FARAD NEWSLETTER

The FARAD Newsletter is an electronic publication from the **Food Animal Residue Avoidance Databank** (FARAD) for veterinarians, animal scientists, extension specialists and the regulatory community.

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The FARAD crew wishes all newsletter readers a happy, healthy and fulfilling new year. Like all of you, we are anxiously waiting to see what happens with the federal budget as FARAD continues to be funded through USDA-CSREES on a year by year basis with sympathetic congressmen using-up their ear marks to keep us in the budget. There is concern about how the 110th Congress is going to handle earmarks as they are often seen as pork [FARAD as a national program is not pork but we get tarred by the same brush]. Bottom line is that, if FARAD is stripped from the budget as an earmark and does not get restored, there will no money for FARAD to continue after July 2007. We just managed survive this once before and it was not pretty. If FARAD can survive another funding lapse, it will take years to restaff the program and even longer to play catch-up. FARAD cannot lobby Congress itself but if any of our readers have suggestions or friends in high places let them or the AVMA know.

FARAD ON CD – 2nd YEAR

This is the second year for the FARAD on CD subscription. If you want to subscribe please see the form at the end of the newsletter for details. The CD features a number of customized

compendia ranging from a complete listing of all FDA Approved Drugs [includes legal citations for the approval and any amendments or additions] to species specific compendia of currently marketed drugs. The subscription is for quarterly issued CDs and the cost is $75 which covers production and mailing costs.

FARAD will be at the North American Veterinary Conference with a booth outside the entrance to the trade exhibit. Please come by and find out more about the CD subscription or have a discussion on residue avoidance issues and the future of FARAD.

OFFICE OF MINOR USES AND MINOR SPECIES [OMUMS]

New Director

Dr. Bernadette Dunham became director of OMUMS at the start of 2007. This follows the retirement of long-time advocate for MUMS, Dr Andrew Beaulieu. FARAD Newsletter readers send their congratulations to Dr. Dunham and best wishes to Dr. Beaulieu for a long and healthy retirement. We wonder if his colleagues gave him one of those mattresses that feature sheep in the advertising or he took out an insurance policy advocated by that duck. Both are minor species that owe much to Andy's efforts on their behalf.

MUMS Designations

FDA's Center for Veterinary Medicine has granted the first minor use and minor species drug designations under the Minor Use and Minor Species Animal Health Act (MUMS.)

The designation of minor use and minor species drugs has been possible since the MUMS Act was signed into law in August of 2004. Designation is a package of incentives loosely modeled on those included in the Orphan Drug Act for human drugs. To be eligible for these, sponsors must apply for designation prior to filing a New Animal Drug Application for FDA approval. At the time that a designated drug gains approval or conditional approval, it is awarded 7 years exclusive marketing rights. This means that FDA will not approve another application for the same drug in the same dosage form for the same intended use until after the 7 years have elapsed. The proposed rule governing designation was published in the Federal Register on September 27, 2005 with comments solicited with a closing date of January 27 2007..

The first drug to receive this designation is Florfenicol (Aquaflor®), and it has been designated for use in controlling conditions in four aquaculture species – catfish, hybrid striped bass, salmonids, and tilapia. Designations that are granted are posted on a list on the Minor Use and Minor Species page of the CVM website.

Any questions about MUMS designations may be directed to Dr. Bernadette Dunham, Center for Veterinary Medicine (HFV-50), 7519 Standish Place, Rockville, MD 20855, 240-276-9090, or e-mail Bernadette.Dunham@fda.gov.

MUMS Indexing

FDA is also soliciting comments on the proposed rule for establishing a drug "Index" under the Minor Use and Minor Species Animal Health Act (MUMS Act). The indexing proposal, which FDA released for comment in August 2006, would permit drug companies to legally market unapproved new animal drugs mostly for minor species that are not used for food. (Exceptions are possible in cases in which a drug could be used for early life stages of food animals, e.g., fish eggs, oyster spat). The rule is intended to help drug manufacturers legally market drugs sold in pet stores and drugs intended for use in wildlife and zoo animals.
Interested persons may submit to the Division of Dockets Management written or electronic comments on this document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number 2006N-0067. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Some Reminders on Extralabel Drug Use in Food-Producing Animals

Drug Use Clarification Act (AMDUCA) of 1994. Prior to AMDUCA, veterinarians were not legally permitted to use an animal drug in any way except as indicated on the label.

