ELIZABETH WARREN
MASSACHUSETTS

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United States Senate

UNITED STATES SENATE
WASHINGTON, DC 20510-2105
P: 202-224-4543

2400 JFK FEDERAL BUILDING
15 NEW SUDBURY STREET
BOSTON, MA 02203
P: 617-565-3170

1550 MAIN STREET
SUITE 406
SPRINGFIELD, MA 01103
P: 413-788-2690

www.warren.senate.gov

July 27, 2018

Scott Gottlieb, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, Maryland 20993

Dear Commissioner Gottlieb:

I am writing to request that you move swiftly to improve oversight of medically-important antibiotics in food animals by finalizing guidance on durations of use and veterinary oversight for all medically important antibiotic drugs administered to animals and publicly posting a list identifying drugs for which durations of use have not yet been set. I appreciate your public commitments to improving oversight of medically-important antibiotics in food animals, but I am concerned that animal drug user fee legislation currently pending in Congress does not contain requirements that would guarantee the FDA must take these steps.

Antibiotic drugs are critical tools for treating serious bacterial infections, but they are becoming less and less effective. Today, resistance has been seen in almost all antibiotics ever developed.[1] The CDC estimates that 2 million people in the U.S. develop antibiotic-resistant infections every year, resulting in over 23,000 deaths and adding as much as $20 billion in health care costs to an already-overburdened system.[2] Overuse of medically important antibiotics in food animals is a critical factor contributing to the growth of drug resistant bacteria that can cause hard-to-treat human diseases. One in five antibiotic-resistant infections in humans come from bacteria in animals and food.[3]

Despite the clear need for the judicious use of antibiotics in animals in order to curb the growth of antibiotic resistance, serious gaps remain in oversight of these drugs. A 2017 Government Accountability Office (GAO) report that I requested along with several of my colleagues found that while the Department of Health and Human Services (HHS) has increased oversight and data collection of medically important antibiotics in food animals in recent years, HHS's regulation of these products still has critical shortcomings.[4] In March of 2017, along with Senators Feinstein and Gillibrand, I sent a letter to then-Secretary Price, asking HHS to take

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[1] P&T, "The Antibiotic Resistance Crisis," C. Lee Ventola, April 2015, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/.
[2] Centers for Disease Control and Prevention, "Antibiotic/Antimicrobial Resistance," https://www.cdc.gov/drugresistance/index.html.
[3] Centers for Disease Control and Prevention, "Antibiotic Resistance from the Farm to the Table," https://www.cdc.gov/foodsafety/challenges/from-farm-to-table.html.
[4] U.S. Government Accountability Office, "Antibiotic Resistance: More Information Needed to Oversee Use of Medically Important Drugs in Food Animals," March 2, 2017, https://www.gao.gov/products/GAO-17-192?mobile_opt_out=1#summary_recommend.

action to implement the GAO's recommendations.[5] Secretary Price never responded to my letter. On April 13, 2018, on behalf of HHS, you sent me a response to the March 2017 letter, confirming that antibiotic resistance "is a serious global public health threat" and that you were "committed to advancing efforts to foster the judicious use of antimicrobial drugs in food-producing animals."[6]

FDA has long acknowledged that using medically-important antimicrobials in food animals for long or unlimited durations increases the risk of antibiotic resistance. In 2013, FDA issued Guidance for Industry (GFI) #213, which called for "explicitly defined duration of dosing" on new drug label indications because "giving antimicrobial drugs to food-producing animals at low levels for long periods of time and in large numbers of animals may contribute to antibiotic resistance." Current FDA guidance requires new drug indications to "have an explicitly defined duration of dosing."[7]

Despite these steps, as of September 2016, one-third of products containing medically-important antibiotics for use in animal feed or water still had label indications that lacked duration limits.[8] The FDA has acknowledged that GFI #213 "does not address some currently approved therapeutics that lack defined durations of use on their labels" and requested information on "how to establish appropriately targeted durations of use" for the remaining one-third of products lacking duration limits. The agency has solicited public comment on this question, but regulations addressing this issue have yet to be issued.

