

**Deliberations of an Advisory Committee Regarding Priorities, Sources, and
Methods for Collecting Animal Antimicrobial Use Data in the United States**

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Abstract

This paper describes the methodological options for food animal antimicrobial use data collection in the United States, including data priorities and methods limitations that were identified by a diverse group of expert stakeholders. Four major categories of antimicrobial use data were identified based on the source of information and its proximity to actual use: end-user data, prescription data, manufacturing data, and distribution data. Criteria were developed to aid in evaluating the overall utility of each methodological option, and attempt was made to develop a qualitative, composite “overall usefulness” score for each option. Consensus was not reached on option scores, therefore, experts individually rated six methodological options relative to the evaluation criteria, and provided comments and rationale for each response. The responses were summarized and presented.

Introduction

The Advisory Committee on Animal Antimicrobial Use Data Collection in the United States was established by the Alliance for the Prudent Use of Antibiotics in order to foster discussion among a diverse group of expert stakeholders and develop consensus regarding the most effective means for gathering data on antimicrobial use in food animals in the United States. Specific objectives and the rationale for the project are described elsewhere in this Supplement (DeVincent and Viola, 2005). This report describes the methodological options for animal antimicrobial use data collection, priorities, and limitations identified by the members of the Advisory Committee.

Methods

In the spring of 2002, Advisory Committee members were recruited from the following stakeholder groups: academics/researchers, government officials, animal health industry representatives, public interest scientists and advocates, food animal producers, and veterinary professionals (see DeVincent and Viola, 2005, for complete list of names). Committee members engaged in a three-step process to develop a strategy for gathering

antimicrobial use data in animals in the United States. The first step was to identify and prioritize “data needs,” or the specific types of information that would be ideal to characterize the quantity of antimicrobial use in animals. Next, the committee considered “potential data sources and methods for gathering data,” again focusing on identifying all possible options. Finally, the Committee considered “limitations” and practical considerations constraining the feasibility or utility of each data collection method. Criteria were also developed to aid in evaluating the overall utility of each methodological option.

At each stage of this process, initial knowledge and opinion were solicited from Committee members via email questionnaire. Responses were then compiled by staff members at APUA and re-submitted to the group for comment and revision.

Additionally, Committee meetings were held in November 2002 and May 2003. All Committee members had an opportunity to review the meeting minutes and project documents. Additional correspondence, initiated by APUA or by individual Committee members, occurred by phone and email throughout the duration of the project.

Results

Assumption of Utility

Initial concerns were raised by several Committee members regarding the difficulty of discussing methodology without first reaching consensus on the utility and specific purpose(s) of animal antimicrobial use data collection. While acknowledging the validity of this concern, the Committee co-chairs decided that the highest priority should be to generate a flexible set of options adequate to meet a broad range of potential policy

goals. Committee members were therefore asked to assume utility and set aside their concerns about specific goals. All agreed to do so.

Initial Data Categories

Four major categories of antimicrobial use data were identified by the Committee based on the source of information and its proximity to actual use. Described below, these categories were labeled as follows: End-User Data, Prescription Data, Manufacturing Data, and Distribution Data.

End-User Data may be obtained from persons having direct knowledge of antimicrobial use in animals—i.e. those who administer antimicrobials to animals. End-Users were divided into three major subcategories: 1) veterinarians (in clinics or ambulatory practices); 2) food animal producers; and 3) companion or sport animal owners (Table 1, items I.A-C).

Where applicable (i.e. for drugs requiring a prescription), Prescription Data may be obtained from those who prescribe and/or dispense antimicrobials to end-users; these may include licensed veterinarians, compounders, and pharmacies (Table 1, item II).

Manufacturing Data include production, exports, and manufacturer sales information (Table 1, items III.A-C). Such data may be obtained from pharmaceutical manufacturers or feed mills.

Finally, Distribution Data may be obtained from points in the distribution network between the manufacturer and the end-user; these may include distributors, veterinarians, buying groups, dealers, and any other individuals included in the distribution network. As the number of parties involved in distribution networks may be large (Viola and

DeVincent, 2005), the Committee believed that it would not be practical to attempt further subdivision of this category (Table 1, item IV).

The Committee briefly considered including a fifth category for illegal use, but most members agreed that such use was probably minimal and could not be reliably quantified.

Priorities by Use Data Category

The Committee considered it to be self-evident that end-users would have the most accurate information regarding the disposition of antimicrobials, including actual purpose and duration of use, lag time between purchase and use, and the fate of expired antimicrobials. Therefore, prior to considering feasibility, cost, and other limitations, the Committee identified End-Use Data as a high priority.

Prescription Data were also prioritized because of their proximity to end-use and inherent verifiability. However, the Committee recognized this information to be inferior in some respects because not all prescriptions are filled and/or used. The Committee also acknowledged that Prescription Data would not be useful for the vast majority of antimicrobial drugs used in food animal production, most of which are sold over-the-counter (Viola and DeVincent, 2005).

