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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, D.C.

The subcommittee met, pursuant to call, at 10:15 a.m., in Room 2322 Rayburn House Office Building, Hon. Michael Burgess [chairman of the subcommittee] presiding.

Members present: Representatives Burgess, Guthrie, 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: Zachary Dareshori, Staff Assistant; 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, External Affairs; Jacquelyn Bolen, Minority Professional Staff; Jeff Carroll, Minority Staff Director; Samantha Satchell, Minority Policy Analyst; Andrew Souvall, Minority Director of Communications, Outreach and Member Services; Kimberlee Trzeciak, Minority Senior Health Policy Advisor; and C.J. Young, Minority Press Secretary.

Mr. Burgess. I now call the subcommittee to order and recognize myself five 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 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 five 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 review several times -- 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 five-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.

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. Gentlelady yields back. Chair thanks the gentlelady.

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

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, and this hearing, Mr. Chairman, is so very important and so I associate my comments with the gentlelady from Tennessee that this is bipartisan, bicameral, and this -- 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, five minutes.

The Chairman. 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 and 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 our witness -- the witness today. We are actually going to get the wisdom of Solomon today, apparently. So we do appreciate that.

And with that, I would yield the remainder of my time to Mr. Mullin, I believe, who is seeking time and 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, five minutes for an opening statement, please.

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 Health 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 five 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 are 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 antimicrobial 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.

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

This concludes with 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 five minutes to give a summary of your opening statement, please.

STATEMENTS OF DR. STEVEN SOLOMON, DIRECTOR, CENTER FOR VETERINARY MEDICINE (CVM), FOOD AND DRUG ADMINISTRATION (FDA)

Mr. 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, 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 process 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 time frame for reviewing categorical exclusion and Animal Drug Availability Act combination medicated feed requests by two-thirds.

We also establish new goals for pre-submission 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 gross. 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:]

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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 and I will begin by recognizing myself for five 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 it been -- has that been more straightforward or more difficult than you would have anticipated?

Mr. 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?

Mr. 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?

Mr. Solomon. So the current user fees represent around 30 percent of the -- of the animal drug -- 35 percent of the staff on the animal drug review side and around 60 percent of -- on the generic drug user fee side.

So those are covered by user fees.

Mr. Burgess. Okay. 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?

Mr. 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 while they're developing -- 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 time frames for some unique aspects of the categorical exclusion in some of our environment findings.

On the generic drug side, we are dramatically reducing the time frames 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?

Mr. 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.

Is -- am I right or wrong about that?

Mr. 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 five-year time frame 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?

Mr. 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 time frame for efficacy requirements, which can be up to five 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?

Mr. 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 five years for the full standard for efficacy, which means substantial evidence of efficacy at the end of that five periods.

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?

Mr. Solomon. Yes. So we recognize that on the pioneer side, most of the submissions are coming in on electronic on the generic side. There is -- 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?

Mr. 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 comes abundant harvest. So what we are doing here goes back to understanding we have to have a good agriculture, even back in the Bible times --

[Laughter.]

-- and from -- 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 around shortening the review time frame for combination medicated fee?

Mr. Solomon. Sure.

So this was an agreement under -- that we worked on during the previous time frame. 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 anti-parasitic drug, for, say, conidia. At the same time

they may be treating an 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 time frame to evaluate these drugs when they combine them together in medicated feeds.

Mr. Guthrie. Okay. 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?

Mr. 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?

Mr. 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 time frame for this agreement?

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

Mr. 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 trying -- moving that agreement forward in the time frame for meeting that assessment so we can evaluate the GMP conditions on the animal side of the house.

Mr. Guthrie. Okay. 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, five minutes for questions, please.

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

Welcome, Dr. Solomon.

Mr. 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 Health 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 about 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 -- some of the changes in the conditional approval process to be very helpful.

Getting back to the -- to the minor uses major species and minor species piece, there are -- my understanding from the

testimony there's only been four, really, applications and only one been approved.

