Guidelines for Veterinarians:
Judicious Use of Antimicrobials in Livestock

The practices and protocols developed and implemented by veterinarians, livestock owners, and personnel responsible for animal care are critical to the promotion and maintenance of animal health and welfare, the conservation of animal resources, and the protection of public health.[1-3] Established biosecurity and therapeutic recommendations, including treatment protocols, are vital to limiting the severity and the spread of disease or infection in livestock.[4] In the event of a disease occurrence, timing is everything.[5,6] The ability to recognize early signs of disease or infection in animals, and to identify those animals with an elevated risk of contracting a particular disease or infection, are vital to the successes of infectious disease prevention, control, and treatment.[2,7] Various tools and/or scoring systems may facilitate the training and day-to-day activities of those responsible for animal care.[2,7]

In California, the use of medically important antimicrobial drugs (MIADs) in livestock must be deemed necessary under the professional judgement of a licensed veterinarian, within the context of a valid veterinarian-client-patient relationship and in accordance with current veterinary medical practice and legal parameters.[a] To effectively and appropriately employ the use of MIADs, a veterinarian must first initiate a general or preliminary diagnosis of disease or infection, or have indication of an elevated risk of contracting a particular disease or infection, in an individual animal or group of animals.[8,b,c] The diagnostic process may incorporate relevant history, production performance, clinical signs, physical examination, and/or diagnostic test results.[9]

Once a veterinarian has identified a possible indication to use medically important antimicrobial drugs (MIADs), judicious use includes careful consideration of the following practices:

These guidelines are intended to serve as an adjunct to professional judgement. The following are based on current scientific principles and state and federal laws regarding MIADs.

1) Antimicrobial therapy should be initiated in a timely manner, often before a definitive diagnosis can be made, in order to minimize the infectious burden to the animal(s) and the environment, reduce the amount of MIADs necessary to affect clinical outcome, improve clinical response to therapy, and diminish the development of antimicrobial resistance.[4,6,10,11]

2) Antimicrobials should be reserved for cases that would be expected to provide a measurable benefit to the clinical outcome.[12] The following indications may be considered when determining the benefit of therapy:

    a) Antimicrobial therapy may be indicated for treatment in animals with evidence of infectious disease before a final diagnosis can be made. Prudently consider the use of MIADs in chronic or moribund cases or those cases that may have no anticipated recovery for production purposes.[12,13]
    b) Antimicrobial therapy may be necessary for control to decrease the risk of a subclinical infection resulting in clinical signs of disease, reduce shedding of infectious bacteria, and minimize chances of disease transmission.
    c) Antimicrobial therapy may be necessary for prevention to address an elevated risk of contracting a particular disease or infection when the ability to predict outcomes to infectious exposure is not possible, but infection is anticipated based on a licensed veterinarian's professional judgment regarding animal-specific risk factors.

[a] Medically important antimicrobial drugs (MIADs) are defined as those listed in Appendix A of the U.S. Food and Drug Administration's Guidance for Industry #152, including critically important, highly important, and important.
[b] As defined in the Veterinary Medicine Practice Act, 16 CCR § 2032.1. Attached in Appendix A.
[c] Allowable and prohibited uses of medically important antimicrobial drugs in livestock are described in 4.5 FAC § 14402. Attached in Appendix D.

d) MIADs shall not be administered to livestock solely for purposes of promoting weight gain or improving feed efficiency.[6,d]

3) Veterinarians are encouraged to work with clients to maintain accurate drug inventory, measures of production performance, and treatment records that include clinical outcomes. Assembly and analysis of this information may aid in monitoring treatment efficacy, reviewing treatment protocols and management procedures, providing objectives for communication and training of those responsible for livestock care on improving disease detection, and optimize identification of animals at risk of an unfavorable outcome and allow for appropriate management. [1,2,7,14]

   a) Veterinarians maintain medical records in compliance with state and federal regulations.[e] Except where disclosure is allowed per California and federal laws, veterinary medical records are considered confidential and are prohibited from disclosure without client consent.[f]

4) Ancillary treatments and supportive care may be used when shown to reduce the need for MIADs, improve clinical response to therapy, or to improve animal welfare with no deleterious effect on treatment outcome.[2,15]