The Committee observed that manufacturers must have accurate knowledge regarding total amount of antimicrobial produced and sold, including amount of active ingredient by weight or volume produced. It may also be possible for them to predict end-use, although their knowledge regarding final outcome after distribution is likely to be incomplete. However, as surrogates for actual input into the system over a given time

period, Manufacturing Data are subject to “stockpiling errors,” or errors due to the fact that all the product produced or sold in a given time period may not be used in that time period. For this reason, Manufacturing Data were judged to be slightly less desirable than End-Use Data, although some Committee members expressed the opinion that a combination of production and/or sales data and more limited end-use data for validation would be ideal.

Distribution Data include the total amount of antimicrobial products sold by distributors, dealers, veterinary clinics, feed stores, clinics, pharmacies, or other sources. Like manufacturer sales data, however, these data do not reflect the fate of antimicrobials once they are sold. Antimicrobials may be used directly by the buyer, or they may be re-sold to a variety of distributors and intermediaries, making it difficult to track sales without double counting (thus rendering comparison to end-use nearly impossible). Distribution Data from points in the network below manufacturer sales were therefore judged to be a less desirable substitute for actual antimicrobial use data, although some members of the Committee felt they could be useful for validation studies and to connect production data to end-use.

Data Needs

The Committee defined “data needs” as the specific information that would ideally be available regarding the use, production, or sale of an antimicrobial drug or drug product. Data needs identified for each data category defined above are summarized in Table 1.

Category	Data Needs
<i>I. End Use Data</i>	
A. Direct Use by Veterinarians	Total quantity administered to animals by:
B. Use by Producers	Name of Drug (chemical name)
C. Use by Companion or Sport Animal Owners	Species/Market Class/Stage of Production Number of Animals Treated Dose (total mg per animal per day) Duration (total days) Indication (purpose of use) Route of Administration

II. Prescription Data

Total quantity prescribed to animals by:

Name of Drug (chemical name)

Species/Market Class/Stage of Production

Number of Animals Treated

Body Weight or Approximate Weight Range

Dose (total mg per animal per day)

Duration (total days)

Indication (purpose of use)

Route of Administration

III. Manufacturing Data

A. Production

Total quantity produced by:

Active Ingredient

Name of Drug (chemical)

Approved Label Claims (includes
species/market class/stage of production;
indication; and route of administration)

Final Formulation

B. Exports

Total quantity exported by:

Active Ingredient

Name of Drug (chemical)

C. Domestic Sales

Total quantity sold by:

Active Ingredient

Name of Drug (chemical)

Approved Label Claims (includes
species/market class/stage of production;
indication; and route of administration)

IV. Distribution Data

Total quantity sold by:

Active Ingredient

Name of Drug (chemical)

Approved Label Claims (includes
species/market class/stage of production;
indication; and route of administration)

Table 1: Major animal antimicrobial use data categories and data needs as identified by the Advisory Committee.

Regarding End-User and Prescription Data (Table 1, items I and II), the Advisory Committee emphasized that antimicrobial use practices vary with animal species and type (e.g. beef or dairy cattle), stage of production, presence/absence of disease and/or indication—presumably with correspondingly different impacts on antimicrobial resistance. When gathering antimicrobial use data, it is therefore critical to describe the animal species treated, numbers of animals treated, total amount of antimicrobial dispensed per animal, and indication. Route of administration may also be important in determining ecological contributions to the development, dissemination, and persistence of antimicrobial resistance.

The Committee decided that Manufacturing and Distribution Data should include the amount of active ingredient in a particular antimicrobial formulation as well as the approved label claim (which includes species, indication, and route of administration) (Table 1, items III and IV). As the goals of the project focused narrowly on domestic antimicrobial use information, the Committee elected to include only rudimentary information on exports. Export data are intended solely for the purpose of subtraction from total production figures (Table 1, item III.B). The issue of imports was not addressed, as antimicrobials cannot be used legally in the United States without Food and Drug Administration (FDA) approval. Manufacturers based outside of the United States, of which there are many, must comply with the same regulations as domestic manufacturers. Illegal importation was not considered because the Committee could not identify reliable and consistent sources of data.

In addition to the specific data needs outlined in Table 1, several Committee members emphasized the importance of collecting ancillary data for use in interpretation of antimicrobial use data. They expressed the opinion that information on contextual variables such as disease status, prevailing market conditions, use of new vaccines, manufacturing shortages, weather patterns, etc., might be crucial in interpreting antimicrobial use data for any given application. Other Committee members contended that a distinction should be made between drug use surveillance and analytical epidemiology. The purpose of public health surveillance, these members emphasized, is to systematically collect, analyze, interpret, and disseminate data for use in decision-making and response to public health concerns. Any fluctuations or unusual trends observed in surveillance data should be investigated through more focused epidemiologic investigations. Accordingly, information regarding antimicrobial use in food animals should be structured to permit further epidemiological analyses.

