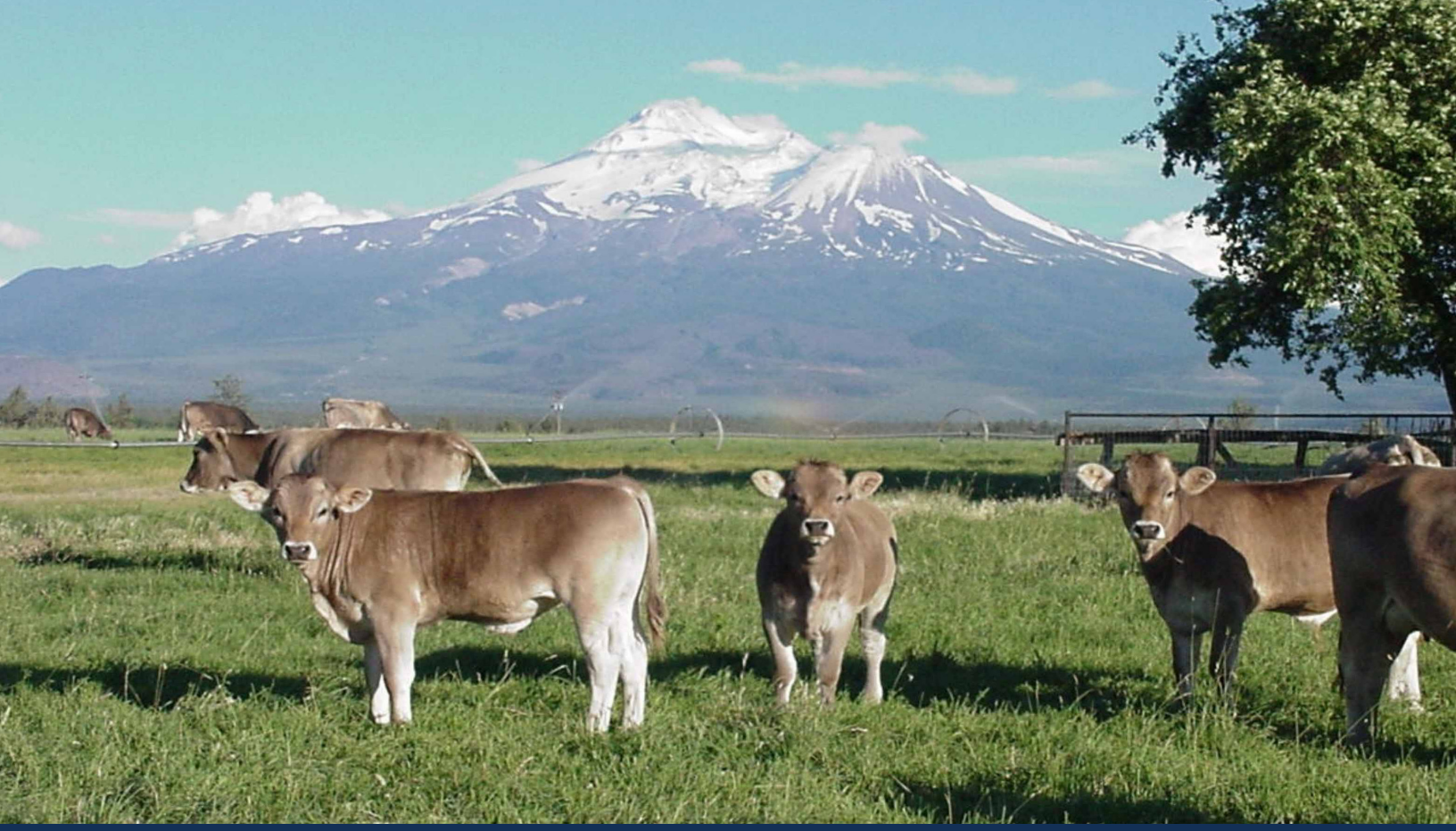

Antimicrobial Use and Stewardship (AUS) Program

Report to the Legislature

California Department of Food and Agriculture

January 2019

Access to Report:
To access this Report online: **https://www.cdfa.ca.gov/ahfss/AUS/**
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CALIFORNIA DEPARTMENT OF FOOD & AGRICULTURE
Karen Ross, Secretary

Statement of the Secretary

Antimicrobial resistance is an important and complex issue recognized in public health, veterinary medicine, food safety, and the environment. A multidisciplinary approach to addressing antimicrobial resistance necessitates collaboration across the state. Livestock producers, veterinarians, consumer and environmental interest groups, elected officials, and regulators came together to combat this serious problem with the development of Senate Bill 27, Livestock: Use of Antimicrobial Drugs law (Chapter 758, Statutes of 2015). Governor Jerry Brown and the California Legislature passed this forward-looking legislation and made State funding available for implementation by the California Department of Food and Agriculture (CDFA). The result of this cooperative effort is the Antimicrobial Use and Stewardship program, which has assembled a team of experienced scientists and qualified staff to protect the efficacy of these drugs crucial to human and animal well-being. California rises as a leader in antimicrobial stewardship policy while momentum grows globally and domestically, as demonstrated through the FDA's complementary objectives for years 2019 to 2023 to continue supporting antimicrobial stewardship in veterinary settings.

The spirit of collaboration that was foundational to the Law's development has continued throughout its implementation. The program spans two divisions, each with complementary expertise - a first for CDFA. As the following pages illustrate, the Antimicrobial Use and Stewardship program has an immense task, especially in a state as large and diverse as California, to enforce legal requirements, monitor antimicrobial use and resistant bacteria, and communicate recommendations to minimize antimicrobial resistance. There are many viewpoints on this topic. The support of multiple national and State agencies, as well as the cooperation of agriculture, consumer, and other organizations across the state, has helped the program accelerate its initial efforts in the first two years and is embodied within this report. The program encompasses much more work than I can cover in these few lines, so I encourage you to review the more detailed information on the following pages.

In California, it is our mandate to identify and work towards reducing antimicrobial resistance associated with livestock. CDFA takes this responsibility seriously, and I am proud to say we are moving ahead with a program founded in science, focused on human and animal health, specific to California's unique needs and priorities, and a first of its kind in the nation, with a look toward the future.

Karen Ross

Karen Ross
Secretary

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State of California
Edmund G. Brown Jr., Governor

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Executive Summary

Antimicrobial drugs are life-saving medications essential for protecting human and animal health. As such, it is imperative to preserve their efficacy. Bacteria that cause disease in both humans and animals are continually acquiring resistance to these medications. In response to this emerging and worrisome trend, the California Legislature passed a first-in-the-nation law requiring veterinary oversight for all uses of medically important antimicrobial drugs in livestock, as of January 1, 2018. From this forward-looking legislation, the California Department of Food and Agriculture (CDFA) established the Antimicrobial Use and Stewardship (AUS) program, tasked with implementing the directives of Food and Agricultural Code 14400-14408. AUS is responsible for assessment, education, and enforcement of antimicrobial use for livestock. A team of veterinarians, epidemiologists, and specialists collect information specific to California on the sale and use of antimicrobial drugs, antimicrobial resistance, and livestock management practices, and utilize this information to develop recommendations and guidelines that will inform livestock producers and veterinarians on antimicrobial stewardship. This Report to the Legislature aims to fulfill the mandate in FAC 14405 (d) by providing the results of outreach activities and monitoring efforts.

The AUS team has conducted extensive outreach and education within the state to raise awareness of the law, promote participation in data collection activities, provide education on antimicrobial stewardship, and help ensure compliance. AUS is estimated to have reached more than 80,000 people, especially livestock owners and veterinarians, through over 120 events, presentations, and publications. Prior to the January 1, 2018 implementation of restrictions on antimicrobial drug sales and use, AUS team members made 841 visits to 605 feed and drug retailers in 53 counties across California to help them prepare for the upcoming changes. Outreach documents were mailed to a total of 372 CDFA-licensed restricted livestock drug retailers and posted on websites following the publication of regulations related to the sale of antimicrobial drugs intended for use in livestock.

The AUS team has utilized a robust collaborative approach throughout the program's development, which remains critical to its ongoing success. In addition to being the first program in CDFA to span two divisions - each with complementary specialties - numerous stakeholder groups are actively engaged in the program, including livestock industry advocates, consumer advocates, public health officials, veterinary medical associations, academic institutions, regulatory authorities, and a variety of in-state and out-of-state subject matter experts. Collaboration with State and federal entities has helped AUS develop program recognition and support while leveraging existing opportunities and resources to advance program goals. Because of the ground-breaking nature of California's endeavors, AUS has been

able to engage in the antimicrobial resistance discussions at a national level and has established a unique collaboration with the National Animal Health Monitoring System to ensure data representative of California will be collected through existing processes. AUS has also supported efforts to leverage external funding and enhance laboratory testing capabilities for antimicrobial resistance.

Through the AUS data collection efforts to date, California is gaining an unparalleled view of antimicrobial use and resistance in its livestock agricultural system. In under two years, greater than 15,000 surveys have been administered to livestock producers across California. Responses representing more than half a million animals across 55 counties in California reflect antimicrobial use and management practices across beef and dairy cattle, sheep, and backyard poultry operations; current efforts include expansion into other production groups, such as commercial poultry and goats. AUS has also initiated on-farm sampling at more than 50 volunteering operations, representing at least 128,000 animals, where samples will be taken over time to evaluate antimicrobial resistance in bacteria. Additionally, AUS is pioneering an approach to monitoring trends in sales of antimicrobials used in feed through the collection and analysis of Veterinary Feed Directives issued in the state. Findings from AUS data collection activities will be reported in multiple formats aimed to provide actionable information to the livestock industry and veterinarians, including peer-reviewed, scientific journals; annual reports; and summary reports accessible to the program's largest stakeholder group - the people of California.

In its first two years, the AUS program has made great strides in the outreach and monitoring enshrined in its mandates. As demonstrated through this Report to the Legislature, the AUS program fulfills the mandates of the law by leveraging strong relationships with key partners to implement a robust monitoring program and develop antimicrobial stewardship guidelines that meet the needs of California's diverse livestock industries and producers. AUS evaluates the quality of data collected using scientifically established methods, including assessment of response rates along with farm size and regional distributions, applying external validation when possible. Research has shown that a relatively small proportion of a population providing survey responses can yield relevant and representative data. By sampling a representative portion of the population, voluntary participation in AUS data-gathering efforts has thus far furnished data that are suitable for statistical analysis and can be expected to represent trends across California agriculture. AUS supports building upon this early success by continuing to utilize voluntary participation and to collect information using current strategies. This pathway supports evidence-based, innovative approaches to minimizing antimicrobial resistance and promoting responsible antimicrobial use in California's animal agricultural industry.

AUS PROGRAM HIGHLIGHTS

2015

- Senate Bill 27 signed into Law

2016

- 1st phase of funding approved
- AUS managers hired onto the team

2017

- AUS website goes live
- CAHFS starts offering MIC testing
- 1st Ad Hoc Advisory meeting
- NAHMS collaboration initiated
- Expert workgroup formed
- Veterinary Feed Directive facility visits initiated
- 1st contracted, on-farm study begins
- 2nd phase of funding approved
- 1st in-house survey mailed out

61,743 individuals (vets, livestock producers, and livestock drug retailers) directly **contacted and informed** of the Law prior to implementation

2018

- All MIADs move under veterinary oversight in CA
- 3rd phase of funding approved
- Longitudinal studies initiated
- Principles of Antimicrobial Stewardship and Judicious Use Guidelines released
- FDA Drug Residue Prevention Cooperative Agreement initiated
- Retailer Sales Regulations published
- "Qualified Individual" trainings begin
- Veterinary Medicine Loan Repayment Program Submissions (5)

44,535 veterinarians, livestock producers, and livestock drug retailers directly **engaged** in ongoing AUS outreach and education efforts

Over half a million animals represented in survey responses across multiple studies

Sampling initiated on **50 voluntary operations, representing** at least **128,000 animals**

LEGEND

Winter · Summer · Spring · Fall

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Definitions

Antimicrobial agent

Any substance of natural, semi-synthetic, or synthetic origin that, at concentrations within the treated human or animal, kills or inhibits the growth of microorganisms by interacting with a specific target. The term antimicrobial is a collective for antiviral, antibacterial, antifungal, antiparasitic, and antiprotozoal agents. For the purpose of this Report to the Legislature, and the focus of the Antimicrobial Use and Stewardship program, the term antimicrobial is used exclusively as it relates to antibacterial (acting against bacteria) properties.

Medically Important Antimicrobial Drugs

Antimicrobial agents important for therapeutic use in humans as described in the U.S. FDA Guidance for Industry #152, Appendix A. This does not include ionophores or other antimicrobial agents not important for human therapeutic use.

The Law

For the purpose of this Report to the Legislature, Livestock: Use of Antimicrobial Drugs, California Food and Agricultural Code (FAC) Sections 14400 - 14408 is referred to by relevant section or generally as "the Law." Some may be familiar with the Law referred to as Senate Bill 27 or SB 27 (2015).

Veterinary Feed Directive

A Veterinary Feed Directive (VFD) is a written (nonverbal) statement issued by a licensed veterinarian that authorizes the use of a VFD drug or combination VFD drug in or on an animal feed. This written statement authorizes the client (the owner of the animal or animals or other caretaker) to obtain and use animal feed bearing or containing a VFD drug or combination VFD drug to treat the client's animals only in accordance with the conditions for use approved, conditionally approved, or indexed by the FDA. A VFD is also referred to as a VFD order. (21 CFR Part 558)

- **VFD drug**
  A drug intended for use in or on animal feed, which is limited to use under the professional supervision of a licensed veterinarian.

- **Combination VFD drug**
  An approved combination of new animal drugs intended for use in or on animal feed under the professional supervision of a licensed veterinarian, and at least one of the new animal drugs in the combination is a VFD drug.

Acronyms

Acronym	Name
AHFSS	CDFA Animal Health and Food Safety Services Division
AMR	Antimicrobial resistance
AST	Antimicrobial susceptibility testing
AUS	CDFA Antimicrobial Use and Stewardship
CAHFS	California Animal Health and Food Safety Laboratory System
CCR	California Code of Regulations
CDC	U.S. Centers for Disease Control and Prevention
CDFA	California Department of Food and Agriculture
CVMA	California Veterinary Medical Association
FAC	California Food and Agricultural Code
FARAD	Food Animal Residue Avoidance and Depletion Program
FDA	U.S. Food and Drug Administration
FFA	Future Farmers of America
IS	CDFA Inspection Services Division
MIAD	Medically important antimicrobial drug
MIC	Minimum inhibitory concentration
NAHMS	USDA National Animal Health Monitoring System
NARMS	U.S. National Antimicrobial Resistance Monitoring System
NASS	USDA National Agriculture Statistics Service
NIFA	USDA National Institute of Food and Agriculture
USDA	United States Department of Agriculture
VCPR	Veterinarian-client-patient relationship
VFD	Veterinary Feed Directive
VIN	Veterinary Information Network
VMTRC	UC Davis Veterinary Medicine Teaching and Research Center (Tulare)

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California's Approach to the Complex Problem of Antimicrobial Resistance

How Bacteria Develop Resistance

The development and spread of antimicrobial-resistant bacteria is a complex process that occurs in human health, animal health, and in the environment. Since the introduction of antimicrobial drugs in the 1940s, illness and death in both people and animals from infectious diseases have been greatly reduced. Unfortunately, as these drugs have been widely used over several decades, bacteria are adapting to be less vulnerable to them. Some bacteria are already resistant to these lifesaving drugs.

Section Highlights

- **The development of antimicrobial-resistant bacteria is a One Health issue, spanning human, animal, and environmental health**
- **AUS is developing a comprehensive, model antimicrobial stewardship and monitoring program in California**
- **AUS has established strong relationships with key collaborators to create evidence-based, innovative approaches to promote antimicrobial stewardship and minimize antimicrobial resistance**

Key Acronyms

- **AUS – Antimicrobial Use and Stewardship**
- **FAC – California Food and Agricultural Code**
- **MIAD – medically important antimicrobial drug**

The evolution of bacterial strains that are resistant to antibiotics is a natural process. Many bacteria produce antimicrobial substances as a communication or defense mechanism. As bacteria have co-evolved with each other, some have developed defense mechanisms to protect themselves from antimicrobial compounds. The resistance mechanism becomes encoded in the bacterial DNA, some forms of which can be transferred between different bacterial organisms, and subsequent generations of the bacteria are no longer affected by antimicrobial compounds that previously could slow their growth or kill them. When exposed to the same or similar compound due to antimicrobial drug use in human and animal populations, those bacteria with antimicrobial-resistant genes are more likely to survive than those without.

The Antimicrobial Use and Stewardship (AUS) Program

The role of antimicrobial use in driving the development and spread of antimicrobial-resistant bacteria is highly nuanced in both human and veterinary medicine. Researchers are still exploring the multitude of contributing factors, such as antibiotic type, method of drug application, type of bacteria, and biology of the animal itself. What is clear is the importance of ensuring antibiotics are used judiciously to reduce potential for resistance, while maintaining animal welfare and health. California is leading the way to preserve the efficacy of antimicrobial drugs by developing antimicrobial stewardship guidelines and best management practices for medically important antimicrobial drugs (MIADs) used in livestock under the nation's first comprehensive, model antimicrobial stewardship and monitoring program. In implementing California's law, Livestock: Use of Antimicrobial Drugs, California Food and Agricultural Code (FAC) Sections 14400-14408 (herein referred to by relevant section or generally as "the Law"), California is paving the way to understand current antimicrobial use and livestock management practices; to monitor trends in antimicrobial resistance in livestock bacterial populations; and to identify best management practices, disease prevention and treatment alternatives, and other key mitigations that may slow the development and prevent the spread of antimicrobial-resistant bacteria associated with livestock.

Passage of California Senate Bill 27, 2015 (Hill), created the California Department of Food and Agriculture (CDFA)'s Antimicrobial Use and Stewardship (AUS) program **(Figure 1)** and brought the administration of all MIADs used in livestock under veterinary oversight. Effective January 1, 2018, the Law prohibits the administration of MIADs to livestock, unless ordered by a licensed veterinarian through a prescription or Veterinary Feed Directive (VFD), pursuant to a veterinarian-client-patient relationship (VCPR). Furthermore, the Law prohibits the administration of MIADs to livestock solely for purposes of promoting weight gain or improving feed efficiency and prohibits regular pattern prophylactic use, unless necessary for a surgical or medical procedure. Improving MIAD use is an intervention, for which slowing or reducing antimicrobial resistance is the desired outcome.

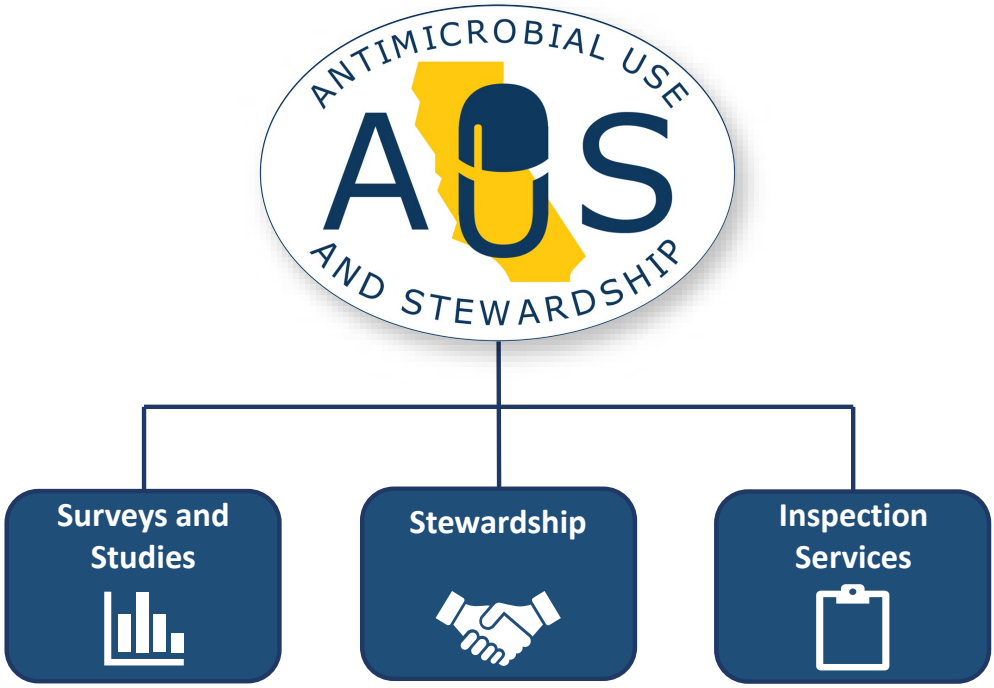


Figure 1. California Department of Food and Agriculture (CDFA) Antimicrobial Use and Stewardship (AUS) Program.

