

United States Senate

WASHINGTON, DC 20510

April 12, 2016

The Honorable Robert M. Califf, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Commissioner Califf:

We write regarding the public health threat of antibiotic resistant bacteria. While we are pleased that significant steps are being taken to reduce the risk of antibiotic resistance stemming from antibiotic use in human medicine, we remain deeply concerned about the use of antibiotics in animals. All use of antibiotics, whether in human medicine or in animal agriculture, can lead to antibiotic resistance. Through previous correspondences with the administration, we have identified clear gaps in current policies to improve the stewardship of antibiotics in food animal production.¹ As you begin your tenure as Commissioner of the Food and Drug Administration (FDA), we ask that you reexamine current policies and create a plan to address these clear gaps.

Too many food animals are still fed low doses of antibiotics continuously throughout their lifespan, putting them at risk of developing resistant bacteria. These bacteria can easily spread to humans through consumption of the animal's meat or through the animal's feces, which often are used to fertilize crops.² FDA data show that, in 2014, nearly 34 million pounds of antibiotics were sold for use in food animals.³ To make matters worse, all data indicate that antibiotic use in food animals is on the rise. From 2009 to 2014, the number of medically important antibiotics sold for use in food animals increased by 23 percent.⁴

We appreciate that the FDA has taken steps to try to address antibiotic overuse in food animals by establishing that using antibiotics to promote animal growth is inappropriate, requiring veterinary oversight for all other uses of antibiotics, and seeking to define the circumstances under which treating healthy animals with antibiotics to prevent a disease is appropriate.⁵ While these efforts represent an important first step, we have serious concerns that critical gaps in these

¹ Warren, Feinstein, Gillibrand letter to Dr. Hamburg, Commissioner, U.S. Food and Drug Administration. Jul. 28, 2014; Warren, Feinstein, Gillibrand letter to Secretaries Hagel, Vilsack, and Burwell, Interagency Task Force for Combatting Antibiotic-Resistant Bacteria. Dec. 15, 2014; Warren, Feinstein, Gillibrand letter to Secretaries Burwell, Vilsack, and Carter, Interagency Task Force for Combatting Antibiotic-Resistant Bacteria. Aug. 17, 2015; Dr. Robert M. Califf responses to Sen. Warren Questions for the Record from HELP Committee Hearing Nov. 17, 2015.

² Centers for Disease Control and Prevention, *Antibiotic Resistance from the Farm to the Table*. Nov. 16, 2015

³ FDA, *2014 Summary Report on Antimicrobials Sold or Distributed for Use In Food-Producing Animals*. Dec. 2015. Web. Pg. 17

⁴ *Ibid.* Pg. 17

⁵ FDA, *Guidance for Industry #209: The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals*. April 13, 2012; FDA, *Guidance for Industry #213: New Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209*. December, 2013; FDA, *Veterinary Feed Directive*, 21 CFR 514 and 558. April 2015.

policies may hinder FDA's ability to have a significant impact on the inappropriate use of antibiotics on farms. We ask that you take immediate action by creating a plan to address the following gaps in the FDA's current policies:

- 1) Enforcement. While FDA policies attempt to disallow the use of antibiotics to promote faster animal growth, in many cases, the dosage instructions for prevention and control uses look a lot like the instructions for disallowed production uses.⁶ This leaves a significant loophole that could allow producers to continue to use the same antibiotics at the same doses, as long as the use of the drugs isn't called "growth promotion." FDA has laid out criteria that veterinarians should follow when determining whether it is appropriate to prescribe an antibiotic for prevention or control.⁷ If followed to the letter, this should make a big difference. However, we are highly concerned with FDA's assertion that the agency will rely on stakeholders, including organizations representing veterinarians and animal producers, to promote compliance with these criteria.⁸ This is problematic because some of these stakeholder organizations, have questioned the link between antibiotic use in animals and antibiotic resistant bacteria.⁹

A strong enforcement plan is necessary to measure the degree to which veterinarians are consulting the criteria before prescribing antibiotics for prevention or control, and to specifically monitor the use of antibiotics that were previously used primarily for growth promotion to ensure they are not being misused. In order to address this significant gap in its enforcement plans, we ask that the FDA put in place strong plan to enforce its appropriate preventive use criteria that does not rely primarily on industry partners.

- 2) Data collection. We understand that the FDA and the United States Department of Agriculture are leading an effort to create a data collection plan that includes collecting data on how antibiotics are used on farms. In its March 2016 draft report, the Presidential Advisory Council on Combatting Antibiotic-Resistant Bacteria (PACCARB) emphasized the importance of on-farm data collection.¹⁰ While we appreciate these efforts, it is important to begin collecting the data as soon as possible in order to have a full picture of the impact of the FDA's policies. For that reason, we ask that the FDA release a public timeline for developing and implementing its data collection plan.

