Optional Column E Explanation Form

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 laypersons as well as scientists.

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1. Registration Number: 14-R-101

2. **Number of animals used in the study (s):** Two experienced pain or distress without alleviation.

3. Specie (common name) of animals used in this study (s). Non-Human Primate

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

Exposure to a test article (pharmaceutical agent).

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)

Studies conducted at Toxikon are performed for sponsors to obtain toxicity information on experimental materials, drugs or chemicals, or to ensure the safety. Regulatory guidelines do not permit the use of analgesic or anesthetics during toxicity determination studies. Toxikon does employ monitoring of animals in order to observe them for adverse clinical signs. When animals are found to be experiencing unexpected pain or distress due to toxicity response or due to research procedures during the course of the study, animals are typically euthanized in a timely manner. Toxikon's IACUC approves and provides post-approval monitoring of all animal use protocols.

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):

Based upon the following standards:

ICH Harmonized Tripartite Guideline. Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies, S3A, 1994. FDA: Published in the Federal Register, Vol. 60, No. 40, March 1, 1995, pages 11264-11268.

ICH Harmonized Tripartite Guideline. Dose Selection for Carcinogenicity Studies of Pharmaceuticals, 1997 (revised). FDA: First published in the Federal Register, Vol. 60, No.40, March 1, 1995, pages 11278- 11281, Revision published in the FR, Vol. 62, No. 233, December 4, 1997, page 64260.