The AUS program is required to gather voluntary information about on-farm MIAD usage, and to address underlying issues that contribute to MIAD use, while evaluating the levels and trends in antimicrobial resistance. This Report to the Legislature addresses the requirements set forth by FAC 14405(d) by describing the results of the program's outreach activities and monitoring efforts to date.

The Law requires CDFA to collect information on:

- Livestock antimicrobial drug sales and usage,
- Antimicrobial-resistant bacteria, and
- Livestock management practices.

The Law furthermore directs that, when applicable, this information be gathered in coordination with the U.S. Department of Agriculture (USDA) National Animal Health Monitoring System (NAHMS) and the National Antimicrobial Resistance Monitoring System (NARMS), from:

- California's major livestock segments,
- Regions with considerable livestock production, and
- Representative segments of the food production chain.

The initial funding for AUS became available July 1, 2016 and was incrementally phased in based on approved legislative funding through FY 2018-19.

As the first program within CDFA to encompass two divisions—Inspection Services (IS) and Animal Health and Food Safety Services (AHFSS)—AUS successfully coordinates resources and combines efforts across multiple teams to ensure a clean and wholesome food supply, while encouraging judicious use of antimicrobials and promoting animal health. The AUS program collaborates with a diverse group of stakeholders to create evidence-based, innovative approaches to minimize antimicrobial resistance and promote responsible antimicrobial use. These partners include academic institutions, other state and federal agencies, public health officials, veterinarians, consumer groups, and livestock producers **(Figure 2)**. Data collection methods used, including surveys and research studies, are guided by other national and international antimicrobial use and resistance monitoring programs and have been customized to fit California's unique needs. This allows for the development of meaningful and practical education and tools to support California veterinarians and producers in making informed decisions regarding disease prevention and judicious use of antimicrobials in livestock.

External Funding Opportunities for AUS

As mandated in FAC Section 14405(e), AUS continues to seek external funding to supplement the general funds supplied by the State budget. Nationally, more funding is prioritized to be spent on antimicrobial use and resistance research in human medicine compared to animal medicine. For example, in the 2016 U.S. federal budget, approximately $793 million dollars were allocated to human health agencies to help combat antibiotic-resistant bacteria. Only $67.6 million dollars were allocated for the same goal in the agencies that deal with animal health.[1,2]

Section Highlights

- **AUS supports and collaborates with researchers seeking federal funding when research efforts are aligned with program goals**
- **California is one of seven states to receive the maximum amount of funding over a three-year term for FDA's Drug Residue Prevention Program**

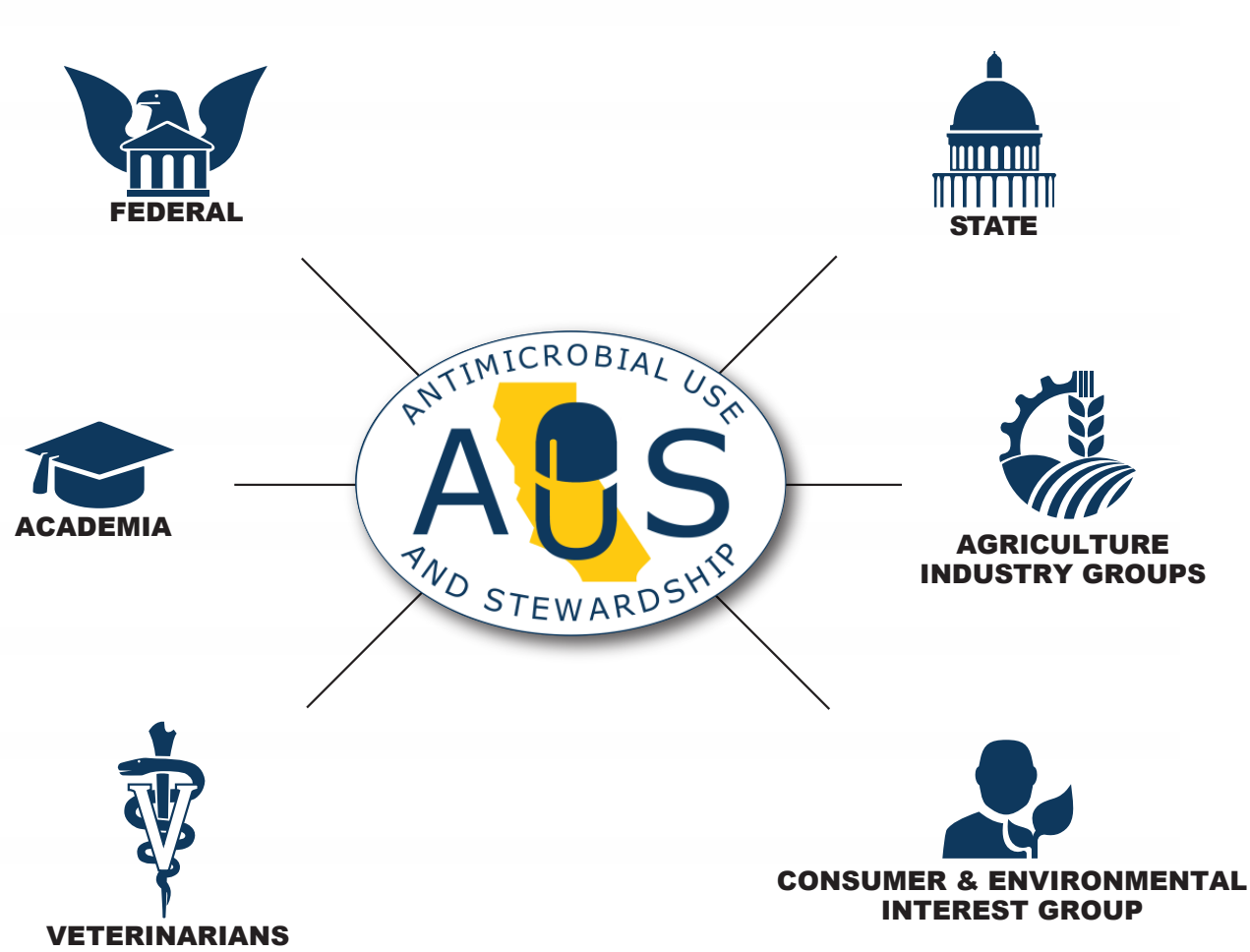


Figure 2. AUS Stakeholder and Collaborator Groups. For additional information on these groups, please see Appendix A.

AUS monitors sources of research funding and makes efforts to collaborate with or support researchers seeking this funding when aligned with the program's goals. While the nature and extent of the program's involvement with these projects varies on a case-by-case basis, AUS' role has included engaging researchers around relevant funding opportunities, serving as expert collaborators, and providing letters of support. AUS supported and collaborated with many academic research, stewardship, and surveillance efforts taking place nationwide, including those of: Washington State University, Ohio State University, North Carolina State University, Oregon State University, California Polytechnic State University - San Luis Obispo, California State University - Chico, University of California - Davis (UC Davis), and the University of Minnesota.

USDA National Institute of Food and Agriculture (NIFA) Veterinary Services Grant Program

In particular, AUS supports and collaborates with multiple universities that have received grant funding or are applying for funding from the USDA NIFA Veterinary Services Grant Program. The purpose of this program is to relieve veterinarian shortages and support veterinary services through education, training, recruitment, placement, and retention of veterinarians, veterinary technicians, and students of veterinary medicine and veterinary technology.

CDC Broad Agency Announcement Proposal Support

AUS supported researchers at UC Davis and Washington State University to apply separately for funding under the Centers for Disease Control and Prevention (CDC)'s Broad Agency Announcement FY2018-OADS-01 "Applied Research to Address Emerging Public Health Priorities." Both project proposals addressed issues related to antibiotic resistance in California, including improving veterinary prescriber antimicrobial stewardship and evaluating potential linkages between resistance profiles of foodborne bacteria and human infections. Unfortunately, neither of these proposals was selected for further development or funding through this mechanism. AUS continues to pursue partnerships with applicants for similar funding opportunities.

FDA Cooperative Agreement

In March of 2018, the Food and Drug Administration (FDA) announced a cooperative agreement called the Drug Residue Prevention Program. This three-year, $175,000-per-year agreement will focus on the judicious use of antimicrobials, follow-up investigations and enforcement action on producers who have multiple drug residue violations (contamination of animal products with drug levels above the legally allowed concentration), occurring within a one-year timeframe, as well as the development of outreach and education materials, and educational visits with recent and historical drug residue violators. CDFA was one of seven states to receive this funding and AUS began participating in the cooperative agreement in Fall of 2018.

Program Stakeholders and Collaborators

A broad array of stakeholders guided development of a comprehensive program within the mandate of the Law, in order to aid producers and veterinarians tackling the problem of antimicrobial resistance. Regular contributors to the development of the program include livestock industry advocates; consumer advocates; public health officials, including the California Department of Public Health; the California Veterinary Medical Board and veterinary medical associations; other leaders in federal and State government; academic institutions; regulatory

Section Highlights

- **Numerous stakeholders are actively guiding program development, assisting with outreach efforts, and collaborating on research development**
- **AUS has ongoing communication with interested stakeholders to provide program updates, receive feedback, and leverage their wide range of exptertise**

Key Acronyms

- **AMR – antimicrobial resistance**

authorities; and in-state and out-of-state subject matter experts. These participants represent a range of expertise and contributions to the AUS program, including guidance regarding program development, assistance with outreach efforts, and collaboration on specific projects. Additionally, AUS works to align with leading federal and State efforts when possible. For more information on AUS stakeholders and collaborators, please see Appendix A.

CDFA produced two annual Strategic Plans, one in 2017 and one in 2018, to provide a framework for the implementation of the program, as well as to guide measurements of success. The Plans were shared with the stakeholder groups to incorporate their input and were posted on the AUS website.

AUS also built upon pre-established networks with universities, government agencies, and others to review current surveillance models in animal agriculture. With the goal of better understanding the links between antimicrobial use patterns in livestock and the development of antimicrobial resistance (AMR), the program collaborated with both national and State partners to incorporate a broad base of expertise and to align with the goals of the National Action Plan for Combating Antibiotic-Resistant Bacteria. **Figure 2** shows a snapshot of the variety of entities engaged with AUS, including leaders in federal, State, and academic efforts as well as veterinary, consumer, and agriculture industry groups.

Ad Hoc Advisory Meetings

Active stakeholder involvement and voluntary commitments are central to the development of a program in a large, diverse, and decentralized agricultural system such as California's. Along with group-specific meetings and communications, program stakeholders participated in the Ad Hoc Advisory Committee, which met six times over the course of 18 months. These gatherings provided entities impacted by the Law an opportunity to voice their perspectives and participate in developing the program direction; additionally, the meetings were a mechanism for AUS to provide updates on budget issues, contract development, and accomplishments. The meetings were held at the CDFA headquarters in Sacramento on the following dates:

- April 11, 2016
- March 14, 2017
- June 12, 2017
- November 27, 2017
- April 3, 2018
- October 2, 2018

Agriculture Industry Contributions

California's animal agriculture industry has been very supportive of and engaged with AUS' efforts to reduce AMR and promote animal health. Organizations such as the California Farm Bureau Federation, California Cattlemen's Association, California Wool Growers Association, California Poultry Federation, and California Sheep Commission have contributed to program development and assisted with multiple AUS projects. This support has included providing advice on and field testing of AUS survey questionnaires and promoting survey participation via newsletters, email, meetings, and conferences. Additionally, the Milk Producers Council and Western United Dairymen helped to promote participation in the surveys administered by the UC Davis Veterinary Medical Teaching and Research Center in its work for AUS.

Veterinary Medical Associations and Academic Experts

The California Veterinary Medical Association and many of the local veterinary medical associations with multiple livestock veterinarian constituents have been instrumental in assisting with program outreach to licensed veterinarians across the state. AUS staff have been invited to speak at several board meetings as well as provide continuing education opportunities to members about the new requirement of the Law and judicious use of antimicrobial drugs in livestock.

Additionally, numerous veterinarians in academia have engaged with the AUS program to provide their knowledge and expertise of the various complexities regarding AMR. These veterinarians have been instrumental in guiding the development of the AUS program as well as disseminating outreach and integrating educational opportunities into the veterinary school curricula.

Consumer and Environmental Interest Group Contributions

Multiple interest groups share concerns related to antimicrobial resistance and seek a collective, public response to this health challenge. Their involvement provides an additional perspective to the program, as they expressly advocate for consumer and environmental interests. Many of these groups also represent a national focus and actively promote wholesale, retailer, and food service antibiotic use policies across the country that align with AUS' focus on judicious use and antimicrobial stewardship. Such groups invested in AUS activities and the implementation of the Law have participated in the Ad Hoc Advisory Committee, as described above, and engaged California leadership in discussions regarding the AUS program.

Federal and State Entities

Numerous federal and State entities are tasked with the mission to protect food safety and public health. These include the Centers for Disease Control and Prevention, U.S. Department of Agriculture, Food and Drug Administration, California Department of Public Health, California Department of Food and Agriculture, California Veterinary Medical Board, and California Board of Pharmacy. Antimicrobial resistance is a complex problem requiring a multidisciplinary approach, thus partnerships with other government agencies engaged in this issue at the state and federal level are crucial to the success and strength of the AUS program in California. For more information on AUS collaborations with federal and State entities, please see Appendix A.

California Animal Health and Food Safety (CAHFS) Laboratory

The CAHFS Laboratory safeguards public health by providing rapid and reliable diagnoses for animal diseases in California, including those affecting humans. Using AUS funds, the CAHFS Laboratory purchased state-of-the-art equipment for monitoring AMR in the state. Testing methods were validated to ensure timely and accurate laboratory results for future studies on AMR. Additionally, efforts were made to educate clients and veterinary practitioners on the advantages of the new testing methods. The micro-broth dilution method of antimicrobial susceptibility testing has been shown to produce more accurate, consistent

results than the disk diffusion method and is the current best practice.[3] This procedure exposes bacteria to varying concentrations of drugs; the resulting measurement is a minimum inhibitory concentration (MIC), which is defined as the lowest concentration of an antimicrobial that will inhibit the visible growth of a microorganism.[4] To date, this new method has been performed on samples collected from a variety of livestock animal species, as shown in **Figure 3**. These diagnostic services and associated guidance are publicly available to veterinary practitioners, allowing them to make appropriate treatment decisions consistent with the intent of the Law. AUS has also supported CAHFS capabilities by utilizing their resources in ongoing studies to characterize pathogens and their susceptibility to antibiotics.

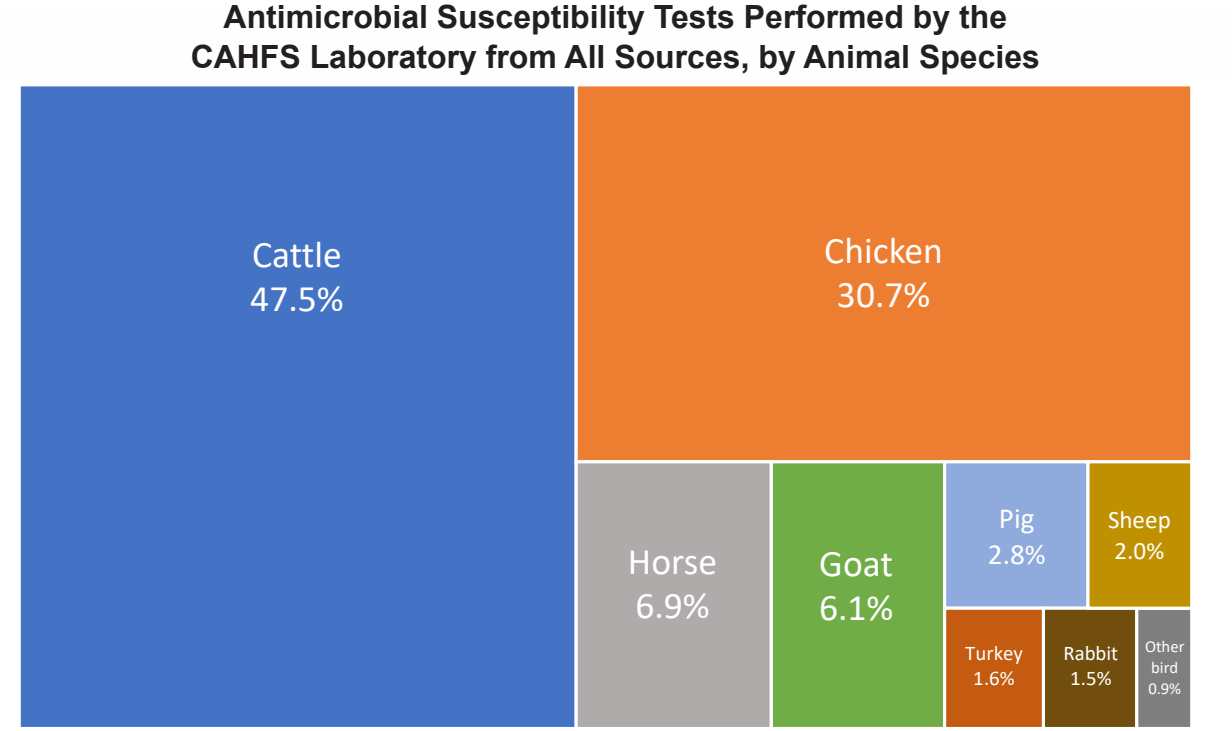


Figure 3. Antimicrobial Susceptibility Tests Performed by the CAHFS Laboratory from All Sources, by Animal Species. Data provided by the California Animal Health and Food Safety (CAHFS) Laboratory. The CAHFS Laboratory provides services for a wide variety of animals, especially livestock, in California. Testing performed using the micro-broth dilution method to determine minimum inhibitory concentrations (MICs) for samples submitted to the Laboratory. Figure represents 1,145 MIC submissions from December 2017 – August 2018.

AUS has also supported CAHFS capabilities by utilizing CAHFS resources in an ongoing study of backyard poultry to characterize pathogens and their susceptibility to antibiotics. Additionally, AUS and CAHFS have initiated a study of stored samples to gain historical information on AMR in California and continue to explore opportunities for trend reporting.

Outreach to Veterinarians, Retail Distributors, and California Livestock Owners

The core tenet of the Law, and the foundation of the AUS program, is veterinary oversight of antimicrobial use, with the first-in-the-nation requirement to have a prescription or VFD to administer any MIAD to livestock, pursuant to a VCPR. Prior to implementation of the Law, many antibiotics were available over-the-counter for use in livestock animals. This gave livestock owners the ability to administer medications to their animals when access to veterinary care may have been limited or perceived to be unnecessary. Due to the concern of imprudent, ineffective, or avoidable antibiotic use contributing to AMR in animals and humans, stakeholders agreed to require veterinary expertise in the decision-making process for use of these lifesaving drugs, prohibit the use of MIADs for production purposes (such as growth promotion or feed efficiency), and limit administration in a regular pattern for disease prevention, unless necessary for a surgical or medical procedure. To inform California veterinarians, livestock drug retailers, and livestock producers of this major change in animal health care, AUS conducted extensive outreach in 2017. Outreach efforts provided stakeholders with resources to facilitate compliance with the Law.

Section Highlights

- **Implementation of the Law presents various challenges to livestock owners, veterinarians, and retail distributors**
- **Regulations were passed to aid in providing timely access to MIADs with a prescription within the context of a valid VCPR**
- **AUS conducted considerable outreach to facilitate compliance with the Law, promote participation in surveys and studies, and provide resources on antimicrobial stewardship**

Key Acronyms

- **MIAD – medically important antimicrobial drug**
- **VCPR – veterinarian-client-patient relationship**
- **VFD – Veterinary Feed Directive**

AUS leverages CDFA's resources to ensure that all parties involved in California's livestock industry are aware of the significant antimicrobial drug use changes mandated by the Law. Since California is geographically large, with vast and remote areas of food animal production activity, CDFA has field offices throughout the state. AUS utilizes CDFA staff at all locations to ensure compliance with the Law and to conduct regular outreach and education to livestock drug retail outlet staff, commercial feed inspectors, drug and feed manufacturers, livestock producers, and private veterinarians in their respective regions across California.

Communicating with Stakeholders Prior to Implementation of the Law

Prior to implementation of FAC Sections 14400-14403 on January 1, 2018, AUS made many efforts to inform veterinarians, feed manufacturers, livestock drug retailers, and livestock owners on understanding their role and responsibilities under this new law.