⁶ Pew Charitable Trusts, *Issue Brief: Gaps in FDA's Antibiotics Policy*, Nov. 30, 2014; FDA Center for Veterinary Medicine, FDA Approved Animal Drug Products. "NADA Number: 138-934 – Pennchlor SP 500, Pennchlor SP 250" www.accessdata.fda.gov/scripts/animaldrugsatfda/details.cfm?dn=138-934; "NADA Number: 091-513 – Stafac" www.accessdata.fda.gov/scripts/animaldrugsatfda/details.cfm?dn=091-513; FDA Center for Veterinary Medicine, FDA Approved Animal Drug Products. "NADA Number: 138-934 – Pennchlor SP 500, Pennchlor SP 250"; "NADA Number: 138-187 – Tylan® 10 Premix, Tylan® 100 Premix, Tylan® 40 Premix" www.accessdata.fda.gov/scripts/animaldrugsatfda/details.cfm?dn=138-187.

⁷ FDA, *Guidance for Industry #213: New Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209*, December, 2013. Page 7

⁸ Thomas A. Kraus, Food and Drug Administration letter to Senator Warren, Sept. 8, 2014. Page 4.

⁹ Christine Hoang, American Veterinary Medical Association (AVMA), on "The Trouble with Antibiotics," PBS Frontline, October 2014; AVMA Antimicrobial Use and Antimicrobial Resistance FAQ; Ron Philips, Animal Health Institute, in Flynn, Dan (27 May 2011) "Ag Coalition Says Antibiotic Facts are on Its Side." *Food Safety News*; Coalition letter to David Hoffman, PBS Frontline Producer, August 2014; Juan Ramon Alaix, Zoetis in Loftus, Peter. (2013 Nov. 19). Zoetis Chief Leads Animal-Health Firm Following Split from Pfizer. *The Wall Street Journal*; Levitt, Tom. "I Don't See a Problem": Tyson Foods CEO on Factory Farming and Antibiotic Resistance." *The Guardian*. Guardian News and Media, 05 Apr. 2016.

¹⁰ Presidential Advisory Council on Combatting Antibiotic-Resistant Bacteria. *Draft Report 1: Initial Assessments of the National Action Plan for Combatting Antibiotic-Resistant Bacteria*. March 2016. pg 11.

- 3) Metrics for evaluation. We have asked the administration numerous times how it plans to evaluate whether the FDA’s policies have been successful or unsuccessful at reducing inappropriate antibiotic use, and to date have not received a concrete answer. At the same time, many different members of the administration – including at the FDA – have stated that if the policies are unsuccessful, additional actions should be considered.¹¹

Clear metrics and benchmarks are necessary in order to effectively determine whether additional actions are called for. The PACCARB agreed in its March 2016 draft report, stating that “limited progress has been made in finalizing a plan for assessing the impact of the two [guidance documents] on the extent of antibiotic use in food animals.”¹² We ask that the FDA create a plan that lays out clear metrics and benchmarks for success, both from currently available data sources and future expected data sources, including a specific timeline for when the FDA would expect each metric or benchmark to be met. In addition, the plan should include options for what additional antibiotic stewardship measures FDA would consider if current efforts are insufficient.

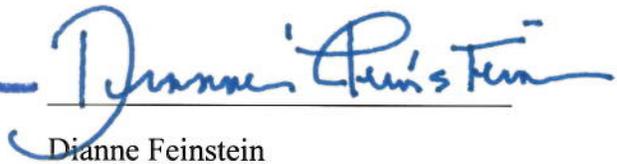
President Obama has made addressing antibiotic resistance a priority of his second term – and effective policies to reduce antibiotic use in animals are a critical part of reducing the public health threat posed by antibiotic resistant bacteria.¹³ The FDA’s current policies are an important first step, but they have clear gaps and alone are not enough. As you begin your work as Commissioner, we ask that you prioritize this issue by creating a plan to address the gaps outlined above and that you share that plan with us no later than June 1, 2016.

We look forward to your response and to continuing to work closely with you on this critical issue.

Sincerely,



Elizabeth Warren
United States Senator



Dianne Feinstein
United States Senator

¹¹ The White House. *National Strategy for Combating Antibiotic-Resistant Bacteria*. Washington, Sep. 2014; Kraus, Thomas A., Associate Commissioner for Legislation, FDA to Senators Warren, Feinstein and Gillibrand, Sep. 8, 2014; President’s Council of Advisors on Science and Technology, Executive Office of the President, *Report to the President on Combating Antibiotic Resistance*, Sep. 2014; James Beard Foundation Food Conference, Panel Discussion with Sam Kass. Nov. 5, 2014.

¹² Presidential Advisory Council on Combatting Antibiotic-Resistant Bacteria. *Draft Report 1: Initial Assessments of the National Action Plan for Combating Antibiotic-Resistant Bacteria*. March 2016. pg 11

¹³ The White House. *Executive Order -- Combating Antibiotic-Resistant Bacteria*. Sept. 18 2014.

Kirsten Gillibrand

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Richard Blumenthal

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