Republic of the Philippines
DEPARTMENT OF AGRICULTURE
Office of the Secretary
Elliptical Road, Diliman, Quezon City

12 October 1993

ANIMAL INDUSTRY
ADMINISTRATIVE ORDER
No. 27
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SUBJECT: **Minimum Requirements for Determining/Evaluating the Efficacy and Safety of Veterinary Drugs to Target Animals**

Pursuant to the provisions of R.A. No. 3720, as amended by Executive Order No. 175, otherwise known as the Food, Drugs and Devices and Cosmetic Act" R. A. 3675 otherwise known as the "Generics Act" of 1988, R.A. 382 known as the "Pharmacy Act", R.A. 6425 known as the "Dangerous Drugs Act of 1972" as amended, R.A. 1556, otherwise known as the "Livestock and Poultry Feeds Act", R.A. 1071, an act to regulate the sale of veterinary biologics and medicinal preparation and R.A. 3101, an act authorizing the Director of the Bureau of Animal Industry, subject to the approval of the Secretary of Agriculture and Natural Resources to promulgate regulations for the preparation, sale, traffic in, shipment, and importation of viruses, sera, toxins or analogous products used for the treatment of domestic animals, and the Memorandum of Agreement dated September 20, 1991 signed by the Department of Agriculture and the Department of Health delineating their functions regarding licensing of establishments engaged in the manufacture, distribution and sale of veterinary drugs, premixes and products likewise registration of veterinary drugs and products such as veterinary biologicals, drugs intended for premixes, water solubles, supplements and animal feeds, the following are hereby promulgated for the information, guidance and compliance of all concerned to define the minimum requirements for establishing efficacy and target animal safety for drugs to be used therapeutically in food-producing animals. The intent of these requirements is to identify drugs which will be of benefit to a developing country and to prevent the use of drugs that are not safe or efficacious.

A. Drugs with a Satisfactory History of Use in Developed Countries

If a drug or combination of drugs has been identifically evaluated and approved for use in a developed country, and the drug has had a satisfactory history of use, the following testing requirements would apply to the various use conditions:

1. Use in same animal species for same claims at same dose confirm its safety and efficacy in a limited number of field cases when used as recommended. This is presented for antibacterial and antiparasitic drugs.

2. Use in same animal species for the same or different claims at a different dose:
   (a) Lower dose – Efficacy studies.
   (b) Higher dose – Efficacy and safety studies.

3. For use in a different animal species or for use of a drug that is not approved or does not have a history of use in another country, both safety and efficacy studies should be conducted.

B. Target Animal Safety Studies

1. Toxicity Test

The objective is to determine the margin of safety between the use level and the dose at which signs of toxicity occur (with a maximum dose of five times the proposed dose).

All available background data and published literature should be used to design the study and focus on the parameters to measure. This include using data collected from laboratory animals to determine safety to humans as well as studies conducted with humans and other animal species.

The general study design for the target animal safety study is to administer the market formulation of the drug to the most sensitive class of animal in the species to which the drug will be administered at 0, 1X, 3X and 5X the maximum proposed dose for three times the maximum intended duration of use. Clinical signs should be monitored and recorded.

Cellular haematological parameters should be measured periodically along with appropriate serum biochemical tests. Results of these test and clinical signs should be compared to results of the same test, and clinical signs obtained before treatment.

If the drug is known or suspected to be quite toxic, the study design can be adjusted to include the following groups – untreated (placebo), maximum, use level, intermediate level above use level, and toxic level.

2. Reproductive Studies

If the drug will be used in breeding or pregnant animals, its effect on breeding and development of the embryo / fetus should be determined.

The following general design is recommended as minimum, and if effects on breeding or pregnant animals are suspected, additional testing should be done with higher doses.

Males should be tested by administering two times the proposed maximum dose every other day for 30 days before the breeding season and for 30 days during the breeding season. The effect on male breeding soundness can be determined by a combination of other evaluations and measurement of breeding success.

The effects on females can be determined by administering the drug at two times the maximum proposed dose at the following times:

a) The three (3) days around ovulation time (the day before ovulation, day of ovulation, and the day after ovulation.

b) Three (3) days during early pregnancy, e.g., days 13, 14, and 15 of pregnancy to address maternal recognition and embryo development.

c) Three (3) days during early gestation, e.g., three days from 30 to 40 days of pregnancy to address early fetal death.

In addition to the above treatment regimen, the drug should be given at five times the proposed dose once during the second and third trimesters of pregnancy.

C. Efficacy Studies

The registrant / sponsor of the drug must develop adequate data to demonstrate that the drug produces the effects (s) claimed on the label. The condition or disease to be treated must be specifically identified on the label as well as the animal species to be treated.

The trials should be adequately defined, designed, and controlled, and they should be conducted by qualified investigators in geographical areas representative of the major production locales of the species of animal involved.

If the optimum dose is not known, early trials with multiple dose levels should be conducted to establish the effective dose for the indicated use. That dose should be confirmed in subsequent controlled field trials. The trials must b e conducted in animals in which the disease has been accurately diagnosed.

Husbandry practices should represent actual production conditions. Demonstration of effectiveness for each claim must be made if the drug is proposed for more than one indication. The major portion of the date must be collected from studies in which the proposed drug dosage form is used.

Experiments must be designed so that an evaluation can be made of the appropriate differences within an animal species, such as weight, sex, breed, age and condition of the animals.

In addition to the observations for effectiveness, the animal should be monitored for signs of toxicity from the use of the drug under field conditions.

Effectiveness may be demonstrated by quantitative and/or qualitative measurements.

Quantitative measurements may use gradual signs of the disease, e.g., severity, pathological lesions at slaughter, microbiological cultures, tests of antimicrobial susceptibility, and appropriate laboratory and serological testing.

Qualitative measurements may include presence of disease signs, isolation of specific etiological entities, morbidity, and mortality.

If a drug dose range rather than a fixed dosage is concluded to be desirable by the registrant sponsor, the conditions under which to administer the lower or the higher end of the dosage range should be specified on the label.

This Order takes effect upon approval.

ROBERTO S. SEBASTIAN
Secretary

RECOMMENDING APPROVAL:

ROMEO N. ALCASID
Director