April 10, 2022

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

Re: **Strengthen FDA's Efforts to Address Antibiotic Resistance, Improve Stewardship**

Dear Commissioner Califf,

As members of Keep Antibiotics Working[1] and partner organizations, we appreciate your experienced leadership of the Food and Drug Administration at a time of great public health peril. We write to ask that you apply your leadership and experience to confront the worsening antibiotic resistance crisis, and the antibiotic overuse that is among the chief reasons for its spread.

As you know, antibiotics have been a lynchpin of the modern medical system for decades. Their ongoing overuse, however, has hastened the emergence and spread of antibiotic resistance to the degree that at least 2.8 million drug-resistant infections occur in the United States each year, according to the Centers for Disease Control and Prevention. A recent study in the Lancet estimated there were nearly 1.3 million deaths worldwide in 2019 directly caused by antibiotic-resistant bacteria, among nearly 5 million deaths "associated with" bacterial drug resistance.[2] Rising numbers of patients suffer infections treatable with only a single antibiotic of last resort, and sometimes not treatable at all. The conduct of modern medicine is under threat, as a result.

Our 64 organizations urge that it is more critical than ever for the FDA to confront the slow-moving resistance pandemic, which often spreads via animals and is exacerbated by livestock husbandry practices. We need information about how and why antibiotics are used across all settings, in order to fully understand and respond to ongoing antibiotic overuse – one of the largest, if not the largest driver of the spread of resistance. Curbing medically important antibiotic use in food-producing animals is especially important; around two-thirds of the nation's medically important drugs are sold for use on animals, not people.[3]

For almost a quarter century, U.S. federal agencies have acknowledged the imperative for a national system to robustly track antibiotic use and resistance, in food production especially. But that system has never been prioritized, funded, or built.[4] Since 2009, the FDA has reported annually on medically important antibiotics and other drugs sold for use in food-producing animals. Sales data are an appropriate proxy for data on actual farm use of antibiotics, since the FDA and other agencies have not found a way to accomplish the latter.[5] The FDA's latest sales data, for instance, show medically important antibiotics to have declined modestly, by 27 percent from 2010 to 2020. Sales initially fell in 2017, after the FDA finished implementing Guidance for Industry #213. Since 2017, however, sales of medically important antibiotics have risen by 8 percent, not fallen.[6]

The FDA must begin to robustly monitor antibiotic use, but also prioritize actions to effectively curb the overuse of these precious medicines. Specifically, we recommend that you commit to the following actions to protect public health:

A. Establish a national stewardship goal to curb medically important antibiotic sales for use in food-producing animals by at least 50% by the end of 2025, relative to 2010 levels. The CDC and others have established concrete targets for reducing antibiotic use in both inpatient and outpatient settings; no such goals exist for non-human uses of these same antibiotics, however.[7] Concrete use reduction targets and specific timelines for reaching them, along with robust antibiotic use tracking to measure progress, seem to have been important factors for several European countries to have realized their antibiotic stewardship goals for food animal production.[8]

1) ***Finalize weight-adjusted reporting of antibiotic sales.*** At the same time, we urge the FDA to take immediate action to finalize a method for reporting antibiotic sales for use in food producing animals on a weight-adjusted basis. A weight adjustment is needed to account for changes in animal populations so that it is clear whether changes in sales are linked to actual changes in antibiotic stewardship, or simply reflect the number of animals raised that year. Normalizing sales reports by the size of the animal population under production would, for the first time, make it transparent how intensively these precious medicines are being used from year to year. Less intensive antibiotic use, of course, is consistent with better antibiotic stewardship. In 2017, the FDA proposed a method to weight-adjust sales as a preferable alternative to reporting raw, non-adjusted sales alone, but no weight-adjusted method was ever implemented.[9]

By December 2022, in other words, the FDA's annual sales summary should include both raw sales, in kilograms of active ingredient, of antibiotics sold for use in food producing animals, plus these same sales on a weight-adjusted basis. Starting at that same time, we urge the FDA to retroactively report sales figures for 2009 to 2021 on a weight-adjusted basis, as well. In doing so, the FDA will finally offer transparent means for determining over that entire period whether stewardship of medically important drugs within the single largest category of their use has improved, worsened, or stalled.

2) ***End administration of antibiotics to entire herds where there are not sick animals.*** The U.S. finished phasing out antibiotics for growth promotion in 2017, but use of the same drugs in healthy animals for disease prevention continues to be legal. If stewardship is the FDA's goal, then preventive use should be disallowed, except in the case of surgery. This will slow the emergence of antibiotic resistance and encourage higher welfare standards in farming operations.

