July 9, 2024

Robert M. Califf, MD
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Dear Commissioner Califf:

I write to express concern that the Food and Drug Administration (FDA)’s revisions to Guidance For Industry #152 (GFI#152) and draft Guidance for Industry #273 (draft GFI#273) would worsen the catastrophic impacts of antimicrobial resistance, caused by the overuse of antibiotics in animal agriculture in concentrated operations. These revisions would undermine the safety standards applied to new animal drugs by allowing animal health concerns to be the determining factor in human safety decisions about drugs used in food-producing animals. This will set a dangerous precedent by prioritizing the needs of the regulated industry over the FDA’s primary mission to protect public health. I urge you to finalize Guidance for Industry that meaningfully protect medically important antibiotics from overuse.

Antimicrobial resistance (AMR) is one of the greatest public health threats of our time. AMR makes routine medical procedures dangerous and common illnesses deadly for people with compromised or weakened immune systems. Drug-resistant infections sicken three million people and kill at least 50,000 people in the United States each year. Just six strains of antimicrobial-resistant pathogens cost the U.S. healthcare system $4.6 billion annually. Infections are a primary or associated cause of death in 50% of cancer patients, because they are difficult or impossible to treat without antimicrobials.1

A primary driver of the spread of antibiotic resistance is the misuse of antibiotics in industrial animal agriculture.2 About two-thirds of the sales of medically important antibiotics are for use in food-animal production.3 Concentrated animal feeding operations create a breeding ground for AMR, due to their crowded conditions and the overreliance on antibiotics to keep animals healthy in an unsanitary and disease-promoting environment.

While the FDA has long recognized the integral connection between antibiotic use in animal agriculture and antibiotic resistance, I am concerned that the FDA is moving backward with respect to this growing public health threat. Under the Federal Food, Drug, and Cosmetic Act (FDCA), drugs used in food-producing animals must be shown to be safe with respect to human health including safe with respect to antibiotic resistance. Current policy allows high and medium risk drugs to be approved if they adopt use

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3 https://www.nrdc.org/bio/david-wallinga-md/antibiotic-use-remains-far-too-intensive-us-livestock
restrictions such that there is a reasonable certainty of no harm to human health. One of these restrictions is that the drug cannot be used more than 21 days in groups of animals. In the proposed draft GFI#152, the FDA replaced the 21-day limit with a rule that “duration of use will be revised on a case-by-case basis in light of, but not limited to, animal species, disease risk period, and animal management husbandry practices, etc.”\(^4\) In doing this, draft GFI#152 replaces a limit which was intended to protect human health with a duration based on animal health. Including factors not related to human health is completely inappropriate; The FDCA and FDA regulations do not allow balancing the human safety of veterinary drugs against animal health benefits.

In Draft GFI#273\(^5\), the FDA further improperly considers the benefits to animal health at the cost of human health. Draft GFI #273 has the human safety goal “to mitigate the development of antimicrobial resistance” (Page 1), but requires all decisions about durations -- the focus of the guidance -- to be based solely upon animal health benefits. In draft GFI #273, data related to human safety (i.e. data on antibiotic resistance) is completely excluded from decision making around durations even though the stated goal is safe use to prevent AMR.

If finalized, these draft GFIs would worsen AMR. Further, the FDA has failed to use its existing authority to collect information on antibiotic use from feed mills and has not created any metrics to measure the progress of its efforts to combat AMR, including targets to reduce antibiotic overuse in animal agriculture.

I write seeking information about the FDA’s efforts to manage the growing crisis of AMR. I ask that you answer the following questions.

1. Does the FDA believe it is appropriate to make human safety decisions based on animal health needs--as it has done in its revisions to GFI#152 and GFI#273--for durations of use intended to protect human health?

2. How will the FDA’s consideration of animal health concerns impact its ability to ensure human safety in the use of animal drugs? Will FDA now begin to consider animal health or economic benefit to the impacted industry when holding hearings on whether to withdraw drugs from the market for safety reasons?

3. Does the FDA believe it has the authority to ask drug sponsors to voluntarily adopt durations that are consistent with existing guidance (i.e. under 21 days as recommended by the original GFI#152)? If not, please explain why the FDA does not have authority for requesting this voluntary action.

4. Given the slow pace of action to address the critical public health threat of antibiotic resistance, what additional resources or authorities does the FDA need to take prompt action to protect public health from antibiotic resistance?

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\(^5\) [https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cvm-gfi-273-defining-durations-use-approved-medically-important-antimicrobial-drugs-fed-food#:~:text=This%20guidance%20provides%20information%20to,animals%20where%20none%20currently%20exist.](https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cvm-gfi-273-defining-durations-use-approved-medically-important-antimicrobial-drugs-fed-food#:~:text=This%20guidance%20provides%20information%20to,animals%20where%20none%20currently%20exist.)
5. It has been over 20 years since the Interagency Task Force on Antimicrobial resistance identified collection of antibiotic use data as a priority.⁶
   a. When does the FDA anticipate creating “functional and efficient systems for collecting antimicrobial use data in animals” as described² in the FDA’s 2019-2023 plan for antimicrobial stewardship in veterinary settings? When does the FDA expect the data collection plan to be finalized, and when will it be implemented?
   b. So far, the FDA has only publicly discussed a public-private partnership.
      i. Why has the FDA not collected feed distribution data from feed mills as recommended by public health advocates⁹?
      ii. What resources would be needed to collect drug distribution data from feed mills?
      iii. How would the resource needs for collecting feed distribution data compare to resource needs for collecting data through a public-private partnership?
      iv. If the FDA does move forward with a public-private partnership how will the agency ensure that the collected data is representative i.e., how will it ensure that those facilities practicing poor antimicrobial stewardship (that will likely not be inclined to participate) are represented?

6. What is the FDA doing to measure its progress on combating antibiotic resistance? Has the FDA adopted any indicators of success such as a reductions in antibiotic use by livestock sectors and reductions in antibiotic resistance in food animal isolates?

Please provide answers to these questions by September 1, 2024.

I strongly urge the FDA to prioritize protecting public health when making decisions about the safety of animal drugs, whether through guidance or regulation, and to not compromise the separation between drug safety reviews and the review of benefits of a drug approval to the regulated industry.

Sincerely,

Cory A. Booker

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⁷ https://www.fda.gov/media/115776/download?attachment
⁸ https://www.regulations.gov/comment/FDA-2022-N-0824-0574