PEER REVIEWED

Survey of treatment practices on Midwest dairy farms

A. M. Schuler, DVM; **C. Rice**; **P. J. Gorden**, DVM, DABVP
Veterinary Diagnostic and Production Animal Medicine, Iowa State University College of Veterinary Medicine, Ames, IA 50011
Corresponding author: Dr. Patrick Gorden, pgorden@iastate.edu

Abstract

The objective of this study was to assess current antimicrobial use practices and veterinarian involvement with these practices on upper Midwest dairy farms. Eighty-five dairy farms ranging in size from 105 to 5,400 lactating cows located in 6 states (SD, NE, IA, MN, WI, and IL) were visited by 2 veterinary students during the summer of 2015. Interns observed farm treatment practices, reviewed individual herd treatment protocols and records, and conducted a standardized survey with farm management assessing mastitis, metritis, lameness, pneumonia, heifer pneumonia, and heifer diarrhea. Results indicate the presence of written treatment protocols varied by disease type. Metritis was the most common disease for which a protocol was found on-farm (49%), followed by mastitis (46%), lameness (39%), adult cow pneumonia (34%), heifer pneumonia (21%), and heifer diarrhea (19%). Ceftiofur was the most common primary antimicrobial selected for the treatment of mastitis (61%), metritis (82%), lameness (54%), and pneumonia (72%). Thirty-nine percent of farms selected enrofloxacin as their primary antimicrobial for the treatment of calf diarrhea. This use of enrofloxacin was also the most common unapproved treatment observed in the study. Results of this study demonstrate an opportunity for veterinarians to educate producers about judicious antimicrobial use on dairy farms.

Key words: dairy, antimicrobials, stewardship, protocols

Résumé

L'objectif de cette étude était d'évaluer les pratiques courantes d'utilisation des antimicrobiens et l'implication des vétérinaires dans ces pratiques dans des fermes laitières du Haut-Midwest Américain. Durant l'été 2015, deux étudiants vétérinaires ont visité 85 fermes laitières comptant entre 105 et 5400 vaches en lactation dans 6 états (Dakota du Sud, Nebraska, Iowa, Minnesota, Wisconsin et Illinois). Les stagiaires ont observé les pratiques de traitement à la ferme et examiné les protocoles de traitement au niveau du troupeau de même que les dossiers. Ils ont aussi mené un sondage standardisé auprès des gestionnaires de la ferme pour évaluer la mammite, la métrite, la boiterie, la pneumonie, la diarrhée et la pneumonie chez les génisses. Dans cette étude, l'existence de documents écrits portant sur les protocoles de traitement variait selon le type de maladie. La métrite était la maladie la plus commune pour laquelle on retrouvait un protocole à la ferme (49%), suivie de la mammite (46%), de la boiterie (39%), de la pneumonie chez les vaches adultes (34%), de la pneumonie chez les génisses (21%) et de la diarrhée chez les génisses (19%). Le ceftiofur était l'agent microbien le plus utilisé pour le traitement de la mammite (61%), de la métrite (82%), de la boiterie (54%) et de la pneumonie (72%). Pour 39% des fermes, l'enrofloxacine était l'agent microbien le plus utilisé pour le traitement de la diarrhée chez les veaux. L'emploi de l'enrofloxacine dans ce contexte représentait aussi l'utilisation non-approuvée d'un traitement la plus fréquente dans cette étude. Ces résultats suggèrent que les vétérinaires ont la chance de sensibiliser les producteurs sur l'utilisation judicieuse des antimicrobiens dans les fermes laitières.

Introduction

Antimicrobial drugs are commonplace on modern dairy farms and are used in both a therapeutic and prophylactic manner.[18] Currently, antimicrobials are used across all classes of dairy animals. The majority of antimicrobial use is represented by 5 different broad categories of disease that include intramammary infections, respiratory disease, uterine infections, digestive problems, and infectious foot diseases. From 2012 to 2014, organic dairy farms represented less than 6% of the total dairy production in the United States.[18] This statistic demonstrates that the majority of farms in the US have the ability to utilize antimicrobials and other drugs in their operation. Guidelines from organizations such as the American Association of Bovine Practitioners and the American Veterinary Medical Association, in conjunction with regulations from the federal government, exist to help producers and veterinarians judiciously utilize antimicrobials when the decision to treat an animal has been made.

Over the last several years, the use of the phrases "judicious antimicrobial use" and "antimicrobial stewardship" has become commonplace in the veterinary and lay literature. Heightened consumer awareness surrounding antimicrobial use in agricultural settings, as well as scrutiny from the public health and human medicine communities,[9] has identified the need to better understand how antimicrobials are being

utilized on farms within the US. Similarly, many restaurant chains and grocery purveyors have implemented position statements limiting or eliminating the use of antimicrobials in production systems that supply meat and dairy products to their operations. On May 22, 2015, Walmart US and Sam's Club US announced new position statements on responsible use of antimicrobials in farm animals. In their announcement, they stated that they would be asking suppliers to:

- Adopt and implement the Judicious Use Principles of Antimicrobial Use from the American Veterinary Medical Association,[1] including accurate record keeping, veterinary oversight, and limiting antimicrobial treatment to animals that are ill or at risk.
- Adopt and implement Voluntary Guidance for Industry #209 from the FDA[21] in their own operations and their industry producer programs, including eliminating growth promotion uses of medically important antibacterials.
- Promote transparency by providing a report on antibiotic management to Walmart and publicly report antibiotic use on an annual basis.

While this is just 1 example of changes that farmers will be asked to undertake in their production systems, it clearly provides a benchmark for the industry to work toward. Currently, there are very little data available regarding the status of judicious antimicrobial practices on US farms, including dairy farms. In addition, there are few accurate data available on the amount of antimicrobials used by the dairy industry, and how these are used for the treatment of disease. The objective of this study was to assess the level of antimicrobial use on dairy farms, the degree in which treatments were under the guidance of a veterinarian's protocols, as well as the farm's subsequent compliance with processing regulations following antimicrobial use on upper Midwest dairy farms.

Materials and Methods

Fourteen veterinarians or veterinary practices from IA (n=5), MN (n=3), WI (n=3), SD (n=1), IL (n=1), and NE (n=1) were asked to identify dairy farms within their practice area that would allow Iowa State University (ISU) summer interns to visit their dairy operation and evaluate treatment practices, treatment protocols, and treatment records. From May 18 through August 07, 2015, 2 veterinary student interns visited 85 dairy cattle operations, all of which had lactating cows with the exception of 2 calf ranches which custom raised dairy replacement heifers. The farms were located in IA (n=30), MN (n=24), WI (n=19), SD (n=6), IL (n=5), and NE (n=1). In total, the farms had 87,262 lactating cows (avg. herd size=1051 [range 105 to 5,400]), most with replacement heifers on site. The study region was divided into 2 segments and each intern was assigned to a region. Region 1 was composed of western IA, southwest MN, SD, and NE. Region 2 was composed of eastern IA, southeast MN, WI, and IL.

