GENERAL REVIEW AND ENFORCEMENT POLICIES

NEW ANIMAL DRUGS FOR INVESTIGATIONAL USE

Statutory authority to exempt new animal drugs from the requirements of an approved new animal drug application is found in Section 512(j) of the Federal Food, Drug, and Cosmetic Act (the Act). This exemption makes it possible for unapproved new animal drugs to be distributed for use by experts, qualified by scientific training and experience, to investigate the safety and effectiveness of animal drugs. In order to distribute a new animal drug for clinical investigations, an exemption from the requirements of an approved new animal drug application (NADA) must be claimed. Claiming an exemption is accomplished by submitting certain information. This body of information is referred to as an investigational new animal drug (INAD). In older records, it may be referred to as a veterinary investigational drug (VID). The regulations describing the procedures and the information requirements for investigational new animal drugs are found in 21 CFR 511.1. Additionally, the regulations describe the requirements for distributing unapproved new animal drugs for tests in vitro and in laboratory research animals. A notice of claimed investigational exemption is not needed for these research activities but the drugs must be labeled and controlled as designated by the regulation.

1. Purpose:

   This guide identifies the purpose of investigational new animal drug exemptions, uses for which they may be granted, and the responsibilities of their sponsors.

2. Purpose of INADs:

   The purpose of INADs is to permit the interstate shipment of unapproved drugs intended for use in animals other than man so that:

   a. Firms can conduct investigations to obtain the safety and effectiveness data needed to support the approval of a new animal drug application for the product.

   b. Individual research may be conducted while, at the same time, the public is being protected from any unsafe residues of the investigational drug in food products.

   c. Special treatment of specific animals with unapproved drugs may be provided for (see Guide 1240.3025).

3. Submission of an INAD Exemption Request:

a. The sponsor of a clinical investigation must submit to the Food and Drug Administration (FDA) a Notice of Claimed Investigational Exemption for a New Animal Drug before the drug may be shipped. This notice will be submitted as an INAD application.

The sponsor may be a pharmaceutical company, veterinary clinic, educational institution, government agency, or individual. The INAD application must be signed by the sponsor or by an agent acting on behalf of the sponsor.

b. The initial submission of information requesting an investigational exemption for a particular drug is considered to be an original INAD. An original INAD will generally be established for each new chemical entity, combination, dosage form, and sponsor.

c. The submission of additional data, protocols, changes in experimental design, or details of individual drug shipments by a sponsor, following FDA's acknowledgement of the original INAD, are considered to be amendments to the original application.

d. Trials using the investigational drug may commence at any time following submission of the investigational exemption to FDA. However, animals treated with the investigational drug may not be used for food until expressly authorized by FDA (see item 6).

4. Responsibilities of the Sponsor:

a. General:

(1) The sponsor shall insure that the new animal drug or animal feed containing the new animal drug will actually be used for tests in animals and will not be used in humans.

(2) The sponsor shall submit to FDA any information with respect to the investigation which may affect a determination on whether there are grounds for terminating the investigational exemption in the interest of the public health.

(3) The sponsor shall assure that the investigation is monitored by a person qualified by scientific training and experience to evaluate information obtained from the investigation. The monitoring of investigations should be conducted

according to acceptable procedures, such as those described in FDA's Conduct of Clinical Investigations: "Responsibilities of Clinical Investigators and Monitors for Investigational New Animal Drug Studies," October 1992.

(4) The sponsor shall promptly investigate and report to FDA and to all investigators any findings associated with the use of the new animal drug that may suggest significant hazard(s) to the target animal or to man as a result of consuming edible products from the animal.

(5) The sponsor shall submit either an environmental assessment pursuant to 21 CFR 25.31 or a claim for categorical exclusion under 21 CFR 25.24

b. Recordkeeping:

(1) The sponsor shall maintain the following information for a period of at least two years:

(a) Names and addresses of the investigators (individuals or organizations) to whom the drug was shipped.

(b) Date, quantity, and batch or code mark for each drug shipment or delivery.

(2) The sponsor shall retain reports received from investigators for a period of two years after the discontinuation of the study or after approval of a new animal drug application.

(3) The sponsor shall make such records and reports available for inspection and copying upon the request of an authorized employee of the Department of Health and Human Services at reasonable times.

c. Selection of Investigators:

(1) The sponsor shall assure that the new animal drug is shipped only to investigators who are qualified by scientific training and experience to evaluate the safety and/or effectiveness of new animal drugs.

(2) Investigators must agree to:

(a) Maintain complete records of the receipt and disposition of each shipment or delivery of the investigational drug.

(b) Furnish adequate and timely reports of the investigation to the sponsor.

(c) Maintain completed copies of all records of the investigation for two years after the discontinuation of the investigation or the approval of a new animal drug application for the product.

(d) Conduct the investigations in accordance with the Good Laboratory Practice for Nonclinical Laboratory Studies regulations (21 CFR Part 58) and the New Animal Drugs for Investigational Use regulations (21 CFR 511.1).

d. Prohibited Activities:

(1) The sponsor shall not unduly prolong distribution of the new animal drug for investigational use.

(2) The sponsor shall not (nor shall any person acting on behalf of the sponsor) represent the new animal drug as being safe or effective for the purposes for which it is being investigated. (This requirement is not intended to restrict the full exchange of scientific information.)

