22R0009

OPTIONAL COLUMN E EXPLANATION FORM

ORAL GAVAGE RISING DOSE TOXICOLOGY STUDY

1. Registration Number: 22-R-0009

2. Number of animals used in this study – 4. 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 animals were dosed with a pharmaceutical compound.

On study day 10, one animal demonstrated emesis, decreased motor activity and a hunched posture, and was therefore euthanized.

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)

22 R0009

OPTIONAL COLUMN E EXPLANATION FORM

TWO WEEK ORAL DOSE RANGEFINDING STUDY

1. Registration Number: 22-R-0009

2. Number of animals used in this study – 12. Number of animals classified as category "E" - 3.

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

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

These animals were dosed with a pharmaceutical compound.

On study day 8 one monkey demonstrated emesis, labored breathing and decreased locomotor activity and was therefore euthanized. On study day 8 a second monkey demonstrated decreased locomotor activity, hunched posture and no food consumption and was euthanized. This monkey demonstrated reduced food consumption and a slight decrease in locomotor activity for two days prior to euthanasia. A third monkey was euthanized as scheduled on study. However, this animal was thin and demonstrated a decrease in food consumption and fecal output over the course of the study.

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):

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