A standardized investigation form was used to evaluate each farm and to assist in consistent data collection. The investigation form included specific, pointed questions related to disease diagnosis, treatment (including antimicrobial used, dose, route, duration, and frequency of administration), recording, and case management. Additionally, any examples of treatment protocols and treatment records on the farm were collected. Each farm was asked for a backup copy of their dairy management computer software program. In order to minimize ambiguity related to disease diagnosis and definition between farms, we concentrated only on common diseases, which are easy to diagnose at the farm level (mastitis, metritis, pneumonia, lameness, heifer pneumonia, and heifer diarrhea). Farm employees were asked to describe what a positive diagnosis for each disease looked like to further help standardize the disease classification across farms.

The farm was notified by the veterinarian at least 48 hours prior to the date of the scheduled evaluation. On the date of the visit, all treatment practices were observed. If multiple sections of a farm were receiving treatment at the same time (e.g., treating the fresh pen and mastitis pen at the same time), the intern went to the location where the majority of the diseases assessed in the study were likely to be treated. If treatment of a specific disease was not observed, appropriate farm staff were questioned about the procedure when a case did occur.

Results and Discussion

One of the objectives of this study was to determine the level of involvement of the veterinarian in treatment practices on the dairy. As these farm visits were arranged through the farm's veterinarian, we assumed that a valid veterinarian-client-patient relationship (VCPR) was in place, and all farms affirmed that they had a valid VCPR. Protocols are an important part of veterinary guidance for drug use on farms; however, when we asked to review those protocols, most farms did not have a written protocol from the veterinarian that was current (<1 year-old). Protocols for treatment of metritis was the most common (49% of farms), while calf diarrhea and pneumonia protocols were the least common available on farms at 26% and 27%, respectively.

This survey utilized local veterinarians to identify farms to include in the study, which may have biased the reality of drug use on dairy farms. As a result, veterinarians were involved with all of the farms at some level. Our observations suggest that many of the treatment practices were influenced by the local veterinarian, as some treatment practices that were questionable tended to be within 1 practice or geographic area. This suggests to us that antimicrobial stewardship programs on dairy farms are going to be highly influenced by treatment practices of the veterinarians of record for the farm. However, there were some treatment practices for which the veterinary practice was not providing guidance or were unaware that a certain practice was occur-

ring on the farm. The 2 treatments for which the veterinarian appeared to have the least amount of input was intrauterine (**IU**) therapy for metritis and treatment of digital dermatitis (**DD**).

Mastitis

At the farm level, mastitis is the infectious disease that affects the highest percentage of dairy cows. According to the National Animal Health Monitoring System (**NAHMS**) 2007 Dairy survey, 18.2% of dairy cows were affected by mastitis, with 16.4% of the total cow population receiving antimicrobial therapy because of this disease. Cows treated for mastitis were present on 85.4% of dairy operations nationwide.[19] Mastitis has previously been reported as the most common disease event that occurs in the lactating dairy herd for which antimicrobial agents are commonly used.[16] In addition to utilizing antimicrobials for the treatment of mastitis, the report also found that 90.1% of operations utilized antimicrobials in a prophylactic manner to prevent infection during the dry period. The majority (72.3%) of farms reported that 100% of lactating cows received antimicrobials at dry-off. Consequently, the highest total percentage of dairy cows treated with an antimicrobial can be attributed to mastitis or mastitis prevention.[12,19,16] In the US, a limited number of antimicrobial classes are available for intramammary (**IMM**) and dry-cow therapy (**DCT**). These include β-lactams (cloxacillin, cephapirin, procaine penicillin G, ceftiofur, and amoxicillin), courmarines (novobiocin), lincosamides (pirlimycin), and macrolides (erythromycin).

Based on data collection from farms and conversations with dairymen, mastitis is the most robust disease event we assessed. Farm protocols were evaluated to determine the most commonly used IMM tube as the farm's primary treatment. Forty-six percent of farms were able to produce a mastitis treatment protocol on the day of the visit. If a farm had treatment protocols or programs that differed by severity score, we assumed that the mildest treatment was the most commonly applied treatment. The most common IMM treatment administered on farm was ceftiofur[a] (60%), followed by cephapirin[b] (25%), and pirlimycin[c] (5%), respectively (Figure 1). Findings of this study were similar to those reported by Oliveira and Ruegg, where 71.6% of animals were treated with IMM ceftiofur.[11] Two farms reported using the non-lactating formulation of ceftiofur[d] for treatment of lactating cow mastitis. This treatment represents a prohibited, extra-label use of cephalosporin antimicrobials according to the current Animal Medicinal Drug Use Clarification Act (AMDUCA) guidelines.[23]

Twenty-nine farms (35%) reported culturing at least some of their clinical cases prior to therapy. Of those 29 farms, 38% cultured all clinical cases and 17% utilized culture to dictate IMM therapy. Three farms were not treating culture-confirmed, gram-negative cases with IMM antibiotics. Culture-based treatment protocols provide dairy farms opportunities to demonstrate judicious antimicrobial use and

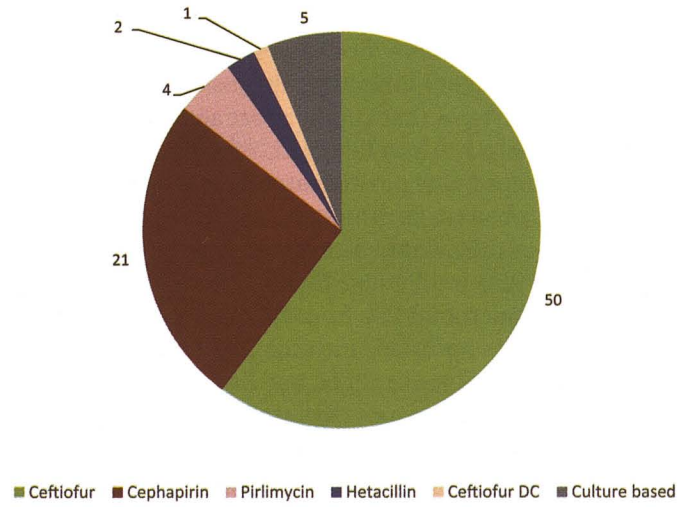

Figure 1. Primary intramammary product used for lactating mastitis treatment on 83 farms. Numbers next to each section of the graph represent the number of farms that reported usage.

may result in decreased antimicrobial use related to mastitis cases.[8] Previous research has demonstrated that milk production was not affected when comparing antimicrobial treatment vs non-antimicrobial treatment in mild clinical cases of mastitis in which no bacteria or coliforms were isolated.[8,14]

The use of systemic antimicrobials for treatment of mastitis is shown in Figure 2. Ampicillin was the most commonly used antimicrobial for systemic treatment (31% of farms). Olivera and Ruegg reported that 48% of severe clinical mastitis cases received systemic therapy and IMM therapy concurrently.[11] Although we did not evaluate the total number of individual treatments in the present study, most farms indi-

