22R 0009

OPTIONAL COLUMN E EXPLANATION FORM

2-WEEK ORAL RANGEFINDING TOXICOLOGY STUDY

1. Registration Number: 22-R-0009

2. Number of animals used in this study – 12. Number of animals classified as category "E" - 4.

3. Species (common name)___Non-human Primate___ of animals used in this study.

4. Explain the procedure producing pain and/or distress.

   These primates were dosed with a pharmaceutical compound.

   On study day 10 two monkeys were euthanized because they were in poor condition, thin and produced feces with blood. Over the few days prior to euthanisia the food ration consumed was decreased for these monkeys. Two other monkeys were found to have decreased food consumption, soft feces, and emesis over a period of days prior to scheduled euthanasia being performed.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see question 6 below)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

22R 0009

OPTIONAL COLUMN E EXPLANATION FORM

26-WEEK TOXICOLOGY STUDY WITH A 4-WEEK RECOVERY

1. Registration Number: 22-R-0009

2. Number of animals used in this study – 40. Number of animals classified as category "E" - 1.

3. Species (common name)____Non-human Primates___ of animals used in this study.

4. Explain the procedure producing pain and/or distress.

These primates were dosed with a pharmaceutical compound.

One primate died on study day 52. The animal experienced labored breathing, decreased motor activity and tremours post dosing this day. Although emesis was observed on day 51, there were no other severe clinical signs in the days preceding death.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see question 6 below)

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)