AUS utilized various methods and outlets to reach a wide range of stakeholders. AUS developed outreach materials in English and Spanish that were distributed to all California dairies, commercial sheep producers, cow-calf producers, and major poultry producers. Well-

known agriculture organizations such as the California Farm Bureau Federation, California Cattlemen's Association, California Wool Growers Association, Western United Dairymen, UC Davis Cooperative Extension, California Poultry Federation, Pacific Egg and Poultry Association, California Pork Producers Association, and Latino Farmers Conference were instrumental in further disseminating information. Outreach materials were distributed to small-scale livestock owners through local and county fairs, livestock sale yards, feed stores, and veterinary clinics.

AUS also made focused efforts to inform veterinarians and livestock owners of the requirements of the Law by giving presentations, webinars, and workshops throughout the state. Many of these events targeted industry leaders and veterinarians who are in positions to share vital information with their affiliates and clients; other events are customized for members of livestock associations and youth agriculture organizations, as well as the small scale, backyard livestock owners. AUS veterinarians conducted presentations to students attending the UC Davis School of Veterinary Medicine, a key asset in the fight against AMR upon graduation and entrance into the work force.

In addition, AUS published multiple articles in various veterinarian and livestock owner newsletters and magazines **(see Figure 4)**. These veterinary news outlets cast a broad net, with *California Veterinarian* being delivered to all licensed veterinarians in the State of California. Articles for producers were published in CDFA's *California Dairy Review*, UC Cooperative Extension newsletters across the state, as well as newsletters distributed by veterinarians to their individual clients.

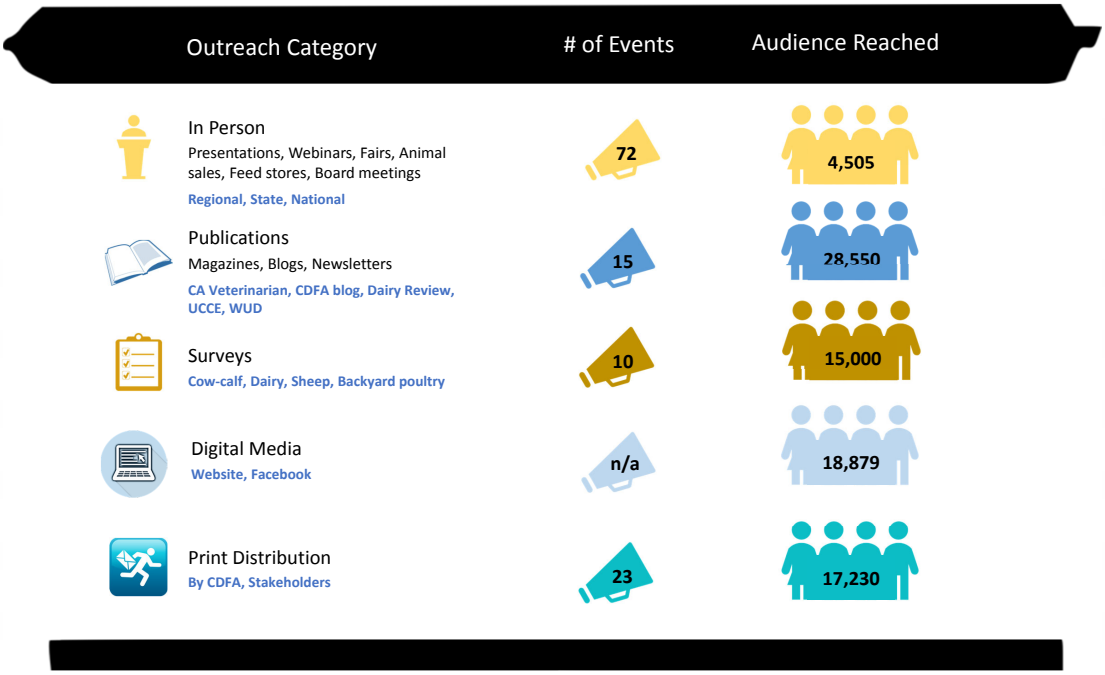


Figure 4. AUS Outreach: Communication Channels and Influence. December 2016 – December 2018.

Inspection Services staff also visited retail feed outlets selling MIADs to share information about the Law's impact on drug sales, provide outreach materials, and answer questions. As shown in **Figure 5**, IS conducted a total of 841 visits to 605 retailers in 53 counties throughout California during the period of March through December of 2017. Stores visited include Restricted Livestock Drug and Feed Retailers licensed by CDFA, as well as retail stores selling livestock and pet care products.

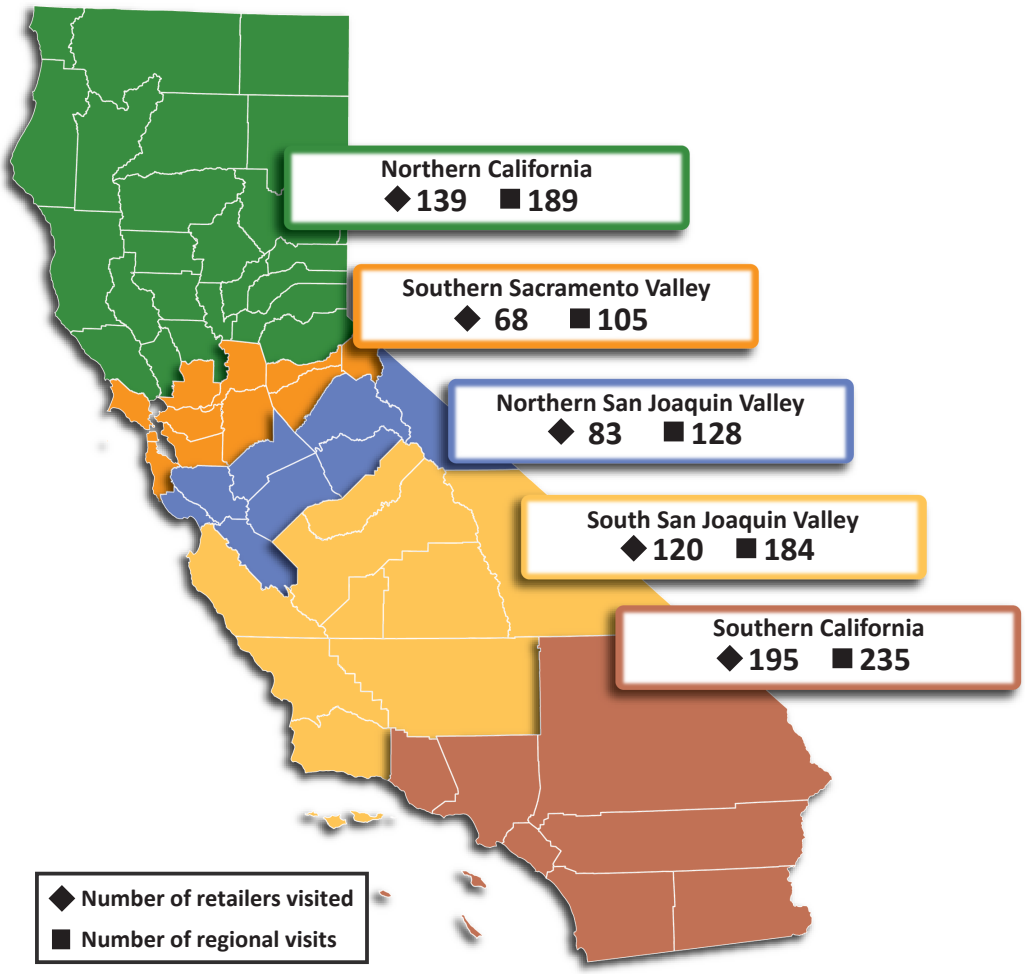


Figure 5. Inspection Services Educational Visits, by Region. March – December 2017.

Retailer Regulations on Drug Access

The Law granted AUS the authority to promulgate regulations regarding the sale of MIADs by Restricted Livestock Drug Retailers licensed with CDFA. The AUS program has worked diligently with input and feedback from stakeholders and sister agencies—including the Board of Pharmacy and Veterinary Medical Board—to develop regulations creating a framework for lawful sale that balances the necessity for tighter controls while maintaining adequate access to MIADs for industry.

On August 16, 2018, IS adopted California Code of Regulations (CCR) Title 3, Sections 5007-5015 clarifying the requirements for CDFA-licensed retailers to sell MIADs. Importantly, these regulations clarify that CDFA-licensed retailers may only sell "California prescription drugs," which are defined in 3 CCR Section 5007(c) as a MIAD intended for use on livestock that is federally labeled for over-the-counter sale but requires a prescription to be sold in California pursuant to Chapter 4.5 of Division 7 of the Food and Agricultural Code.

The regulations developed pursuant to FAC Section 14403 require a Restricted Livestock Drug licensed retailer selling California prescription drugs to:

- Hire a California licensed pharmacist, either on a consulting basis or as part of the retailer's staff;
- Employ at least one qualified individual who meets training requirements as set forth in the regulations;
- Maintain detailed information of drug sales logs, including a copy of the prescription from the prescribing veterinarian; and
- Develop store-specific, written procedures for the receipt, storage, inventory, sale, and disposal of California prescription drugs. There is a three-year record retention requirement for these documents.

A "qualified individual" is a person who is 18 years or older and has completed an approved training course covering topics such as applicable laws and regulations, drug residue hazards, antimicrobial resistance science, reading prescriptions and product labels, and safe storage and handling practices. An initial training program course developed in cooperation with the Food Animal Residue Avoidance and Depletion (FARAD), a USDA-funded university consortium, was held on October 24, 2018 in Sacramento, California. A second training was held on December 4, 2018 in Tulare, California and AUS is working with FARAD to host additional training sessions, with the eventual goal to make this training available online.

In addition to hosting qualified individual training, AUS program staff have begun conducting outreach to help retailers understand the requirements to sell California prescription drugs in compliance with the new regulations. Staff developed outreach documents which were mailed to a total of 306 restricted livestock drug retailers and posted on the AUS and Livestock Drug Program websites. **Figure 6** shows how the new regulations affected what retailers can sell. The program visited a total of 61 retailers beginning in October 2018 to explain the new regulations, answer questions, and verify compliance with the new requirements. See Appendix B for a list of California prescription drugs.

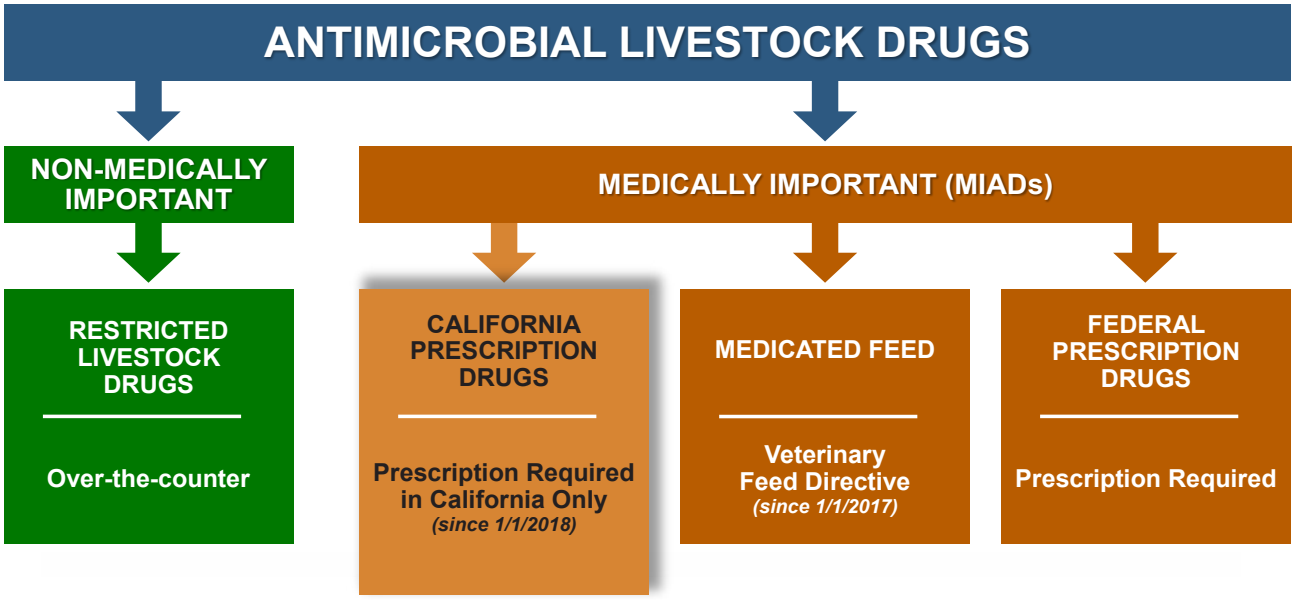


Figure 6. Federal and State Retail Classifications of Antimicrobial Livestock Drugs.

Restricted Livestock Drug Retailer License Program

Included in the educational materials provided to retailers prior to the implementation of the Law on January 1, 2018 was information about the Restricted Livestock Drug Retailer license program. The program has been in existence since 1967 in accordance with FAC Sections 14321-14330. A license, costing $50 annually, is required to sell any Restricted Livestock Drug, which is defined in 3 CCR Section 5000(e) as any livestock drug which, if improperly administered, is dangerous to the health of livestock or to humans who consume products from livestock, and includes products such as hormones, antibiotics, Type A medicated articles, and drugs with a withdrawal period. Any livestock drug that requires a prescription based on federal law is exempt from this provision.

Under FAC Section 14403, licensed retailers may sell California prescription drugs provided they adhere to additional requirements. Among these requirements, a licensed retailer must adhere to certain recordkeeping standards (FAC Section 14329 and 3 CCR Section 5004) for all sales of restricted livestock drugs. For each drug sold, a retailer must record:

- Drug or trade name, route of administration, quantity, and lot number;
- Date of sale;
- Name, address, and telephone number of the purchaser; and
- Signature of purchaser.

Licensed retailers selling California prescription drugs must also retain certain additional information (3 CCR Section 5010) for each sale, including:

- A copy of the prescription with a unique transaction number,
- Indication that the drug is a California prescription drug, and
- Identification of the qualified individual selling the drug.

These sales records requirements cover only the products that remain federally over-the-counter and are sold in California by Restricted Livestock Drug Retailers. The AUS program does not have oversight over the sale of federal prescription drugs or where the California prescription drug was sold by a California Board of Pharmacy-licensed facility.

AUS has created sample sales logs for retailers and plans to conduct more compliance visits and reviews of sales records for livestock drug retailers as part of their outreach and educational efforts. In 2019, the program will begin enforcement action on retailers not maintaining adequate sales logs.

Before implementation of the Law, there was no active collection of the federal over-the-counter drug data. While there is no baseline data available from these sales records, this information will be collected for California by AUS moving forward.

Addressing Limited Access to Veterinary Care

FAC Section 14404(b) mandates that AUS consult with livestock owners, licensed veterinarians, and other relevant stakeholders to ensure timely access to treatment for producers in rural areas with limited access to veterinary care. In consultation with livestock producers and veterinarians across the state, and considering feedback from presentations, workshops, surveys, and online reporting tools, many livestock owners and agricultural groups were concerned regarding the challenges of finding a veterinarian, including that:

AUS leverages relevant national and State efforts to increase access to veterinary services in regions with an apparent shortage situation.

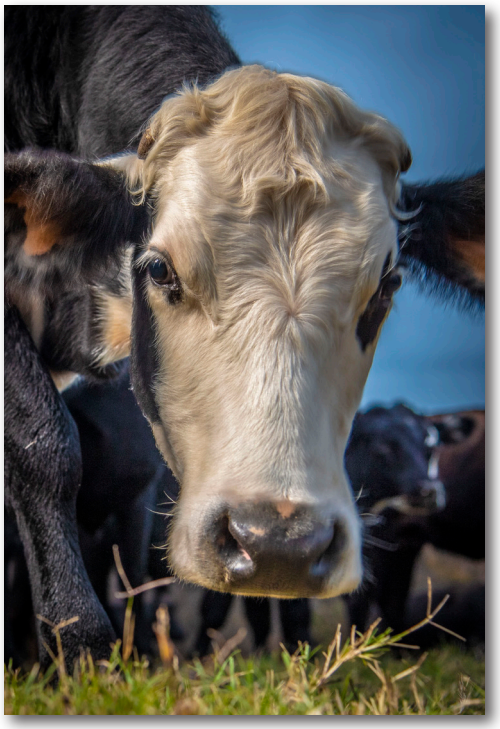
- Extremely rural communities may use a veterinarian on a routine basis, but their ranches are too remote for a veterinarian to reach in order to provide timely emergency care, as in the case of a sudden outbreak or injury;
- Some rural, suburban, and even urban communities with livestock have difficulty finding veterinarians who are knowledgeable or able to provide care for particular livestock species (e.g., sheep, goats, poultry, rabbits); and
- Some owners who raise livestock animals for personal use, or those with low profit margins, find it cost-prohibitive to use a veterinarian, leading to owner and veterinary concerns regarding animal welfare.

AUS has identified underserved regions and populations of California using veterinary location mapping, the AUS veterinarian shortage online reporting tool, surveys, and anecdotal reports from presentations and workshops. With this information, AUS leverages relevant national and State efforts to increase access to veterinary services in regions with an apparent shortage situation.

These efforts have included involvement with USDA National Institute of Food and Agriculture (NIFA) programs. For example, CDFA assists with designating regions with a veterinary shortage that may qualify new practitioners who work in the identified area for financial support through the USDA NIFA Veterinary Medical Loan Repayment Program. Additionally, AUS collaborated with North Carolina State University, a 2017 recipient of the USDA NIFA Veterinary Services Grant award, on the development of training modules for rural, mixed-animal veterinarians that address residue avoidance and antimicrobial stewardship in livestock. AUS also supported a USDA NIFA Veterinary Services Grant proposal from Washington State University to better understand practitioner implementation of antimicrobial stewardship guidelines and prepare veterinary students to work more effectively with clients.

AUS has developed a guidance document on the VCPR, called the *Youth Agriculture Model*, to address the unique challenges of the younger livestock producers in California. Leaders in 4-H and Future Farmers of America (FFA), as well as commercial livestock producers, have voiced concerns regarding the vulnerability of the youth agriculture population regarding access to veterinary care. The California Veterinary Medical Board advised AUS, so as to ensure that the VCPR practice model for youth agriculture is compliant with California VCPR regulations. Materials have been distributed to the California Agricultural Teachers' Association and 4-H statewide and county offices. This outreach offers an opportunity to discuss the importance of the VCPR with future California farmers, and strengthen their support for the veterinarian-producer partnership.

Non-commercial and small-scale producers impacted by the Law may also face limited access to veterinary care. Presentations and direct communication with organizations and subgroups within this industry focus on issues that are not traditionally addressed. These are crucial outreach opportunities; by identifying and approaching smaller segments of producers, AUS will be better positioned to understand their unique challenges and provide contacts for further clarification and discussion of concerns.



To better understand private veterinary practice demographics in California and identify practitioners who would be willing to expand their practice to include underserved livestock populations, AUS developed the Veterinary Services and Expansion Questionnaire. The survey was promoted and distributed with the help of the California Veterinary Medical Association (CVMA). The majority of respondents indicated they would be interested in further education specifically focusing on livestock veterinary care, even if they were not currently able or willing to expand their practice. AUS plans to conduct more such surveys of the California veterinary profession in the coming years; this initial survey was useful not only for outreach, but also in helping assess effective methods for surveying veterinarians in the state.

To further support practitioners interested in expanding their practice, AUS veterinarians provided continuing education at the CVMA Pacific Veterinary Conference on the judicious use of antimicrobials in livestock to small animal veterinarians interested in treating livestock. Likewise, for the Veterinary Information Network (VIN) Rounds Webinar, AUS veterinarians provided an easily accessible, online, continuing education session called *Antimicrobial Policy + Implementation* to small animal veterinarians interested in treating livestock.

Finally, to promote veterinary access for California's diverse population of livestock owners, AUS collaborated with the UC Cooperative Extension to make their very popular poultry website available in Spanish. According to the U.S. Census Bureau, 44.6% of California's 39 million residents speak a language other than English at home. Over 9.5 million California residents (28%) identify Spanish as the most spoken language in their homes. Particularly in Southern California, veterinary access and information available in Spanish is a crucial component of bird care. The webpage provides science-based information regarding commercial and backyard poultry to this audience. Information on antibiotic use, avian diseases, biosecurity, and basic husbandry, among other topics, is also provided. Users can contact experts, including veterinarians who treat backyard flocks, via the website contact links.

Ongoing Outreach Efforts

Education and outreach is ongoing as AUS continues to engage with stakeholders and promote voluntary surveys and research efforts to monitor trends in antimicrobial use and AMR while receiving valuable feedback for the program. AUS veterinarians continue to be invited to give presentations for livestock producers and veterinarians. AUS program leaders are optimistic regarding the interest shown by the livestock industry and veterinary profession in responsible antimicrobial use and reducing AMR.

