



# FDA Proposal Would Support Fight Against Antibiotic-Resistant Bacteria

Biomass method would adjust antibiotic sales data by livestock population, provide valuable information

## Overview

Data on how and why medically important antibiotics are used in agricultural settings—and how this usage changes over time—are central to ensuring the judicious use of these drugs. However, information is [currently limited](#), with the only national estimates of antibiotic use in food animal production derived from [antibiotic sales data](#). Since publishing the 2016 data, the Food and Drug Administration (FDA) reports on antibiotic sales have included [estimates by major food animal species](#)—chickens, cows, pigs, and turkeys. But much more detailed information is needed.

In 2017, FDA [proposed](#) a [method](#) that uses animal population estimates to [contextualize antibiotic sales](#) data. This approach, known as animal biomass adjustment, can help explain trends and fluctuations in antibiotic use, which may be affected by differences or changes in animal populations, such as animal life span, species and production class differences, or management practices. The methodology thus provides important context for sales data.

The Pew Charitable Trusts applauds FDA's commitment to implementing a biomass methodology and urges the agency to do so without delay. Pew provided [public comments](#) on the technical merit of FDA's biomass proposal, as did several other organizations, including veterinary and animal agriculture industry associations, consumer groups, pharmaceutical companies, and individual stakeholders. More than a year later, FDA has not taken any concrete action to finalize the proposal, although the agency's recently released [five-year plan](#) identifies completing a biomass method by 2021 as one of its immediate priorities.

To aid in this important effort, Pew reviewed and analyzed the [42 public comments submitted](#) on this topic to FDA between Aug. 15 and Nov. 13, 2017. Pew's review of these public comments identified four key recurring concerns related to the finalization of the biomass method. Although most of these concerns are valid, they can be effectively addressed, and should not deter the agency from finalizing the biomass adjustment method.

## **Issue 1: Antibiotic sales data provide imperfect insights on actual antibiotic use**

Various stakeholders expressed fundamental concerns about the value of antibiotic sales data, regardless of any specific biomass adjustments.<sup>1</sup> Comments cited this data source's limitations, including that sales do not necessarily represent actual quantities used because of issues such as stockpiling, and the inherently limited information that sales data can provide about exactly why, how, and when the drugs were used.<sup>2</sup> For example, some comments stated that antibiotic sales estimates can be, and have been, misinterpreted as actual use data and that applying a biomass adjustment could encourage additional inaccurate interpretations.<sup>3</sup> Moreover, because sales data are now broken out by major food animal species, some expressed concerns that use of these data could lead to inappropriate and potentially misleading comparisons across animal species.<sup>4</sup> Finally, several commenters mentioned that sales data, which are reported by weight, do not account for drug potency (the amount of drug required to produce the intended effect), which may lead to unintended consequences, such as incentives to switch to stronger drugs that are more important to public health.<sup>5</sup>

**Resolution: Antibiotic sales data provide valuable insights into use trends, however, Pew acknowledges the data's limitations and recognizes the importance of ensuring appropriate analysis and interpretation.** Data can be imperfect—yet still insightful for assessing trends. Biomass-adjusted sales data are important for three key reasons:

- 1. Sales data are well established, useful, and the only publicly available and nationally representative source to estimate total antibiotic use in U.S. food animal production.** Although sales estimates are not perfect, they provide crucial data points and valuable insights.<sup>6</sup> In fact, sales data are widely accepted as an important source of information on antibiotic use, with many countries and regions relying largely or exclusively on these data because they have been collected for many years and because the alternative—gathering reliable on-farm data about antibiotic use—is methodologically challenging and costly.<sup>7</sup> For example, the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) has been tasked with collecting and assessing trends in antibiotic sales across European countries and has annually collected and reported the data since 2009.<sup>8</sup> Similarly, the World Organisation for Animal Health (OIE)—the 182 member intergovernmental organization responsible for improving animal health—established systems that collect and monitor antibiotic sales data across its members.<sup>9</sup>

Sales data are a useful tool for tracking policy impacts. Organizations such as the Codex Alimentarius Commission of the United Nations have recognized the value of sales data for the surveillance of antibiotic consumption in animals.<sup>10</sup> In the U.S., the Presidential Advisory Council on Combating Antibiotic-Resistant

Bacteria (PACCARB) also recognized the value of sales data, establishing national goals to prioritize the improved collection of sales data to strengthen surveillance efforts.<sup>11</sup> In addition, sales data actually informed FDA's focus on drugs administered through feed and water when the agency developed its Guidance for industry [209](#) and [213](#); over time, sales data will also provide insight into how effective these policies are in reducing the injudicious use of antibiotics. In the U.K., sales data have been used to develop national antibiotic reduction targets established by the Responsible Use of Medicines in Agriculture Alliance.<sup>12</sup>

