January 19, 2024

Response of Keep Antibiotics Working to The U.S. Food and Drug Administration's (FDA), Center for Veterinary Medicine (CVM) Environmental Scan

William T. Flynn, DVM, MS
Deputy Director, Center for Veterinary Medicine
U.S. Food and Drug Administration
Response by email to: CVMOfficeoftheCenterDirector@fda.hhs.gov

1. CVM published the Animal Veterinary Innovation Agenda in September 2023. How do the objectives and actions laid out in the agenda impact the sectors your organization represents or engages with? What additional objectives and actions would improve the agenda?

Response:

The Keep Antibiotics Working Coalition (KAW) sees the CVM Innovation agenda as a symptom of the FDA's ongoing failure to prioritize public health over the interests of the regulated industries (i.e. livestock and animal drugs). The FDA consistently takes decades to advance actions aimed at addressing critical public health issues like antimicrobial resistance. Now, the FDA is shifting even more resources to get additional products and more diverse products approved even faster all the while failing to make sure that existing products are safe.

2. CVM is enhancing its information technology and digital environment. As we advance this initiative, what should we consider that will help us meet your organization and stakeholder needs?

Response:

The FDA should focus on making sure that information on its website is up to date and accurate before spending resources on new information technology. For example, making sure that the NARMS methodology is clearly described and identifiable. There needs to be greater emphasis on effective communication over information technology. The agency should be careful to make sure that new communication technologies like Tableau do not obscure to the same degree as they provide information.

3. How would you like to see CVM more involved in advancing One Health priorities?

Response:
The FDA should prioritize its public health mission when addressing the One Health priority of antibiotic resistance. Instead, we see weak action over very long timelines. For example, the FDA first sought comment on duration limits in 2016 yet still has not developed a final rule seven years later, and implementation is not likely to be completed within 10 years of first taking comment. Creating an on-farm data collection program was a priority in the early 2000s but no program yet exists to collect this data, and the sales data that is available is only available because Congress mandated that the FDA report it. At the same time, the FDA downplays the significance of the sales data as an indicator of use, echoing industry talking points to undermine accountability. CVM has put significant effort into reducing timelines for new drug approvals but has not done anything similar for protecting public health. The criticisms about sluggishness and slow decision-making identified by the external review of the FDA Food Safety program also apply to CVM. We have repeatedly asked CVM to create and report upon indicators of progress for the One Health priority of antimicrobial resistance but the agency has consistently ignored these calls for accountability.

In adopting a One Health framework, we would like the FDA to take a broader perspective on the animal health and environmental impacts of its decisions. CVM's regulatory decisions around antibiotic use have been instrumental in creating a livestock production system in the U.S. that is highly dependent on antibiotics - particularly the swine and beef cattle industries. Where continuous harvest either for eggs or milk precludes routine antibiotic use or where market pressure has driven change such as the meat chicken industry, there are thriving productive industries that do not rely on routine antibiotics.

In cattle and swine, the antibiotics approved by the FDA allow unhealthy conditions to be covered up by routine antibiotic use. For example, feedlot cattle rely on tylosin to prevent liver abscesses created by unhealthy high energy diets, and the maker of carbadox advertises its use for pigs in crowded conditions. In addition to antibiotic resistance, the antibiotics that the FDA has approved have also contributed to other negative impacts of animal agriculture. These impacts include: animal welfare impacts of confinement, environmental contamination from concentrated animal feeding operations and serious equity and environmental justice challenges created by the current concentrated livestock raising system.

There are other serious potential One Health issues likely to be exacerbated by the Innovation Agenda. We are concerned that the FDA does not adequately take into consideration animal health and welfare when considering intentional genomic alterations. CVM has failed to regulate antibiotic residues in the byproducts of ethanol production and we are concerned that it will similarly fail to regulate the use of these drugs in the production of cultured meat. Nor does the FDA take into consideration the impacts on the structure of agriculture including how novel

technologies can lead to even further consolidation of animal agriculture. It should be part of the FDA's public health mission to understand the FDA's role in creating a system where 75% of the feedlot cattle are fed on just 2% of farms. How does this impact animal health, antibiotic resistance, food safety, and environmental justice? How does CVM's One Health vision and commitment to racial equity take into consideration these broader implications of the agency's actions?

