STATEMENT

OF

STEVEN SOLOMON, D.V.M., MPH

DIRECTOR, CENTER FOR VETERINARY MEDICINE

FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

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UNITED STATES SENATE

"IMPROVING ANIMAL HEALTH:

REAUTHORIZATION OF FDA ANIMAL DRUG USER FEES"

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Introduction

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

I recently returned to CVM as the Director after more than 20 years serving in other roles in FDA. This is a very exciting time for veterinary therapeutics necessary to protect both animal and human health. Advances in biotechnology are leading to the development of innovative, new animal drug products and approaches that offer the promise of a safer and healthier future for the people and animals we serve.

According to the American Veterinary Medical Association, more than half of American households include pets, most of whom are viewed as part of their families. Overall, this includes approximately 70 million dogs, 74 million cats – and a diverse assortment of birds, fish, and other animals. Our companion animals are living longer as promising new products are being developed to treat chronic and insidious diseases. In recent years, FDA has approved innovative treatment options, including two treatments for navicular disease in horses, one of the most common causes of lameness. The drugs, for the first time, target bone changes commonly caused by the disease. FDA has also approved new oncology treatments for dogs targeting canine-specific tumors. The drugs represent a significant advance for veterinary medicine which

traditionally relies on oncology treatments approved for humans to treat cancer in animals. These approved animal drugs contain canine-specific dosing instructions and safety information. Stem cell therapies offer great promise for future veterinary treatments and cures. Meanwhile, approval of the first generic version of a vital heartworm treatment has alleviated a shortage of this critically important treatment for dogs – and provided a safe, effective, and more affordable alternative for pet owners.

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

FDA considers timely review of the safety and effectiveness of new animal drug applications (NADAs) to be central to the Agency's mission to protect and promote human and animal health. ADUFA and AGDUFA are highly successful programs that facilitate the availability of approved products for food-producing and other animals and foster a flexible, risk-based review framework to accommodate innovative approaches to drug development. Prior to initiating these user fee programs, FDA's CVM had a large backlog of overdue submissions, and sponsors had to wait on average 500 days for pioneer drug review responses and 700 days for generic drug

review responses. As a result of ADUFA and AGDUFA user fees, CVM eliminated the backlog in applications and has dramatically reduced the time needed to review animal drug applications and other submissions. Both programs help FDA to maintain a stable scientific and technical workforce, improve timely communications with drug sponsors, and achieve other efficiencies in the drug approval process while maintaining science-based regulatory standards for drug safety and efficacy.

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

Status of FDA's Reauthorization Activities

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

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

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

ADUFA Background

The five-year reauthorization cycles for ADUFA – and AGDUFA – have supported continuous program innovation, evaluation, and improvement. Through successive reauthorizations, program enhancements have evolved and expanded to include extensive communication and consultation between drug sponsors and FDA throughout drug development. ADUFA I enabled FDA to increase the number of staff dedicated to animal drug review by approximately 30 percent. ADUFA II included important measures to enhance communications with industry,

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

develop and implement electronic submission capability for applications and submissions, and added pre-approval foreign inspection goals. It also supported 10 public workshops on mutually agreed upon topics.

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

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

FDA continues to improve communications, timeliness, and predictability of foreign pre-approval inspections. As a result of ADUFA III, sponsors may voluntarily submit a list of foreign manufacturing facilities they anticipate including in their applications subject to pre-approval inspections for the following fiscal year. Six sponsors voluntarily submitted such lists

in FY 2016, allowing better planning for all parties involved and timely execution of good manufacturing practice (GMP) inspections by FDA.

Also as part of ADUFA III, FDA agreed to two long-term goals. First, we agreed to explore the possibility of pursuing statutory changes to expand the use of conditional approval. FDA is continuing work on the goal of exploring the feasibility of statutory revisions to expand the use of conditional approvals to other appropriate categories of new animal drug applications beyond the current FD&C Act authority provided under the Minor Use and Minor Species Animal Health Act of 2004 (MUMS Act). CVM formed a Conditional Approval Working Group that has conducted preliminary activities to evaluate the feasibility, practicality, criteria, and potential requirements for expanding the use of conditional approval to certain major uses in major species. FDA is committed to continuing to explore through a public and transparent process the expanded use of conditional approval consistent with the Agency's mission to protect and promote public health. In our second long-term goal, FDA agreed under ADUFA III to explore the feasibility of statutory revisions that may modify the current requirement that the use of multiple new animal drugs in the same medicated feed each be subject to a separate approved application. The Agency held a public meeting on March 16, 2015, to discuss this issue with stakeholders. In FY 2016, CVM fulfilled its commitment as outlined in the ADUFA III goals letter and provided written recommendations concerning the use of multiple new animal drugs in the same medicated feed for consideration through the *Federal Register* on May 2, 2016.[2] This proposal formed the basis for process changes being recommended in ADUFA IV.

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

ADUFA Performance

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

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

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

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

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the Regulation of Combination Drug Medicated Feeds," May 2, 2016, available at *https://www.regulations.gov/docket?D=FDA-2014-N-1050*.

Proposal for ADUFA IV

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

Additionally, ADUFA IV offers the following recommendations:

- Eliminating the Offset Provision, which will allow any excess collections to be more readily available for use by FDA for the process for the review of animal drug applications.
- In conjunction with eliminating the Offset Provision, for any fiscal year the Workload Adjuster is invoked in which FDA had excess collections in the second preceding fiscal year, provide for FDA to reduce the workload-based fee increase by the amount of excess

collections. If FDA did not have excess collections in the second preceding fiscal year, FDA will collect the full amount of the workload-adjusted fee revenue.

- Continuing to authorize recovery of collection shortfalls; however, provide for any fee increase to recover shortfalls to be reduced by the amount of remaining prior year excess collections not already applied for purposes of reducing workload-based fee increases.
- Modifying the Workload Adjuster base years from ADUFA II (FY 2009 through FY 2013) to ADUFA III (FY 2014 through FY 2018) to ensure the adjuster adequately captures changes in FDA's workload during ADUFA IV.

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

AGDUFA Background

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

Electronic submissions have grown from approximately 3 percent of submissions in FY 2011 to 58 percent in FY 2017.

AGDUFA II included further enhancements. FDA added flexibility with a second-cycle shortened review process for key submission types, such as protocols, data submissions, and applications that significantly impact the generic new animal drug approval timeline. Qualifying submissions receive a significantly reduced second-cycle review to shorten approval timelines. FDA also made multiple enhancements to the CMC technical section, similar to the ADUFA changes noted above.

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

AGDUFA Performance

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

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

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

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

Proposal for AGDUFA III

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

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

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

Additionally, AGDUFA III offers the following recommendations:

- Eliminating the Offset Provision, which will allow any excess collections to be more readily available for use by FDA for the process for the review of generic new animal drug applications.
- In conjunction with eliminating the offset provision, for any fiscal year the Workload Adjuster is invoked in which FDA had excess collections in the second preceding fiscal year, provide for FDA to reduce the workload-based fee increase by the amount of excess

collections. If FDA did not have excess collections in the second preceding fiscal year, FDA will collect the full amount of the workload-adjusted fee revenue.

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

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

Conclusion

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

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