MCFA

Minor Crop Farmer Alliance

Via Electronic Docket Submission http://www.regulations.gov December 13, 2023

Michal Freedhoff, Ph.D.
Assistant Administrator; Office of Chemical Safety and Pollution Prevention
U.S. Environmental Protection Agency
1201 Constitution Ave. N.W.
Washington, DC 20004

Re: *Pesticides; Concept for a Framework To Assess the Risk to the Effectiveness of Human and Animal Drugs Posed by Certain Antibacterial or Antifungal Pesticides; Notice of Availability and Request for Comment*. Docket Identification Number EPA-HQ-OPP-2023-0445.

Dear Dr. Freedhoff:

These comments are submitted on behalf of the members of the Minor Crop Farmer Alliance ("MCFA") in response to the subject *Pesticides; Concept for a Framework To Assess the Risk to the Effectiveness of Human and Animal Drugs Posed by Certain Antibacterial or Antifungal Pesticides; Notice of Availability and Request for Comment* ("Framework Concept"), originally published by the Environmental Protection Agency ("Agency") in the Federal Register on September 26, 2023 (88 Fed. Reg. 65998-9).

MCFA is an alliance of national and regional organizations and individuals representing growers, shippers, packers, handlers, and processors of various agricultural commodities, including food, fiber, turf grass, nursery and landscape crops. MCFA's members are extremely interested in the development and safe use of pest management tools including crop protection chemicals that are safe for applicators, workers, and the public, and do not represent an unreasonable adverse risk to the environment, including humans and non-target organisms such as pollinators and endangered and threatened species. While our commodities are often called "minor crops" or "specialty crops," they contribute to the diverse and highly nutritious diets available for the global population, and to safe and aesthetic surroundings for our homes, schools, and places of business. These U.S. farmers grow more than 500 types of fruit, vegetable, tree nut, flower, ornamental nursery, and turf grass crops in addition to the major bulk (row) commodity crops. Specialty crop production accounts for more than $60 billion, or approximately 40% of total U.S. crop receipts.

Antibacterial and antifungal pesticides have been used by specialty crop growers in U.S. agriculture for more than 70 years to address destructive plant pests and diseases that can attack their commodities. Without being able to access these tools, significant adverse impacts to specialty crop growers regarding their ability to produce marketable crops can be anticipated. Consequently, MCFA's members have a strong interest regarding how the Framework Concept is developed by the Agency. To that end, we offer these initial comments.[1]

[1] While MCFA appreciates that the Agency provided an opportunity for interested stakeholders to comment on the Framework Concept, the allotted comment period (approximately 78 days) was too short in view of the nature of the issues involved. The relatively short comment period also occurred during the same time in which interested stakeholders such as MCFA were having to prepare comments on additional outstanding Agency actions. It is not clear why the Agency could not have meaningfully extended the comment period in this instance. Providing some additional time for filing comments would have permitted MCFA to go into greater depth in commenting on the Framework Concept.

MCFA has been involved in reviewing the potential for human disease resistance associated with the use of certain antimicrobial pesticides for several years, including working with the involved Federal agencies such as EPA, FDA, and USDA, in reviewing and commenting on the Codex Task Force on Antimicrobial Resistance ("TFAMR"). The information developed in that process can help inform the Agency in determining how to structure the Framework Concept. That process grew out of a concern principally associated with the use of antibiotics in animal production for reasons other than the health of the animal. In particular, this included the use of antibiotics to stimulate the growth of food animals. One of the effects from such use was the presence of antibiotic residues in the foods derived from the treated animal. The subsequent consumption of the products from the treated food animal created a potential pathway for resistance to the antibiotic in humans. FDA has now initiated a strategy to promote the judicious use of medically important antimicrobial drugs in food animals. It is directed to phasing out the use of these products to enhance the growth or improve feed efficiency for food production purposes. It is also tightening up on the therapeutic uses of these animal drugs including requiring their specific authorization by a licensed veterinarian in accordance with the procedures FDA has developed.

However, the TFAMR also expanded its review to include horticultural uses of antibiotics. Field data and other information were presented demonstrating that because of environmental degradation in particular, the horticultural use of antibiotic pesticides did not present a realistic pathway to impact antibiotic resistance in humans. Further, the use of these products in specialty crop production occurs where there is little or no opportunity for interaction with the human pathogens that can lead to antibiotic resistance in humans or food animals. Studies that the Agency required the registrants of antibiotics in plant agriculture to conduct included surveillance and monitoring phyllosphere and rhizosphere bacteria for shifts in background resistance levels in comparisons of treated acreage to non-treated acreage.

Multiple multi-year studies following an EPA established protocol were conducted on multiple crops for streptomycin, oxytetracycline, and kasugamycin by the registrants of these antibiotics, and the results from multiple states including California, Florida, and Michigan were submitted to the Agency. These studies clearly demonstrate that changes in resistance levels did not occur. Thus, in certain bacterial species (that were identified by molecular methods), resistance was not detected in non-treated or treated samples with an antibiotic pesticide. Additionally, in some bacterial species recovered from untreated plant or soil samples, inherent resistance was detected, but the incidence of this resistance did not increase in treated samples.

Concerning the Framework Concept, MCFA will focus on two issues. The first concerns the types of pesticides and organisms that should be evaluated under the Framework Concept. The second concerns the potential mitigation strategies available to address the potential risk of antimicrobial resistance in humans or animals from pesticide use.

