USDA Annual Report
Registration #: 22-R-0145

Explanation of Category 'E' Animals

1. Number of Animals and Species Used in:

Pain Research

Used: 72 Rabbits
Number of Category E animals: 33 Rabbits

Model Development for early discovery research

Used: 39 Rabbits
Number Category E animals: 6

General Toxicology

Used: 214 Dogs
Number of Category E animals: 19

Reproductive Toxicology

Used: 262 Rabbits
Number of Category E animals: 36

2. Procedure Used:

Pain Alleviation Research
33 rabbits - Used in the testing of potential new pain medications that show no bioavailability in rodents. The rabbits were monitored continuously throughout the procedure. They were subjected to the minimal amount of pain, for the minimal amount of time necessary to assess potential pain medication efficacy. The rabbits were humanely euthanized as soon as study objectives were met.

Model development for early discovery research
6 Rabbits – While developing an animal model for wound repair and fibrosis, the rabbits in the control group did not receive analgesics in order to determine the effects of analgesics on study data. The rabbits were under veterinary supervision throughout the study. The results of the model development and analgesia assessment studies determined that presurgical analgesic alleviated post surgical pain and did not compromise study confidence.

General Toxicology
11 dogs: During a dose range finding study, two (2) dogs developed lesions at the site of infusion that did not adequately respond to veterinary intervention. Therefore, they were

humanely euthanized prior to study completion. On a different study, two (2) animals died unexpectedly and seven (7) animals were found moribund or developed significant clinical signs that resulted in humane euthanasia.

8 dogs: During a toxicity evaluation study for an anti-cancer agent, one (1) animal was humanely euthanized prior to study completion. Seven (7) animals showed signs of toxicity such as abnormal gait and/or general malaise. Under veterinary supervision, these animals were evaluated and maintained on the study until the planned end dates.

Reproductive Toxicology Studies
36 rabbits:
During one exploratory study, seven (7) animals either died acutely or were euthanized for humane reasons.

During a different study, seven (7) animals died acutely; 13 other rabbits exhibited clinical signs such as lack of appetite, reduced food consumption & decreased activity. Under veterinary supervision, these animals were evaluated and maintained on the study until the planned end dates.

During another study, nine (9) animals exhibited various clinical signs such as hypothermia, incoordination and reduced food consumption. Five (5) of the rabbits with the most severe clinical signs were humanely euthanized prior to the end of study. The other four (4) remained under veterinary supervision; these animals were evaluated and maintained on the study until the planned end dates.

For all toxicology studies, the test compound produced unexpected toxicity. Thus it was not the procedure itself, but the sequelae, that caused the adverse affects.

3. Justification for procedure:

Pain Alleviation Research
New pharmaceuticals aimed at controlling pain are needed to help alleviate human suffering. Research compounds are tested as potential analgesics; therefore no other analgesics or anesthetics can be used while data are being collected. Animals are euthanized as soon as the study is completed.

Model development for early discovery research
Excessive scarring is a major health issue resulting from the abnormal resolution of burns, traumatic injury and complication of surgical procedures. These studies are required to evaluate compounds for the treatment of excessive and/or hypertrophic scarring.

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

Reproductive Toxicity Testing
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 on human pregnancy.

4. Procedure required by:

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