental controls, the human food safety, but allows a 5-year timeframe to demonstrate the efficacy of the product while it can be on the market.

We've had discussions with industry that, in order to help spur innovation, trying to get this applied to major species under certain conditions, the conditions being that it's got to be for serious illness or disease in major species that really have unmet veterinary medical needs or public health needs and for studies that have difficulty in demonstrating efficacy.

So things that we would envision would be more chronic disease conditions, things like congestive heart failure or chronic renal disease, osteoarthritis—things that it would be difficult to do the efficacy studies because you need to measure things over time.

We think additional approval would be a welcome addition to try and get additional products on the market.

Mr. BUTTERFIELD. Can you describe the safety requirements that must be met for conditional approval?

Dr. SOLOMON. So the safety requirements have to be met exactly the same as for any other approval. So there is no difference in the safety that needs to be demonstrated before marketing.

The only difference on conditional approval is the timeframe for efficacy requirements, which can be up to 5 years after the product starts marketing.

Mr. BUTTERFIELD. Would any of the drug companies that we deal with have an incentive to provide a drug under conditional approval that it does not believe to be effective?

Dr. SOLOMON. So there's a requirement in the conditional approval that they need to submit status reports on an annual basis, as least as it's currently applied to minor use, minor species, on the progress they're making on the efficacy requirements. And then, if they do not meet it, they need to come in at 5 years for the full standard for efficacy, which means substantial evidence of efficacy at the end of that 5 period.

If not, the way the MUMS Act works and what we would hope in any future one, is that product is no longer allowed to be marketed. So it gives them time to do the efficacy studies—those challenging efficacy studies that are meeting unmet veterinary medical needs.

Mr. BUTTERFIELD. Dr. Solomon, I appreciate the work that the FDA has done to expedite the process of approval for animal drugs, and I really appreciate your testimony earlier about how it was 28 years ago when the trucks would back up to your building. I can just envision that now.

In your testimony, you mentioned that the agreement recommends that 100 percent of the applications be submitted electronically and only 58 percent of applications were submitted in fiscal year 2017 that way.

Will the FDA provide any support to help with that transition to electronic applications, what I call 21st century technology?

Dr. SOLOMON. Yes. So we recognize that, on the pioneer side, most of the submissions are coming in on electronic on the generic side. These are generally smaller companies, newer companies.

We want to provide assistance to try and get there, and it also includes some IT enhancements in the funding to help CVM support making that transition over so we can get everyone to the 100 percent submission goal.

Mr. BUTTERFIELD. And are the sponsors ready to make that transition, or do they have some anxiety about it?

Dr. SOLOMON. I think they're generally anxious to try and do it. I think they see the efficiencies in it. But I think it's a great question for the panel coming up.

Mr. BUTTERFIELD. All right. All right. Thank you.
I yield back, Mr. Chair.

Mr. BURGESS. Gentleman yields back. Chair thanks the gentleman.

Chair recognizes the gentleman from Kentucky, the vice chairman of the committee, Mr. Guthrie.

Mr. GUTHRIE. Thank you very much.

Actually, I can't let the chairman's comment of the wisdom of Solomon this morning go. I know you probably hear that all the time, and I apologize.

But trying to be a little more disciplined myself, as Solomon talked about, and trying to read the proverbs of the day—of the chapter of the month, and so today being the 14th Proverbs—and if you read Proverbs every day, there's always something you're going to face.

So Proverbs 14:4 says, "Where there are no oxen, the manger is empty, but from the strength of an ox come abundant harvests." So what we are doing here goes back to understanding we have to have a good agriculture, even back in the Bible times—

[Laughter.]

Mr. GUTHRIE [continuing]. And proclaimed by Solomon, which is the standard of wisdom.

And some of the questions they've already—I guess some of your testimony piqued all of our interest, because I am going to kind of touch on it again because I was going to ask that.

But first, can you please explain ADUFA IV performance goals, specifically centered around shortening the review timeframe for combination medicated fees?

Dr. SOLOMON. Sure.

So this was an agreement that we worked on during the previous timeframe. So there's a number of medicated fees that combine various different drugs, usually for different type conditions.

So there might be some combination that there might be a need for an antiparasitic drug, for, say, Coxidia. At the same time they may be treating a bacterial-infection-type area.

So, in the medicated feed area, we wanted to not subject each of them to a separate approval requirement when each drug had already gone through an approval combination.

When we put these two combinations together, we need to make sure that they're not interfering with each other—the two drugs together.

Putting drugs in the feed supply is often the most efficient way to get it into food-producing animals.

So we worked with the industry to come up with a shortened timeframe to evaluate these drugs when they combine them together in medicated feeds.

Mr. GUTHRIE. OK. Thanks.

And the second question, I was going to talk about the electronic submission, and it was kind of asked but at the very end you said that would be a good question for the next panel, why we haven't gotten a higher percentage from 58 to 100 percent, and we'll do that—ask them that.

What kind of challenges are you seeing from—for some reason, they're not—obviously, I don't know if it's all their issues for not getting the 100 percent, but what kind of challenges, from your

perspective, do you think the next panel should be looking at to address?

Dr. SOLOMON. So I think my understanding is, this is mainly some of the newer companies. Often, we have companies that are new on the generic side to this and just simply haven't developed the structure for all the electronic pieces.

We give lots of guidance on what we expect in a submission, how to put it together, how to facilitate the electronic entry. We have a pathway for moving it.

We are going to try and provide, you know, help desk assistance for anyone that needs assistance in getting that electronic review.

So we all benefit from getting the electronic review process, and we want to work with the industry to get to that objective.

Mr. GUTHRIE. Do you think 100 percent is attainable by 2019?

Dr. SOLOMON. We will work closely with them to try and meet that goal.

Mr. GUTHRIE. That's a good answer.

So, and Dr. Burgess talked a little bit about the U.S.-European Union good manufacturing practices for animal drug facilities. What is the timeframe for this agreement?

And I know you said they're doing the human and then the animal. But what's the timeframe for the agreement, and when do you expect to see that?

Dr. SOLOMON. So, the way the agreement is drafted, the agreement got signed on the human side in March of 2017, and they're still going through the assessment. A number of the E.U. countries have already been reviewed and are now part of the agreement.

In December, we met with the European Union to lay out our goals and objectives for trying to move it on the animal side, and we have an objective by making a determination by July of 2019 whether we are going to be successful in moving that agreement forward in the timeframe for meeting that assessment so we can evaluate the GMP conditions on the animal side of the house.

Mr. GUTHRIE. OK. Well, thank you very much, and that concludes my questions. I appreciate your testimony.

I yield back.

Mr. BURGESS. Chair thanks the gentleman. Gentleman yields back.

Chair recognizes the gentleman from Oregon, Dr. Schrader, 5 minutes for questions, please.

Mr. SCHRADER. Thank you very much, Mr. Chairman. I appreciate it.

Welcome, Dr. Solomon.

Dr. SOLOMON. Thank you.

Mr. SCHRADER. Very impressive, the results you guys have gotten as a result of the previous ADUFA agreements. The performance measures speak for themselves—95 to 100 percent success in all the different areas.

Most agencies would die to have that sort of track record at the end of the day, and you're stepping up and willing to reduce time lines and do some more with a little assistance from industry.

I guess the comment I would make is that it's just great to see these public-private partnerships. I mean, that's ideally the way things are supposed to work. We are in this together. It's not one

versus the other, but helping one another get the job done for humans and, in this case, for our animal friends.

As a veterinarian, I am very interested in the conditional use approval process. Frankly, in the animal field, we are a smaller population, usually not quite as remunerative as it is with our human medical colleagues, and as a result the conditional use process is critical for us to be able to access some of these medications in a more timely manner and make them available to our patients, and, frankly, some of the work that's done on our patients benefits our human colleagues at the end of the day.

So I am very interested in the potential expansion of the conditional use process, you know, when you were before the HELP Committee, you indicated that you felt that at least for the minor species, minor use, it was working pretty well. But we are getting a little behind the time line. It was 2015, I think, at one point, and looking at the expansion of the scope, you alluded to it, I think, in your comments both to the Chair and to Mr. Butterfield.

But when do you think we are going to be finishing this expansion and hopefully getting to full conditional use for the major species as well as the minor?

Mr. SOLOMON. So thank you for your interest in our issues. So, once again, it needs statutory language to expand it for the additional approval in major species.

Once again, this is not for all uses. This is for significant, serious disease conditions, unmet veterinary or medical needs.

We certainly could see this for certain zoonotic diseases that may arise where you need to get a drug out. You want to show that the product is safe, which needs to be shown beforehand. Some of the efficacy requirements may come later, but in critical public health issues, which I am sure you recognize, it might be out there.

So we met earlier this year with the drug industry. We shared the interest in moving this forward. Our staffs have been working really closely on this issue over the past month and a half.

And, if Congress is interested in the conditional approval, we would love the opportunity to provide some technical assistance on that issue.

Mr. SCHRADER. Great. I would like to see that move forward, because there are unmet needs and there are some difficult processes. Neither one of those, I think, would be a good justification for some of the changes in the conditional approval process to be very helpful.

Getting back to the minor-uses-major-species and minor species piece, my understanding from the testimony, there's only been four, really, applications and only one been approved.

Is there a problem in the process here, or do you need some more help from us?

Dr. SOLOMON. So it is a little disappointing. We'd hoped that we'd have—that incentive would be more products out there. Of the four products, one was an aquaculture product that got approved—clearly, a needed area of resources.

Two of them demonstrate some of the challenges. So two were drugs to fight cancer. One drug, simply the firm withdrew it because it was not demonstrating efficacy. They didn't have the right

doses, so they determined, "Let me take this off the market, go do some more work and come back."

One just couldn't get the efficacy standard and therefore had to be withdrawn, and we have another one that's currently in the pipeline that looks promising.

Mr. SCHRADER. You're seeing the incentives seem to be OK? It's just maybe a company is getting used to the process or getting familiar with the opportunity?

Dr. SOLOMON. Once again, firms that are looking for the—usually in the minor species—are generally small firms, and while the economic incentives for major species are often a challenge compared to the human side, it's even more challenging on the minor species side.

Mr. SCHRADER. OK.

And then ADUFA III accelerated the process quite a little bit, replaced the end review amendment process and shorter second-round reviews.

Any problems with safety as a result of doing those things? Any problems crop up as a result of making the process more efficient?

Dr. SOLOMON. No. I think safety is always a paramount concern and, once again, our process doesn't just stop with the approval process.

We have postmarketing activities that monitor the safety of drugs. We have the largest adverse event database in the world.

We work with other countries on harmonizing that data, and we use that data if we ever have to make adjustments to a product and work with industry to continue to ensure the safe use of animal drugs.

Mr. SCHRADER. Very good. Thank you, and I yield back.

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

The Chair recognizes the gentleman from Indiana, Dr. Bucshon, 5 minutes for questions, please.

Mr. BUCSHON. Thank you, Mr. Chairman.

This year's ADUFA includes a new goal for tissue residue method validation.

First, can you explain what this is, in layman's terms, and then describe how this validation of tissue residue methods may have led to delays in the approval of new drugs in the past?

And then could you walk us through how you plan to meet the new review goal of 120 days for this measure?

Dr. SOLOMON. So thank you.

So a tissue residue method is for an animal drug that's going to be used in food-producing animals. We need to develop a method—industry needs to develop a method and then we need to do validation of the method to make sure that the levels and the determination of the safety in meat, milk, or eggs has been determined and this is the method that would be used to evaluate that in the food supply once the product's on the market.

We have an office of research as part of CVM that does this work. This is the first time we actually put a goal time period to be able to meet the objective of developing the tissue residue method and validating that method, and because of the agreement we are now able to hire additional resources and research scientists

that can work out in our office of research to be able to support the tissue residue method.

Mr. BUCSHON. So protecting the public health and providing the best animal health and welfare can only be achieved through continued advancements in innovation.

I hear of a need for more innovation in animal health due to the unmet medical needs. What are some of the ways the agency can spur innovation to meet some of these needs?

Dr. SOLOMON. So we are doing a lot of different work to communicate with firms early and be able to get new products on the market.

One of the ways is we do different surrogate end points. One example is, there's a disease called Addison's disease, which is a low level of cortisol. Cortisol levels are hard to measure because they're a natural hormone in the body, so we've used surrogate end points to measure sodium and potassium ratios rather than looking at the end point. We use different clinical designs.

So I talked earlier about the use of drugs in food-producing animals. So, if you're trying to reduce pain you can't ask the cow, you know, "On a score of zero to 10, how painful are you?"

So we actually worked on it in designing a method with the firm that the animals have a foot lameness problem and we actually figured out how to use pressure mats to determine how much weight they're putting on it.

If they're less painful, these pressure mats will be able to weigh the difference about how much weight they're putting on those mats. So we use those methods.

We use data from foreign countries so we approved a drug for noise aversion. Dogs—some animals get very scared when there's thunder or fireworks, and so we use data actually gathered in European studies, transferred that data because we work closely with our international colleagues to try and get that data to be able to suffice and reduce the number of animals that are used in studies.

We use other methods such as—we approved a drug for a follicle-stimulating hormone, which is a drug for super ovulation. We did that review using literature review and meta-analysis without having to use clinical studies.

We used every technique that we can to try and get innovative products to market by early communication with the firm in designing how these studies should look.

Mr. BUCSHON. Great. Thank you.

I yield back, Mr. Chairman.

Mr. BURGESS. Chair thanks the gentleman. Gentleman yields back.

Chair recognizes the gentlelady from Indiana, Mrs. Brooks, 5 minutes for questions, please.

Mrs. BROOKS. Thank you, Mr. Chairman, and thank you for being here.

Can you talk a little bit about the improved wait times and what the average wait times are for pioneer drug review responses and generic drug review responses, respectively?

Dr. SOLOMON. So there's two ways that a firm can put drugs onto the market. One way is to wait and put all their submissions of all their technical sections—their target animal safety, their efficacy

studies, their environmental review, their human food safety if it's for food-producing animals—and submit that.

We determined a long time, working with industry, a much better way is to do a phase review process where the firms come in much earlier in the developmental process, meet with us early, talk about those kinds of design of the studies there, and therefore work on each section as they have the appropriate resources and they're gathering the data, submit that data to us, and then that technical section gets a review.

So the wait times are a little—it's not the same way as it is on the human side, because most of these are phased review processes.

We are working with the firm as they're doing the studies, submitting those pieces, and we are continuing to meet our—that's the way that the performance goals are written to have the timeframes.

As mentioned now several times, we've been very successful in achieving our timeframe for each of those actual submission timeframes.

Mrs. BROOKS. I understand, though, that prior to the ADUFA fee process and user fee programs that there used to be, like, 500 days average wait time, 700 for generic. What have you gotten those down to, on average, now? And I appreciate it's an average but—

Dr. SOLOMON. Right.

Mrs. BROOKS [continuing]. What kind of timeframe are we looking at now?

Dr. SOLOMON. So we are getting closer towards these 180-day timeframes. You know, it depends how many times—what the work looked like, the quality of the submissions.

But we've dramatically reduced the timeframes from where we used to be prior to the use fees.

Mrs. BROOKS. And congratulations. Anything else you need with respect to either the process or resources to increase that wait time—or, to decrease that wait time, rather?

Dr. SOLOMON. The user fee agreements and our work with industry are important to get reauthorized. So we are anxious to get that done.

Mrs. BROOKS. Can you talk to us a little bit about what are some of the unmet needs in animal medicines? And I am sure there are many.

Dr. SOLOMON. Right.

Mrs. BROOKS. Some of the most concerning ones to you.

Dr. SOLOMON. So continued oncology treatment for cancer treatments. As our pets are living longer, we are getting more cancers in our companion animals. Right now, a lot of the drugs used are human oncology treatments. The veterinarians would greatly appreciate the opportunity to be able to have drugs that have been demonstrated for the efficacious—for the canine or equine or the horse or the dog or the cat-type tumors.

The chronic renal diseases, as our pets are living longer, they're getting more care. We are seeing more osteoarthritis, arthritic conditions, the same thing we see at our older ages.

We'd love to have drugs for renal disease, congestive heart disease problems that we see. There's no shortage of unmet veterinary medical needs out there.

Mrs. BROOKS. And finally, can you talk to us a little bit about the conditional approval process and hearing more about how that will impact the industry?

Dr. SOLOMON. So, once again, we think conditional approval for those type diseases I just talked about where, once again, they come in with their package as normal for safety.

They come in for the same package for the environmental controls, human food safety—all those conditions. It's only on the efficacy. So it changes the requirement from a reasonable—substantial evidence of efficacy, too.

They have to show reasonable expectation and they need to meet that standard within the next 5 years and with the current proposals that we are looking at.

So it gives them time for those diseases that are more chronic, insidious diseases that are harder to measure during a clinical trial because you're monitoring these conditions over a much longer period of time.

Mrs. BROOKS. Thank you. I yield back.

Mr. BURGESS. Chair thanks the gentlelady. The gentlelady yields back.

The Chair recognizes the gentlemen from New York, Mr. Collins, 5 minutes for questions, please.

Mr. COLLINS. Thank you, Mr. Chairman. Thank you, Dr. Solomon. I am going to step back just a second. As we added these user fees, I am assuming all that money goes towards personnel in your office?

Dr. SOLOMON. Correct.

Mr. COLLINS. And whether percentage of your budget or the number of folks, how significant is this to your staffing levels?

Dr. SOLOMON. So on the pioneer side on animal drug, it supports 28 percent of our animal drug review costs—what our costs are to run the program—and on the generic drug, it's 62 percent. So there are significant contributions to our overall—

Mr. COLLINS. But absolutely a direct result, this money is what's bringing our wait times down?

Dr. SOLOMON. Absolutely.

Mr. COLLINS. So when you mentioned, you know, some veterinarians are using human drugs, is there an approval process they have to go through, cancer or otherwise, to take a human cancer treatment and use it in an animal? Do they have to come to your agency to get approval to do that?

Dr. SOLOMON. They do not. So there is authorization for extra-label use and veterinarians can use human drugs in animals without a review. That preference would be from the veterinary community, to have drugs that are specifically approved for animals. And so that's why the conditional approval, for example, would be advantageous.

Mr. COLLINS. If they do this, I mean, I would think it would helpful to the industry if they also compile data at some point so other veterinarians could have a better feel whether this drug is working or not.

Is that just option—it's not mandatory that they do so as they're using—

Dr. SOLOMON. So many of these drugs approved in humans may have gone through animal studies. So a lot of times veterinarians will take a look at those animal studies and, in fact, we've had drugs that have been approved.

Much of the work was done during the human approval. We had some drugs for pain in animals. We had some drugs for appetite stimulation in dogs. Much of the work, when they came in with a submission, was done for those drugs when they were approved on the human side, and that information was transferred over, submitted to the approval process, and we went through approval.

Mr. COLLINS. Although I think a lot of the animal portions of human drug trials are more for safety issues than efficacy?

Dr. SOLOMON. That's correct.

Mr. COLLINS. So, now, I am very familiar with the human side. But on the animal side, is there the equivalent of a phase one, a phase two, a phase three, or is it just a lot more data driven—they do their work, they come to you with a submission? Or do they have to go through anything remotely resembling what we do in human trials?

Dr. SOLOMON. So there are some similarities about the type of data that they need to submit. We use a different process than the phased process.

But they do go through those same type of aspects. So they do clinical trials on a small number of animals to evaluate safety. They look at safety issues by giving various doses of the drug to determine the safety.

Once safety is looked at, then they start doing efficacy trials, and that may be both clinical trials and field trials that may be done throughout the—

Mr. COLLINS. But, I mean, that's almost exactly the way we do human trials. But is it as formalized, or is folks developing animal drugs have a lot more latitude in all those areas to bring a drug to market and then—is your involvement more of a review of that data that they've built without being quite under the same scrutiny as human trials?

Dr. SOLOMON. So we don't put them through the phases in the same way the same type data is collected. But we work very closely with them on each of those aspects.

So they come in early in the developmental process, sit down with us, what's it going to demonstrate to show the target animal safety? What are we going to need for the clinical efficacy?

Each drug is unique, because once again we are using different approaches. Are we using different surrogate end points? Are we using data from human trials? Are we—

Mr. COLLINS. Well, my time is almost up. But is the patent protection similar for this development as it is, and then generics can come on board after 17 years or whatever it happens to be?

Dr. SOLOMON. So I need to get back to you on the patent issues. We do have exclusivity issues where the drugs are either for 3 years or 5 years when a pioneer comes on before a generic product can come on the market.

Mr. COLLINS. So significantly reduced time compared to human drugs?

Dr. SOLOMON. On the exclusive marketing, yes.

Mr. COLLINS. Very good. Well, thank you. This is very informative.

I yield back.

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

The Chair recognizes the gentleman from Florida, Mr. Bilirakis, 5 minutes for questioning.

Mr. BILIRAKIS. Thank you, Mr. Chairman. Appreciate it.

Dr. Solomon, would you briefly explain how ADUFA and AGDUFA improved FDA regulations as far as the public health is concerned and how the most recent proposed changes will benefit FDA and public health?

Dr. SOLOMON. So, by getting new products, new animal drugs to the market, many of these drugs are very important for food-producing animals, which directly affects public health.

When we get a new antimicrobial, for example, for use for treating a disease in food-producing animals, we have the resources to try and do the human food safety aspect of that review.

That review includes all the toxicology review, the residue review, which I talked about before with the tissue residue method. But it also looks at the microbial review process. Is this a product that could affect humans and is medically important in humans, and therefore could cause antimicrobial resistance? So that's all part of the review process that directly affects public health.

Mr. BILIRAKIS. OK. Very good.

How has consolidation in the industry impacted the review process?

Dr. SOLOMON. So, on the pioneer side, there's been considerable consolidation that's taken place. From our perspective, they become more familiar with it and therefore the submissions—they understand better the products out there.

It also has an effect that sometimes it reduces the number of applications. So when a company has had mergers in several drugs, they often look at their portfolio, and it may result in some products being withdrawn from the market.

Mr. BILIRAKIS. OK. What are the consequences of not reauthorizing these user fee programs?

Dr. SOLOMON. So I hope no one wants to go down that path, because it's significant.

Mr. BILIRAKIS. Tell us why.

Dr. SOLOMON. Again, we've achieved these timely review processes. It would create instability in the industry. We've become very predictable on the timeframes and the pathways for these products.

It would be significant in terms of our staff. We have 115 staff that are currently employed using the user fees. Depending on the timing of when reauthorization would look, we would have to give notices, and it would make great challenges for our future staffing.

People would not want to come to work for the Center of Veterinary Medicine, where we have outstanding scientists and review-

ers, veterinarians that come on if there was uncertainty about this pathway.

Mr. BILIRAKIS. Well, thank you.

Mr. Chairman, I yield back the balance of my time. Thank you.

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

The Chair recognizes the gentleman from Virginia, Mr. Griffith, 5 minutes for questions, please.

