**Background:**
This Compliance Policy Guide (CPG) provides regulatory guidance for the development of cases resulting from the use of animal drugs contrary to label directions ("extra-label use") by non-veterinarians in food-producing animals. It also provides guidance on measures that can be taken by non-veterinarians to ensure proper drug use and avoid illegal residues (See CPG 7125.06 (Sec. 615.100) for guidance on proper drug use by veterinarians).

Extra-label use of drugs by non-veterinarians in food-producing animals is a significant public health concern and a contributing factor in illegal residues in edible animal tissue. Such use of drugs is illegal under the Federal Food, Drug, and Cosmetic Act (the Act). Under the Act, virtually all drugs that are intended for use in animals are subject to extensive pre-market approval requirements. New animal drugs (those drugs that are not generally recognized as safe and effective for their labeled conditions of use) may not be marketed unless they are the subject of an approved new animal drug application (NADA). A new animal drug that has not been approved is "unsafe" under Section 512 of the Act, and adulterated under Section 501(a)(5).

The pre-market approval process ensures that when animal drugs are used in accordance with the labeled directions (type of animal, medical conditions, dosage, route of administration, and any other precautions or instructions for the safe and effective use of the product, including withdrawal and milk discard times) milk, eggs, and the edible tissues of slaughtered animals treated with a drug will not contain potentially harmful or violative drug residues. The withdrawal time is the period following the last treatment with the drug during which the animal may not be offered for slaughter and during which products from this animal such as milk and eggs may not be offered for sale. The length of the withdrawal period is based upon the time necessary for drug residues in the animal to deplete to levels that are shown to be safe.

The withdrawal period is based on residue studies conducted under the labeled conditions of use (type of animal, dosage, route of administration) to ensure that residues above levels that have been shown to be safe will not be present in animal products used as human food. Those levels, called tolerances or safe concentrations, represent the amount of drug legally permitted in the edible tissue of the animal. The withdrawal period enables the animal to metabolically reduce the drug level in its tissues to levels that are not of public health concern.

**POLICY: Use of Drug Products Contrary to Label Directions**
A new animal drug is "unsafe" under Section 512(a)(1) of the Act and adulterated under Section 501(a)(5) when it is not used in accordance with its approved label directions. Therefore, use of an unapproved new animal drug or of an approved new animal drug contrary to label directions constitutes a violation of the Act.

Use by veterinarians and non-veterinarians (e.g., livestock and poultry producers, herdsman, dealers, haulers, etc.) of veterinary drug products in food-producing animals contrary to label directions is illegal. Uses that are contrary to label directions would include ignoring labeled withdrawal times or milk discard times, using the product in a species not indicated on the label, using the drug to treat a condition not indicated on the label, administering the drug at a different dosage than stated on the label, or otherwise failing to follow label directions for use and administration of the drug.

FDA, in the exercise of its regulatory discretion, allows veterinarians, acting in a valid veterinarian-client-patient relationship and in accordance with the conditions outlined in CPG 7125.06 (See Sec. 615.100) ("Extra Label Use of New Animal Drugs in Food-Producing Animals") to consider the use of a new animal drug contrary to label directions when the health of the animal is immediately threatened and suffering or death would result from failure to treat the affected animal(s). This policy applies only to licensed veterinarians who administer, prescribe, or dispense drugs in accordance with the policy guide and applicable state laws. If the veterinarian does not personally administer the drugs, certain labeling information is required, as explained in CPG 7125.06 (See Sec. 615.100). Also, no drug residues above permitted levels may be present in the final food product whenever a drug is used in an extra-label manner by a veterinarian.

**Avoiding Drug Residues Through Proper Drug Use**
The presence in food of a residue of a new animal drug above permitted levels causes the food to be adulterated under Section 402(a)(2)(D) of the Act. The ability of persons who produce and sell food-producing animals and animal products such as milk and eggs to have systems to monitor and control the use of animal drugs is an indispensable adjunct to providing appropriate therapy and is essential to avoiding illegal residues. Such systems also enable federal and state officials to monitor the food supply and ensure that it is free of harmful drug residues. Failure to establish and utilize such systems can result in adulteration of live food-producing animals, for reasons explained in the following paragraphs.

