

32R 0003

intravenous dextrose injections if needed. The animals do not show clinical indications of 'distress'. They are reported here as required by Policy #11. There are no alternative models or experimental paradigms that replace measurement of basal blood glucose levels in higher mammals over time.

Pharmaceutical intervention with sedatives, tranquilizers or analgesics would have no effect on the animals' well being but would invalidate the experimental objectives.

Dogs

1

Toxicology

E.Y.

This dog was used in the early toxicological evaluation of drug candidates. In these studies the degree of toxicity was unexpectedly severe. Test compound administration was suspended and the animal was provided with symptomatic veterinary care. Despite careful study design, supportive care, and adjustments to study protocols, animals in toxicology studies used in the evaluation of new drug candidates may experience unanticipated events. These studies are required by U.S. and O.U.S. regulations and guidelines for animal studies to support human clinical trials; specifically CFR Volume 62, #227 and ICH M3.

Rabbits

37

Cardiovascular Research

Rabbits are used in studies of compounds that have antithrombotic activity previously observed in *in vitro* test systems. In studies where agents are evaluated for oral bioavailability, the animal must be fasted for a period long enough to assure that the stomach is empty and that there would be no interference between ingesta and the absorption of the compound. In the rabbit this period has been determined to be up to forty six hours. These activities have been reviewed and approved by the Institutional Animal Care and Use Committee and have been observed by the veterinary staff. The animals do not show clinical indications of 'distress'. They are reported here as is required by Policy #11. There are no alternative models or experimental paradigms that replace normal gastric emptying time in the rabbit. Pharmaceutical intervention with sedatives, tranquilizers or analgesics would have no effect on the animals' well being but would invalidate the experimental objectives as they have effects on gastrointestinal activity.

Gerbils

353

Cardiovascular Research

These gerbils were used as an animal model of (b)(4) infarction (stroke) in search of therapies that could remedy the condition in man. The end point of the experimentation is histological changes (b)(4) and their modulation with experimental drug therapies. Some of the animals may exhibit subtle changes in behavior which are presumed to be associated with some degree of distress. Anesthetics, analgesics, tranquilizers or other drugs would mask, exacerbate, or otherwise alter neurological assessment and/or test compound effect and thus would adversely affect interpretation of the data.

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Gerbils

106

Infectious Disease Research

Gerbils were used in evaluating potential therapies for bacterial otitis media. In these short term studies animals may experience febrile responses and/or middle ear discomfort. All compounds used in this experimentation are first tested in one or more *in vitro* systems and only those showing potential efficacy are used in animal models. The anatomy of gerbil ear drainage channels closely mimics the anatomy of the human ear making the animal uniquely suited to the study of this disease. Anesthetics, analgesics, tranquilizers or other drugs would mask, exacerbate, or otherwise alter behavioral assessment and/or test compound effect and thus would adversely affect interpretation of the data.

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