The World Health Organization (WHO) has called for an end to the practice of preventive use citing major concerns that it contributes to antibiotic resistance.[10] In January 2022, a new EU veterinary medicine regulation went into effect that prohibits administration of antibiotics to groups of food animals for disease prevention.[11]

B. Develop comprehensive, national systems to monitor and report pertaining to farm-level antibiotic use and resistance, using a One Health approach.

1) ***Monitor antibiotic use***. The continued lack of national systems to track antibiotic use at the farm level leaves a critical gap in national pandemic preparedness, as well.

Feed mills are an important potential source of this information since existing rules require all facilities that handle medically important antibiotics keep records pertaining to the amount of these drugs mixed into 'medicated feeds' under a veterinarian's feed directive, the reason for that directive, and information on the animals receiving the medicated feed.[12] Around two-thirds of all medically important antibiotics sold for use in food producing animals are mixed by feed mills into medicated feeds, and information about these are potentially available to the FDA.[13]

In order to collect and analyze information about the remaining one-third of these antibiotics used in livestock, including the minority prescribed for sick animals, the FDA should coordinate and collaborate with agency partners in the USDA and Department of Health and Human Services (HHS) to ensure more robust tracking of antibiotic use on farms and feedlots to help curb the overuse of antibiotics in food-animal production.

2) ***Monitor for new and emerging pathogens, specifically including antibiotic-resistant bacteria, at the farm level.*** As the nation considers how to strengthen its preparedness to identify and respond to the spread of new and potentially pandemic infectious threats, the FDA must do its part to ensure strong farm-level disease surveillance, including full integration of the agency's efforts to track antibiotic use and resistance into broader pandemic readiness plans. With three out of four emerging infections arising in animals[14], it is impossible to adequately identify emerging pandemic threats without monitoring one of the most important interfaces of human and animal health – farms and feedlots. We urge the FDA to collaborate with HHS and the White House to develop One Health early warning systems to monitor for emerging pathogens with pandemic potential and antibiotic-resistant strains before they spread.

C. **Commit the FDA to on-time achievement of the antibiotic stewardship goals in its current Action Plan.** In 2023, the FDA's Center for Veterinary Medicine (CVM) will reach the end of its current Five-Year Action Plan for Supporting Antimicrobial Stewardship in Veterinary Settings.[15] The agency is not on track to complete that Plan's overly-modest goals, however. Leadership is needed to ensure the current goals will be fully met, if not exceeded.

1) ***Update FDA's medically important antibiotics (MIA) list.*** Specifically, we ask for CVM to act with more urgency to update the agency's list of medically important antibiotics. The last update took place nearly two decades ago, in 2003, when the FDA published the list as part of GFI#152.[16] Without delay, CVM should finish reviewing public comments to its concept paper, "*Potential Approach for Ranking of Antimicrobial Drugs According to Their Importance in Human Medicine*,"[17] and publish a draft guidance as soon as possible. The latter should include FDA's commitment to update the list at least every three years – and even more frequently, when appropriate.

2) ***Ensure that feed antibiotics carry meaningful, clearly defined duration limits.*** We also call for a clear and expedited timeline on CVM's *still-draft* 2021 proposal to set clearly defined duration limits for medically important antibiotics.[18] The current draft proposal, "*Defining Durations of Use for Medically Important Antimicrobial Drugs Intended for Use In or On Feed*," delays placing duration limits on product labels until 2030 or even later.[19] This threatens antibiotic stewardship and public health. Continuous use of medically important antibiotics in herds of food animals clearly increases the risk of antibiotic

resistance.[20] In order to meet the CVM's professed antibiotic stewardship goal to combat resistance, durations must be established that are sufficiently concrete and short.

We welcome the opportunity to assist your office in actions to combat antibiotic resistance in the future, and therefore request a meeting with you and your staff to discuss the aforementioned recommendations. To arrange, please respond to Dr. David Wallinga at dwallinga@nrdc.org. Thank you for your consideration.

Sincerely,

Daniel P. McQuillen, MD, FIDSA, FACP
President
Infectious Diseases Society of America

Devin Jopp, EdD, MS
CEO, Association for Professionals in Infection Control and Epidemiology

Ramanan Laxminarayan, PhD, MPH
Director
Center for Disease Dynamics, Economics, and Policy (CDDEP)

Victoria Maizes, MD
Executive Director
Andrew Weil Center for Integrative Medicine at the University of Arizona

David Wallinga, MD
Senior Health Officer
NRDC

Pam Runquist
Executive Director
Humane Society Veterinary Medical Assoc.

