

OCT 21 2015

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: 22-R-0148

2. Number 22 of animals used in this study.

3. Species (common name) Hamster of animals used in the study.

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

The animals are being utilized to study the pathogenic bacterium *Clostridium difficile*, the most common cause of diarrhea in hospitalized patients. Ninety-percent of *C. difficile* infections are associated with current or recent use of antibiotics. As a model of human disease, the animals are administered clindamycin by a subcutaneous injection and subsequently inoculated with the *C. difficile* organism by oral gavage. Within 48 hours animals begin showing signs and symptoms of disease, including diarrhea (i.e. "wet tail") as well as reduced activity, responsiveness and feeding. Animals are monitored three times daily during this period of time and animals in obvious distress are humanely euthanized.

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)

We explored the possibility of using medication to relieve animal suffering. However, the use of opioids can cause constipation, nausea and weight loss (Thomas. 2008. J. Pain Symptom Manage. 35:103-13) which would confound our observations of diarrhea and weight loss which are used to assign moribund status. Similarly, treatment of diarrhea with anti-diarrheals (e.g. bismuth) would interfere with the onset of diarrhea and confound assignment of moribund status. Therefore, we utilized frequent observation combined with an objective scoring system to assign moribund status and perform humane euthanasia on animals in distress. This strategy allows us to obtain scientifically meaningful data from the studies while simultaneously limiting animal suffering to a minimum.

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 _____