Exploring Existing Monitoring Systems

As California is the first state in the U.S. to pass legislation requiring the monitoring of antimicrobial use and antimicrobial resistance (AMR) in livestock, it has the opportunity to demonstrate how a novel, successful program can be designed to put the current and future needs of diverse livestock populations at the forefront. Data reported by the AUS program are used for monitoring and to inform the development of recommendations and new outreach materials focused on stewardship and judicious use of antimicrobials. Significantly, the data gathered through the AUS program reflects California's unique livestock assets while also being comparable to national and international efforts where possible.

Section Highlights

- **AUS researched other systems in the U.S. and internationally as guidance**
- **The design of a monitoring system should be tailored to the specific needs of the program**
- **AUS coordinates with national efforts, including NAHMS and NARMS, where possible**
- **AUS will identify and focus efforts on livestock populations and practices of highest risk for fostering AMR in California**

Key Acronyms

- **AMR – antimicrobial resistance**
- **MIAD – medically important antimicrobial drug**
- **NAHMS – National Animal Health Monitoring System**
- **NARMS – National Antimicrobial Resistance Monitoring System**
- **VFD – veterinary feed directive**

Multiple programs are already in place, both in the U.S. and abroad, to monitor antimicrobial use and AMR. The AUS team gathered and evaluated information on these programs and their methodologies through a literature review, participation in webinars, and consultation with food and agriculture experts and government entities, such as the European Food Safety Authority. CDFA has prioritized the assessment of these varying systems and incorporation of those aspects that make sense for the specific demographics of California agriculture, while collaborating with existing U.S. surveillance efforts when feasible and appropriate.

International Efforts

The literature review focused on antimicrobial use and AMR monitoring and reporting systems worldwide to determine which, if any, strategies may be applicable in California. One pattern AUS researchers identified was that data collection efforts tend to prioritize the largest and most economically valuable industries.[5,6]

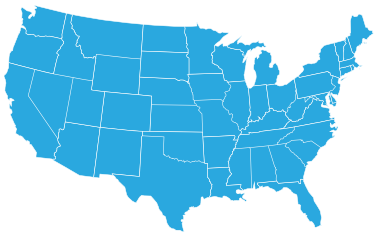
Worldwide, antimicrobial drug sales data are largely employed as a proxy for use. This is because the collection of actual on-farm usage data is highly resource-intensive. Although there is no consistent metric for reporting antimicrobial use internationally, many European countries report this data utilizing a variation of a Defined Daily Dose calculation that is standardized for a given species based on various factors such as estimated weight at treatment, active ingredient, main indication for use, and route of administration.[6-8]

Although useful, sales data have known limitations. Sales data may be reported in the aggregate, rather than by animal species, and may not be comparable across reporting entities. Trying to compare total sales data across geographic areas risks misinterpretation, so establishing dependable antimicrobial use information by animal species is considered essential.[9] Another issue is that many calculations incorporating sales data utilize assumptions and estimations about the way a product is used and the timing of use, rather than actual on-farm usage data, which can lead to inaccuracies in the results.[10] Thus, sales do not necessarily reflect what is administered to livestock,[9] nor do they provide insight into the reason for use of the drugs. Overall, a decrease in AMR does not always occur in tandem with decreasing antimicrobial sales figures.[11] Other factors may be more important in AMR than antimicrobial consumption as measured through sales, highlighting the value of applying other antimicrobial use data in addition to sales data.[12]

Across systems reviewed by AUS, AMR in livestock is most commonly monitored through samples from healthy animals, sick animals, samples taken at slaughter, and samples from retail meat. Each of these sample types has different advantages and provides valuable information.[13,14] Both indicator bacteria and zoonotic bacteria offer important insights for AMR monitoring. Indicator bacteria are those that generally do not cause disease yet easily acquire resistance and are commonly found in the intestinal tract of different species, including humans. Zoonotic bacteria are important because they may transfer resistance from animals to humans and may cause human infection.[14] Reports from other surveillance systems show that minimum inhibitory concentrations (MICs) determined by micro-broth dilution methods are commonly used to assess drug resistance in these bacteria.[5,15]

In some European countries, antimicrobial use and AMR metrics are used to target regulation and benchmarking to meet national reduction targets; however, simply reducing use does not consistently result in reduced AMR.[5,16,17] There has been limited research into the impacts of reduced antimicrobial use on animal health and welfare in Europe.[5]

Much of the data reported in other countries is obtained through mandatory reporting systems,[5] which differs from current California Law (FAC Section 14405(c)). To gain perspective from a system that relies on voluntary participation, AUS participated in a webinar with representatives from the Canadian Integrated Program for Antimicrobial Resistance Surveillance. That program provides monetary incentives to participants at selected sentinel sites. Although the program began in 2004, its publishable data are available from 2014, demonstrating the considerable amount of time such a system takes to establish. AUS research efforts to look at international systems led to the conclusion that the design of a country's surveillance program should be tailored to the specific needs of the program and country.[14]



National Efforts

In the U.S., the FDA plays the lead role in regulating the use of antimicrobial drugs in livestock and other animal species. Starting in 2008, the FDA required drug sponsors to annually report the amounts of active antimicrobial drug ingredients in their products that were sold or distributed for use in food-producing animals.[18] Reports on this sales information, which is provided on a national scale only, have been made available by the FDA since 2009.[19] More recently, in 2016, the FDA started requiring drug sponsors to estimate the proportions of each drug meant for administration to different livestock species and to provide those estimates in their annual reports. The "2017 Summary Report on Antimicrobials Sold or Distributed for Use in Food-Producing Animals," which was the first such report to be released following national changes to increase veterinary oversight of antimicrobials, was published in December 2018.

The FDA's rule requiring veterinary oversight of the administration of identified drugs in animal feed or water, through a VFD or a prescription, respectively, came into effect on January 1, 2017. FDA has conducted outreach on VFDs and is initiating enforcement of the VFD regulations through reviews of a sample of VFDs found at manufacturers and distributors. From this information, FDA plans to begin a trace forward and back inspection, including visits with the issuing veterinarian and with the producer. To better understand how antimicrobial drugs are being used, the FDA has funded two multiyear studies of antimicrobial use that encompass nationwide beef, dairy, poultry, and swine populations. The goal of the studies, in addition to suggesting sustainable means to collect usage data, is to identify metrics for reporting use in the context of other on-farm data, such as animal health outcomes. Results of these studies will be made available by FDA upon completion. AUS has participated in meetings with the researchers on these two projects, so as to be part of the discussion on appropriate U.S. metrics for antimicrobial use.

Recently, the FDA released a five-year plan, *Supporting Antimicrobial Stewardship in Veterinary Settings: Goals for Fiscal Years 2019-2023*, that outlines a phased approach to attaining key goals and objectives for the near term, including enhancing monitoring of antimicrobial use and AMR in animals and fostering antimicrobial stewardship.

The USDA's National Animal Health Monitoring System (NAHMS) systematically collects, analyzes, and disseminates data, collected primarily through in-person interviews, on animal productivity, health, and management across multiple livestock production sectors.[20] While NAHMS includes questions about antimicrobial use in its surveys, in 2017 it implemented a more in-depth assessment of use in beef feedlot and swine production sectors. At the time of writing, reports from these in-depth studies were not yet published.

The National Antimicrobial Resistance Monitoring System (NARMS), which was established in 1996, is the primary entity for AMR monitoring in the U.S. A collaboration between USDA, FDA, and CDC, the system monitors resistance trends of intestinal bacteria identified in food animals at slaughter (USDA), retail meats (FDA), and ill people (CDC). California is

one of 15 states where retail meat is sampled under the program. In addition to antimicrobial susceptibility testing, NARMS also conducts genetic characterization of identified bacteria. The information gathered by NARMS is presented publicly through a variety of reports, including the *NARMS Integrated Report* and the NARMS Now interactive webpage. Where NARMS data presented in these forums are not broken down by state, AUS has made a request to obtain California-specific data. Unfortunately, the results of NARMS testing cannot be linked to the food animal's state of origin, as animals and meat frequently cross state borders during processing and marketing. For this reason, retail samples collected through NARMS in California may not be indicative of foodborne pathogens or AMR on farms in California and do not necessarily reflect the impact of antimicrobial use practices in California.

FAC Section 14405(b) directs AUS not to duplicate the efforts of NAHMS and NARMS partners and, to the extent feasible, to coordinate with them.

California Wholesale-level Medically Important Antimicrobial Drug (MIAD) Sales

AUS worked with the California State Board of Pharmacy to evaluate collection of MIAD sales information at the wholesale level. The wholesale level was selected because the California State Board of Pharmacy has the authority under CCR Title 16, Section 1782 and Business and Professions Code Sections 4081 and 4332 to collect information at this level of the drug distribution chain. Moreover, wholesale numbers could theoretically account for the maximum amount of MIAD sales in the state; collecting this information would require fewer data exchanges than information sought at the retail level.

A preliminary assessment revealed that the data found at the wholesale level were flawed in many respects. Numerous firms indicated that they were unable to determine if the drugs would be used in livestock, so their reported sales figures sometimes included non-livestock applications. Although detailed specifications were given for providing the data, most firms did not report in the requested format and many were missing key pieces of requested information. Additionally, some firms reported resource challenges in meeting this unusual information request. The burden was especially significant for small firms, one of which reported needing 70 person-hours to fulfill the request.

Based on the significant challenges encountered in this initial process, it has been determined that wholesale pharmaceutical data will not meet the needs of the AUS program. The data received in this pilot process were incomplete; following up to obtain the missing information and reformat all the data for analysis would require a substantial amount of personnel time. Most importantly, it is not possible to ascertain at the wholesale level whether the drugs were used, or intended for use, in livestock species nor whether the drugs were used or intended for use in the State of California. Future efforts to collect MIAD sales data would best be focused on Veterinary Food Animal Drug Retailers and indicator drugs or formulations that are highly likely to be intended for use in livestock residing in California.

Focus on Risk in California

In developing the first statewide antimicrobial use and resistance monitoring program in the country, AUS is laying the groundwork for a risk-based system through which data can be compared over time, detecting relevant change and sharing representative information with California's livestock industry to promote behaviors that mitigate the development of AMR. AUS is engaged with experts in the field of antimicrobial use and AMR monitoring and reporting, within California and nationally, and is committed to remaining up-to-date on scientific literature and national efforts in order to implement a system that is evidence-based, meaningful, and sustainable. Overall, evaluations of foreign programs demonstrated the challenges of comparing data broadly between countries or geographic areas.[5,9,21-24] The information AUS is gathering, as described below, will help to identify the livestock populations and practices in California most at risk for fostering AMR. The monitoring system will be refined to focus efforts on the areas of highest risk, as determined through scientific evidence and AUS data collection processes.

Creating a Monitoring System for California's Diverse Livestock Population

AUS formulated an initial approach to antimicrobial use and AMR data collection, key features of which are summarized in **Figure 7**. This approach focuses on launching studies to obtain an accurate picture of current livestock management practices and animal health in California, as they relate to antimicrobial use and AMR, and to assess the best ways to engage livestock industries in these efforts. These studies serve to build a solid foundation and establish a process for the ongoing, risk-based monitoring efforts of the AUS program and will include longitudinal studies, so that findings can be compared over time. Information collected will also serve to inform AUS' antimicrobial stewardship and other outreach materials, as well as be published through various channels to be shared with livestock owners, veterinarians, the scientific community, and the public.

Section Highlights

- **Information now being gathered through a variety of means will shape subsequent risk-based monitoring and stewardship activities and will also be shared with stakeholders**
- **Both indicator and zoonotic bacteria collected from farms are evaluated for resistance to drug classes important in human medicine**
- **AUS assesses the representativeness of data collected to ensure it is statistically relevant**

Key Acronyms

- **AST – antimicrobial susceptibility testing**
- **CAHFS – California Animal Health and Food Safety Laboratory**
- **MIAD – medically important antimicrobial drug**
- **NAHMS – National Animal Health Monitoring System**
- **VFD – veterinary feed directive**

Approach to Data Gathering

FAC Section 14405 (b)(2) mandates that AUS gather data on all of California's major livestock segments, as well as regions with considerable livestock production, and representative segments of the food production chain. Accordingly, AUS has initiated early data collection efforts focused on California's relatively large and economically valuable cattle and poultry industries; dairy, beef, and poultry are three of the top 10 commodities in California agriculture.[25] As mentioned above, this practice is consistent with priorities of antimicrobial use and AMR surveillance in other countries. Additionally, AUS' data collection efforts leverage opportunities provided through federal partners, such as NAHMS, and industry support.

As the output of any monitoring system is only as good as the data it collects, AUS strives to collect representative data that will provide a meaningful understanding of antimicrobial use and resistance in California's livestock. FAC Section 14405(d)(1) requires data collected voluntarily to be "statistically relevant," which is interpreted in the context of this program to mean that the data are reasonably unbiased and representative of the population. "In the context of research, bias is the introduction of systematic error, subconsciously or otherwise, in the design, data collection, data analysis, or publication of a study."[26] While statistical methods are available for working with data sets of any size, biased data inherently lack quality and are not reliable for making valid statistical inferences.[27-30] Therefore, AUS data collection processes are aimed, first and foremost, to minimize bias and to obtain information from a sample population that is representative of the larger livestock population in California. As comprehensive baseline data about California's livestock populations and their management may be limited, unknown, or unpublished, AUS evaluates representativeness of its data primarily through comparisons of sampled herd sizes and geographic locations with alternative, available sources of data, such as NASS and NAHMS – a process undertaken by other organizations conducting surveys.[31]

Many of AUS' data collection activities, both in-house and contracted through external researchers, utilize surveys to assess information on antimicrobial use, management practices, and animal health across the state. Survey response rates are dependent upon many factors, including survey content and survey sponsor.[32-34] Additionally, it has been noted in previous studies that survey response rates have tended to be higher in smaller (<1000 participants) surveys as compared to larger ones.[35,36] Although response rates to surveys have generally been in decline for many years,[31,35,37-39] responses from a relatively small proportion of the population can provide valid and representative results.[31,40-43] For example, following years of a declining response rate, the Pew Research Center determined, through comparison with data from federal sources, that information obtained from a 2012 survey with a 9% response rate was an accurate representation of the studied population.[31] As described above, AUS takes a similar approach in evaluating how representative its data is of the larger livestock population in California.

Information from producer groups and industry indicate that mail surveys remain the best way to reach most producers in California, especially as available contact lists most frequently contain mailing addresses. Despite the availability of other survey modes and techniques aimed to improve response rates, mail surveys can continue to achieve superior response

rates[37,40,44,45] and can be the most cost-effective approach.[37,46] Mail surveys can provide assurance of anonymity, which helps to encourage participation. Additionally, the information provided in the survey packet serves as outreach to inform recipients about the Law and the AUS program. For these reasons, AUS has focused its in-house efforts on mail surveys, in conjunction with information gathered through contracted on-farm sampling and longitudinal studies, and will continue to explore electronic reporting and other data-gathering methods for use in future activities.

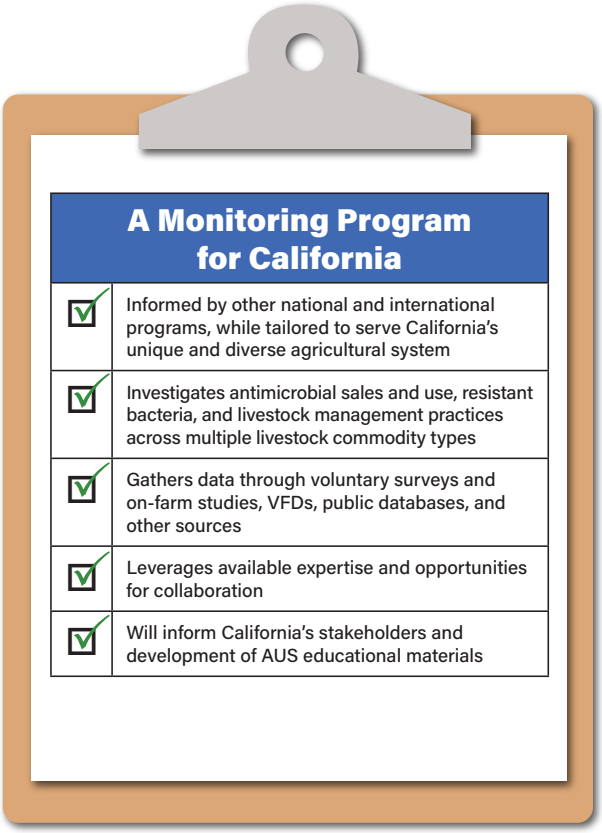


Figure 7: Key Qualities of California's Monitoring Program.

Goals of Antimicrobial Use Reporting

In California, the goals of antimicrobial use reporting are to monitor trends, to inform the development of educational materials that are relevant for producers, and to promote antimicrobial stewardship and judicious use practices that mitigate the development and persistence of AMR. AUS has focused its efforts on information gathering and the use of multiple strategies to determine, in an incremental manner, how best to accomplish these goals in California. As mentioned above, collecting antimicrobial sales data represents one way to look at usage. Although useful, sales data represent only part of the whole picture of antimicrobial use in California's livestock. Veterinary antimicrobial prescriptions and VFDs, like prescriptions authorized in human medicine, are a form of permission to purchase or obtain the prescribed drug and do not necessarily reflect the actual amount of medicine administered to the animal or group.

Conversations in antimicrobial use metrics development meetings emphasize the differences in record keeping, management practices, and animal health considerations across and within livestock production types. Each industry requires a different approach to optimize monitoring and reporting efforts, and producers must see business value in the information. As noted by the European Union and Canada, consistency of metrics used across countries is critical.[5,6,13,47] However, discussions around metrics also note the dangers in aggregating use numbers to represent all livestock, because the meaning of different metrics varies across industries. For these reasons, AUS has complemented collection of VFD sales data with surveys and studies that gather on-farm use information, customized for each livestock production type.

On-Farm Sampling for Antimicrobial Resistance

The determination of appropriate, evidence- and risk-based AMR monitoring and reporting methods is of vital importance to the AUS program. AMR data need to be relevant for California while also comparable to other efforts, where possible. This applies not only to the drugs tested, but also the testing procedures and reporting methods.

As mentioned above, AMR in livestock can be monitored through samples taken at different points in the food production chain. To address the AUS program's immediate priorities, on-farm sampling provides the main source of AMR data. On-farm sampling provides information that is not available elsewhere, can most directly be linked to use in livestock, and readily translates to inform stewardship practices for California's producers. Furthermore, samples taken from the same farms over time, when linked with usage data, can provide valuable information on the effects of antimicrobial use and other management practices on AMR.

On-farm sampling provides information that is not available elsewhere, can most directly be linked to use in livestock, and readily translates to inform stewardship practices for California's producers.

Selecting Microbes and Drugs to Test for Antimicrobial Resistance

Bacteria are the focus of AUS' monitoring efforts, as directed by FAC Section 14405. Review of other monitoring systems shows that isolates of *E. coli* and *Enterococcus* species are most commonly chosen as indicator bacteria.[5,13,14] *Salmonella* species and *Campylobacter* species are commonly chosen to represent foodborne bacteria, especially as they are the leading bacterial causes of foodborne illness in the U.S.[5,13,14,48] AUS studies are currently evaluating each of these bacteria.

The Law focuses AUS priorities on medically important antimicrobial drugs (MIADs); thus, antimicrobial drugs and drug classes that are important to human health should be considered for antimicrobial susceptibility testing (AST). AST determines to which antimicrobial drugs a particular bacterium—as identified by its physical traits—is most sensitive. As mentioned in the Program Stakeholders and Collaborators section, AUS funding enabled the CAHFS Laboratory to offer micro-broth dilution methods for AST, consistent with best practices in other AMR monitoring systems.

Many drugs important in livestock health are in the same drug classes as MIADs but may differ in specific molecular structure. In order to provide information most relevant for livestock producers and veterinarians, AUS may test for drugs specific to livestock production that fall into MIAD classes.

In addition to AST, other methods of detecting and characterizing antimicrobial-resistant bacteria are emerging. Denmark's DANMAP 2015 Report notes future directions in this area involve using next generation whole genome sequencing to identify resistance genes in parallel with AST.[6] When scientists better understand the relationship between a bacterium's genetic code and its susceptibility, it can be studied with a higher level of precision and new resistance genes can be identified.

AUS is collecting both genetic and clinically relevant information on bacterial samples, with an eye toward future data needs. These monitored variables will be adapted and modified based on AUS experiences and as scientific research evolves and further informs understanding about the causes of AMR and best practices for AMR monitoring.

About the Livestock Industry Surveys and Contracted Studies

In 2017 and 2018, AUS initiated multiple surveys and studies in priority livestock groups, both in-house and contracted through external researchers, to help identify the most effective approach for long-term antimicrobial use and AMR monitoring in California. These focus on assessing antimicrobial sales, use, and resistance trends, as well as related animal management and health information. Details about each of these efforts can be found in the next sections.