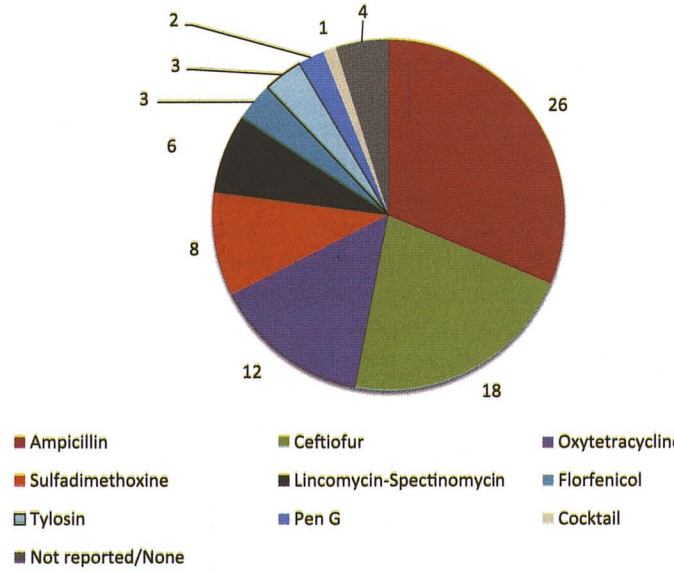

Figure 2. Primary systemic antimicrobial product used for lactating mastitis treatment on 83 farms. Numbers next to each section of the graph represent the number of farms that reported usage.

cated that they used a systemic antimicrobial in combination with IMM therapy for treatment of mastitis cases considered to be more severe. Other notable systemic antimicrobials used included ceftiofur (22%), oxytetracycline (**OTC**) (14%), sulfadimethoxine (10%), lincomycin-spectinomycin[e] (7%), florfenicol[f] (4%), tylosin[g] (2%), procaine penicillin G (2%), and "cocktail" (1%). Four farms (5%) reported not using systemic treatments for mastitis therapy or did not report any usage.

The selection of antimicrobials for treatment of mastitis was vast, although these choices may prove to have limited benefit for their intended use. Dairymen polled in this survey felt that the use of parenteral therapy would provide stronger, more effective treatment against the intramammary infection. However, in considering the pharmacokinetics of the choices utilized in this survey, many of these antimicrobials have poor penetration into the mammary gland and would not achieve effective drug concentrations.[25]

The use of sulfadimethoxine (n=8) was the most common prohibited systemic mastitis treatment found in the study. According to 21 CFR 530, extra-label use of sulfonamide antimicrobials is prohibited in lactating dairy cattle.[22] Sulfonamides were also reported by Oliveira and Ruegg to be the most common prohibited systemic treatment for mastitis.[11] Six farms in the current study reported utilizing lincomycin-spectinomycin, and 1 farm reported using a "cocktail" of antimicrobials for systemic mastitis therapy. Lincomycin-spectinomycin is not approved for use in lactating dairy cattle. The powder form was commonly found on-farm, and was reconstituted by farm staff. Because of the substantial variability in mixing practices as well as the fact that a well-established withdrawal time does not exist, nor is there an established allowable residue limit, lincomycin-spectinomycin should be considered an extremely high-risk antimicrobial (in relation to a violative residue) when used on-farm. On the date of the visit, the contents of the cocktail were unclear. In the case of the farm utilizing the aforementioned "cocktail," the veterinarian of record had not been consulted regarding appropriate antimicrobial compounding, withdrawal times, or approved therapies prior to its administration. Fifty-one farms (61% of the 83 that reported mastitis therapy usage) reported using flunixin meglumine for treatment of mastitis, and 23 farms (28%) reported using a steroid, either dexamethasone or isoflupredone acetate.

All farms were asked to describe their dry-cow therapy program. Ceftiofur hydrochloride[d] and cephapirin benzathine[h] were the most common dry-cow IMM therapies utilized (41% each; Figure 3). Of the 79 farms that described their dry-cow program, 37 (47%) reported using an internal teat sealant in addition to IMM dry-cow treatment.

Metritis

The use of antimicrobials for the treatment of metritis is commonplace on most dairy farms in the US. In the USDA survey, reproductive diseases affected 12.5% of lactating

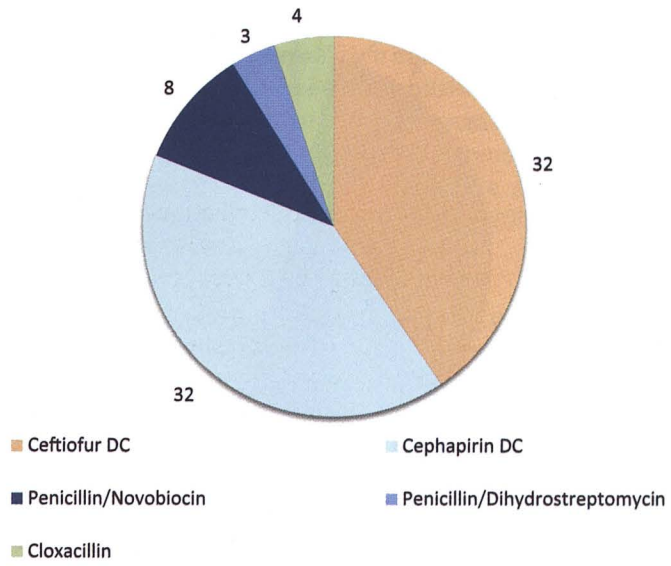

Figure 3. Primary intramammary dry-cow therapy used on 79 farms. Numbers next to each section of the graph represent the number of farms that reported usage.

cows, with antimicrobial use to treat reproductive disorders in the study representing 7.4% of all cows. Classes of antimicrobials utilized for the treatment of non-mastitis diseases reported in the NAHMS survey were aminocyclitols, aminoglycosides, β-lactams, florfenicol, macrolides, sulfonamides, and tetracyclines.[19]

In the current study, antimicrobials were either administered systemically, intrauterine, or via both routes. Forty-nine percent (20/41) of farms had metritis treatment protocols available on the day of the visit, and of all the conditions assessed in this study, metritis was the condition most likely to have a written protocol on-farm. Farms were asked to tell us what their primary systemic antimicrobial (first-line therapy) was (Figure 4), as well as the secondary antimicrobial used to treat metritis (Figure 5). The use of a secondary antimicrobial could be based on severity of the infection or on a perceived lack of response to the primary treatment. A ceftiofur-based product was the most commonly used antimicrobial for the treatment of metritis (88%). The use of ceftiofur sodium[i,j] for treatment of metritis is extra-label, and is considered a prohibited use[23] as 2 other ceftiofur products with label claims for the treatment of metritis currently exist. Two farms reported using an ampicillin product compounded from a different formulation of ampicillin not approved for use in cattle. It was not, however, compounded from bulk product. Additionally, 1 farm reported using sulfadimethoxine for the treatment of metritis. The use of this product is prohibited for treatment of metritis under the AMDUCA guidelines.[22]