Mr. GRIFFITH. Thank you very much.

All right. So what can we do to help to bring some of these ideas that you talked about, the antimicrobials that are being used, and trying to make sure that we have drugs for the animals but that they don't affect humans?

What can we do to move that process along to make it a little quicker?

Dr. SOLOMON. So we are working very closely on the antimicrobial resistance issue. It's a significant public health issue.

We work on judicious use policies, both on the human side—my counterparts work on the human side, we work on the animal side of that issue.

We work closely with industry to withdraw all the claims for use that was production uses for feed efficiency and growth promotion. Industry worked over the past 3 years. As of January of last year, all those were withdrawn.

We continue to work at monitoring both sales of antimicrobials and monitoring, through our national antibiotic resistance monitoring system, antibiotic usage.

Our colleagues at the American Veterinary Medical Association put out to the veterinary profession principles of good stewardship of antimicrobial use and principles about how to apply that and the definitions associated with that. Our American Association of Veterinary Medical Colleges has developed curriculum to be able to educate the new generation on what judicious use looks like.

We continue to need to work both domestically and internationally on getting better data to monitor antimicrobial resistance over time.

Mr. GRIFFITH. All right, I am going to shift gears on you, and feel free to tell me that it's not my department, but I had some folks come to me recently—and I represent the part of Virginia that has Virginia Tech, where a lot of research is being done—and they were talking about genetically modified calves.

And when they finished with their testing on, you know, rearranging the genes in the calf, they have to kill the mother. I am trying to figure out why. Do you have any help—can you help me there?

Because why would the mom be affected by a genetically modified calf when the calf is placed there out of a test tube, and it has nothing to do with her other than she's the vehicle in which the calf is being—

Dr. SOLOMON. So I don't think I can answer the question on the mother.

Mr. GRIFFITH. And that's fair. I thought that might be the case.

Dr. SOLOMON. But in a genetically modified animal, they do need to go to a review process to make sure these animals are safe, and

if someone's going to eat them that the modification makes it safe for people to eat.

Mr. GRIFFITH. And I recognize it's not necessarily your field, but it's something we might want to look at at some point, Mr. Chairman, is that they get that with the genetically modified calf, and so when they finish their experiment they understand they have to kill the calf. But I can't figure it out.

Now, you know, it's not my field. So maybe there's a small country lawyer—there's some obvious answer. But if you could maybe see if you could find me the right person to answer that question. Why does the mother have to be killed because, you know, the mama is a valuable asset, and when you're doing research and you suddenly have to start killing off assets that—I can't figure out nor could this individual who brought this to me figure out why the mother also has to be killed.

The calf, I get. You don't want to put that calf into the marketplace, and maybe you don't want to put mom in the marketplace, but you could use her again if she's able to have more than one. They're not able to do that right now. But I appreciate it.

Dr. SOLOMON. We are happy to take a look into the issue.

Mr. GRIFFITH. And I appreciate that.

And with that, Mr. Chairman, most of my questions having previously been asked, I yield back.

Mr. BURGESS. Chair thanks the gentleman. Gentleman yields back.

Chair recognizes the gentleman from Illinois, Mr. Shimkus, 5 minutes for questions.

Mr. SHIMKUS. Thank you, Mr. Chairman. Sorry I am late. We were at another hearing. I am sure you have heard that before, and I wish I would have been here for Kurt Schrader's questions, since he's a veterinarian, and I would have loved to hear. Maybe I will check his questions for the record.

But the last—we started going into this antimicrobial resistance discussion, and the only thing I wanted to raise was—and I know you have all talked about the conditional approval authority extensively, which is good.

How might you, in this antimicrobial resistance, can expand and improve your antimicrobial resistance provision as we move to—I call it AGDUFA—AGDUFA III?

Dr. SOLOMON. So I think there's opportunities under—if conditional approval for serious medical conditions that are treating public health issues, there's opportunities for alternatives to antibiotics to be potentially used under conditional approval, and I think we'd welcome those opportunities. We have approved a drug that's an alternative to antibiotics. It's given to dairy cows to try and prevent mastitis. It increases the number of neutrophils in the bone marrow to be able to fight infections. I think we are looking for other innovations that could be used as alternatives to antimicrobials, and I think conditional approval may be another incentive to try and get those products to the market.

Mr. SHIMKUS. Yes, and I should have asked this question first to set up the second one, but what are the barriers you have right now under current law on this debate?

Dr. SOLOMON. So the conditional approval Congress approved for only minor use in major species or minor species.

In order to use it in major species under the unique conditions that we've defined, it needs new statutory authority because it was—right now, efficacy needs to be demonstrated at the same time as target animal safety, human food safety, the environmental review process.

The conditional approval allows all the human food safety. The other pieces—the technical sections to be reviewed allows the product on the market 5 years. Industry can demonstrate the efficacy, comes back in and gets the full approval.

Mr. SHIMKUS. Do you agree with that, Schrader?

Mr. SCHRADER. Yes. Yes, I do. I mean, he outlined a current process and stuff. But we do need to expand the conditional use opportunities for major species. I think—

Mr. SHIMKUS. Good enough for me. Yield back my time. Thank you.

Mr. BURGESS. Chair thanks the gentleman. Gentleman yields back.

The Chair recognizes the gentleman from Oklahoma, Mr. Mullin, 5 minutes for questions, please.

Mr. MULLIN. Well, that is good timing. Thank you, Mr. Chairman, and Dr. Solomon, thank you so much for you taking the time to be with us.

A couple questions that I have. Wwhat is the timing? We've been talking a lot about conditional approvals. What's the timing on this? Do we know what we are looking at, how we can more predict in the industry level?

Dr. SOLOMON. So, once again, I think we've worked very hard with industry over the long period of time but more expeditiously recently to try and get a common understanding of conditional approval.

I think there's a good understanding of the scope that we've described here about its use for challenging efficacy issues, serious medical conditions.

So we'd be interested in, you know, if Congress wants to take this on we'd welcome the opportunity to give some technical assistance to it.

There may be some remaining issues that would need to be worked through, through either a guidance or a regulatory process. But getting the statutory authority while ADUFA/AGDUFA would be an opportunity.

Mr. MULLIN. Do you know what you would need from Congress? Because I am committed to working with you, and the industry is wanting to work with you.

We are wanting to see this move forward, I mean, because under—I mean, as we know, underneath the idea, which passed in 2004, we've only seen, what, four different drugs that's actually been able to come out of it, and I don't think that was the intent. Originally, the intent was to help incentivize the industry on coming up with new ways and new paths to build—to be able to produce and enhance the treatment for the animals.

So what would you need from Congress? How could I work with you? Because, in all seriousness, I really want to see this go as far as what Congress I think first intended in 2004 for it to go to.

Dr. SOLOMON. So once again, in 2004, it was for the minor species and minor uses.

Mr. MULLIN. Right.

Dr. SOLOMON. We are now having discussions—can we expand that to major species under unique conditions? We would welcome the opportunity to work on technical assistance to try and—

Mr. MULLIN. Who needs to be at the table on that?

Dr. SOLOMON. The industry is, clearly, at the table.

Mr. MULLIN. Right.

Dr. SOLOMON. American Veterinary Medical Association, a lot of people that are sitting here today.

Mr. MULLIN. Are we the ones missing at the table then? I mean, you said you're welcome to work with Congress on this. I am just looking for a path. How do we need to inject ourselves into this conversation without confusing it?

Dr. SOLOMON. I think technical assistance for some language that I think has been floating around. Once again, this is a recent development.

We recognize this. We've recognized timeframes are challenging, but we welcome the opportunity to try and get this important piece added.

Mr. MULLIN. Well, we worked with industry some as far as looking for language that's needed. Have you had a time to look at it yet?

Dr. SOLOMON. So we've had staff working very closely with the industry on that piece.

Mr. MULLIN. But you haven't got a look at it yet?

Dr. SOLOMON. We would like the opportunity, sort of taking that language if we get requested by Congress and be able to provide formal agency review of it.

Mr. MULLIN. I guess that's where I am confused. Is it simply me saying, "I want you to look at it," or is there—and I am confused here—does it take actual legislation for us to give you—

Dr. SOLOMON. I think its only request that if Congress is—which sounds, you know, a lot of interest here on conditional approval. If you came to us we'd be happy to provide technical assistance to give a formal agency position to try and have it in front of you to decide to include it in the ADUFA/AGDUFA—

Mr. MULLIN. Well, let me talk with the committee so I am not stepping in front of the chairman on this and find out for sure what the committee wants.

But I was under the understanding that's where we are wanting to move to. But I will get back to you personally, and then I look forward to working with you moving forward with it.

Dr. SOLOMON. We welcome that opportunity. Thank you.

Mr. MULLIN. Thank you, sir.

And with that, Mr. Chairman, I will yield back.

Mr. BURGESS. Gentleman yields back.

The Chair would observe that the gentleman might want to work with the primary author of the bill. Oh, that is the gentleman. So, yes.

[Laughter.]

But we will work with you, Mr. Mullin.

Mr. MULLIN. I don't want to overstep the committee because you have been very gracious to me.

Mr. BURGESS. We will work with you, absolutely.

Chair now recognizes the gentleman from Texas, Mr. Green, 5 minutes for your questions, please.

Mr. GREEN. Thank you, Mr. Chairman. I apologize for being late.

Thank you, Dr. Solomon, for being here today, and as you explained in your testimony, over the last 2 years FDA has been working to finalize recommendations for reauthorization of the animal drug user fees and has held negotiations with regulated animal drug and generic animal drug industries in order to reach an agreement on both financial and performance goals for the next 5 years.

These recommendations were finalized and transmitted to Congress for consideration early this year. Dr. Solomon, you noted that the FDA is currently delivering predictability—high levels of performance against the ADUFA and AGDUFA goal commitments for a timely review.

Under ADUFA IV and AGDUFA III, do you believe this high level of performance will continue?

Dr. SOLOMON. With the additional resources that have been negotiated and put forward, yes, we are committed to continue to meet the high levels of performance.

Mr. GREEN. Is this why the performance recommendations for most of the submission types for pioneer drugs remains consistent with the current goals?

Dr. SOLOMON. That's correct.

So once again, we've reduced timeframes for most of those submissions. We added four new areas this time, of particular importance to some of those commitments for early communication with the industry early in the development process.

Mr. GREEN. For generic animal drug submissions, FDA's performance goal review times have been shortened. Can you explain how the FDA plans to meet those new timeframes?

Dr. SOLOMON. So there was significant new resources associated with the generic drug. The industry really wanted to be able to get the generic drugs to the market sooner, and so they committed additional resources.

We plan on hiring the scientific support staff to be able to conduct those reviews. There has been a tremendous increase in generic drug submissions over the past couple years.

The workload has increased tremendously. In fact, we had over a 50 percent increase in the last year on generic drug submissions.

Mr. GREEN. Thank you.

Can you explain how the financial recommendations in the AGDUFA III negotiated agreement have changed from AGDUFA II? Additionally, can you explain the rationale for those changes? Is it mainly just an increased funding?

Dr. SOLOMON. So there's increased funding. We also made the funds more readily available. So one of the conditions is, historically there used to be a process where, if there's excess collections

of funds, you'd have to wait to the last year of the agreement in order to be able to use them.

We negotiated with industry. They would like and we would like to be able to use those funds earlier. There were some changes in the inflation index that took place to make it a variable inflation index, and there was changing the base years that we were using for the negotiations. So all agreed upon.

Mr. GREEN. Are there any other performance and financial recommendations from the new proposal that should be highlighted?

Dr. SOLOMON. The tremendous changes on the generic drug side dramatically reduce the timeframes associated with those. So I think the industry and FDA would be very excited about meeting those new timeframes, because they're significant reductions.

Mr. GREEN. I want to thank you, Dr. Solomon. These performance and financial goals are critical aspects to the ADUFA and the AGDUFAs and will chart the course for the next 5 years.

I am pleased that the FDA and the animal health industries have reached agreement and look forward to the swift reauthorization of these important programs.

And Mr. Chairman, I yield back.

Mr. BURGESS. Chair thanks the gentleman.

The Chair recognizes the gentleman from North Carolina, Mr. Hudson, 5 minutes for your questions, please.

Mr. HUDSON. Thank you, Mr. Chairman. Thank you, Dr. Solomon, for your time today.

In my home State of North Carolina, agriculture is the number-one industry. Poultry is the number-one sector, making up 40 percent of our State's total farm income.

All told, it's about \$4 billion a year, or 10 percent of our total State product. One issue that pops up continually for our chicken and turkey farmers is blackhead disease. This highly transmittable disease can wipe out an entire turkey flock in weeks, disrupts breeding cycles for chickens, causes millions of dollars in damage to my farmers back home.

This disease occurs sporadically but has a high impact every time it strikes a farmer's flock. Unfortunately, no medication exists at this moment to treat or cure this disease, meaning that if your flock is hit, it's guaranteed to hurt.

Because this disease requires a spontaneous biological event to occur, it's almost impossible to create controlled trials to study the disease or the efficacy of the drug.

One thing my colleagues, Markwayne Mullin and Dr. Bucshon, noted earlier and I've been examining is the conditional approval that's gotten a lot of attention here in this hearing—a pathway for major use, major species.

Blackhead disease is just one disease of many where a conditional approval pathway would help drug makers get medications to farmers and pet owners that are currently unviable for the traditional approval pathway.

So in your testimony you note that the CVM is committed to continuing to explore conditional pathways. Do you agree that the conditional approval pathway for major use in major species would help bring innovative therapies that can treat diseases like blackhead disease to market?

Dr. SOLOMON. I do. We've done a lot of work on blackhead. We've recognized that's one of those unmet veterinary medical needs out there.

We've asked for the industry, in the turkey industry that suffers from this the most, that they may be eligible under our minor use, minor species, but we need data presented to try and do that.

If they're unable to meet that, then this new conditional approval proposal would be welcome. It's a challenging disease to treat because of many of the sporadic conditions, seasonal nature of it. It would be one that, you know, demonstrating efficacy over a longer period of time could be valuable tool in the arsenal.

Mr. HUDSON. Right. Well, I appreciate that, and my colleague Markwayne Mullin and others have I think clearly established that we want to work with you on this and, you know, we welcome any feedback you have on any requirements that make conditional approval pathway feasible—you know, what you need from us to move forward on this, and rather than continue to beat that dead horse, I would just ask do we have your commitment that we'll move as quick as we can together to find a way forward on this?

Dr. SOLOMON. We are ready, willing, and able to work with you on that issue.

Mr. HUDSON. Great. I appreciate that very much.

Unrelated to conditional use, but just out of curiosity for me: Off the top of your head, what's the longest amount of time that CVM has spent reviewing a single drug?

Dr. SOLOMON. That's probably the genetically engineered salmon, which went on for a significant period of time for a lot of different reasons.

Mr. HUDSON. What do you think just in general the reasons for long review cycles are?

Dr. SOLOMON. So for that particular review, that was unique—the first genetically engineered animal for food-producing animals. You need to develop how are you going to evaluate the safety, the efficacy of something that's so new and novel.

It was one also of great concern from an environmental area, which is part of our requirement, you know, what's the potential for a genetically engineered animal to get loose—either get into the wild, even though they're sterile animals—poses lots of different challenges, looking at our typical review process with something unique.

Now that we've been through those processes, we've answered many of those questions.

Mr. HUDSON. Well, just in a more typical review process, you know, what are some of the reasons that these sometimes take longer?

Dr. SOLOMON. So data quality is an important issue for us. We constantly are working with the industry—the more higher quality the data, then we'd have to go back to these issues.

Efficacy requirements in certain disease conditions can be very challenging. We've been challenged, for example, on heartworm disease. We try and—as there's been resistance to various new—some of the different parasites—it becomes more difficult to demonstrate efficacy over a period of time.

So it's kind of, evolution of some of the disease conditions over time poses challenges on proving efficacy.

Mr. HUDSON. Well, I appreciate your testimony very much.

Mr. Chairman, I will yield back.

Mr. BURGESS. Chair thanks the gentleman.

Chair recognizes the gentleman from Georgia, 5 minutes for your questions, please.

Mr. CARTER. Thank you, Mr. Chairman.

Thank you, Dr. Solomon, for being here. Appreciate that very much.

Let me ask you something. It's my understanding in a new animal drug application that the drug sponsors are responsible or submitting information, and it's quite detailed and quite thorough.

From what I understand, in the application it's going to include information on the drug's chemistry, the composition, the component ingredients, manufacturing methods, facilities and controls, proposed labeling—on and on and on.

And not only that, but also if the drug product is intended for use in a food-producing animal, that it also has to be proven for human use, and I am just—and all this burden falls on the drug sponsors.

And it just appears that it's more than even what—the guidelines for animal drug are more stringent than they are for human drug applications. And I am just interested to know, first of all, do you think that's true, and secondly, if it is, why is that?

Dr. SOLOMON. So, just to take a step back, so with all due respect to my human colleagues on review, they have one species to deal with.

Often we have to deal with multiple species. So many of the applications, they don't want to market it in multiple species at the same time.

And that's a challenge, because there's different pharmacology versus pharmacokinetics in different species out there. We also have the responsibility in food-producing animals to make sure that this is going to be safe for humans.

So, once again, I think our safety and efficacy and environmental reviews are very similar to the human side. But when it comes to either multiple species or the human food safety issues, they're unique to the animal side. But that's part of our responsibility to the American public to make sure that the food is safe.

Mr. CARTER. Fair enough. Good answer. Thank you.

I want to talk to you about animal drug compounding. This is certainly something that the FDA has—or drug compounding period is something the FDA has been involved in here recently, and rightfully so.

But when it comes to animal drug compounding, it's my understanding that it's legal only in very specific circumstances, according to the FDA, and as a result of the Drug Quality Security Act, there were some changes that were made and, from what I understand, the FDA rescinded their initial guidelines and that they are now looking at and coming up with new guidelines.

Are you familiar with that, and what kind of time line are we looking at here?

Dr. SOLOMON. So we did have a guidance on compounding. As you're very well aware, it's a challenging issue to find the right balance.

There is some need for compounding out there. We don't want that to either prove a safety issue to animals, and we don't want that to undermine the approval of pioneer or generic drugs.

So compounding within a veterinarian/client/patient relationship is something important because veterinarians need access to that. So our previous guidance, there was confusion about applying the DQSA, the Drug Quality Security Act, which does not apply to the animal side of the house.

Mr. CARTER. Right.

Dr. SOLOMON. We wanted to clarify that it was never intended to apply to that.

Mr. CARTER. Thank you.

Dr. SOLOMON. It also—back to my multiple species issues, the previous guidance only addressed compounding for companion animals, and as I've sort of talked about several times now, we have the challenge of compounding for food-producing animals, companion animals, and minor species.

So we decided to rescind that compounding guidance. We are working on it. We expect over the next several months to be able to issue a new compounding guidance, where it would be, once again, cover the whole spectrum of the species, be clear about not applying the DQSA, trying to apply that right balance of where compounding is appropriate, and we'd welcome the opportunity once that's out to come brief Congress.

Mr. CARTER. OK. Are you soliciting the input of the animal drug compounders while you're formulating this?

Dr. SOLOMON. We are talking to lots of stakeholders and, once again, this will be another proposal. So we welcome the opportunity when this comes out for a proposal to continue to engage with folks.

Mr. CARTER. Well, thank you for mentioning accessibility, because that's extremely important. I can tell you, as a practicing pharmacist for over 30 years before I became a Member of Congress, this was something we typically worked with our veterinarians and, you know, it was very detailed.

So the accessibility part of it is very important, as well. Good. Thank you very much, and I yield back, Mr. Chairman.

Mr. BURGESS. Gentleman yields back. The Chair thanks the gentleman.

I believe that concludes questions from Members for your panel, Dr. Solomon. We do, again, want to thank you for being with us and providing your expert testimony today, and certainly as we work through this we will take what you have shared with us today to heart.

And we are going to have the briefest of transitions to our second panel. Dr. Solomon, you're excused, and we'll ask our second panel to take their places.

Dr. SOLOMON. Thank you very much.

[Pause.]

Mr. BURGESS. So I thank our second panel of witnesses, and I want to thank you for being here today, taking time to testify before the subcommittee.

We are going to give each of you an opportunity to give an opening statement, and that will be followed by questions from Members.

So today, on our second panel we are going to hear from Dr. Rachel Cumberbatch, the Director of Regulatory Affairs, Animal Drugs, at the Animal Health Institute; Mr. Bill Zollers, chairman of Generic Animal Drug Alliance; and Dr. Michael Topper, president of the American Veterinary Medical Association.

We appreciate each of you being here with us today.

Dr. Cumberbatch, you're now recognized for 5 minutes to summarize your opening statement.

STATEMENTS OF RACHEL CUMBERBATCH, D.V.M., DIRECTOR, REGULATORY AFFAIRS, ANIMAL DRUGS, ANIMAL HEALTH INSTITUTE; BILL ZOLLERS, PH.D., CHAIR, GENERIC ANIMAL DRUG ALLIANCE; AND MICHAEL J. TOPPER, D.V.M., PH.D., PRESIDENT, AMERICAN VETERINARY MEDICAL ASSOCIATION

STATEMENT OF RACHEL CUMBERBATCH

Dr. CUMBERBATCH. Thank you, Mr. Chairman.

I am a veterinarian here today on behalf of the Animal Health Institute, a trade association that represents companies that make medicines for animals.

I am here to ask Congress to reauthorize the animal drug user fee program, also known as ADUFA, and to provide a pathway for sponsors to meet unmet medical needs by enhancing opportunities for innovation.

The animal health industry makes important contributions to the American economy. Fueled by \$9.9 billion in sales of medicine, the U.S. animal health industry employs over 21,000 workers and generates more than \$1.2 billion in wages.

It accounts for \$1.2 billion in taxes and maintains a positive trade balance. Furthermore, animal health products directly contribute to the economy of other industries, including veterinary services, animal production, meat and dairy production, and pet services.

Combined, these four industries generated \$548 billion in output, created more than 1.4 million jobs, and paid over \$52 billion in wages in 2016 alone.

These contributions extend to every State, in every congressional district where people own pets and families rely on the availability of safe food.

The Animal Health Institute strongly supports the ADUFA program. This new agreement builds on the success of this program. Funding will increase from \$118 million in ADUFA III to a total of \$150 million in this 5-year agreement.

This includes a one-time influx of funds that will be devoted to information technology so that CVM can transition to electronic filing of new animal drug submissions and can eliminate all paper submissions.

Current inflation and workload adjustment factors remain as they are while AHI has agreed to allow FDA to reinvest surplus funds into the program.

Existing sentinel timeframes will remain the same or be slightly reduced, and all current review process changes from the previous ADUFA agreement will remain in place.

There is one important piece of business from ADUFA III which we are asking Congress to help us complete. ADUFA III contained a provision that FDA and AHI would enter into discussions on how to more broadly extend the conditional approval process.

