ConsumersUnion®

POLICY & ACTION FROM CONSUMER REPORTS

Comments of Consumers Union on the
Food and Drug Administration (FDA) Request for Comments on
"Collecting On-Farm Antimicrobial Use and Resistance Data"
Docket No. FDA-2015-N-2768

Michael Hansen, Senior Scientist
November 30, 2015

Consumers Union (CU), the public policy and advocacy arm of Consumer Reports,[1] welcomes the opportunity to comment on possible approaches the Food and Drug Administration (FDA), U.S. Department of Agriculture (USDA), and Centers for Disease Control and Prevention (CDC) may take for collecting on-farm antimicrobial use and resistance data.

We are glad that FDA, in collaboration with USDA and CDC, is undertaking this project to collect data on how antibiotics are used on-farm, and also strongly agree that such usage data are needed to help government and stakeholders meet four goals: 1) assess the adoption rate of changes under Guidance for Industry (GFI) #209 and #213; 2) gauge the success of additional antibiotic stewardship efforts and guide their continued development; 3) better understand the associations between antibiotic use practices and resistance; and 4) provide greater transparency about antimicrobial use in food-producing animals.

We agree with others in the broader public health community that there should be a consistent standard used for the type of antimicrobial data that would be most useful in answering these four goals. We believe such data must have four characteristics, including that it must be: 1) quantitative; 2) comprehensive (from all food animal species and production classes, and including purpose of use); 3) ongoing; and 4) unbiased (e.g., not based on voluntary participation). We need quantitative, comprehensive, ongoing and unbiased data in order to accurately estimate on-farm antimicrobial usage and resistance.

The current federal proposals could represent positive steps—but need to be strengthened significantly in order to provide the data needed to guide public policy.

---

[1] Consumers Union is the public policy and advocacy arm of Consumer Reports. Consumers Union is an expert, independent, nonprofit organization whose mission is to work for a fair, just, and safe marketplace for all consumers and to empower consumers to protect themselves. It conducts this work in the areas of food and product safety, telecommunications reform, health reform, financial reform, and other areas. Consumer Reports is the world's largest independent product-testing organization. Using more than 50 labs, auto test center, and survey research center, the nonprofit organization rates thousands of products and services annually. Founded in 1936, Consumer Reports has over 8 million subscribers to its magazine, website, and other publications.

Based on the analysis presented below, we believe that the antimicrobial data collected by USDA—either through the National Animal Health Monitoring System (NAHMS) survey, the Collaboration in Animal Health and Food Safety Epidemiology (CAHFSE) pilot study, the Agricultural Resource Management Survey (ARMS), on-farm research studies, or the proposed annual Antibiotic Use Survey—may be of some use, but are seriously flawed for use in making an accurate estimate of antimicrobial usage or resistance, in large part due to the fact that the vast bulk of the data gathered are not unbiased because the data come from voluntary participation in surveys. USDA admits that the larger the farm, the lower the likelihood to participate in such surveys.[2]

In contrast, the antimicrobial data gathered by FDA, while not fully meeting the four goals for the collection of such data, do come closer to meeting those goals than the data collected by USDA. Thus, FDA's recent proposed rule on antimicrobial animal drug sales and distribution[3] is a step in the right direction since it recognizes the importance of species-specific data on antimicrobial use for understanding, monitoring and managing antimicrobial resistance. This proposed rule is flawed, however, because it only requires the drug sponsor to provide ***estimates*** of species-specific use data, which are not an accurate substitute for the actual collection of species-specific antimicrobial drug use data. We urge FDA to require data reporting on specific species usage, including the purpose for the antimicrobial use.

In addition, we believe that FDA could gain quantitative, accurate information on the precise amounts of medically important antimicrobials used in food-producing animal species for specific purposes (e.g., for growth promotion, or for disease prevention, control, or treatment) through the annual reporting of data regarding antimicrobial drugs added to animal feed. This reporting by veterinarians and feed mills, in a standardized format, is already required as part of the recently finalized Veterinary Feed Directive[4] (VFD) rule. Requiring that the data gathered under the VFD rule be turned over to FDA and made part of the annual data reported to the public is actually the single most important step FDA could take at this time to gain the most accurate data on species-specific use of antimicrobials for each purpose. The data would meet the four criteria of an effective data collection system (e.g., that the data be quantitative, comprehensive, ongoing and unbiased) and would enable a meaningful analysis of those factors related to the development and spread of antimicrobial resistance as a result of use of antimicrobials of importance in human medicine.