Regarding the types of pesticides and human pathogens that should be evaluated, the U.S. Center for Disease Control ("CDC") should be requested to provide the Agency with lists of medically important organisms and medically important drugs to clearly establish the potential problems. The definition of "medically important" should only include drugs that would be reasonably expected to be used for medical treatments. Current lists of "medically important" drugs include drugs that were once used for human treatment but are now obsolete either because of the development of resistance from prescription overuse or the introduction of new drugs that are more effective treatments. Drugs that have not been routinely used for 30 years or more should not be defined as "medically important." EPA should not expend valuable resources conducting risk assessments or resistance screens on drugs that are no longer used for human treatments.

Additionally, the list should consist of bacteria and fungi named at the species or genus level and should include molecular sequence data for species identification. The types of high priority pesticides with usage in agriculture and medicine currently include the bactericide classes aminoglycosides and tetracyclines, and the fungicide classes triazoles and benzimidazoles. As noted above, it is clear there are extensive field data and other information demonstrating that the horticultural uses of antibiotic pesticides do not present a legitimate scientific pathway for resistance to antibiotics in humans or animals to develop. These products degrade quickly once they are introduced into the environment. Consequently, the Agency should review the available field data and based on the weight-of-evidence, confirm that the use of these antibiotic pesticides is understood and not a significant concern regarding the potential to facilitate antibiotic resistance in humans or animals.

Regarding fungicides that are also used as medical treatments in humans, it is believed that additional field data are needed to better understand the potential for such use to impact antimycotic resistance in humans or animals. This is not to suggest that use of this fungicide segment does facilitate resistance in humans. MCFA is simply not aware of any data available that can reasonably and scientifically inform the Agency on the potential of these products to have such an affect.

To determine the magnitude of the potential problem, field data are needed. Laboratory data are not a reliable and valid method for determining resistance development in this instance. Laboratory data may result in postulating misleading concepts on how and to what extent resistance can develop in practical applications. Numerous examples in the literature describe resistance being induced by laboratory methods (and the resistance mechanisms were explored), but this has not been observed under field conditions. Field data provides the best evidence of the potential risk because it reflects the potential impacts of real-world conditions including the potential for environmental degradation to occur as well as the potential presence of the pool of fungi that can cause the resistance issues in humans and food animals to develop. If such data are not available, then it should be developed. With such data, the Agency will be in a better position to define the scope of the problem and potential approaches in helping to resolve it. If these reliable data already exist, then the Agency can perform an appropriate risk assessment to understand the magnitude of the issue and appropriate responses.

Regarding mitigation associated with fungicides that have related uses in humans, it appears that the only potential area where there may be an opportunity for the fungicide and the pool of fungi to interact under conditions that may impact resistance in humans and food animals, involves the composting of treated material. Composting generates a high-temperature environment. The presence of fungicide residues coupled with the potential presence of the pool of fungi of concern in a relatively warm environment, may present a potential pathway of concern regarding antimicrobial resistance. If so, then mitigation restrictions precluding the composting of treated commodities may be warranted.

Other established agricultural mitigation practices that are widely accepted and used by plant agriculturists include: rotating or tank-mixing antimicrobials that have alternate modes of action ("MoA") and have proven efficacy against the target pathogen; limiting the number of applications of a specific mode of action per season; minimizing the overall frequency of applications; restricting preharvest intervals to minimize residues on the harvested crop; following labeled rates to avoid targeted organisms being exposed to sub-lethal chemical concentrations; and, avoiding antimicrobial usage where high populations of human pathogens exist. These practices demonstrate that plant agriculture is already implementing strategies to help prevent potential antimicrobial resistance selection in the environment.

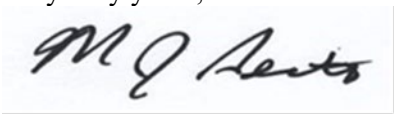
The dynamics and mechanism of antimicrobial resistance development and spread in human pathogens are poorly understood. Moreover, mechanisms for resistance development in clinical pathogens directly resulting from the application of antimicrobials to plant agriculture have not been positively elucidated. Considering that antibiotic use in plant agriculture accounts for less than one percent (<1%) of the total

amount of antibiotics used clinically and in animal agriculture, antimicrobial resistance mitigations should focus on where most of the antibiotics are being used, especially where water and soil are contaminated with animal and human excreta from treated subjects, on discharges of waste from hospitals and feedlots, and where decontamination is not done at sewer treatment facilities that may result in contaminated waterways.

Fungicides are extensively used in plant agriculture, and until recently, antimicrobial resistance in human pathogens from agricultural use has only been the focus for triazole fungicides that are also used in human medicine. Since *Aspergillus fumigatus* is an environmentally ubiquitous, non-target fungus, occurrence of antimicrobial resistance in this organism should not be viewed as a general indictment against the established and judicious use of antimicrobials or fungicides in plant agriculture. Still, with the potential antimicrobial resistance development in *A. fumigatus* (or other fungi) within the framework of Integrated Pest Management, triazole fungicide applications in plant agriculture should potentially be subject to additional mitigation steps. These may include, for example, restricting the number of applications, establishing minimum re-treatment intervals, requiring resistance management by rotation with antifungal products having a different MoA, and as discussed above, prohibiting composting of treated crops.

MCFA appreciates the opportunity to provide comments on the Framework Concept. We look forward to working with the Agency as its approach is further developed.

Very truly yours,



Michael J. Aerts
Chair; MCFA Technical Committee

Cc: Susan Jennings, U.S. Environmental Protection Agency