PreClinical Research Services, Inc.
Registration Number: 84-R-0072

Column E Explanation

1. **Number of animals used in this study:**

   A total of 64 dogs were used for acute synovitis studies.

2. **Species of animals used in this study:** Canine

3. **Explain the procedure producing pain or distress:**

   The dog urate model and kaolin – carrageenan (K/C) model were used to induce an acute synovitis that manifests as local inflammation and lameness. The urate model induced lameness peaked at 2- 6 hr post IA urate injection and resolved by 24 hours. The K/C model induced lameness peaked at ~10 hr post IA urate injection and resolved by 34 hours. The K/C model was less severe and more consistent than the urate model.
   No long term consequences to the acute inflammation have been reported for either model and several studies have utilized repeat injections in the same joint after a period of rest with no adverse effects. Animals were treated with analgesics following the 8 or 12 hour evaluation (urate model) or 24 hour evaluation (K/C model), if lameness persisted.

4. **Scientific or regulatory justification for withholding of pain/distress relief:**

   Analgesics were withheld because the study evaluated the potential analgesic effect of the experimental compound and the administration of an analgesic would confound the results. Meloxicam is known to be effective in this model system and was included as a positive control.
   The dog urate model was chosen due to the temporary nature of the inflammation as there is no need to induce long term pain and lameness to investigate the analgesic effects the test articles.
   The K/C model was developed to allow for the assessment of long acting, novel osteoarthritis treatments for dogs. Similarly to the urate model, analgesics were withheld because the studies involved are designed to evaluate the potential analgesic effect of the experimental compound and the administration of an analgesic would confound the results. Meloxicam and carprofen are known to be effective in these model systems and serves as both a positive control and as the rescue analgesia as needed.

5. **What, if any, federal regulations require this procedure?**

   N/A