5) Appropriate antimicrobial selection should be made based on knowledge of the identified or suspected pathogen(s), compliance with federal regulatory requirements, and the expected efficacy of the drug as determined by available scientific medical evidence, the clinical experience of the veterinarian, results of initial treatment, and/or antimicrobial susceptibility.[9,16,19,g]

   a) Carefully consider the use of combination antimicrobial therapy for cases with impaired host defenses, polymicrobial infections, or emergence of resistance is shown to be reduced. Limit combinations to those with predictable synergistic effects, where effective, broad spectrum antimicrobials are not available.[5,8,10,18]
   b) Antimicrobial susceptibility testing should be performed by laboratories using current and validated methods approved by the Clinical and Laboratory Standards Institute.[13,17]
   c) Interpretation and application of antimicrobial susceptibility test results to the individual animal or the herd requires the knowledge and expertise of a licensed veterinary medical professional.[17] Consults with veterinary specialists may be useful on a case-by-case basis.

[d] Allowable and prohibited uses of medically important antimicrobial drugs in livestock are described in 4.5 FAC § 14402. Attached in Appendix D.

[e] 16 CCR 2032.3, 16 CCR 2032.2, and 21 CFR Part 558

[f] BPC 4857

[g] The Animal Medicinal Drug Use Clarification Act (AMDUCA) permits Extralabel Drug Use (ELDU) in food-producing animals, by or on the lawful order of a licensed veterinarian within the context of a valid veterinarian-client-patient relationship, if criteria are met as defined in Title 21 in the Code of Federal Regulations, Part 530. Attached in Appendix B. A veterinarian must select a drug that is labeled for its intended use and that contains the same active ingredient which is in the required dosage form and concentration, except where a veterinarian finds that the approved drug is clinically ineffective for its intended use. See www.FARAD.org for more informative resources on ELDU.

6) Establish optimal antimicrobial therapy regimens for the treatment, control, or prevention of disease or infection as supported by relevant clinical trials and principles of veterinary medicine.[9,13] Use must comply with federal and state legal requirements.[h,i]

   a) Utilize an adequate dose, route of administration, and appropriate dosing frequency, to achieve and maintain steady-state drug concentration above the known or predictable minimum inhibitory concentration of the identified or likely pathogen(s).[6,8,19,20]
   b) Target methods of drug delivery, such as local or regional therapy, when feasible and likely to achieve the desired drug concentration at the site of infection.[10,13]
   c) Duration of therapy should be long enough to achieve the desired clinical response but short enough to minimize the risk of adverse effects and selection of resistant bacteria.[6,8,13,19-21,j]
   d) In circumstances when multiple animals are affected or at risk of contracting a disease or infection, antimicrobials should be administered to the fewest number of animals necessary.
   e) MIADs may not be used to prevent disease in a regular pattern, unless in relation to surgery or to a medical procedure.[k] Examples of MIADs used in a regular pattern to prevent disease include, but are not limited to:
      i) MIADs given to prevent disease beyond the period of elevated risk determined in the professional judgement of the licensed veterinarian.
      ii) MIADs given to prevent disease out of habit in a recurrent manner solely based on the animal's age or weight, the calendar date, or a life stage event of the animal(s) without the presence of an elevated risk of a particular disease or infection determined in the professional judgment of the licensed veterinarian.

7) Avoid oversupplying MIADs beyond the anticipated needs of therapy for ill or at-risk animals.[1]

[h] AMDUCA permits ELDU in food-producing animals, by or on the lawful order of a licensed veterinarian within the context of a valid veterinarian-client-patient relationship, if criteria are met as defined in Title 21 in the Code of Federal Regulations, Part 530. Attached in Appendix B. ELDU ("Off-Label Use") is any use of an FDA-approved drug that differs from instructions on the approved product label (species, animal production class, dose, volume per injection site, route, frequency, duration, or indication). See www.FARAD.org for more informative resources on ELDU.

[i] Allowable and prohibited uses of medically important antimicrobial drugs in livestock are described in 4.5 FAC § 14402. Attached in Appendix D.

[j] Currently, there is a dearth of scientific literature to support evidence-based decisions on effective duration of antimicrobial therapies in the practice of veterinary medicine on livestock animals.

