Johns Hopkins Center for a Livable Future
Bloomberg School of Public Health
615 North Wolfe Street, W7010
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January 4, 2013

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

The statements made herein are our own and do not necessarily reflect the views of the Johns Hopkins University.

RE: Animal Drug User Fee Act (ADUFA) Reauthorization (Docket No. FDA-2011-N-0656)

To Whom It May Concern:

The Johns Hopkins Center for a Livable Future (CLF) is an academic research and education center based at the Bloomberg School of Public Health that investigates the interconnections among food systems, public health, and the environment. CLF has conducted and supported numerous studies of antimicrobial use in food animal production and antimicrobial resistance.

As public health scientists, we believe it is imperative that antimicrobials be used responsibly in food animal production to minimize the development and propagation of antimicrobial resistance. An essential component of any effort to assure responsible use is the monitoring of antimicrobial sales and use. We have devoted substantial time over the past 14 months to recommending public health enhancements to the Animal Drug User Fee Act (ADUFA) that would strengthen such monitoring. Unfortunately, despite numerous meetings and comments by CLF and other public health and medical groups, these recommendations were not included or acknowledged in FDA's draft recommendations.

CLF first presented its ADUFA recommendations to FDA at a public meeting in Rockville, MD held on November 7, 2011. We included these recommendations in a written comment submitted to the agency on December 7, 2011. In 2012, we met with FDA three times (on February 27, May 17, and September 13) to discuss ADUFA. We understand that allied organizations like the Pew Campaign on Human Health and Industrial Farming and the Keep Antibiotics Working coalition, joined by public health and medical associations like the American Public Health Association, the American Medical Association, and the American Academy of Pediatrics, met on several occasions with the agency and submitted written comments as well. None of the recommendations that CLF or allied groups made was included or acknowledged in the draft recommendations.

We have attached the November 2011 comment to this comment for FDA's review. We hope that FDA will consider these recommendations and include them in the agency's final recommendations to Congress, which we understand will be transmitted next week.

We understand that FDA has established a separate process for the enhancement of antimicrobial sales and use monitoring initiated by an advanced notice of proposed rulemaking (ANPR) published on July 27, 2012. CLF submitted a comment in response to the ANPR that echoed the ADUFA recommendations made earlier. A number of these recommendations could require enhancements to FDA's current statutory authority. The most viable pathway for such enhancements would be ADUFA, which is seen by FDA, drug sponsors, and members of Congress as must-pass legislation. The agency sought public health enhancements (e.g., drug safety authorities) in its recommendations to Congress on the latest Prescription Drug User Fee Act (PDUFA) earlier this year. It is unclear why the agency is able and willing to seek public health enhancements to PDUFA while it is reluctant to take action via ADUFA.

CLF is disappointed by the exclusion of public health enhancements from the draft recommendations issued last month, as they address the critical need for additional data to protect the health of the public and require nothing else of the agency or drug sponsors. CLF nevertheless remains open to working with FDA, should the agency decide that stronger action is warranted. Please contact us with questions about this comment or antimicrobial resistance more generally.

Sincerely,

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Attachment

The Johns Hopkins Center for a Livable Future
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December 7, 2011

Division of Dockets Management (HFA-305)
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RE: Public Comment on the Animal Drug User Fee Act (Docket No. FDA-2011-N-0656)

Thank you for the opportunity to submit a comment regarding the Animal Drug User Fee Act of 2008 (ADUFA II) as the U.S. Food and Drug Administration (FDA) prepares for Congressional reauthorization of this legislation. We are public health researchers at The Johns Hopkins Center for a Livable Future (CLF) who examine the use of antimicrobial drugs in food animal production, selection for antimicrobial-resistant bacteria, and the potential for subsequent human infection. Our comment focuses on a provision of ADUFA II that requires annual reporting of antimicrobial sales and distribution data and the release of a summary of these data to the public each year. We believe that the data collected under ADUFA II and the public summary of these data, in their current form, do not enable public health officials, veterinarians, and scientists to properly evaluate the relationship between antimicrobial use and resistance. As FDA prepares the legislation that will become ADUFA III, we urge the agency to ensure that additional data, described below, are collected under the new statute, and that a greater fraction of these data is released to the public.

CLF and the wider public health community have long been concerned that the widespread use of antimicrobial drugs in food animal production selects for antimicrobial-resistant bacteria at production facilities and leads to the release of antimicrobial drug residues to environmental media, where the residues may select for resistance genes in off-farm bacteria as well. These resistant bacteria can infect food animals and spread to and infect human populations through myriad dietary and environmental pathways, resulting in clinical diseases for which fewer and limited treatment options are available. FDA, as an agency of the U.S. Public Health Service (PHS), is tasked with ensuring that the ways in which drugs are used in veterinary medicine are safe for both animals and humans, and should ensure that public health officials (e.g., in PHS and state and local health departments), veterinarians, and scientists have adequate information to understand antimicrobial use and resistance.