When asked about IU therapy for metritis, 58% of farms reported that they treated at least some cases of metritis with various products administered by this route. In total, 14 respondents reported different compounds were utilized

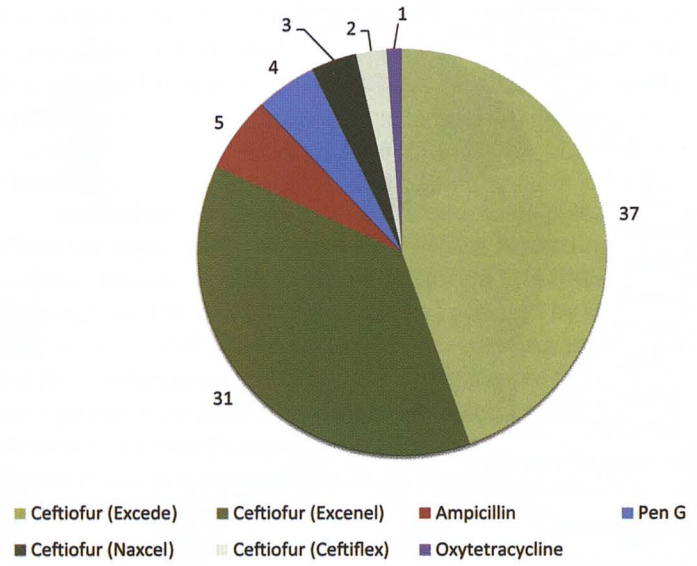

Figure 4. Primary systemic antimicrobial used for treatment of metritis on 83 farms. Numbers next to each section of the graph represent the number of farms that reported usage.

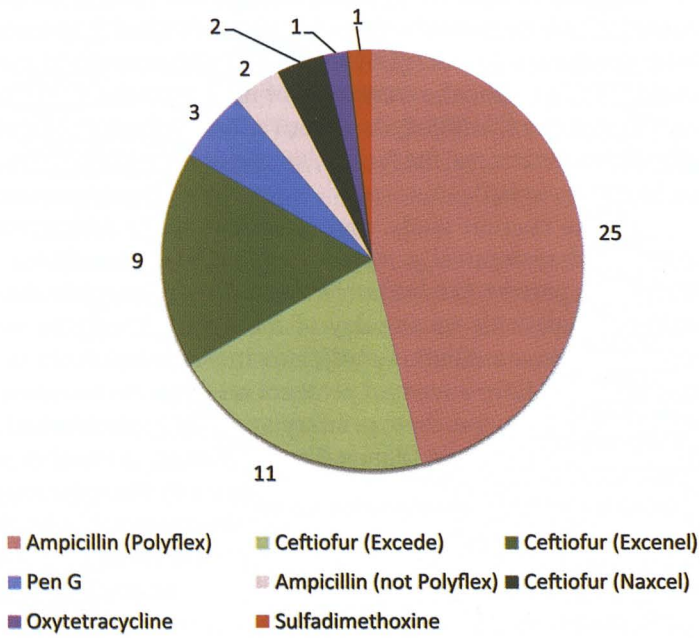

Figure 5. Secondary systemic antimicrobial used for treatment of metritis on 83 farms. Numbers next to each section of the graph represent the number of farms that reported usage.

for IU treatment of metritis. Therapeutic products utilized ranged from commonplace (OTC; 66%) to rare (Q-cleanse; n=1), and many products were used without veterinary oversight. Farms using OTC were using either the water soluble hydrochloride formulation, or the 100 or 200 mg injectable formulations. Determining the exact dosage was often difficult because the unit of measure was sometimes an obscure term, such as "1/3 of a capful". However, the dose was determined to range from 2 grams to 15 grams. In the latter, instructions were to place 150 mL of oxytetracycline (100 mg/mL) in 1 liter of water, with the entire volume to be infused. Figure 6 shows the number of farms using each of 6 different products for IU therapy. Additionally, 8 other products were reportedly utilized to treat metritis using the IU route of administration.

Intrauterine therapy for metritis has been a subject of several clinical research studies in recent years.[3,7,10] Results from those studies yielded mixed results, dependent on the specific outcome that was assessed in regards to the effectiveness of a given treatment. Although many studies have evaluated the use of various antimicrobials for treating metritis, with the exception of OTC few have assessed the necessary withdrawal time following IU administration.[2,5,6] It is the experience of 1 of the authors (PJG) that many producers use OTC for IU therapy because of the perception that it does not get into milk when using this route of administration. Work by our research group demonstrated that OTC is absorbed from the lumen of the uterus, and is present in the plasma and milk within a matter of minutes. Additionally, cows treated with a high initial metritis severity score had a higher maximum concentration and area under the concentration curve compared to cows with lower severity scores.[6] This is an area of opportunity for veterinarians to work with producers to educate them about the risks and/or benefits associated with using IU therapy when treating metritis, especially in light of new milk testing protocols for the tetracycline family of drugs that have been adopted within the Pasteurized Milk Ordinance.[24]

Pneumonia in Lactating Cattle

According to the NAHMS Dairy 2007 report, respiratory disease was the most common infection in dairy cattle requir-

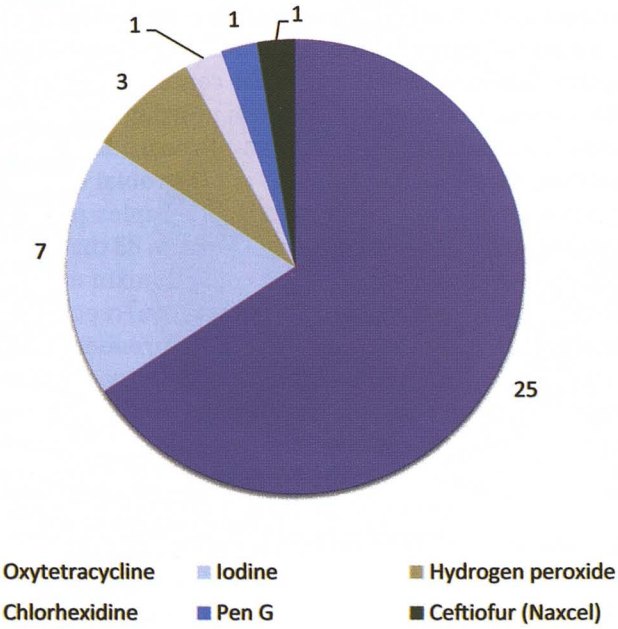

Figure 6. Products used for intrauterine metritis therapy for 38 of the 48 farms that reported using intrauterine therapy. Numbers next to each section of the graph represent the number of farms that reported usage.

ing antimicrobial therapy (96.4%); however, only 2.9% of all dairy cows were identified as having respiratory disease.[18]

In the current survey, 11 different products were used for primary treatment of pneumonia in adult cattle. Of these, 62 farms (74%) utilized 1 of the ceftiofur products as their primary choice (Figure 7). Similarly, Pol and Ruegg also found that the ceftiofur class of antibiotics was most commonly used for treatment of respiratory disease in adult cows.[12] Figure 8 shows the farms' secondary choices for treatment of adult-cow pneumonia, with ampicillin being the most common choice (41%). Treatment protocols were less common for pneumonia (39% of farms) than for mastitis and metritis therapies.

