

FDA's Proposed Method for Adjusting Antimicrobial Sales Data Using a Biomass Denominator

Challenges to Changing Antibiotic Use in Food Animal Production: Economics, Data, and Policy

A USDA-ERS/Farm Foundation Workshop

September 7, 2018

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Background

- The use of an animal biomass denominator to adjust antimicrobial sales data has been implemented in Europe (PCU), and more recently in Canada and the OIE
- FDA-CVM formed a working group to determine if those methods could be utilized similarly in the U.S.
- It was determined that a biomass denominator more specific to the U.S. would be appropriate
 - Accounts for domestic animal populations and animal weights
 - Differences in food animal management practices and antimicrobial drug approvals

Definitions - Biomass

- **Biomass Denominator:** the **population** of a given livestock species in the U.S. multiplied by the average **weight** of that species
 - To be assessed at the drug class level
 - For each of the four major food-producing species—cattle, swine, chickens, and turkeys

- **Target Animal Biomass (TAB):** the biomass denominator for each species for a specific antimicrobial drug class

ESVAC Method

- Animal populations
 - Include major species with further breakdown into slaughter and livestock categories, some minor species, and imported/exported animals
- Animal weights
 - Assign standard weights to each of the categories and these are used across countries and years
 - Currently use average weight at treatment
- Denominator (Population Correction Unit) includes the populations and weights for all species for all drug classes

ESVAC Method

$$\frac{\text{Total Sales (mg)}}{\left[\sum (\text{population} \times \text{standard weight})_{\text{animal category}} \right] (\text{kg})}
 \quad \text{OR} \quad
 \frac{\text{Antimicrobial Drug Class Sales (mg)}}{\left[\sum (\text{population} \times \text{standard weight})_{\text{animal category}} \right] (\text{kg})}$$

FDA's Proposed Biomass Denominator Method

- **August 15, 2017** – FDA proposed a method to adjust annual data on the amount of antimicrobials sold for use in the U.S. based on annual animal population
 - Utilizes FDA's annually reported antimicrobial sales and distribution data, estimated sales by species (as of 2016)
 - Takes into account annually reported domestic animal populations and weights
 - Applies a **target animal biomass** (TAB) denominator to estimated sales data, by species, for medically important antimicrobial drug classes