Conditional approval is currently available only for minor uses and minor species products. These efforts aim to find a way to expand a pathway to major species applications.

Those discussions took place and were productive, bringing each side to near agreement on an approach. However, when we got to the ADUFA IV, CVM was precluded from discussing this issue as part of the agreement.

More than a year ago, this committee commendably came together and approved the 21st Century Cures Act to spur innovation in human therapies. By all indications, it is working, and now we ask that you include in this legislation a measure to similarly spur innovation in animal health.

Conditional approval for animal health products exist at the EPA as well as the U.S. Department of Agriculture and, as we said, it also exists for minor use, minor species at the FDA.

Expanding the current authority to major species would drive innovation and, most importantly it would lead to the approval of new products for serious diseases which there are no available treatments and which it is difficult for clinical effectiveness to be proven via controlled studies.

Thank you for holding this hearing on this important piece of legislation, and thank you for the opportunity to speak to you today about how keeping animals and humans safe using medicines also helps with public health.

Thank you.

[The prepared statement of Dr. Cumberbatch follows:]

Testimony of Dr. Rachel Cumberbatch
Animal Health Institute
Subcommittee on Health, Energy and Commerce Committee
March 14, 2018

Mr. Chairman and members of the Committee:

Thank you for holding a hearing on this important piece of legislation, and for the opportunity to speak to you today about the important human and animal health benefits that result from using medicines to keep animals healthy.

My name is Dr. Rachel Cumberbatch and I am a veterinarian here today on behalf of the Animal Health Institute, a trade association that represents companies that make medicines for animals. I am here today to ask Congress to reauthorize the Animal Drug User Fee (ADUFA) program and provide a pathway for sponsors to meet unmet medical needs by enhancing opportunities for innovation.

The animal health industry makes important contributions to the American economy. Fueled by \$9.9 billion in sales of medicines, the U.S. animal health industry employs 21,257 workers, accounts for more than \$1.2 billion in wages and \$1.2 billion in taxes and maintains a positive balance in trade.

Furthermore, animal health products directly contribute to the economic activity of other industries including veterinary services, animal production, meat and dairy production, and pet services.

Combined, these four industries generated \$548 billion in output, created almost 1.4 million jobs, and paid over \$52 billion in wages in 2016. These contributions extend to every state, and every Congressional district, where people own pets and where people rely on food to be safe.

But the contribution of animal health goes far beyond dollars and cents. Over 67% of U.S. households own pets, with nearly half owning a dog and over one-third owning a cat. In total, American households

own approximately 393 million pets. These households rely on routine veterinary care and animal health products to keep pets healthy. Animal owners can enjoy their companions without the fear of exposure to diseases like rabies or pests like fleas and ticks. As pet owners look for solutions to increase the length and quality of life for their pets, cutting edge treatments for pet health problems, such as arthritis and cancer, are becoming more common. These are the statistics behind what we call the human-animal bond, and this bond is strengthened by medicines to both treat and prevent diseases in pets and keep families safe by preventing the transfer of disease from pets to humans.

Animal health products also give veterinarians, and livestock and poultry producers, the necessary tools to protect the health and well-being of 9 billion food producing animals annually. A vital first step in producing safe meat, milk and eggs is keeping animals healthy. Veterinarians work hard to prevent disease in animals, but it is important for them to have medicines available when needed to treat a disease or disease threat.

The statutory standard for Food and Drug Administration (FDA) approval of animal drugs under the Federal Food, Drug and Cosmetic Act is the same as that for human drugs: they must be proven to be safe and effective. As a result, the animal drug approval process looks much like the human drug approval process: animal drug companies submit data packages to demonstrate safety, efficacy, and the ability to meet the same stringent FDA manufacturing standards. It is a costly process, requiring as much as \$100 million and 7-10 years to bring an animal drug to market. In the case of food animals, the standard to ensure that meat, milk, and eggs are safe for human consumption adds an additional set of requirements that increases the cost and time to market.

The market for animal drugs, however, is nothing like the market for human drugs. Our products are used to treat seven different major species of animals and many more minor species. A blockbuster animal drug will have sales of \$100 million, and the vast majority of animal health products have a

market size of around \$1 million. There is no Medicare or Medicaid and, except in rare cases, no employer supported health insurance -- the cost of animal drugs is borne in full by the animal owner.

Animal health companies rely on a rigorous, efficient, predictable and science-based review process at the FDA's Center for Veterinary Medicine (CVM) to provide these products that are not only safe and effective, but also affordable. The Animal Drug User Fee Act, first enacted in 2003, made it possible for our companies to bolster funding at CVM so that the agency can meet performance standards to improve the efficiency and predictability of the animal drug approval process.

This new ADUFA agreement builds on the success of this program. Funding will increase from a total of \$118 million in ADUFA III to a total of \$150 million over the five years, including a one-time influx of funds that will be devoted to information technology so that CVM can transition to electronic filing of new animal drug submissions and eliminate all paper submissions. Current inflation and workload adjustment factors remain as is while AHI has agreed to allow FDA to use over collection of funds from one year for program needs in subsequent years. Existing sentinel timeframes will remain the same or be slightly reduced, and all current review process changes from the previous ADUFA agreement will remain in place.

In addition to reducing the time for combination clearances, FDA agreed to work on three important efforts.

1. CVM agreed to work towards implementing the US/EU agreement on mutual recognition of Good Manufacturing Practices inspections, which were negotiated during the last months of the previous Administration.
2. FDA will implement a new performance metric of 120 days for FDA validation of tissue residue methods with additional dedicated funds to accomplish this metric. This process has taken considerable time in the past and delayed approval of new drugs.

3. CVM will institute an expedited meeting schedule for critical pre-NADA submission conferences.

The agreement contains some technical corrections in the Act to permit user fees to apply to Minor Use/Minor Species Drug Application reviews, as well as a change in a label requirement on indexed minor species products. It also provides an amendment to legally require the NADA number be placed on the labels of all approved products. While identification of the NADA on labels has been voluntarily adopted by most AHJ member for many years this requirement for all sponsors of approved products will differentiate - for the producer and veterinarian - legally approved versus unapproved or illegally manufactured products.

There are also a number of minor changes made to the performance standards in an effort to create new efficiencies.

Passage of this important legislation will have several benefits:

1. FDA/CVM benefits by having additional resources to meet its mission of protecting public health.
2. Animal health sponsors benefit from a stable and predictable review process, allowing them to make informed decisions about the investment risks of research and development dollars.
3. Veterinarians benefit from having new and innovative medical advances available to treat, control and prevent diseases in their patients.
4. Livestock and poultry producers, and the veterinarians on whose advice they rely, also have the tools needed to keep food animals healthy.

5. Pet owners benefit by having their animals live longer and healthier lives, increasing their enjoyment of these companions.
6. Consumers reap the food safety benefits that come as a result of the availability of additional tools to keep food animals healthy.

There is one important piece of unfinished business from ADUFA III which we are asking Congress to help complete. ADUFA III contained a provision that FDA and AHI would enter into discussions on how to more broadly extend the conditional approval process currently available only to minor use/minor species products to major species applications. Those discussions took place and were productive, bringing each side to near agreement on an approach. However, when negotiations began for ADUFA IV, FDA/CVM was precluded from considering this issue as part of the agreement.

More than a year ago, this committee commendably came together and approved the 21st Century Cures Act to spur innovation in human therapies. By all indications, it is working, and now we ask you to include in this legislation a measure to similarly spur innovation in animal health.

This is a tool that exists in other areas of animal health. Conditional approval exists at the Environmental Protection Agency which reviews flea and tick products. It exists at the U.S. Department of Agriculture that reviews veterinary vaccines. It even exists at FDA, where Congress in 2004 authorized conditional approval for minor uses and minor species. Expanding this current authority to major species would drive innovation and approval of new products for serious diseases for which there are no available therapies and for which it is difficult to establish clinical effectiveness via controlled studies. This is often the case where a long term progressive condition takes time to manifest, or where there is a lack of effective disease models for use in controlled studies. Conditional approval could also aid in the research and discovery in pursuit of alternative therapies to antibiotics.

Authorizing conditional approval in no way reduces safety. Conditional approval requires sponsors to provide safety and meet all technical packages but changes the efficacy standard from “substantial evidence” to “reasonable expectation” of efficacy. Sponsors can then market the product while continuing to collect effectiveness data to satisfy the “substantial evidence” requirement and gain full approval. A case can be made that conditional approval authority could improve animal safety. Providing a veterinarian with a product that has been proven to be safe and has a reasonable expectation of efficacy would provide that veterinarian with a better-defined expectation for the product than the unapproved drug and off-label human drug now currently used to address unmet medical needs.

Mr. Chairman, CVM has a rigorous, science-based approval process that provides to the American public the products necessary to protect public health by protecting animal health. Every year scientists uncover new diseases in animals, some of which potentially pose a threat to human health. As more animals are raised to feed the planet and as animals are reared closer to people, we will continue to need new medicines to protect animal and human health.

The reauthorization of ADUFA will continue to provide the agency the resources necessary to maintain and improve this approval process, provide new and innovative products to allow our pets to live longer and healthier lives, and contribute to food safety by keeping food animals healthy. I urge you to pass an enhanced ADUFA that improves upon the agreement by authorizing the Agency to extend the conditional approval pathway to spur innovation in animal health.

Mr. BURGESS. Thank you for your testimony.

Dr. Zollers, you're recognized for 5 minutes for a summary of your opening statement, please.

STATEMENT OF BILL ZOLLERS

Dr. ZOLLERS. Thank you.

Good morning. My name is Bill Zollers, and I serve as the chairman of the Generic Animal Drug Alliance, also known as GADA.

We are an independent professional trade organization that represents the interests of the generic animal drug industry. We represent sponsors, manufacturers, distributors, suppliers, and service providers of generic animal drugs.

Our products and processes are regulated by the FDA Center for Veterinary Medicine. Our members are focused on the development, regulatory approval, and marketing of high-quality generic drugs to livestock and pets.

I would like to thank the committee for inviting me to testify today on behalf of GADA in support of the reauthorization of the Animal Generic Drug User Fee Act.

The GADA has previously provided testimony to this subcommittee in support of AGDUFA I in 2008 and AGDUFA II in 2013.

Just like with human generic drugs, generic animal drugs provide cost-effective alternatives to pioneer drugs. Lower-cost generic animal drug options help contribute to the safety of the Nation's food supply, the treatment of diseases in animals, and the ability of owners to provide care to their pet family members.

However, the potential cost savings from generic animal drugs cannot be achieved without broad availability. It is critical that the CVM regulatory review and approval process for generic drugs is both efficient and predictable.

Prior to the implementation of AGDUFA I, a CVM review cycle of a generic application could take as long as 2 years. In most cases, multiple review cycles are needed. So if an application required three review cycles, it could easily take more than 6 to 8 years to receive approval.

In the time it took to get an application approved, the market for a generic drug could change, making it no longer cost effective. This created a disincentive for companies to pursue generic animal drug approvals and denied the public cost-effective generic drugs.

The industry remembers this time in our history. No one involved in the approval process for generic drugs wants to see these conditions return. Therefore, the industry is stepping up again to support reauthorization of AGDUFA.

Since AGDUFA began, CVM has reduced the review time of an application to a more predictable 270 days. We believe the shorter review times are helping contribute to the growth of our industry.

As part of the current reauthorization of AGDUFA III, the industry has agreed to significantly increase our financial contributions so that generic submissions could receive even shorter review periods that are equivalent to pioneer drug submissions.

As currently written, AGDUFA III will further shorten some critical submission review times from 270 days to 180 days.

The industry is comprised of many small companies and product markets that are much smaller than those for human generic drugs. Therefore, it remains vital that congressional appropriations continue to be provided to the Center for Veterinary Medicine to significantly support the review of generic drug applications.

Appropriations must continue at an increased level that enables CVM to meet its public health mission and the important public policy goal of providing generic drug options for farmers and pet owners.

We believe AGDUFA III provides the review time targets that industry requires to counterbalance the financial investment being made in support of CVM's needed resources to build capacity and balance the realities of a small but growing generics industry.

The proposed AGDUFA III enhancement concerning e-submissions should make the approval process more efficient. Also, the proposed revisions to the overcollections that offset provisions will more immediately reduce the financial burden if overpayments are made by the industry.

Overall, we are hopeful that the reduction and review times will lead to a shortened time from project initiation to approval, allowing generic products to come to market sooner.

In conclusion, the GADA supports the proposed legislation for reauthorization of AGDUFA.

Thank you.

[The prepared statement of Dr. Zollers follows:]



March 14, 2018
US House of Representatives
Committee on Energy and Commerce
Subcommittee on Health

Dear Honorable Members:

The Generic Animal Drug Alliance (GADA) is providing testimony to the Subcommittee on Health of the Committee on Energy and Commerce in support of the re-authorization of the Animal Generic Drug User Fee Act of 2018 (AGDUFA). The GADA has previously provided testimony to this Subcommittee in support of AGDUFA I in 2008 and AGDUFA II in 2013. The GADA is an independent professional trade organization that represents the interests of generic animal drug companies. We are the only trade organization that represents the interests of sponsors, manufacturers, distributors, suppliers and service providers of generic animal drugs. Our products and processes are regulated by the Food and Drug Administration, Center for Veterinary Medicine (FDA/CVM). Our members are focused on the development, regulatory approval and marketing of high quality generic drugs for livestock and pets.

Just like with human generic drugs, generic animal drugs provide significant benefits to the public by providing cost-effective alternatives to their pioneer drug counterparts. Lower cost generic animal drug options help contribute to the safety of the nation's food supply, the treatment of diseases in animals that can be transmitted to humans, and the ability of owners to provide care to their pet family members. However, the potential cost savings to famers

and pet owners from generic animal drugs cannot be achieved without broad availability. Therefore, it is critical that the CVM regulatory review and approval process for generic drugs is both efficient and predictable.

AGDUFA was a successful first step in achieving these goals. Prior to the implementation of AGDUFA I, a single CVM review cycle of a generic application could take longer than two years. In most cases, multiple review cycles are needed, so if an application required three review cycles, it could take more than six to eight years to receive approval. In the time it took to get an application approved, the entire market for a generic drug could change, making it no longer cost-effective to market. This created a disincentive for companies to pursue generic animal drug approvals and denied the public cost-effective veterinary generic drugs. The industry remembers this time in our history. No one involved in the approval process for generic drugs wants to see these conditions return. Therefore, the industry is stepping up again to support the reauthorization of AGDUFA.

Since AGDUFA began, CVM has reduced the review time of an application to a more predictable 270 days. In addition, CVM implemented several process enhancements and increased communications with industry. We believe the shorter more predictable review times are helping contribute to the growth of our industry. As part of the current reauthorization of AGDUFA III, the industry has agreed to significantly increase our financial contributions so that the generic industry could receive even shorter review periods that are equivalent to those experienced by the sponsors of pioneer drugs. As currently written, AGDUFA III will further shorten some critical submission review cycle times from 270 days to 180 days.

The industry is comprised of many small companies and product markets that are much smaller than those for human generic drugs. Therefore, it is vital that Congressional appropriations continue to be provided to the Center of Veterinary Medicine to significantly support the review of generic drug applications. For this to be achieved, appropriations must continue at an increased level that enables CVM to meet its public health mission and the important public policy goal of providing generic drug options for farmers and pet owners.

We believe AGDUFA III provides the review time targets that industry requires to counterbalance the financial investment being made in support of CVM's needed resources to build capacity and balance the realities of a small but growing generics industry. In addition, the proposed AGDUFA III enhancement concerning e-Submissions should make the approval process more efficient. Also, the proposed revisions to the overcollections and offset provisions will more immediately reduce the financial burden if overpayments are made by the industry. This will also make funding more efficiently ready for use by CVM to continue to improve the generic drug review process. Overall, we are hopeful that the reduction in review times will lead to a shortened time from project initiation to approval allowing generic products to come to market sooner.

In conclusion, the GADA supports the proposed legislation for re-authorization of AGDUFA. Without timely reauthorization, we will return to the untenable situation pre-AGDUFA when lengthy application reviews served as a disincentive to companies pursuing generic animal drugs. It remains critical for the continued viability of the veterinary generic drug industry that

the FDA/CVM review process maintains and improves predictability and efficiency.

Reauthorization of AGDUFA is critical to continuing to make the pursuit of generic animal drug approvals viable and to increase the number of safe and effective generic animal drugs on the market.

Sincerely,

The Generic Animal Drug Alliance

Mr. BURGESS. Chair thanks the gentleman.

Dr. Topper, you're recognized for 5 minutes for a summary of your opening statement, please.

STATEMENT OF MICHAEL J. TOPPER

Dr. TOPPER. Thank you, and good morning.

Like was stated, I am Dr. Mike Topper. I have the privilege of being the president of the American Veterinary Medical Association, and on behalf of the AVMA I appreciate the opportunity to discuss the importance of reauthorizing the Animal Drug User Fee Act and the Animal Generic Drug User Fee Act.

The AVMA was founded in 1863, and we represent over 91,000 individual member veterinarians engaged in the many segments of professional veterinary medicine, including private practice, public health, biomedical research, and many others.

The FDA Center for Veterinary Medicine's collection and effective utilization of user fees are important to veterinarians.

By providing new animal drugs with a predictable pathway to market, these fees help provide veterinarians with access to new and additional tools that can potentially improve treatment outcomes, provide alternatives to existing therapies, fill unmet medical needs in veterinary medicine, and ultimately improve patient care, which is the center of veterinary practice.

The AVMA supports user fees for new animal drug applications when the fees are supplemental to appropriations and directed toward expediting the review process for new animal drug products.

There simply are not enough approved drugs for use in animals. Comparisons of FDA data show there are 23 times the number of approved labeled indications for human use as there are for animal use, and when comparing animal drug products approved for minor use and minor species to its human model, which is the orphan drug program, that number increases to 26 times.

Thankfully, through the Animal Medicinal Drug Use Clarification Act of 1994 and its extra-label drug use provision, veterinarians are provided with greater treatment options.

Of course, there are necessary and appropriate restrictions of extra-label drug use in food-producing animals.

In instances where extra-label drug use is allowed in food and companion animals, it is a vital tool that allows veterinarians to use animal and human medications labeled for certain indications for other clinical instances in which that therapy may be effective but for which it is not labeled.

Our veterinary medical education, clinical training, and understanding of the pharmaceutical products we use enable us to navigate these uncertain waters. But driving innovation and increasing the number of improved medications will ultimately lead to better patient care, especially in instances where extra-label drug use is prohibited.

Some diseases and conditions lack treatment options due to the extended course of the disease or the difficult nature of study.

Examples in which human drugs are used in an extra-label manner in animals include treatments for heart disease, pain management, gastrointestinal disorders, diabetes, immune-mediating diseases, and cancer.

While university studies, data collected in foreign countries, anecdotal evidence, and other alternative information all assist in selecting appropriate extra-label therapies, the knowledge that a drug used for therapy has been fully evaluated by the FDA and shown to be safe and effective is invaluable.

We have also been encouraged by recent attention given to the topic of expanding conditional approval beyond minor use and minor species. Extending its applicability to major uses and major species would increase the tools in a veterinarian's pharmaceutical tool box.

A greater number of approved animal drugs helps to ensure that veterinary patients receive the best care, and this is the goal of clinical veterinarians across the country.

So thank you for the opportunity to speak on this important topic today. We appreciate the attention the subcommittee is giving to this issue and the commitment to addressing the unmet needs in veterinary medicine.

Timely passage of this legislation is needed to continue programs that increase the availability of pharmaceutical resources in the treatment of animal diseases.

We look forward to working to increase the number of approved animal drugs for the benefit of our patients, their owners, and our communities.

Thank you again, and I am happy to answer any questions.
[The prepared statement of Dr. Topper follows:]

United States House of Representatives
Committee on Energy and Commerce
Subcommittee on Health

Hearing
“Reauthorization of Animal Drug User Fees 2018:
ADUFA and AGDUFA”

March 14, 2018

Testimony of
Michael J. Topper, DVM, PhD, DACVP
President, American Veterinary Medical Association

Introduction

Thank you, and good morning Chairman Burgess, Ranking Member Green, and Members of the Subcommittee. I am Dr. Mike Topper, President of the American Veterinary Medical Association. On behalf of the AVMA, I appreciate the opportunity to discuss the importance of reauthorizing the Animal Drug User Fee Act (ADUFA) and the Animal Generic Drug User Fee Act (AGDUFA).

Founded in 1863, the AVMA represents over 91,000 individual member veterinarians engaged in the many segments of professional veterinary medicine, including private practice, public health, biomedical research, and more. As an association, we are devoted to advancing the science and art of veterinary medicine and advocating on behalf of the veterinary profession.

Background and Support

The U.S. Food and Drug Administration Center for Veterinary Medicine's (FDA CVM) collection and effective utilization of drug sponsor user fees are important to veterinarians. By providing new animal drugs with a predictable pathway to market, these fees provide veterinarians with access to new and additional tools that can potentially improve treatment outcomes, provide alternatives to existing therapies, fill unmet medical needs in veterinary medicine, and ultimately improve patient care, which is the center of veterinary practice.

A drug that is approved by the FDA has been shown through rigorous studies to be safe and effective for its labeled indication. This gives the veterinarian confidence when selecting the drug for use in their patients. Unfortunately, there simply are not enough FDA approved drugs for use in animals. In fact, there are far fewer than there are approved for use in human medicine. With seven major species and innumerable minor species, all of which have many varied diseases and conditions to treat, veterinary access to FDA-approved medications for use in numerous diverse species is critical.

Each animal is different, and therapeutics that are used to treat dogs do not act exactly the same in cats, nor in horses, cattle, turkeys, parakeets, koi fish, or any other animal species. The inherent pharmacokinetic and pharmacodynamic differences in each species

provide very real hurdles to overcome in the treatment of our patients when there are few options with which to help them. Our veterinary medical education, clinical training, and understanding of the pharmaceutical products we use enable us to navigate these uncertain waters, but driving innovation and increasing the number of approved medications will ultimately lead to better patient care, especially in instances where extralabel drug use (ELDU) is prohibited.

The FDA defines “major species” as horses, dogs, cats, cattle, pigs, turkeys, and chickens. “Minor species” are all remaining animal species. A “minor use” in a major species is defined by FDA in regulation as a drug for a condition that occurs infrequently or in a limited geographic area and in only a small number of animals each year.

A small number of animals is defined by FDA in regulation as fewer than 50,000 horses; 70,000 dogs; 120,000 cats; 310,000 cattle; 1,450,000 pigs; 14,000,000 turkeys; and 72,000,000 chickens. These numbers translate to very small populations, and the availability of animal drugs to treat rare diseases in these limited populations is low.