Florfenicol was listed by 1 farm as their primary or first-line therapy for treatment of pneumonia, and 4 farms listed it as their secondary choice. Florfenicol is only approved for use in dairy cattle under 20 months of age. Florfenicol has no established tolerance level in milk or edible tissues from cull dairy cattle, and therefore no withdrawal times have been established for florfenicol following use in lactating dairy cattle. In addition, 2 farms reported that tulathromycin was the secondary choice when treating pneumonia in adult cattle. According to their treatment protocols, tulathromycin was to be used only in dry cows with pneumonia. One of these farms indicated they only used tulathromycin for severe cases of adult-cow pneumonia. When tulathromycin was used on this farm, milk from treated cows was never placed in the saleable milk supply, and the cow was culled from the herd when the labeled slaughter withdrawal had expired. Treatment protocols for the second farm did not indicate any withholding time for milk following tulathromycin therapy or stipulate testing for milk residues once the cow calved. Like florfenicol, tulathromycin has no established tolerance level in milk or edible tissues from dairy cattle, and therefore no withdrawal time has been established for dairy cattle. Administering florfenicol or tulathromycin to lactating dairy cattle should be accompanied by an extended withdrawal period for meat and milk, where applicable, as there is zero tolerance for these products in tissue and milk.

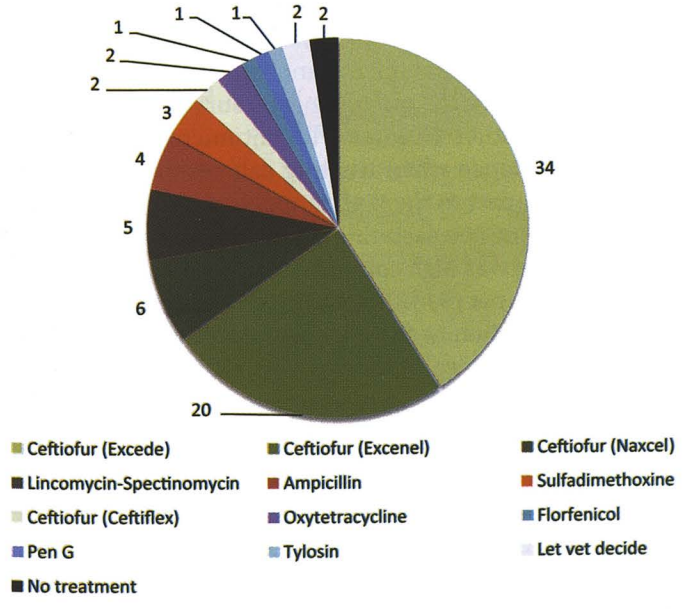

Figure 7. Primary antimicrobial used for treatment of pneumonia in adult cattle on 84 farms. Numbers next to each section of the graph represent the number of farms that reported usage.

Lameness

Lameness affected 10.0% of lactating cows in the USDA survey. Antimicrobial use to treat lameness in the study represented 7.1% of all cows.[19] Figures 9 and 10 show the primary and secondary antimicrobials used for the treatment of infectious lameness other than digital dermatitis (**DD**) in the current study. Ceftiofur containing products were by far the most commonly used products on participating dairy farms (90%). As mentioned previously, using ceftiofur at an extra-label dose, route, duration, and/or frequency is not allowed under FDA regulations. One farm reported interdigital administration of ceftiofur in severe cases of foot rot, which represents a prohibited, extra-label use of the product.[23]

It is important to note that the selection of antimicrobials used to treat lameness was done with little owner involvement. Over 30 farms did not provide answers related to antibiotic use to treat lameness, instead indicating that these decisions were made by a hoof trimmer or veterinarian. Although many farms did not provide answers about how they treated lameness, 34% were able to retrieve a lame-cow treatment protocol, which was comparable to the number of farms that had pneumonia and mastitis treatment protocols available on the farm.

Topical treatment of DD was the most common method utilized by the dairymen to treat this disease (98%; Figure

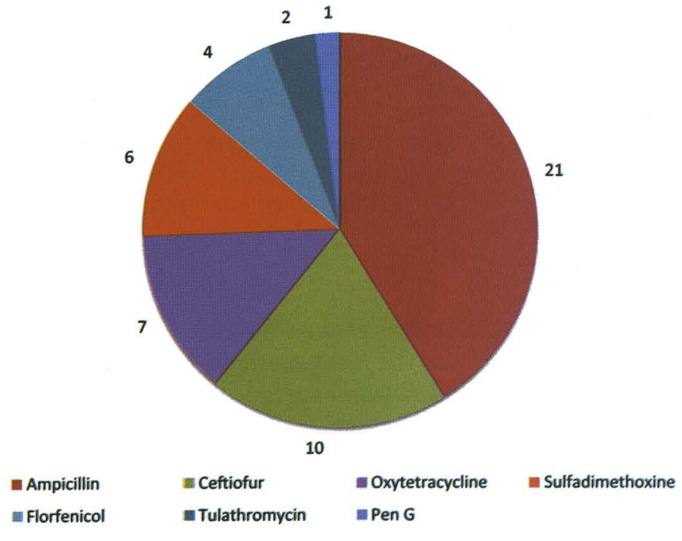

Figure 8. Secondary antimicrobial used for treatment of pneumonia in adult cattle on 51 farms that reported a secondary choice. Numbers next to each section of the graph represent the number of farms that reported usage.

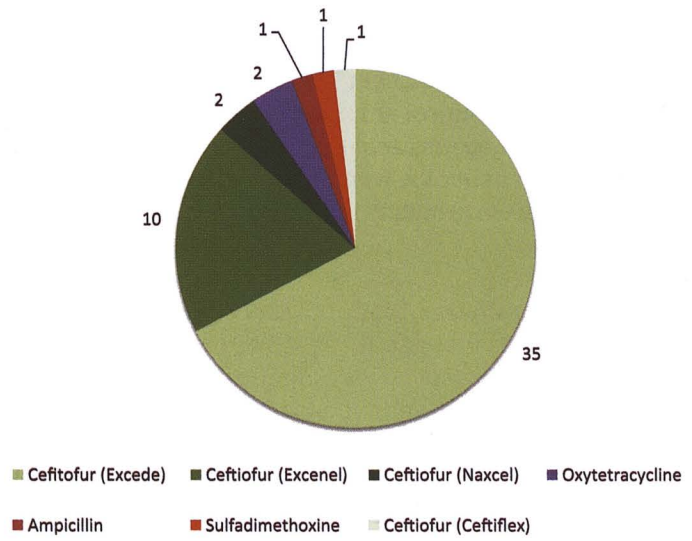

Figure 9. Primary antimicrobial choice for treatment of infectious lameness other than digital dermatitis on 51 farms that reported usage. Numbers next to each section of the graph represent the number of farms that reported usage.