Following the passage of AMDUCA, veterinarians gained the right to prescribe/dispense the "extralabel" use of drugs but the Food and Drug Administration (FDA) places limits the extralabel use of drugs to protect public health.

Extralabel drug use [ELDU] occurs when the drug's actual or intended use is in a manner not in accordance with the approved labeling. For instance, ELDU occurs when administration is:

- for a species not listed on the label;
- for an indication, disease or other condition, not on the label;
- is at a dosage level or frequency not on the label; or
- by a route of administration not on the label.

The ELDU rule allows veterinarians legally to go beyond label directions in using animal drugs, and permits them to use legally obtained human drugs in animals. However, the rule does not permit ELDU in animal feed. Further, ELDU must take place within the confines of a valid veterinarian-client-patient relationship. This means that the veterinarian must have sufficient knowledge of the animal to make a preliminary diagnosis on which the intended use of drugs is based. In the case of food producing animals, the veterinarian is responsible for establishing a "substantially extended withdrawal time" that is "supported by appropriate scientific information." This latter requirement is one that FARAD is especially geared up to help practitioners meet.
ELDU is limited to cases in which the health of the animal is threatened, or suffering or death may result from a lack of treatment. ELDU is not an option where the drug use is to enhance production.

Veterinarians can consider ELDU in food-producing animals only when no approved drug is available for use that contains the same active ingredient in the required dosage form and concentration, or that the veterinarian finds that there is no approved drug that is clinically effective for the intended use.

In summary, the veterinarian must:

- Make a careful diagnosis or evaluation of the conditions to be treated;
- Establish a substantially extended drug withdrawal period that is supported by scientific evidence;
- Take the steps necessary to be sure the withdrawal period is met and no illegal drug residues occur in food from the treated animals; and
- Institute procedures to make sure the treated animal's identity is known. And that records relating to details of the ELDU are retained for the required two years.

The AMDUCA regulation places requirements on the veterinarian to properly label the drugs used extralabel and to give the livestock owner complete instructions about proper use of the drug and withdrawal times. Veterinarians remain responsible for any voliative drug tissue residues that occur because of ELDU under their supervision.

Under no circumstances can a non-veterinarian order the extralabel use of a drug in animals. This is the reason that FARAD's consultative services have to be limited to veterinarians.

Prohibited from extralabel use

AMDUCA also gives FDA the right to prohibit the use of certain drugs from use in food producing animals when their use can be a hazard to human health.

The prohibition can be against all uses of a drug, or against the use in limited species, or limit use to certain indications, dosages, forms, routes of administration, or a combination of factors.

The list currently includes:

- Chloramphenicol
- Clenbuterol
- Diethylstilbestrol
- Dimetridazole and Other nitroimidazoles (including metronidazole)
- Furazolidone, nitrofurazone, other nitro furans (including topical administration)
- Fluoroquinolones
- Glycopeptide
- Ipronidazole
- Gentian Violet
- Phenylbutazone animal and human drugs in female dairy cattle 20 months of age or older
- Sulfonamide drugs in lactating dairy cattle (except approved use of sulfadimethozine, sulfabromomethazine, and sulfaethoxpyridazine

There were two new prohibitions added last year. They were for drugs used to treat influenza in humans. These drugs, or classes of drugs, are prohibited from use in chickens, turkeys, and ducks:

- Adamantanes (amantadine and rimantadine)
- Neuraminidase inhibitors (oseltamivir and zanamivir)

REF: FDA Veterinarian, 2006, Volume XXI, No. III.

