What is an ADE?

In common terms, an adverse drug event (**ADE**) is either an undesired side effect, or the lack of a desired effect. The Center for Veterinary Medicine (**CVM**) defines an ADE as "*any side effect, injury, toxicity, or sensitivity reaction (or failure to perform as expected) associated with use of an animal drug, whether or not determined to be attributable to the drug*."

What are the FDA Center for Veterinary Medicine's specific areas of interest?

The primary purpose of our ADE monitoring system is to detect problems, or "side effects" associated with the use of FDA-approved animal drugs. During the research studies that lead to drug approval, only a limited number of animals are treated. Because of this, effects or problems that only occur rarely may not be discovered until after the drug has been widely marketed and used in a clinical setting.

Lack of effectiveness is also an adverse event. The majority of reports of this nature involve anesthetics, tranquilizers, and anthelmintics. These reports can be difficult to evaluate, but a group of similar reports will prompt further investigation.

CVM gives careful consideration to any reports of adverse events occurring in humans as a direct result of using or administering an animal drug or in other situations involving accidental human exposure. Product defects or any unintended effect on the environment and/or wildlife would also be considered adverse events.

Does CVM review reports that involve the extra-label use of animal drugs?

The reporting of ADEs associated with extra-label use is important to the veterinary profession. Under the Animal Medicinal Drug Use Clarification Act of 1994, veterinarians can administer drugs more freely in an extra-label manner. About one-third of the reports on file involve extra-label use. We are also interested in ADEs involving human drugs used in veterinary practices, and in ADEs involving animal drugs marketed without FDA approval.

Who monitors reports of ADEs for products used to treat animals?

The FDA Center for Veterinary Medicine monitors reports of ADEs for animal drug products, medicated feeds, and animal devices under the Federal Food, Drug, and Cosmetic Act.

Animal vaccines and most biologics (e.g., rabies vaccines) are regulated by the United States Department of Agriculture (**USDA**) under the Federal Virus, Serum and Toxin Act.

Most of the products used topically for the control of ectoparasites and insects on animals are regulated by the Environmental Protection Agency (**EPA**) under the Federal Insecticide, Fungicide and Rodenticide Act.

The United States Pharmacopeia (**USP**) operates an independent, non-government reporting program called the Veterinary Practitioner's Reporting Program. USP will forward reports of ADEs to the appropriate regulatory agency and the drug company, at the discretion of the person reporting. This program has the support and endorsement of the American Veterinary Medical Association. The USP program is not affiliated with FDA.

Are there any laws that require reporting of ADEs?

Reporting by veterinary medical professionals is entirely voluntary. However, Federal regulations require that drug companies of FDA-approved animal drugs send FDA all information concerning adverse drug events reported to, or coming to the attention of, the company. Products regulated by USDA and EPA do not have the same reporting requirements as animal drugs.

Who submits these reports?

Roughly ninety-five percent of the reports are submitted by drug companies after learning of the adverse event from a veterinarian or animal owner. The other five percent of reports are submitted by veterinarians and animal owners directly to CVM or USP.

How many reports does CVM receive each year?

Veterinarians at CVM evaluate over 18,000 reports annually. This estimate includes reports of product defects.

If I decide to report an ADE, who should I contact?

You should first call the drug company for an FDA-approved animal drug. Inform them that you wish to report an ADE, and ask to speak to a technical services veterinarian. The technical services veterinarian should ask a series of questions about the event, complete a form called the FDA 1932, and forward the report to CVM. We suggest the drug company as your first point of contact because many companies will also offer clinical advice or diagnostic assistance. CVM does not provide these services. Drug company phone numbers can usually be obtained from product labeling, or from the publications **Compendium of Veterinary Products** (North American Compendiums Inc.) and **Veterinary Pharmaceuticals and Biologics** (Veterinary Medicine Publishing Company).