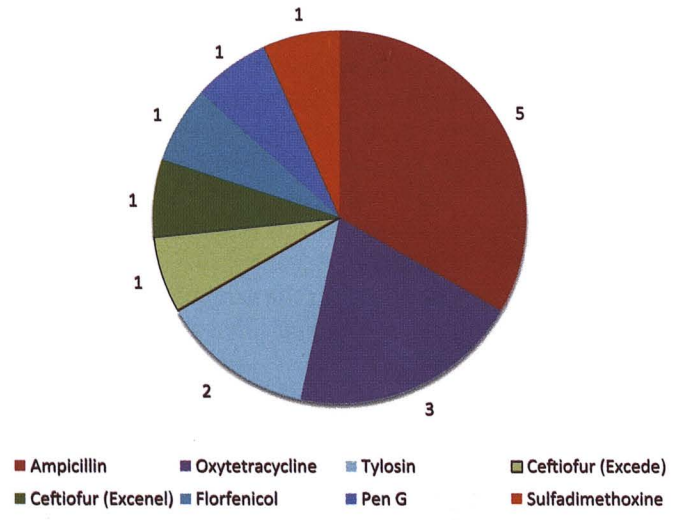

Figure 10. Secondary antimicrobial choice for treatment of infectious lameness other than digital dermatitis for 15 farms that reported usage. Numbers next to each section of the graph represent the number of farms that reported usage.

11). Oxytetracycline (either water-soluble powders or injectable formulations) was the most commonly used therapy to treat DD topically, followed by various mixtures of copper sulfate or lincomycin powder. One farm treated DD with parenteral ampicillin, and another used parenteral sulfadimethoxine for the treatment of DD, a prohibited, extra-label use of the product.[22]

Calf Pneumonia

Figures 12 and 13 show the primary and secondary antimicrobials used to treat respiratory disease in calves.

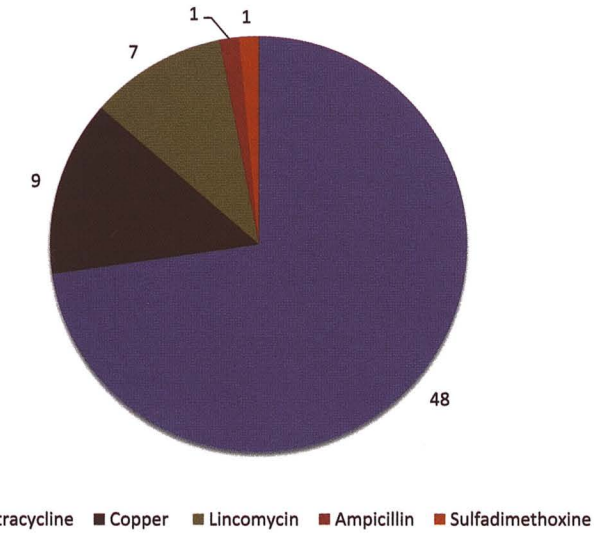

Figure 11. Products utilized for treatment of digital dermatitis for 66 farms that reported usage. Numbers next to each section of the graph represent the number of farms that reported usage.

Tulathromycin[k] (34%) and enrofloxacin[l,m] (29%) were the most common primary antimicrobials used to treat respiratory disease in replacement heifers. Florfenicol (21%) and enrofloxacin (17%) were the most common secondary antimicrobials used to treat respiratory cases, i.e., those that relapsed. All of the primary antimicrobial treatments shown in Figure 12 represent approved uses (if the drug was administered according to label directions). Results of this survey are in contrast to reports by Sawant et al and Zwald et al who reported that 48% of respondents utilized ceftiofur for treatment of calf pneumonia,[17] and 80% of conventional dairy farms had ceftiofur available to treat the disease.[26] In the current study, only 8% and 5% of dairy farms utilized ceftiofur for their primary and secondary calf pneumonia treatments, respectively. There was higher compliance with label instructions when treating calf pneumonia on surveyed dairies than when treating other diseases with antimicrobials. The high level of compliance when treating calf respiratory disease may be due in-part to the high number of antimicrobials labeled for treating non-lactating dairy animals for pneumonia. Although there was high compliance with label instructions, only 21% of farms (9/42) had written treatment protocols in place. In addition to the absence of treatment protocols, record keeping for calf diseases was difficult to assess for herds that were visited. In many cases, records of calf treatments appeared to be highly dependent on the individual administering the treatments. While the majority of farms had a record book in the calf treatment area to record treatments, the records did not appear to be current at the time of the farm visit. Regardless of whether or not an animal is lactating, record keeping requirements for antimicrobial treatments are the same as those for lactating cows.[24]

In addition to legal requirements, there are other practical reasons for keeping good treatment records. Rossini noted

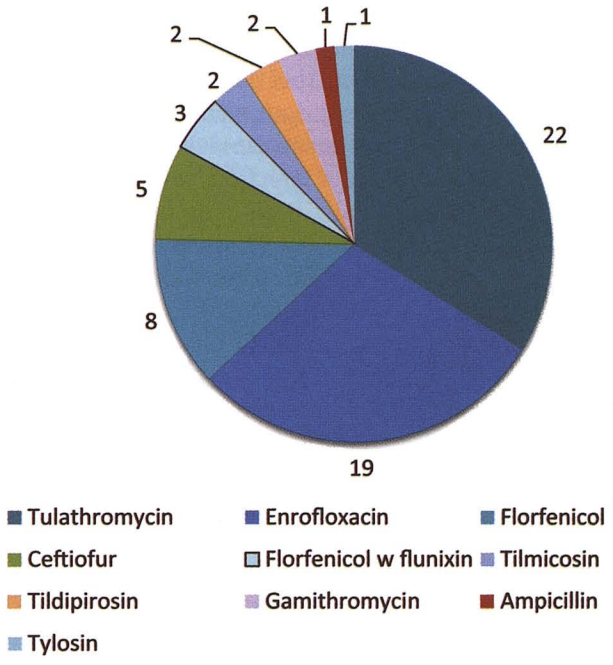

Figure 12. Primary antimicrobial for treatment of respiratory disease in replacement heifers for 66 farms that reported usage. Numbers next to each section of the graph represent the number of farms that reported usage.