## **2. Biomass-adjusted sales data provide meaningful insight into antibiotic consumption in animals—and are less likely to be misinterpreted—than sales data alone.**

Because variations in the size and composition of the animal populations are accounted for, biomass-adjusted sales estimates can be valuable in monitoring antibiotic use trends.<sup>13</sup> Other countries, such as Canada, and the EU already use them to help track antibiotic consumption.<sup>14</sup> In 2017, for the first time, OIE included biomass-adjusted data to report global antibiotic consumption.<sup>15</sup> Scientific studies have also used this type of data to evaluate global trends in animal antibiotic consumption.<sup>16</sup>

Adjusting sales data with biomass helps provide the context needed to assess trends in antibiotic use and track progress in improving the use of these drugs, as highlighted in a joint monitoring and evaluation report published by the Food and Agriculture Organization (FAO), World Health Organization (WHO), and OIE on the cross-sectional Global Action Plan established by those same organizations.<sup>17</sup> The addition of such contextual information helps minimize the risk of data misinterpretation—for instance, compared to species-specific antibiotic sales data without any adjustment. For this reason alone, as FDA stated when reporting its proposed biomass methodology, such adjustment is beneficial.<sup>18</sup>

## **3. Sales data collection complements, rather than precludes, the collection of actual antibiotic use data.**

Biomass-adjusted sales data will not and should not replace the collection of antibiotic use data—both types of data can and should be collected in parallel as they permit different types of insights into antibiotic use. As one case in point, a study of Danish and Dutch national animal sales data concluded that monitoring both national sales and use data can be a useful option; it is the preferred method in the Netherlands.<sup>19</sup> Similarly, a review examining methods for quantifying antibiotic use trends explained that there is an inherent tradeoff between comprehensiveness—to what extent the population can be sampled—and resolution (how much detail can be captured, such as detailed farm-level information and monthly antibiotic use).<sup>20</sup> Therefore, combining highly detailed but small primary data sets, such as use data collected on a small number of farms, with comprehensive, secondary sources—such as national sales estimates—may be helpful when large, nationally representative on-farm data are not readily available.<sup>21</sup> Almost all of the organizations that submitted comments to FDA highlighted the importance of on-farm data collection efforts and the need for FDA to focus on supporting such efforts, such as by collaborating with the U.S. Department of Agriculture (USDA). Use data are essential to better understanding how and why antibiotics are used—for example, by helping to understand for what reasons antibiotics were used and contributing to the broader effort to combat the emergence of antibiotic-resistant bacteria.

Pilot projects and periodic surveys are underway and should be continued and expanded. However, it is not currently feasible to collect on-farm use data in a robust, quantitative, and comprehensive way across all food-producing species that would ensure that the data are broadly actionable. As highlighted in a 2017 report from the Government Accountability Office (GOA), “benchmarking and measuring producers’ use and veterinarians’ prescriptions of antibiotics would require major infrastructure and technological investments for data capture, analysis, and reporting.”<sup>22</sup> Even if collection of nationally representative use data were to become feasible and widely adopted, the collection of biomass-adjusted sales data should not be discontinued.

Antibiotic sales and on-farm use data have inherent but distinct limitations. On-farm use data are limited by factors such as selection bias from voluntary participation (i.e., there is no required reporting of use data in the U.S.), the cost and resources required to collect accurate data, and lack of standardization across collection methods.<sup>23</sup> Sales data are limited by a lack of detail about how the drugs are actually used, the time delay between purchase and use of a drug, and variations in external factors, such as changing treatment practices.<sup>24</sup> These limitations emphasize why gathering and combining data from multiple sources is important to provide a comprehensive understanding of antibiotic use patterns and allow for science- and evidence-based decision-making.

## **Issue 2: FDA’s proposed approach for calculating biomass is not sufficiently described, lacks transparency, and may slightly overestimate the size of the animal population**

Multiple stakeholders expressed concerns with FDA’s proposed technical approach. Several commenters highlighted a lack of detail regarding exactly how the agency will calculate biomass. Other commenters questioned the lack of clarity on how average animal weights will be calculated and whether the estimates will be accurate.<sup>25</sup> In addition, several commenters questioned the choice to use average animal weight at the time of slaughter instead of at an earlier time in the animal’s life when treatments with antibiotics are most likely, as this choice may overestimate biomass. Stakeholders also expressed concerns that there will be improper comparisons across countries and regions if methodological differences in how these countries estimate biomass cannot be properly accounted for. These differences include the types of data average animal weights are based on, how potential year-to-year variations in slaughter weight from market forces and seasonal variations are addressed, and how weight differences across animal production classes are accounted for. Amid these concerns, most stakeholders agreed with FDA that using data from USDA’s National Agricultural Statistics Service and Economic Research Service is the most appropriate and best available information on animal populations in the U.S.,<sup>26</sup> and a few commenters agreed with the overall proposed method to calculate the biomass denominator.<sup>27</sup>