Furthermore, in 2015, the FDA implemented the Veterinary Feed Directive (VFD), which was intended to put an end to the use of medically-important antibiotics for the promotion of faster animal growth and feed efficiency, and to bring antibiotics used in feed and water under veterinary supervision.[9] While the VFD is an important step in improving the oversight of antibiotics, it does not extend veterinary oversight to drugs administered by other routes, like injections or tablets.[10] H.R. 5554, the "Animal Drug and Animal Generic Drug User Fee Amendments of 2018 would require a report from the FDA by September 2019 on how the agency "will incorporate veterinary oversight for all approved medically important antimicrobial drugs administered to animals that are not yet subject to veterinary oversight."[11] However, it is imperative that the FDA not just report on its progress but actually take concrete actions to extend veterinary oversight to all medically important antibiotics used in animals.

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[5] Letter from Senators Feinstein, Gillibrand and Warren and Representatives DeLauro and Slaughter to HHS Secretary Thomas E. Price and USDA Acting Deputy Secretary of Agriculture Michael Young, March 16, 2017.
[6] Letter from FDA Commissioner Scott Gottlieb to Senator Elizabeth Warren, April 13, 2018.
[7] FDA, Guidance For Industry 213, https://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf.
[8] Food and Drug Administration, "FDA Seeks Public Input on Next Steps to Help Ensure Judicious Use of Antimicrobials in Animal Agriculture," September 12, 2016, https://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm520110.htm.
[9] FDA, "Veterinary Feed Directive (VFD)," https://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/ucm071807.htm.
[10] U.S. Government Accountability Office, "Antibiotic Resistance: More Information Needed to Oversee Use of Medically Important Drugs in Food Animals," March 2, 2017, https://www.gao.gov/products/GAO-17-192?mobile_opt_out=1#summary_recommend.
[11] Animal Drug and Animal Generic Drug User Fee Amendments of 2018, H.R.5554, https://www.congress.gov/bill/115th-congress/house-bill/5554/text?q=%7B%22search%22%3A%22animal+drug+user+fee%22%7D&r=2.

At a House Energy and Commerce hearing on July 26th, you spoke about the need to improve the FDA's efforts to limit antibiotic resistance, stating: "We are going to be taking some additional steps to look at antibiotic use in animal feed, the length of the duration of use and the indications in which they are used, and plan to have some additional policy steps that we should be announcing within the next couple of months to continue to advance what we've already done in that regard to reduce the use of antibiotics in animal feed, and limit one route by which we're seeing resistance develop."[12]

While I welcome these statements, I am concerned that animal drug user fee legislation currently pending in Congress contains no requirements that the FDA carry out these promised actions. In order to address my continued concerns with this legislation and with persistent gaps in our nation's oversight of animal antibiotics, I ask that you swiftly provide answers to the following questions:

(1) Will you commit to reviewing the durations of use of all approved indications of medically important antibiotics labeled for use in animals?

(2) Will you commit to posting on the internet website of the FDA and updating every six months a list of all medically-important antibiotics labeled for use in animals and indicating which products on this list lack a duration of use in their labels or lack data supporting the duration of use?

(3) Will you commit to issuing a draft guidance to establish appropriately-targeted durations of use for medically-important antibiotics? Please provide the date by which you plan to issue this guidance.

(4) Will you commit to swiftly finalizing that guidance? Please provide the date by which you plan to finalize this guidance.

(5) Will you commit to issuing FDA guidance to bring all medically-important antibiotics under veterinary supervision? Please provide the date by which you plan to issue this guidance.

(6) Will you commit to swiftly finalizing that guidance? Please provide the date by which you plan to finalize this guidance.

Thank you for your continued attention to this issue. I look forward to your prompt response.

Sincerely,

Elizabeth Warren
United States Senator

[12] House Committee on Energy and Commerce, Subcommittee on Health, "21st Century Cures Implementation: Updates from FDA and NIH," July 25, 2018, https://energycommerce.house.gov/hearings/21st-century-cures-implementation-updates-from-fda-and-nih/.