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COLUMN E EXPLANATION – 2017
Facility Registration No: 23-R-0061

Guinea Pigs: The 102 guinea pigs listed in Column E of the Annual Report were used on guinea pig sensitization evaluations, in compliance with Organization for Economic Co-operation and Development (OECD), U.S. Environmental Protection Agency (EPA) and/or International Organization for Standardization (ISO) testing guidelines. The purpose of these studies is to assess the sensitization potential of a substance following repeated dermal exposure. Dermal irritation and occasional abnormal systemic reactions can occur during these studies. The test guideline citations for these studies are as follows:

- OECD Guidelines for Testing of Chemicals
  - Test Guideline No. 406, Skin Sensitization, Adopted by the Council on July 17, 1992
- EPA Health Effects Test Guidelines
  - OCSPP 870.2600, Skin Sensitization, effective March 2003

These are regulatory-driven protocols and there are no current provisions in these test guidelines to permit the use of analgesia or anesthetics. NSAIDs and opioids are known to interfere with dendritic cell and T-cell responses, which are key events in the adverse outcome pathway (AOP) for delayed-type hypersensitivity (skin sensitization) reactions. Any pharmacologic control of pain that would lead to either enhancement or mitigation of delayed-type hypersensitivity is contraindicated by the interests of hazard identification for risk assessment and public health protection.

Rabbits: Thirty-five rabbits listed in Column E of the Annual Report were used in dermal irritation/corrosion studies in compliance with Consumer Product Safety Commission (CPSC), EPA, and/or OECD testing guidelines. The purpose of these studies is to determine the irritant or corrosive effect of a substance when applied to the skin. Dermal irritation and occasional abnormal systemic reactions can occur during these studies. The test guideline citations for these studies are as follows:

- CPSC Federal Hazardous Substance Act
  - 16 CFR 1500.41, Primary Dermal Irritation
- OECD Guidelines for Testing of Chemicals
  - Test Guideline No. 404, Acute Dermal Irritation/Corrosion, Adopted by the Council July 28, 2015
- EPA Health Effects Test Guidelines
  - OCSPP 870.2500, Acute Dermal Irritation, effective August 1998

These are regulatory-driven protocols and there are no current provisions in the test guidelines to permit the use of analgesia or anesthetics. Opioids and NSAIDs are known modulators of wound-healing. Skin recovery from chemical irritation, or wound-healing, is an important aspect of skin irritation studies, and is a measure of reversibility. Any pharmacologic control of pain that would lead to either enhancement or mitigation of healing is contraindicated by the interests of hazard identification for risk assessment and public health protection.

One additional rabbit exhibited signs of pain and/or distress and was not relieved. This animal was used on an eye irritation/corrosion study. The test guideline citation is below:

- OECD Guidelines for Testing of Chemicals
  - Test Guideline No. 405, Acute Eye Irritation/Corrosion, Adopted by the Council October 2, 2012

There was a total of 77 rabbits used on 27 eye irritation/corrosion studies. All animals were treated prophylactically with sustained-release buprenorphine, and buprenorphine treatment was continued for 14 of these rabbits until the time of euthanasia. However, one rabbit that met the criteria for continued treatment was inadvertently not continued due to technical error. Fortunately, the pain-indicating signs were minor, and were no longer present at the subsequent observation timepoint. The laboratory staff were retrained to prevent any future occurrence.

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