Jeff Carter
Executive Director
Physicians for Social Responsibility

Steve Roach
Safe and Healthy Food Program
Food Animal Concerns Trust

Jason Newland MD, Med
Pediatric Infectious Diseases Physician
SHARPS (Sharing Antimicrobial Reports for Pediatric Stewardship) Collaborative

Phoebe Schreiner
Executive Director
Center for Agricultural Development & Entrepreneurship (CADE)

Matt Wellington
Public Health Campaign Director
U.S. PIRG

Steve Heilig, MPH
Director, Public Health and Education
San Francisco Marin Medical Society

Nadira Narine
Program Director
Interfaith Center on Corporate Responsibility

Amanda Strawderman
Program Director
Clean Water for NC

Bob Martin
Director, Food System Policy
Johns Hopkins Center for a Livable Future

Michael Hansen
Senior Scientist
Consumer Reports

Mimi Brody
Director of Federal Affairs
Humane Society Legislative Fund

Connor Kippe
Policy Analyst & Advocate
Toxic Free NC

Katie Huffling, DNP, RN
Executive Director
Alliance of Nurses for Healthy Environments

Carrie Apfel
Senior Attorney
Sustainable Food and Farming Program
Earthjustice

Geoff Horsfield
Government Affairs Manager
Environmental Working Group

Jenn Engstrom
State Director
CALPIRG

Robert M. Gould, MD
President
San Francisco Bay Physicians for Social Responsibility

Kari Hamerschlag
Deputy Director, Food and Agriculture
Friends of the Earth

Christian John Lillis
Executive Director
Peggy Lillis Foundation

Michael Roberts, Executive Director
Resnick Center for Food Law and Policy
UCLA School of Law

Amanda Hitt
Director, Food Integrity Campaign
Government Accountability Project

Andrew Decoriolis
Executive Director
Farm Forward

Sherri Dugger
Executive Director
Socially Responsible Agriculture Project (SRAP)

Belita Cowan
President
Lymphoma Foundation of America

Peter Brandt
Managing Attorney, Farm Animals
Animal Protection Litigation
Humane Society of the United States

Michael J. Martin, MD
President
Physicians Against Red Meat (PhARM)

Jaydee Hanson
Policy Director
Center for Food Safety

Kara Shannon
Director of Farm Animal Welfare Policy
American Society for the Prevention of Cruelty to Animals (ASPCA)

Bruce Friedrich
CEO, The Good Food Institute
Western Nebraska Resources Council

Tarah Heinzen
Legal Director
Food & Water Watch

Abe Scarr
Director
Illinois PIRG

Shedd Farley
Director, Linda and Gene Farley Center for Peace, Justice and Sustainability

DeEtta Bilek
Executive Board
OFARM

Laura Rogers
Managing Director
Antibiotic Resistance Action
Director
George Washington University Association

Cameron Harsh
U.S. Programs Director
World Animal Protection

Kristin Urquiza
Co-Founder, Co-Executive Director
Marked by COVID

April Desclos
Pure Farms, Pure Waters Campaign
Waterkeeper Alliance

Sally Greenberg
Executive Director
National Consumers League

Emily Scarr
State Director
Maryland PIRG

Charlie Fisher
State Director
OSPIRG

Eddie Dutton
Executive Director
South Florida Cancer Association

Danny Katz
Director
CoPIRG

Gretchen Dubeau
Executive and Legal Director
Alliance for Natural Health USA

Ariana Guilak
Environmental Health Program Coordinator
As You Sow

Danielle Koonce
Community Organizer
EJCAN

Tina Stevens, PhD
Director
Alliance for Humane Biotechnology

Hannah Connor
Senior Attorney, Environmental Health
Center for Biological Diversity

Ben Lilliston
Director of Rural Strategies
Institute for Agriculture and Trade Policy