**Resolution: Pew agrees that FDA should provide additional details about the proposed biomass calculation and align the method with existing ones to the extent feasible, although ultimately, any one of the proposed methods may be acceptable as long as it is implemented appropriately and consistently used to track changes.** The technical issues that stakeholders raised should not detract FDA from swiftly finalizing the biomass method for three key reasons:

1. **Several countries and organizations have successfully established biomass adjustments specific to their unique needs (e.g., comparisons across countries or over time) and country situation, and there is value in developing a U.S.-specific method.** The differences between the U.S. animal agriculture industry and those in other countries—for instance, regarding average animal weights, slaughter ages, age composition of animal populations, and data availability—warrant development of a U.S.-specific biomass methodology. One key difference among established methods is how animal weight is calculated. Organizations such as OIE use the animal’s weight at slaughter as a proxy for how much it weighed when treated with antibiotics in their biomass method, while the ESVAC and Canada’s methods estimate animal weight based on when treatment with antibiotics is most likely during an animal’s life.<sup>28</sup> This is important because an animal’s weight at treatment may be considerably lower than its weight at slaughter, which in turn will lead to lower biomass estimates.<sup>29</sup> In addition, average animal weights may differ across countries and regions, due to differences in breeds,

husbandry practices, or typical age at slaughter, among other factors.

Some other methodological differences stem from variations in the available data on animal populations. These variations include whether data on the weight of animals at slaughter is readily available or has to be estimated based on the weight of carcasses, and whether information on the composition of animal populations—for instance, the fraction of adult versus newborn animals—is readily available. The OIE method uses whatever data is available for a given region, providing established, standardized approaches for estimation where needed.<sup>30</sup> In contrast, ESVAC’s and Canada’s methods are tailored to use the data systems available in their respective countries.<sup>31</sup>

2. **The FDA method can be transparently described and largely aligned with existing methods.** Given the various options available for calculating animal weights, it is crucial for FDA to provide a sufficiently detailed and transparent description of its method. Moreover, the general approach can and should be largely aligned with existing methods. Similarity in approaches across entities and geographic regions can reduce confusion and the potential for misinterpretation, help support international coordination efforts, and allow for comparisons across different settings where appropriate.
3. **A comparison of trends is possible with any of the proposed or established methodological choices.** ESVAC has compared results of its biomass estimation to those derived using different approaches and found strongly correlated results.<sup>32</sup> A key purpose for FDA’s proposed biomass adjustments is to track changes in antibiotic use within the U.S. over time. Such trends will be minimally affected by the chosen method. As long as FDA is clear and consistent with its biomass approach, tracking national antibiotic use will be achievable with any of the established or proposed approaches.

### **Issue 3: Inappropriate comparisons with biomass-adjusted sales estimates from other countries may lead to inappropriate conclusions about U.S. antibiotic use**

Several commenters expressed a concern that country-to-country comparisons of biomass-adjusted sales data might be problematic due to potentially inaccurate extrapolations and misinterpretations. A few organizations explicitly expressed concerns about how comparisons of biomass-adjusted sales data across countries could possibly affect the export of U.S. animal proteins and products.<sup>33</sup>

**Resolution: Pew acknowledges the potential risk of inappropriate comparisons, including across different countries and geographic regions.** The differences discussed above can make it difficult to compare data across countries. However, these challenges should not deter FDA from finalizing the biomass adjustment method for three key reasons:

1. **Initiatives are underway to find appropriate approaches for comparing data from different countries or regions.** WHO’s Global Action Plan recommends implementing systems to collect and analyze antibiotic use data to better understand trends and the appropriateness of antibiotic use.<sup>34</sup> Reports from organizations such as OIE provide harmonized estimation methods and address the appropriateness of comparing data from different countries and regions.<sup>35</sup> For example, the most recent OIE report analyzed biomass-adjusted sales data by regions instead of individual countries, and supported animal population data obtained by global data sets with available country-specific data sources to account for challenges in comparing geographical regions and different data collection efforts.<sup>36</sup> The OIE report also addressed the limitations of its analysis, such as recognizing the differences between its approach and existing biomass methodologies, highlighting the distinct purpose and goals of the OIE biomass method, and noting the limited specificity of data given

the global scope of the OIE analysis. In another notable example, ESVAC applied two different methods of calculating biomass using EU data sources to address data limitations in one of the EU countries and then compared the two sets of results to determine how well the methods corresponded.<sup>37</sup> Similarly, scientific research has compared estimates based on the current ESVAC method to those based on an approach that accounts for the longevity of different species and, based on those findings, recommended ways to quantitatively adjust for an animal's life span when calculating biomass.<sup>38</sup>