A January 2018 review of FDA CVM’s Green Book and Orange Book that list approvals of animal drug products and human drug products, respectively, revealed the difference between the two is staggering. In fact, comparisons show there are twenty-three times as many approved labeled indications for human use than there are for animal use. The picture is equally dire for animal drug products approved for Minor Use and Minor Species (MUMS), a program modeled after the Orphan drug program. There have been approximately twenty-six times the number of approved label indications through the Orphan Drugs process as through the MUMS program. For all species treated by a veterinarian, most approved indications are for use in one of the seven major species, but these disparities highlight the need for more approved drug products for major uses, minor uses, and minor species. The lack of approved animal drug products limits treatment options in these patients.

Thankfully, through the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA) and its ELDU provision, veterinarians with a valid existing veterinarian-client-patient relationship (VCPR) are provided with greater prescribing options so that animals may receive treatment with therapeutics that are not labeled for that indication.

However, this is not a panacea for the lack of options that are labeled for use in animals. Veterinarians must use the safety and efficacy data available to them from veterinary literature, alternate sources, and extrapolate data from other studies, data from other medications, and data from human medicine.

To understand the unique needs of veterinarians and complicated nature of veterinary therapeutic options when there is no labeled drug available, an understanding of extralabel drug use is beneficial. Under the Federal Food, Drug, and Cosmetics Act, the FDA has the authority to regulate human and animal drugs. If a use is not indicated on the animal drug label, it is deemed unsafe by the FDCA unless it meets specific criteria for use under AMDUCA. ELDU is the term that describes the use of an approved drug in a manner that differs in any way from the drug's approved labeling. This includes deviations from FDA-approved labeling such as:

- In a species not listed on the label;
- For an indication not listed on the label;
- At a different dose or frequency than listed on the label; or
- Via a different route of administration than listed on the label.

It is easy to see that drug labels provide essential information to veterinarians.

AMDUCA appropriately allows ELDU only on the lawful order of a licensed veterinarian in the context of a valid VCPR. ELDU is also limited to circumstances when the health of the animal is threatened, or suffering or death may result from failure to treat. Further, many drugs are prohibited from ELDU for food-producing animals, and ELDU is prohibited in the feed of food-producing animals.

Because of the relative lack of approved animal drug products, ELDU as allowed under AMDUCA is a vital tool in veterinary medicine. It allows veterinarians to use medications that are approved for use in one species in another, or to use the treatment for one disease to treat a different or similar disease. Veterinarians often look to ELDU of approved animal drug products or approved human drug products to fill a void where there is no appropriate medication approved for that indication.

Understandably, there are necessary and appropriate restrictions on ELDU in food-producing animals that further limit treatment options. The production of safe and wholesome food from healthy animals raised in a healthful environment is part of a science-based food safety system, and some drugs are prohibited from use in these species entirely. In non-food animals, veterinarians are understandably allowed more flexibility and ELDU is permitted if there is no appropriate approved animal drug labeled for that indication. However, in these circumstances, veterinarians are still often left with minimal options to choose an appropriate medication.

For instance, there are few drugs approved for use in cats. In some circumstances, medicines that may be used freely in dogs cannot be used in cats because they are metabolized differently. Non-steroidal anti-inflammatory pain medications are one example. These medicines, while approved and commonly used in long-term treatment of our canine patients for osteoarthritis and other conditions, may have dire consequences when given long-term to our feline patients due to potentially harmful side effects. Theoretically, human pain medications could be used for pain management in an extralabel manner, except this is often medically inappropriate due to toxicity in both feline and canine species. This leaves many feline patients with no approved medication, and limited options for treatment via ELDU due to the dangerous side effects of these medications.

Many diseases and conditions, due to the extended course of disease, difficult nature of study, or difficulty in enrolling patients in clinical studies, also lack treatment options. There are many examples in which human drugs are used in an extralabel manner in animals, including treatments for heart disease, pain management, gastrointestinal disorders, diabetes, behavioral conditions, immune-mediated diseases and disorders, and neoplasia. While university studies, anecdotal evidence gathering, and other alternative information all assist in selecting appropriate extralabel therapies, the knowledge that a drug used for therapy has been evaluated by the FDA and shown to be safe and effective is invaluable.

For these reasons, the AVMA supports user fees for new animal drug applications when the fees are directed toward expediting the review and approval process for animal drug

products. The bipartisan and bicameral discussion draft text circulated by the Committee would accomplish this objective.

To ensure adequate availability of veterinary drugs, the AVMA prefers to see Congressional funding of the FDA Center for Veterinary Medicine for the New Animal Drug Application approval process indexed to keep pace with cost increases. However, we recognize that user fees are a valuable tool to expedite the review of new animal drug applications, which ultimately puts new animal drugs in the hands of veterinary practitioners to apply to their daily practice.

We appreciate the attention Congress is giving to this legislation to reauthorize user fees and provide veterinarians with more important tools with which to treat their patients. We feel that more work is needed to attain the program's ultimate goal of more and expedited drug approvals.

Further, we have been encouraged by recent attention given to the topic of expanding Conditional Approval beyond minor uses and minor species. Extending its applicability to major uses and major species would increase the number of tools in a veterinarian's pharmaceutical toolbox. A greater number of approved animal drugs helps to ensure that veterinary patients receive the best care, which is the ultimate goal of clinical veterinarians across the country.

Conclusion

Thank you for the opportunity to provide testimony on this important topic today. We appreciate the attention the Subcommittee is giving to this issue and the commitment to addressing the unmet needs in veterinary medicine. We look forward to working with the Committee and FDA CVM to increase the number of approved animal drugs for the benefit of our patients, their owners, and our communities. Thank you again, and I am happy to answer any questions.

Mr. BURGESS. Thank you, Dr. Topper, and I want to thank each of you for your testimony, and we'll move into the second round of questions from Members. Let me begin by recognizing myself for 5 minutes.

And let me just ask in a very general sense—and I will ask it to each of you—how the adoption of the user fees, going back to their initiation, how does it fundamentally change the industry?

So I realize that's pretty broad, and you have already addressed that to some degree. But give me the sound bite, and Dr. Cumberbatch, we'll start with you and then we'll come down the line.

Dr. CUMBERBATCH. Thank you very much for the question.

The user fee programs has helped with consistency. Sponsors now know when they will hear back from FDA. Also, as Dr. Solomon mentioned, it has allowed them to hire and to increase the number of reviewers, which has been very important for helping them meet the goals of the time lines.

Thank you.

Mr. BURGESS. Yes, Dr. Zollers.

Dr. ZOLLERS. Yes. As Dr. Solomon indicated, on the generic side of things, we've seen a tremendous increase in workload on the CVM side, and I think that in itself talks to the success of the user fee program.

Ten years ago, when we had 2-year review cycles and we had 12 or 14 members of GADA at that time, and now today we have 270-day review cycles, an increased workload, and over 30 members of GADA. So that is all indicative of the growth of our industry.

Mr. BURGESS. Dr. Topper.

Dr. TOPPER. Yes, sir. I agree with my colleagues. It has really helped in bringing new animal drugs to the market faster, and we need to continue with this because that's what our patients need.

Mr. BURGESS. So, now, we've been through—I guess this is the fourth iteration for the animal drug user fee and the third for the generic animal drug user fee.

How has that evolved over time? Do you think that is something where we've been able to build on the previous levels and increase the availability and timeliness of products?

And, again, Dr. Cumberbatch, we'll start with you and then come down the line.

Dr. CUMBERBATCH. Thank you.

In ADUFA I we began with decreasing the backlog, and now we are moved on to looking at how we can improve efficiency. From here, we will look at how communication can be improved and work towards ADUFA goals not just during negotiations for this agreement but all through the 5-year agreement and able to work together to look at how do we best review products and ultimately get additional tools for veterinarians onto the market.

Mr. BURGESS. Yes, Dr. Zollers.

Dr. ZOLLERS. Yes, I would agree with a lot of what Rachel just said.

Again, for AGDUFA I, getting through that shock and awe of the 2-year review cycle and now getting it down to something manageable, now we are focused on how do we reduce the timeframe from the time we initiate the project until it's actually approved.

And we are having very good conversations and good communication with CVM throughout this process, and we'll continue to so we can try to improve this process even more before we get to AGDUFA IV 5 years from now.

Mr. BURGESS. Yes, sir. Dr. Topper.

Dr. TOPPER. And, yes, sir, we have been building up all along, and we look forward to this new one building even better, moving things faster, and if we build different things into this, as we heard earlier, it'll just make it better.

Mr. BURGESS. To that end—and we'll start with you this time, Dr. Topper, and move back the other way. The electronic submission—do you see that as being—ultimately that's going to be helpful, correct?

Dr. TOPPER. Yes, sir. It should speed it up. It should decrease the cost to somebody who's providing, because it's electronic and they don't have to back up that truckload or send a computer or a hard drive in.

So it will be readily available to the reviewers, and they will not have to transcribe it from paper to their own electronic means.

Mr. BURGESS. Dr. Zollers.

Dr. ZOLLERS. Yes. We are totally in favor of the electronic system.

Mr. BURGESS. Dr. Cumberbatch.

Dr. CUMBERBATCH. As Dr. Solomon mentioned, a majority of sponsors of pioneer drugs use the electronic submission system already.

What we do see is a need to look at the efficiency—how much data are we putting in. Electronic submissions are very helpful for CVM in getting those to the reviewers.

What we are trying to find is a good way for sponsors to be able to get this information in an efficient way.

Mr. BURGESS. Well, I want to thank each of you for your testimony today, and Dr. Topper, in your testimony you talked about, you know, kind of the differences between humans and animals, having spent a lifetime in practicing medicine, to think that you have got those—both the major and minor classes of animals to consider.

You give the anti-inflammatory that you gave to your dog to your cat, and you're in big trouble. I am sensitive to the problems that you face, and we want you to be able to do your best work. So thank you each for testifying today.

Mr. Green, I will recognize you for 5 minutes for questions, please.

Mr. GREEN. Thank you, Mr. Chairman. I hope you didn't have any patients that would bite you.

[Laughter.]

Mr. BURGESS. How much time do you have?

[Laughter.]

Mr. GREEN. He was an OB/GYN. Thank you, Mr. Chairman.

Dr. Topper, I am interested in your perspective as a veterinarian on the use of antimicrobials in food-producing animals and the growing public health concerns regarding antimicrobial resistance.

I understand that the use of the medically important antimicrobial drugs in treating food-producing animals is necessary,

but I also have concern over the overuse and what steps both the FDA and the animal health providers should be taking to reduce the risks of resistance.

Can you explain how these antimicrobial resistance happens and what impact it can have on both the animal and human health?

Dr. TOPPER. Yes, sir. I can talk to the first part, for sure, about how the AVMA along with other of our colleagues are very much concerned about antimicrobial resistance, and we are taking as many steps for our members and providing them with information about the judicious use of antimicrobials, as you heard Dr. Solomon talk about, and we have just developed a stewardship for our members to follow in looking at these.

So we have been taking an active role in working with the Centers for Veterinary Medicine for the veterinary fee directive so that all antimicrobials that are put in food have to be under the direction of a veterinarian-client-patient relationship and they have to have that fee directive.

Most of the other veterinarians, we know through their judicious use of the antimicrobials, they are working to reduce the number that are being used. So we support that.

To talk about how antimicrobial resistance happens would probably be a lot longer than we would have here. And so we can probably provide you with plenty of literature as to how that antimicrobial resistance occurs. But I am not ready to talk about it at this time, if that's OK.

Mr. GREEN. How has greater data collection improved veterinarian awareness regarding the overuse of the antimicrobial drugs, and what additional steps should the FDA be taking to address the concerns?

Dr. TOPPER. Well, the FDA is monitoring. We do the residue, like Dr. Solomon talked about, during the formulation and the approval process of the drug. They have to be able to detect it in the meat products. And so, as they approve those methods, that will help detect the antimicrobial uses, as they go forward.

Mr. GREEN. OK. Do you know what the American Veterinarian Medical Association is doing to educate its members on the importance of addressing these antimicrobial resistances, and how can veterinarians be good stewards of antimicrobials when treating food-producing animals?

Dr. TOPPER. Yes, sir. Like I said, we do have and along with our industry partners—that's the bovine practitioners, the swine veterinarians, and the avian pathologists—have developed therapeutic guidelines for the judicious use of antibiotics, and we have just approved in our AVMA's house of delegates our stewardship policy and the core principles of antibiotic use.

So we are very much educating our members, and they do understand that there is this great need in public health.

Mr. GREEN. Well, part of our other jurisdiction on this committee is the need to do medical research and looking at the next, you know, vaccinations, the next treatment, because we do have a growing resistance of—both in humans and I was going to see if that happens with animals—that you use these antimicrobials and then over a period of time they develop a resistance to them. Does that happen in animals as well as we see in humans?

Dr. TOPPER. Yes, sir, it does happen in animals also. Again, as we talked about, different species react to different antibiotics in different ways. So it is a problem in animals also.

Mr. GREEN. And the concern about growing antimicrobial resistance is a real one and further compounded by the need for the development of new antibiotics and will still be effective in the face of the resistance, and I hope we continue to work closely with the CVM and the CDR to ensure that safe and effective antibiotics are available when needed.

Dr. TOPPER. Yes, sir.

Mr. GREEN. Mr. Chairman, I will yield back my time.

Mr. BURGESS. Chair thanks the gentleman. Gentleman yields back.

Chair recognizes the gentleman from Oklahoma, 5 minutes for your questions, please.

Mr. MULLIN. Thank you, Mr. Chairman, and I want to thank the panel for the great work and the time and dedication you have spent to bring us to this point.

Working with the agency and industry I know is no easy task. But that's how we—as you can see, that's the best way, the easiest way for us to move forward with any type of legislation. So thank you both—everybody for being here.

Dr. Cumberbatch, I want to ask you a question. Can you explain the difference between the animal market and the human drug market and elaborate on some of the differences and the challenges that we face?

Dr. CUMBERBATCH. Absolutely. Thank you.

You know, as Dr. Solomon said, size is one of the differences in the animal market and the human market. Also, as a veterinarian, when I talk about a treatment protocol, price has to be one of the topics that we talk about and what the availability is of the medication and what my expectation is as a veterinarian that this is going to work for your particular situation.

And it is important to have very good data so that I can share that with an animal owner, and that is why it's important to have new, innovative, well-studied drugs on the market for veterinarians to use.

Mr. MULLIN. So what do you think are some of the unmet needs that are in the animal market that we need to try to address?

Dr. CUMBERBATCH. We've had the opportunity to hear about a number, but osteoarthritis is one that I know we see every day. I hear stories where the cat's hiding under the bed or "My dog doesn't want to play ball anymore—he seems more tired," or "My horse won't jump."

You know, these seem like changes in behavior, but that's sometimes pain, and it's—osteoarthritis can happen over a period of time, and it's difficult to study because it does take that time.

In cattle, we have chronic diseases as well like Johne's disease that eventually is fatal, and most importantly, it decreases production and can spread throughout a herd, and that's devastating to our small farmers.

Mr. MULLIN. Well, as a cattle owner, which—you know, I don't think we could quite make a living off our cattle because I still

think the fastest way to become a millionaire running cattle is start with two million—you will get to a million.

[Laughter.]

But I am glad I have other things that can help offset the ranch. But it's still a way of life. It's the way I was raised. It's the way we raise our kids.

You know, the biggest traffic jam coming out of our house is usually the cattle that want to, for some reason, hang around the driveway and use the bathroom on it. But that's a whole another thing.

But there are issues that we run about—my colleague from Texas was talking about the antibiotics and the overuse of it.

But there has to be a common area that's reached here, because I can tell you personally in our experience—and I am surrounded by other cattle owners—when we took away the ability to actually buy medicated feed, it actually cost the consumers more and, in my opinion, can be even more devastating, moving forward, because unlike children, you're not out there watching your cattle necessarily every day on a one-on-one basis.

When you buy cattle out of a stockyard or a sale barn, you buy a trailer full of them. Before you mix them into your herd, you want to be able to make sure that they've not carrying something that is going to infect the herd.

We've seen an increase, especially in my area this year, because we have such high swings with temperatures from low to high, with pneumonia coming in.

And used to, when we would bring our cattle back from the barns, which it is very common for them to develop a cough, as you guys are aware of, or a runny nose, we could catch a lot of that before we'd turn them out into the pastures, because we would feed them some medicated feed.

Now we are running into a situation where we have a choice. Instead of sending them just medicated feed, which we are not going to overuse because it's too expensive to use all the time, we have to vaccinate them to be preemptive on this by having to give them a shot that they may not need or we take the chance of infecting the entire herd.

So which one is—as us, which one do we decide to do? It's very expensive to sit there and time consuming to give everybody a shot when you're buying them in pot bellies—which pot bellies, by the way, for us are those big trailers—and you're dumping them to the lot.

So when we are having this conversation about overmedicating, I understand the concerns—me too. But there has to be some common area to work with. And so, while we've been working with the panel, make sure you're not leaving out the stakeholders like myself or other cattle producers or the stockyards, because I know you have been hearing from the stockyards on this, too.

So I want to work, moving forward, with this. But I don't know that what we've done right now is the right approach.

So with that, Mr. Chairman, I will yield back.

Mr. BURGESS. Gentleman yields back. Chair thanks the gentleman.

Chair recognizes the gentleman from Oregon, Dr. Schrader, 5 minutes for your questions, please.

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

I will kind of jump on Markwayne's discussion a little bit, because I think there's a lot of misinformation out there over the use of antimicrobials and their contribution to human resistance to drugs.

There certainly could be a factor. I spent a lot of time reading a lot of the studies that have been generated since the '70s, and there's lots of inference but no study that I've seen there's any direct causation.

That doesn't mean we shouldn't be judicious or smart about how we use antimicrobials in veterinary medicine or on the ranch.

I think every one of us wants to do the right thing, and I would applaud the CVM's recent suggestions that, you know, in certain situations when there is the right climatic conditions or whatever that, under proper veterinary supervision, that certain therapeutic uses of antimicrobials could be used on a mass basis to prevent more disease and, frankly, suffering to these animals that Markwayne and others raise on our farms and ranches.

So I just want us to be cognizant of that, and I will tell you this: In my veterinary practice there were times when, if I did not use an antimicrobial at the appropriate time, that the disease spread would have been much bigger, and there was also a chance for a virulence to increase and these animals—or these bugs, if you will—to mutate and go stronger yet.

And to my good colleague from Texas, the real world of resistance is called biology. You know, if you ever watched "Jurassic Park"—might have been a fun movie, but one thing that is absolutely true there is the real-world plants and animals mutate over time. That could be for good things, and it could also be for bad things.

So whether or not we get engaged at all in trying to prevent that, things are still going to change. We should do our best to, you know, fight resistance in the ways we can.

But it's going to happen anyway, and that's why drug innovation—the whole hearing we are having here today for our animal friends—speed these things to marketplace, because we are going to need ever newer and smarter ways to treat these animals, whether it's on an anti-inflammatory, antimicrobial side.

So ending my soliloquy here, Dr. Topper, do you see expanding conditional approval as negatively affecting FDA safety and efficacy standards in any way?

Dr. TOPPER. No, sir, because, like Dr. Solomon said, they will be doing this all along, and it will just get some of these drugs that are right now maybe out on extra-label drug use. But we still have that great unmet medical need, and this will help very much if this is added to the bill.

Mr. SCHRADER. I would agree.

Talking about extra-label use, a little different than conditional use. How do the two processes work in synergy, or how are they different?

Dr. TOPPER. I will do my best, to my knowledge of them. The extra-label drug use, again, are approved drugs that are already on

the market. They have met FDA efficacy. They may be for humans or they may be for another animal species. So, hopefully, they were safe in that species.

This conditional would be specific for the species intended for use. So it would then have the same safety studies done for that species, and the efficacy would be increased upon as time goes along.

So the difference would be that it will be—in my knowledge that it would be for the species intended for use and not just using something approved for a different—

Mr. SCHRADER. And to your earlier comments, it's just another tool in the toolbox for enabling veterinarians who, again, the market—real-world marketplace—cost matters. Dr. Zollers, say, can't yet take advantage of all these great new drugs necessarily that are coming out.

I think it was the chairman and others indicated or you had indicated earlier, you know, 23 human products for every veterinary product that's developed out there.

So this is just a great way, a safe way, an efficacious way for veterinarians to have access, hopefully, to some of the same opportunities that we do in the human field, and I would argue that our food safety is critical to human safety—the whole public health aspect that Dr. Cumberbatch talked about.

Dr. Cumberbatch, if I could come to you. You know, again, we talked earlier about very few conditional approvals have even been requested, much less granted at this time.

From your standpoint—maybe Dr. Zollers, if you have an opinion on this—you know, what are the barriers? Is it just familiarity with this new process, or are there some barriers, given some of these companies are pretty small?

Dr. CUMBERBATCH. Thank you, Dr. Schrader.

You know, right now conditional approval is for minor use, minor species, and by definition that is a very small market.

And so, by expanding this, it would allow companies to bring forward products to a bigger market for that unmet need and in no way would this be taking away or preventing companies from coming forward and still utilizing MUMS as it currently is.

Mr. SCHRADER. All right. Dr. Zollers, if I may, real quick.

Dr. ZOLLERS. Yes. I would just say right now small companies—it comes down to how much money can they make in revenue, can they make with this process, and a lot of them, a lot of times these just don't pan out.

Mr. SCHRADER. Got you.

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

Mr. BURGESS. Chair thanks the gentleman. Gentleman yields back.

Chair recognizes the gentleman from Georgia, 5 minutes for your questions, please.

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

Dr. Cumberbatch, I will start with you. Earlier, when Dr. Solomon was here, they asked him about the process by which the new animal drug application process and how thorough it was and

how much information that the drug manufacturers had to submit along with a new animal drug application.

And I just wanted to ask you, from your perspective, do you think that's an impediment for new animal drug breakthroughs in any way, that it's so detailed and so, for lack of a better word, so laborious?

Dr. CUMBERBATCH. Bringing a new product to market takes time. It takes investment. In fact, we have a survey that shows that it can take up to 10 years and \$100 million to bring a product to market.

Now, as we were talking about with Congressman Mullin, as well, at the end of the day it comes down to what can an animal owner pay for this. These products need to be at a reasonable price point, as well.

And so, yes, having a long review, an expensive review, ultimately can hinder our ability to get new products onto the market.

Mr. CARTER. So you do believe that perhaps just a different level of data might be sufficient and still provide the protection that we need and—because there is a balancing act, we all know there, and, quite honestly, from my perspective, FDA, a lot of times, has—not just FDA but all of Federal agencies have the tendency to overreact sometimes and overrequire.

So is it your feeling that it could be done safely with less information?

Dr. CUMBERBATCH. We are committed to working with FDA to look at those efficiencies while making sure that we maintain safety and quality in the products.

Mr. CARTER. Mr. Chairman, we don't have any kind of abbreviated like we do with the drug approvals—we don't have any kind of abbreviated application in this area, do we?

Mr. BURGESS. In the generic space, you certainly do.

Mr. CARTER. In the generic space for animal control?

Mr. BURGESS. Yes.