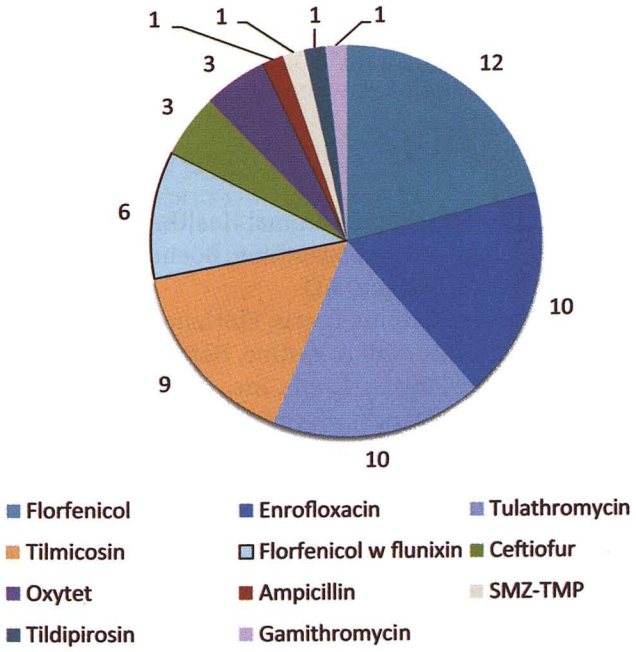

Figure 13. Secondary antimicrobial for treatment of respiratory disease in replacement heifers for 57 farms that reported usage. Numbers next to each section of the graph represent the number of farms that reported usage.

that calves with respiratory disease were older at first calving and were more likely to leave the herd than their adult herdmates.[15] By recording calf disease events and treatments to meet regulatory requirements, records are available to make management decisions impacting their operation.

Calf Diarrhea

Fifty-four farms provided information about antimicrobial use relating to treatment of diarrhea in heifers. Figures 14 and 15 show the primary and secondary antimicrobial selections for the treatment of diarrhea in calves. As shown in the graphs, a variety of different antimicrobials (n=11) were utilized for the treatment of diarrhea in calves, with enrofloxacin being the most commonly used. Forty percent of farms reported enrofloxacin was their primary treatment for calf diarrhea. Enrofloxacin was also the most common

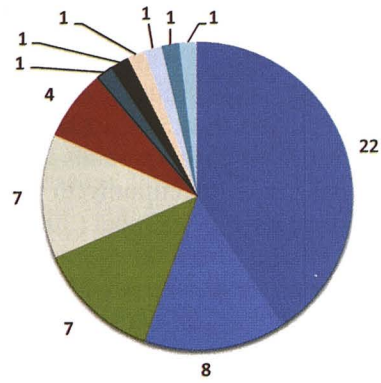

Figure 14. Primary antimicrobial for treatment of diarrhea in calves for 54 farms that reported usage. Numbers next to each section of the graph represent the number of farms that reported usage.

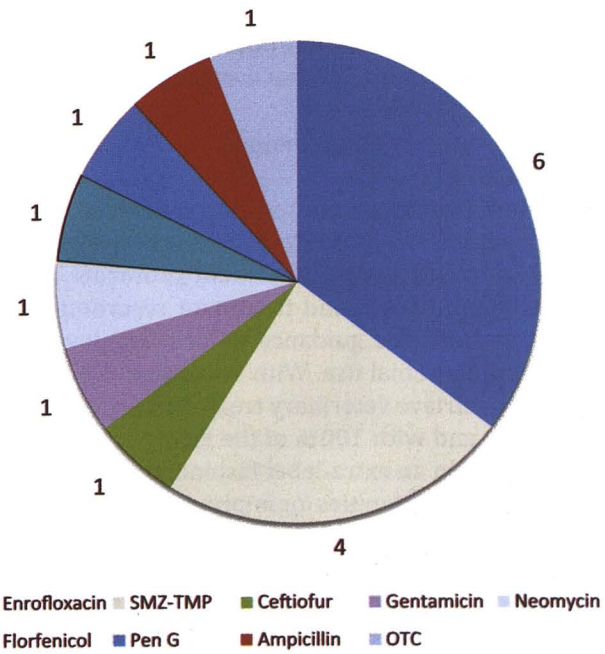

Figure 15. Secondary antimicrobial for treatment of diarrhea in calves for 17 farms that reported usage. Numbers next to each section of the graph represent the number of farms that reported usage.

secondary or follow-up antimicrobial treatment for calf diarrhea. Of the 6 farms using enrofloxacin as a secondary treatment option, none were using enrofloxacin as their primary treatment for calf diarrhea. Interestingly, procaine penicillin G was the second most commonly used primary diarrhea therapy. Of the 11 antimicrobials used for the treatment of calf diarrhea on the study farms, only OTC and neomycin are labelled for treatment of *E. coli* diarrhea in calves. Twenty-six percent of farms in this study had written protocols for the treatment of calf diarrhea.

The use of enrofloxacin for the treatment of calfhood diarrhea represents a prohibited, extra-label use of a fluoroquinolone.[4] In several instances, producers acknowledged that the use of enrofloxacin was prohibited for this use, but still chose to use it as first-line therapy for calf diarrhea. Sawant et al reported that 36% of the calf population in Pennsylvania received antimicrobials for the treatment of enteritis. In that study, spectinomycin was the most common antimicrobial used extra-label (30% of farms) to treat calf enteritis.[17] Findings from the current study indicate that spectinomycin is no longer the most common antimicrobial used extra-label to treat calf diarrhea, likely because spectinomycin is not as readily available in more recent years. As a proportion of the total farms reporting usage, more farms are utilizing enrofloxacin in an extra-label manner today than were utilizing spectinomycin in an extra-label manner in the 2007 study.[17] The findings of this study and conversations with farm personnel suggest a wide-spread perception that enrofloxacin is extremely effective for treatment of neonatal calf diarrhea, and is therefore acceptable to use even though it is a prohibited, extra-label use. The AVMA has issued judicious antimicrobial use guidelines that encourages dairy practitioners to educate producers through protocol development and direct teaching about why fluoroquinolone use or any other illegal, extra-label therapy is not acceptable.[1]

Conclusions

As new processor testing requirements and stewardship programs are put into place, veterinarians will be asked to write and update treatment protocols on farms, help implement disease and treatment recording systems for herds, and provide guidance to farm employees about judicious antimicrobial use. With fewer than 50% of farms being able to retrieve veterinary treatment protocols for the investigators, and with 100% of the farms utilizing at least 1 antimicrobial in an extra-label fashion, the dairy industry has significant opportunities for improving antimicrobial use.

It is highly unlikely that there will be a large number of new antimicrobials introduced for use in food-producing animals, and just as unlikely that there will be an increase in the number of labeled indications for currently available antimicrobials. Therefore, the veterinary community must be diligent to ensure antimicrobial use policies stipulated by regulatory agencies are followed. If this does not occur, there will be increased calls outside the veterinary community for the exclusion of all extra-label therapy in food producing animals. If this occurs, tremendous welfare issues within the dairy industry could result due to the lack of effective labeled products for the wide array of infectious processes that dairy veterinarians face on a daily basis. The herd veterinarian offers a tremendous resource and knowledge base for dairy herds regarding disease identification, judicious antimicrobial use, and record keeping on-farm.

Veterinarians utilizing sound pharmacological data and having a solid understanding of legal requirements associated with antimicrobial use can be leveraged by farms as a resource to implement on-farm systems that enhance consumer confidence, assure a food supply that is free of violative residues, provide risk management to the producer, and most importantly, improve the health of the cow.

