Defining antimicrobial stewardship is pivotal to our ability as veterinarians to continue to address the health and welfare of our patients in the coming decades. This may be due to both regulatory and antimicrobial resistance contributions.

Antibiotic use monitoring has the potential to be both a useful benchmarking tool which can promote and support antibiotic stewardship in veterinary medicine, and also the potential to be a merciless, untargeted policy hammer which sets back animal welfare a couple of decades. There are several steps which can help us achieve the first, and avoid the latter.

First, Defining Stewardship

Stewardship has a different meaning between physicians and veterinarians. The Infectious Disease Society of America has a stewardship definition which does not include infection prevention. In human medicine, infection prevention and antibiotic stewardship are considered two separate but overlapping processes. However, in veterinary medicine, it is rare that two separate people or groups address these two issues, they are addressed together. Therefore, the concept of antibiotic stewardship in veterinary medicine is all encompassing, including disease prevention and the judicious use of antibiotics when they are needed (Figure 1).

**Figure 1: Components of an Antibiotic Stewardship Program**

Within this stewardship cycle, there are aspects of antibiotic use which may be benchmarked to make the veterinarian and their clients aware of the primary disease challenges being experienced by others, and how they are being addressed. The nature of different production systems creates a situation in which the optimal antibiotic stewardship benchmarking metrics are often specific to the species, and even the production system type within species.
The American Veterinary Medical Association (AVMA) recently defined antimicrobial stewardship and core principles. Antimicrobial stewardship refers to the actions veterinarians take individually and as a profession to preserve the effectiveness and availability of antimicrobial drugs through conscientious oversight and responsible medical decision-making while safeguarding animal, public, and environmental health. Core principles as defined by the AVMA are… “Antimicrobial stewardship involves maintaining animal health and welfare by implementing a variety of preventive and management strategies to prevent common diseases; using an evidence-based approach in making decisions to use antimicrobial drugs; and then using antimicrobials judiciously, sparingly, and with continual evaluation of the outcomes of therapy, respecting the client’s available resources.” More details on the principles are provided on the AVMA website.

The American Association of Bovine Practitioners has developed a guideline on Implementing Antimicrobial Stewardship Guidelines for veterinarians. These may be accessed by searching “AABP Guidelines”.

Attributes of a useful antibiotic use monitoring system

Table 1 illustrates what we would like to have, and like not to have in an antibiotic use monitoring system. To change this from a wish list to a reality list, switch “easy” and “resource intensive”; Table 1 now becomes two lists of associated characteristics of monitoring systems and programs. You can have easy, or you can have useful, but it is very difficult to have both. This is a problem in communication regarding antimicrobial use programs. If all that is wanted is justification for policy, then nothing on the left side of Table 1 matters; the left side is only of interest to those wishing to move antibiotic stewardship forward.

<table>
<thead>
<tr>
<th>What we would like…</th>
<th>We would not like it to be…</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coupled to cause</td>
<td>Uncoupled to cause for use</td>
</tr>
<tr>
<td>Accurate</td>
<td>Approximate</td>
</tr>
<tr>
<td>Granular</td>
<td>Aggregate</td>
</tr>
<tr>
<td>Current</td>
<td>Significant lag</td>
</tr>
<tr>
<td>Easy</td>
<td>Resource intensive</td>
</tr>
<tr>
<td>Enables benchmarking</td>
<td>Policy driver only</td>
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</tbody>
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Appropriate Numerators for Beef Cattle

The implication of all discussion of numerators and denominators in this paper is that they are associated with cause for use. With that in mind, there are three basic components of numerators which allow for evaluation of use from different perspectives.

The amount of drug used is dependent on both the number of animals receiving the dose and the regimen (primarily dose, frequency, and duration here) required to achieve a clinical effect. This clinical (in-vivo) potency against target pathogens is a driver of the required treatment,
control, or prevention regimen, but so are factors such as bioavailability from any route other than intravenous administration, protein binding, metabolism to metabolites with varying degrees of activity, and elimination characteristics. These clinical realities make the comparison of relative kgs of use for different antibiotics a useless exercise, because the same factors affecting the regimen for clinical effect also affect the potential for selection of resistant organisms. The reality of resistance selection is that the outcome is dependent on both the antibiotic and the bacterial population which is exposed to the antibiotic.

Two things more useless than using kg of actual use to compare antibiotic groups are using sales data to do it, or combining all drug classes together to compare between species or countries. Neither of these approaches provides useful tools to the person at the point of the use decision.