If you prefer not to call the drug company, you can contact **CVM** toll-free at (888) FDA-VETS. Please provide the information as requested by the telephone instructions. We can also provide a supply of prepaid mailers (Form FDA 1932a). These mailers are available by writing or telephoning CVM, and are also available through the CVM Internet site at (www.fda.gov/cvm/forms/fda1932a.pdf).

If the ADE involves a product other than a drug, the following numbers may be useful. The phone number to reach **USDA** regarding biologics (vaccines) is (800) 752-6255. The phone number to reach **EPA** regarding topical insecticides is (800) 858-7378. A third option for reporting is the Veterinary Practitioners' Reporting Network (**USP-PRN**) sponsored by the United States Pharmacopeia. The USP-PRN program is an independent, non-government reporting program. The phone number to reach USP regarding any animal medicinal product is (800) 4-USPPRN.

What happens after I report an ADE?

Each ADE report is evaluated by a veterinarian and entered in a computer database. The reviewer assigns codes to items that describe the drug(s) and animal(s) involved. These items become separate fields of information. The reviewer also enters a brief clinical description of the ADE, and makes an assessment of whether the event is judged to be drug related using an algorithm scoring system.

CVM publishes an annual summary of ADE reports. The summary provides the number of reports and the clinical signs associated with each drug in the database. The information is limited to those reports that were assessed as at least "possibly drug related". The publication is available from the FDA Center for Veterinary Medicine. CVM also provides the ADE annual summary on a World Wide Web Internet server (**www.fda.gov/cvm)**

Other information and reports from the database can be requested on an individual basis by filing a written Freedom of Information (**FOI**) request. For more information about filing a request, you can contact the FDA FOI Staff at (301) 827-6500.

What actions result from reports of ADEs?

A group of similar reports submitted in a short period of time may alert CVM and the drug company to a problem with a

particular lot of drug. This may result in a product recall of the affected lot.

Another outcome would be for a label change to include new information gleaned from reported ADEs. The changes may include new warnings, contraindications or human safety information. In very rare instances, a drug may be removed from the market due to problems discovered by ADE reporting.

At times, CVM may require the involved drug company to issue a "Dear Doctor" letter to veterinarians informing them of the type of actions that had resulted from ADE reports.

Why should veterinarians in practice care about reporting an ADE?

Veterinarians in practice depend on the information available on drug labeling to make informed choices about the risks and benefits associated with the use of a drug. The purpose of ADE monitoring is to ensure that animal drug labeling is adequate and accurate.

In spite of the highest standards for safety and effectiveness that exist for FDA approval, not everything is known about a drug when it is first marketed. Due to the limited size and controlled nature of pre-marketing clinical trials, only the most common adverse events will be observed and included in product labeling at the time of FDA approval. An accurate safety profile emerges only after a product is marketed and the number and spectrum of animals receiving the drug increases.

As a practicing veterinarian, you are in a unique position to observe adverse clinical outcomes associated with the use of drug products. Some of these problems may only be associated with extra-label drug use. You can assist in the development of a complete safety profile by reporting adverse events. Such reports are often the first signal that a problem exists. By participating in the reporting program and contributing to our knowledge of animal drugs, you provide a valuable service to animals, the public, and your colleagues in the veterinary profession.

Where can I obtain information for a specific drug concerning potential adverse reactions?

The drug manufacturer is usually the best source for this type of information. Other sources include the FDA Center for Veterinary Medicine, the FDA/CVM Internet World Wide Web server (www.fda.gov/cvm), the National Animal Poison Control Center (www.napcc.aspca.org), the USP (www.usp.org), and veterinary computer networks such as VIN and NOAH. *(04/01)*

FDA/CVM Adverse Drug Event Reporting System
Division of Surveillance (HFV-210)
FDA/Center for Veterinary Medicine
7500 Standish Place
Rockville, MD 20855-2773

U.S. Food and Drug Administration
Center for Veterinary Medicine

Pharmacovigilance of Animal Drugs

Adverse Drug Event Reporting System

A monitoring program for adverse events associated with the use of drugs in animals

and

Why your participation is important!

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