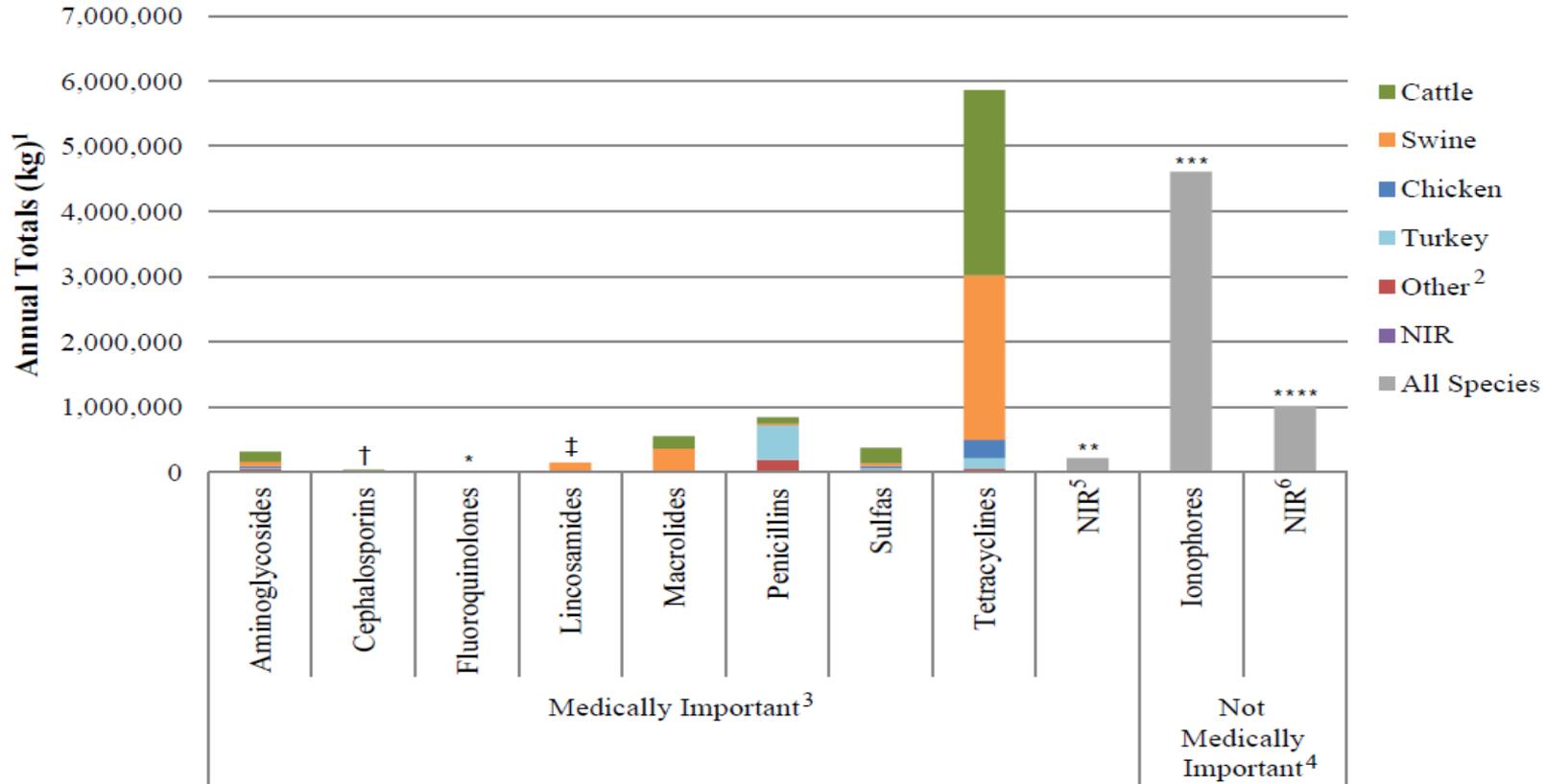
Key Elements

- Antimicrobial sales and distribution data (by species) reported annually to FDA
- Annually reported animal populations in the U.S.
- Annually reported animal weights in the U.S.
- Animal drug approvals in the U.S.
- Limitations on the use of certain antimicrobial drugs and/or drug classes in the U.S.
- Focuses on trends in antimicrobial sales relative to U.S. livestock populations

Antimicrobial Sales and Distribution Data

- The amount of antimicrobials sold or distributed for use in food-producing animals has been reported annually to FDA by animal drug sponsors since 2009
- As of 2016, the reports now include species-specific estimates
 - For the four major food-producing species (cattle, swine, chickens, turkeys) as identified on the approved drug label
 - An “other species/ unknown” category may include use in other species, extralabel uses, or unknown uses

2016 US Domestic Sales and Distribution Medically Important Antimicrobials



Medical Importance, Drug Class, and Estimated Species

Animal Categories and Population Data



- Annually reported livestock populations include subcategories specific to the U.S. livestock population and drug approvals in the U.S.
- Method will utilize animal number data reported by U.S. Department of Agriculture (USDA)
 - Annual totals of slaughtered animals
 - Inventory of livestock at a single timepoint
 - Annual totals of animals imported into or exported from the U.S.

