Column E Explanation

20 NOV 2016

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: 41-R-0074

2. Number of animals used in this study: 21

3. Species (common name) of animals used in this study: Guinea Pig

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

   Guinea Pig Maximization Test: A positive control test is required to be performed and valid within 3 months of device testing. Each test uses 18 guinea pigs. The study is comprised of two Induction Phases and a Challenge Phase. Induction I is a series of 6, 0.1mL intradermal injections along the dorsum of the animal. The injections are a combination of Freund's Complete Adjuvant, NaCl, and a control article (positive or negative). Induction II involves a topical application of the control (positive or negative) article on gauze to the intrascapular area. The animal is bandaged to maintain contact for 48 hours. The challenge phase consists of topical application of both the positive and negative control to contralateral flank for 24 hours. The areas of contact are scored at 24 and 48 hours after patch removal for edema and erythema. Additional studies were completed in order to find an appropriate positive control.

   The Guinea Pig Maximization Test positive control was downgraded to a category C, following refinement of the positive control, effective February 10, 2017 with the caveat that animals receiving a score of 3 (associated with intense erythema and/or swelling) will be evaluated by a veterinarian and may be upgraded to category E if warranted. One positive control was run prior to this change. Three animals were upgraded to category E following this change.

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

   The study is designed to test the sensitization potential of medical devices in accordance with ISO 10993-10. The use of anesthetics, analgesics or tranquilizers is prohibited due to the potential molecular interaction between drugs and compounds associated with the device. This interaction may cause a response (inhibitory or synergistic) that could affect the outcome of the study and crease a false positive or negative.

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 _____ CFR_____

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1. Registration Number:

   41-R-0074

2. Number of animals used in this study:

   3

3. Species (common name) of animals used in this study:

   Hamster

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

   This was an internal study to validate the buccal irritation procedure. The procedure comprised of 4 doses of a positive control article into the buccal pouch of Hamsters. Dosing was completed at 1 ± 0.1 hour intervals by placing a braided cotton coupon soaked with 1mL of the article into one buccal pouch (the contralateral pouch was left empty to serve as control tissue). The coupon remained in place for a minimum of 5 minutes, then was removed and the buccal pouch rinsed with normal saline. Each animal's buccal pouch was scored prior to the initial dose, just after the final dose, and 24 ± 2 hours after the final dose, prior to euthanasia.

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

   This study is designed to test the irritation potential of medical devices. This positive control validation study was performed in accordance with ISO 10993-10 to ensure reproducibility and sensitivity, and to demonstrate a positive control response. The use of anesthetics, analgesics or tranquilizers is prohibited due to the potential molecular interaction between drugs and compounds associated with the device. This interaction may cause a response (inhibitory or synergistic) that could affect the outcome of the study and crease a false positive or negative.

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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