The number of regimens are more straightforward to quantify from use records, although a regimen may result in only a day or so of actual exposure up to more than 200 days if used for an entire feeding period. The regimens are indicative of the number of animals exposed to a drug, without consideration of the nature of the regimen (dose, duration, frequency).

The days of exposure give an idea of how long the antibiotic pressure for potential resistance selection is present. The next logical question would then be “how long is too much”? Herein lies the problem; other than thinking that the shorter the better, we really don’t have concrete evidence for how the combination of magnitude and duration of exposure serves to minimize or maximize the selection for resistant bacteria. And the next challenge is how many days of exposure to assign to single injection treatments, which are common in cattle.

Appropriate Denominators for Beef Cattle

After looking for a denominator for kg of use, one is tempted to completely discard the kg numerator. But, the kg metric has become a staple of antibiotic use monitoring and is likely here to stay. One proposed denominator for kg of drug is an estimate of the mass of animals sold during the monitoring period, or the estimated mass of the population as some point during the monitoring period. The problem with the population mass is that it requires estimating some type of average mass, which may not reflect the size of the animals at the time of exposure. When looking at a policy goal of comparing species, then this is one of the few options, but don’t confuse it with something that can meaningfully drive stewardship through management decisions at the production level. Biomass as a denominator has been proposed in the United States, with comments on this approach recently being requested by the Food and Drug Administration Center for Veterinary Medicine (FDA/CVM).³

Another option for a denominator to pair with the kg numerator is the number of animals rather than mass, whether sold or determined at a consistent time point during the monitoring period. This would make the most sense for comparing antibiotic use within specific segments for a species; however, this denominator loses clarity across species because it does not take mg/kg dosing realities into consideration.

When the numerator is number of animals exposed (regimens) or duration of exposure, then a time component makes the most sense. In feedlot, the term “days on feed”, or DOF, describes
the period an animal has been in the feedlot. The DOF values can be added up and divided by 365 to derive a fairly intuitive “animal year”. The results are values for number of regimens and number of days exposure per animal year.

What sources of data are available?

Data collection sources in feedlots vary across the spectrum of production systems and sites. In some cases, there are available sources of batch-specific ration antibiotic inclusions coupled with individual animal treatment records which contain weight, drug, dose, indication, and duration. At the opposite end, some records may consist only of purchase receipts coupled with verbal protocols. In the authors experience with evaluating antibiotic use records across multiple species and segments within these species, one of the major lessons of the antibiotic use monitoring programs is that perhaps broader incorporation of a consistent antibiotic record format would also lead to advancing understanding of the disease pressures being encountered.

What do the Metrics Tell Us?

Looking at all 3 components of antibiotic use monitoring, we have…

• an estimate of total amount of different antibiotics used as expressed by kg in relation to some type of animal mass or population number,
• an estimate of the total number of animals exposed in relation to a time period (animal year), and,
• an estimate of the total duration of exposure for these animals during an animal year.

The big concept is that these components of measuring use are only truly valuable for advancing antibiotic stewardship at the treatment decision level when they are…

• associated with cause for this use,
• as determined by treatment records.

When these components are in place, the antibiotic use metrics are in reality a proxy for disease pressure on a production system. Looking again at Figure 1, that makes sense as our first obligations are case definitions, diagnostics, and then non-antibiotic alternatives for disease prevention, control, and treatment.

What are others doing?

There is a wealth of literature, both reporting antibiotic use, and providing input into the most appropriate metrics. A comprehensive review is beyond the scope of these proceedings; however, there are some key papers which highlight thoughts on collecting and applying antibiotic use data. For the purposes of beginning to explore the subject of antibiotic use metrics, the paper by Collineau, et al., is an excellent start with summaries of different metrics and their characteristics.4 There is one especially telling quote from the abstract for this paper; “… there is a clear lack of standardization, resulting in poor transparency and comparability”.

Summary
The choosing of reasonable metrics for monitoring antibiotic use in food animals starts with the end goal. When there is a commitment to providing the resources to drive antibiotic use at the level of those making the use decisions, then it is clear that use record-based systems are worth their higher resource requirements. This is especially clear when it is recognized that successful antibiotic use monitoring becomes a proxy for disease pressure due to being closely correlated with cause for the use. Other, less granular, approaches such as sales-based estimates coupled with an extrapolated animal population estimate are sufficient only for macro-monitoring of use trends. The basic question is whether the desired outcome is providing a tool for advancing stewardship at the end-user level, or rather to provide a crude instrument for policy pressure where the only goal is reduction.