[k] Allowable and prohibited uses of medically important antimicrobial drugs in livestock are described in 4.5 FAC § 14402. Attached in Appendix D.

Appendix A

Title 16, California Code of Regulations, Section 2032.1 – Veterinarian-Client-Patient Relationship

(a) It is unprofessional conduct for a veterinarian to administer, prescribe, dispense or furnish a drug, medicine, appliance, or treatment of whatever nature for the prevention, cure, or relief of a wound, fracture or bodily injury or disease of an animal without having first established a veterinarian-client-patient relationship with the animal patient or patients and the client, except where the patient is a wild animal or the owner is unknown.

(b) A veterinarian-client-patient relationship shall be established by the following:

(1) The client has authorized the veterinarian to assume responsibility for making medical judgments regarding the health of the animal, including the need for medical treatment,

(2) The veterinarian has sufficient knowledge of the animal(s) to initiate at least a general or preliminary diagnosis of the medical condition of the animal(s). This means that the veterinarian is personally acquainted with the care of the animal(s) by virtue of an examination of the animal or by medically appropriate and timely visits to the premises where the animals are kept, and

(3) The veterinarian has assumed responsibility for making medical judgments regarding the health of the animal and has communicated with the client a course of treatment appropriate to the circumstance.

(c) A drug shall not be prescribed for a duration inconsistent with the medical condition of the animal(s) or type of drug prescribed. The veterinarian shall not prescribe a drug for a duration longer than one year from the date the veterinarian examined the animal(s) and prescribed the drug.

(d) As used herein, “drug” shall mean any controlled substance, as defined by Section 4021 of Business and Professions code, and any dangerous drug, as defined by Section 4022 of Business and Professions code.

(e) No person may practice veterinary medicine in this state except within the context of a veterinarian-client-patient relationship or as otherwise permitted by law. A veterinarian-client-patient relationship cannot be established solely by telephonic or electronic means.

(f) Telemedicine shall be conducted within an existing veterinarian-client-patient relationship, with the exception for advice given in an “emergency,” as defined under section 4840.5 of the code, until that patient(s) can be seen by or transported to a veterinarian. For purposes of this section, “telemedicine” shall mean the mode of delivering animal health care services via communication technologies to facilitate consultation, treatment, and care management of the patient.

Note: Authority cited: Sections 686 and 4808, Business and Professions Code. Reference: Sections 686, 2290.5, 4021, 4022 and 4883, Business and Professions Code.

Appendix B

Title 21, Code of Federal Regulations, Part 530 – Extralabel Drug Use in Animals

Authority: 15 U.S.C. 1453, 1454, 1455; 21 U.S.C. 321, 331, 351, 352, 353, 355, 357, 360b, 371, 379e.

Source: 61 FR 57743, Nov. 7, 1996, unless otherwise noted.

Subpart A—General Provisions

§530.1 Scope.

This part applies to the extralabel use in an animal of any approved new animal drug or approved new human drug by or on the lawful order of a licensed veterinarian within the context of a valid veterinary-client-patient relationship.

§530.2 Purpose.

The purpose of this part is to establish conditions for extralabel use or intended extralabel use in animals by or on the lawful order of licensed veterinarians of Food and Drug Administration approved new animal drugs and approved new human drugs. Such use is limited to treatment modalities when the health of an animal is threatened or suffering or death may result from failure to treat. This section implements the Animal Medicinal Drug Use Clarification Act of 1994 (the AMDUCA) (Pub. L. 103-396).

§530.3 Definitions.

(a) *Extralabel use* means actual use or intended use of a drug in an animal in a manner that is not in accordance with the approved labeling. This includes, but is not limited to, use in species not listed in the labeling, use for indications (disease or other conditions) not listed in the labeling, use at dosage levels, frequencies, or routes of administration other than those stated in the labeling, and deviation from the labeled withdrawal time based on these different uses.

(b) *FDA* means the U.S. Food and Drug Administration.

(c) The phrase *a reasonable probability that a drug's use may present a risk to the public health* means that FDA has reason to believe that use of a drug may be likely to cause a potential adverse event.

(d) The phrase *use of a drug may present a risk to the public health* means that FDA has information that indicates that use of a drug may cause an adverse event.

