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:

   41-R-0074

2. Number of animals used in this study:

   156

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.

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:

   18

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

   Guinea Pig

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

   Closed-Patch (Buehler) 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 nine induction phases and a challenge phase. For the induction phases, three times a week for three weeks a positive control soaked gauze or blank gauze (negative control) is applied topically and bandaged to maintain contact for 6 hours. The challenge Phase consists of all animals receiving a positive control soaked gauze. The animal is bandaged to maintain direct contact for 6 hours. The area of contact is then scored 24 and 48 hours later for erythema and edema.

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 ISO10993-10. 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 create a false positive or negative.

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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:

   Rabbit

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

   A positive control test is required to be performed and valid within 3 months of device testing. Each test uses 3 rabbits. Each rabbit is dosed with topical application of a positive control (12.33% formaldehyde) and negative control (0.9% NaCl) via cutaneous patches. The patches are wrapped to maintain contact with the skin for 4 hours. Observations of the injection sites are conducted at 1 hour, 24 hours, 48 hours, and 72 hours post-patch removal and graded for edema and erythema.

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 irritation potential of medical devices in accordance with ISO10993-10. 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 create 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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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:

   Guinea Pig

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

   Over the course of the year 3 animals suffered limb injuries which caused moderate lameness. Each animal was evaluated by a veterinarian who elected to survive the animal with close monitoring but no treatment due to study requirements; the animals were euthanized 1 day, 4 days, and 5 days post veterinary evaluation. These animals were upgraded to pain category 'E' at time of veterinary evaluation due to the unknown nature of the injury and prohibited treatment.

   The animal that was euthanized 1 day post veterinary evaluation was did not reach the full term of the study, however, the other two animals were survived through the end of the study which enabled the scientist to obtain study outcomes and prevent additional animal usage.

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 studies utilizing guinea pigs (Guinea Pig Maximization Test & the Closed-Patch (Buehler) Test) are 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):

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