22R0009

OPTIONAL COLUMN E EXPLANATION FORM

2-WEEK IV TOXICOLOGY STUDY

1. Registration Number: 22-R-0009

2. Number of animals used in this study – 24. Number of animals classified as category "E" - 6.

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.

One animal in the high dose group was found dead on study day 4. The other five animals in this dose group demonstrated a decrease in food consumption and fecal oputput over three days prior to being 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).

22R0009

OPTIONAL COLUMN E EXPLANATION FORM

EMBRYO-FETAL DOSE RANGE FINDING DEVELOPMENT STUDY IN RABBITS

1. Registration Number: 22-R-0009

2. Number of animals used in this study – 12. Number of animals classified as category "E" - 1.

3. Species (common name)____Rabbits___ of animals used in this study.

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

These animals were dosed with a pharmaceutical compound.

One animal was found moribund and 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).

2) Guideline on detection of toxicity to reproduction for medicinal products published in the Federal Register on September 22, 1994 (FR 48746).