(e) The phrase *use of a drug presents a risk to the public health* means that FDA has evidence that demonstrates that the use of a drug has caused or likely will cause an adverse event.

(f) A *residue* means any compound present in edible tissues that results from the use of a drug, and includes the drug, its metabolites, and any other substance formed in or on food because of the drug's use.

(g) A *safe level* is a conservative estimate of a drug residue level in edible animal tissue derived from food safety data or other scientific information. Concentrations of residues in tissue below the safe level will not raise human food safety concerns. A safe level is not a safe concentration or a tolerance and does not indicate that an approval exists for the drug in that species or category of animal from which the food is derived.

(h) *Veterinarian* means a person licensed by a State or Territory to practice veterinary medicine.

(i) A *valid veterinarian-client-patient relationship* is one in which:

(1) A veterinarian has assumed the responsibility for making medical judgments regarding the health of (an) animal(s) and the need for medical treatment, and the client (the owner of the animal or animals or other caretaker) has agreed to follow the instructions of the veterinarian;

(2) There is sufficient knowledge of the animal(s) by the veterinarian to initiate at least a general or preliminary diagnosis of the medical condition of the animal(s); and

(3) The practicing veterinarian is readily available for followup in case of adverse reactions or failure of the regimen of therapy. Such a relationship can exist only when the veterinarian has recently seen and is personally acquainted with the keeping and care of the animal(s) by virtue of examination of the animal(s), and/or by medically appropriate and timely visits to the premises where the animal(s) are kept.

§530.4 Advertising and promotion.
Nothing in this part shall be construed as permitting the advertising or promotion of extralabel uses in animals of approved new animal drugs or approved human drugs.

§530.5 Veterinary records.
(a) As a condition of extralabel use permitted under this part, to permit FDA to ascertain any extralabel use or intended extralabel use of drugs that the agency has determined may present a risk to the public health, veterinarians shall maintain the following records of extralabel uses. Such records shall be legible, documented in an accurate and timely manner, and be readily accessible to permit prompt retrieval of information. Such records shall be adequate to substantiate the identification of the animals and shall be maintained either as individual records or, in food animal practices, on a group, herd, flock, or per-client basis. Records shall be adequate to provide the following information:

(1) The established name of the drug and its active ingredient, or if formulated from more than one ingredient, the established name of each ingredient;

(2) The condition treated;

(3) The species of the treated animal(s);

(4) The dosage administered;

(5) The duration of treatment;

(6) The numbers of animals treated; and

(7) The specified withdrawal, withholding, or discard time(s), if applicable, for meat, milk, eggs, or any food which might be derived from any food animals treated.

(b) A veterinarian shall keep all required records for 2 years or as otherwise required by Federal or State law, whichever is greater.

(c) Any person who is in charge, control, or custody of such records shall, upon request of a person designated by FDA, permit such person designated by FDA to, at all reasonable times, have access to, permit copying, and verify such records.

Subpart B—Rules and Provisions for Extralabel Uses of Drugs in Animals

§530.10 Provision permitting extralabel use of animal drugs.
An approved new animal drug or human drug intended to be used for an extralabel purpose in an animal is not unsafe under section 512 of the act and is exempt from the labeling requirements of section 502(f) of the act if such use is:

(a) By or on the lawful written or oral order of a licensed veterinarian within the context of a valid veterinarian-client-patient relationship; and

(b) In compliance with this part.

§530.11 Limitations.
In addition to uses which do not comply with the provision set forth in §530.10, the following specific extralabel uses are not permitted and result in the drug being deemed unsafe within the meaning of section 512 of the act:

(a) Extralabel use in an animal of an approved new animal drug or human drug by a lay person (except when under the supervision of a licensed veterinarian);

(b) Extralabel use of an approved new animal drug or human drug in or on an animal feed;

(c) Extralabel use resulting in any residue which may present a risk to the public health; and

(d) Extralabel use resulting in any residue above an established safe level, safe concentration or tolerance.