Voluntary participation helps to engage livestock producers, create program buy-in, and ensure that AUS' stewardship materials are evidence-based, meaningful, and practical for California's many different livestock industries. Survey content has been identified as the most important factor in stimulating response rates.[32,33] AUS' focus on industry buy-in helps to promote participation by ensuring that survey content not only aligns with program goals, but also addresses industry's needs, uses of antimicrobials, and priorities. Additionally, pursuant to the mandates of FAC Section 14407, and in alignment with the National Action Plan on Combating Antibiotic-Resistant Bacteria,[49] data collected by AUS is held confidential. Maintaining this producer confidentiality encourages participation and meaningful responses.

Following data collection, validation, and analysis processes, results from these surveys and studies will be shared in a multitude of ways in order to be useful and accessible to a variety of audiences.

Livestock Industry Surveys

The AUS Surveys and Studies team works to fulfill the mandates set forth in the Law regarding data collection and validity, with one veterinarian specialist and two epidemiologists focused on survey development, data collection, data analysis, and reporting. In the first two years of the program, this small team has implemented two in-house, statewide surveys: a survey of cow-calf beef producers mailed out in October 2017 and a survey of commercial sheep producers mailed out in June 2018. As mentioned previously, mail-out surveys were chosen in order to reach a wide range of producers and provide assurance of anonymity. Industry feedback supports this approach, as opposed to electronic means; moreover, mailing address contact information is most readily available.

Section Highlights

- **The AUS Surveys and Studies team has implemented two in-house, statewide surveys**
- **Both surveys effectively engaged livestock owners across the state, with responses mirroring California's livestock demographics**
- **AUS' in-house data collection and monitoring activities feed directly into stewardship activities**
- **Results will also be shared directly with livestock owners and the public through various channels, including summary and annual reports**

Key Acronyms

- **FFA – Future Farmers of America**
- **NAHMS – National Animal Health Monitoring System**
- **NASS – National Agricultural Statistics Service**
- **VFD – veterinary feed directive**

Results from AUS' in-house data collection and monitoring efforts will be shared through formal and informal channels, as appropriate to program goals and audiences. Results for each study will be shared in summary and commodity-specific reports within six months of completing all study activities and in the AUS annual report at the end of the fiscal year. More in-depth analyses may be considered for publication in peer-review journals. As the processes of data collection, validation, analysis, and publication are resource- and time-intensive, AUS also may discuss preliminary information with industry groups in order to guide analytical queries and receive feedback on program materials. Internally, in an ongoing process, preliminary and final results from AUS' in-house efforts inform stewardship resources and guide program efforts. Findings presented below are preliminary, as data analysis is currently ongoing for all surveys and studies.

Cow-Calf Beef Survey

The beef sector was identified as a major livestock industry important to California.[50] The preeminence of this industry, coupled with the support and partnership of the California Cattlemen's Association, made beef cow-calf producers an ideal population for AUS' first in-house survey. Cow-calf operations represent herds mostly made up of breeding cows and their offspring for production of feed stock destined for beef. The AUS Cow-Calf Beef Survey was developed in collaboration with multiple stakeholders, including expert guidance and feedback from federal partners at USDA NAHMS and researchers at UC Davis. Additionally, AUS worked closely with the California Cattlemen's Association to develop and pre-test the survey form, as well as promote participation, and continues to collaborate regarding useful ways to report findings.

The AUS Cow-Calf Beef Survey was mailed out to 11,589 presumed cow-calf producers across California in October 2017. USDA National Agricultural Statistics Service (NASS) Agriculture Census data from 2012, the most recent published census, reported 10,925 beef cow ranches in California, representing 1,324,558 beef cattle and calves, which would include cow-calf operations.[51] At least one survey was mailed to each of the 58 counties in California; survey distribution is similar to that of the most current USDA NASS estimations of beef cow ranches[52] and beef cows[53] across the state.

Along with promoting participation in the Cow-Calf Beef Survey through AUS social media, presentations and outreach, and other CDFA networks, the survey was also promoted by the California Cattlemen's Association to its members, with AUS staff being invited to speak at multiple regional meetings and attend the Annual Conference. In total, AUS received 937 completed surveys. This demonstrates a response rate of 8.1% (937 responses/11,589 surveys mailed), which is similar to that observed in a recent, published survey of cattle producers (9%).[54] These AUS survey responses represent 8.6% of beef cow ranches in California.[51] Additionally, surveys received reported a total of 180,690 beef cattle, representing 13.6% of estimated total beef cattle and calves across California.[51]

The survey questionnaire focused on calendar year 2016, the year prior to implementation of the FDA's VFD final rule and California's Law, and asked about animal management practices, including antibiotic use, as well as animal health, decision-making, and veterinary engagement. Asking about practices prior to federal and State changes surrounding antimicrobial use provided the opportunity to collect baseline data in this industry. The survey responses received represent management practices from 55 of California's 58 counties. The three counties with no responses each represent less than 0.5%

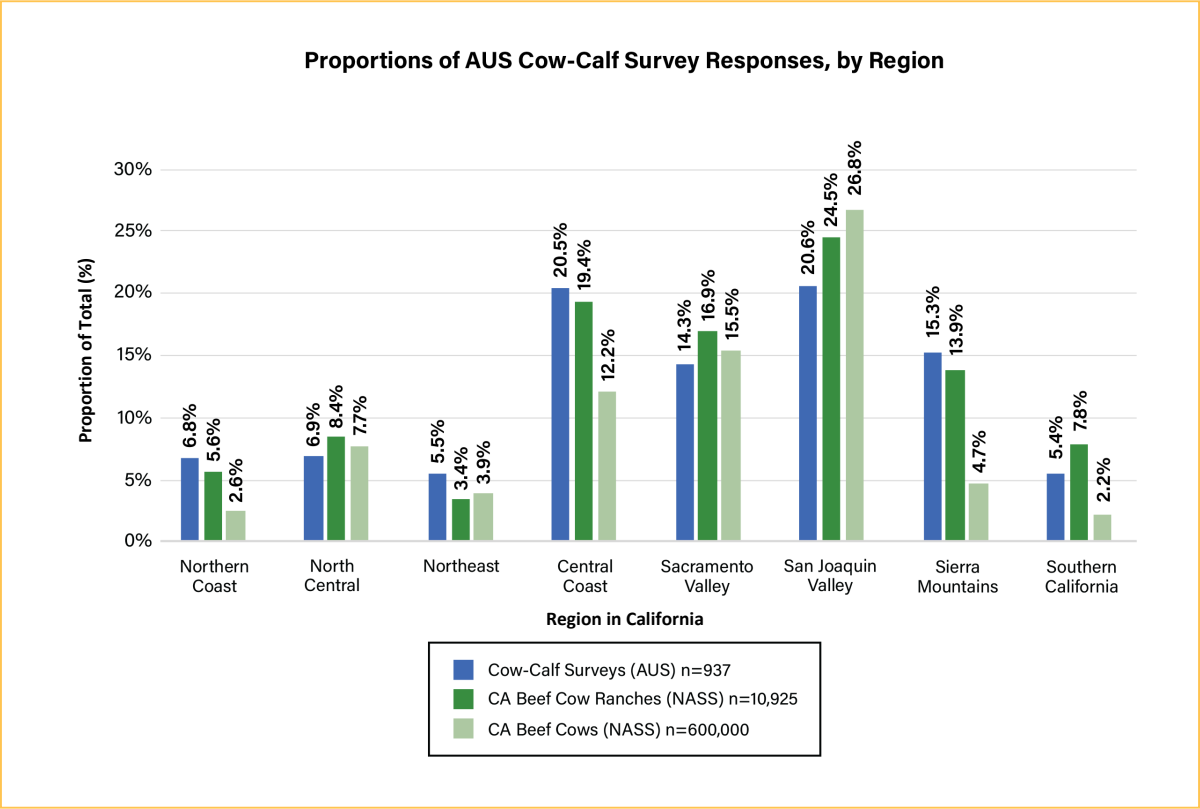


Figure 8. Proportions of AUS Cow-Calf Survey Responses, by Region. Proportions of AUS 2017 Cow-Calf surveys compared with proportions of NASS total beef cow ranches (2012) and total beef cows (2016), per California region.

of California's beef cow ranches[52] and less than 0.15% of beef cows;[53] one of these counties has no county-level beef cow estimates reported. Survey response distribution, as shown in **Figure 8**, is similar to that of the most current USDA NASS estimations of beef cow ranches[52] and beef cows[53] across regions of California. Regions used in Figure 8 are modeled after NASS-designated regions and are used to aggregate responses across the state, protecting respondent confidentiality. These regions do not necessarily reflect regions that will be meaningful for future analysis and AUS reporting.

The range of herd sizes reported in surveys received compare to NASS estimations for beef cow ranches per herd size, as shown in **Figure 9**. The AUS Cow-Calf Beef Survey represents a higher proportion of responses from larger cow-calf operations; this difference is primarily driven by the larger number of herds with 1 to 9 beef cattle included in NASS estimates compared with AUS survey responses. For AUS' survey, smaller farms may be less likely to self-identify as cow-calf operations. This herd size group of 1 to 9 beef cattle, although including a large proportion of California's ranches, represents less than 5% of California's total beef cattle.[51] In terms of impact, larger operations are more likely to contribute to the food supply and their management practices affect more cattle across California.

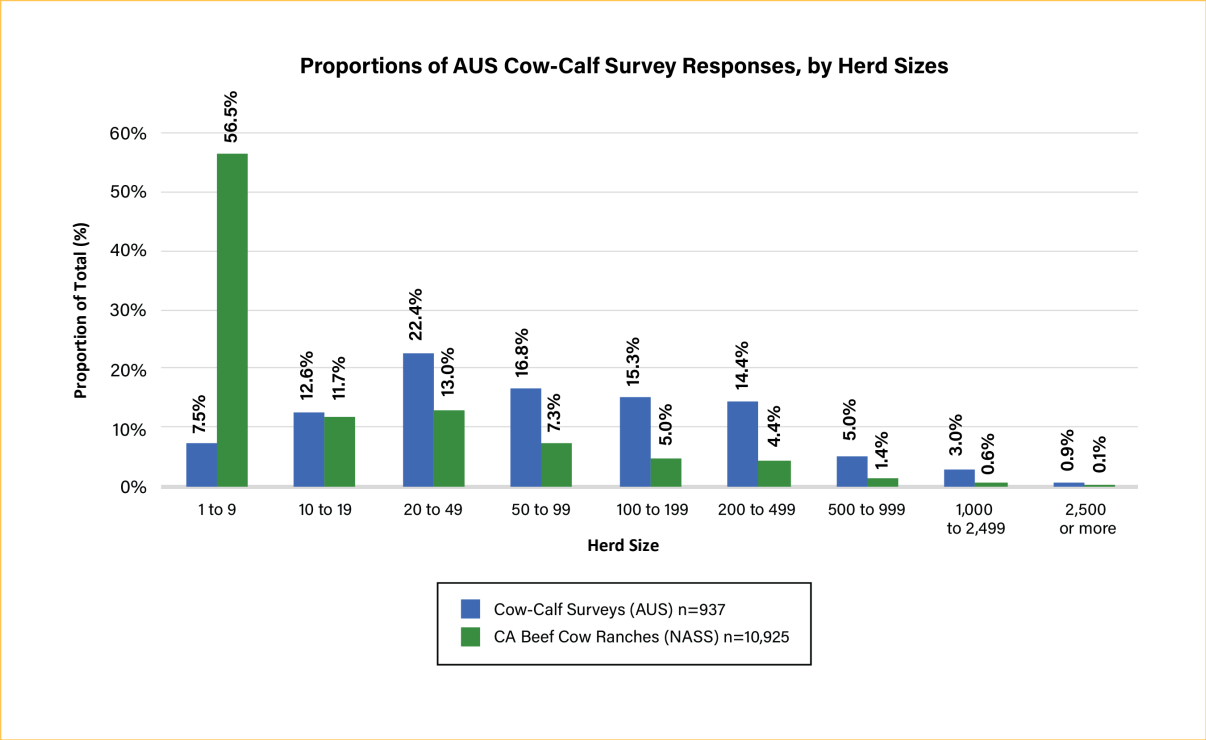


Figure 9. Proportions of AUS Cow-Calf Survey Responses, by Herd Sizes. Proportions of AUS 2017 Cow-Calf surveys reporting each herd size compared with herd size proportions of NASS total beef cow ranches (2012) in California.

With responses reflecting the distribution of beef cow ranches and beef cows across the state, including responses from most of the counties in California and a range of operation sizes, the Cow-Calf Beef Survey successfully engaged a diverse group of producers throughout the state. Analysis of survey data is ongoing in preparation for dissemination of findings.

Commercial Sheep Survey

AUS adapted the mail-out survey instrument used for cow-calf producers for application to commercial sheep operations. The commercial sheep producers were asked about their antimicrobial use and animal health management practices for the year of 2017. After acquiring the advice of sheep experts interviewed during the initial survey planning process, it was determined that hobbyists, backyard sheep owners, and youth agriculture (4-H and FFA) utilize practices that appear to vary from commercial producers. Surveying these groups at the same time as commercial producers would require an impractically long and complicated survey questionnaire. These groups were excluded from this survey and will be engaged at a future date.

AUS met with the California Sheep Commission board ahead of the survey's release to explain the purpose and intended uses of the data, and to promote engagement. The California Wool Growers Association and California Sheep Commission each expressed their strong support for the survey and actively requested participation from their members. Four members of the California Wool Growers Association volunteered to pretest the survey questionnaire. Their valuable feedback helped assure the questionnaire was understandable and applicable to the commercial sheep producers of California.

The survey was mailed out to 658 commercial sheep producers; 109 surveys were completed and returned. This gave a response rate of 16.6%. Surveys were received from 40 of the 51 (78%) counties to which they were mailed across California. The 109 surveys comprised antimicrobial use and health management practices for operations responsible for 111,145 total sheep. This is 18.5% of all sheep in California as determined by NASS.[55] **Figure 10** uses NASS 2012 data to demonstrate that AUS was successful in primarily capturing the commercial sheep operations. This can be seen when looking at the 1 to 24 sheep category; NASS census captured many more operations in this group.[56] Other than the 1 to 24 sheep category, the data show that the AUS survey responses had a similar distribution of herd sizes compared with the NASS 2012 Census data. This demonstrates the AUS survey responses garnered good representation of all different sizes of commercial sheep operations. It is worth noting the AUS survey captured more large operations, including eight sheep operations which had 5,000 or more sheep. Analysis for distribution of findings is ongoing.

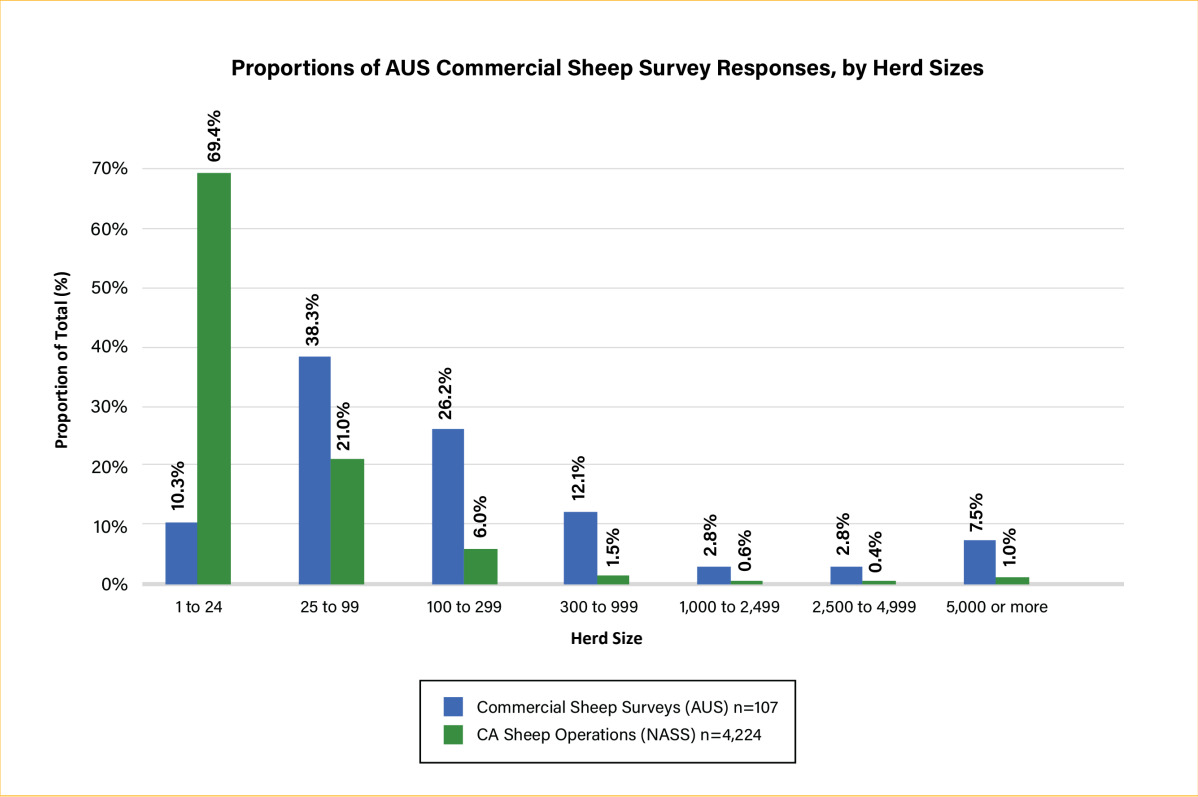


Figure 10. Proportions of AUS Commercial Sheep Survey Responses, by Herd Sizes. Proportions of AUS 2018 Commercial Sheep surveys reporting each herd size compared with herd size proportions of NASS total sheep operations (2012) in California.

Contracted Studies of the Livestock Industry

Section Highlights

- **AUS' contracted studies leverage available expertise and opportunities for collaboration, while encouraging voluntary participation**
- **Survey responses to date representatively mirror statewide livestock populations**
- **Studies now in progress will evaluate on-farm antimicrobial use and resistance**

Key Acronyms

- **MIAD – medically important antimicrobial drug**
- **NAHMS – National Animal Health Monitoring System**
- **NASS – National Agricultural Statistics Service**
- **VMTRC –Veterinary Medicine Teaching and Research Center (Tulare)**

As mentioned earlier, AUS works with university researchers to conduct a number of studies. A side benefit of being able to leverage researcher expertise is the increased likelihood of participation associated with university-sponsored studies. It has been observed that study sponsor is an important factor in increasing response rates, and that surveys conducted by universities have been found to receive greater returns than those conducted by other survey sponsors.[32,34] The information obtained from the studies described below will be published in peer-reviewed, scientific journals by the research investigators, and is expected to further inform the growing body of scientific literature on antimicrobial use and AMR in livestock. Given the 18 - 24 month timeframe commonly involved with the peer review process, preliminary, summary information from contracted studies may be shared directly with AUS to inform AUS antimicrobial stewardship materials, such as those targeted at the dairy and poultry industries. Data are fully protected from any disclosure of individual information, in accordance with FAC Section 14407, and are aggregated into regional or statewide values to ensure confidentiality of respondents.

Dairy Calf Studies

Under a contract with AUS, researchers at the UC Davis Veterinary Medicine Teaching and Research Center (VMTRC) surveyed California dairies and calf nurseries about management practices and antimicrobial use in pre-weaned calves. Questionnaires were mailed to 1,413 producers throughout the state in June-July 2017, with an overall response rate of 12.3%. Regional response rates were similar across the dairying regions of the state, with regions based on identified differences in management practices between the three milk sheds[57] (**see Table 1**). Most responding dairies (49.7%) were from greater southern California (GSCA, which included southern San Joaquin Valley), with smaller proportions responding from the northern San Joaquin Valley (NSJV, 34.3%) and northern California (NCA, 16.0%). The distribution of survey respondents is very similar to the actual distribution of dairies in the state: GSCA 43.7%, NSJV 40.4%, and NCA 15.8%.[58] Responses were received from 20 of the 30 (66.7%) counties to which they were mailed. Counties with licensed dairies that were not represented in the survey responses had very few dairies (average 1.8 dairies per county, range 1-4). A total of 23,120 calves were represented by the survey data. The herd sizes of responding dairies are strikingly similar to the distribution of dairy herd sizes reported by NASS in 2012, with the exception that more large herds (2,500 or more) were captured by the VMTRC survey **(see Figure 11)**.

Table 1. Response Rates and Numbers of Milking Cows, by Region, in AUS Dairy Surveys. Response rates and numbers of milking cows represented in total and by dairy region for AUS-funded studies (2017-18) of antimicrobial use in dairy calves and adult dairy cows.

