the NHPs were included in the other aspects of the environmental enrichment program. After the study, they were returned to their normal social housing.

Thirty-six Rhesus NHPs were single housed with IACUC approval for sample collection (urine, stool, or bile) for up to 7 days or post dosing observation for 2 days or special food restrictions for up to 5 days. Apart from the social housing, the NHPs were included in the other aspects of the environmental enrichment program. After the study, they were returned to their normal social housing.

Thirty-two Rhesus NHPs were singly housed for evaluation of novel drugs to (b) (4) Apart from the social housing, the NHPs were included in the other aspects of the environmental enrichment program. The exception was IACUC approved.

Eleven canines had exceptions from the exercise program for study related reasons but were housed in 100% of space requirements. The canines were either a (b) (4) (b) (4) complete collection of excreta (urine and feces). The studies occurred up to seven times and lasted 4-36 days. These exemptions were reviewed and approved by the IACUC.

B) General Column 'E" Justification Statement

Site 1

One dog on an IACUC approved study to determine the (b) (4) (b) (4) developed acute terminal condition, although it had no clinical signs at its last observation. Due to lack of clinical signs veterinary medical intervention was not possible. Necropsy was not remarkable. The IACUC approved the study and reviewed the incident.

Site 2

Five hundred and forty-four hamsters developed acute terminal complications or were humanely euthanized in an IACUC-approved study to determine the (b) (4) The use of pain relief

and supportive care would alter the results of the study, therefore they were not used. The animals were closely monitored and those animals with significant health issues were humanely euthanized.

One guinea pig that was part of a study examining (b) (4) (b) (4) Blood was collected under general anesthesia using the . The serum was examined to determine antibody titer and in some cases, functional *in-vitro* assays. The technique is only performed by trained veterinary technicians. Subsequent to this procedure and after the effects of procedure-related anesthesia had worn off sudden death appeared to have occurred in the absence of signs. Only a very small percentage of these procedures were associated with this complication and death was usually due to internal hemorrhage. Due to the lack of signs and sudden death, medical intervention could not be administered. The study was approved by the IACUC.

One rabbit developed acute terminal complications while on IACUC approved studies (b) (4) The acute nature of illness prevented any medical intervention. The study was the effect of (b) (4) (b) (4)

Twenty-three rabbits developed terminal complications on IACUC approved studies that evaluate the potential (b) (4) (b) (4) test article(s) administered to rabbits. Conduct of these procedures is required by the FDA and other foreign regulatory agencies [ICH S5(R2) also published in Federal Register, Vol. 59, No. 183, September 22, 1994, pg 48746-48752].

Eighteen dogs in IACUC-approved studies developed significant medical complications. The studies examined if there are (b) (4) (b) (4) The animals were closely monitored during the study by veterinary and research staff. Most of the dogs were humanely euthanized after not being responsive to symptomatic treatment. The guidelines for toxicity testing that were followed are outlined in Section IVB.1., General Guidelines for Designing and Conducting Toxicity Studies of the Redbook 2000 with 2007 revision, Toxicological Principles for the Safety Assessment of Food Ingredients, Guidance for Industry M3(R2), Nonclinical Safety Studies for the Conduct of Human Clinical Trials for Pharmaceuticals, June 2009, ICH Guidelines.

One dog on a (b) (4) mandated by the FDA (ICH S7A guidelines) developed an acute terminal medical condition before it could be humanely euthanized. The study is approved the IACUC.

Four Rhesus NHPs developed acute complications while on an IACUC approved study for (b) (4) in NHPs. The animals were closely monitored during the study by veterinary and research staff. The acute nature of the complication prevented veterinary intervention in 3 NHPs and the 4th was humanely euthanized. The GLP guidelines for toxicity testing are outlined in Section IVB.1., General Guidelines for Designing and Conducting Toxicity Studies of the Redbook 2000 (with 2007 revision), Toxicological Principles for the Safety Assessment of Food Ingredients Plus, the guidelines for toxicity testing are outlined in Section IVB.1., General Guidelines for Designing and Conducting Toxicity Studies of the Redbook 2000 (with 2007 revision), and Toxicological Principles for the Safety Assessment of Food Ingredients. The studies were conducted in accordance with these guidelines and were approved by the IACUC.