Unfortunately, the language of ADUFA II and its interpretation by FDA have limited the information that is made available to public health and veterinary stakeholders. Under ADUFA Section 512(l) (21 U.S.C. §360b(l)), sponsors of drugs that contain an antimicrobial active ingredient are required to submit an annual report to FDA on the amount of each antimicrobial active ingredient in the drug that is sold or distributed for use in food-producing animals. A summary of these sales and distribution data is to be prepared by FDA and released to the public each year. Since passage of ADUFA II, FDA has released summary reports for 2009 and 2010. These reports have contained sales and distribution data reported by drug class, with domestic and international sales reported separately. No other data have been included.

These summaries do not provide sufficient information for public health officials, veterinarians, and scientific experts to monitor changes in antimicrobial use or the relationship between antimicrobial use and resistance. Furthermore, they do not allow for the evaluation of efforts by physicians, veterinarians, and the public health community to combat antimicrobial resistance by reducing overall use of antimicrobial drugs. Reduction in antimicrobial drug use is attempted through improvements to judicious use guidelines for human and veterinary health professionals, and education of providers and clients on good antimicrobial stewardship. The availability of high-quality, relevant, and timely data on antimicrobial use under ADUFA would help to evaluate the success of these efforts and suggest improvements to them.

For these reasons, we urge FDA to send a revised and improved version of ADUFA to Congress for reauthorization that requires both additional reporting of sales and distribution data by drug sponsors, and that allows FDA to make a greater fraction of these data public. Specifically, we ask FDA to do the following:

1. Include additional data already required of drug sponsors under ADUFA (e.g., monthly sales, target species, indications for use, and route of administration) in the public summary reports. These data would allow public health scientists to correlate ADUFA sales and distribution data with resistance data from the National Antimicrobial Resistance Monitoring System (NARMS), which is currently reported by month and species. These data would also assist veterinary professionals in treating animals under their care, as improved knowledge of local patterns of antimicrobial use could help inform prescribing decisions by veterinarians confronted with herd-level animal health problems related to drug-resistant pathogens.

2. Revise ADUFA to require reporting of whether antimicrobial drugs are distributed in medicated feed. Medicated feed, because it is offered *ad libidum* to animals, may or may not

be consumed in the intended dose or for the intended duration, and can therefore enhance selective pressures for antimicrobial-resistant bacteria.[1]

3. Report sales and distribution of antimicrobial drugs by class regardless of the number of distinct sponsors. ADUFA II prohibits the reporting of separate sales and distribution data for drug classes with fewer than three distinct sponsors of approved drugs in that class. These classes are instead grouped together in "not independently reported" (NIR) and "not independently reported export" (NIRE) categories in public summaries. The NIR and NIRE categories represent 11 percent, by weight, of antimicrobial drugs distributed domestically in 2010, and 95 percent, also by weight, of antimicrobial drugs exported during the same year, respectively. Both categories include fluoroquinolones and streptogramins, two drug classes considered "critically important" to human medicine by the World Health Organization. Given their importance, the public health and veterinary communities must have access to sales and distribution data for these drug classes.

4. Revise ADUFA so that antimicrobial sales and distribution data are collected at the state level. These data would provide veterinary practitioners, public health officials, and scientific experts on antimicrobial use and resistance with information on geographic usage patterns that can be compared with geographic resistance patterns to better understand causal relationships. Similar geographic relationships have been seen with other chemicals used in agriculture, such as pesticides. Requiring drug sponsors to provide information on where antimicrobial drugs are distributed is especially important in light of the concentration of food animal production in particular regions of the country, which may result in heightened levels of exposure to antimicrobial drugs in these regions.

Adoption of these recommendations would significantly improve the utility of ADUFA antimicrobial drug sales data for veterinarians, public health officials, and scientific experts. As FDA prepares ADUFA for Congressional reauthorization, the CLF would be willing to serve as a technical resource for FDA staff. Please do not hesitate to contact us with questions about our recommendations in the process revising ADUFA, or with more general questions about the use of antimicrobial drugs in animal agriculture and the ecology of antimicrobial resistance.

Sincerely,

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[1] Love DC, Davis MF, Bassett A, Gunther A, Nachman KE. Dose imprecision and resistance: free-choice medicated feeds in industrial food animal production in the United States. *Environ Health Perspect*. 2011;119(3):279-283.

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