

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 – 36. Number of animals classified as category "E" - 9.
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.

Seven animals were found dead on this study. The other two categorized as category "E" experienced soft stool and decreased fecal output for the two 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).
- 2) Guideline on detection of toxicity to reproduction for medicinal products published in the Federal Register on September 22, 1994 (FR 48746).

22R0009

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EMBRYO-FETAL DOSE-RANGE FINDING DEVELOPMENT STUDY IN RABBITS

1. Registration Number: 22-R-0009
2. Number of animals used in this study – 36. Number of animals classified as category "E" - 26.
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.

Twenty-six animals on this study demonstrated decreased food consumption and no fecal output. Nine of these animals were euthanized due to the clinical signs. The others were euthanized as scheduled by 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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