If FDA believes either of these two steps exceeds the agency's current legal authority, it should ask Congress to provide that authority without delay.

Detailed comments

[2] Slide 3 in MacDonald, J. 2015. Future Work with ARMS. Presented at Collecting On-Farm Antimicrobial Use and Resistance Data Public Meeting, Washington, D.C. Sept. 30, 2015: http://www.fda.gov/downloads/AnimalVeterinary/NewsEvents/WorkshopsConferencesMeetings/UCM464315.pdf.

[3] 80 Fed Reg 97, pp. 28863-28872, May 20, 2015. At: http://www.gpo.gov/fdsys/pkg/FR-2015-05-20/pdf/2015-12081.pdf.

[4] 80 Fed. Reg. 104, pp. 31708-31735, June 3, 2015. At: http://www.gpo.gov/fdsys/pkg/FR-2015-06-03/pdf/2015-13393.pdf.

Characteristics of useful data

We fully agree with FDA that accurate data on antimicrobial usage and resistance are needed to assess the changes in antimicrobial use that have resulted from implementation of FDA's Judicious Use Policy on antimicrobials as laid out in two Guidance for Industry (GFI) documents: 1) The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals (GFI #209)[5] and 2) Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions With GFI #209 (GFI #213).[6] The intent of these two GFIs is to reduce use of antimicrobials for food animal production. To the extent that we could have accurate data for antimicrobial use and bacterial resistance from the same farm, it could dramatically improve our understanding of the precise association between antimicrobial use and resistance.

However, for the data on antimicrobial usage and resistance in food animal production to be truly useful in understanding the connection between antimicrobial use and antimicrobial resistance, it should have four characteristics, including that it must be: 1) quantitative, 2) comprehensive, 3) ongoing and 4) unbiased. First, the data must be quantitative rather than qualitative. We must know the precise quantities of antibiotics used on farms; knowing only qualitative information, such as whether an antibiotic is used for a given purpose, is far less useful. Second, the data should be comprehensive. This means knowing not just the total quantity of antimicrobials used on a farm, but also which particular food animal species are being treated with which antibiotic(s), how many of the animals are being treated, for which particular purpose the antimicrobial was administered (e.g., for growth promotion, or for disease prevention, control or treatment), and duration of use. Third, the data should be ongoing, ideally being taken at regular intervals, such as every year, in order to be able to determine if implementation of GFIs #209 and #213 have actually lead to a reduction in antimicrobial use. Finally, the data should be unbiased, which means that it should not be based on voluntary reporting initiatives that can suffer from selection bias.

USDA programs

USDA programs which gather data about on-farm antimicrobial use and resistance can be found throughout the agency, including in the Animal and Plant Health Inspection Service (APHIS), the Agricultural Research Service (ARS), and the Economic Research Service (ERS). Although the programs differ in a number of ways, they all have one thing in common: participation in the various programs is voluntary. Thus, the data that come from these studies

---

[5] FDA. 2012. Guidance for Industry (GFI) #209: The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals. 26 pp. At: http://www.fda.gov/downloads/animalveterinary/guidancecomplianceenforcement/guidanceforindustry/ucm216936.pdf.

[6] FDA. 2012. Draft Guidance for Industry (GFI) #213: 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. 18 pp. At: http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf.

are fundamentally biased, since the population that is being sampled consists of those farmers, processors, and others who agree to be part of a study.

Animal and Plant Health Inspection Service (APHIS)
National Animal Health Monitoring System

The major USDA program that gathers data about on-farm antimicrobial use and resistance is housed in APHIS: the National Animal Health Monitoring System (NAHMS). NAHMS is a national program that both sends out questionnaires and takes biological samples (for various bacteria, including pathogens) from various commodities, including swine, dairy animals, beef cows/calves, poultry, sheep, and others. This is the largest government program that monitors food animal health. The commodity surveys are sent out periodically, but not on a regular schedule, and at relatively long intervals. Thus, swine has been sampled every 5-6 years (e.g. 1990, 1995, 2000, 2006, 2012), dairy animals every 3-5 years (1992, 1996, 2000, 2006, 2012), and poultry every 3-8 years (1996, 2004, 2010, 2013).[7] In addition, the data collected in the surveys is often qualitative or not comprehensive when it comes to antimicrobial use. Thus, data on antimicrobial use in feed and water is often qualitative (only whether the farm has used an antimicrobial, not how much), the data on antimicrobial use by injection just asks for the primary product used, not how much or when it was used. In addition, participation in the NAHMS surveys is voluntary. In terms of the biological samples taken, NAHMS has focused heavily on *Salmonella*, and culturing some of those samples to further characterize the *Salmonella* (such as to serotype it) and identify resistance to various antimicrobials.