Potential Data Sources and Methods

Potential data sources were defined as those individuals, agencies, or other entities that could potentially provide antimicrobial use information. Committee members agreed to initially list potential sources without regard to legal, financial, or other limitations and constraints. Potential methods for collecting this information were similarly defined as the means by which the necessary information could be gathered from the data sources. Potential data sources and methods identified by the Committee are summarized in Table 2.

Category	Data Sources	Potential Methods
<i>I. End User Data</i>		
A. Direct use by veterinarians	1. Hospitals, clinics, and ambulatory practices	<ul style="list-style-type: none"> a. Require veterinarians to record all direct use b. Enroll sentinel practices that keep track of use electronically c. Ask individual practices to record use for a defined period of time d. Periodically survey a cross-section of veterinarians
B. Use by producers	<ul style="list-style-type: none"> 1. Food animal producers 2. Market research companies 3. Cooperative extension agents 	<ul style="list-style-type: none"> a. Require all producers to record use b. Enroll sentinel farms that keep track of use electronically c. Ask individual producers to record use for a defined period of time d. Periodically survey a cross-section of producers e. Drug use reporting data from on-farm quality assurance programs a. Purchase from market research companies (applicable data may be limited to indication, dose, and duration) a. Interviews with individual farmers

- C. Use by companion and sport animal owners
 - 1. Companion and sport animal owners
 - a. Periodically survey a cross-section of owners

II. Prescription Data

- 1. Veterinarians
 - a. Require veterinarians to record all prescriptions
 - b. Enroll sentinel practices that keep track of prescriptions electronically
 - c. Ask individual practices to record prescriptions for a defined period of time
 - d. Periodically survey a cross-section of veterinarians
- 2. Pharmacies
 - a. Conduct periodic surveys
 - b. Establish an electronic capture system

III. Manufacturing Data

- A. Production
 - 1. Manufacturers and feed mills
 - a. Request voluntary disclosure by manufacturers
 - 2. CVM
 - a. Require reporting by NADA/ANADA sponsors and publicly disclose data
- B. Exports
 - 1. Manufacturers
 - a. Request voluntary disclosure by manufacturers

	2. CVM	a. Modify current data reporting requirements and publicly disclose data reported by NADA/ANADA sponsors
C. Domestic Sales	1. Manufacturer and feed mills	a. Request voluntary disclosure by manufacturers
	2. CVM	a. Modify current data reporting requirements and publicly disclose data reported by NADA/ANADA sponsors

IV. Distribution Data

- | | |
|---|---|
| 1. Distributors, Veterinarians, Compounders, Pharmacies, Dealers, Buying Groups, etc. | a. Require or request voluntary reporting to centralized database |
| | b. Implement tracking system |

Table 2: Potential data sources and methods.

Considerations and Limitations

After listing potential data collection methods, the Committee turned its attention to practical considerations and limitations of potential data collection methods. The sections below detail the major concerns expressed by Committee members, grouped by row number in Table 2. Except where objections are noted, statements attributed to “the Committee” reflect a consensus of opinion.

(I.A.1.a) Require veterinarians to record all direct use

Many Committee members commented that requiring veterinarians to track and report all direct use of antimicrobials would be impractical due to high costs. As the practice of veterinary medicine is regulated by the states, it would also be difficult to coordinate reporting requirements and formats. Some Committee members observed that many veterinary practices operate on small profit margins, making adherence to labor-intensive reporting requirements burdensome. In clinics where electronic records are already kept through specialized prescription software, the issue would likely be one of data compatibility (Reid-Smith and DeVincent2005).

(I.A.1.b) Enlist sentinel practices that track use electronically

The Committee noted significant potential for bias in a surveillance system based solely on collecting information from sentinel practices. For example, it would be difficult to include practices that did not track prescriptions electronically, and these practices may provide better record-keeping than the ones that track prescriptions manually. Concerns were also raised regarding incentives; those practices most willing to participate would not necessarily be representative of the entire industry. The Committee recognized, however, that such bias is not uncommon in field-based information gathering. All agreed that criteria for enrollment would have to be chosen carefully and that methodological concerns, such as how to deal with practices that drop out of the program, would have to be addressed.

One Committee member suggested that veterinary teaching hospitals might be particularly appropriate as sentinel sites, because comprehensive medical records would be available for large numbers of animals and many of them would likely have been

exposed to antimicrobials. However, as another Committee member pointed out, many of these facilities are referral centers. Animals might reasonably be expected to have more severe illnesses requiring more intensive treatment, including the use of antimicrobials, than in primary care settings. Therefore, while useful for detecting overall trends in resistance under these unique circumstances, antimicrobial use data from veterinary teaching hospitals are unlikely to be representative of trends in antimicrobial use at primary treatment facilities or in food animal production.