	Calf Survey	Adult Survey*
Survey Response Rate		
Northern California (NCA)	12.3%	7.4%
Northern San Joaquin Valley (NSJV)	10.5%	9.4%
Greater Southern California (GSCA)	14.0%	8.3%
State Total	**12.3%**	**10.8%**
Adult Cattle Represented **		
NCA	7,810 (8.6%)	7,203 (7.9%)
NSJV	61,614 (9.9%)	59,445 (9.6%)
GSCA	147,610 (14.7%)	92,051 (9.1%)
State Total	**217,034 (12.6%)**	**168,876 (9.8%)**

* Preliminary data available at the time of writing. An additional survey reminder went out in October 2018 and will likely increase the survey response rate.

** Denominator data from CDFA 2017 Annual Dairy Statistics

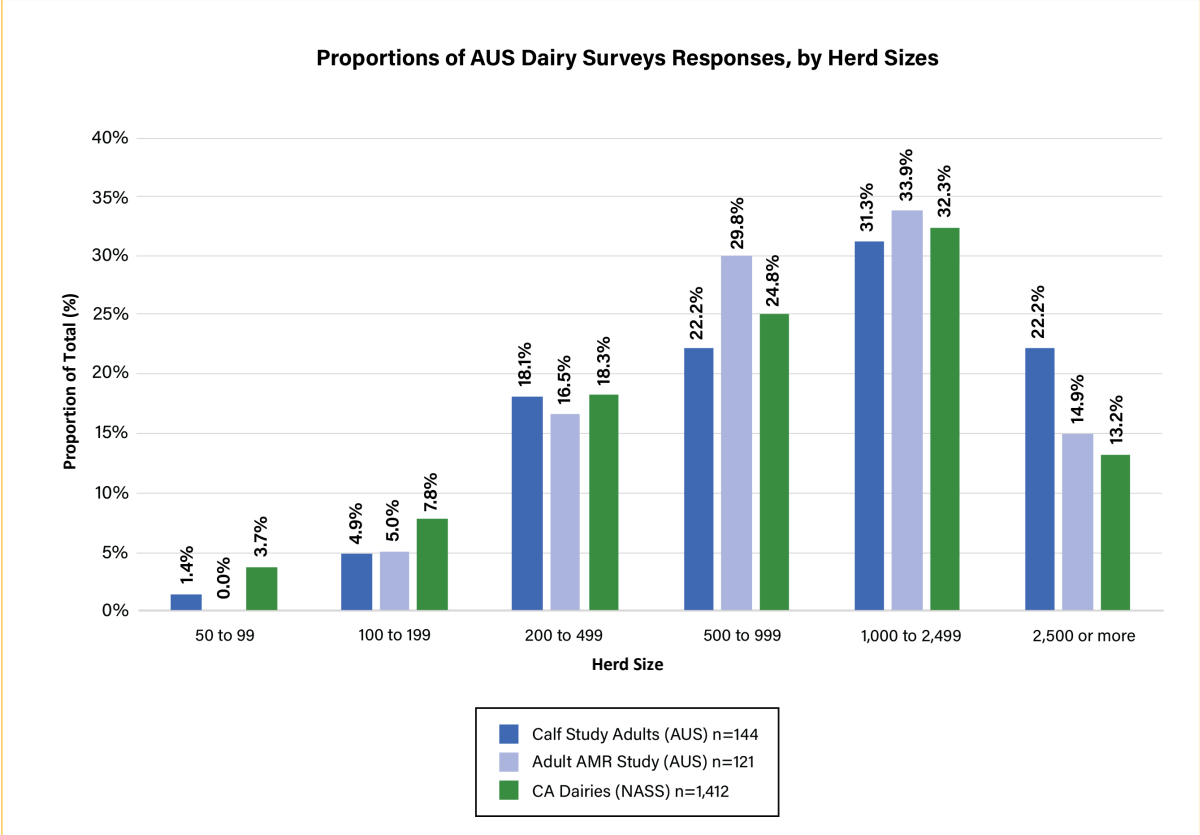


Figure 11. Proportions of AUS Dairy Surveys Responses, by Herd Sizes. Proportions of AUS 2017 Calf Study and AUS 2018 Adult Dairy AMR Study surveys reporting each milking herd size compared with NASS milking herd size (2012) proportions in California.

A subset of operations that raise dairy calves was enrolled in on-farm studies of antimicrobial use and AMR that incorporated both longitudinal and cross-sectional survey designs. The enrolled farms had a total population of 88,463 calves and 27,875 milking cows, from which calves to be sampled were identified.

Adult Dairy Cattle Studies

AUS also contracted the UC Davis VMTRC to study antimicrobial use in California's adult dairy cows. A survey was mailed out to 1,282 California dairies in late July 2018 to gather information on antimicrobial use and other dairy health and husbandry practices. After an initial reminder, the preliminary overall survey response was 10.8%, with regional response rates summarized in **Table 1**. At the time of writing, a second reminder has been sent and is expected to boost the number of returned surveys. For comparison, a relatively recent, mailed survey of California licensed dairies elicited a response rate of 14.7%,[57] while a survey of Canadian dairies administered both online and by mail around the same time period had a 9% response rate.[54]

Longitudinal studies like this one reveal relationships between management and medication practices, as well as changes in animal microbiomes (that is, the community of microorganisms, such as bacteria, that live in or on the animal) over time.

Calculations using herd size proportions from NASS 2012 Census data[59] resulted in nearly identical response rates to those using CDFA data in the denominator. Initial survey returns suggest that the herd sizes of participating dairies closely approximate the distribution of herd sizes reported by NASS in 2012 as shown in **Figure 11**. Using CDFA's definition of a dairy, which differs from that of NASS, herds under 50 head are not shown.

A total of 10 dairies have been identified for enrollment in an on-farm, longitudinal study of antimicrobial use, AMR, and disease pressures (that is, disease factors that may favor the growth of microbes that develop or maintain resistance to antimicrobial agents). By committing to the longitudinal study, the participating dairies have voluntarily agreed to repeated measures of the same farms and animals over a one-year period. The data gathered will allow researchers to evaluate variations in measured characteristics by season. Additionally, previously stored samples from the researcher's earlier study of antimicrobial therapy in dairy cows will be more deeply evaluated for indicators of resistance.

Longitudinal studies like this one reveal relationships between management and medication practices, as well as changes in animal microbiomes (that is, the community of microorganisms, such as bacteria, that live in or on the animal) over time. They also help provide the clarity needed to develop risk-based monitoring systems. The results of these investigations will provide insight into antimicrobial use on California's dairy farms as well as the observed effects of use practices on AMR.

Commercial Poultry Study

AUS has contracted a study through the University of Minnesota to expand existing national efforts focused on commercial poultry production. This involves a longitudinal study of antimicrobial use and resistance on California broiler chicken and turkey farms, with data being collected in collaboration with the California Poultry Federation over a two-year period. The study will describe antimicrobial use on participating farms and evaluate AMR in samples from those farms. The researcher will also explore historical usage for commercial laying hens, turkeys, and broiler chickens in California. At the time of writing this report, study enrollment is ongoing.

NAHMS Goat Study

AUS has developed a solid working relationship with the USDA NAHMS and NASS programs. The strength and timeliness of these collaborations will allow the 2019 NAHMS Goat Study to be expanded to include 400 additional goat producers in California to obtain a representative sample for the state. The NAHMS 2019 Goat Study is a two-phase study in line with previous national USDA research; phase I involves a general management survey of goat producers administered by NASS and phase II involves a more in-depth NAHMS survey with biological sampling.

In the first partnership of its kind, AUS worked with NASS and NAHMS to expand both phases of the study in California and has agreed to contribute CDFA personnel resources to accomplish the additional data collection in phase II. Additionally, CDFA has committed to provide funding in the amount of $68,000 for NASS to fulfill its role in the phase I study expansion. Following data collection from both phases, NAHMS will perform a California-specific analysis of the data, applying the same methodology used for national data, and report these results back to AUS. This collaboration not only fulfills the mandate of FAC Section 14405(b) to avoid duplication of monitoring efforts, but also allows AUS to obtain information that is representative of the goat industry in California and can be compared with national-level results reported by NAHMS.

Salmonella Retrospective Study

Building on prior work to evaluate AMR in *Salmonella* from cattle, AUS funded a contracted project with UC Davis to streamline testing for resistance genes to two specific classes of antimicrobial drugs that are important in treating human cases of infection with this organism. As future funding becomes available, additional work in this area could provide a unique opportunity to look retrospectively at resistance in a foodborne pathogen through stored samples. This would allow researchers to identify and analyze resistance trends from 2002-2016, prior to changes in medically important antimicrobial drug (MIAD) uses in livestock, and to identify genetic elements that make the bacteria resistant to drugs commonly used to treat human disease from *Salmonella*.

Backyard Livestock Producer Studies

Currently, three studies have been contracted through UC Davis and California Polytechnic State University - San Luis Obispo focused on antimicrobial use and animal management practices, on-farm AMR, and communication networks for backyard livestock producers. Backyard producers are a key study population as they represent a diverse group that have the potential to be missed by common mechanisms of communication, education, and surveillance, such as through industry groups or publications. Little is known about backyard livestock production practices, including usage of veterinary services, common animal health problems, antimicrobial use practices, and AMR. Thus, it is essential to address this population in California and explore opportunities for increased education and outreach.

One study contracted through UC Davis is focusing on backyard poultry and involves a survey on use of antimicrobials and parallel assessment of AMR in backyard flocks. This study aims to help fill knowledge gaps associated with backyard poultry production and provide needed education, thereby improving food safety and backyard bird health. It will also provide information about antimicrobial drug usage in backyard poultry and explore associated AMR across California over all four seasons.

For this study, a total of 162 backyard poultry owners from 32 counties across the state participated in an initial survey. Average reported flock size across these participants was 12.7 chickens, ranging from 1 to 107 chickens. Based on this participatory survey, 16 paired backyards across California (i.e., 16 backyards that used antibiotics in their chickens and 16 that did not use antibiotics in their chickens), representing approximately 430 chickens total, were selected for a follow-up study assessing AMR in backyard chickens and their coop environment on a quarterly basis for one year, from the summer of 2018 to the spring of 2019. Quarterly sampling allows for repeated measures of the same flocks and evaluation of variations over time. For these backyard poultry samples, the CAHFS Laboratory is performing antimicrobial susceptibility testing in collaboration with UC Davis researchers.

Broadening the focus beyond backyard poultry, two additional studies concentrate on approaches to engaging backyard livestock producers in general. One of these, contracted through California Polytechnic State University - San Luis Obispo, targets backyard producer communication networks, specifically assessing the feasibility of reaching this group through local social hubs, such as feed stores. This pilot study in San Luis Obispo has the potential for expansion to other areas of California to better aim outreach and education efforts.

Another study, contracted through UC Davis, addresses backyard producers' knowledge gaps regarding antimicrobial use and AMR. This project focuses on using workshops to develop, evaluate, and promote AMR mitigation strategies and judicious use of antimicrobials. As part of this study, informational workshops are planned for the six regions of: Marin-Sonoma; San Joaquin-Stanislaus; Contra Costa-Alameda; Fresno, Kings and Tulare; Yolo, Solano, and Sacramento; and Santa Clara County. The workshops for Marin-Sonoma and San Joaquin-Stanislaus have already been completed. A needs assessment was performed via a pre-workshop survey and attendees received follow-up information in the form of a newsletter.

VFD Data Collection

In addition to the above studies, AUS performed inspection visits to facilities that initially expressed interest to the FDA in producing or distributing feeds requiring VFDs. FAC Section 14406 grants CDFA the authority to request and receive copies of VFDs from owners, veterinarians, and feed distributors. Federal law requires each party to maintain a copy of the VFD for two years. In Spring 2017, AUS and Commercial Feed Inspection Program personnel visited all 105 facilities that initially expressed interest to FDA in producing or distributing feeds requiring VFDs. During this initial visit, program staff distributed outreach materials and surveyed whether the location planned to manufacture and/or distribute feeds requiring a VFD in the future.

Section Highlights

- **VFDs for 2017 and 2018 have been collected, in coordination with extensive outreach and education**
- **California has comparatively few facilities that manufacture and/or distribute feeds requiring VFDs**
- **AUS will summarize and analyze VFD data - the first known program nationwide to do so**

Key Acronyms

- **MIAD – medically important antimicrobial drug**
- **VFD – veterinary feed directive**

Beginning in February 2018, the program visited all locations that intended to manufacture and/or distribute VFD feed as well as new locations expressing interest to FDA in this activity. During this process, the program collected VFDs from 2017 **(see Figure 12)**. In addition, the tonnage of feed produced per MIAD ingredient type was recorded. Information from this collection will inform future analysis and study design by the program.

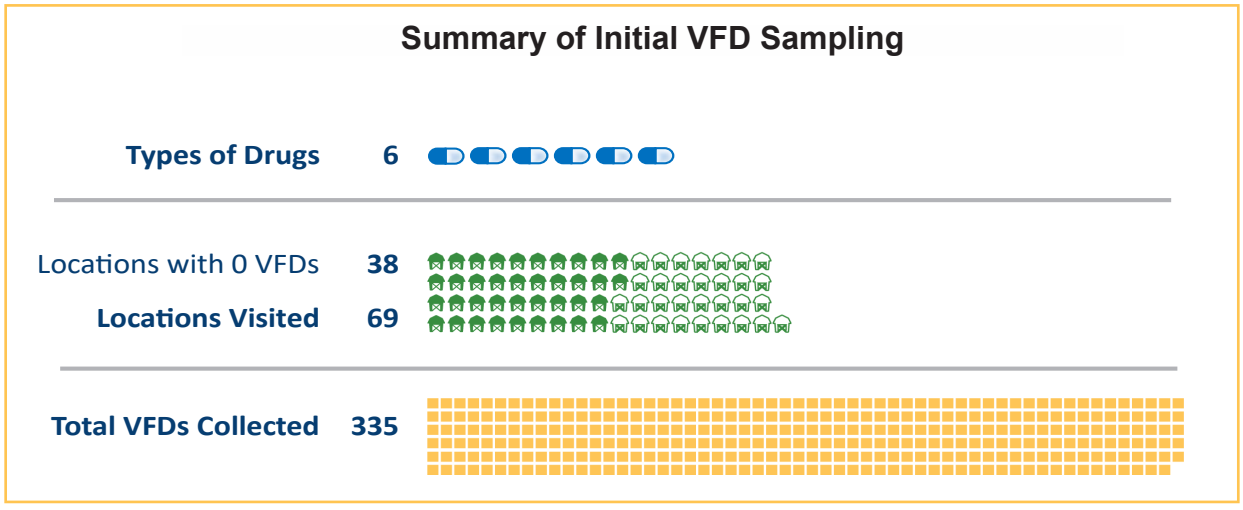


Figure 12. Summary of Initial VFD Sampling. VFD: Veterinary Feed Directive.

Nationwide, the total number of facilities on the VFD intent list is 9,482 as of October 2018. California currently ranks 26th among all the states, with just 130 facilities on the VFD intent list **(see Figure 13)**. For comparison, the top 10 states have 373 to 896 facilities. Of the 130 listed California facilities, currently only 56 actually manufacture and/or distribute VFD feeds.

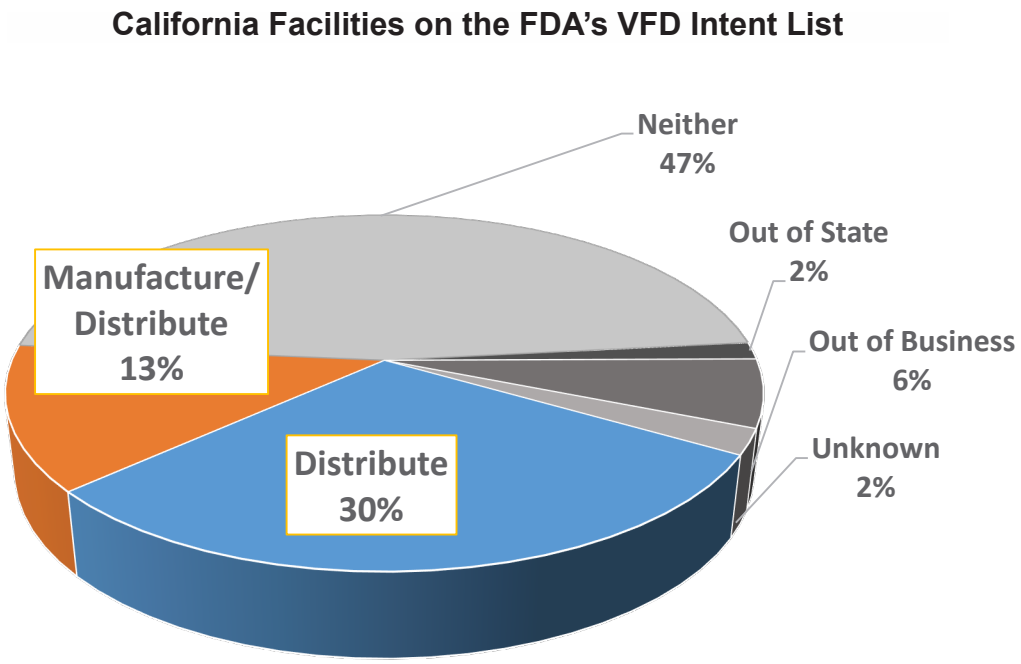


Figure 13. California Facilities on the FDA's VFD Intent List. This represents the breakdown of the 130 California facilities on the U.S. Food and Drug Administration (FDA)'s Veterinary Feed Directive (VFD) Intent list, as of October 2018.

The Law requires the collection of all VFDs filled in California, which will be summarized and analyzed to inform AUS stewardship outreach. No other states or federal entities have expressed similar plans for comprehensive analysis of these documents. Therefore, VFDs and related information on the amounts of medicated feed sold and/or produced in California cannot currently be compared to other states.

The program will continue to look at and analyze the data received from these collections. Data are fully protected from any disclosure of individual information, in accordance with FAC Section 14407, and will be aggregated to provide confidentiality of those submitting the VFD information to the program.

Summary of AUS Data Collection Efforts

As described in the sections above, AUS has taken a comprehensive and thoughtful approach to building an incremental, risk-based antimicrobial use and resistance monitoring system that is meaningful in California and aligns with the intent of the Law. This includes drawing on best practices from other monitoring systems, both national and international, and expertise from other State and federal programs, industry groups, and academia. As this program is the first of its kind in the nation, it is essential that AUS carefully assess the best ways to collect and report data that is useful for California.

As this program is the first of its kind in the nation, it is essential that AUS carefully assess the best ways to collect and report data that is useful for California.

In its first years, AUS initiated data collection efforts across the state to obtain a representative picture of current antimicrobial sales, use, and resistance, as well as animal health concerns and communication networks. This includes executing CDFA's authority to collect VFDs from all licensed livestock feed manufacturers in California. In addition to this sales data, antimicrobial use information is being obtained from surveys of producers and review of treatment records for livestock agricultural operations. In multiple studies, use data is paired with findings from on-farm sampling for antimicrobial resistance.

The AUS program collects data from willing participants through the aforementioned surveys and studies; this information is held confidential. Data collected by AUS through voluntary methods has demonstrated its potential for the future. AUS tailors survey content to industry priorities and leverages university relationships where appropriate to increase participation.[32,34] Across both AUS' in-house survey efforts and contracted studies, responses have been received from producers across the state, representing varying herd sizes that mirror the range and distribution of operations and animals in California. This voluntarily shared information is statistically relevant, as it provides representative data for further analysis. Gathering this data from voluntary participants while maintaining confidentiality ensures that these findings are meaningful and encourages participation in future monitoring efforts.

AUS' mailed surveys have been demonstrated to be effective tools for collecting information from livestock producers statewide. Despite a historical decline in mailed survey response rates,[31,35,37-39] California industry and scientific literature[31,40-43] continue to support the value of this data-gathering method. AUS survey results to date consistently reflect the broader herd/flock sizes and distributions in California and studies with comparable response rates have proven to show statistically relevant results. Thus far, participation has improved for each subsequent in-house survey the AUS team has administered. This demonstrates that as AUS refines its monitoring methods, and the program gains more recognition from producers and veterinarians, AUS can anticipate increased engagement.

The findings from AUS surveys, as well as from on-farm sampling for resistance, provide ongoing data to support the development of evidence-based stewardship materials and resources and lay the foundation for methods of long-term monitoring of antimicrobial use and AMR in California. Preliminary information is also discussed with livestock producer groups, including their leadership, to help ensure the analytical process develops findings that are informative and actionable. Additionally, following analysis, results will be shared in annual, commodity-specific, and summary reports published by AUS. Certain analyses, including findings from AUS' contracted studies, are expected to contribute to the growing body of scientific literature through publication in peer-reviewed, scientific journals.