USDA has recognized some of the drawbacks of the commodity surveys and has proposed numerous changes, many of which we strongly support. USDA plans to enhance the NAHMS commodity surveys, by asking more questions about antimicrobial use and practices, linking of the sample on-farm collections for pathogens and commensals, and increasing the number and breadth of resistance testing. We agree with this plan, and specifically urge USDA to require the following.

First, the antimicrobial data should be quantitative and comprehensive. For antimicrobial use in feed or water, this means taking data on the specific antimicrobial used, dosing levels, inclusion rates in feed, the number of animals that are treated, for how long and for which particular purposes.

Second, the surveys should happen far more frequently than every 5-7 years. They should occur every year or every other year so that changes in antimicrobial use and resistance can be more readily tracked over time.

Third, in terms of the biological sample collections, we agree with USDA that it should be extended beyond *Salmonella* to include *E. coli*, *Campylobacter*, *Enterococcus*, MRSA, *Clostridium difficile* and *Listeria*. The number and breadth of resistance testing should also be

[7] USDA-APHIS. 2015. Historical and Current Antimicrobial Use Data Collection and Analysis. Presented at Collecting On-Farm Antimicrobial Use and Resistance Data Public Meeting, Sept. 30, 2015: http://www.fda.gov/downloads/AnimalVeterinary/NewsEvents/WorkshopsConferencesMeetings/UCM464324.pdf.

expanded, so that all collections of pathogens and commensals include information of the level of resistance to various antimicrobials for each species or sample collected.

Fourth, the on-farm biological samples should be linked to the surveys so that it is possible to know which farms the particular samples come from and what the antimicrobial use practices were on that farm. Ideally, samples from the same farms could be tracked over time, so that government officials and the broader public health community can more accurately assess the changes that are seen in the data. On-farm data has proven useful abroad, such as in Denmark, as a way of drawing food producers' attention to the necessity of more judicious use when they do not meet the industry norm.

Fifth, we also urge further molecular characterization of pathogens. Presently, USDA and CDC use pulse-field gel electrophoresis (PFGE) for molecular typing. Given that sequencing technology has dramatically improved over the years, we urge USDA and CDC to use whole genome sequencing (WGS) for the pathogens they collect. WGS means that the entire genome is sequenced so as to more accurately be able to link pathogens with disease outbreaks, compared to PFGE which is a cruder measure. Indeed, CDC has recently noted that WGS is the future of food safety.[8]

Economic Research Service

Every year, the Economic Research Service conducts a survey of U.S. farms, called the Agricultural Resource Management Survey (ARMS), along with the National Agricultural Statistics Service (NASS). The ARMS is meant to be representative of U.S. agriculture and is USDA's primary source of farm financial data, with some 22,000 farms responding each year.[9] The hog and poultry (broilers) versions of ARMS have included data on antimicrobial use. The ARMS data can be useful because they represent a large representative sample of producers.

However, the ARMS data have some significant drawbacks. First, the data gathered on antimicrobial use is largely qualitative, such as whether or not the farm operator uses antibiotics for a particular use. Second, for antimicrobials put in feed, the farm operators may not know whether there are antimicrobials in the feed, since many farm operators are contract growers who are supplied with the feed by an integrated agricultural enterprise. Indeed, USDA notes that "don't know" is a common response on these surveys, which is why USDA contacts integrators for information on feed costs.[10] Third, the antimicrobial questions have only been asked of the hog and poultry (broilers) sectors, but not of the dairy and cow-calf operations, and the surveys are only periodic, happening about every 5 years for hogs, poultry (broilers), and dairy.

---

[8] Centers for Disease Control and Prevention (CDC). 2015. Future of Food Safety: Whole Genome Sequencing, Sept. 9, 2015. At: http://www.cdc.gov/genomics/public/features/food_safety.htm#Sep9.