Mr. CARTER. We do? OK. But not for the new drugs, and obviously that wouldn't work as well.

Let me ask you, Dr. Cumberbatch—I will start with you. From what I understand, the electronic submission that the applications are going to have to be submitted electronically starting on October of 2018—do you think you're all going to be prepared for that? Are you ready for that? Is that sufficient time?

Dr. CUMBERBATCH. The pioneer companies have been utilizing the e-submitter, and so I am confident, yes, AHI members will be ready for that transition.

Mr. CARTER. Any recommendations in that process that, you know, thus far you having input into that process?

Dr. CUMBERBATCH. The communication is key. Developing the templates that they use for the e-submission. The time that it would take for a sponsor to put the data in that they collect is important. It adds to that time and that administrative burden.

And so increased communication, working together on what those templates look like. They have also hoped to provide webinars and training. These are all very important.

Mr. CARTER. Great.

Dr. Topper, just very quickly I wanted to ask you—you know, one of the concerns and certainly one of the experiences I had as a practicing pharmacist was the price of some of these medications, particularly for the companion animals and, you know, unlike human patients where you have insurance and have a co-pay, you know, there is no insurance or co-pay for these animals and for these types of drugs particularly.

Is there anything that you can really recommend that manufacturers might be able to do to lower the cost of some of these medications besides take a cut in profit?

Dr. TOPPER. Well, you raise a very difficult issue, and it's a complex issue. To ensure that the drugs are safe and efficacious, then they have to go through this process.

So anything we can do to speed up the process and make it more efficient, hopefully, will result in drug-lowering costs and, especially as the drugs move to generic types, then that should lower the cost also. But it's complicated, as we know, even in human medicine.

Mr. CARTER. Great. Well, I thank all of you for being here. It's been a very interesting hearing today.

Thank you, Mr. Chairman. I yield back.

Mr. BURGESS. Gentleman yields back. The Chair thanks the gentleman.

Seeing no additional Members wishing to ask questions, Mr. Green, did you have anything on redirect?

Mr. GREEN. No, Mr. Chairman. I think the job's been done, but I do have some concerns because our next half will be trying to find, you know, some of the solutions for the drug resistance we have. But appreciate the efforts.

Mr. BURGESS. Very well.

Again, seeing no further Members wishing to ask questions, I want to thank our witnesses for being here today. I would like to submit statements from the following for the record: the Agriculture Value Chain Coalition.

Pursuant to committee rules, I remind Members they have 10 business days to submit additional questions for the record. I ask that witnesses submit their response within 10 business days upon receipt of those questions.

And without objection, the subcommittee is adjourned.

[Whereupon, at 12:20 p.m., the committee was adjourned.]

[Material submitted for inclusion in the record follows:]

.....
 (Original Signature of Member)

115TH CONGRESS
 2D SESSION

H. R. _____

To amend the Federal Food, Drug, and Cosmetic Act to reauthorize user fee programs relating to new animal drugs and generic new animal drugs.

 IN THE HOUSE OF REPRESENTATIVES

M. _____ introduced the following bill; which was referred to the
 Committee on _____

A BILL

To amend the Federal Food, Drug, and Cosmetic Act to reauthorize user fee programs relating to new animal drugs and generic new animal drugs.

1 *Be it enacted by the Senate and House of Representa-*
 2 *tives of the United States of America in Congress assembled,*

3 **SECTION 1. SHORT TITLE.**

4 This Act may be cited as the “Animal Drug and Ani-
 5 mal Generic Drug User Fee Amendments of 2018”.

6 **SEC. 2. TABLE OF CONTENTS; REFERENCES IN ACT.**

7 (a) TABLE OF CONTENTS.—The table of contents for
 8 this Act is as follows:

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- Sec. 1. Short title.
 Sec. 2. Table of contents; references in Act.

TITLE I—FEES RELATING TO ANIMAL DRUGS

- Sec. 101. Short title; finding.
 Sec. 102. Definitions.
 Sec. 103. Authority to assess and use animal drug fees.
 Sec. 104. Reauthorization; reporting requirements.
 Sec. 105. Savings clause.
 Sec. 106. Effective date.
 Sec. 107. Sunset dates.

TITLE II—FEES RELATING TO GENERIC ANIMAL DRUGS

- Sec. 201. Short title; finding.
 Sec. 202. Authority to assess and use generic new animal drug fees.
 Sec. 203. Reauthorization; reporting requirements.
 Sec. 204. Savings clause.
 Sec. 205. Effective date.
 Sec. 206. Sunset dates.

TITLE III—MISCELLANEOUS PROVISIONS

- Sec. 301. Electronic submissions.
 Sec. 302. Index of legally marketed unapproved new animal drugs for minor species.
 Sec. 303. Misbranded drugs and devices.

1 (b) REFERENCES IN ACT.—Except as otherwise spec-
 2 ified, amendments made by this Act to a section or other
 3 provision of law are amendments to such section or other
 4 provision of the Federal Food, Drug, and Cosmetic Act
 5 (21 U.S.C. 301 et seq.).

6 TITLE I—FEES RELATING TO 7 ANIMAL DRUGS

8 SEC. 101. SHORT TITLE; FINDING.

9 (a) SHORT TITLE.—This title may be cited as the
 10 “Animal Drug User Fee Amendments of 2018”.

11 (b) FINDING.—Congress finds that the fees author-
 12 ized by the amendments made in this title will be dedi-
 13 cated toward expediting the animal drug development

1 process and the review of new and supplemental animal
2 drug applications and investigational animal drug submis-
3 sions as set forth in the goals identified for purposes of
4 part 4 of subchapter C of chapter VII of the Federal Food,
5 Drug, and Cosmetic Act, in the letters from the Secretary
6 of Health and Human Services to the Chairman of the
7 Committee on Energy and Commerce of the House of
8 Representatives and the Chairman of the Committee on
9 Health, Education, Labor, and Pensions of the Senate as
10 set forth in the Congressional Record.

11 **SEC. 102. DEFINITIONS.**

12 Section 739 (21 U.S.C. 379j-11) is amended—

13 (1) by amending paragraph (1) to read as fol-
14 lows:

15 “(1)(A) The term ‘animal drug application’
16 means—

17 “(i) an application for approval of any new
18 animal drug submitted under section 512(b)(1);
19 or

20 “(ii) an application for conditional ap-
21 proval of a new animal drug submitted under
22 section 571.

23 “(B) Such term does not include either a new
24 animal drug application submitted under section

1 512(b)(2) or a supplemental animal drug applica-
 2 tion.”; and

3 (2) in paragraph (8), by adding at the end the
 4 following:

5 “(I) The activities necessary for implemen-
 6 tation of the United States and European
 7 Union Good Manufacturing Practice Mutual In-
 8 spection Agreement with respect to animal drug
 9 products subject to review, including implemen-
 10 tation activities prior to and following product
 11 approval.”.

12 **SEC. 103. AUTHORITY TO ASSESS AND USE ANIMAL DRUG**
 13 **FEES.**

14 (a) FEE REVENUE AMOUNTS.—Section 740(b) (21
 15 U.S.C. 379j–12(b)) is amended—

16 (1) in paragraph (1)—

17 (A) in subparagraph (A)—

18 (i) by striking “2014” and inserting
 19 “2019”; and

20 (ii) by striking “\$23,600,000” and in-
 21 serting “\$30,331,240”; and

22 (B) in subparagraph (B)—

23 (i) by striking “2015 through 2018”
 24 and inserting “2020 through 2023”; and

1 (ii) by striking “\$21,600,000” and in-
2 serting “\$29,931,240”; and

3 (2) in paragraph (2), in the matter preceding
4 subparagraph (A), by striking “determined” and in-
5 serting “established”.

6 (b) ANNUAL FEE SETTING; ADJUSTMENTS.—

7 (1) INFLATION ADJUSTMENT.—Section
8 740(e)(2) (21 U.S.C. 379j–12(e)(2)) is amended—

9 (A) in the matter preceding subparagraph
10 (A)—

11 (i) by striking “For fiscal year 2015”
12 and inserting “(A) For fiscal year 2020”;
13 and

14 (ii) by inserting “multiplying such
15 revenue amounts by” before “an amount”;

16 (B) by redesignating subparagraphs (A),
17 (B), and (C) as clauses (i), (ii), and (iii), re-
18 spectively;

19 (C) by striking the flush text at the end;
20 and

21 (D) by adding at the end the following new
22 subparagraph:

23 “(B) COMPOUNDED BASIS.—The adjustment
24 made each fiscal year after fiscal year 2020 under
25 this paragraph shall be applied on a compounded

1 basis to the revenue amount calculated under this
2 paragraph for the most recent previous fiscal year.”.

3 (2) WORKLOAD ADJUSTMENTS.—Paragraph (3)
4 of section 740(c) (21 U.S.C. 379j–12(e)) is amended
5 to read as follows:

6 “(3) WORKLOAD ADJUSTMENTS.—

7 “(A) IN GENERAL.—For fiscal year 2020
8 and subsequent fiscal years, after the fee rev-
9 enue amounts established under subsection (b)
10 are adjusted for inflation in accordance with
11 paragraph (2), the fee revenue amounts shall be
12 further adjusted for such fiscal year to reflect
13 changes in the workload of the Secretary for
14 the process for the review of animal drug appli-
15 cations, subject to subparagraphs (B) and (C).

16 With respect to such adjustment—

17 “(i) such adjustment shall be deter-
18 mined by the Secretary based on a weight-
19 ed average of the change in the total num-
20 ber of animal drug applications, supple-
21 mental animal drug applications for which
22 data with respect to safety or effectiveness
23 are required, manufacturing supplemental
24 animal drug applications, investigational
25 animal drug study submissions, and inves-

1 tigational animal drug protocol submis-
2 sions submitted to the Secretary; and

3 “(ii) the Secretary shall publish in the
4 Federal Register the fees resulting from
5 such adjustment and the supporting meth-
6 odologies.

7 “(B) REDUCTION OF WORKLOAD-BASED
8 INCREASE BY AMOUNT OF CERTAIN EXCESS
9 COLLECTIONS.—For each of fiscal years 2021
10 through 2023, if application of the workload ad-
11 justment under subparagraph (A) increases the
12 fee revenue amounts otherwise established for
13 the fiscal year under subsection (b), as adjusted
14 for inflation under paragraph (2), such fee rev-
15 enue increase shall be reduced by the amount of
16 any excess collections, as described in sub-
17 section (g)(4), for the second preceding fiscal
18 year, up to the amount of such fee revenue in-
19 crease.

20 “(C) RULE OF APPLICATION.—Under no
21 circumstances shall the workload adjustments
22 under this paragraph result in fee revenues for
23 a fiscal year that are less than the fee revenues
24 for that fiscal year established under subsection

1 (b), as adjusted for inflation under paragraph
2 (2).”.

3 (3) FINAL YEAR ADJUSTMENT.—Section
4 740(c)(4) (21 U.S.C. 379j–12(c)(4)) is amended—

5 (A) by striking “2018” each place it ap-
6 pears and inserting “2023”; and

7 (B) by striking “2019” and inserting
8 “2024”.

9 (c) EXEMPTION FROM FEES.—Section 740(d) (21
10 U.S.C.379j–12(d)) is amended—

11 (1) in the subsection heading, by inserting “;
12 EXEMPTION FROM FEES” after “REDUCTION”;

13 (2) by striking the heading of paragraph (1)
14 and inserting “WAIVER OR REDUCTION”; and

15 (3) by adding at the end the following:

16 “(4) EXEMPTIONS FROM FEES.—

17 “(A) CERTAIN LABELING SUPPLEMENTS
18 TO ADD NUMBER OF APPROVED APPLICA-
19 TION.—Fees under this section shall not apply
20 with respect to any person who—

21 “(i) not later than September 30,
22 2023, submits a supplemental animal drug
23 application relating to a new animal drug
24 application approved under section 512,
25 solely to add the new animal drug applica-

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9

1 tion number to the labeling of the drug in
2 the manner specified in section 502(w)(3);
3 and

4 “(ii) otherwise would be subject to
5 fees under this section solely on the basis
6 of such supplemental application.

7 “(B) CERTAIN ANIMAL DRUG APPLICA-
8 TIONS.—Fees under paragraphs (2), (3), and
9 (4) of subsection (a) shall not apply with re-
10 spect to any person who is the named applicant
11 or sponsor of an animal drug application, sup-
12 plemental animal drug application, or investiga-
13 tional animal drug submission if such applica-
14 tion or submission involves the intentional
15 genomic alteration of an animal that is in-
16 tended to produce a drug, device, or biological
17 product subject to fees under section 736, 738,
18 744B, or 744H.”.

19 (d) CREDITING AND AVAILABILITY OF FEES.—

20 (1) AUTHORIZATION OF APPROPRIATIONS.—
21 Section 740(g)(3) (21 U.S.C.379j–12(g)(3)) is
22 amended—

23 (A) by striking “2014 through 2018” and
24 inserting “2019 through 2023”;

1 (B) by striking “determined” and inserting
 2 “established”; and

3 (C) by striking “paragraph (4)” and in-
 4 serting “paragraph (5)”.

5 (2) EXCESS COLLECTIONS.—Section 740(g) (21
 6 U.S.C.379j-12(g)) is amended by striking paragraph
 7 (4) and inserting the following:

8 “(4) EXCESS COLLECTIONS.—If the sum total
 9 of fees collected under this section for a fiscal year
 10 exceeds the amount of fees authorized to be appro-
 11 priated for such year under paragraph (3), the ex-
 12 cess collections shall be credited to the appropria-
 13 tions account of the Food and Drug Administration
 14 as described in paragraph (1).

15 “(5) RECOVERY OF COLLECTION SHORT-
 16 FALLS.—

17 “(A) IN GENERAL.—Subject to subpara-
 18 graph (B)—

19 “(i) for fiscal year 2021, the amount
 20 of fees otherwise authorized to be collected
 21 under this section shall be increased by the
 22 amount, if any, by which the amount col-
 23 lected under this section and appropriated
 24 for fiscal year 2019 falls below the amount

1 of fees authorized for fiscal year 2019
2 under paragraph (3);

3 “(ii) for fiscal year 2022, the amount
4 of fees otherwise authorized to be collected
5 under this section shall be increased by the
6 amount, if any, by which the amount col-
7 lected under this section and appropriated
8 for fiscal year 2020 falls below the amount
9 of fees authorized for fiscal year 2020
10 under paragraph (3); and

11 “(iii) for fiscal year 2023, the amount
12 of fees otherwise authorized to be collected
13 under this section shall be increased by the
14 cumulative amount, if any, by which the
15 amount collected under this section and
16 appropriated for fiscal years 2021 and
17 2022 (including estimated collections for
18 fiscal year 2022) falls below the cumulative
19 amount of fees authorized for such fiscal
20 years under paragraph (3).

21 “(B) REDUCTION OF SHORTFALL-BASED
22 FEE INCREASE BY PRIOR YEAR EXCESS COL-
23 LECTIONS.—

24 “(i) IN GENERAL.—Subject to clause
25 (ii), the Secretary shall, in such manner as

1 the Secretary determines appropriate, re-
2 duce any fee increase otherwise applicable
3 for a fiscal year under subparagraph (A)
4 by the amount of any excess collections
5 under this section for preceding fiscal
6 years (after fiscal year 2018).

7 “(ii) WORKLOAD-BASED FEE AC-
8 COUNTING.—In applying clause (i), the
9 Secretary shall account for the reduction of
10 workload-based fee revenue increases by
11 excess collections under subsection
12 (c)(3)(B), in such manner as needed to
13 provide that no portion of any excess col-
14 lections described in clause (i) is applied
15 for purposes of reducing fee increases
16 under both such subsection (c)(3)(B) and
17 this paragraph.

18 “(C) RULE OF APPLICATION.—Under no
19 circumstances shall adjustments under this
20 paragraph result in fee revenues for a fiscal
21 year that are less than the fee revenues for that
22 fiscal year established in subsection (b), as ad-
23 justed or otherwise affected under subsection
24 (c).”.

1 **SEC. 104. REAUTHORIZATION; REPORTING REQUIREMENTS.**

2 Section 740A (21 U.S.C. 379j-13) is amended—

3 (1) in subsection (a), by striking “2013” and
4 inserting “2018”;

5 (2) by striking “2014” each place it appears in
6 subsections (a) and (b) and inserting “2019”; and

7 (3) in subsection (d), by striking “2018” each
8 place it appears and inserting “2023”.

9 **SEC. 105. SAVINGS CLAUSE.**

10 Notwithstanding the amendments made by this title,
11 part 4 of subchapter C of chapter VII of the Federal Food,
12 Drug, and Cosmetic Act (21 U.S.C. 379j-11 et seq.), as
13 in effect on the day before the date of enactment of this
14 title, shall continue to be in effect with respect to animal
15 drug applications and supplemental animal drug applica-
16 tions (as defined in such part as of such day) that on or
17 after October 1, 2013, but before October 1, 2018, were
18 accepted by the Food and Drug Administration for filing
19 with respect to assessing and collecting any fee required
20 by such part for a fiscal year prior to fiscal year 2019.

21 **SEC. 106. EFFECTIVE DATE.**

22 The amendments made by this title shall take effect
23 on October 1, 2018, or the date of the enactment of this
24 Act, whichever is later, except that fees under part 4 of
25 subchapter C of chapter VII of the Federal Food, Drug,
26 and Cosmetic Act, as amended by this title, shall be as-

1 sessed for animal drug applications and supplemental ani-
2 mal drug applications received on or after October 1,
3 2018, regardless of the date of the enactment of this Act.

4 **SEC. 107. SUNSET DATES.**

5 (a) AUTHORIZATION.—Section 740 of the Federal
6 Food, Drug, and Cosmetic Act (21 U.S.C. 379j–12) shall
7 cease to be effective October 1, 2023.

8 (b) REPORTING REQUIREMENTS.—Section 740A of
9 the Federal Food, Drug, and Cosmetic Act (21 U.S.C.
10 379j–13) shall cease to be effective January 31, 2024.

11 (c) PREVIOUS SUNSET PROVISION.—Effective Octo-
12 ber 1, 2018, subsections (a) and (b) of section 107 of the
13 Animal Drug User Fee Amendments of 2013 (Public Law
14 113–14) are repealed.

15 **TITLE II—FEES RELATING TO**
16 **GENERIC ANIMAL DRUGS**

17 **SEC. 201. SHORT TITLE; FINDING.**

18 (a) SHORT TITLE.—This title may be cited as the
19 “Animal Generic Drug User Fee Amendments of 2018”.

20 (b) FINDING.—Congress finds that the fees author-
21 ized by the amendments made in this title will be dedi-
22 cated toward expediting the generic new animal drug de-
23 velopment process and the review of abbreviated applica-
24 tions for generic new animal drugs, supplemental abbrevi-
25 ated applications for generic new animal drugs, and in-

1 vestigational submissions for generic new animal drugs as
 2 set forth in the goals identified for purposes of part 5 of
 3 subchapter C of chapter VII of the Federal Food, Drug,
 4 and Cosmetic Act, in the letters from the Secretary of
 5 Health and Human Services to the Chairman of the Com-
 6 mittee on Energy and Commerce of the House of Rep-
 7 resentatives and the Chairman of the Committee on
 8 Health, Education, Labor and Pensions of the Senate as
 9 set forth in the Congressional Record.

10 **SEC. 202. AUTHORITY TO ASSESS AND USE GENERIC NEW**
 11 **ANIMAL DRUG FEES.**

12 (a) **FEE REVENUE AMOUNTS.**—Subsection (b) of sec-
 13 tion 741 (21 U.S.C. 379j–21) is amended to read as fol-
 14 lows:

15 “(b) **FEE REVENUE AMOUNTS.**—

16 “(1) **IN GENERAL.**—Subject to subsections (c),
 17 (d), (f), and (g), for each of fiscal years 2019
 18 through 2023, the fees required under subsection (a)
 19 shall be established to generate a total revenue
 20 amount of \$18,336,340.

21 “(2) **TYPES OF FEES.**—Of the total revenue
 22 amount established for a fiscal year under para-
 23 graph (1)—

1 “(A) 25 percent shall be derived from fees
2 under subsection (a)(1) (relating to abbreviated
3 applications for a generic new animal drug);

4 “(B) 37.5 percent shall be derived from
5 fees under subsection (a)(2) (relating to generic
6 new animal drug products); and

7 “(C) 37.5 percent shall be derived from
8 fees under subsection (a)(3) (relating to generic
9 new animal drug sponsors).”.

10 (b) ANNUAL FEE SETTING; ADJUSTMENTS.—

11 (1) INFLATION ADJUSTMENT.—Section 741(c)
12 (21 U.S.C. 379j–21(c)) is amended—

13 (A) by redesignating paragraphs (2)
14 through (4) as paragraphs (3) through (5), re-
15 spectively; and

16 (B) by inserting after paragraph (1) the
17 following:

18 “(2) INFLATION ADJUSTMENT.—

19 “(A) IN GENERAL.—For fiscal year 2020
20 and subsequent fiscal years, the revenue
21 amounts established under subsection (b) shall
22 be adjusted by the Secretary by notice, pub-
23 lished in the Federal Register, for a fiscal year,
24 by multiplying such revenue amounts by an
25 amount equal to the sum of—

- 1 “(i) one;
- 2 “(ii) the average annual percent
- 3 change in the cost, per full-time equivalent
- 4 position of the Food and Drug Administra-
- 5 tion, of all personnel compensation and
- 6 benefits paid with respect to such positions
- 7 for the first 3 of the preceding 4 fiscal
- 8 years for which data are available, multi-
- 9 plied by the average proportion of per-
- 10 sonnel compensation and benefits costs to
- 11 total Food and Drug Administration costs
- 12 for the first 3 of the preceding 4 fiscal
- 13 years for which data are available; and
- 14 “(iii) the average annual percent
- 15 change that occurred in the Consumer
- 16 Price Index for urban consumers (Wash-
- 17 ington-Baltimore, DC-MD-VA-WV; not
- 18 seasonally adjusted; all items less food and
- 19 energy; annual index) for the first 3 of the
- 20 preceding 4 years for which data are avail-
- 21 able multiplied by the average proportion
- 22 of all costs other than personnel compensa-
- 23 tion and benefits costs to total Food and
- 24 Drug Administration costs for the first 3

1 of the preceding 4 fiscal years for which
2 data are available.

3 “(B) COMPOUNDED BASIS.—The adjust-
4 ment made each fiscal year after fiscal year
5 2020 under this paragraph shall be applied on
6 a compounded basis to the revenue amount cal-
7 culated under this paragraph for the most re-
8 cent previous fiscal year.”.

