KEEP ANTIBIOTICS WORKING
The Campaign to End Antibiotic Overuse
www.KeepAntibioticsWorking.org

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Recommendations on the FDA's Five-Year Plan to Address Antibiotic Resistance and Improve Antibiotic Stewardship in Animals

Five years ago, former Food and Drug Administration Commissioner Scott Gottlieb, MD announced a new effort by the Food and Drug Administration (FDA) to advance antimicrobial stewardship in veterinary settings. Gottlieb emphasized the public health imperative for these efforts, saying: "Our aim is to reduce the overuse of antimicrobial drugs and combat the rising threat of resistance."

From the outset, Keep Antibiotics Working and its member groups expressed concern that the FDA's first and still current five-year action plan was far too vague to ensure Dr. Gottlieb's worthy goals would be met. Whether in human or non-human settings, progress around antibiotic stewardship cannot be tracked and/or verified until antibiotic use itself is being quantitatively estimated or measured. Estimates or direct measures of antibiotic use are inextricably tied to the ability to track antibiotic stewardship, and whether it is improving or worsening over time.

While Congress has required the FDA to report antibiotic sales for use in food-producing animals since 2009, the FDA has refused to consider these sales data as a proxy for antibiotic use. At the same time, the FDA has failed to move forward with any alternative approach to collect or estimate antibiotic use in animals.

Predictably, the FDA's failure to create any meaningful indicators to quantifiably measure or estimate annual antibiotic use in food animal production, or to quantify changes in veterinary antibiotics stewardship, translates directly into the Agency's inability to document any public health benefit from its veterinary stewardship efforts to date. Verifiable progress around stewardship at the national level requires the quantifiable measurement of antibiotic use, or at least an estimation of antibiotic use. By definition, FDA must establish an indicator or measure of stewardship before it tracks progress to improve veterinary antimicrobial use, and thereby combat the rising threat of resistance.

Although FDA also seeks to develop strategies to promote stewardship in the use of antimicrobials in companion animals, there have been several outbreaks of antimicrobial resistant diseases attributed to misuse and overuse of antimicrobials and the lack of appropriate veterinary oversight in the commercial pet industry. This overuse pales in comparison with the volume of antimicrobials used in food production, but due to the close connection between people and their pets, this overuse by the commercial pet industry cannot be ignored.

Tracey Forfa, J.D. the Director of the Center for Veterinary Medicine (CVM), testified recently before the House Energy and Commerce subcommittee on health that the CVM would release a new 5-year

plan by the end of 2023. The new plan would cover the period from fiscal years 2024 through 2028. However, the CVM cannot and will not deliver on Dr. Gottlieb's five-year-old goals to reduce antimicrobial overuse and to combat the rising resistance threat until the Agency makes significant improvements as it develops a new five-year-plan. Specifically, we recommend the CVM make the following changes:

1. To better reflect the public health urgency of the rising resistance threat, and the core public health aim articulated by Dr. Gottlieb in 2018, we urge the new plan be titled "FDA's Five-Year Plan to Address Antibiotic Resistance and Improve Antibiotic Stewardship in Animals." The current plan's title fails to reflect the public health goal of not merely "supporting" veterinary antimicrobial stewardship, but actually improving it.

Moreover, the FDA to date has failed to offer a sound scientific basis for why its plan should only discuss stewardship with respect to settings where there is veterinary oversight. Veterinary oversight is not required for almost half of the antibiotics used in food-producing animals, e.g. those drugs which are not considered medically important. However, there is abundant and ever-growing evidence that use of these non-medically important antibiotics in U.S. food animals impacts selection pressure for and spread of antibiotic resistance which may ultimately affect human medicine.

2. The new plan must also include indicators for the population-level improvements the FDA seeks in antibiotic stewardship and antibiotic resistance as a result of its purported efforts to promote stewardship and address resistance. These indicators should be based upon currently available data such as antibiotic sales and data collected through the National Antimicrobial Resistance Monitoring System.

While it is important to complete actions that are reported in FDA Track, it is a basic matter of accountability that the FDA cannot and should not assume these actions are necessarily improving stewardship or reducing resistance. By our definition, the indicators must be clear measures of progress towards the overarching public health goals to improve stewardship and reduce antibiotic resistance—for example, a reduction in the use of all medically important antibiotics by 50% by 2025, or no observed decrease in the percent *E. coli* bacteria collected from food animal sources that have been found to be pan-susceptible. The Center for Disease Control (CDC) uses indicators for progress towards improved stewardship and reductions in resistance in human medical settings that conform to this definition. By contrast, the FDA has never established indicators of stewardship that conform to this definition. To date, the FDA's supposed "indicators" under its stewardship plan instead have been metrics which are independent of any public health relevant goal

3. Include a goal to complete work on creating a system to collect additional antibiotic use data by the end of the five-year plan. The FDA should not assume that a public-private partnership is the best approach but rather should transparently report other options and their pros and cons, including, for example, the agency's use of its existing authority under Veterinary Feed Directive (VFD) regulations to request feed distribution records.

4. Include a goal to complete work on duration limits to limit the high extent of use of medically important antibiotics currently allowed by existing approvals. Set a goal, by the end of calendar year 2025 to include a default duration of 21 days for sponsors that do not wish to submit data supporting a longer duration. The FDA should also clarify what a duration on a drug label means since some veterinarians and drug sponsors believe it is appropriate to skip a day and start another round of antibiotics once a duration limit has been reached. This undermines the public health goal of limiting the extent of use of antibiotics to reduce the risk of resistance.

5. Commit to conduct research on co- and cross-resistance and develop policies to address the findings. This should include looking at the role of non-medically important antibiotics in the selection for and dissemination of resistance to medically important antibiotics.

6. Continue to implement the NARMS Strategic Plan and create a new plan for when the current plan ends in 2025. Making isolate-level data available more frequently is needed since these data include information not available through the FDA's NARMS Now Webpage.

7. Include pet industry members into antimicrobial resistance discussions. Commercial companion animal breeders, distributors, and pet stores need to be required to keep records on antimicrobial use, similar to the Veterinary Feed Directive. Antimicrobials would only be prescribed and administered within a valid veterinary client patient relationship (VCPR).

8. Include a goal to address illegal and unethical marketing of veterinary antimicrobials both for food-producing and companion animals including the promotion of unapproved uses on company websites and drug sponsor recommendations for duration of use longer than approved duration.

9. Work with other agencies, particularly USDA-APHIS, to review the enforcement of existing requirements, especially the need for a valid VCPR. FDA/CVM, USDA, and CDC must work together and share their expertise on the need for antibiotic stewardship, so that antibiotic stewardship is addressed in a consistent manner across these agencies.