Data comparability was also mentioned as a concern for sentinel sites. Temporary regional variation, caused by events such as disease outbreaks, climatic fluctuations, or market conditions, were recognized as potential problems for data collected from sentinel sites. If national in scope, however, some Committee members felt that this type of fluctuation would even out over time. Since data collection would be continuous, aggregation and period of analysis would be limited by data volume and data management capacity.

(I.A.1.c) Record use at selected practices for a finite time period

Asking individual practices to record all antimicrobial use for a defined period of time would be subject to many of the same methodological limitations as sentinel sites. The increased flexibility afforded by collecting data from a greater number of practices for discrete time periods might mitigate some of the bias inherent in fixed sentinel sites. Incentives would still be an issue, but the cost of providing incentives (e.g. monetary) for a limited time period would likely be lower. Committee members observed that the time period and selection of sample practices would remain critical to minimize bias.

(I.A.1.d) Periodically survey a cross-section of veterinary practices

This option would involve asking veterinarians to retrospectively record antimicrobial use during a defined time period. Committee members observed that the existing National Animal Health Monitoring System (NAHMS) program of the United States Department of Agriculture (USDA) (see Viola and DeVincent, 2005), could serve as a model. As others observed, however, no comprehensive list of veterinary practices has yet been compiled by any government agency, making the target population difficult to identify. Several Committee members suggested that the extensive list of veterinarians available through the American Veterinary Medical Association might be used for this purpose. The Committee agreed that the incentive for participation by veterinary practices might be insufficient.

An additional limitation would be the possible inaccuracy and recall bias introduced by asking veterinarians to retrospectively recall use. Alternatively, as previously noted, prospective recording could be burdensome to some veterinary practices, particularly those that currently lack electronic record systems.

(I.B.1.a-d) Require all producers to record use, enlist sentinel farms, sample individual farms for a defined time period, or survey producers

In general, the limitations for these methods as applied to producers are the same as those listed for veterinarians (see I.A.1.a-d, Table 2). Periodic surveys of producers are already conducted by the NAHMS Program but could be expanded to include more specific information on antimicrobial use. However, Committee members noted several

limitations with the NAHMS program that affect the usefulness of currently available data: 1) data reporting is not mandatory (although the response rate is generally high); 2) data are often collected retrospectively through completion of questionnaires; 3) data are reported in summary reports to protect anonymity of respondents; and 4) historically, data have not been collected more often than once every five years.

(I.B.1.e) On-farm quality assurance programs

Quality assurance programs such as the program sponsored by the National Pork Board (<http://www.porkboard.org/PQA/manualHome.asp>) provide producers with forms and organizational infrastructure for accurate record-keeping. Participation by producers is generally voluntary. Committee members emphasized that the intent of on-farm quality assurance programs is generally educational only; data collection methods are neither rigorous nor consistent. The Committee believed that these data should not be considered as an accurate source for antimicrobial use information unless program requirements are significantly altered.

(I.B.2) Market research companies

Limitations on data purchased from market research companies such as Doane Market Research, Inc. (see Viola and DeVincent, 2005) include the fact that methods used by market research companies to obtain antimicrobial use data are often proprietary, making it impossible to evaluate data quality. In addition, corporate data collection methods are not transparent, and data available from market research companies may also be limited to indication, dose, and duration.

(I.B.3) Extension Service personnel

Although the USDA Extension Service plays an important role in advancing knowledge and promoting human and animal health, the Committee concluded that Extension Service personnel have limited access to relevant information on the quantity of animal antimicrobial use at any particular farm. Information they could provide would likely be qualitative rather than quantitative.

(I.C.1) Survey companion and sport animal owners

Theoretically, pet and horse owner surveys would be subject to the same limitations listed under I.B.1.d. The Committee did not consider this possibility at length.

(II.1.a) Require veterinarians to record prescriptions

The utility of this data collection method would obviously be limited to the subset of antimicrobial drug use in food animal production that occurs by veterinary prescription. Most Committee members felt that requiring veterinarians to record prescriptions would be subject to the same limitations as requiring them to record actual use in clinics, hospitals, and ambulatory practices (see I.A.1.a). However, one member observed that requiring clinics to record prescriptions might be more feasible than requiring them to record actual antimicrobial use, as it should impose fewer limitations on actual practice. It was also noted that hand-written prescriptions or those submitted directly to a pharmacy by telephone would not be captured by practice management and labeling software. New database management software might be needed for this purpose.

(II.1.b-d) Enlist sentinel practices, sample individual practices for a defined time period, or survey veterinarians

Limitations would be similar to those noted for end-use by veterinarians (See I.A.1.b-d).

