United States Senate
WASHINGTON, DC 20510

December 15, 2014

Secretary Chuck Hagel
U.S. Department of Defense
1300 Defense Pentagon
Washington, DC 20301

Secretary Tom Vilsack
U.S. Department of Agriculture
1400 Independence Avenue, SW
Washington, DC 20250

Secretary Sylvia Burwell
U.S. Department of Health and Human Services
200 Independence Avenue
Washington, DC 20201

Dear Secretaries Hagel, Vilsack, and Burwell:

On September 18, 2014, the president issued an executive order to address the public health threat of antibiotic-resistant bacteria, which, according to estimates from the Centers for Disease Control and Prevention (CDC), cause at least two million illnesses and 23,000 deaths in the United States each year.[1] As the co-chairs of the interagency Task Force for Combating Antibiotic-Resistant Bacteria, you are charged with developing a National Action Plan to implement the president's *National Strategy for Combating Antibiotic-Resistant Bacteria.* The first guiding principle of the *National Strategy* is that "misuse and over-use of antibiotics in health care and food production continue to hasten the development of bacterial drug resistance, leading to the loss of efficacy of existing antibiotics."[2] Of the millions of pounds of medically important antibiotics sold each year, nearly 75 percent are used in food animal production and the CDC estimates that antibiotic-resistant bacteria from contaminated food cause more than 400,000 infections in the United States each year.[3] The way antibiotics are used in animal agriculture poses a clear threat to human health and it is critical that the National Action Plan directly addresses gaps in current policies designed to curb such misuse and over-use.

Antibiotic resistant bacteria are most likely to develop when low doses of antibiotics are administered continuously – the type of regimen used frequently in food animals to promote faster animal growth and contain and prevent disease. To address these concerns, the Food and Drug Administration (FDA) released guidance documents #209 and #213 and a proposed rule on Veterinary Feed Directives (VFDs), prescription-like documents issued by veterinarians for antibiotics delivered through feed. The goal of these policies is to limit the use of antibiotics to circumstances when they are necessary to protect the health of the animal. The policies establish that using antibiotics for growth promotion is inappropriate, bring all other uses of antibiotics under veterinary oversight, and clearly define the circumstances when using antibiotics for disease prevention and control is appropriate.[4]

While the FDA's policies are a step in the right direction, we are concerned that the FDA may lack the authority to ensure veterinarians adhere to the criteria for determining an appropriate preventive use laid out in its guidance documents, that the FDA does not have a clear mechanism for collecting the data necessary to evaluate whether its policies effectively reduce the public health threat, and that the administration has no clear metrics or benchmarks that will be used to determine success or a need for future action. Given the current administration-wide effort that is underway to address this issue, we

[1] Exec. Order No. 13676. 79 FR 56931 (September 18, 2014), "Combating Antibiotic-Resistant Bacteria."
[2] The White House. *National Strategy for Combating Antibiotic-Resistant Bacteria.* Washington, September 2014.
[3] The Center for Science in the Public Interest, *Antibiotic Resistance in Foodborne Pathogens, 2013;* The Pew Charitable Trusts, *Record-High Antibiotic Sales for Meat and Poultry Production, 2011*; CDC, *Antibiotic resistance in foodborne germs is an ongoing threat.* Jul. 1 2014.
[4] FDA, *Guidance for Industry #209: The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals*. Apr. 13, 2012.

have a number of questions about how the interagency Task Force plans to address the gaps in enforcement, data collection, and policy evaluation while developing the National Action Plan:

Enforcement. Even after production uses are removed from antibiotic labels, many approved antibiotic uses to contain or prevent diseases will still allow for the same continuous low dose antibiotic regimens known to facilitate the development of antibiotic-resistant bacteria.[5] For this reason and in order to prevent unnecessary antibiotic use, it is critical that the FDA finalize the VFD rule to bring all medically important antibiotics used in feed under veterinary supervision and that veterinarians closely follow the criteria outlined in Guidance #213 for determining an appropriate preventive use. We are concerned that the FDA may not have the authority to enforce compliance with these criteria and we are unaware of any veterinary training modules used by the United States Department of Agriculture (USDA) or the American Veterinary Medical Association that instruct veterinarians in the FDA's criteria. According to the FDA, the agency plans to work in collaboration with the USDA and the CDC, as well as organizations representing veterinarians, animal producers, and other stakeholders to promote judicious antibiotic use.[6] Representatives from many of these organizations, however, have publically voiced doubts about the need to reduce antibiotic use and the impact that the FDA's policies will have on the amount of drugs used.[7]