AJ Albrecht
Director of Government Affairs
Mercy for Animals

Amalie Lipstreu
Policy Director
Ohio Ecological Food and Farm Association

Marie Burcham
Policy Director
The Cornucopia Institute

Nancy Utesch
Founder
Kewaunee CARES

Nicole Walter
Advocate
WashPIRG

Laura Braden
Lead Regulatory Counsel
The Good Food Institute

Emma Horst-Martz
Advocate
PennPIRG

Kathleen Schuler, MPH
Policy Director
Health Professionals for a Healthy Climate

Nicole Fox
Campaign Organizer
WisPIRG

Samantha Guerrero
Community Organizer
Idaho Organization of Resource Councils

[1] Keep Antibiotics Working consists of 19 organizations advocating jointly to curb farm overuse of antibiotics, which hastens the spread of hard-to-treat superbugs, and puts at risk many of the era's top medical advances.
[2] Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet*. 2022 Feb 12;399(10325):629-655.
[3] David Wallinga, Eili Klein, and Alisa Hamilton,"U.S. Livestock Antibiotic Use is Rising, Medical Use Falls," November 18, 2021.
[4] See Keep Antibiotics Working, "On Farm Antibiotic Data Collection: Always a priority but never an implemented," accessed March 10, 2022. The FDA's own Science Advisory Board highlighted the need for on-farm antibiotic use data in 2007 and 2017. The Government Accountability Office (GAO) also has made recurrent recommendations for on-farm data collection in reports issued in 2004, 2011, and 2017. And the 2001 Interagency Task Force on Antimicrobial Resistance, co-chaired by the CDC, the FDA, and the National Institutes of Health, made collection of antibiotic use data and better surveillance a top priority in its Public Health Action Plan.
[5] European authorities regularly issue a fully integrated analysis of sales or 'consumption' of antimicrobial agents and occurrence of AMR in bacteria from humans and food-producing animals, jointly prepared by the European Centre for Disease Prevention and Control (Europe's CDC equivalent) and the European Food Safety Authority (Europe's FDA equivalent). Those reports confirm that reducing antibiotic sales is a desirable goal to contain the spread of antibiotic resistance. See European Medicines Agency (EMA) website, ECDC/EFSA/EMA second joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals, July 2017.
[6] U.S. Food & Drug Administration, Center for Veterinary Medicine. "Annual Summary Report on Antimicrobials Sold or Distributed in 2019 for Use in Food-Producing Animals." FDA, December 15, 2020. On their face, U.S. stewardship efforts around antimicrobials in food producing animals seem to be much less effective than in Europe., where the latest (2020) sales for use in livestock were 43% lower, on a weight-adjusted basis, than they were in 2010; over that same period, sales declined by around 60% or more in France, the Netherlands, Germany and the United Kingdom.
[7] CDC. Antibiotic Use in the United States, 2021 Update: Progress and Opportunities. Atlanta, GA: US Department of Health and Human Services, CDC; 2021; CDC. What Do We Know About Antibiotic Use in Outpatient Settings? Last reviewed November 13, 2020; The PEW Charitable Trusts. Health Experts Establish Targets to Improve Hospital Antibiotic Prescribing. March 2021.
[8] David Wallinga, Lidwien Smit, Meghan Davis, Joan Casey, Keeve Nachman, A Review of the Effectiveness of Current US Policies on Antimicrobial Use in Meat and Poultry Production, *Current Environmental Reports* (in press).
[9] In fact, the FDA's European counterpart has been reporting sales on a weight-adjusted basis for the past 12 years, considering this measure of antibiotic 'consumption' to be a reasonable proxy for actual antibiotic use on farms.
[10] World Health Organization, "Stop using antibiotics in healthy animals to prevent the spread of antibiotic resistance," November 7, 2017.
[11] Center for Infectious Disease Research, Economics and Policy, "New EU Rules on Antibiotic use on Farms take Effect," January 28, 2022.
[12] Steve Roach (blog), "Feed Mills and Antibiotic Use Data," November 2, 2021.
[13] FDA Annual Summary Report, 2020.
[14] CDC, Zoonotic Diseases, last reviewed July 1, 2021.
[15] Center for Veterinary Medicine | FDA, Supporting Antimicrobial Stewardship in Veterinary Settings: Goals for Fiscal Years 2019-2023, September 2018.
[16] FDA's current method for ranking drugs by medical importance is described in Appendix A of the CVM's Guidance for Industry #152: Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern, October 23, 2003.
[17] Center for Veterinary Medicine | FDA, "Potential Approach for Ranking of Antimicrobial Drugs According to Their Importance in Human Medicine," *FDA,* October 13, 2020.
[18] Center for Veterinary Medicine | FDA. "FDA Seeks Public Comment on Potential Approach for Defining Durations of Use for Certain Medically Important Antimicrobial Drugs for Food Animals." *FDA*, February 22, 2021.
[19] Center for Veterinary Medicine | FDA. "FDA-TRACK: Progress on FDA's Support of Antimicrobial Stewardship in Veterinary Settings." *FDA*, May 26, 2021.
[20] U.S Food and Drug Administration, New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209, December 2013.