(II.2) Pharmacies

Prescription veterinary drugs are not typically dispensed by retail pharmacies in the United States. However, pharmacies could potentially provide data on extra-label prescriptions of human drugs dispensed for animal use that would likely be missed by other methods for collecting prescription data. Committee members were not certain of the extent of this practice or whether existing pharmacy databases allow for differentiation of prescription data based on the species (i.e. human versus animal) of the intended recipient. Potential limitations include cost and accessibility.

(III.A.1) Request voluntary reporting of production information from manufacturers and feed mills

Several Committee members, including those with direct knowledge of the pharmaceutical industry, were skeptical that manufacturers would voluntarily disclose production information. They observed that companies have no incentive to disclose such data, which is generally considered proprietary because of its potential to reveal market share to competitors.

(III.A.2) Require manufacturers to report production information and publicly disclose data

Pharmaceutical manufacturers are currently required to report annual sales data and annual amounts exported to the U.S. Food and Drug Administration's Center for Veterinary Medicine (CVM) on the anniversary date of New Animal Drug Application (NADA) or Administrative New Animal Drug Application (ANADA) approval, but production data are not currently reported. Production information may differ from sales in a given reporting period if the entire inventory is not sold. Production data are also more useful if exports are of interest. Because the limitations on collection of production and sales data would presumably be the same, they are discussed below.

Committee members strongly suggested that these data would be more useful if reported on a single date specified by CVM. Additionally, data are reported in terms of unit quantity sold (e.g. number of vials of a systemic injectable drug, bags of feed premix, or bottles of oral tablets) rather than by active ingredient. Retroactively converting these data into kilogram or pound quantities of active ingredient for each drug and/or drug class might be complicated and inaccurate unless standardized.

Moreover, public disclosure of the information is limited unless there are three or more manufacturers of a given drug product. To some extent, reporting data aggregated by drug class could circumvent this limitation. For newer antimicrobials, however, this would not be possible until the period of exclusivity for the pioneer/discovery manufacturer expired and ANADAs were approved. One Committee member suggested that reporting rolling averages from a multi-year database might circumvent manufacturer concerns regarding proprietary sales information. Three or five year intervals were

suggested, or, to further frustrate attempts to misuse the data, three years might be randomly selected from a five year period. As an added benefit, such a reporting scheme would also solve the problem of interpretability introduced by variable reporting periods.

(III.B.1-2) Request or publicly disclose production information from exporters

Export data would be necessary for the purpose of subtraction from total antimicrobial production data. These data are already reported to CVM (see above). Limitations on public disclosure would presumably be similar to those listed for domestic manufacturers (III.A.1-2)

(III.C.1-2) Request or publicly disclose sales information from manufacturers and feed mills

Limitations would be similar to those for production information (See III.A.1-2).

(IV.1) Distribution data

Finally, the Committee considered distribution data to be of lowest priority, partially because of the complexity of distribution networks for different drug products and the difficulty of tracking drugs through the system while avoiding duplication. The Committee discussed a centralized national reporting or tracking system as a potential method. It was acknowledged, however, that no such system currently exists and that such a system would be extremely costly to implement and maintain. One Committee member suggested that the goal should not be to comprehensively track the movement of every drug product; a smaller sample might provide valuable descriptive data.

Evaluation Matrix

In attempting to determine the overall merit of the potential data collection methods outlined in Table 3, the Committee found it useful to define the following evaluation criteria: 1) feasibility; 2) representativeness; and 3) data quality. Feasibility was defined to include considerations such as current incentives, likelihood of stakeholder participation, cost of implementation, perceived political will or legal constraints, etc. Several members noted that the feasibility criterion is particularly problematic, cautioning against an *a priori* assumption that any method is “feasible” given sufficient political will and funding. Most agreed that a more objective feasibility assessment might be an appropriate subject for a follow-up study. Representativeness was intended as a measure of external validity, or how well collected data correspond to actual conditions. Data quality, on the other hand, measured internal validity or freedom from error in data collection.

Based on these criteria, Committee members suggested creating an evaluation matrix in which potential data collection methods could be rated according to each criterion and a composite “overall usefulness” score could be calculated by averaging across rows (Figure 1). Committee members generally agreed that the development of the evaluation matrix would be useful to policy-makers attempting to prioritize use data collection methods.

	Feasibility	Representativeness	Data Quality	Overall Usefulness
Option A				
Option B				
Option C				

Figure 1: Sample evaluation matrix for selected data sources/collection methods. Under the scheme proposed by the Advisory Committee, the “Overall Usefulness” column would contain an average or composite of the ratings across each row.