Antimicrobial Stewardship Guidelines and Best Management Practices

Antimicrobial stewardship is a commitment to reducing the need for antimicrobial drugs by implementing livestock management practices that aid in the prevention of infectious disease. In addition, it means using antimicrobial drugs selectively and responsibly to optimize animal health and minimize the risk for developing AMR. Antimicrobial stewardship in veterinary medicine places the veterinarian as the authoritative overseer of these lifesaving drugs. Veterinarians have long taken a comprehensive approach to the diagnosis, management, and prevention of diseases in livestock. As part of this approach, veterinarians make deliberate therapeutic decisions with the intent of optimizing animal health, while protecting food safety and public health.

Section Highlights

- **AUS has established five principles for a successful statewide stewardship plan**
- **The *Guidelines for Judicious Use of Antimicrobials in Livestock* have been developed and species-specific guidelines are forthcoming**
- **AUS Stewardship efforts are guided by the results of data collection and analysis activities that are ongoing for California livestock populations**

Key Acronyms

- **AMR – antimicrobial resistance**
- **MIAD – medically important antimicrobial drug**

With substantial input from a diverse group of renowned California and national leaders in livestock production, veterinary medicine, and the science of AMR, AUS has established the five principles shown in **Figure 14** as the foundation to a successful statewide antimicrobial stewardship plan.

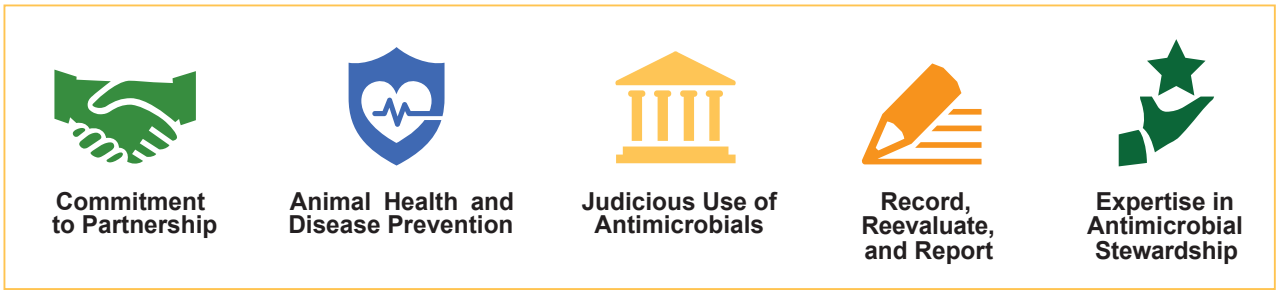


Figure 14. Principles of Antimicrobial Stewardship.

Based on these principles, AUS is working in collaboration with the California Veterinary Medical Board, California Department of Public Health, and university and cooperative extension experts to provide guidelines for implementation of a complete and robust antimicrobial stewardship plan by veterinarians and livestock owners.

The *Guidelines for Judicious Use of Antimicrobials in Livestock* for the general public and veterinarians were developed as a top priority for the AUS program and published in July 2018. These documents reflect months of consensus building between all stakeholder groups and recognized experts in the field, with a solid backing of peer-reviewed research. They cover the current science-based recommendations for veterinarians in livestock production regardless of species or production type, outline federal and State requirements pertaining to the therapeutic use of MIADs in livestock, and employ sociological considerations to ensure the documents' approachability, readability, and impact.

AUS is also developing a species-specific set of guidelines. These guidelines are the cornerstone of an antimicrobial stewardship plan, as they will assist veterinarians and livestock owners in developing animal health and disease prevention programs to address the unique challenges faced by each operation, farm, or ranch. In addition to being species-specific, the guidelines will be specific to the production class (e.g., beef, dairy, pre-weaned calf, or lactating cow), due to the vast differences in disease pressures and physiology between each species and production class of livestock.

AUS stewardship efforts are based on data gathered by surveys and studies that are ongoing in California's livestock populations. In order to have a major impact on the progression of AMR, the guidelines will also be syndrome-specific, addressing the top diseases that necessitate the use of MIADs, as revealed through findings of AUS data collection activities. These methods of antibiotic stewardship intervention have demonstrated success in improving antimicrobial use by physicians in human hospitals.[60-62]

A robust and systematic literature review will validate the quality and applicability of the available scientific literature to generate recommendations for each species, production class, and syndrome. Recommendations for livestock owners and veterinarians may include information on early recognition of selected cases, diagnostic options, and measures for disease prevention and control, as well as effective and practical alternative strategies to treat the disease or infection. Program contracts for species-specific syndrome guidelines are underway. Contracted groups will draw on the knowledge of Californian experts to provide solutions for some of the common problems identified through AUS' surveys and studies.

Many California producers currently belong to programs that incorporate new scientific techniques and approaches to production, marketing, and maintaining animal health and welfare to give added value, such as the Beef Quality Assurance program. Management practices that mitigate the development and spread of AMR and/or aid in the prevention of important diseases will be incorporated into these existing programs so they are accessible to those who need them and to prevent redundancy. For livestock owners not belonging to these groups, the resources will be published on the AUS public website. By providing easy-to-use information and tools to discuss with their veterinarian, AUS hopes to help producers make appropriate progressive changes on their individual farms.

Addressing Concerns

Section Highlights

- **AUS is responsive to questions and concerns that arise and is quick to issue clarification in its education and outreach**

In many ways, California's new Law provides a window into discussions already underway in the scientific community surrounding the use of antimicrobial drugs in people and livestock. More work needs to be done on the part of the State to support producers looking through that "window" and to ensure they have an informed view. For example, two important issues affecting producers are product knowledge and access to veterinary and pharmaceutical services. An additional priority for AUS, during implementation of FAC Sections 14400-14408, is to clarify with producers which drugs are regulated under the Law, and the difference between antimicrobial resistance mitigation vs. drug residue avoidance.

AUS program staff made a substantial effort to inform the regulated public (livestock owners and veterinarians) of the Law's requirements. As previously described, this effort was multifaceted and included multiple in-person meetings and presentations with a reach of nearly 1,000 leaders in the veterinary profession and animal agriculture industries within California. Educational materials were developed in English and Spanish and distributed to thousands of producers prior to January 2018. In addition, AUS maintains a Facebook page, an official webpage, and an open line of direct communication via email or phone. The program promptly responds to questions or concerns in relation to the requirements of the Law or AUS' information gathering efforts to promote clarity regarding the Law and to be transparent as a program.

Confusion Surrounding Which Drugs are Regulated

As the AUS team began presenting at producer meetings and speaking with livestock owners, some confusion arose among participants surrounding which drugs were considered antimicrobial drugs. Many believed that vaccines and anthelmintics (dewormers, or drugs that kill parasites) were included in the new restrictions. These over-the-counter medications help producers reduce the occurrence of disease and can be applied on the farm at the owner's convenience and preference. Fear of losing easy access to these drugs clouded the AUS message. On receiving this feedback, updates were made to AUS outreach documents to address this distinction **(see Figure 15)** and were distributed through CDFA Branches and other channels.

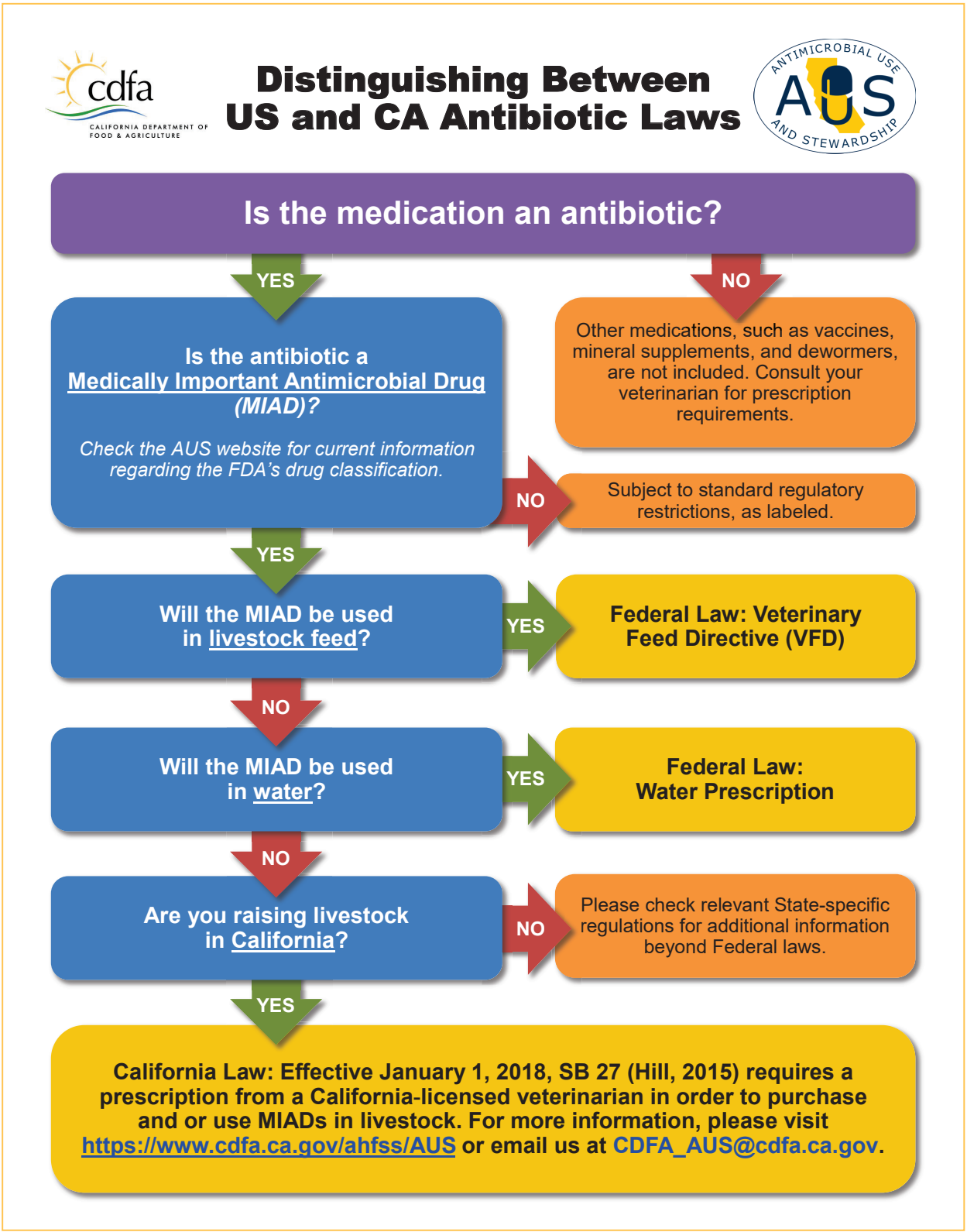


Figure 15. Example of Outreach Materials Provided to the Regulated Public. Example of outreach developed and provided by AUS to clarify confusion surrounding the Law.

Antimicrobial Resistance vs. Residues

Another concern was the distinction between resistance and residues; these topics are often confused and misunderstood. Antimicrobial resistance is the evolution of strains of bacteria that are resistant to antibiotics, whereas drug residues are the impurities associated with veterinary drugs that remain in any edible portion of an animal product. Residues usually occur due to inappropriate drug use or from further inaccuracies in animal identification, record keeping, and not following a recommended withdrawal period that is scientifically established.

Depending on their concentration level, such residues can harm humans who consume the product. Over the past decade, residue violations have reduced substantially, thanks to increased oversight and collaborative efforts; additional restrictions and scrutiny of antibiotic use was frustrating to many producers who felt they were already taking measures to be compliant with existing residue laws. In response to this concern, AUS tailored outreach materials to distinguish these two concepts, and to clarify that a veterinarian can help ensure antibiotic use will not result in residues, while also reducing antimicrobial resistance impacts.

Conclusion and Future Directions

California's Law represents forward-thinking and ambitious legislation that has set out to protect animal and public health in California through the monitoring and study of antimicrobial use and resistance, which directly support educational outreach and the development of stewardship guidelines. The California Antimicrobial Use and Stewardship program (AUS) has undertaken numerous endeavors in outreach, monitoring, and education to fulfill the mandate set forth by the Law and to establish systems and methods to ensure current and future success of the program. Throughout all AUS activities and efforts, the program has sought and developed collaboration with State entities and federal agencies, as well as with other key stakeholders. Through the willing participation of Californians, AUS has established a practical system for collecting statistically relevant data on antimicrobial use, antimicrobial resistance (AMR), and animal health management practices from the major livestock segments, representative segments of the food production chain, and regions with considerable livestock production. These efforts, coupled with the collection of retail data and veterinary feed directives (VFDs) statewide, have established a sound foundation for AUS to build upon in the years to come. All data collected for AUS feeds directly into efforts to create meaningful antimicrobial stewardship guidelines for California's livestock producers and veterinarians.

All data collected for AUS feeds directly into efforts to create meaningful antimicrobial stewardship guidelines for California's livestock producers and veterinarians.

AUS works with multiple State and federal partners, as well as university researchers, to collect information across California's diverse livestock production types, coordinating with existing systems and efforts where possible. In doing so, AUS has established a model for how the program will continue to grow and expand in future years. Early data collection activities are prioritized to provide high impact in California; in under two years, AUS efforts have resulted in more than 15,000 surveys administered to livestock producers across California. Responses representing more than half a million animals across 55 counties in California reflect antimicrobial use and management practices across beef and dairy cattle, sheep, and backyard poultry operations. Additionally, AUS has initiated on-farm sampling at more than 50 volunteering operations, representing at least 128,000 animals, where samples will be taken over time to evaluate antimicrobial resistance in bacteria. AUS data collection activities are ongoing, and the program will continue to initiate studies, including additional longitudinal efforts, looking at other production types important to California, with an anticipated focus on goats and commercial poultry in the near future. Data collection methods will continually be evaluated and modified as appropriate to meet the program's evolving needs and priorities. Participation and engagement among California's livestock producers is critical to meaningful and sustainable collection of information. AUS will continue to pursue collaboration with its research partners, California-licensed veterinarians, and with livestock owners across the state to engender long lasting and effective change.

AUS continues to collaborate with and educate livestock owners and veterinarians on the requirements of the Law and the foundations of antimicrobial stewardship. AUS published the *Principles of Antimicrobial Stewardship* to outline for stakeholders the major components of implementing a holistic approach to antimicrobial stewardship. A key part of this approach is the responsible use of these lifesaving drugs, guided by veterinarians, whose relationships with livestock owners are vital to maintaining productivity, animal health and welfare, as well as a safe and secure food supply. The *Guidelines for Judicious Use of Antimicrobials in Livestock* were published to highlight the relevant laws regarding drug use in livestock species and to give specific information about how the veterinarian-client-patient relationship (VCPR) works to ensure safe, effective, and beneficial antimicrobial use.

In addition to continued efforts to refine outreach and communications to meet producers' needs and ensure compliance with the Law, the program's priorities going forward are to collect data that are meaningful and actionable. As the program gains increased recognition and its findings are shared back with California audiences, as well as with the larger scientific community via peer-reviewed publications, AUS anticipates increased participation in its information gathering and monitoring activities.

Moving forward, national efforts may provide additional opportunities for the AUS program to grow and receive external support. The stated goals of the FDA's recently released five-year plan, *Supporting Antimicrobial Stewardship in Veterinary Settings, Goals for Fiscal Years 2019 – 2023*, reiterate California's approach to monitoring use and resistance, as well as a focus on veterinary oversight and antimicrobial stewardship. California's AUS program will continue to move forward with its established model, a path which parallels the FDA's anticipated direction and priorities. The achievements demonstrated by AUS, coupled with the long-term systems and partnerships established by the program, assure that the Law is, and will continue to be, fully enacted. California has taken the lead with its steps toward combating antimicrobial resistance in livestock and is contributing to the protection of animal and human health now and into the future.

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Appendix A
Program Stakeholders and Collaborators

This appendix provides additional information on AUS' collaborators and stakeholders. The following supplements that which is included in the body of the Report, where detailed explanation of specific collaborations can be found. Italicized text below emphasizes AUS interactions with described entities.

Federal Entities

Centers for Disease Control and Prevention (CDC)

CDC is the leading national public health institute in the U.S., within the Department of Health and Human Services. Its main goal is to protect public health and safety through disease and injury control and prevention. As such, the CDC embodies expertise in the nation's most pressing public health issues, including antimicrobial use and resistance.

AUS monitors CDC activities and funding opportunities to harmonize efforts and goals across public and animal health perspectives.

AUS contacted CDC scientists involved with the National Antimicrobial Resistance Monitoring System (NARMS) program in early 2017 to make initial introductions and discuss possible opportunities for future collaborative efforts. AUS also reached out to the California Emerging Disease Program, the California Department of Public Health Microbial Diseases Laboratory, and the Los Angeles Public Health Department as they are collaborating with the CDC on a resistance gene monitoring project in California. In addition, AUS has provided letters of support to researchers applying for CDC funding of antimicrobial use and resistance research projects.

U.S. Food and Drug Administration (FDA)

FDA is an agency within the U.S. Department of Health and Human Services that protects the public health by helping to ensure the safety, effectiveness, and security of human and veterinary drugs, as well as vaccines, other biological products, and medical devices for human use. The FDA also helps to ensure the safety and security of the nation's food supply.

The CDFA Inspection Services Division's Livestock Drug Program has had a long-standing working relationship with the FDA. The program has historically maintained several contracts with FDA for feed inspections, process inspections, bovine spongiform encephalopathy inspections, and tissue residues investigations. These contracts have evolved over the years to include medicated feed inspections and, more recently, Veterinary Feed Directive inspections.

National Antimicrobial Resistance Monitoring System (NARMS)

Established in 1996, NARMS is a collaborative program of the U.S. Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), and the U.S. Department of Agriculture (USDA Food Safety and Inspection Service (FSIS)), as well as participation by state and local public health departments and universities. This national public

health surveillance system tracks changes in the antimicrobial susceptibility of enteric (intestinal) bacteria found in ill people (performed by CDC), retail meats (by FDA), and food animals (by USDA). The NARMS program helps promote and protect public health by providing information about emerging bacterial resistance, how resistant infections differ from susceptible infections, and the impact of interventions designed to limit the spread of resistance. NARMS data are used by FDA to make regulatory decisions designed to preserve the effectiveness of antibiotics for humans and animals. In addition to monitoring antimicrobial susceptibility, NARMS conducts epidemiologic investigations examining risk factors and clinical outcomes of infections with specific bacterial subtypes or subsets of bacteria that exhibit particular resistance patterns.

AUS has been in contact with scientists involved with the NARMS program to make initial introductions and discuss possible opportunities for future collaboration. Additional discussion about testing methodologies is planned for early 2019.

In order not to duplicate efforts, AUS has obtained NARMS data on retail meat samples collected in California through online resources. Other state-level data (from slaughter sampling and Hazard Analysis and Critical Control Points (HACCP) programs) from California that are not publicly available online through NARMS have been requested directly.

Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB)

PACCARB is comprised of human and animal health experts who provide advice, information, and recommendations to the Health and Human Services Secretary on federal programs and policies intended to support and evaluate the implementation of U.S. government activities related to combating antibiotic-resistant bacteria. PACCARB works together to ensure the continued effectiveness of antibiotics and slow the threat of resistant germs for the future by complementing progress made in other federal efforts, specifically the National Action Plan for Combating Antibiotic-Resistant Bacteria.

AUS maintains valuable relationships with PACCARB voting and recent members. Through these relationships and by observing public hearings, AUS is kept abreast of all new and relevant PACCARB information and resolutions.

The National Action Plan provides a roadmap to guide the Nation in rising to the challenge of antibiotic resistance and potentially saving thousands of lives. The Action Plan outlines federal activities to enhance domestic and international capacity to prevent and contain outbreaks of antibiotic-resistant infections; maintain the efficacy of current and new antibiotics; and develop and deploy next-generation diagnostics, antibiotics, vaccines, and other therapeutics. Implementation of the Action Plan requires the sustained, coordinated, and complementary efforts of individuals and groups around the world, including public and private sector partners, healthcare providers, healthcare leaders, veterinarians, agriculture industry leaders, manufacturers, policymakers, and patients.

AUS has aligned many of its goals with those of the National Action Plan for Combating Antibiotic-Resistant Bacteria, with particular attention to the following objectives:

- Objective 1.3: Identify and implement measures to foster stewardship of antibiotics in animals

- Objective 2.4: Enhance monitoring of antibiotic-resistance patterns, as well as antibiotic sales, usage, and management practices, at multiple points in the production chain for food animals and retail meat
  - Sub-objective 2.4.2: Enhance collection and reporting of data regarding antibiotic drugs sold and distributed for use in food-producing animals
  - Sub-objective 2.4.3: Implement voluntary monitoring of antibiotic use and resistance in pre-harvest settings to provide nationally representative data while maintaining producer confidentiality

U.S. Department of Agriculture (USDA)

USDA is a large, multifaceted federal agency with roles in policy, regulation, research, education, trade, and foreign affairs. Over 150 years, the USDA has impacted the lives of generations of Americans through their work on food safety, nutrition, agriculture, economic development, science, natural resource conservation, and other issues.