We would like to see CVM prioritize public health when making decisions related to feed safety. CVM's current deregulation of *Salmonella* and other pathogens in feed threatens both animal and human health. CVM's current policy on serotypes of *Salmonella* that create an animal health risk is not based on science or evidence. It ignores the major serotypes of *Salmonella* causing health problems in US food animals, as indicated by clinical data, and ignores the risk to human health from *Salmonella* transmitted through feed. CVM has never provided any justification scientific or otherwise on how it chose the *Salmonella* serotypes selected for regulatory action. The agency's language around the risk of *Salmonella* contamination of feed is even weaker than that of the feed industry.

One thing that would be helpful would be to have someone in a position of authority at CVM whose goal is to ensure that the center prioritizes its public health mission when making decisions. Dr. Flynn while leading agency efforts on antibiotic resistance clearly positions himself as balancing public health and animal drug and food industry interests. The approach chosen by CVM to address antibiotic resistance either through voluntary guidance or public-private partnerships makes this worse.

4. Based on your organization's mission, what changes, challenges, or opportunities can you identify, from the human, animal or environmental health sectors, will potentially have an impact on your organization's work and on CVM in the next five years? What can CVM do now to prepare our Center and help your organization and its stakeholders, to meet those changes, challenges, or opportunities?

5. What are some of the strengths and weaknesses of CVM's legal authorities?

KAW believes that the FDA has sufficient authority to take greater action on antibiotic resistance, but instead chooses an approach that prioritizes industry interests over public health. We see this with respect to antibiotic drug approvals that are inappropriate (FDA's own risk analysis found specific uses create a human health problem but the FDA failed to act after sending sponsors a letter), with the FDA's failure to collect antibiotic use data from feed mills, with the FDA's failure to prohibit advertising a drug for use longer than the duration, or even to the FDA's language surrounding antibiotic stewardship- refusing to support "reducing use" but only mentioning "reducing the need for use", affirming all current use is appropriate.

It would be helpful if CVM would support legislation that would make it easier to withdraw approval of veterinary drugs that create a human health risk. The Keep Antibiotics Working coalition crafted phase-out legislation similar to the re-registration requirements for pesticides based on conversations with CVM, but the agency never supported legislation which would give the agency new authorities. Over the 20+ years of KAW, we have never seen the agency support legislation that would strengthen oversight of veterinary medicines. However, the agency has consistently supported weakening oversight - most recently with expanded conditional approvals.

6. In what ways could CVM improve communication with your organization?

7. Please provide any additional feedback that you would like to share with respect to the topics included in this questionnaire or on other matters impacting your organization.

KAW promotes a One Health approach to antimicrobial resistance. Our biggest concern is that CVM inappropriately prioritizes industry interests over public health, at times adopting industry rhetoric to the detriment of public health. Keep Antibiotics Working effectively argued for the restriction of non-therapeutic uses of antibiotics meaning uses that CVM had previously defined as sub-therapeutic and even at times called non-therapeutic i.e. uses for disease prevention and growth promotion. CVM then adopted that terminology using industry framing, making non-therapeutic only apply to growth promotion, and then supported the U.S. government in international venues (e.g. Codex Alimentarius) to change the terminology in international standards to meet the industry definition. More recently KAW has effectively argued that GFI #152 which is focused on “microbiological safety” recommends that drugs at high and medium risk for antimicrobial resistance not be used for more than 21 days and that the agency should consistently apply that recommendation across guidance. Instead of following our recommendation to be consistent across guidance in a way that protects public health, the agency has rewritten GFI #152, so that now a guidance on “microbiological safety” includes balancing animal health interests against human health, contrary to longstanding FDA policy. Draft GFI #273 is similar to Draft #152 in balancing human and animal health but goes even further. GFI #273 has the human and animal safety goal to “mitigate the development of antimicrobial resistance”, but requires all decisions about durations - the focus of the guidance - to be based solely upon extremely limited efficacy data such as, a duration that covers any situation that “might sometimes be encountered in the United States.”

CVM has stated that it has chosen to use voluntary guidance to address antimicrobial resistance because of the difficulty and resources needed for a contested withdrawal once a human health concern has been identified. By creating guidance that requires balancing

animal and human health needs (draft GFI#152 and draft GFI#273) in the context of improving drug safety, the FDA undermines its own authority to withdraw drugs based on human health concerns because the regulated industry will always argue that any drug is needed for animal health, welfare, and food safety (see withdrawal of fluoroquinolones and on-going effort on carbadox). In the future, when the FDA argues that it is inappropriate in a hearing on human safety to consider animal health concerns, the drug sponsor and allied industries can point to these guidances as evidence that the FDA's own policies require balancing human and animal health when making decisions related to drug safety.

KAW appreciates the opportunity to comment and hopes that our call for greater accountability and greater emphasis on the primary public health mission of the FDA is heeded.