

**Category E**  
10/2020-9/2021 Fiscal Year

**Species:** Canine

**Studies:**

(b) (4) -PH40

**Number of Animals:**

9

**Max Duration:**

10 days/dosing

Inflammatory pain

**Procedure Summary:**

Beagle dogs underwent unilateral injections of kaolin suspension in order to create a model of inflammatory pain. Lameness and paw edema were assessed ~1-2 days prior to kaolin injection, and 4, 28, 52, 76, 100, 124, 148, 172, and 244 hours after kaolin injection. Lameness lasted ~7 days following kaolin injection. All animals received a single dose. After minimum 35 day monitoring period, the twenty of the animals were given an additional 14 day washout period, then redosed.

**Explanation for use of Dogs:**

Dogs are a defined model for the assessment of pain and inflammation. Additionally, dogs were the target species for this test article application for the two studies listed above. Dogs are chosen as the subjects in these research studies since the ultimate goal was the development of therapies to treat pain and inflammation in dogs. As such, for many later stage investigational pain therapies, assessments in dog models of pain prove to be the most highly translatable preclinical models.

**Explanation for why analgesics cannot be used:**

The purpose of this study was to assess the effectiveness of novel analgesics (test article) and meloxicam (control article) in reducing inflammation-induced pain behaviors following kaolin injections, and as such we could not administer pain relieving agents without compromising the study endpoints. The inflammatory pain state lasts from ~1 to ~2 weeks post-injection. Over the course of the study, animals were assessed frequently by trained staff to determine any changes in lameness and inflammation. Animals were also evaluated frequently by a test facility veterinarian. This also provided a frequent and thorough assessment of the animals' welfare during the course of the study.

Care for injury or lameness not associated with the study-specific procedures may include hot compresses, cold compresses, and routine wound care procedures, application of topical antiseptics, routine bandage care, and administration of antibiotics if the injured tissue is infected.

The kaolin induced inflammation resolved over time and the animals enrolled on these studies returned to a baseline state after a period of time.

Eight of the nine animals had been transferred off study onto the facility holding protocol prior to the beginning of this reporting period. One animal was transferred off study onto the holding protocol on 10/9/2020.

No other dogs were categorized as E throughout the rest of the reporting period.

Category E  
10/2020-9/2021 Fiscal Year

**Species:** Guinea Pig

**Number of Animals:** 80

**Max Duration:** 91 days

**Studies:** (b) (4) -PH14

#### Procedure Summary:

Osteoarthritic pain was induced by an injection into the left knee on day -21. Hind limb weight bearing was assessed prior to and 1, 2, 3, 4, 6, 8, and 10 weeks after Day 0 dosing.

#### Explanation for use of Guinea Pigs:

The test article was intended to treat canines and felines and, as such, needs to be tested in animals prior to approval. Guinea pigs are useful studying pain behavior in response to osteoarthritis (OA). Furthermore, Guinea pigs are relatively easy to handle and have sufficient joint size to evaluate biomarkers. In addition, the Guinea pig has been the most widely used model to evaluate inflammatory biomarkers related with OA. In light of the multifaceted general reasons to use Guinea pig model, it was hoped that this study could establish the model as suitable in particular for assessing the effects of test articles on the pain associated with bearing weight on a weight-bearing joint afflicted with OA. Additionally, the test article had a significantly greater affinity to guinea pig nerve growth factor than to rat nerve growth factor and, as such, testing in rats would not have been valid. Finally, due to genetic variations in the targeted protein, the protein homology between Guinea pigs and canine/felines was more closely matched than in rats or mice.

#### Explanation for why analgesics cannot be used:

It was necessary to induce an osteoarthritic pain state that will be treated with the test article. A negative control group was given only vehicle. This was necessary to determine how well the pain state was induced in this model. Anesthetics, (isoflurane) were used for the surgical procedure for all animals, and buprenorphine SR was administered once immediately following the injection for all animals. Beyond these however, analgesics such as nonsteroidal anti-inflammatory drugs or opiates were not to be used. Treatment of pain could have interfered with the development of the pathology and resultant pain behaviors, resulting in those animals not meeting study requirements.