USDA Annual Report
Registration #: 22-R-0145

Explanation of Category 'E' Animals

1. Number of Animals and Species Used in:

Pharmacokinetic Evaluation of Investigational Drugs
Used: 7 Cynomolgus macaques
Number Category E animals: 2

General Toxicology
Used: 305 Dogs
Number of Category E animals: 40

Reproductive Toxicology
Used: 80 Rabbits
Number of Category E animals: 15

2. Procedure Used:

Pharmacokinetic Evaluation of Investigational Drugs
2 Cynomologus macaques – During testing, two animals had a compound related reaction resulting in death. The animals were under veterinary supervision throughout the study.

General Toxicology
5 dogs: During a repeat dose study, four animals displayed mild to moderate decreased activity and vomiting. On another study, one animal displayed decreased activity and was cold to the touch. The animals were monitored throughout the study and the veterinarian determined that the signs were not severe enough to remove the animals from study.

35 dogs: Details below for four separate toxicology studies for anti-cancer agents. During all studies, the dogs were under veterinary supervision and treated as appropriate.
Study 1: Twelve animals displayed signs including red discolored feces, decreased activity; and vocalization. Of these, six animals were humanely euthanized before the planned end of study.
Study 2: Two animals displayed decreased activity and one animal vocalized.
Study 3: Twelve animals displayed mild to marked decreased activity, vomiting and liquid feces. One was found dead and five were humanely euthanized prior to the end of study.
Study 4: Nine animals displayed signs of vomiting and diarrhea, both containing red material. On necropsy, gastric and intestinal ulcers were noted. One died acutely and eight were subsequently humanely euthanized before the end of study.

Reproductive Toxicology
6 rabbits: During one exploratory study, two animals died acutely after showing inappetance. Four animals were humanely euthanized after six days of decreased appetite euthanized prior to the planned end of study.

9 rabbits: During a different exploratory study, 9 animals displayed decreased appetite for greater than four days. All animals humanely euthanized prior to the planned end of study.

3. Justification for procedure:

Wound Repair Research
Excessive scarring is a major health issue resulting from the abnormal resolution of burns, traumatic injury and complications from surgical procedures. These studies are required to evaluate compounds for the treatment of excessive and/or hyertrophic scarring.

Pharmacokinetic Evaluation of Investigational Drugs
Pharmacokinetic (PK) studies provide information on drug absorption, metabolism, distribution, and excretion. This information is essential for interpreting results from drug distribution and safety studies. Animal PK data is also essential for setting up clinical studies in man. PK studies are conducted by administering a drug candidate to an animal and measuring the amount of drug in biological fluids and tissues over a period of time.

General Toxicology
National and international regulatory agencies require safety studies prior to the approval of any new drug. These assessments safeguard the human population from potentially harmful effects from experimental candidates and new drug products. The goal of these studies is to investigate the toxicity of a new drug or formulation.

Reproductive Toxicology
These studies are required to evaluate potential effects of new compounds on embryo-fetal development when administered during gestation. The studies also evaluate potential effects to the pregnant doe.

4. Procedure required by:

Reproductive & General Toxicology Studies: Agency: FDA; Federal Food, Drug, and Cosmetic Act CFR: 505 (4) (i) (1) (A)