9 (2) WORKLOAD ADJUSTMENTS.—Paragraph (3)
10 of section 741(c) (21 U.S.C. 379j–21(c)), as redesign-
11 nated, is amended to read as follows:

12 “(3) WORKLOAD ADJUSTMENTS.—

13 “(A) IN GENERAL.—For fiscal year 2020
14 and subsequent fiscal years, after the fee rev-
15 enue amounts established under subsection (b)
16 are adjusted for inflation in accordance with
17 paragraph (2), the fee revenue amounts shall be
18 further adjusted for each such fiscal year to re-
19 flect changes in the workload of the Secretary
20 for the process for the review of abbreviated ap-
21 plications for generic new animal drugs, subject
22 to subparagraphs (B) and (C). With respect to
23 such adjustment—

24 “(i) this adjustment shall be deter-
25 mined by the Secretary based on a weight-

1 ed average of the change in the total num-
2 ber of abbreviated applications for generic
3 new animal drugs, manufacturing supple-
4 mental abbreviated applications for generic
5 new animal drugs, investigational generic
6 new animal drug study submissions, and
7 investigational generic new animal drug
8 protocol submissions submitted to the Sec-
9 retary; and

10 “(ii) the Secretary shall publish in the
11 Federal Register the fees resulting from
12 this adjustment and the supporting meth-
13 odologies.

14 “(B) REDUCTION OF WORKLOAD-BASED
15 INCREASE BY AMOUNT OF CERTAIN EXCESS
16 COLLECTIONS.—For each of fiscal years 2021
17 through 2023, if application of the workload ad-
18 justment under subparagraph (A) increases the
19 fee revenue amounts otherwise established for
20 the fiscal year under subsection (b), as adjusted
21 for inflation under paragraph (2), such fee rev-
22 enue increase shall be reduced by the amount of
23 any excess collections, as described in sub-
24 section (g)(4), for the second preceding fiscal

1 year, up to the amount of such fee revenue in-
2 crease.

3 “(C) RULE OF APPLICATION.—Under no
4 circumstances shall workload adjustments
5 under this paragraph result in fee revenues for
6 a fiscal year that are less than the fee revenues
7 for that fiscal year established under subsection
8 (b), as adjusted for inflation under paragraph
9 (2).”.

10 (3) FINAL YEAR ADJUSTMENT.—Paragraph (4)
11 of section 741(c) (21 U.S.C. 379j–21(c)), as redesign-
12 ated, is amended by—

13 (A) striking “2018” each place it appears
14 and inserting “2023”; and

15 (B) striking “2019” and inserting “2024”.

16 (c) FEE WAIVER OR REDUCTION; EXEMPTION FROM
17 FEES.—Subsection (d) of section 741 (21 U.S.C. 379j–
18 21) is amended to read as follows:

19 “(d) FEE WAIVER OR REDUCTION; EXEMPTION
20 FROM FEES.—

21 “(1) FEE WAIVER OR REDUCTION.—The Sec-
22 retary shall grant a waiver from or a reduction of
23 1 or more fees assessed under subsection (a) where
24 the Secretary finds that the generic new animal drug

1 is intended solely to provide for a minor use or
2 minor species indication.

3 “(2) EXEMPTION FROM FEES.—Fees under this
4 section shall not apply with respect to any person
5 who—

6 “(A) not later than September 30, 2023,
7 submits a supplemental abbreviated application
8 for a generic new animal drug approved under
9 section 512, solely to add the application num-
10 ber to the labeling of the drug in the manner
11 specified in section 502(w)(3); and

12 “(B) otherwise would be subject to fees
13 under this section solely on the basis of such
14 supplemental abbreviated application.”.

15 (d) CREDITING AND AVAILABILITY OF FEES.—Sec-
16 tion 741(g) (21 U.S.C. 379j–21) is amended by striking
17 paragraph (3) and inserting the following paragraphs:

18 “(3) AUTHORIZATION OF APPROPRIATIONS.—
19 For each of the fiscal years 2019 through 2023,
20 there is authorized to be appropriated for fees under
21 this section an amount equal to the total revenue
22 amount established under subsection (b) for the fis-
23 cal year, as adjusted or otherwise affected under
24 subsection (c).

1 “(4) EXCESS COLLECTIONS.—If the sum total
 2 of fees collected under this section for a fiscal year
 3 exceeds the amount of fees authorized to be appro-
 4 priated for such year under paragraph (3), the ex-
 5 cess collections shall be credited to the appropria-
 6 tions account of the Food and Drug Administration
 7 as described in paragraph (1).”.

8 **SEC. 203. REAUTHORIZATION; REPORTING REQUIREMENTS.**

9 Section 742 (21 U.S.C. 379j–22) is amended—

10 (1) in subsection (a), by striking “2013” and
 11 inserting “2018”;

12 (2) in subsection (b), by striking “Committee
 13 on Health, Education, Labor, and Pensions” and in-
 14 serting “the Committee on Health, Education,
 15 Labor and Pensions”;

16 (3) by striking “2014” each place it appears in
 17 subsections (a) and (b) and inserting “2019”; and

18 (4) in subsection (d), by striking “2018” each
 19 place it appears and inserting “2023”.

20 **SEC. 204. SAVINGS CLAUSE.**

21 Notwithstanding the amendments made by this title,
 22 part 5 of subchapter C of chapter VII of the Federal Food,
 23 Drug, and Cosmetic Act (21 U.S.C. 379j–21 et seq.), as
 24 in effect on the day before the date of enactment of this
 25 title, shall continue to be in effect with respect to abbre-

1 viated applications for a generic new animal drug and sup-
2 plemental abbreviated applications for a generic new ani-
3 mal drug (as defined in such part as of such day) that
4 on or after October 1, 2013, but before October 1, 2018,
5 were accepted by the Food and Drug Administration for
6 filing with respect to assessing and collecting any fee re-
7 quired by such part for a fiscal year prior to fiscal year
8 2019.

9 **SEC. 205. EFFECTIVE DATE.**

10 The amendments made by this title shall take effect
11 on October 1, 2018, or the date of the enactment of this
12 Act, whichever is later, except that fees under part 5 of
13 subchapter C of chapter VII of the Federal Food, Drug,
14 and Cosmetic Act, as amended by this title, shall be as-
15 sessed for abbreviated applications for a generic new ani-
16 mal drug and supplemental abbreviated applications for
17 a generic new animal drug received on or after October
18 1, 2018, regardless of the date of enactment of this Act.

19 **SEC. 206. SUNSET DATES.**

20 (a) **AUTHORIZATION.**—Section 741 of the Federal
21 Food, Drug, and Cosmetic Act (21 U.S.C. 379j-21) shall
22 cease to be effective October 1, 2023.

23 (b) **REPORTING REQUIREMENTS.**—Section 742 of the
24 Federal Food, Drug, and Cosmetic Act (21 U.S.C. 379j-
25 22) shall cease to be effective January 31, 2024.

1 (c) PREVIOUS SUNSET PROVISION.—Effective Octo-
2 ber 1, 2018, subsections (a) and (b) of section 206 of the
3 Animal Generic Drug User Fee Amendments of 2013
4 (Public Law 113–14) are repealed.

5 **TITLE III—MISCELLANEOUS**
6 **PROVISIONS**

7 **SEC. 301. ELECTRONIC SUBMISSIONS.**

8 (a) NEW ANIMAL DRUG APPLICATIONS AND ABBRE-
9 VIATED APPLICATIONS FOR A GENERIC NEW ANIMAL
10 DRUG.—Section 512(b) (21 U.S.C. 360b(b)) is amended
11 by adding at the end the following:

12 “(4) Beginning on October 1, 2018, all applications
13 or submissions pursuant to this subsection shall be sub-
14 mitted by electronic means in such format as the Sec-
15 retary may require.”.

16 (b) CONDITIONAL APPROVAL OF NEW ANIMAL
17 DRUGS FOR MINOR USE AND MINOR SPECIES.—Section
18 571(a) (21 U.S.C. 360ccc(a)) is amended by adding at
19 the end the following:

20 “(4) Beginning on October 1, 2018, all applications
21 or submissions pursuant to this subsection shall be sub-
22 mitted by electronic means in such format as the Sec-
23 retary may require.”.

1 **SEC. 302. INDEX OF LEGALLY MARKETED UNAPPROVED**
 2 **NEW ANIMAL DRUGS FOR MINOR SPECIES.**

3 Effective on October 1, 2018, section 572(h) (21
 4 U.S.C. 360ccc-1(h)) is amended—

5 (1) by amending paragraph (1) to read as fol-
 6 lows:

7 “(1) ‘LEGAL STATUS—In order to be legally
 8 marketed, a new animal drug intended for a minor
 9 species must be Approved, Conditionally Approved,
 10 or Indexed by the Food and Drug Administration.
 11 THIS PRODUCT IS INDEXED—MIF.’ (followed
 12 by the applicable minor species index file number
 13 and a period) ‘Extra-label use is prohibited.’;” and
 14 (2) in paragraph (2), by striking “other ani-
 15 mals” and inserting “food-producing animals”.

16 **SEC. 303. MISBRANDED DRUGS AND DEVICES.**

17 (a) IN GENERAL.—Section 502(w) (21 U.S.C.
 18 352(w)) is amended—

19 (1) in subparagraph (1), by striking “; or” and
 20 inserting “;”;

21 (2) in subparagraph (2), by striking the period
 22 and inserting “; or”; and

23 (3) by adding at the end the following:

24 “(3) for which an application has been ap-
 25 proved under section 512 and the labeling of such
 26 drug does not include the application number in the

1 format: ‘Approved by FDA under (A)NADA # xxx-
2 xxx’, except that this subparagraph shall not apply
3 to representative labeling required under section
4 514.1(b)(3)(v)(b) of title 21, Code of Federal Regu-
5 lations (or any successor regulation) for animal feed
6 bearing or containing a new animal drug.”.

7 (b) APPLICABILITY.—Section 502(w)(3) of the Fed-
8 eral Food, Drug, and Cosmetic Act, as added by sub-
9 section (a), shall apply beginning on September 30, 2023.



February 26, 2018

The Honorable Lamar Alexander
Chairman
Committee on Health, Education, Labor
and Pensions
U.S. Senate
Washington, D.C. 20510

The Honorable Patty Murray
Ranking Member
Committee on Health, Education, Labor
and Pensions
U.S. Senate
Washington, D.C. 20510

The Honorable Greg Walden
Chairman
Committee on Energy and Commerce
U.S. House of Representatives
Washington, D.C. 20515

The Honorable Frank Pallone
Ranking Member
Committee on Energy and Commerce
U.S. House of Representatives
Washington, D.C. 20515

Dear Chairman Alexander, Ranking Member Murray, Chairman Walden, and Ranking Member Pallone,

As representatives of the U.S. food value chain, we urge you to reject any amendments to the reauthorization of the Animal Drug User Fee Act (ADUFA) that could undermine or conflict with the National Bioengineered Food Disclosure Standard Act (the Disclosure Act or the Act). Congress passed the Disclosure Act in 2016 with overwhelming bipartisan support, and President Obama signed it into law. The Act provides the framework for the United States Department of Agriculture (USDA) to provide consumers with consistent, truthful, and non-misleading information they may wish to have about their food in a way that does not stigmatize the use of technology to produce that food. USDA is currently implementing the Disclosure Act through rulemaking.

When considering the Disclosure Act, Congress was explicit that the Act must prevent a patchwork of bioengineered food disclosure regulations, as the existence of such would likely

cause widespread consumer confusion. Consequently, Congress set the definition of “bioengineered” food, thus establishing the scope of the uniform mandatory disclosure standard. Those foods that meet the definition of a “bioengineered food” fall within the uniform disclosure mandate. The Act sets out a number of options for compliance and recognizes the 30-plus years of proven safety of bioengineering in food and agriculture.

It is important for Congress to fully support the framework set out in the Disclosure Act and the authority vested in USDA to implement that framework. To do that, Congress must reject any attempts to undermine the Act. We are extremely concerned that a proposed amendment to S. 2434, the Animal Drug and Animal Generic Drug User Fee Amendments of 2018 would do just that. The proposed amendment would require a separate and conflicting mandated label for a specific bioengineered food product that is already covered by the Disclosure Act. If this provision becomes law, it will undermine the congressionally-mandated USDA uniform disclosure standard and generate consumer confusion as the proposed FDA label would mandate different disclosure language from that required by the Disclosure Act. Consumers would likely be left wondering as to the differences in disclosures.

As you work over the next few weeks to finalize the reauthorization of ADUFA, we ask that you oppose inclusion of this harmful bioengineered food labeling provision from any final bill.

Sincerely,

Agricultural Retailers Association
 American Farm Bureau Federation
 American Feed Industry Association
 American Seed Trade Association
 American Soybean Association
 Animal Health Institute
 Biotechnology Innovation Organization
 Corn Refiners Association
 Enzyme Technical Association
 National Association of State Departments of Agriculture
 National Association of Wheat Growers
 National Black Growers Council
 National Cattlemen’s Beef Association
 National Corn Growers Association
 National Council of Farmer Cooperatives
 National Grain and Feed Association
 National Milk Producers Federation
 National Oilseed Producers Association
 National Pork Producers Council
 National Renderers Association
 National Turkey Federation
 North American Meat Institute
 North American Millers’ Association

GREG WALDEN, OREGON
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FIFTEENTH CONGRESS
Congress of the United States
House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115

Majority (202) 225-2327
Minority (202) 225-3641

April 5, 2018

Dr. Steven Solomon
Director
Center for Veterinary Medicine
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993


Dear Dr. Solomon:

Thank you for appearing before the Subcommittee on Health on March 14, 2018, to testify at the hearing entitled "Reauthorization of Animal Drug User Fees 2018: ADUFA and AGDUFA."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on April 19, 2018. Your responses should be mailed to Zack Dareshori, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, DC 20515 and e-mailed in Word format to zack.dareshori@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,



Michael C. Burgess, M.D.
Chairman
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment



JUL 23 2018

The Honorable Greg Walden
Chairman
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515

Dear Chairman Walden:

Thank you for providing the Food and Drug Administration (FDA or the Agency) with the opportunity to testify at the March 14, 2018, hearing before the Committee on Energy and Commerce, entitled "Reauthorization of Animal Drug User Fees: ADUFA and AGDUFA." This letter is a response for the record to questions posed by the committee.

If you have further questions, please let us know.

Sincerely,

A black rectangular box redacting the signature of John Martin.

John Martin
Principal Associate Commissioner
for Legislative Affairs

The committee's questions are restated below in bold, followed by FDA's response.

The Honorable Gus M. Bilirakis

- 1. Would you walk us through what actions FDA has taken over the past few years and is currently undertaking with regard to antimicrobial resistance in animals – specifically those for consumption?**

Antimicrobial resistance (AMR) is a serious global public health threat. FDA, in close coordination with other government and public health stakeholders, including the U.S. Department of Agriculture (USDA), has taken a leading role in addressing this critical threat by implementing judicious use policies to promote antimicrobial stewardship and by enhancing surveillance through systems such as the National Antimicrobial Resistance Monitoring System.

Over the past few years, FDA has made a number of important changes with regard to antimicrobial use in animals.

In December 2013, FDA requested through guidance for industry (GFI) #213 that animal drug sponsors of medically-important antimicrobials used in animal feed and water revise the labels of these products to remove indications for growth promotion and to require veterinary oversight for the remaining therapeutic uses. The policy outlined in GFI #213 was fully implemented in January 2017, with all affected animal drug sponsors making the requested changes to their labels. It is important to note that the cooperation of the affected animal drug sponsors was voluntary; however, because they have now revised their labeling consistent with the recommendations in GFI #213, the use of these products in the feed or drinking water of food-producing animals for production (e.g., growth promotion) purposes is now illegal in the U.S. and their use for therapeutic purposes requires authorization from a licensed veterinarian.

To build on the progress made by GFI #213, FDA sought public input on establishing appropriately-targeted durations of therapeutic use of medically-important antimicrobial drugs in food-producing animals. FDA has evaluated the comments received and is in the process of developing a specific strategy for addressing this issue. The strategy developed will need to consider the approved use conditions of these products on a product-by-product basis and any changes to such use conditions will need to be based on sound science and available evidence.

FDA also has issued a final rule revising the annual reporting requirements for drug sponsors of antimicrobials sold or distributed for use in food-producing animals. The additional data FDA will gather as a result of that rulemaking 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.

FDA is also funding two grants for antimicrobial use data collection. These collection efforts are intended to provide part of the baseline information on antimicrobial use practices in the

Page 3 -- The Honorable Greg Walden

four major food-producing animal species (cattle, swine, chickens, turkeys), which is a critical element in measuring the overall impact of FDA's judicious use strategy. We also expect these data collection efforts to provide important information on methodologies to help optimize long-term strategies to collect and report such antimicrobial use data.

Finally, FDA has also been working in close collaboration with the USDA Animal and Plant Health Inspection Service (APHIS) Center for Epidemiology and Animal Health, and has provided input on surveys they have conducted on antimicrobial use in certain animal agriculture settings. We also expect the results of these surveys to provide useful information for assessing antimicrobial use practices in veterinary settings.

2. How do these user fee programs foster innovation in drug development?

ADUFA and AGDUFA are highly successful programs that have accelerated the review of innovative new animal drugs – and more affordable generic alternatives – advancing both animal and human health. The programs have enabled FDA to dramatically reduce the time needed to review pioneer and generic animal products for premarket approval, improve timely communications with sponsors, and achieve other efficiencies in the drug review process, while helping ensure that the drugs are safe and effective.

Innovative new animal products and approaches are being developed that offer the promise of a longer and healthier life for our pets and other animals. In recent years, FDA has approved new oncology treatments for dogs targeting canine-specific tumors and innovative therapies targeting bone changes in horses to treat a common cause of performance-ending lameness. We also approved the first generic version of a vital heartworm treatment that alleviated a shortage of this critically important treatment for dogs. And promising new stem cell therapies offer future veterinary treatments and cures.

FDA employs cutting edge methods of analysis and approaches to arrive at safety and efficacy conclusions including the following:

- Use of pharmacokinetic/pharmacodynamic information
- In vitro testing of product characteristics
- Meta-analysis of broad sources of information such as published literature
- New statistical analyses and presentations of data
- Risk analysis methodologies

The Honorable Frank Pallone, Jr.

Dr. Solomon, it's clear that the user fee programs for animal drugs have been a success, just as the other user fee programs at FDA have been. I'm pleased that FDA, the animal drug industry, and other stakeholders have once again worked together to reach agreement on a path forward.

1. Since the implementation of the animal drug user fee programs, how has FDA's new animal drug review process improved?

Before these programs were initiated, FDA's Center for Veterinary Medicine 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. Because of additional resources provided through the animal drug user fee programs, FDA maintains a stable scientific and technical workforce and provides the animal drug industry with more timely and predictable premarket product review. These programs have been highly successful and have enabled CVM to eliminate the backlog in applications, dramatically reduce the time needed to review animal drug applications and other submissions, improve timely communications with drug sponsors, and achieve other efficiencies in the drug approval process. FDA has met or exceeded virtually all performance goals established under both programs, without sacrificing scientific standards for safety and efficacy.

2. What has FDA learned since the first authorization of the animal drug user fees and how have the agreements evolved over time to further streamline the review process since the first authorization?

The five-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.

Under the current ADUFA III agreement, FDA has made multiple enhancements to the chemistry, manufacturing, and controls (CMC) technical section of the new animal drug application (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 (INAD) file, and permits certain prior approval manufacturing supplements to be resubmitted as Supplements – Changes Being Effectuated in 30 Days (CBE-30s).

FDA continues to improve communications, timeliness, and predictability of foreign pre-approval inspections. Sponsors may now voluntarily submit a list of foreign manufacturing facilities they anticipate including in their applications subject to pre-approval inspections for the following fiscal year, permitting better planning and timely execution of FDA good manufacturing practice (GMP) inspections.

Under the current AGDUFA II agreement, 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.

FDA also 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.

The ADUFA IV and AGDUFA III agreements 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.

3. Without the animal drug user fee programs, would animal drug development suffer?

The animal drug user fee programs have enabled FDA to dramatically reduce the time needed to review pioneer and generic animal products for premarket approval, improve timely communications with sponsors, and achieve other efficiencies in the drug review process, while helping ensure that the drugs are safe and effective.

In the absence of these programs, FDA would be forced to lay off a significant share of our scientific workforce, delaying the review of new animal drugs, creating uncertainty and frustration for industry, and delaying the availability of new safe and effective treatments. In the AGDUFA program, approximately 60 percent of our staff are funded by user fees. In the ADUFA program, approximately 35 percent of CVM's workforce is funded by user fees. The loss of such a large number of staff would be devastating.

4. In your opinion, what are the most significant new proposals in ADUFA IV and AGDUFA III and how do they further improve the animal drug review process at FDA?

Both agreements build on the success of prior program achievements, propose additions to current performance goals to further enhance review, and include financial recommendations to enhance program stability.

In ADUFA IV, FDA adds an additional four new performance goals to enhance the exchange of scientific information. FDA will reduce timeframes for certain medicated feed applications and environmental impact submissions from 180 days to 60 days. We also establish new goals for timely pre-submission conferences and tissue residue method demonstrations.

The ADUFA IV recommendations also require 100 percent electronic submission starting in FY 2019 to help facilitate efficient review and an FDA commitment to work on implementing the U.S.-European Union Good Manufacturing Practices Inspection Mutual Recognition Agreement for animal drug facilities.

Page 6 – The Honorable Greg Walden

The AGDUFA III negotiated agreement includes a significant, additional financial commitment from the animal generic drug industry that reflects the industry's growth. These resources will help support significantly decreased review times for generic submissions and provide greater review predictability. Like the ADUFA IV recommendation, AGDUFA III also requires 100 percent electronic submission starting next year.

Dr. Solomon as you have previously explained, these animal drug user fee agreements are critical to ensuring animal health and safety and streamlining FDA's animal drug approval process.

These user fee programs help to maintain a stable workforce at the agency to review new animal drug applications, while cutting down on review times and improving FDA's efficiency. In addition, the agreements also help to bring certainty to industry regarding the review and approval of innovative and generic animal drugs, provide necessary treatments for animal health providers, and ensure the health and well-being of our animals.

- 5. Can you explain why it is so critical that the animal drug user fee and animal generic drug user fee programs are reauthorized before the sunset date?**
- 6. What will happen if the animal drug user fee agreements are not reauthorized in a timely manner? Could there be disruptions in the approval process?**
- 7. Would delays impact the agency's ability to retain subject matter experts to review new animal drug applications?**

If reauthorization is delayed, we could risk having to lay off many employees. As a longer-term consequence, a delay will make it more difficult for FDA to attract and retain skilled scientists and medical reviewers, and undermine product innovation.

The loss of large numbers of dedicated staff would be devastating. In the AGDUFA program, approximately 60 percent of our staff are funded by user fees. In the ADUFA program, approximately 35 percent of the FTE are funded by user fees. With the loss of FTE, review times would return to the pre-user fee timeframes which exceeded 500 days for pioneer products and 700 days for generic products.