Estimates of Animal Weights

- Animal weights in the U.S. vary annually based on reported data
- Examples of weights to be utilized for species subcategories include:
 - Average weight at slaughter
 - Weights for animals imported to or exported from the U.S.
 - Annual average weights for livestock kept longer than 1 calendar year (e.g., dairy cattle, sows, and beef cattle)

Target Animal Biomass

- **Target Animal Biomass (TAB):** the biomass denominator for each species for the antimicrobial drug class
- When applied to antimicrobial sales data for a specific drug class (expressed in mg), results in an adjusted **mg/TAB** which can be applied for each major species

Example Biomass Denominator Adjustment for a Single Drug Class

mg/TAB value for Cattle =

$$\frac{\text{All sales of an antimicrobial drug class for use in cattle (mg)}}{(\text{Population} \times \text{Annual average weight})_{\text{cattle}} \text{ (kg)}}$$

mg/TAB value for Swine =

$$\frac{\text{All sales of an antimicrobial drug class for use in swine (mg)}}{(\text{Population} \times \text{Annual average weight})_{\text{swine}} \text{ (kg)}}$$

mg/TAB value for Chickens =

$$\frac{\text{All sales of an antimicrobial drug class for use in chickens (mg)}}{(\text{Population} \times \text{Annual average weight})_{\text{chickens}} \text{ (kg)}}$$

mg/TAB value for Turkeys =

$$\frac{\text{All sales of an antimicrobial drug class for use in turkeys (mg)}}{(\text{Population} \times \text{Annual average weight})_{\text{turkeys}} \text{ (kg)}}$$

Analysis and Reporting

- Data reporting must meet statutory requirements to protect confidential business information
- Goals of the method are to focus on analysis of trends in antimicrobial sales relative to the U.S. livestock populations
- Percent change may be the primary metric proposed for analysis and reporting of annual trends
- FDA-CVM is considering alternative reporting systems for sharing the antimicrobial sales adjusted by a biomass denominator

Public Comments on Proposed Method

- **November 15, 2017** - Public comment period for the proposed U.S.-specific biomass denominator method closed
 - FDA received feedback from various stakeholders and has reviewed the comments
- Majority of the comments encouraged collection of on-farm antimicrobial use data
 - Recommendations for FDA-CVM to collaborate with USDA on collection of on-farm antimicrobial use data
 - Significant preference for antimicrobial use data rather than further analysis of sales data

Public Comments on Proposed Method

- Many comments were not in favor of the proposed method, some included recommendations to withdraw the proposal
 - Unknown level of uncertainty for the sales by species estimates, and therefore concerns with the utility of any resulting adjusted data
 - Proposed method does not take dose, potency, or number of animals exposed into account
 - Potential for misinterpretation and unintended competition or inappropriate comparisons (between species and/or countries)
 - Is not a good indicator for measuring antimicrobial stewardship
 - Adjusted data based on estimates should not be used for policy decisions

Public Comments on Proposed Method

- Some provided insight into production group categorization and animal weights to consider
- Some recommended collection and reporting of antimicrobial use data for humans and companion animals
- Of the comments in favor of applying a biomass denominator, additional recommendations included:
 - Identify and describe the uncertainty and limitations of the data
 - Provide clarity and context in reporting to allow for appropriate interpretation
 - FDA should consider international harmonization with EU and/or OIE, or a discussion of the differences in methods to allow for accurate interpretation

Summary

- FDA-CVM received valuable feedback on the proposed U.S.-specific biomass denominator method
- While many of the comments were not in favor of additional analysis of estimated sales by species data, FDA-CVM continues to believe that a biomass denominator provides important context when considering antimicrobial sales data
 - Further refinement of the method may be needed, and FDA-CVM is open to considering additional feedback as we move forward
 - On-farm antimicrobial use data, antimicrobial resistance data, and other data are also very important and will help inform antimicrobial stewardship efforts

References

- European Surveillance of Veterinary Antimicrobial Consumption (ESVAC):
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000302.jsp
- FDA 2016 Summary on Antimicrobials Sold or Distributed for Use in Food-Producing Animals:
<https://www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM588085.pdf>
- FDA's Proposed Method for Adjusting Data on Antimicrobials Sold or Distributed for Use in Food-Producing Animals, Using a Biomass Denominator:
<https://www.fda.gov/downloads/animalveterinary/safetyhealth/antimicrobialresistance/ucm571099.pdf>



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