The Act defines food as "(1) articles used for food or drink for man or other animals... and (3) articles used for components of any such article." 201(f). Food-producing animals, even though not in their final, edible form, have been held to be food under the statute (United States v. Tomahara Enterprises Ltd., Food, Drug Cosm. L. Rep. (CCH) 38,217 (N.D.N.Y. 1983) (live calves intended as veal are food). More generally,
Section 402(a)(4) provides that a food shall be “deemed” to be adulterated “if it has been prepared, packed, or held under insanitary conditions whereby...it may have been rendered injurious to health.” The phrase “insanitary conditions” in §402(a)(4) is not limited to filth or bacteria. Indeed, the courts have construed “insanitary conditions” in §402(a)(4) to comprehend a variety of conditions that may render food injurious to health. See United States v. Nova Scotia Food Products Corp., 417 F. Supp. 1364, 1369-70 (E.D.N.Y. 1976), rev’d on other grounds, 568 F.2d 240 (2d cir. 1977); United States v. 1200 Cans, Pasteurized Whole Eggs, 339 F. Supp, 131, 140-41 (N.D. Ga. 1972). Thus, in the context of holding food-producing animals, FDA believes that “insanitary conditions” could include a lack of adequate controls concerning treatment of food-producing animals with drugs.

The “may have been rendered injurious to health” standard requires a reasonable possibility of injury. See United States v. Lexington Mill & Elevator Co., 232, U.S. 399, 411 (1914); see also Berger v. United States, 200 F.2d 818 (8th Cir. 1952). In FDA’s view, failure to maintain adequate controls with respect to use of animal drugs could result in a reasonable possibility of injury to human health because illegal drug residues often result from a lack of such controls, and illegal drug residues could have adverse toxicological effect on consumers, ranging from acute to chronic reactions.

Under the circumstances described above, FDA may regard live animals raised for food as adulterated under 402(a)(4). Persons involved in raising, handling, transporting, holding, and marketing food-producing animals are encouraged to establish systems to ensure that animal drugs are used properly and to prevent potentially hazardous drug residues in edible animal products. These control systems should include the following measures:

a. Identifying and tracking animals to which drugs were administered, in order to preclude the sale of edible animal tissue, milk, or eggs containing illegal residues (identification may be by specific animal identification, pen or lot, quarantine/segregation, or other means);

b. Maintaining a system of medication/treatment records that, at a minimum, identifies the animal(s) treated (individual animals, pens, lots, etc.), the date(s) of treatment, the drug(s) administered, who administered the drug(s), the amount administered, and the withdrawal time prior to slaughter (and when milk, eggs, etc. can be used, if appropriate);

c. Properly storing, labeling, and accounting of all drug products and medicated feeds;

d. Obtaining and using veterinary prescription drugs only through a licensed veterinarian based on a valid veterinarian-client-patient relationship; and

e. Educating all employees and family members involved in treating, hauling, and selling the animals on proper administration techniques, observance of withdrawal times, and methods to avoid marketing adulterated products for human food.

Establishing and maintaining such systems should help producers avoid marketing milk, eggs, or edible animal tissue containing illegal residues and avoid regulatory action based on Sections 402(a)(2)(D), 402(a)(4), or 501(a)(5).

Persons who do not administer medications but who purchase or lease animals for milking or sale for slaughter (such as livestock dealers) should also establish and implement a record-keeping system. This system should include information on the source of the animal and whether the animal has been medicated (when, with what drug, and the withdrawal period) to preclude marketing of edible animal tissue, milk or eggs, that may contain illegal residues.

Such persons may also be subject to regulatory action if they market animals containing illegal residues and have failed to take reasonable precautions to prevent the sale of adulterated food.

Regulatory Action Guidance:
FDA investigators should determine the extent of the misuse of drugs in food-producing animals during the course of their inspections or investigations, such as when following up on an illegal tissue residue report from United States Department of Agriculture/Food Safety and Inspection Service or other information concerning improper drug use. The occurrence of an illegal tissue residue will be regarded as prima facie evidence of improper drug use, and may be an appropriate subject for enforcement action. Of course, before recommending such action, FDA will also consider whether evidence of proper drug usage, as described under the “Policy” section above, exists to demonstrate that every reasonable effort has been made to preclude residues.

CVM is prepared to recommend regulatory action when drugs are misused as described above. If the misuse involves administration contrary to labeled directions, the drug itself is adulterated under Section 501(a)(5). If an illegal residue is involved, the food is adulterated under Section 402(a)(2) (D). Further, if an illegal residue is involved and inadequate control measures are documented, the food (edible animal tissue, milk, or eggs) may also be adulterated under Section 402(a)(4). Except in egregious situations, a Warning Letter is ordinarily the appropriate action of choice. Compliance Program 7371.006, Illegal Drug Residues in Meat and Poultry, provides additional regulatory guidance for illegal residues. Drug residues in milk should be handled according to Compliance Programs 7318.003, Milk Safety Program and 7371.008, National Drug Residue Milk Monitoring Program.

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