§530.12 Labeling.
Any human or animal drug prescribed and dispensed for extralabel use by a veterinarian or dispensed by a pharmacist on the order of a veterinarian shall bear or be accompanied by labeling information adequate to assure the safe and proper use of the product. Such information shall include the following:

(a) The name and address of the prescribing veterinarian. If the drug is dispensed by a pharmacy on the order of a veterinarian, the labeling shall include the name of the prescribing veterinarian and the name and address of the dispensing pharmacy, and may include the address of the prescribing veterinarian;

(b) The established name of the drug or, if formulated from more than one active ingredient, the established name of each ingredient;

(c) Any directions for use specified by the veterinarian, including the class/species or identification of the animal or herd, flock, pen, lot, or other group of animals being treated, in which the drug is intended to be used; the dosage, frequency, and route of administration; and the duration of therapy;

(d) Any cautionary statements; and

(e) The veterinarian's specified withdrawal, withholding, or discard time for meat, milk, eggs, or any other food which might be derived from the treated animal or animals.

§530.13 Extralabel use from compounding of approved new animal and approved human drugs.
(a) This part applies to compounding of a product from approved animal or human drugs by a veterinarian or a pharmacist on the order of a veterinarian within the practice of veterinary medicine. Nothing in this part shall be construed as permitting compounding from bulk drugs.

(b) Extralabel use from compounding of approved new animal or human drugs is permitted if:

(1) All relevant portions of this part have been complied with;

(2) There is no approved new animal or approved new human drug that, when used as labeled or in conformity with criteria established in this part, will, in the available dosage form and concentration, appropriately treat the condition diagnosed. Compounding from a human drug for use in food-producing animals will not be permitted if an approved animal drug can be used for the compounding;

(3) The compounding is performed by a licensed pharmacist or veterinarian within the scope of a professional practice;

(4) Adequate procedures and processes are followed that ensure the safety and effectiveness of the compounded product;

(5) The scale of the compounding operation is commensurate with the established need for compounded products (e.g., similar to that of comparable practices); and

(6) All relevant State laws relating to the compounding of drugs for use in animals are followed.

(c) Guidance on the subject of compounding may be found in guidance documents issued by FDA.

Subpart C—Specific Provisions Relating to Extralabel Use of Animal and Human Drugs in Food-Producing Animals

§530.20 Conditions for permitted extralabel animal and human drug use in food-producing animals.
(a) The following conditions must be met for a permitted extralabel use in food-producing animals of approved new animal and human drugs:

(1) There is no approved new animal drug that is labeled for such use and that contains the same active ingredient which is in the required dosage form and concentration, except where a veterinarian finds, within the context of a valid veterinarian-client-patient relationship, that the approved new animal drug is clinically ineffective for its intended use.

(2) Prior to prescribing or dispensing an approved new animal or human drug for an extralabel use in food animals, the veterinarian must:

(i) Make a careful diagnosis and evaluation of the conditions for which the drug is to be used;

(ii) Establish a substantially extended withdrawal period prior to marketing of milk, meat, eggs, or other edible products supported by appropriate scientific information, if applicable;

(iii) Institute procedures to assure that the identity of the treated animal or animals is carefully maintained; and

(iv) Take appropriate measures to assure that assigned timeframes for withdrawal are met and no illegal drug residues occur in any food-producing animal subjected to extralabel treatment.

(b) The following additional conditions must be met for a permitted extralabel use of in food-producing animals an approved human drug, or of an animal drug approved only for use in animals not intended for human consumption:

(1) Such use must be accomplished in accordance with an appropriate medical rationale; and

(2) If scientific information on the human food safety aspect of the use of the drug in food-producing animals is not available, the veterinarian must take appropriate measures to assure that the animal and its food products will not enter the human food supply.

(c) Extralabel use of an approved human drug in a food-producing animal is not permitted under this part if an animal drug approved for use in food-producing animals can be used in an extralabel manner for the particular use.

§530.21 Prohibitions for food-producing animals.
(a) FDA may prohibit the extralabel use of an approved new animal or human drug or class of drugs in food-producing animals if FDA determines that:

(1) An acceptable analytical method needs to be established and such method has not been established or cannot be established; or

(2) The extralabel use of the drug or class of drugs presents a risk to the public health.

(b) A prohibition may be a general ban on the extralabel use of the drug or class of drugs or may be limited to a specific species, indication, dosage form, route of administration, or combination of factors.