USDA National Agricultural Statistics Service (NASS)

NASS conducts hundreds of surveys every year and prepares reports covering multiple aspects of U.S. agriculture. NASS is committed to providing timely, accurate, and useful statistics in service to U.S. agriculture by reporting objective and unbiased statistics; working with State field offices, universities, and State Departments of Agriculture; and safeguarding the privacy of farmers, ranchers, and other data providers, with a guarantee that confidentiality and data security continue to be top priorities.

AUS is collaborating with NASS to expand Phase I of the NAHMS 2019 Goat Survey. Local NASS personnel have also provided their expertise to AUS on how to understand and use the date NASS publishes.

USDA National Animal Health Monitoring System (NAHMS)

The USDA Animal and Plant Health Inspection Service (APHIS) initiated NAHMS in 1983 to collect, analyze, and disseminate data on animal health, management, and productivity across the U.S. NAHMS conducts national studies on the health and health management of domestic livestock populations. These studies are designed to meet the information needs of the industries associated with these commodities, as identified by people within those industries. Each animal group is studied at regular intervals; NAMHS provides the science-based, statistically sound information essential for policy decision-making.

In the short time since its inception, AUS has developed a solid working relationship with USDA NAHMS. AUS personnel have made three visits to NAHMS headquarters in Fort Collins, Colorado, to learn about national antimicrobial surveillance efforts, participate in discussions about study and metric development, and discuss future collaboration. The cooperation established with NAHMS has allowed AUS to communicate with NAHMS experts throughout the planning, development, review, testing, and administration of AUS surveys. Additionally, NAHMS provided suggestions to AUS for data analysis and reporting, as well as data security procedures. NAHMS has, in turn, solicited AUS input and feedback on NAHMS survey instruments and utilized AUS-developed survey questions in their national surveys.

USDA Veterinary Medical Loan Repayment Program (VMLRP)

The USDA National Institute of Food and Agriculture (NIFA) VMLRP places veterinarians in rural communities that have demonstrated a veterinary shortage situation, in exchange for limited financial assistance with student loan repayment for up to three years.

CDFA nominates regions with a veterinary shortage that, if selected by USDA, may qualify new practitioners who work in the identified area for financial support through the USDA NIFA Veterinary Medical Loan Repayment Program.

USDA Veterinary Services Grant Program (VSGP)

The USDA National Institute of Food and Agriculture (NIFA) VSGP is designed to support education and extension activities, as well as practice enhancement initiatives, that will enable veterinarians, veterinary students, veterinary technicians, and veterinary technology students to gain specialized skills. The VSGP also provides veterinary practices with additional resources (e.g., equipment, personnel) needed to more effectively mitigate veterinary service shortages in the U.S.

AUS collaborated with and supported recipients and applicants of the USDA NIFA Veterinary Services Grant award.

State Entities

California Department of Public Health (CDPH)

CDPH aims to optimize the health and wellbeing of the people in California by fulfilling a comprehensive range of responsibilities. These include but are not limited to infectious disease control and prevention, food safety, environmental health, laboratory services, and patient safety. The California Antimicrobial Stewardship Program Initiative of the CDPH Healthcare-Associated Infections (HAI) Program provides guidance and support for California healthcare facilities to implement antimicrobial stewardship programs, which promote and measure appropriate antimicrobial use by optimizing selection, dosing, route, and duration of therapy. They concentrate on improving patient outcomes while minimizing adverse events associated with antimicrobial use, including toxicity, *Clostridium difficile* infections, and the emergence of antimicrobial resistant organisms. The CDPH HAI Program has developed multiple antimicrobial stewardship program educational materials for hospitals, nursing homes, and outpatient care.

CDPH has been an invaluable resource during the initial phases of AUS antimicrobial stewardship program development. Staff from this program shared key elements of the HAI Antimicrobial Stewardship Program as well as challenges. CDPH reviewed and approved of the AUS Principles of Antimicrobial Stewardship and the Judicious Use Guidelines prior to their release. The relationship between CDPH and CDFA helps bridge the gap between the human and animal health.

California State Board of Pharmacy

Under of the authority of the Department of Consumer Affairs, the California State Board of Pharmacy (Pharmacy Board) protects and promotes the health and safety of Californians by pursuing the highest quality of pharmacist care and the appropriate use of pharmaceuticals through education, communication, licensing, legislation, regulation, and enforcement. The Pharmacy Board has jurisdiction over sales of prescription drugs in the state and licensing of Veterinary Food Animal Drug Retailers (VFADRs).

AUS and the Pharmacy Board have evaluated means for collecting medically important antimicrobial drug (MIAD) sales information in California, as well as assessed the utility of available sales data.

California Veterinary Medical Board (VMB)

Operating under the authority of the Department of Consumer Affairs, the California VMB is the governing authority responsible for protecting consumers and animals by regulating licensees, promoting professional standards, and diligent enforcement of the California Veterinary Medicine Practice Act. Senate Bill 361, which also passed into law in 2015 at the same time as Senate Bill 27, instituted compulsory continuing education (CE) for California veterinarians on judicious use of antimicrobials. This new CE requirement is advertised in the California VMB renewal notices to veterinarians when they renew their license every two years.

The California VMB has been integral to the development of AUS outreach materials, as its approval of AUS documents ensures the materials comply with state laws and regulations pertaining to veterinary practice. The California VMB website provides a link to the AUS website to engage California-licensed veterinarians with the AUS program and access information on CE opportunities fulfilling the new CE on the judicious use of antimicrobials requirement.

Academia

University of California (UC)

UC is a public university system in California with world-renowned programs and a multitude of distinguished faculty. The College of Agriculture and Environmental Sciences is ranked #1 in the world and nation for plant and animal sciences. The School of Veterinary Medicine, also ranked #1 both nationally and worldwide, has shaped the field of veterinary medicine through the development of dynamic veterinary treatments and key discoveries related to animal, human and environmental health.

■ UC Cooperative Extension (UCCE)

Cooperative Extension is a nationwide network of land-grant university researchers and educators who solve problems in agriculture, the environment, and human and community well-being. The UCCE has an educational and research branch, the UC Division of Agriculture and Natural Resources, within the UC Davis College of Agriculture and Environmental Sciences. Extension advisors are based in over 50 county offices throughout California and focus on providing evidence- and science-

based information to industry and the public and work with them to solve real-world concerns. Many of these experts are at the intersection of rangeland management, production services, small farms outreach, and animal health. Farm advisors are instrumental in implementation studies, contributing to the progressive nature of California agriculture through evidence-based scientific research and outreach.

Many Cooperative Extension specialists have contributed to AUS' understanding of regional differences in California agriculture, and provided key insight into real-time farm applications of scientific principles.

UC Davis School of Veterinary Medicine

The UC Davis School of Veterinary Medicine serves the people of California by providing educational, research, clinical service, and public service programs of the highest quality to advance the health and care of animals, the health of the environment, and public health, and to contribute to the economy. To carry out this mission, the school trains students in the professional Doctor of Veterinary Medicine program, Master of Preventive Veterinary Medicine program, graduate clinical residency program and graduate academic Master of Science and Doctor of Philosophy (PhD) programs.

AUS funding has supported the development of research proposals and projects from UC Davis-affiliated veterinary professionals in livestock herd health and medicine to study and evaluate antimicrobial use as well as antimicrobial resistance patterns in samples from sick animals as well as from young, healthy animals on the farm.

UC Davis Veterinary Medical Teaching and Research Center (VMTRC)

The VMTRC is a multi-purpose facility that provides clinical training in dairy production medicine to veterinary students and residents, as well as high quality laboratory services to dairy veterinarians, producers, and other industry professionals in areas such as milk safety. Its researchers are well-placed in the heart of California's dairy country and maintain ongoing relationships with many dairy producers in the area.

AUS has partnered closely with the UC Davis VMTRC in Tulare to draw on its valuable expertise and evaluate antimicrobial use and resistance in dairy cattle. AUS funding for longitudinal studies has enabled the VMTRC to purchase equipment needed to test samples for antimicrobial resistance and the presence of antimicrobial resistance genes.

The opportunity to study the impacts of FAC Sections 14400-14408 and potential to provide meaningful information to California's livestock industry led UC Davis, including the VMTRC, to create a research road map on antimicrobial resistance prevention and control in dairy cattle that identifies key avenues to advance knowledge on mitigating antimicrobial resistance.

UC Davis Western Institute for Food Safety and Security (WIFSS)

WIFSS is a collaborative program between the UC Davis School of Veterinary Medicine and the UC Davis College of Agricultural and Environmental Sciences that serves the global community by conducting research, developing training, and providing outreach programs that enhance the health and security of people, animals, and the environment.

WIFSS conducted the preliminary literature reviews that informed AUS program design. The growing body of literature is reviewed continuously and held in the AUS library.

California Animal Health and Food Safety Laboratory System (CAHFS)

CAHFS is a group of four laboratories across the state that protects public and animal health in partnership with the CDFA and the UC Davis School of Veterinary Medicine. CAHFS provides rapid and reliable diagnostics and surveillance for endemic and foreign animal diseases, including those that affect humans.

The AUS program has provided funding for CAHFS to purchase and validate state-of-the-art equipment to enhance antimicrobial susceptibility testing capabilities.

California State Universities (CSU)

Colleges of Agriculture and affiliated Campus Centers and Institutes at California state universities — California State University - Chico, California State University - Fresno, California State Polytechnic University - Pomona, and California Polytechnic State University - San Luis Obispo — extend research, scholarship, and practical training for undergraduate students. In addition, the Agriculture Research Institute works for Californians through the four CSU colleges of agriculture to conduct applied agriculture and natural resource research to improve the economic efficiency and ensure the sustainability of California agriculture.

AUS supported and provided guidance for multiple research projects developed at California Polytechnic State University - San Luis Obispo, which were aimed at providing educational materials, understanding how small-scale livestock producers acquire information, and how these producers also use veterinarians as advisors. AUS is also coordinating efforts with California State University - Chico to assess best management practices for sheep producers.

Out-of-state Universities

The U.S. has multiple world-renowned schools of veterinary medicine at land grant universities in various states that play a crucial role in studying cutting-edge topics related to animal health and welfare. University faculty with expertise in livestock AMR and food safety conduct research that informs national and international policy development.

The AUS program currently collaborates with prominent expert researchers in livestock AMR from Kansas State University, The University of Minnesota, Colorado State University, Washington State University, and The Ohio State University.

Food Animal Residue Avoidance and Depletion Program (FARAD)

As a university-based, national program, FARAD is a key resource for safeguarding our nation's animal-source food supply against accidental contamination with violative residues of drugs, pesticides or other agents that could compromise food safety. FARAD provides tools for veterinarians to ensure therapeutic regimens comply with federal laws regarding drug residues and food safety.

AUS has collaborated with FARAD to develop a training program for CDFA-licensed retailers who wish to sell antimicrobial products in accordance with the newly adopted regulations. In addition, FARAD has assisted the program by developing educational materials regarding VFD drugs and combination VFD drugs, as well as which drugs require a prescription in California. The transition of these products to prescription status in California has highlighted a knowledge gap for pharmacists, as the typical curriculum often does not include training for veterinary patients. To address this gap, the program utilized FARAD's expertise to create a website with information for pharmacists who have limited experience dispensing medications for food-producing animals.

Veterinarians

Veterinary Medical Associations (VMA)

As one of the largest veterinary medical associations in the U.S., the California Veterinary Medical Association (CVMA) serves over 7,200 members and is a vocal advocate for animals and veterinary professionals throughout the State. The CVMA is a respected source of pertinent information in all segments of the veterinary profession and helps to improve animal and human health in an ethically and socially responsible manner. In addition, the local VMAs cater to the specific interests and needs of the region, especially for livestock veterinarians serving dense agriculture communities.

The California Veterinary Medical Association (CVMA) and many of the local veterinary medical associations have been instrumental in assisting with program outreach to licensed veterinarians across the state. AUS staff have been invited to speak at several board meetings as well as provide continuing education opportunities to statewide and local members about the new requirement of the Law and judicious use of antimicrobial drugs in livestock.

Veterinary Information Network (VIN)

VIN serves the global veterinary community by connecting veterinarians with specialized skills and knowledge, provides instant access to vast amounts of up-to-date veterinary information, practice management resources, and online continuing education courses. More than one out of five veterinarians around the world use VIN as a source of information when making clinical decisions.

AUS assisted VIN in educating veterinarians of all disciplines in livestock medicine and the judicious use of antimicrobials through delivery of a rounds presentation on Antimicrobial Use Policy and Implementation.

Agriculture Industry Groups

Agriculture is a major industry for the Golden State. With 76,400 farms and ranches, California agriculture is a $54 billion-dollar industry that generates more than $100 billion in related economic activity. California agriculture is a large and diverse industry encompassing more than 400 plant and animal commodities. Its members may belong to associations or operate as individual producers. These groups include:

- Ag Association Management Services, Inc
- Agriculture Council of California
- California Cattlemen's Association
- California Farm Bureau Federation
- California Grain & Feed Association
- California Pork Producers Association
- California Poultry Federation
- California Sheep Commission
- California Wool Growers Association
- Dairy CARES
- Foster Farms
- Pacific Egg and Poultry Association
- Milk Producers Council
- Western United Dairymen

California's livestock industry organizations have been very supportive of and engaged with AUS' efforts to reduce antimicrobial resistance and promote animal health, with some groups assisting in AUS survey development and promotion. Their support includes providing advice on and field testing of survey questionnaires, promoting survey participation via newsletters, sharing information at meetings and conferences, and distributing emails to members. Additionally, many of these groups regularly engage in and provide feedback on AUS program development by participating in the AUS Ad Hoc Advisory committee and meetings and/or as members of AUS mailing lists.

Consumer and Environmental Interest Groups

Multiple interest groups share concerns related to antimicrobial resistance and seek a collective, public response to this health challenge. Their stated priorities include the environment, public health and safety. The groups' engagement has helped to bring this issue to the forefront through interactions with government entities and efforts to effect marketplace changes. These groups include:

- California Advocates, Inc.
- California Public Interest Research Group
- Center for Food Safety
- Consumers Union
- Environmental Working Group
- National Resources Defense Council
- Pew Charitable Trusts
- Public Health Institute
- Roots of Change

AUS welcomes guidance and feedback from all stakeholders by encouraging participation in the AUS Ad Hoc Advisory Committee, engaging California leadership in discussions regarding the AUS program, and subscribing to AUS mailing lists.

Appendix B
List of California Prescription Drugs

CALIFORNIA PRESCRIPTION DRUGS

Prescription required for purchase and use in California effective January 1, 2018

Product Name, Brand, or Trademark	Drug Ingredient	Route of Admin	Container Type	Company Name
5-WAY CALF SCOUR BOLUS	Oxytetracycline	Bolus	Bottle	AGRI
AGRI-CILLIN PROCAINE PENICILLIN G	Penicillin	Injectable	Bottle	AGRI
AGRIMYCIN 100	Oxytetracycline	Injectable	Bottle	AGRI
AGRIMYCIN 200	Oxytetracycline	Injectable	Bottle	AGRI
ALBADRY PLUS SUSPENSION DRY COW FORMULA	Penicillin	Injectable	Syringe	ZOETIS
ALBON 5 g BOLUS	Sulfadimethoxine	Bolus	Packet	ZOETIS
ALBON 15 g BOLUS	Sulfadimethoxine	Bolus	Packet	ZOETIS
BACTRACILLIN G	Penicillin	Injectable	Bottle	ASPEN
BACTRACILLIN G BENZATHINE FOR CATTLE	Penicillin	Injectable	Bottle	ASPEN
BIO-MYCIN 200	Oxytetracycline	Injectable	Bottle	BIV
CALF SCOUR BOLUS ANTIBIOTIC	Oxytetracycline	Bolus	Jar	DURVET
COMBI-PEN-48	Penicillin	Injectable	Bottle	BIMEDA
DI-METHOX INJECTION - 40%	Sulfadimethoxine	Injectable	Bottle	AGRI
DURAMYCIN 72-200	Oxytetracycline	Injectable	Bottle	DURVET
DURAMYCIN-100	Oxytetracycline	Injectable	Bottle	DURVET
DURA-PEN	Penicillin	Injectable	Bottle	DURVET
HANFORD'S US VET GO-DRY DRY COW MASTITIS TREATMENT	Penicillin	Other	Syringe	HGCM
HANFORD'S US VET MASTI-CLEAR	Penicillin	Other	Syringe	HGCM
LINCOMIX 100 SWINE	Lincomycin	Injectable	Bottle	ZOETIS
LINCOMIX 300 SWINE	Lincomycin	Injectable	Bottle	ZOETIS
LINCOMYCIN 300 SWINE	Lincomycin	Injectable	Bottle	DURVET
LIQUAMYCIN LA-200	Oxytetracycline	Injectable	Bottle	ZOETIS
LIQUID SPECTOGARD SCOUR-CHEK ORAL SOLUTION FOR PIG	Spectinomycin	Oral	Bag	BIMEDA
NOROMECTIN INJECTION FOR CATTLE	Ivermectin	Injectable	Bottle	NORBROOK
NOROMECTIN PLUS INJECTION FOR CATTLE	Ivermectin	Injectable	Bottle	NORBROOK
NOROCILLIN STERILE USP	Penicillin	Injectable	Bottle	NORBROOK
NOROMYCIN 300 LA	Oxytetracycline	Injectable	Bottle	NORBROOK
OXY 500 CALF BOLUS	Oxytetracycline	Bolus	Bottle	BIV

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CALIFORNIA PRESCRIPTION DRUGS

Prescription required for purchase and use in California effective January 1, 2018

Product Name, Brand, or Trademark	Drug Ingredient	Route of Admin	Container Type	Company Name
OXYTET 100	Oxytetracycline	Injectable	Bottle	NORBROOK
OXYTETRACYCLINE INJECTION 200	Oxytetracycline	Injectable	Bottle	NORBROOK
PEN-AQUEOUS FOR CATTLE, SWINE, SHEEP & HORSES	Penicillin	Injectable	Bottle	ASPEN
PENICILLIN G PROCAINE	Penicillin	Injectable	Bottle	IBA
PENICILLIN INJECTABLE	Penicillin	Injectable	Bottle	DURVET
PRO-PEN-G INJECTION	Penicillin	Injectable	Bottle	BIMEDA
SULFAMED 40% INJECTION	Sulfadimethoxine	Injectable	Bottle	MWI
SULFAMED INJECTION 40%	Sulfadimethoxine	Injectable	Bottle	BIMEDA
SUPRA SULFA III BOLUS	Sulfamethazine	Bolus	Tub	ASPEN
SUSTAIN III SUSTAINED RELEASE BOLUS	Sulfamethazine	Bolus	Jar	DURVET
SUSTAIN III SUSTAINED RELEASE BOLUS (72 HOURS)	Sulfamethazine	Bolus	Box or Jar	BIMEDA
SUSTAIN III SUSTAINED RELEASE CALF BOLUS	Sulfamethazine	Bolus	Jar	BIMEDA
SUSTAIN III SUSTAINED RELEASE CALF BOLUS	Sulfamethazine	Bolus	Jar	DURVET
TERRAMYCIN OPTHALMIC OINTMENT	Oxytetracycline	Topical	Tube	ZOETIS
TERRAMYCIN SCOURS TABLETS	Oxytetracycline	Oral	Bottle	ZOETIS
TERRA-VET 100	Oxytetracycline	Injectable	Bottle	ASPEN
TERRA-VET 200	Oxytetracycline	Injectable	Bottle	ASPEN
TETROXY-LA	Oxytetracycline	Injectable	Bottle	BIMEDA
TODAY LACTATING COWS	Cephapirin	Injectable	Syringe	BIV
TOMORROW DRY COW	Cephapirin	Injectable	Syringe	BIV
TYLAN 200	Tylosin	Injectable	Bottle	ELANCO
TYLAN 50	Tylosin	Injectable	Bottle	ELANCO
TYLOVED 200 MG/ML	Tylosin	Injectable	Bottle	VEDCO
VET ONE PENONE PRO	Penicillin	Injectable	Bottle	MWI
VET ONE SULFAMED 40% INJECTION	Sulfadimethoxine	Injectable	Bottle	MWI
VET ONE VETRIMYCIN 100	Oxytetracycline	Injectable	Bottle	MWI
VET ONE VETRIMYCIN 200	Oxytetracycline	Injectable	Bottle	MWI

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