At the May 2003 meeting, the Committee discussed how the criteria might best be applied to several of the potential data collection methods identified above. Consensus could not be reached during the meeting, so a follow-up questionnaire was distributed in order to provide Committee members with an opportunity to express their views in more detail. Respondents were asked to rate six methodological options relative to the evaluation criteria, providing comments and rationale for each response. The sections below attempt to qualitatively characterize responses for each option listed on the questionnaire. It should be acknowledged, however, that these six single-method options by no means exhaust the range of possibilities available to policymakers. The ideal set of options would undoubtedly involve combinations of data collection methods. Unfortunately, time constraints prevented the Committee from attempting to identify and evaluate the merits of options involving combinations of data collection methods.

Option 1: All practices/producers record all prescriptions/use indefinitely

The majority of respondents considered the feasibility of this method to be low. One member suggested that feasibility might be improved if it was incorporated into a

mandatory quality assurance program. Conversely, most Committee members rated the likely representativeness of such a system to be high, as it would effectively constitute a “census” of use. In terms of data quality, one Committee member suggested that it would be “a database nightmare.” Overall, most Committee members rated the overall usefulness of this method as low. One member commented that uniform implementation of electronic prescription management software would alter his rating to medium or high depending on the record collection and processing systems.

Option 2: Sentinel practices/farms track use electronically

Many Committee members rated feasibility of collection by sentinel practices as high. However, most classified its representativeness as low to medium. Two noted that there would be some volunteer bias towards more compliant farms unless sampling was random. Most Committee members rated data quality as high, one suggesting that data quality should be higher with sentinel sites than if all practices/farms recorded use because volunteers would be more interested and more vigilant about record-keeping. Overall, the majority of members rated usefulness of the sentinel option as medium.

Option 3: Selected practices/producers record all prescriptions/use for a defined period of time

Opinion on the feasibility of this option varied widely. Approximately half of the group rated the representativeness of this option as medium; issues raised included the selection criteria of the practices/producers and resultant bias from volunteer

participation. Most of the Committee also rated data quality and overall usefulness as medium.

Option 4: Periodically survey a cross-section of veterinarians/producers

Opinion on surveys was also highly variable. Most Committee members rated feasibility as high. Half of the group evaluated representativeness as medium, but the range of evaluations was high to low. Members commented that “a random sample is essential but a low response rate and inherent bias is inevitable” and “representativeness depends upon the sampling methods.” Similar comments accompanied the data quality ratings, which were also variable. One member who rated the data quality low remarked that it is difficult to collect high quality quantitative data with a survey. Overall usefulness ratings were mixed, but one member who classified this option as highly useful commented “descriptive data are moderately useful for interpretation of data from manufacturers and end-users but highly useful for the further development/evaluation of prudent use/clinical practice guidelines and practitioner education.”

Option 5: Solicit production and sales information from manufacturers

Most Committee members rated feasibility for voluntary disclosure as low. Responses for representativeness ranged from low to high, with several commenting that it depends on the sampling scheme. Several Committee members also noted that sales data are not necessarily representative of use. Most rated data quality as high, presumably because the manufacturers should have accurate data on their own sales.

However, many Committee members rated overall usefulness of information gathered from the manufacturers on a volunteer basis as low.

Option 6: Publicly disclose production information obtained by FDA from manufacturers

Opinion on the feasibility of public disclosure of production information was evenly dispersed from low to high. Opinion on representativeness tended to be on the higher end of the spectrum, with one member commenting “in theory this should be a census of manufacturers and therefore should have high representation among manufacturers but would have low representation of actual use.” Others argued that manufacturing data should closely mirror actual use as manufacturers have an incentive to know their markets. Almost all Committee members agreed that data quality of information obtained from CVM would be high. Opinion on overall usefulness was split, with one Committee member stating, “...overall usefulness would be high, but only when paired with end-user data.”

Conclusion

As discussed above, the ideal animal antimicrobial use data collection strategy would likely combine two or more of the methods identified by the Committee. In formulating and implementing a plan to collect animal antimicrobial use data, policy-makers will have to contend with economic, legal, political, and social constraints while remaining cognizant of the need for a data set that is sufficiently robust for use in risk assessment. The findings of the Advisory Committee on Animal Antimicrobial Use Data Collection in the United States should facilitate this process by providing policy-makers

with a set of methodological options from which to piece together a solution. To the extent that constraints and data needs are similar elsewhere, the analyses should also be useful to public health officials and policy-makers in other nations who are attempting to respond to recommendations of the World Health Organization and other groups to implement national animal antimicrobial use surveillance systems.

While the identification, categorization, and evaluation of methodological options for collecting animal antimicrobial use data in the United States were the primary objectives of this project, in retrospect it is clear that there was also inherent value in engaging stakeholders in dialog on this issue. Chosen for the diversity of interests they represented, the Committee members displayed exemplary willingness to take part in open and honest exchange. Indeed, given the underlying political and philosophical differences of opinion, the extent to which Advisory Committee members were able to work together to meet the technical challenge of defining methodological options is truly remarkable. Moreover, having participated in the policy process at this early stage, the constituencies they represent are more likely to be invested in developing and implementing a long-term solution to this complex problem.