§530.22 Safe levels and analytical methods for food-producing animals.
(a) FDA may establish a safe level for extralabel use of an approved human drug or an approved new animal drug when the agency finds that there is a reasonable probability that an extralabel use may present a risk to the public health. FDA may:

(1) Establish a finite safe level based on residue and metabolism information from available sources;

(2) Establish a safe level based on the lowest level that can be measured by a practical analytical method; or

(3) Establish a safe level based on other appropriate scientific, technical, or regulatory criteria.

(b) FDA may require the development of an acceptable analytical method for the quantification of residues above any safe level established under this part. If FDA requires the development of such an acceptable analytical method, the agency will publish notice of that requirement in the Federal Register.

(c) The extralabel use of an animal drug or human drug that results in residues exceeding a safe level established under this part is an unsafe use of such drug.

(d) If the agency establishes a safe level for a particular species or category of animals and a tolerance or safe concentration is later established through an approval for that particular species or category of animals, for that species or category of animals, the safe level is superseded by the tolerance or safe concentration for that species or category of animals.

§530.23 Procedure for setting and announcing safe levels.
(a) FDA may issue an order establishing a safe level for a residue of an extralabel use of an approved human drug or an approved animal drug. The agency will publish in the Federal Register a notice of the order. The notice will include:

(1) A statement setting forth the agency's finding that there is a reasonable probability that extralabel use in animals of the human drug or animal drug may present a risk to the public health;

(2) A statement of the basis for that finding; and

(3) A request for public comments.

(b) A current listing of those drugs for which a safe level for extralabel drug use in food-producing animals has been established, the specific safe levels, and the availability, if any, of a specific analytical method or methods for drug residue detection will be codified in §530.40.

§530.24 Procedure for announcing analytical methods for drug residue quantification.
(a) FDA may issue an order announcing a specific analytical method or methods for the quantification of extralabel use drug residues above the safe levels established under §530.22 for extralabel use of an approved human drug or an approved animal drug. The agency will publish in the Federal Register a notice of the order, including the name of the specific analytical method or methods and the drug or drugs for which the method is applicable.

(b) Copies of analytical methods for the quantification of extralabel use drug residues above the safe levels established under §530.22 will be available upon request from the Communications and Education Branch (HFV-12), Division of Program Communication and Administrative Management, Center for Veterinary Medicine, 7500 Standish Pl., Rockville, MD 20855. When an analytical method for the detection of extralabel use drug residues above the safe levels established under §530.22 is developed, and that method is acceptable to the agency, FDA will incorporate that method by reference.

§530.25 Orders prohibiting extralabel uses for drugs in food-producing animals.
(a) FDA may issue an order prohibiting extralabel use of an approved new animal or human drug in food-producing animals if the agency finds, after providing an opportunity for public comment, that:

(1) An acceptable analytical method required under §530.22 has not been developed, submitted, and found to be acceptable by FDA or that such method cannot be established; or

(2) The extralabel use in animals presents a risk to the public health.

(b) After making a determination that the analytical method required under §530.22 has not been developed and submitted, or that such method cannot be established, or that an extralabel use in animals of a particular human drug or animal drug presents a risk to the public health, FDA will publish in the Federal Register, with a 90-day delayed effective date, an order of prohibition for an extralabel use of a drug in food-producing animals. Such order shall state that an acceptable analytical method required under §530.22 has not been developed, submitted, and found to be acceptable by FDA; that such method cannot be established; or that the extralabel use in animals presents a risk to the public health; and shall:

(1) Specify the nature and extent of the order of prohibition and the reasons for the prohibition;

(2) Request public comments; and

(3) Provide a period of not less than 60 days for comments.

(c) The order of prohibition will become effective 90 days after date of publication of the order unless FDA publishes a notice in the Federal Register prior to that date, that revokes the order of prohibition, modifies it, or extends the period of public comment.

(d) The agency may publish an order of prohibition with a shorter comment period and/or delayed effective date than specified in paragraph (b) of this section in exceptional circumstances (e.g., where there is immediate risk to the public health), provided that the order of prohibition states that the comment period and/or effective date have been abbreviated because there are exceptional circumstances, and the order of prohibition sets forth the agency's rationale for taking such action.