1. In light of the disagreements among stakeholders and their competing interests, what tools are available to the administration to encourage compliance with FDA criteria for determining an appropriate preventive use of antibiotics?
2. Does the administration need additional authorities to ensure compliance?
3. How will the administration measure the rate of adoption of the Guidance #213 guidelines among veterinarians?
4. When does the administration plan to finalize the VFD rule?

Data Collection. The *National Strategy* sets a goal of ending non-judicious antibiotic use and directs the Task Force to develop mechanisms to assess progress toward this goal through "enhanced data collection on sales and use." According to a letter the FDA sent to us on September 8th, the FDA has access to data on antibiotic sales and distribution and can measure resistance patterns in food samples, but does not have any clear mechanism for collecting data on how antibiotics are actually being used in food animal production.[8] The USDA has the authority to conduct voluntary surveys of producers regarding on-farm practices – including antibiotic use – but the USDA's current surveys do not collect antibiotic usage data on indications, route of administration, and antibiotic types that allow for scientific examination of the relationship between usage practices and resistance trends. Without this critical on-farm information, the administration will be unable to attribute any change in antibiotic sales or distribution, or any shift in antibiotic resistance patterns, to the FDA's policies.

5. USDA surveys are voluntary and depend on the participation of producers. Are these surveys an effective means of collecting the valid on-farm antibiotic use data – across all of the major food-producing species in the U.S. – necessary to evaluate current FDA policies? If not, what agency and department will be tasked with obtaining this data?

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[5] 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.

[6] Kraus, Thomas A., Associate Commissioner for Legislation, FDA to Senators Warren, Feinstein and Gillibrand, Sept. 8, 2014.

[7] 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*.

[8] Kraus, Thomas A., Associate Commissioner for Legislation, FDA to Senators Warren, Feinstein and Gillibrand, Sept. 8, 2014.

6. We understand that the USDA does not currently have the necessary resources to conduct comprehensive surveys of on-farm antibiotic use practices and that a large scale study can cost up to $1.5 million. In its fiscal year 2016 budget request, does the administration plan to request additional funds to perform a study on on-farm antibiotic use practices within the budget caps?
7. What is the first step toward developing a new data collection mechanism (as directed by the *National Strategy)* that will be included in the February 15, 2015 Action Plan?

Policy Evaluation. If the FDA's policies to curb antibiotic misuse and over-use are unsuccessful, the *National Strategy* calls for "further action." The FDA, the President's Council of Advisors on Science and Technology, and White House Senior Policy Advisor for Nutrition Policy Sam Kass agree that additional measures may be necessary.[9] It is troubling, however, that neither the FDA nor the administration has given any indication of what would constitute success of FDA policies and what result would trigger additional actions. We continue to strongly believe that clear metrics and benchmarks are needed in order to evaluate the outcomes of policy changes and determine if future action is necessary to protect public health.

8. If the FDA's guidance documents succeed in reducing the continuous low-dose use of antibiotics in food animal production, what changes will you expect to see (in sales data, in VFDs, or any other currently collected data point) and when will you expect to see these changes?
9. What additional metrics and benchmarks for evaluating the FDA policies will be published as a part of the Action Plan?
10. What agencies and departments will be responsible for running the evaluation?
11. If FDA policies are unsuccessful, what next steps will the administration consider to continue addressing the misuse and over-use of antibiotics in animal agriculture?

We appreciate your responses to these questions by January 15, 2015. If you have any questions, please contact Melea Atkins in Senator Warren's office at 202-224-4543.

Sincerely,

Elizabeth Warren
U.S. Senator

Dianne Feinstein
U.S. Senator

Kirsten E. Gillibrand
U.S. Senator

CC: President Barack Obama; Commissioner Margaret Hamburg, U.S. Food and Drug Administration

[9] 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.