2. **FDA has a long history of taking steps to limit data misinterpretation risks.** For years, FDA's annual reports on animal antibiotic sales estimates have clearly stated the limitations on how the data may be appropriately interpreted and used—for example, by clarifying that reported sales do not necessarily represent actual use for a specific indication in a species.<sup>39</sup> Similar qualifications could be provided in the reporting of biomass-adjusted sales data and would help guide the interpretation of such data going forward. Transparency about methodological differences across countries and a focus on national trends can help prevent inappropriate comparisons and data misinterpretation. Where the U.S. chooses to differ in approach from entities such as OIE, Canada, and ESVAC, FDA can provide a description of the differences, explain why the chosen method is most appropriate for the U.S, and discuss how these differences may have affected the biomass and adjusted antibiotic sales estimates.
3. **Biomass adjustments actually reduce the risk of inappropriate country-to-country comparisons.** By accounting for differences in animal populations across countries, biomass-adjusted sales data may actually reduce the risk of drawing inappropriate conclusions. One study explored appropriate comparisons using Danish and Dutch national animal sales data. It concluded that country-to-country comparisons based on sales figures alone risk being misinterpreted partially due to differences in age and composition of the animals and dosage of the antibiotics.<sup>40</sup> However, country-to-country comparison data can be and has been useful, and biomass adjustments can help with interpretation of the data.<sup>41</sup>

## **Issue 4: Finalizing and using the biomass adjustment method will place undue scrutiny on antibiotic use in livestock**

Some comments suggested that the lack of comparable biomass-adjusted sales data for human medicine might result in undue scrutiny on antibiotic use in animal agriculture because no comparable biomass-adjusted sales data exist for human health care.

**Resolution: Considerably more data is already available on antibiotic use in human medicine than in animal agriculture.** Hospitals are required to report hospital-acquired infections to the National Healthcare Safety Network (NHSN).<sup>42</sup> Using this data reporting system, approximately 800 hospitals nationwide also voluntarily report antibiotic use—based on pharmacy data—to NHSN, and some states, including Missouri, and Tennessee starting in 2021, require such reporting.<sup>43</sup> There are also numerous data collection and reporting mechanisms in place via the Centers for Disease Control and Prevention and national organizations that track antibiotic use and resistance rates in U.S. health care facilities.<sup>44</sup> Such data is also used to guide policy. An analysis of national ambulatory health care survey data, for instance, found that antibiotic prescribing on the outpatient side varies by the recipient's age and geographic region and that about 30 percent of antibiotic prescriptions are unnecessary.<sup>45</sup> Although it is true that FDA does not collect and report sales data for human health care settings on an annual basis, the agency has reported sales data in previous years; moreover, as cited above, many other data streams provide information on how antibiotics are used in human health care.<sup>46</sup>

## Conclusion

Although concerns and limitations exist about the use and application of biomass adjustments in the U.S., this approach is undoubtedly an important step forward in better understanding the antibiotic sales data we currently have available. FDA can and should finalize the proposed biomass adjustment method as soon as possible. In doing so, the agency should clearly articulate limitations to the methodology and how the biomass-adjusted sales data can and cannot be used.

Biomass is not a replacement for actual antibiotic use data, and the U.S. should continue to pursue other data sources to complement sales data. Several factors beyond those accounted for by biomass can impact antibiotic sales. These include changes in use patterns (e.g., shifts to drugs with higher potency or changes in administration routes) or animal disease pressures—for instance, due to an increased number of disease outbreaks. Having multiple data sources that capture antibiotic sales, on-farm antibiotic use, and antibiotic stewardship practices will help provide a comprehensive picture of antibiotic stewardship and help explain the impact that these and other external factors have on the data.

As outlined above, biomass-adjusted sales data have limitations—as do all data sources—but the concerns should not deter FDA from quickly finalizing this important methodology. Biomass-adjusted data have the potential to provide better insight into how antibiotics are used than the unadjusted sales data currently available, and the risk of misinterpretation is lower. If the agency is transparent in its approach while also remaining vigilant in pursuing other sources of data, then all stakeholders will benefit from an improved understanding of antibiotic use.

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**For further information, please visit:**

[pewtrusts.org/antibiotic-pipeline](https://pewtrusts.org/antibiotic-pipeline)

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