What's the -- is there a problem in the process here or do you need some more help from us?

Mr. 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 aquiculture product that got approved -- clearly, a needed area of resources.

Two of them demonstrate some of the challenges. So two were cancer-causing -- 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 okay? It's just maybe a company is getting used to the process or getting familiar with the opportunity?

Mr. 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. Okay.

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?

Mr. 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 post-marketing 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 date 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, five 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 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?

Mr. Solomon. So thank you.

So a tissue residue method is for a 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 any -- 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 products go on the market.

We work -- 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 people that -- 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?

Mr. 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 of 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 use of the 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, five 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?

Mr. 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 kind 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 time frames.

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

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 --

Mr. Solomon. Right.

Mrs. Brooks. -- what kind of time frame are we looking at now?

Mr. Solomon. So we are getting closer towards these 180-day

time frames. You know, it depends how many times -- what the work looked like, the quality of the submissions.

But we've dramatically reduced the time frames 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?

Mr. 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.

Mr. Solomon. Right.

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

Mr. 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. We would -- 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?

Mr. 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 five 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, five 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?

Mr. Solomon. Correct.

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

Mr. Solomon. So on the -- 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?

Mr. 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?

Mr. Solomon. They do not. So that -- 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 --

Mr. 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?

Mr. 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?

Mr. 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.

Then they -- 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?

Mr. 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?

Mr. Solomon. So I need to get back to you on the patent issues. We do have exclusivity issues where the drugs are either for three years or five 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?

Mr. 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, five 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?

Mr. 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 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. Okay. Very good.

How has consolidation in the industry impacted the review process?

Mr. 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. Okay. What are the consequences of not

reauthorizing these user fee programs?

Mr. Solomon. So I hope no one wants to go down that path because it's significant.

Mr. Bilirakis. Tell us why.

Mr. Solomon. Again, we've achieved these timely review processes. It would create instability in the industry. We've become very predictable on the time frames 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 who not want to come to work for the Center of Veterinary Medicine where we have outstanding scientists and reviewers -- 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 he gentleman. The gentleman yields back.

The chair recognizes the gentleman from Virginia, Mr. Griffith, five 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?

Mr. Solomon. So we are working very closely on the antimicrobial resistant 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 there 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, and I am going to shift gears on you, and feel free to tell me that 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 -- 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 --

Mr. 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.

Mr. Solomon. But in a genetically modified animal they do need to go to a review process to make sure these animals are safe and is someone's going to eat them that the modification makes it safe for people to eat.

Mr. Griffith. And just -- 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.

Mr. 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,

five 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?

Mr. 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. Yeah, 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?

Mr. 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 five 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, five 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 -- a couple questions that I have -- what is -- what 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 -- how we can more predict in the industry level?

Mr. 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 describe 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 be -- welcome the opportunity to give some technical assistance to it.

There may be some remaining issues that would need to be worked 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.

Mr. Solomon. So once again, in 2004 it was for the minor species and minor uses.

Mr. Mullin. Right.

Mr. 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?

Mr. Solomon. The industry is, clearly, at the table.

Mr. Mullin. Right.

Mr. Solomon. American Veterinary Medical Association, a lot of people that are sitting here today.

Mr. Mullin. Are we the ones missing at that table then? I mean, if 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?

Mr. 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 time frames 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 -- have you had a time to look at it yet?

Mr. 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?

Mr. 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 --

Mr. 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 -- 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.

Mr. 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 -- we will -- we will work with you, absolutely.

Chair now recognizes the gentleman from Texas, Mr. Green, five 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 two 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 five 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?

Mr. 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?

Mr. Solomon. That's correct.

So once again, we've reduced time frames 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 time frames?

Mr. 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?

Mr. 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?

Mr. Solomon. The tremendous changes on the generic drug side dramatically reduce the time frames associated with those. So I think the industry and FDA would be very excited about meeting those new time frames 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 AGDUFA programs and will chart the course for the next five 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, five 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. An issue -- 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, making -- 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?

