FARAD Digest

Breaking new ground

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In December 1996, final regulations for the implementation of the Animal Medicinal Drug Use Clarification Act (AMDUCA) were implemented by the FDA-Center for Veterinary Medicine (FDA-CVM). Food animal veterinarians now may use drugs legally in an extra-label manner, provided there are data to support the human food safety of such use. The Food Animal Residue Avoidance Databank (FARAD) is a USDA-sponsored program whose purpose is to help prevent or minimize the occurrence of chemical residues in food animal products. The FARAD comprises a comprehensive, unique database of pharmacokinetic and toxicokinetic information on veterinary drugs and other chemicals and, therefore, is a valuable information resource to aid food animal veterinarians in complying with AMDUCA regulations.

Residue and pharmacokinetic information is used by FARAD personnel to help develop withdrawal recommendations for some extra-label drug uses and to aid in the mitigation of other problem residues (eg, pesticides, environmental contaminants, mycotoxins). In addition, FARAD generally serves as a clearinghouse for a wide variety of residue avoidance information, such as milk and meat residue tests, the latest regulatory guidance from the FDA-CVM, tolerances, action and safe levels, and up-to-date drug label information.

The "FARAD Digest" will be an ongoing *JAVMA* feature designed to assist veterinarians with the implementation of AMDUCA by providing the data required to use drugs without incurring costly illegal residues. Articles published in this feature will describe the rationale and processes used to develop extra-label withdrawal recommendations that comply with AMDUCA. In addition, articles will cover late-breaking developments from FDA-CVM regarding extra-label drug use as well as other residue avoidance topics. This introductory article describes the FARAD program and how it is currently organized and provides some practical tips on how to best access FARAD. In the future, many withdrawal recommendations for drugs commonly used extra-labelly in food animals will be published in the "FARAD Digest."

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Development and Current Organization of FARAD

The FARAD was developed in 1982 as part of the USDA's national Residue Avoidance Program, which was designed to help producers and veterinarians prevent violative residues via education rather than regulation. It is a cooperative project of North Carolina State University (NCSU), the University of California-Davis (UC-Davis), and the University of Florida. Originally, FARAD consisted of 3 regional access centers located at NCSU, UC-Davis, and the University of Illinois National Animal Poison Control Center, but it was recently reorganized and now consists of only 2 access centers, an eastern regional access center located at NCSU and a western regional access center located at UC-Davis.

How to Access FARAD

As part of the reorganization of FARAD, a toll-free telephone number (888-US-FARAD [888-873-2723]) routes calls to both regional access centers. Calls placed before 11:00 AM Pacific time are routed to the North Carolina office, and calls placed after that time are routed to the California office. Although anyone may call the FARAD regional access centers to request residue avoidance information, only veterinarians will be provided extra-label withdrawal recommendations.

FARAD Information Resources

Two sites on the World Wide Web are maintained by the FARAD. The addresses for these sites are *http://ace.orst.edu/info/farad* and *http://cptc.ncsu.edu/farad*.

The first site contains a complete, up-to-date, searchable listing of label information for all veterinary drugs approved for use in food animals in the United States. The second site provides additional background information about FARAD and describes some of the resources available.

Additional resources available from FARAD include the FARAD Compendium (a comprehensive compendium of FDA-CVM approved food animal drugs) and 2 Windows-based computer programs "The Veterinarian's Guide to Residue Avoidance Management (VetGRAM)," which contains complete label information for all approved food animal veterinary drugs, and the "Producer's Guide to Residue Avoidance Management (ProGRAM)," which contains label information for over-the-counter drugs only. Both contain in-

formation about commercial residue test kits, tolerances, and action and safe levels for drugs and other chemicals. These programs allow users to quickly locate drug label information for a particular species and to search based on indications for use.

When to Call FARAD

Most calls to FARAD are requests for withdrawal recommendations for extra-label drug use. Veterinarians who intend to use a drug in an extra-label manner in food animals and who need advice on establishing a safe withdrawal period should call FARAD before the drug is used. The FARAD personnel will assist veterinarians in establishing an appropriate withdrawal interval, and if there are no suitable pharmacokinetic or residue data available to determine a withdrawal recommendation, FARAD personnel will advise the caller. Withdrawal recommendations will not be made for drugs in which extra-label use is prohibited (Appendix).

Callers to FARAD should have the following information available: species of animal, dose (mg/kg of body weight or mg/lb), treatment regimen (how many doses and at what interval), route of administration, and trade name of the drug. The dose should be expressed in units of mg or international units per kg of body weight, which allows rapid comparison of the proposed dose with doses contained in our database. If this is not possible, callers should provide information about the volume of the injection (ml or cc), weight of the animal, and concentration of the drug formulation used.

Because FARAD operates with a restricted budget, it may be necessary to leave a message on an answering machine. Usually, FARAD personnel return calls within 1 or 2 hours; however, in some cases, particularly for unusual requests, determination of withdrawal recommendations may take 2 days or more.

Requests for information also may be sent to the FARAD, using the following e-mail addresses: *farad@ucdavis.edu* (California) or *farad@ncsu.edu* (North Carolina) or fax numbers: 916-752-0903 (California) or 919-829-4358 (North Carolina). All e-mail and fax requests should include complete dosing information and a telephone number in case additional information is needed. All FARAD withdrawal recommendations are subject to change as new data become available.

Extra-label Withdrawal Recommendation Development

Withdrawal recommendations for extra-label use of drugs are derived in several ways. In some cases, the proposed extra-label use actually may be an approved label use in another country. In this case, the foreign withdrawal time will be used and slightly extended to ensure an extra margin of safety. If there are no data available from any foreign sources, pharmacokinetic or residue data in the FARAD database may be used to calculate a withdrawal time. If there are extensive kinetic data (time-concentration data), FARAD personnel will conduct a pharmacokinetic analysis of the data to determine the time at which the meat or milk concentration would be expected to reach the tolerance or detection limit for the particular drug. When a withdrawal time is calculated pharmacokinetically, additional time may be added to provide a greater margin of safety to account for variables (health status, breed, sex, age, individual difference) that affect how rapidly individual animals metabolize and excrete the drug. For meat, times may be extended even longer because of the greater variability and longer periods over which tissue residues deplete.

Some residue studies do not report sufficient pharmacokinetic data to conduct an independent pharmacokinetic determination of a withdrawal interval, but do state when milk or meat residues were no longer detected. In this case, the time it takes for the residue concentration to become undetectable is taken as the initial withdrawal recommendation, to which the same safety factors, as described, are applied.

Appendix

Drugs and classes of drugs for which extra-label use in food animals is prohibited by FDA-CVM

Chloramphenicol
Clenbuterol
Diethylstilbestrol
Dipyrone
Fluoroquinolones (eg, enrofloxacin, sarafloxacin)
Furazolidone (except for approved topical uses)
Nitrofurazone (except for approved topical uses)
Nitroimidazoles (eg, dimetridazole, ipronidazole)
Sulfonamides in lactating dairy cattle (with the exception of approved uses of sulfadimethoxine, sulfabromomethazine sodium, and sulfaethoxy-pyridazine)