[9] MacDonald, J. 2015. Using ARMS Data for Analyses of Antibiotics Use in Livestock. Presented at Collecting On-Farm Antimicrobial Use and Resistance Data Public Meeting, Sept. 30, 2015: http://www.fda.gov/downloads/AnimalVeterinary/NewsEvents/WorkshopsConferencesMeetings/UCM464312.pdf.

[10] *Ibid*.

Perhaps the most important drawback of the ARMS is that participation is voluntary, so that means we are probably getting a biased sample of the population. USDA recognizes this problem, noting that ARMS gets a 60 to 65% response rate, yet the "response is inversely related to farm size and production keeps shifting to the larger farms."[11] Admitting that the larger producers tend not to participate in the ARMS suggests that any results from this survey are or will be skewed toward the practices of small producers and not the major suppliers of the livestock.

As part of the ARMS, USDA is thinking of conducting an Annual Antibiotic Use Survey, which would be designed to provide annual estimates of antimicrobial use in feed or water in multiple production types so as to monitor the use trends relative to FDA Guidance #209 and #213. NAHMS would be developing the survey questions. Unfortunately, the major drawback of this proposed survey is that on-farm participation would be voluntary. Given that USDA has admitted that larger farms tend not to participate, unless USDA can ensure more uniform participation, the value of such a survey's results would be limited.

FDA programs

The antimicrobial data gathered by FDA, while not fully meeting the four goals for the collection of such data, are consistently better (in terms of being quantitative, comprehensive, ongoing and unbiased) than those collected by USDA. The data gathered as part of the Animal Drug User Fee Amendments (ADUFA) of 2008 are quantitative and more comprehensive than those collected by USDA.

FDA's recent proposed rule on antimicrobial animal drug sales and distribution[12] is a step in the right direction, since it recognizes the importance of species-specific data on antimicrobial use for understanding, monitoring and managing antimicrobial resistance. This proposed rule is flawed, however, because it only requires the drug sponsor to provide ***estimates*** of species-specific use data, which are not an accurate substitute for the actual collection of species-specific antimicrobial drug use data.

There are several reasons why this is problematic. First, FDA has not provided evidence that the drug sponsors have the information to make accurate estimates. Indeed, as the Generic Animal Drug Alliance (GADA) noted in its comments on the ANPR, "it is impractical to obtain and provide such additional sales estimates and distribution data by individual species with any reasonable degree of accuracy … once the product is sold by the drug manufacturer (i.e., drug sponsor) to the primary customer, there is no practical means for the drug sponsor to further trace the ultimate use of the product to an individual animal species."[13]

---

[11] Slide 3 in MacDonald, J. 2015. Future Work with ARMS. Presented at Collecting On-Farm Antimicrobial Use and Resistance Data Public Meeting, Washington, D.C. Sept. 30, 2015: http://www.fda.gov/downloads/AnimalVeterinary/NewsEvents/WorkshopsConferencesMeetings/UCM464315.pdf.

[12] 80 Fed Reg 97, pp. 28863-28872, May 20, 2015. At: http://www.gpo.gov/fdsys/pkg/FR-2015-05-20/pdf/2015-12081.pdf.

[13] Comment to ANPR by Generic Animal Drug Alliance. At: http://www.regulations.gov/#!documentDetail;D=FDA-2012-N-0447-0036.

Second, FDA already has evidence that drug sponsors are not accurate in reporting antimicrobial sales and distribution data. Presently, as part of section 105 of ADUFA, drug sponsors report the numbers of each drug product sold as well as the amount of antimicrobial active ingredients associated with such product(s). FDA reports that drug sponsors seem to have a problem with accurately converting their product sales data into active ingredient sales data. As FDA notes, "our experience has shown great variability in reporting accuracy when sponsors are asked to convert product sales data into active ingredient sales data. … Therefore, FDA believes this approach [drug sponsor only submits product sales data and allows FDA to calculate total amount of antimicrobial active ingredient in those products] will … greatly increase the accuracy of the final results." If the companies have such difficulty in accurately transforming product sales data into the total amount of antimicrobial active ingredient use (i.e., multiplying the number of units of the specific drug product sold by the amount of each active ingredient in that specific drug product), we are concerned that they may also have difficulty accurately estimating the species-specific use of each antimicrobial active ingredient.

