Toxikon Corporation
14-R-0101
Annual Report of Research Facility
2019-2020

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. Annual Reports and explanations should NOT include PII information such as names (principle investigators and research staff), addresses, protocols, meeting notes (either in part or in full), the animal room numbers, grant information, veterinary care programs, and the like. 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):** 7122; 2;

3. **Specie (common name) of animals used in this study(s).** Guinea Pig; Rabbits

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

Guinea Pigs: Injection (intra dermal) of FCA and Application of Positive Control for production of allergic response.

Rabbits: Three died shortly after intravenous administration of a medical device extract.

5. **Attach or include with the reason(s) for why anesthetics, analgesics and tranquilizers could not be used.** (For Federally mandated testing, see question 6 below)

Guinea Pigs:

The FCA induced lesions are required by the FDA accepted testing method required for skin sensitization. The positive control application is also required by the FDA accepted testing method required for skin sensitization as a validation of the test system. Toxikon IACUC policy 001 outlines monitoring of the FCA lesions.

The pain and distress could not be relieved by use of analgesics because the FDA is concerned that analgesics have the potential to affect the sensitization rates of the guinea pigs. The use of analgesics could interfere with the study as there is a potential for drugs to interact (inhibit or enhance a response) with the test articles that are being evaluated. Animals exhibiting FCA induced lesion sites are reported to veterinary services for appropriate care as per IACUC policy 001.

Rabbits:

Studies conducted at Toxikon are performed for sponsors to obtain toxicity information on experimental materials, drugs or chemicals, or to ensure the safety of a new lot of material. Regulatory guidelines do not permit the use of analgesic or anesthetics during toxicity and febrile determination studies. However, Toxikon does employee a step approach, exposing one or two animals at a time, thus minimizing the total number of animals needed. Toxikon's IACUC approves and monitors 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):**

Guinea Pig:

FDA, CDRH, June 16, 2016, Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluations and testing within a risk management process"

ISO 10993-10, 2010, Biological Evaluation of Medical Devices – Part 10: Tests for Irritation Sensitization.

ISO 10993-12, 2012, Biological Evaluation of Medical Devices – Part 12: Sample Preparation Reference Materials

OECD 406, Organization for Economic Co–Operation and Development (OECD), Guidelines for the Testing of Chemicals, "Skin Sensitization", adopted 17 July, 1992.

Rabbit:

ISO 10993-11, 2012, Biological Evaluation of Medical Devices – Part 11: Tests for Systemic Toxicity

ISO 10993-12, 2012, Biological Evaluation of Medical Devices – Part 12: Sample Preparation Reference Materials

USP 41, National Formulary 36, 2018. <151> Pyrogen Test.

All Studies:

ISO/IEC 17025, 2017, General Requirements for the Competence of Testing and Calibration Laboratories.

Signature of Institutional Official	**Date**
(b) (6), (b) (7)(C)	11/11/20

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