If there's a reasonable expectation that ADUFA and AGDUFA will not be reauthorized by September 30th, FDA would have to notify those employees affected no later than 60 days prior to their expected release date. The Agency, however, would have to perform a substantial analysis prior to sending out the RIF notices to determine what steps would be necessary to adjust drug review and the personnel engaged in those activities.

A topic that often comes up in relation to the reauthorization of animal drug user fees is antimicrobial resistance given that the Center for Veterinary Medicine at FDA is also charged with evaluating antimicrobial animal drugs. Dr. Solomon, as you know, antibiotic

resistance is a grave public health threat as the use of antimicrobials in food-producing animals can result in the emergence of antimicrobial resistance in bacteria that can be transferred to humans and can ultimately reduce the effectiveness of antibiotics in humans.

8. Can you discuss the steps FDA has taken recently to address the public health concerns related to antimicrobial resistance and help reduce or limit the use of antimicrobials in food-producing animals?

Antimicrobial resistance (AMR) is a serious global public health threat. FDA, in close coordination with other government and public health stakeholders, including USDA, has taken a leading role in addressing this critical threat by implementing judicious use policies to promote antimicrobial stewardship and by enhancing surveillance through systems such as the National Antimicrobial Resistance Monitoring System.

Over the past few years FDA has made a number of important changes with regard to antimicrobial use in animals.

In December 2013, FDA requested through guidance GFI #213 that animal drug sponsors of medically important antimicrobials used in animal feed and water revise the labels of these products to remove indications for growth promotion and to require veterinary oversight for the remaining therapeutic uses. The policy outlined in GFI #213 was fully implemented in January 2017, with all affected animal drug sponsors making the requested changes to their labels. It is important to note that the cooperation of the affected animal drug sponsors was voluntary; however, because they have now revised their labeling consistent with the recommendations in GFI #213, the use of these products in the feed or drinking water of food-producing animals for production (e.g., growth promotion) purposes is now illegal in the U.S. and their use for therapeutic purposes requires authorization from a licensed veterinarian.

To build on the progress made by GFI #213, FDA sought public input on establishing appropriately-targeted durations of therapeutic use of medically-important antimicrobial drugs in food-producing animals. FDA has evaluated the comments received and is in the process of developing a specific strategy for addressing this issue. The strategy developed will need to consider the approved use conditions of these products on a product-by-product basis and any changes to such use conditions will need to be based on sound science and available evidence.

FDA also has issued a final rule revising the annual reporting requirements for drug sponsors of antimicrobials sold or distributed for use in food-producing animals. The additional data FDA will gather as a result of that rulemaking 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.

FDA is also funding two grants for antimicrobial use data collection. These collection efforts are intended to provide part of the baseline information on antimicrobial use practices in the four major food-producing animal species (cattle, swine, chickens, turkeys), which is a critical element in measuring the overall impact of FDA's judicious use strategy. We also expect these data collection efforts to provide important information on methodologies to help optimize long-term strategies to collect and report such antimicrobial use data.

Finally, FDA has also been working in close collaboration with the USDA APHIS Center for Epidemiology and Animal Health, and has provided input on surveys they have conducted on antimicrobial use in certain animal agriculture settings. We also expect the results of these surveys to provide useful information for assessing antimicrobial use practices in veterinary settings.

9. How do we balance the need for medically important uses of antimicrobials in food producing animals with efforts to limit or reverse resistance concerns?

FDA believes that the concept of "antimicrobial stewardship" in the animal agriculture setting encompasses a number of important principles, including the following judicious use principles: 1) Antimicrobial drugs should only be used in food-producing animals when necessary to treat, prevent, or control disease, and not for production (e.g., growth promotion) purposes; and 2) when antimicrobial use is necessary, they should be used in an optimal manner under the supervision of a licensed veterinarian.

10. How has access to antimicrobial drug sales and distribution data helped to improve FDA's efforts to address antimicrobial resistance?

FDA believes this information enhances the Agency's understanding of antimicrobials entering the marketplace and supports the assessment of FDA's ongoing efforts to encourage the judicious use of antimicrobials in food-producing animals to help ensure the continued availability of safe and effective antimicrobials for animals and humans.

While sales data provide insight regarding antimicrobial drugs being sold and distributed, FDA believes additional data should be considered when assessing the progress of efforts to foster judicious antimicrobial use, including actual use data, animal demographics and animal health data, and data on resistance. FDA continues to work with Federal, academic, and industry partners to obtain more information about how, when, and why animal producers and veterinarians use medically important antimicrobial drugs.

11. For the first time this past year FDA's summary report on antimicrobials sold or distributed for use in food-producing animals included species-specific estimates. How did FDA determine these estimates and what advantage does inclusion of specific estimates have in data collection efforts?

Since 2008, sponsors of approved or conditionally approved new animal drug applications for a drug containing an antimicrobial active ingredient, must annually report to FDA on the amount of each such ingredient in these drug products sold or distributed for use in food-producing animals. FDA summarizes this information and makes it available to the public in its annual summary reports.

The species-specific estimates were reported for the first time as part of the 2016 annual summary report. FDA established, through notice and comment rulemaking, the additional requirement that drug sponsors submit species-specific estimates as part of their annual report on the quantity of antimicrobials sold or distributed for use in food-producing animals. Drug sponsors are required to provide a species-specific estimate of the percentage of each product that was sold or distributed domestically in the reporting year for use in any of the following animal species categories, but only for such species that appear on the approved label: cattle, swine, chickens, turkeys. The total of the species-specific percentages reported for each product must account for 100 percent of its sales and distribution; therefore, a fifth category of "other species/unknown" must also be reported. Sponsors must submit each year's report to FDA no later than March 31.

Given that many antimicrobial new animal drug products are approved and labeled for use in more than one animal species, the additional species-specific data improves our understanding of how antimicrobials are sold or distributed for use in major food-producing species and will help further target efforts to ensure judicious use of medically important antimicrobials.

Dr. Solomon, the public health crisis resulting from antimicrobial resistance is very concerning and I'm interested in FDA's guidance on judicious use of antimicrobials for food-producing animals and whether FDA's policy has improved veterinary practice in this area.

There is wide agreement that antibiotics should only be used when necessary. As you discussed briefly in your testimony, greater awareness of the harms of antibiotic resistance should result in changes to how antibiotics are utilized in animal agriculture and how FDA is monitoring antimicrobial usage in food-producing animals.

12. Will you further discuss FDA's policy on judicious use of antimicrobials in food producing animals, which aims to maximize therapeutic efficacy while also minimizing the selection of resistant microorganisms?

The goal of FDA's judicious use strategy is focused on mitigating antimicrobial resistance by eliminating the use of medically important antimicrobials in food-producing animals for production (e.g., growth promotion) purposes and limiting therapeutic use to legitimate animal health needs (i.e., disease treatment, control, and prevention) that are under veterinary oversight.

It's essential that we take steps to ensure that all uses of antimicrobials, in both veterinary and human healthcare settings, are judicious and consistent with the principles of antibiotic stewardship. FDA continues to work with Federal, academic, and industry partners to obtain more information about how, when, and why animal producers and veterinarians use medically important antimicrobial drugs. Additional information about how these antimicrobials are being used on the farm will help the agency to assess associations between antibiotic use practices and antimicrobial resistance.

13. Why is it so important to have veterinary oversight or consultation when utilizing medically important antimicrobials in food-producing animals?

Veterinarians play a critical role in diagnosing disease and in the decision-making process related to instituting measures to treat, control, or prevent disease. Veterinary oversight of medically important antimicrobials ensures that prescribing decisions are based on professional judgements about the risk of a specific bacterial disease and whether it would be appropriate in a particular situation to use medically important antimicrobials for prevention purposes. Such factors include whether: (1) there is evidence that the drug will be effective in treating the particular disease; (2) such preventive use is consistent with accepted veterinary practice; (3) the use is intended to address particular bacteria; (4) the use is appropriately targeted to animals at risk of developing a specific disease; and (5) there are no reasonable alternatives for intervention.

14. What is the status of implementation on FDA's judicious use policy and how has implementation progressed since the guidance was first published in 2013?

In January 2017, FDA completed its three-year initiative to eliminate the use of medically important antimicrobial drugs for production purposes (e.g., growth promotion) and require veterinary oversight for the remaining therapeutic uses of these drugs in the feed or drinking water of food producing animals. All affected animal drug sponsors voluntarily worked with FDA to make the requested changes to their product labels. All 292 affected animal drug applications were either aligned with the Agency's recommendations or, in some cases, were voluntarily withdrawn by the drug sponsor. As a result of the changes made by animal drug sponsors to align their products with FDA's recommendations in GFI #213, medically-important antimicrobials can no longer legally be used in the feed or drinking water of food-producing animals for production (e.g., growth promotion) purposes and can only be used for therapeutic purposes in the feed or water of food-producing animals with the oversight of a licensed veterinarian.

FDA finalized updated Veterinary Feed Directive (VFD) regulations in June 2015 to facilitate veterinary oversight of feed-use antibiotics. These regulations went into effect October 1, 2015. The updated VFD regulations provide veterinarians a framework for authorizing the use of medically important antimicrobials in feed.

Based on inspection activities carried out by FDA's Office of Regulatory Affairs (ORA) and state feed regulatory programs, implementation of the VFD Final Rule has generally gone

well. Of the approximately 190 VFD orders inspected during the 2017 VFD Inspection Assignment, nearly 100% have been signed by a veterinarian aware of the state or federal veterinarian-client-patient relationship (VCPR) requirements that apply in the state where they are issuing the VFD order. Based on this observation, we believe affected stakeholders have been learning and adopting the practices necessary for ensuring compliance with the VFD regulation and supporting antimicrobial stewardship.

15. What additional steps do you believe FDA and industry should be taking to further address the harms of antimicrobial resistance? Are there additional tools that FDA needs to better address antimicrobial resistance?

Last January, FDA published its key initiatives for the next five years, which include the following:

- Align antimicrobial drug products with the principles of antimicrobial stewardship in veterinary settings.
- Support efforts to foster stewardship of antimicrobials in veterinary settings.
- Assess the impact of strategies intended to curb the emergence of antimicrobial resistance associated with the use of antimicrobial drugs in veterinary settings.

FDA continues to work with Federal, academic, and industry partners to obtain more information about how, when, and why animal producers and veterinarians use medically important antimicrobial drugs. Should FDA identify further steps that are necessary to address the potential harm of antimicrobial resistance, we will work with our Congressional partners to request additional tools or authorities, as appropriate.

GREG WALDEN, OREGON
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FIFTEENTH CONGRESS
Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
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Majority (202) 225-2927
Minority (202) 225-3641

April 5, 2018

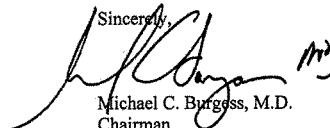
Dr. Rachel Cumberbatch
Director, Regulatory Affairs, Animal Drugs
Animal Health Institute
1325 G Street, N.W.; Suite 700
Washington, DC 20005

Dear Dr. Cumberbatch:

Thank you for appearing before the Subcommittee on Health on March 14, 2018, to testify at the hearing entitled "Reauthorization of Animal Drug User Fees 2018: ADUFA and AGDUFA."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on April 19, 2018. Your responses should be mailed to Zack Dareshori, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, DC 20515 and e-mailed in Word format to zack.dareshori@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Michael C. Burgess, M.D.
Chairman
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment

Attachment — Additional Questions for the RecordThe Honorable Gus M. Bilirakis

1. **Would you walk us through the benefits of ADUFA and AGDUFA to industry and why these programs have a track record of success?**

The Animal Drug User Fee Act (ADUFA) has been successful in providing additional resources to the Food and Drug Administration (FDA) to enable the agency to meet agreed-upon performance goals. ADUFA provides about 44% of the funding for the animal drug review process at FDA. The program has provided stability and predictability for sponsors and has helped modernize the review process through items such as electronic submissions and communications and the scheduling of conference calls and meetings. This stability allows sponsors to make informed decisions about the investment risks of research and development dollars. Pet owners benefit by having their animals live longer and healthier lives, and livestock and poultry producers have the tools needed to keep food animals productive and healthy.

Looking forward, AHI hopes to engage FDA's Center for Veterinary Medicine (CVM) on potentially more meaningful improvements for ADUFA V to incentivize innovation and streamline the review process. Such improvements could include increased market exclusivity to encourage more innovation and new technologies; implementation of a concurrent two cycle chemistry, manufacturing and control review process; and using a risk-based approach to determine the need for submission of raw data from laboratory and clinical studies and simplifying the drug review process and associated requirements.

2. **You mention in your testimony that conditional approval authority exists in other areas of animal health with the exception of major species. Why is that and how does not having this authority in major species ultimately affect public health?**

There are several unmet medical needs where veterinarians, livestock and pet owners have no or limited treatment options necessary to address disease threats. These unmet needs can lead to illness and death among animals. There are well-defined public health benefits to keeping all animals healthy, largely due to the number of zoonotic diseases which can pass back and forth between animals and humans. Authorizing the agency to extend conditional approval status for animal drugs would modernize the FDA approval process and allow faster access to new animal drugs that can treat or potentially prevent serious diseases. We have seen success of licensing of vaccines and biologics at USDA and believe that the program, expanded to a similar market in animal drugs, would also be successful.

Conditional approval does not currently exist for major species because it has not been authorized in law. The Food and Drug Administration would like to offer this pathway but has made it clear they need Congressional authorization. Congress last addressed the issue of conditional approval in animals when it passed the Minor Use/Minor Species Act in 2003. The ability to treat more diseases in food animals will contribute to a safer food supply. The ability to treat more diseases and conditions in companion animals will allow animal owners to enjoy the companionship and health benefits of pet ownership without fear of disease spread.

The Honorable Frank Pallone, Jr.

1. Dr. Cumberbatch, can you briefly summarize why you believe the ADUFA and AGDUFA programs, respectively, are critical to the development of animal drug products?

The chief benefit from ADUFA is ensuring an efficient and predictable review process by which the industry can effectively plan a project timeline, therefore providing a greater incentive to invest in new technologies. The dedicated resources provided for by the user fee program enable FDA to have qualified staff to review submissions in a timelier manner. Because of this, sponsors can better plan their research projects since they can better estimate when the FDA review will be completed for certain technical sections, allowing for better informed decisions about research and development investments. Increased predictability and communication is critical to the development of animal drug products because it encourages increased research in new therapeutic areas and fosters opportunities for new entrants in the animal health industry.

2. How has the animal health industry evolved since the implementation of ADUFA and AGDUFA and how have the animal drug user fee programs improved the animal drug application review process at FDA?

The primary aim of ADUFA was to establish a degree of predictability as to when FDA would render a decision on a new animal drug application or technical section leading to the filing of an application under the phased review process. Prior to ADUFA, animal drug sponsors had no assurance when the agency would respond to a submission even though the statutory time frame of 180 days was required. The timeframe was often exceeded, generating a backlog of applications and submissions. The dedicated resources provided for by the user fee program has enable FDA to have qualified staff to review submissions in a timelier manner. User fees collected under ADUFA have fixed some of the problems related to unpredictability by eliminating the backlog within the first year of ADUFA I and establishing sentinel submission time frames in which the agency is required to render a response whether positive or negative. Because of this, sponsors can now better plan their research projects since they can better estimate when the FDA review will be completed for certain technical sections, allowing for better informed decisions about research and development investments.

Increased predictability and communication has encouraged increased research in new therapeutic areas and fostered opportunities for new entrants in the animal health industry.

3. Can you provide examples of how the ADUFA and AGDUFA programs, respectively, have helped your industry to innovate and have resulted in bringing more products to the market?

The chief benefit from ADUFA is ensuring an efficient and predictable review process by which the industry can effectively plan a project timeline, therefore providing a greater incentive to invest in new technologies. In ADUFA II the FDA agreed to sponsor a series of technical workshops to explain the current thinking on requirements for safety and efficacy testing, manufacturing, and for other data requirements under the Act. These workshops were important

for sponsors to better understand what FDA would expect for study designs and outcomes. CVM also instituted an iVET program with CVM teams dedicated to new technology platforms supporting both small and large companies. Overall, the communication aspect under ADUFA has enabled industry to better understand the FDA expectations, allowing sponsors to invest in the development of new and innovative technologies.

4. In your opinion, what are the most significant new proposals in ADUFA IV and AGDUFA III and how do they further improve the animal drug review process at FDA?

An important goal for FDA to act on is implementation of the US/EU mutual recognition agreement on Good Manufacturing Practice inspections. Due to globalization, many FDA approved animal drugs are also sold and manufactured in the European Union member countries. Inspections are required before a product can be approved and marketed. Regulatory GMP inspections continue to be done as long as the drug is being manufactured. FDA has traditionally required inspectors to conduct on-site inspections of those foreign facilities. Due to scheduling priorities and logistical considerations, these inspections can be a lengthy process and may cause significant delays in approval. Though FDA has agreed in prior ADUFA agreements to speed the process of foreign inspections, delays remain in certifying foreign manufacturing sites. The ability for FDA to accept the inspection reviews of competent authorities in the EU without having to conduct their own inspections will improve the timing of these decisions and potentially accelerate the approval of important new products. This effort is already underway for human drugs and it is important that FDA work to leverage that effort to include animal health products as well. Inspections of animal drug manufacturing sites are usually scheduled at foreign sites when there are associated human drug inspections in the region. If mutual recognition of foreign authority inspections is only implemented for human drugs, the site inspections for animal drugs will likely suffer further delays because the coordination between human and animal drug inspections will no longer be possible.

5. Can you explain why it is so critical that these programs are reauthorized before the sunset date of September 30, 2018?

As with consideration of other user fee programs, if Congress does not reauthorize the ADUFA program by the sunset date the program will cause the initiation of sunset procedures, including the layoffs of some 120 FDA employees. Even a temporary disruption would cause harm to the drug approval process at the operational level and thus slow the momentum within CVM for reviewing submissions and the overall approval process. This unpredictability would inhibit companies from moving forward on projects where timelines and costs could not be accurately forecast. Overall this would lead to a setback in bringing much-needed animal health products to the market.

6. Given the lack of robust utilization of the conditional approval pathway under the minor use/ minor species approach, why does industry believe this process might be more successful for other types of animal drug products?

Since 2004 FDA has conditionally approved four animal drugs through MUMS – one to control mortality in catfish due to bacterial disease and three to treat specific cancers in dogs. Unfortunately, the program is underutilized because the definition of minor use in a major species is narrow in scope. Developing a product that costs millions of dollars for a small market is unfeasible. The current limits of 50,000 horses and 70,000 dogs, for example, are small considering the fact there are 7.6 million horses and nearly 90 million dogs in the U.S. The final cost of the product would be higher than the market could bear because animal owners pay the full cost of medical treatment out of pocket.

A key reason to expand the conditional approval process is to drive innovation and approval of new molecular entities for serious diseases for which there are no available therapies and for which it is difficult to establish clinical effectiveness via controlled studies. This is often due to the time needed for a long term progressive condition to manifest or lack of effective disease models for use in controlled studies. Expanding the pathway to major uses in major species changes that equation and allows companies to consider a fuller range of opportunities. There are several unmet medical needs where veterinarians, livestock and pet owners have no or limited treatment options necessary to address disease threats. Authorizing the agency to extend conditional approval status for animal drugs would modernize the FDA approval process and allow faster access to new animal drugs that can treat or potentially prevent serious diseases. We have seen success of licensing of vaccines and biologics at USDA and believe that the program, expanded to a similar market in animal drugs, would also be successful.

7. Should conditional approval be expanded in certain cases for other animal drugs applications, what are some examples of conditions or potential therapies that could improve animal health and could be an effective use of this process?

CVM and AHI held two years of discussion to determine the need for expansion of conditional approval to other categories of new animal drugs and agreed to a set of criteria for products that would qualify:

- Unmet medical needs (including new disease outbreaks)
- Life threatening, emerging, sporadic and/or chronic disease conditions
- Delayed onset or delayed progression of disease.
- Diseases which would require an extended time period of evaluation in order to enroll enough animals to adequately power the study.

AHI has developed a list of unmet medical needs in different animal species that are examples of the diseases and conditions that could be addressed, and that list is attached as Appendix A. While this list is not comprehensive, it illustrates the diversity and seriousness of the need across animal health.

8. FDA's gold standard of safety and efficacy is the cornerstone by which the agency reviews new drug applications. Do you believe that by expanding conditional approval and permitting sponsors to keep products on the market while gathering effectiveness data there will ultimately be more fully approved products on the market in the long-term?

Yes. For certain products that treat conditions that meet the definition of an unmet medical need, this new pathway would address situations where it is difficult to establish clinical effectiveness via controlled studies. By providing flexibility in the timeline for gathering this data, expanding conditional approval creates a greater incentive for sponsors to consider these innovative therapies. Conditional approval also requires sponsors to demonstrate annual progress toward substantial evidence of efficacy and full approval. The availability of more approved drugs may improve animal safety by reducing the current use of unapproved or human drugs off-label with therapies that have been tested in the target animal and have full data packages that support their safety and efficacy. As in the traditional approval pathway, sponsors would be required to complete all safety testing prior to receiving conditional approval. FDA would also maintain control and oversight of the drug, thus upholding FDA's gold standard of safety while allowing the sponsor to prove efficacy.

9. What are some of the major improvements this proposal makes from the current goals and how will these proposals create new efficiencies for FDA?

In ADUFA IV, FDA has agreed to allow for a reduced review time for medicated feed combination drugs and establish a new performance standard for validating tissue residue methods and implement a mutual recognition process for GMP inspections of manufacturing facilities within the European Union.

There have been considerable delays for sponsors that gain approval of a new animal drug intended for medicated feed to be able to market that product since food animal producers frequently use two or three drugs in combination in medicated feeds. FDA must ensure that the combinations are safe and effective, so each combination must be separately approved. FDA has agreed to substantially shorten this process which will allow important new food animal products to be marketed sooner.

All new animal drugs used in food-producing animals are tested for residue potential, and FDA establishes a tolerance, or maximum residue level, permitted in food animal products. The agency requires the sponsor to submit for validation by FDA and USDA a suitable laboratory testing method that regulatory authorities can use to monitor the safety of meat, milk and eggs. Because these validation procedures have not been part of the ADUFA program, timing of this process has been uncertain and has been a cause for significant delays in FDA approval of products. FDA has now agreed to establish a 120-day performance timeframe for rendering a decision on the residue method.

FDA has agreed to work towards the US/EU mutual recognition agreement on Good Manufacturing Practice inspections. FDA has always required that their inspectors conduct on-site inspections of foreign facilities, such as those in the EU. These inspections can delay approvals if scheduling or logistical complications occur. Efforts to streamline inspections are

already underway for human drugs and it is important to FDA work to leverage current efforts to include animal health products as well.

10.Dr. Cumberbatch – do you believe the electronic submission requirements included in this discussion draft will improve the efficiency of the animal drug approval process at FDA?

