

NOV 20 2012

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Addendum to the FY2012 APHIS Form 7023 Submission for North Carolina State University USDA Registration #55-R-005/842

Category E Report for the Reporting Period of FY2012

Category E Study #1

- 1. Registration Number: 55-R-005**
- 2. Number of animals used under Column E conditions in this study: 6 dogs**
- 3. Species (common name): Dog**
- 4. Explain the procedure producing pain and/or distress, including reason(s) for species selected:**

The purpose of this pilot study is to determine the ability of a single injection of a new extended release formulation of buprenorphine to treat post-surgical pain in dogs. It is also the purpose of this study to assess the validity of a refined model of clinical orthopedic postoperative pain. In private practice, dogs routinely experience procedures such as arthrotomies, fracture repairs, etc. would typically benefit from non-NSAID analgesics that could offer effective postoperative analgesia for a longer time than the current formulations. Six dogs will be randomized as to which subcutaneous injection (saline or extended release buprenorphine) they are to receive for the initial stifle arthrotomy, a procedure that involves incising and opening the skin and stifle joint capsule and then suturing both closed – no other manipulation, administration or excision is performed on the joint. All dogs will receive a SQ injection of extended release buprenorphine or saline not more than 60 minutes prior to being placed under general anesthesia and undergoing a stifle arthrotomy of one of the hindlegs. All dogs will be recovered from the anesthesia and monitored for clinical pain for up to 72 hours. Observations will continue for up to 7 days postoperatively. Rescue analgesia (Meloxicam – an NSAID COX2 Inhibitor) will be administered to any dog that scores a 5/5 on the Glasgow Pain Scale (Part C Short Form). If Meloxicam is administered, it will be continued for a further 3 doses, once every 24 hours for a total of 4 days. Following administration of rescue analgesia, the dog will be evaluated 2 hours later. Upon completion of the 72 hour postoperative pain assessments and one week daily observation period, dogs will be allowed to continue to recover with no further drug administration unless needed, as deemed by a score of 5/5 on the Glasgow Pain Scale. After a 1-3 month rest period, the same stifle arthrotomy will be performed on the alternate knee of each dog, and they will receive the treatment that they did not receive for the initial surgery (cross-over study).

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5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see item 6 below):

The goals of this study are to 1) evaluate the effectiveness of a new extended release formulation of buprenorphine for postoperative analgesia, and 2) evaluate whether this more refined model of postoperative pain is adequate for assessment of pain relief. In order to demonstrate that the dogs do have an adequate pain response, only half of the dogs will receive the test analgesic, and the other half will receive a placebo injection (saline). Any dog that scores 5/5 on the Glasgow Pain Scale (Part C Short Form) during the 7 day observation period will receive rescue analgesia (meloxicam for up to 4 days). If the dog(s) continue to score 5/5 on the Glasgow Pain Score, the rescue analgesia will continue with Meloxicam for up to 2 days or longer based on the Glasgow Pain Score.

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Addendum to the FY2012 APHIS Form 7023 Submission for North Carolina State University USDA Registration #55-R-0005 /842

Exceptions to Standards Report for the Reporting Period of October 1, 2011 through September 30, 2012

Species: Pony, Cattle, and Goat

Number Affected: 5 ponies, 5 cattle, 5 goats

Exception to Standards: Hay is withheld from animals for 36 hrs prior to embalming to reduce the level of fermenting ingesta and organisms in the GI tract. Animals are allowed access to grain until 12 hrs prior to embalming and have free access to water until euthanized.

Standard: 9CFR Ch.1. Pt.3, Subpt. A. Sec. 3.9

Justification: This is done to reduce post-mortem gas accumulation in the gut, which interferes with perfusion of the organs with embalming fluid and leads to poor fixation of the cadaver.

Species: Dog

Number Affected: 6

Exceptions to Standards: Dogs were maintained in cages in the procedures lab that permit most postural adjustments and movements, but do not meet the floor space requirements. Medium sized dogs (15 kgs.) were needed for this study. The dogs were housed in these units for periods of 24-48 hours for drug metabolism and pharmacokinetic studies.

Addendum to the FY2012 APHIS Form 7023 Submission for North Carolina State University USDA Registration #55-R-0005 /842-Exceptions to Standards Report

Standard: 9CFR Ch.1. Pt.3, Subpt. A. Sec. 3.6(c) (1) i and iii. Primary enclosures. Additional requirements for dogs-Space: Each dog housed in a primary enclosure must be provided a minimum amount of floor space, calculated as described in this portion of the regulations. The interior height must be 6 inches higher than the head of the dog.

Justification: The investigators were concerned about the potential for catheters to become dislodged, soiled, or otherwise compromised if dogs remained in their normal runs for the duration of these studies. The University Attending Veterinarian and members of the IACUC examined the metabolism units, and considered them adequate for the limited period that the dogs will be housed in them. The metabolism units, after allowing for removal of space for water bowl, provide 10.6 sq. ft. and approximately 2-4 inches above the top of the head. Because the dogs were being provided less than the required floor and headspace, the investigator agreed to the following accommodations:

- No dog was kept in the metabolism units for more than 48 hrs (during sampling portion of the protocol)
- Throughout the duration of stay in the metabolism units, each dog was exercised on a leash for 5-10 minutes every two hours during the study, with the exception of the night-time hours when the lights are turned off in the room.
- Unit hygiene was maintained by cleaning as frequently as necessary whenever soiling of the cage was observed.
- Dogs received an approved diet and continual access to water while in the metabolism units.
- Each dog was removed from the unit at least once each hour during the first 6 hours and allowed to exercise for 5 minutes.
- The PI or co-PI, both licensed veterinarians, inspected each dog throughout the stay in the metabolism units for any clinical signs or lesions associated with this period of confinement.

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Species: Cats

Number Affected: 37

Exception to Standards: Elevated Resting Surfaces were removed from cat pens for up to 10 days following surgery for lymph node removal surgery.

Standard: 9CFR Ch.1. Pt.3, Subpt. A. Sec. 3.6 (b) (iv)(4): Each primary enclosure housing cats must contain a resting surface or surfaces that, in the aggregate, are large enough to hold all the occupants of the primary enclosure at the same time comfortably. The resting surfaces must be elevated, impervious to moisture, and be able to be easily cleaned and sanitized, or easily replaced when soiled or worn. Low resting surfaces that do not allow the space under them to be comfortably occupied by the animal will be counted as part of the floor space.

Justification: Removal of the elevated resting surfaces will decrease the jumping activity of the cats following surgery. This change will facilitate healing of the incisions and help avoid dehiscence of the surgical wounds. Sutures are removed at 7-10 days after surgery, so this is an appropriate duration for the restriction. Cats are not restricted otherwise and remain in a group-housed setting.