(e) If FDA publishes a notice in the Federal Register modifying an order of prohibition, the agency will specify in the modified order of prohibition the nature and extent of the modified prohibition, the reasons for it, and the agency's response to any comments on the original order of prohibition.

(f) A current listing of drugs prohibited for extralabel use in animals will be codified in §530.41.

(g) After the submission of appropriate information (i.e., adequate data, an acceptable method, approval of a new animal drug application for the prohibited extralabel use, or information demonstrating that the prohibition was based on incorrect data), FDA may, by publication of an appropriate notice in the Federal Register, remove a drug from the list of human and animal drugs prohibited for extralabel use in animals, or may modify a prohibition.

(h) FDA may prohibit extralabel use of a drug in food-producing animals without establishing a safe level.

Subpart D—Extralabel Use of Human and Animal Drugs in Animals Not Intended for Human Consumption

§530.30 Extralabel drug use in nonfood animals.
(a) Because extralabel use of animal and human drugs in nonfood-producing animals does not ordinarily pose a threat to the public health, extralabel use of animal and human drugs is permitted in nonfood-producing animal practice except when the public health is threatened. In addition, the provisions of §530.20(a)(1) will apply to the use of an approved animal drug.

(b) If FDA determines that an extralabel drug use in animals not intended for human consumption presents a risk to the public health, the agency may publish in the Federal Register a notice prohibiting such use following the procedures in §530.25. The prohibited extralabel drug use will be codified in §530.41.

Subpart E—Safe Levels for Extralabel Use of Drugs in Animals and Drugs Prohibited From Extralabel Use in Animals

§530.40 Safe levels and availability of analytical methods.
(a) In accordance with §530.22, the following safe levels for extralabel use of an approved animal drug or human drug have been established: [Reserved]

(b) In accordance with §530.22, the following analytical methods have been accepted by FDA: [Reserved]

§530.41 Drugs prohibited for extralabel use in animals.
(a) The following drugs, families of drugs, and substances are prohibited for extralabel animal and human drug uses in food-producing animals.

(1) Chloramphenicol;

(2) Clenbuterol;

(3) Diethylstilbestrol (DES);

(4) Dimetridazole;

(5) Ipronidazole;

(6) Other nitroimidazoles;

(7) Furazolidone.

(8) Nitrofurazone.

(9) Sulfonamide drugs in lactating dairy cattle (except approved use of sulfadimethoxine, sulfabromomethazine, and sulfaethoxypyridazine);

(10) Fluoroquinolones; and

(11) Glycopeptides.

(12) Phenylbutazone in female dairy cattle 20 months of age or older.

(13) Cephalosporins (not including cephapirin) in cattle, swine, chickens, or turkeys:

(i) For disease prevention purposes;

(ii) At unapproved doses, frequencies, durations, or routes of administration; or

(iii) If the drug is not approved for that species and production class.

(b) The following drugs, families of drugs, and substances are prohibited for extralabel animal and human drug uses in nonfood-producing animals: [Reserved]

(c) [Reserved]

(d) The following drugs, or classes of drugs, that are approved for treating or preventing influenza A, are prohibited from extralabel use in chickens, turkeys, and ducks:

(1) Adamantanes.

(2) Neuraminidase inhibitors.

[62 FR 27947, May 22, 1997, as amended at 67 FR 5471, Feb. 6, 2002; 68 FR 9530, Feb. 28, 2003; 68 FR 14134, Mar. 24, 2003; 71 FR 14377, Mar. 22, 2006; 77 FR 745, Jan. 6, 2012]

The most current version may be found on the Electronic Code of Federal Regulations website: https://www.ecfr.gov/cgi-bin/text-idx?SID=3fba2570d1166f25cadaa2e0065b7e95&mc=true&node=pt21.6.530&rgn=div5

Compliance Policy Guide 615.115 – Extralabel Use of Medicated Feeds for Minor Species

Prior to 1994, the Federal Food, Drug, and Cosmetic Act (the FD&C Act) did not permit the extralabel use of animal drugs, but the Agency exercised enforcement discretion regarding extralabel use of animal drugs provided certain criteria were met. These criteria were published in Compliance Policy Guide 7125.06 and were largely incorporated into the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA). AMDUCA amended the FD&C Act to permit extralabel uses under certain conditions. The regulations promulgated pursuant to AMDUCA are codified at 21 CFR part 530.