Yes. eSubmitter has already been widely used by CVM and has improved the ease with which information can be shared among reviewers and sent from sponsors to CVM. In short, electronic submission is more efficient than large amounts of physical documents, for industry and agency alike. In addition to eliminating a significant amount of paper, eSubmitter reduces the time needed to copy and assemble paper submissions. It also allows for complete electronic archiving and storage of documents.

While eSubmitter is an important step forward, inputting information into the system and understanding what is required for different sections within the template continues to require significant industry time because of tight restrictions on acceptable file types. AHI is working with CVM to improve the eSubmitter program. Most AHI members currently use electronic submissions and work closely with CVM when troubleshooting issues.

GREG WALDEN, OREGON
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FIFTEENTH CONGRESS
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April 5, 2018

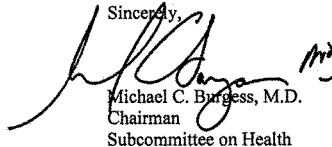
Dr. Bill Zollers
Chairman
Generic Animal Drug Alliance
9 Newport Drive; Suite 200
Forest Hill, MD 21050

Dear Dr. Zollers:

Thank you for appearing before the Subcommittee on Health on March 14, 2018, to testify at the hearing entitled "Reauthorization of Animal Drug User Fees 2018: ADUFA and AGDUFA."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on April 19, 2018. Your responses should be mailed to Zack Dareshori, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, DC 20515 and e-mailed in Word format to zack.dareshori@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Michael C. Burgess, M.D.
Chairman
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment

Attachment — Additional Questions for the Record**The Honorable Gus M. Bilirakis**

Would you briefly explain the importance to industry and public health of efficient and predictable review periods for generic animal drugs?

For public health, AGDUFA has provided additional resources for FDA-CVM to make the thorough review process more efficient and predictable in terms of timing. This capacity leads to sustainability of the regulatory review process for generic veterinary drugs. The benefit of AGDUFA to the FDA-CVM review process further protects the public health by resulting in the approval of safe and effective veterinary generic drug products. This ultimately leads to a longer, healthier lifespan for our family pets and a safer food supply for the public.

For industry, efficient and predictable review cycles allow Sponsors of veterinary drugs to plan more effectively and to choose generic drug development projects that will lead to a positive financial outcome. As mentioned in the GADA testimony on March 14, 2018, prior to the implementation of AGDUFA, a CVM review cycle of a generic drug application could take longer than 700 days. In many cases where the regulatory process required multiple review cycles, it could easily take 6 to 8 years to receive an approval for a generic drug. This was a major disincentive to the generic drug Sponsors. Without the re-authorization of AGDUFA, we fear that a lack of funding will result in a number of CVM reviewers losing their jobs, and a return to the longer and unsustainable timeframes for regulatory review cycles. This is the main reason industry is stepping forward again to support the reauthorization of AGDUFA III. Ideally, industry would like to see increases in Congressional budget appropriations to the veterinary generic drug approval process.

The Public and the Sponsors of generic drugs have a financial interest in an efficient and predictable regulatory process. For the Public, the financial interest is that generic animal drugs provide a cost-effective alternative to pioneer drugs. For the Sponsor, a predictable regulatory review and approval process ultimately leads to a better financial position. When a veterinary drug company sells high-quality, safe generic drugs, this not only leads to better lives for our family pets and a safer food supply, but it also helps to stimulate the economy, create and/or sustain jobs, and provide a return on investment to shareholders.

The Honorable Frank Pallone, Jr.

Since the first iteration of the ADUFA and AGDUFA programs, these agreements have worked to streamline the animal drug approval process at FDA while also ensuring that animal drugs for both pets and food-producing animals are safe and effective.

I'm interested in hearing GADA's perspective on why the animal drug user fee programs are so important and why we must ensure the timely reauthorization of these programs.

1. Dr. Zollers, can you briefly summarize why you believe the ADUFA and AGDUFA programs, respectively, are critical to the development of animal drug products?

The ADUFA and AGDUFA programs provide key funding to assist the FDA-CVM in protecting the public health by ensuring the safety, efficacy and security of veterinary drugs and by ensuring the safety of our nation's food supply. Without

these additional ADUFA and AGDUFA resources provided by the industry, the FDA-CVM has told us that review times would increase significantly and therefore the review process would lose efficiency and increase the time to approval for generic animal drugs. The uncertainty created due to the lack of ADUFA and AGDUFA funding would set back the ability to bring new pioneer and generic drugs to the Public to promote advances in health for veterinary medicine.

2. How has the animal health industry evolved since the implementation of ADUFA and AGDUFA and how have the animal drug user fee programs improved the animal drug application review process at FDA?

The ADUFA and AGDUFA programs have created a predictable review cycle allowing the Sponsor to plan and anticipate better. To speak specifically to the AGDUFA program, part of the evolution of the generic veterinary drug industry over the last 9 years has included new CVM interpretations of the requirements for a veterinary generic drug. There is some debate as to whether all the new requirements effectively lead to safer drug products. It is a struggle for industry to balance the support for AGDUFA as we know that growing the FDA-CVM capacity is likely to lead to additional drug development requirements that may not contribute to the safety of drugs in a measurable way.

Upon evaluation of the FY2017 AGDUFA Performance Report and the FY2017 AGDUFA Financial Report, GADA notes that over the last 9 years there are more sponsors and interest in seeking approval of generic animal drugs. This is evidenced by the reported increase in sponsors and based on the increase in the JINAD sentinel submissions, which are indicative of a significant increase in workload. However, there is not a corresponding significant increase in generic drug approvals by FDA-CVM. The output of approvals does not follow the same increased trajectory as the workload involved in the process to approval. GADA is hopeful that this increased workload, which is reflective of significant interest by the Sponsor, will show up in the number of approvals in the coming years.

3. Can you provide examples of how the ADUFA and AGDUFA programs, respectively, have helped your industry to innovate and have resulted in bringing more products to the market?

Given that GADA's testimony on March 14, 2018 was focused on AGDUFA, we will speak to that User Fee program. The focus of the generic industry through the AGDUFA program has been to eliminate the backlog of submissions under review in 2008 and decrease the review cycle from greater than 700 days down to the proposed 180 days in AGDUFA III. There have been great strides in accomplishing these goals. However, this has not translated into a significant increase in the number of generic drug products approved over the last 9 years.

There are really no good specific examples of innovative generic approval regulatory pathways that have resulted directly from the AGDUFA program. GADA continues to support innovative ways that might improve the efficiency of the review process and lessen the burdensome requirements without sacrificing safety.

4. In your opinion, what are the most significant new proposals in ADUFA IV and AGDUFA III and how do they further improve the animal drug review process at FDA?

The GADA testimony on March 14, 2018 was focused on AGDUFA III. The most significant improvement in AGDUFA III is the reduction in the submission review cycles. For Phased submissions, the review goes from 270 days to 180 days and the reduction in the administrative ANADA review cycle goes from 100 days to 60 days. These reductions put generic drug application review cycles on par with the pioneer drug applications. These reductions in review cycle timeframes come with a very high cost to industry, as the total cost of AGDUFA III (~\$95 million) will approximately double from the total cost of AGDUFA II (~\$47 million to ~\$50 million).

Industry willingly supports AGDUFA III. However, industry will be unwilling to increase its contribution in the future if we do not see an increase in product approvals. It will simply get to a point where it does not make financial sense. As industry has doubled our dollars going from AGDUFA II to AGDUFA III, we have not seen a similar increase in generic drug products approved. In addition, we have seen little or no increases in Congressional budget appropriations allocated to the veterinary generic drug approval process.

5. Can you explain why it is so critical that these programs are reauthorized before the sunset date of September 30, 2018?

Upon sunset of the AGDUFA III User Fee program, the review cycles for generic drug applications would likely go from the current 270 days to in excess of 700 days, as was the review cycle timeframe before AGDUFA. A number of reviewers at FDA-CVM would lose their jobs because no funding would be available unless additional Congressional budget appropriations were provided. This would be a lose-lose-lose situation for FDA-CVM, industry and the public.

For public health, AGDUFA has provided additional resources for FDA-CVM to make the thorough review process more efficient and predictable in terms of timing. This capacity leads to sustainability of the regulatory review process for generic veterinary drugs. The benefit of AGDUFA to the FDA-CVM review process further protects the public health by resulting in the approval of safe and effective veterinary generic drug products. This ultimately leads to a longer, healthier lifespan for our family pets and a safer food supply for the public.

For industry, efficient and predictable review cycles allow Sponsors of veterinary drugs to plan more effectively and to choose generic drug development projects that will lead to a positive financial outcome. As mentioned in the GADA testimony on March 14, 2018, prior to the implementation of AGDUFA, a CVM review cycle of a generic drug application could take longer than 700 days. In many cases where the regulatory process required multiple review cycles, it could easily take 6 to 8 years to receive an approval for a generic drug. This was a major disincentive to the generic drug Sponsors. Without the re-authorization of AGDUFA, we fear that a lack of funding will result in a number of CVM reviewers losing their job and these longer and unsustainable timeframes for regulatory review cycles will return. This is the main reason industry is stepping forward to support the reauthorization of AGDUFA III. Ideally, industry would like to see increases in Congressional budget appropriations to the veterinary generic drug approval process.

The Public and the Sponsors of generic drugs have a financial interest in an efficient and predictable regulatory process. For the Public, the financial interest is that generic

animal drugs provide a cost-effective alternative to pioneer drugs. For the Sponsor, a predictable regulatory review and approval process ultimately leads to a better financial position. When a veterinary drug company sells high-quality, safe generic drugs, this not only leads to better lives for our family pets and a safer food supply, but it also helps to stimulate the economy, create and/or sustain jobs and provide a return on investment to shareholders.

FDA has been working since May 2016 to finalize recommendations for the reauthorization of the animal drug user fee programs and as part of this process FDA held negotiations with the regulated animal drug and generic animal drug industries to reach agreement on both financial and performance goals for ADUFA IV and AGDUFA III.

6. What are some of the major improvements this proposal makes from the current goals and how will these proposals create new efficiencies for FDA?

In AGDUFA III, the most significant improvements for industry are the reduction in the Phased submission review cycle from 270 days to 180 days, and the reduction in the administrative ANADA review cycle from 100 days to 60 days. This puts generic drug application review cycles on par with that of the pioneer drug applications. In AGUFA III, the overcollections and offset provisions have been refined and improved to allow funding to be more effectively and efficiently ready for use by FDA-CVM to continue to improve the generic drug review process.

GADA is cautiously optimistic that these shorter review times will not result in multiple review cycles. Overall, we are hopeful that the reduction in review times will lead to a shortened time from project initiation to approval, allowing generic products to come to market sooner.

7. Dr. Zollers – do you believe that the electronic submission requirements included in this discussion draft will improve the efficiency of the animal drug approval process at FDA?

The electronic submission process has already been available to Sponsors for a number of years. According to the FY 2017 Performance Report to Congress for AGDUFA, in FY2013, 48% of generic product related submissions were via the electronic pathway. In FY2017, 58% of generic product related submissions were via the electronic pathway. Each year, adoption of the electronic submission process increases. CVM has told industry that e-Submissions improve the efficiency of the generic drug review process.

FDA-CVM requested that AGDUFA III include the provision that 100% of submissions be electronic. Industry has accepted this proposal, although we realize there will be an initial burden on Sponsors not currently using the e-Submission pathway. FDA-CVM is providing a webinar training series to allow Sponsors the opportunity to learn how to establish and utilize the e-Submission process. GADA is also reaching out to all of its member companies and associates to assist in connecting them to the resources needed to establish the e-Submission pathway.

This will allow CVM to eliminate the “paper” process submission system; essentially allowing FDA-CVM to move to one system: electronic. This will save time, money and effort and CVM can invest these efficiencies in other aspects of regulatory review. GADA understands that potential efficiency gains that can be made. GADA supports the transition to 100% electronic submissions.

GREG WALDEN, OREGON
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FIFTEENTH CONGRESS
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April 5, 2018

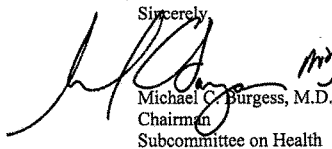
Dr. Michael Topper
President
American Veterinary Medical Association
1910 Sunderland Place, N.W.
Washington, DC 20036

Dear Dr. Topper:

Thank you for appearing before the Subcommittee on Health on March 14, 2018, to testify at the hearing entitled "Reauthorization of Animal Drug User Fees 2018: ADUFA and AGDUFA."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on April 19, 2018. Your responses should be mailed to Zack Dareshori, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, DC 20515 and e-mailed in Word format to zack.dareshori@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Michael C. Burgess, M.D.
Chairman
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment



April 19, 2018

The Honorable Michael Burgess, Chair
The Honorable Gene Green, Ranking Member
U.S. House Committee on Energy and Commerce
Subcommittee on Health
2125 Rayburn House Office Building
Washington, D.C. 20515

**Answers, Questions for the Record for the March 14, 2018 hearing entitled
"Reauthorization of Animal Drug User Fees 2018: ADUFA and AGDUFA" from AVMA
President Dr. Mike Topper**

Dear Chairman Burgess and Ranking Member Green,

Thank you for the opportunity to testify at the March 14, 2018 hearing entitled "Reauthorization of Animal Drug User Fees 2018: ADUFA and AGDUFA." On behalf of AVMA President Dr. Mike Topper, please find attached the answers to submitted questions for the record. If you have questions or require further information, please do not hesitate to contact Dr. Lauren Stump at lstump@avma.org or 202.289.3211.

Sincerely,



Kent McClure, DVM, JD
Chief Government Relations Officer

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The AVMA is the nation's leading representative of the veterinary profession, speaking for more than 91,000 member veterinarians across the United States who care passionately about protecting animal health, animal welfare and human health. Informed by its members' unique scientific training and knowledge, the AVMA advocates for policies that advance the practice of veterinary medicine and support the crucial work of veterinarians nationwide.

April 19, 2018
 The Honorable Michael Burgess, Chair
 The Honorable Gene Green, Ranking Member
 U.S. House Committee on Energy and Commerce
 Subcommittee on Health

Answers to Questions for the Record, hearing entitled "Reauthorization of Animal Drug User Fees 2018: ADUFA and AGDUFA" from AVMA President Dr. Mike Topper

The Honorable Gus M. Bilirakis

Question 1: In your testimony, you mentioned the need for new and innovative medicines to fulfil unmet needs for veterinarians. Would you walk us through some of the unmet needs your members see in their practices?

Answer 1: There are numerous examples of unmet animal drug needs in veterinary medicine given the number of different animals that we treat. It is not economically feasible for a drug company to develop a treatment for a disease or condition that occurs uncommonly or in only one species. Further, it is not economically feasible for drug companies to go through the development and approval process for a drug for each of seven major species of animals, much less each of innumerable minor species of animals. Nor is it practical for drug companies to go through the same approval process for different, but similar, indications. Certain diseases are difficult to study due to inherent difficulties in constructing long-term studies, enrolling the required number of patients, and in studying people's pets or other owned animals, among other factors. Specific examples include a lack of commercial eye drops to treat common herpesvirus eye infections in cats, immune-modulating or gene-targeted therapies to decrease the severity of a fatal condition called degenerative myelopathy in dogs, local analgesics for use during procedures such as castration or dehorning in food animal species, and drugs to treat or prevent a fatal infection called blackhead in turkeys. More generally, targeted therapies for immune-mediated conditions would improve treatment outcomes and decrease potential side effects, and the development of more selective anti-inflammatories or other pain medications for arthritis in cats, for which there is no proven safe drug for long-term treatment, would also be a great step forward. Not only is the development of therapies for use for their labeled indication important, but the safety and efficacy data they provide is enormously beneficial when extralabel drug use (ELDU) provisions in the Federal Food, Drug, and Cosmetic Act apply. ELDU allows veterinarians to legally use a drug approved for one species or condition to treat a different species or a different condition in which that therapy is effective, but not labeled. Development of additional therapies and the generation of additional safety and efficacy data will benefit both approved uses and ELDU and are critical for improving the health and well-being of our pets, and through food animals, the quality and safety of our food supply.

Question 2: Would you explain some of the challenges that exist for veterinarians and veterinary therapeutic options in the context of extralabel drug use?

Answer 2: Extralabel drug use (ELDU) is a vital provision in the Federal Food, Drug, and Cosmetic Act that allows veterinarians to effectively treat their patients despite a lack of a drug specifically labeled for that condition. Veterinarians do not enjoy access to the same number of approved therapies as human physicians and practitioners, as there are roughly 25 times the number of approved drugs for use in humans as there are for use in all animal species. Even in human medicine, where there is much greater access to approved drugs, there is often the need to use them in a manner that differs from their approved labeling. In many cases there is no financial incentive for manufacturers to develop animal-specific products or to go through an approval process in each species of animal for which a drug may have use, and an understanding of ELDU becomes critical. Under ELDU provisions, veterinarians may use a drug approved for one animal or purpose in a different animal or for a different purpose when a more appropriate therapy does not exist. For example, many anesthetics and pain medications used daily by veterinarians in hospital or clinic procedures are approved only for use in humans, but they are no less vital to our animal patients for the same purposes. Veterinarians regularly perform the complex task of interpreting multiple sources of data including labeled animal and human drug data, independent studies, foreign research and data, and historically successful clinical endpoints to choose the most appropriate therapy for their patients. Conditional approval is a process through which a manufacturer is able to market their product after proving full safety data and a reasonable expectation of efficacy, but while still gathering final efficacy data. Currently this process is only allowed in the approvals process for minor uses and minor species, and it would be a transformative improvement to the user fee agreements if this were expanded to major uses in major species, and if this improvement included allowing ELDU of these conditionally approved drugs. Allowing ELDU of these drugs, within the current legal and regulatory framework, would further increase options available for treating animal patients, especially for all those species that are not one of the seven major species and for more uncommon conditions. Expanding this under the existing legal and regulatory framework would keep existing prohibitions on uses of antimicrobials and certain other drugs in food producing animals, and continue to prohibit ELDU of medicated animal feed. Allowing for ELDU of conditionally approved products would have no impact to any FDA policy to address antimicrobial resistance.

The Honorable Frank Pallone, Jr.

I'm interested in your perspective on how the ADUFA and AGDUFA programs have improved animal health, as well as the nation's food supply. Animal drug development and approvals are critical to ensuring that our companion pets lead longer and healthier lives and that our food-producing animals are safe for human consumption.

Question 1: Can you explain how the animal drug user fee agreements have improved animal health, both for pets and food-producing animals?

Answer 1: Animal drug user fee agreements and animal generic drug user fee agreements have improved animal health for pets and food-producing animals by providing veterinarians with additional tools with which to treat their patients. In recent years, the veterinary community has seen the approval of several new animal drugs, partly in thanks to the streamlined and predictable pathway provided by ADUFA and AGDUFA. Examples of improvements include a transdermal solution for cattle to treat pain in cases of a debilitating and painful disease called footrot, and which also treats the fever associated with pneumonia. In pigs, a first-in-class, animal-only antimicrobial that is not considered medically important in human medicine, Avilamycin, was developed to reduce a disease called scours that causes devastating diarrhea in weaned pigs. We have seen approval of a drug for use in horses to relieve certain types of a condition called colic, which can cause significant pain in the gastrointestinal tract and be fatal. These user fee agreements have also contributed to the approval of many therapies that improve the comfort and well-being of our pets. For example, a new drug was developed to target and inhibit a step in the pathway in a dog's response to allergens, and provides them more effective relief from allergies. An insulin product approved for use in both dogs and cats also allows for improved management of diabetes mellitus in many instances. In addition to these, there are many other examples of improvements that have been made, leading to improved animal health for pets and livestock.

Question 2: As a veterinarian, what are the benefits of increasing the efficiency of the animal drug approval process? Does ADUFA and AGDUFA help bring new and innovative products to the market faster in order to help treat animal patients?

Answer 2: By increasing the efficiency of the animal drug approval process and providing a predictable path to market, veterinarians have been provided with new and more efficacious therapies for some conditions in animals. This would not have been possible without user fee agreements. In an ideal scenario, there would be both robust pioneer and generic industries providing veterinarians and their patients with approved products for multiple uses and all species. However, the costs associated with developing this number of approved products and the every-day realities of veterinary practice that require cost-efficiencies and effectiveness make this unlikely. ADUFA and AGDUFA have helped bring new and state-of-the-art products to market, and there are improvements that can be made to the conditional approval process to further increase the number of approved drugs to both major species and minor species under the existing legal and regulatory framework surrounding extralabel drug use.

Question 3: Can you discuss why the FDA gold standard of safety and efficacy is so critical when treating animal patients?

Answer 3: The FDA review process provides veterinarians and animal owners with assurances in regard to the use of drug products in animal patients. It provides veterinarians with safety and efficacy data that would not otherwise be available to them. When an animal drug is FDA-approved to treat a specific condition, a veterinarian must choose that drug to treat the patient unless circumstances that warrant extralabel drug use (ELDU) apply, as defined in statute in the Animal Medicinal Drug Use Clarification Act of 1994 and in FDA regulations. However, for the majority of conditions that veterinarians must treat in numerous animal species, there are no drugs specifically labeled for that use. ELDU is a vital provision within the Federal Food, Drug, and Cosmetic Act that allows veterinarians to treat their patients despite a lack of a labeled therapy, protecting both animal and human health. For example, many analgesics and other drugs used daily by veterinarians are approved only for use in humans, but they are no less vital to our animal patients in those instances. Even in human medicine, where there is much greater access to approved drugs, there is often the need to use them in a manner that differs from their approved labeling. Legal restrictions on use in food animals are in place to safeguard human health, such as banning ELDU of medicated animal feed, and appropriate restrictions on the use of medically-important antimicrobials and certain other drugs. In both food and companion animals, veterinarians regularly perform the complex task of interpreting multiple sources of data including drug labels, independent studies, foreign research data, and historically successful clinical endpoints while applying their medical knowledge of unique pharmacokinetic and pharmacodynamic principles for many drugs and species in order to choose the most appropriate therapy for each specific patient. To determine the best course of action when ELDU is required, as in cases when no appropriate labeled therapy exists, veterinarians use their medical knowledge and training to analyze existing sources of safety and efficacy data, including data from FDA-approved animal drugs. When full approval is possible, feasible, and practical, a fully approved-drug can yield an abundance of information to veterinarians for both its labeled indication and in cases when ELDU is required. Drugs conditionally approved for use in animals provide full safety data and preliminary efficacy data in at least one animal species, and that data can be translated to other uses in that same species and across species as well. FDA safety and efficacy data is the gold standard, and ADUFA and AGDUFA's capability to provide veterinarians with an increase in this data can improve the health of animals regardless of the labeled indication when ELDU is legally allowed. Improving both the conditional approvals process through expansion to major species and allowing ELDU of conditionally approved drugs would be a transformative improvement to the user fee agreements. Allowing for ELDU of conditionally approved products would have no impact to any FDA policy to address antimicrobial resistance.