(3) The sponsor shall not commercially distribute nor test-market the new drug until a new animal drug application is approved pursuant to Section 512(c) of the Act. This does not preclude the sponsor from recovering the cost of drug production shipped to the investigator.

e. Contract Research Organizations:

(1) A "contract research organization" is a person that assumes, as an independent contractor with the sponsor, one or more of the obligations of a sponsor, e.g., protocol design, selection of investigators, monitoring of investigations, evaluation of reports, and preparation of materials to be submitted to FDA.

(2) Any or all of the obligations of the sponsor may be transferred to a contract research organization. Any such transfer shall be in writing and, if not all

obligations are transferred, shall describe each of the obligations being assumed. If all obligations are transferred, a general statement to that effect is acceptable. Any obligation not covered by the written description shall be deemed not to have been transferred.

(3) A contract research organization that assumes any obligation(s) of a sponsor shall comply with the specific regulations applicable to the obligation(s) assumed.

5. Authorized Uses of Investigational New Animal Drugs:

a. New animal drugs for tests in vitro and in laboratory research animals:

(1) A shipment or delivery of a new animal drug or an animal feed containing a new animal drug intended solely for tests in vitro or in animals used only for laboratory research purposes shall be exempt from Sections 512(a) and 512(m) of the Act provided the following conditions are met:

(a) The new animal drug or feed containing the new animal drug must bear the following labeling before the article is shipped or delivered to the investigator:

CAUTION: Contains a new animal drug for investigational use only in laboratory research animals or for tests in vitro. Not for use in humans.

(b) The person distributing or causing the distribution of the new animal drug shall use due diligence to assure that the consignee is regularly engaged in conducting research and that the drug is actually used for in vitro tests or for testing in animals used only for research.

(c) The sponsor is not required by law to notify FDA of the shipment or delivery of new animal drugs for tests in vitro or in laboratory animals; however, such notification is encouraged.

(2) The person distributing or causing the distribution of the new animal drug is responsible for assuring that adequate records are maintained.

(3) Any species of animal may potentially be used in laboratory studies.

Laboratory research, however, must be the animal's sole intended function. Animals used for food purposes or for livestock (breeding) purposes, or animals which are kept as pets, are not considered to be laboratory animals.

(4) A new animal drug is not exempt from the requirements of Section 512(a) of the Act when its intended use is the prevention or treatment of a naturally occurring disease of laboratory animals.

b. New animal drugs for clinical investigation in animals:

A shipment or other delivery of a new animal drug or feed containing a new animal drug intended for clinical investigational use shall be exempt from Sections 512(a) and 512(m) of the Act if all of the following conditions are met:

(1) Prior to shipment, the sponsor shall submit in triplicate to FDA a "Notice of Claimed Investigational Exemption for a New Animal Drug," including a signed statement containing the following information:

(a) The identify of the new animal drug.

(b) Copies of all labeling and other pertinent information to be supplied to the investigators.

(c) The name and address of each investigator. (Most of this information will be supplied in amendments to the original INAD.)

(d) The approximate number of animals to be treated and the number of control animals. If this information is not available, the amount of new animal drug to be shipped must be provided.

(e) Approximate dates of the beginning and end of the experiment or series of experiments.

(f) The maximum daily dose(s) to be administered to a given species, the size of animal, the maximum duration of administration, and the method(s) of administration.

(g) A statement containing the name and address of the contract research organization (if any) to which the sponsor has transferred any

obligation(s) for the conduct of the clinical investigation, identification of the study or studies involved, and a listing of the obligation(s) transferred.

(2) If the product is to be administered to food-producing animals, the following additional information must be submitted:

A commitment that edible products from the investigational animals shall not be used for food without prior authorization.

(3) The labeling of the new animal drug or feed containing the new animal drug must bear the following statements:

CAUTION: Contains a new animal drug for use only in investi- gational animals in clinical trials. Not for use in humans. Edible products of investigational animals are not to be used for food unless authorization has been granted by the U.S. Food and Drug Administration or by the U.S. Department of Agriculture.

If the product container is too small to accommodate a label with sufficient space to bear the caution statements, the statements may be included on the carton label and other labeling on or within the package from which the product will be dispensed.

(4) The person distributing or causing the distribution of the new animal drug or feed containing the new animal drug shall use due diligence to assure that it will actually be used for tests in animals and will not be used in humans.

(5) The person distributing or causing the distribution of the new animal drug or feed containing the new animal drug shall assure that adequate records are maintained.

(6) If any of the information specified above is omitted or inadequate, FDA may withhold the assignment of an INAD number or may refuse authorization until the information is provided.

6. Authorization for Use of Edible Products:

a. Food products (meat, milk, or eggs) from animals treated with investigational new animal drugs may only be marketed after receipt of authorization. The request for authorization shall be made according to the procedures in 21 CFR 511.1(b)(5). The following information must be submitted before authorization may be granted:

(1) Information to show that food derived from animals treated at the maximum dose administered and at the proposed withdrawal period, if any, does not contain unsafe residues of the drug or its metabolites.

(2) The name and location of the packing plant where the animals will be processed. (This requirement may be waived on request.)

b. The granting of an authorization does not exempt the investigational animals or their products from compliance with other applicable inspection requirements.

7. Imported Investigational New Animal Drugs or Bulk Drug Substances Intended for Use in Manufacturing Investigational New Animal Drugs:

See 21 CFR 511.1(b)(9) and Guide 1240.3032 for special notification requirements for imported new animal drugs and drug substances for investigational use.