HORSING AROUND

CLENBUTEROL

FDA's Center for Veterinary Medicine [CVM] has recently posted an alert on its web site http://www.fda.gov/cvm/CVM_Updates/ClenbuterolSupp.htm warning veterinarians and horse owners of the deaths of several horses in Louisiana associated with the use of an unapproved product labeled as "Clenbuterol HCL'. Boehringer Ingelheim Vetmedica, Inc. is the only manufacturer of approved clenbuterol products which are sold under two different tradenames:

- Ventipulmin ® Syrup (under the Boehringer name),
- Aeropulmin ® Syrup (under several different distributor names)

If readers are uncertain about the safety of a particular drug packet they have, it should be labeled : *"NADA 140-973 Approved by FDA "*

CVM asks that horse owners and veterinarians who are aware of horse injuries or deaths that may have been caused by "Clenbuterol HCL" report this to the FDA office in their area. The numbers for the office can be found at: http://www.fda.gov/opacom/backgrounders/complain.html.

Please remember that clenbuterol is **PROHIBITED** from use in food producing animals. The reason for this prohibition is the serious CNS side effects reported in France, Italy and Spain after people ate liver and muscle from cattle treated with clenbuterol. Clenbuterol was also implicated in the death of a cyclist in the Barcelona Olympics .

USDA TESTING FOR HORSE RESIDUES

Before reading further, please note that all drugs approved by FDA-CVM for use in horses are restricted to those animals not intended for human consumption. Readers will be aware of pending legislature regarding slaughterhouses for horses destined for consumption in Europe and Asia and that these slaughterhouses come under the control of USDA-FSIS. In the 2004 FSIS Red Book [table 119] there is data from 17 horses sampled under an exploratory testing program and three had violative positive results [2 for penicillin and 1 for phenylbutazone]. Please note that phenylbutazone is not approved for use in horses in the European Community except for companion and competing animals where a detailed record ["Passport"] has to be kept for that animal's lifetime with the assumption that the animal will not enter the food chain. Thus there is

a zero maximum residue level [MRL] which is synonymous with FDA's tolerance for equine carcasses which mean none of the tissues should contain detectable levels of phenylbutazone.

FARAD does not provide withdrawal information on horses intended for overseas markets but suggests interested people consult medical and pharmacological texts written specifically for readers in those countries.

NARMS 2004 Annual Report Notes Enhanced Meat Sampling

FDA's Center for Veterinary Medicine (CVM) has posted the National Antimicrobial Resistance Monitoring System – Enteric Bacteria (NARMS) Retail Meat Annual Report for 2004 on its Web site at: http://www.fda.gov/cvm/NARMSReport2004.htm. The primary purpose of the NARMS retail meat surveillance program is to monitor the prevalence of antimicrobial resistance among foodborne pathogenic and commensal organisms, in particular, *Salmonella*, *Campylobacter*, *Enterococcus* and *E. coli*. The project includes both active surveillance for foodborne diseases and related epidemiologic studies designed to help public health officials better understand foodborne diseases in the United States.

The results generated by the NARMS retail meat program establish a reference point for analyzing trends of antimicrobial resistance among these foodborne bacteria.

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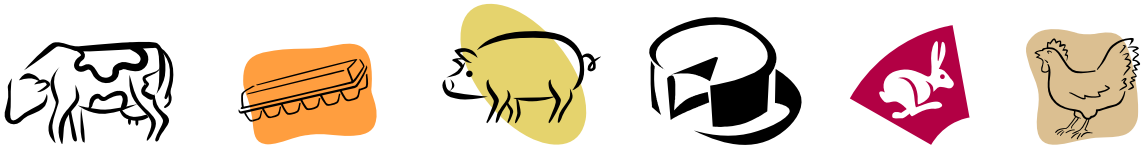
2nd Edition!

.FARAD on CD

A Searchable Compilation of FDA Approved Food Animal Drugs



CD Includes:

- Complete Compendium of all FDA Approved Animal Drugs
- Species Specific Compendia of currently marketed animal drugs
- Searchable PDF files, printable reports, species specific abstracts, and regulatory information
- Quarterly Updates (disks will be sent in January, April, July, and October). Subscriptions will be pro-rated so renewal will be solicited in December for the coming year.
- The CD contains no extra-label information because, while .FARAD provides withdrawal intervals for specific clinical situations, it is not permitted to promote extra-label use of drugs.
- Annual Subscription is $75 (January through December). The subscription is being handled by DHIA Services. Readers can order on-line .FARAD web site at www.farad.org