We further disagree with FDA's proposal to only require species-specific antimicrobial use estimates for four food-producing animals: cattle, swine, chickens, and turkeys. As part of this proposal, FDA proposes a fifth category for "other species/unknown." Thus, FDA would lump data on minor food animal species with data on companion animals and data from unknown sources. This proposal does not allow the broader public health community to distinguish between minor food-producing species, companion animals and unknown sources. As an example, FDA refers to an antimicrobial product that is approved for use only in cattle, sheep and dogs, and the sponsor estimates that 50% of annual sales were for cattle, 10% for sheep and 40% for dogs. This would be reported as cattle 50% and species/unknown 50%. Consequently, it would not be possible to know that the 50% unknown was actually 10% for a minor food animal species (sheep) and 40% for a companion animal, and 0% for an unknown species. Thus, **we urge FDA to at least require reporting for other/minor food species, in addition to data on cattle, swine, chickens and turkeys, and to not lump data from companion animals with data from other sources.**

We also urge FDA to require indicating the purpose—growth promotion, or disease prevention, control or treatment—for antimicrobial use, since such data are needed to help gauge the success of antimicrobial stewardship efforts. We believe that antimicrobials should only be used to treat sick animals and should not be used for routine disease prevention purposes. In this regard, we also urge FDA to stop classifying disease prevention as a "therapeutic" use. To the extent possible, it would be even more useful to know the actual disease for which the antibiotics were being used.

FDA should require reporting of data from Veterinary Feed Directives (VFDs)

There is an alternative to estimation as a way to obtain accurate species-specific data on antimicrobial use in food-producing animals. That alternative can be found within FDA's existing authority in the recently finalized Veterinary Feed Directive (VFD) rule.[14] A VFD drug

[14] 80 Fed. Reg. 31708. 2015. At: http://www.gpo.gov/fdsys/pkg/FR-2015-06-03/pdf/2015-13393.pdf.

is an approved animal drug for use in or on animal feed, and must be used under the professional supervision of a licensed veterinarian.[15] All VFD drugs can only be manufactured by a feed mill that has a medicated feed mill license, which has to be obtained from the FDA. The finalized VFD rule allows for electronic requests and record keeping, and transitions new animal drug products containing medically important antimicrobial drugs from an over-the-counter status to a status that requires veterinary oversight.

The VFD rule requires that both the veterinarian and the feed mill retain copies of the VFD which includes, among other things, the name of the animal drug, the animal species, the number of animals to be fed the medicated feed, the location of the animals, the date of treatment, and the indication for which the VFD was issued. Since some 74% (e.g., 6,828,506 kg out of 9,196,803 kg) of all medically important antimicrobials used in food-producing animals in 2013 were distributed via feed,[16] requiring that the data gathered as part of the VFD be turned over to FDA and made part of the annual data reported to the public is actually the single most important step FDA could take to gain the most accurate data on species-specific use of antimicrobials. This would enable a meaningful analysis of those factors related to the development and spread of antimicrobial resistance as a result of use of antimicrobials of importance in human medicine.

Since VFD orders include information on the location of the animals to be treated, it will be possible to exclude intermediate distributors and identify what feed was actually sent to farms. Also, given that there are already over 1,300 VFD feed distributors and FDA projects 300 additional distributors each year, it will be very easy to maintain the confidentiality of the drug distribution information, compared to the situation for information collected under section 105 of ADUFA, where there were only 23 reporting companies that sell these antimicrobial drugs.

Presently, VFD users are required to maintain records and share them among farms, feed distributors, and veterinarians, and make them available to FDA on request. We simply recommend that such records be *required* to be shared with FDA. To reduce the reporting and analysis burden and analysis on FDA and feed mill distributors, FDA could require only larger distributors to submit data, or could collect data from a selected sample of distributors.

VFD-related data from feed mills would provide accurate data on the amounts of antimicrobials mixed in feed, not estimates. Thus, **FDA should require annual reporting of VFD data by feed mills in a standardized format. FDA should also aggregate those data into a publicly available registry that reports data for each separate food-producing animal species, by use.**

Thank you for your consideration of our comments.

---

[15] FDA. 2009. Guidance for Industry #120. Veterinary Feed Directive Regulation Questions and Answers. 11 pp. At: http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM052660.pdf.

[16] See Table 11a in FDA. 2015. 2013 Summary Report on Antimicrobials Sold or Distributed for Use in Food-Producing Animals. At: http://www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM440584.pdf.

Respectfully submitted,

Michael Hansen, Ph.D.
Senior Scientist
Consumers Union