22R0009

OPTIONAL COLUMN E EXPLANATION FORM

AN EXPLORATORY EMBRYO-FETAL DEVELOPMENT DOSE RANGE-FINDING STUDY

1. Registration Number: 22-R-0009

2. Number of animals used in this study – 100. Number of animals classified as category "E" - 25.

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.

This compound has expected pharmacologic signs. These animals demonstrated dilated pupils, biting and chewing, and increased respiration. These signs were not considered so severe that intervention was necessary.

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).

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

22R0009

OPTIONAL COLUMN E EXPLANATION FORM

A MODIFIED ORAL EMBRYO-FETAL DEVELOPMENT DOSE RANGE-FINDING STUDY

1. Registration Number: 22-R-0009

2. Number of animals used in this study – 10. Number of animals classified as category "E" - 2.

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.

Two animals demonstrated diarrhea for three days. There were no further clincial signs noted on these animals and they were euthanized as scheduled.

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).

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