Mr. Solomon. I do. It is -- 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 mean 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?

Mr. 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?

Mr. 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?

Mr. 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 -- what are some of the reasons that these sometimes take longer?

Mr. 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 five 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, they -- 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 labelling -- 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 falls -- 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 than -- 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?

Mr. 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 pharmakinetics 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?

Mr. Solomon. So we did have a guidance of 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 veterinary-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.

Mr. Solomon. We wanted to clarify that it was never intended

to apply to that.

Mr. Carter. Thank you.

Mr. 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. Okay. Have you -- are you soliciting the input of the animal drug compounders while you're formulating this?

Mr. 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 practising 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.

Mr. 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 we are going to hear -- 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 five minutes to summarize your opening statement.

STATEMENTS OF DR. RACHEL CUMBERBATCH, DIRECTOR, REGULATORY AFFAIRS, ANIMAL DRUGS, ANIMAL HEALTH INSTITUTE; DR. BILL ZOLLERS, CHAIRMAN, GENERIC ANIMAL DRUG ALLIANCE; DR. MICHAEL TOPPER, AMERICAN VETERINARY MEDICAL ASSOCIATION

STATEMENT OF DR. CUMBERBATCH

Ms. 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 ever 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 five-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 time frames 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. But 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:]

**********INSERT 2**********

Mr. Burgess. Thank you for your testimony.

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

STATEMENT OF DR. ZOLLERS

Mr. 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 focussed on the development, regulatory approval, and marketing of high-quality generic drugs for 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 the 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 two years. In most cases, multiple review cycles are needed. So if an application required three review cycles, it could easily take more than six to eight 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 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:]

**********INSERT 3**********

Mr. Burgess. Chair thanks the gentleman.

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

STATEMENT OF DR. TOPPER

Mr. 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, 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 prescribing 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 educations 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:]

**********INSERT 4**********

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 five 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.

Ms. 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.

Mr. 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 two-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.

Mr. 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.

Ms. 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 five-year -- the five-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.

Mr. 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 two-year review cycle and now getting it down to something manageable, now we are focused on how do we reduce the time frame 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 five years from now.

Mr. Burgess. Yes, sir. Dr. Topper.

Mr. 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?

Mr. Topper. Yes, sir. It should speed it up. It should decrease the cost to a -- 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.

Mr. Zollers. Yes. We are totally in favor of the electronic system.

Mr. Burgess. Dr. Cumberbatch.

Ms. Cumberbatch. As Dr. Solomon mentioned, a majority of sponsors of pioneers drugs use the electronic submission system already.

What we do see is a need to look at the efficiency -- how much data are we -- 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, the -- kind of the differences between humans and animals, having spent a lifetime in practising 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 -- 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 five 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?

Mr. 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 okay.

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?

Mr. Topper. Well, the FDA is monitoring. We do the disease -- 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. Okay. Do you know what the American Veterinarian Medical Association is doing to educate its members on the importance of addressing these antimicrobial resistance and how can veterinarians be good stewards of antimicrobials when treating food-producing animals?

Mr. 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 they -- over a period of time they develop a resistance to them. Does that happen in animals as well as we see in humans?

Mr. 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.

Mr. 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 five 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 -- 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?

Ms. 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?

Ms. Cumberbatch. We've had the opportunity here 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 -- as a cattle owner which, you know, we -- 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 is 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 by 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 got -- they're 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 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 pre-emptive 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 over medicating, 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, five 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 they -- 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 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?

Mr. 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?

Mr. 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 it -- 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 indicate 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.

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 -- what -- 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?

Ms. 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 -- 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.

Mr. 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 five 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?

Ms. 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 over require. So is it your feeling that it could be done safely with less information?

Ms. 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? Okay. But not in the -- 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?

Ms. 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?

Ms. 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 practising 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?

Mr. 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, the -- 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 -- he 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.]