Endnotes

[a]Spectramast LC®, ceftiofur hydrochloride, Zoetis, Florham Park, NJ
[b]Today®, cephapirin sodium, Boehringer Ingelheim Vetmedica, Inc., St. Joseph, MO
[c]Pirsue®, pirlimycin hydrochloride, Zoetis, Florham Park, NJ
[d]Spectramast DC®, ceftiofur hydrochloride, Zoetis, Florham Park, NJ
[e]L-S 50 Water Soluble® powder, linocmycin-spectinomycin, Zoetis, Florham Park, NJ
[f]Nuflor®, florfenicol, Merck Animal Health U.S. Headquarters, Madison, NJ
[g]Tylan® 200, tylosin, Elanco Animal Health, Greenfield, IN
[h]Tomorrow®, cephapirin benzathine, Boehringer Ingelheim Vetmedica, Inc., St. Joseph, MO
[i]Naxcel®, ceftiofur sodium, Zoetis, Florham Park, NJ
[j]Ceftiflex®, ceftiofur sodium, VetOne, Boise, ID
[k]Draxxin®, tulathromycin, Zoetis, Inc., Parsippany, NJ
[l]Baytril®100, enrofloxacin, Bayer Animal Health, Shawnee Mission, KS
[m]Enroflox® 100, enrofloxacin, Norbrook® Inc., Overland Park, KS

Acknowledgements

The authors would like to thank Zoetis, Inc. for sponsoring the internships that led to the completion of this survey.

References

1. American Veterinary Medical Association (AVMA). Judicious use of antimicrobials for dairy cattle veterinarians. 2016.
2. Anderson KL, Moats WA, Rushing JE, Wesen DP, Papich MG. Potential for oxytetracycline administration by three routes to cause milk residues in lactating cows, as detected by radioimmunoassay (Charm II) and high-performance liquid chromatography test methods. *Am J Vet Res* 1995; 56:70-77.

3. Armengol R, Fraile L. Comparison of two treatment strategies of cows with metritis in high-risk lactating dairy cows. *Therio* 2015; 83:1344-1351.
4. Code of Federal Regulations. 21 CFR 530.5. Food and Drug Administraition. April 1, 2015.
5. Dinsmore RP, Stevens RD, Cattell MB, Salmon MD, Sundlof SF. Oxytetracycline residues in milk after intrauterine treatment of cows with retained fetal membranes. *J Am Vet Med Assoc* 1996; 209:1753-1755.
6. Gorden PJ, Ydstie JA, Kleinhenz MD, Wulf LW, Gehring R, Lee CJ, Wang C, Coetzee JF. A study to examine the relationship between metritis severity and depletion of oxytetracycline in plasma and milk after intrauterine infusion. *J Dairy Sci* 2016; 99:8314-8322.
7. Hehenberger EM, Doherr MG, Bodmer M, Steiner A, Hirsbrunner G. Diagnosis and therapy of retained fetal membranes, puerpal metritis, and clinical endometritis in cattle: Results of the online-survey among Swiss practitioners. II. Puerperal metritis and clinical endometritis. *Schweiz Arch Tierheillkd* 2015; 157:503-512.
8. Lago A, Godden M, Bey R, Ruegg PL, Leslie K. The selective treatment of clinical mastitis based on on-farm culture results: II. Effects on lactation performance, including clinical mastitis recurrence, somatic cell count, milk production, and cow survivial. *J Dairy Sci* 2011; 94:4457-4467.
9. Landers TF, Cohen B, Wittum TE, Larson EL. A review of antibiotic use in food animals: perspective, policy, and potential. *Public Health Rep* 2012; 127:4-22.
10. Machado VS, Oikonomou G, Ganda EK, Stephens L, Milhomem M, Freitas GL, Zincola M, Pearson J, Wieland M, Guard C, Gilbert RO, Bicalho RC. The effect of intrauterine infusion of dextrose on clinical endometritis cure rate and reproductive performance of dairy cows. *J Dairy Sci* 2015; 98:3849-3858.
11. Oliveira L, Ruegg PL. Treatments of clinical mastitis occurring in cows on 51 large dairy herds in Wisconsin. *J Dairy Sci* 2014; 97:5426-5436.
12. Pol M, Ruegg PL. Treatment practices and quantification of antimicrobial drug usage in conventional and organic dairy farms in Wisconsin. *J Dairy Sci* 2007; 90:249-261.
13. Raymond MJ, Wohrle RD, Call DR. Assessment and promotion of judicious antibiotic use on dairy farms in Washington State. *J Dairy Sci* 2006; 89:3228-3240.
14. Roberson JR, Warnick LD, Moore G. Mild to moderate clinical mastitis: Efficacy of intramammary amoxicillin, frequent milk-out, a combined intramammary amoxicillin, and frequent milk-out treatment versus no treatment. *J Dairy Sci* 2004; 87:583-592.
15. Rossini K. Effects of calfhood respiratory and digestive disease on calfhood morbidity and first lactation production and survival curves. Thesis. Virginia Polytechnic Institute and State University, 2004.
16. Saini V, McClure JT, Leger D, Dufour S, Sheldon AG, Scholl DT, Barkema HW. Antimicrobial use on Canadian dairy farms. *J Dairy Sci* 2012; 95:1209-1221.
17. Sawant AA, Sordillo LM, Jayarao BM. Antimicrobial use on dairy herds in Pennsylvania. *J Dairy Sci* 2005; 88:2991-2999.
18. Sneeringer S, Macdonald J, Key N, McBride W, Matthews K. Economics of antibiotic use in U.S. livestock production, ERR-200. U. S. Department of Agriculture, Economics Research Service (ERS), 2015.
19. U.S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS). Dairy 2007, Part III: Reference of dairy cattle health and management practices in the United States, 2007. USDA-APHIS-VS, CEAH. Fort Collins, CO. #N482.0908, 2008.
20. U.S. Department of Agriculture, Economic Research Service. Organic market overview. 2016. http://www.ers.usda.gov/topics/natural-resources-environment/organic-agriculture/organic-market-overview.aspx
21. U.S. Department of Health and Human Services (USDHHS). The judicious use of medically important antimicrobial drugs in food-producing animals: Guidance for industry #209. 2012. 1-26.
22. U.S. FDA (United States Food and Drug Administration). Extra-label drug use in animals. Federal Register, 1996; 61:57732-57746.
23. U.S. FDA (United States Food and Drug Administration). New animal drugs; cephalosporin drugs; extra-label animal drug use; order of prohibition. Federal Register, 2012; 77:725-745.
24. U.S. FDA (United States Food and Drug Administration). IMS-a-50-Actions of the 2015 National Conference on Interstate Milk Shipments. 2015. Available at: http://www.idfa.org/docs/default-source/d-news/ims-a-50.pdf. Accessed January 17, 2016.
25. Ziv G, Sulman G. Absorption of antibiotics by the bovine udder. *J Dairy Sci* 1975; 58:1637-1644.
26. Zwald AG, Ruegg PL, Kaneene JB, Warnick LD, Wells SJ, Fossler C, Halbert LW. Management practices and reported antimicrobial usage on conventional and organic dairy farms. *J Dairy Sci* 2004; 87:191-201.