The issues on which consensus could not be reached-- most notably the ideal combination of data collection methods-- are also instructive. Many of the differences of opinion among Committee members regarding choice of methods almost certainly stem from deeper disagreements regarding the perceived need for, and utility of, animal antimicrobial use data—differences that the Committee members agreed to set aside at the outset. The broader issue of appropriate animal antimicrobial use policy is highly controversial in the United States, with individual positions influenced by factors such as

personal beliefs, professional training, and institutional constraints. Precisely because they represent such a broad spectrum of interests, the views of the experts who comprised the Committee can help to define and articulate stakeholder views on antimicrobial use policy as they relate to the narrower question of animal antimicrobial use data collection.

In this spirit of open and ongoing dialog, therefore, Committee members were provided with an opportunity to make brief concluding statements following final review of this manuscript. The statements below were provided in response to the following question: “Assuming that there is utility to animal antimicrobial use data collection, which of the methods or combination of methods identified by the Committee would be most appropriate for implementation in the United States?” The views expressed below reflect the opinions of the individual respondents only and are not endorsed or recommended by the organizations or institutions with which they are affiliated.

Frederick J. Angulo, DVM, MPVM, PhD, Diplomate ACVPM (Epidemiology),
Chief, FoodNet and NARMS Activities, Foodborne and Diarrheal Diseases Branch,
National Center for Infectious Disease, US Centers for Disease Control and Prevention
As acknowledged by the World Health Organization and numerous other public health organizations, in the efforts to combat increasing antimicrobial resistance, surveillance of antimicrobial use in food animals is essential for directing focused interventions aimed at reducing the overuse and misuse of antimicrobial agents in food animals. An absence of drug use surveillance does not preclude interventions, but may result in unnecessarily broad actions. Many countries have established national surveillance programs to monitor use of antimicrobial agents in food animals; similar surveillance is needed in the

United States. Such surveillance would complement surveillance of antimicrobial resistance among bacteria that are commonly transmitted from food animals to humans currently included in the National Antimicrobial Resistance Monitoring System (NARMS). Surveillance of use of antimicrobial agents in food animals in the United States need not be burdensome but should include mandatory reporting of the quantities of antimicrobial agents produced and distributed; these data could be provided by modifying, and releasing for surveillance purposes, the current annual reports to FDA by the drug sponsors.

Richard Carnevale, VMD, Vice President, Regulatory, Scientific, and International Affairs, Animal Health Institute

Thomas R. Shryock, PhD, Senior Microbiology Technical Advisor, Elanco Animal Health

Sentinel farms that already electronically capture antibiotic use data offer the best near-term opportunity to implement a national, but representative, monitoring program, perhaps overseen by the USDA (e.g. NAHMS). Data on the antibiotic susceptibility of bacterial isolates from the farm, veterinary care records of disease and clinical outcome, dosing, etc., should also be entered into the electronic database so that the data can be analyzed statistically for trends, correlations, etc. The data would be useful to support prudent antibiotic use practices, risk assessments, and clinical effectiveness evaluations. Expansion of the program to include more sites and more data would possible.

David A. Dargatz, DVM, PhD, Epidemiologist, Centers for Epidemiology & Animal Health, Veterinary Service, Animal and Plant Health Inspection Service, US Department of Agriculture

While there are potentially problems with any collection of data, those collected closest to the endpoint of interest would seem to be of the greatest interest. With attention to potential impacts of sampling and reporting bias, end user studies would seem to have the highest overall value in addressing who uses antimicrobials, how they are used, when they are used, where they are used and why they are used. All are pertinent issues (though they are not the only important issues) in trying to address the ecology of antimicrobial resistance.

John R. MacMillan, PhD, Vice President Research and Environmental Affairs, Clear Springs Foods, Inc.; President, National Aquaculture Association

Assuming there is utility to animal antimicrobial use data collection, the best method of data collection in the domestic aquaculture industry appears to be collection directly from domestic drug manufacturers. There are only two drug companies that manufacture antimicrobial drugs approved (therapeutic use only) for very limited use in the domestic aquaculture industry. These two companies have readily provided annual sales information. While this information cannot be used to differentiate use amongst the aquatic animal species raised (there are over 35 different species produced in the US), the data provided enables some measure of relative risk estimation.

Scott A. McEwen, DVM, DVSc, Diplomate ACVP, Professor, Department of Population Medicine, University of Guelph

Representative, ongoing, national antimicrobial use monitoring data are essential for proper interpretation of national antimicrobial resistance surveillance and for risk assessment. At a minimum, complete national production and importation data (kg active ingredient) should be publicly available on an annual basis. This information should be supplemented with periodic surveys of end users (along the lines of current NAHMS surveys) and data from representative sentinel veterinary practices and farms to determine patterns of use with respect to species, animal type, indication and route of administration.