AMDUCA does not permit extralabel use of medicated feeds. However, when there are no approved treatment options available and the health of animals is threatened, and suffering or death would result from failure to treat the affected animals, extralabel use of medicated feed may be considered for treatment of minor species. Because of the need to have therapeutic options available for treatment of minor species, and to help ensure animal safety and human food safety, FDA is issuing this revised CPG to provide guidance to FDA staff with respect to factors to consider when determining whether to take enforcement action against a veterinarian, animal producer, feed manufacturer, and/or feed distributor for the extralabel use of OTC and VFD medicated feeds in minor species. In general, the Agency will not recommend or initiate enforcement action against the veterinarian, animal producer, feed mill, or other distributor when extralabel use is consistent with this document.

Appendix C

Definitions of Antimicrobial Use for Treatment, Control and Prevention:

The American Veterinary Medical Association (AVMA) professional policies provide guidance on the practice of veterinary medicine. The AVMA encourages its members to voluntarily adhere to policies impacting the practice of veterinary medicine, as these policies are developed by peers on behalf of the profession. AVMA policies are not, and do not supersede, law or regulation. AVMA's concise definitions[l] of treatment, control and prevention of individual animals and animal populations alleviate confusion and assist veterinarians in clearly communicating their intentions when prescribing or recommending antimicrobial use.[m]

Antimicrobial prevention of disease (synonym: prophylaxis):
1) Prevention is the administration of an antimicrobial to an individual animal to mitigate the risk for acquiring disease or infection that is anticipated based on history, clinical judgement, or epidemiological knowledge.
2) On a population basis, prevention is the administration of an antimicrobial to a group of animals, none of which have evidence of disease or infection, when transmission of existing undiagnosed infections, or the introduction of pathogens, is anticipated based on history, clinical judgement or epidemiological knowledge.

Antimicrobial control of disease (synonym: metaphylaxis):
1) Control is the administration of an antimicrobial to an individual animal with a subclinical infection to reduce the risk of the infection becoming clinically apparent, spreading to other tissues or organs, or being transmitted to other individuals.
2) On a population basis, control is the use of antimicrobials to reduce the incidence of infectious disease in a group of animals that already has some individuals with evidence of infectious disease or evidence of infection.

Antimicrobial treatment of disease:
1) Treatment is the administration of an antimicrobial as a remedy for an individual animal with evidence of infectious disease.
2) On a population basis, treatment is the administration of an antimicrobial to those animals within the group with evidence of infectious disease.

[l] AVMA Definitions of Antimicrobial Use for Treatment, Control and Prevention can be found at https://www.avma.org/KB/Policies/Pages/AVMA-Definitions-of-Antimicrobial-Use-for-Treatment-Control-and-Prevention.aspx

[m] Smith, D.R., et al. The AVMA's definitions of antimicrobial uses for prevention, control, and treatment of disease. *J Am Vet Med Assoc.* 2019 Apr 1;254(7):792-797. doi: 10.2460/javma.254.7.792

Appendix D

Division 7, Food and Agriculture Code, Chapter 4.5 – Livestock: Use of Antimicrobial Drugs

§14402.

(a) Beginning January 1, 2018, a medically important antimicrobial drug may be used when, in the professional judgment of a licensed veterinarian, the medically important antimicrobial drug is any of the following:

(1) Necessary to treat a disease or infection.

(2) Necessary to control the spread of a disease or infection.

(3) Necessary in relation to surgery or a medical procedure.

(b) A medically important antimicrobial drug may also be used when, in the professional judgment of a licensed veterinarian, it is needed for prophylaxis to address an elevated risk of contraction of a particular disease or infection.

(c) A person shall not administer a medically important antimicrobial drug to livestock solely for purposes of promoting weight gain or improving feed efficiency.

(d) Unless the administration is consistent with subdivision (a), a person shall not administer a medically important antimicrobial drug in a regular pattern.

(Added by Stats. 2015, Ch. 758, Sec. 1. (SB 27) Effective January 1, 2016.)

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