JAN 1 4 2013

Column E Explanation

This form is intended as an aid to completing the Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

1. Registration Number: 33-R0008

2. Number 1 of animals used in this study.

3. Species (common name) dog of animals used in the study.

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

   One animal died due to test article-related toxicity.

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 Item 6 below)

   Administration of pain relieving drugs could have masked the potential "toxic" effects of the test compound. This was unavoidable in a "toxicity" study of this type.

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):

   Agency Not applicable (N/A) CFR N/A

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1. Registration Number: 33-R-0008

2. Number 1 of animals used in this study.

3. Species (common name) dogs of animals used in the study.

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

One animal died due to test article-related toxicity.

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 Item 6 below)

Administration of pain relieving drugs could have interfered with the study endpoints and complicated the interpretation of study results. This was unavoidable in a "toxicity" study of this type.

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):

Agency Not applicable (NA) CFR NA

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1. Registration Number: 33-R0008

2. Number 5 of animals used in this study.

3. Species (common name) ferret of animals used in the study.

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

One animal accidental death due to gavage error; animal died immediately after dosing.

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 Item 6 below)

Four animals died due to test article toxicity; administration of pain relieving drugs could interfere with study endpoints (i.e., survival). This was unavoidable in a "toxicity" study of this type.

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):

Agency Not applicable (N/A) CFR N/A