Richard Reid-Smith, DVM, DVSc, Epidemiologist, Antimicrobial Resistance Surveillance Unit, Laboratory for Foodborne Zoonoses, Population and Public Health Branch, Health Canada

An optimal approach to animal antimicrobial use data collection would combine manufacturer and sentinel site end-user (producers and veterinarians) data collection in an ongoing basis, reported annually. Sites should be selected by random sample although volunteers would be acceptable initially. Periodic surveys of a larger population of veterinarians and producers on estimated use and use patterns would aid interpretation of sentinel data and adjust program design. Ideally data collection would move quickly to an electronic format; be at the active ingredient level but aggregated for reporting when necessary to protect proprietary information; and protect the confidentiality of sentinel sites.

Randall S. Singer, DVM, MPVM, PhD, Assistant Professor, Department of Veterinary Pathobiology, University of Minnesota

I see two methods that would be appropriate for animal antimicrobial use data collection, depending on the goals. One method would be to require a log of all uses, similar to the controlled substances log. Such a log there would include information on use quantity, indication, amount/route, etc. This approach would probably be opposed vehemently because of the additional burden it would place on producers and veterinarians. Second would be a well-characterized group of sentinel practices/clinicians that could be followed longitudinally. This approach would have the advantage of accounting for the seasonality of disease, but the key would to this approach is the phrase “well-characterized.” The quality of supplemental data collected with the use quantity information would be the key to the utility of the dataset.

Paul Sundberg, DVM, PhD, Diplomate ACVPM, Assistant Vice President Science & Technology, National Pork Board

With the assumption that there is utility to recording animal antimicrobial use data collection, the most appropriate method for implementation in the United States at this time is a cross-sectional survey of antimicrobial users. There is precedent for this method in the USDA-APHIS National Animal Health Monitoring System.

The challenge is to recognize the strengths and limitations of the survey method. These are described in this document. With acknowledgement of these strengths and

limitations, attempts at simplistic associations or solutions to a complex issue will be avoided. Before limited resources are devoted to one method of data collection, all stakeholders should be engaged to provide input into appropriate objectives and the best methods to achieve them.

Linda Tollefson, DVM, MPH, Assistant Surgeon General, US Public Health Service; Deputy Director, Center for Veterinary Medicine, US Food and Drug Administration

Drug use data are essential to evaluate the development of antimicrobial resistance and to target mitigation strategies intended to prolong the effectiveness of antimicrobials used in food-producing animals. Data generated from monitoring antimicrobial use can be used in conjunction with surveillance of antimicrobial resistance to inform and educate all stakeholders, to develop national and international policies for the containment of antimicrobial resistance, and to evaluate the impact of the implementation of the prudent use of antimicrobials and other interventions designed to mitigate or contain antimicrobial resistance. The most useful and reliable data are those maintained by the drug sponsors. Currently, the drug companies are required under 21 CFR 514.80(b)(4)(i) to report quantities of product marketed on the anniversary date of approval of their new animal drug application (NADA or ANADA). Sponsors typically provide a quantity for each of the dosage forms marketed but the information is not differentiated by animal species, label indication(s), route of administration or geographic region. The FDA is prohibited from providing this information to the public for individual products as it is considered proprietary information. The data collection requirements would need to be modified to make the data more relevant for the purposes

described above. This would require notice and comment rulemaking to revise the current regulation.

Lyle P. Vogel, DVM, MPH, Diplomate ACVPM, Director, Scientific Activities
Division, American Veterinary Medical Association

I believe that the animal antimicrobial use data collection methodology needs to mimic the National Health Care Survey (NHCS) and National Ambulatory Medical Care Survey (NAMCS). Because NAMCS is one segment of the multi-purpose, eight surveys of the NHCS, human antimicrobial prescription data can be correlated with other reportable parameters that include patient characteristics and medical diagnoses. Collection of animal use data by periodic surveys of veterinarians and producers that includes pertinent information similar to the NHCS meets the recommendation of WHO Principle 23 – publicly available at regular intervals, compared to resistance data, and “be structured to permit epidemiological analyses” (World Health Organization 2000).

David Wallinga, MD, MPA, Antibiotic Resistance Project Director, Institute for
Agriculture and Trade Policy

We need to collect and compile antimicrobial use data to more effectively limit unnecessary use, reduce the threat from resistance and help keep antimicrobials working for sick animals and humans. The public health demands comprehensive, verifiable, publicly available data on antimicrobial use, regardless of potential limitations imposed by currently inadequate collection infrastructure, weak regulatory authority or disinterest on the part of pharmaceutical producers, retailers, policy makers,

practitioners or others. Establishing such a system is well within the capabilities and resources of the public health entities in United States government. Other countries, albeit smaller than the U.S., have done it. A good first step would be to require that all uses of antimicrobials be prescribed and to develop a system to record and compile prescriptions.

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