According to the Paperwork Reduction Act of 1995, an agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a valid OMB control number. The valid OMB control number for this information collection is 0579-0036. The time required to complete this information collection is estimated to average 2 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

OMB APPROVED
0579-0036

This report is required by law (7 U.S.C. 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

Interagency Report Control No. 0180-DOA-AN

Fiscal Year2018

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

REGISTRATION NUMBER: 74-R0081

Customer Number: 1502

2. HEADQUARTERS RESEARCH FACILITY *(Name and Address, as registered with USDA, Include ZIP Code)*

University of North Texas Health Science Center
3500 Camp Bowie Blvd
Fort Worth Texas 76107

Telephone: 817-735-2017

3. REPORTING FACILITY *(List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)*

FACILITY LOCATIONS *(Sites)* *See Attached Listing*

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY *(Attach additional sheets if necessary or use APHIS FORM 7023A.)*

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress on these animals and the reasons such drugs were not used must be attached to this report.)*	F. TOTAL NUMBER OF ANIMALS (Cols. C + D + E)
4. Dogs	0	0	0	0	0
5. Cats	0	0	0	0	0
6. Guinea Pigs	0	0	75	0	75
7. Hamsters	0	0	535	251	786
8. Rabbits	0	0	21	0	21
9. Non-human Primates	0	0	0	0	0
10. Sheep	0	0	0	0	0
11. Pigs	0	0	4	0	4
12. Other Farm Animals	0	0	0	0	0
13. Other Animals					

ASSURANCE STATEMENTS

1.) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.

2.) Each principal investigator has considered alternatives to painful procedures.

3.) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4.) The attending veterinarian for this research facility has appropriate authority to ensure the provisions of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer (C.E.O.) or Legally Responsible Institutional Official (I.O.))
I certify that the above is true, correct, and complete (7 U.S.C. Section 2143).

SIGNATURE OF C.E.O. OR I.O.	NAME AND TITLE OF C.E.O. OR I.O. *(Type or Print)*	DATE SIGNED
Anuja Ghorpade	ANUJA GHORPADE, VP RESEARCH	12/18/2018

APHIS FORM 7020
JUL 2013

Column E Explanation
Registration Number: 74-R-0081 **Fiscal Year 2018**

1. Study One:
Number of animals used in this study: 251
Species used in this study: Hamster
Explanation of procedure producing pain and/or distress:
Animals associated with this model may experience pain or distress as a result of infection and/or treatment with a compound. Historically, animals often do not manifest any signs of pain or distress prior to death, and 75% of the animals in those studies have either remained healthy and normal or have been euthanized to prevent prolonged suffering. Signs that indicate a severe disease state as a result of Clostridium difficile infection include lethargy, acute/chronic diarrhea, hypothermia, >15% decrease in body weight, reduced water/food intake, and swollen peritoneum. In addition to the possible effects related to the infection, treatment with test articles (compounds) could also induce negative effects in an animal as well. Signs of test article related effects include acute paralysis, increased respiratory/heart rates, and a rough coat. To prevent treatment related effects, all compounds evaluated in this model are pre-screened for potential toxicity by the sponsors and selected dosing regimens will be based on what has been safely used for evaluating other test articles in this model.
All animals associated with this protocol will be monitored for severe disease every 6 to 8 hours throughout the duration of a study (up to 50 days). An clinical observation sheet for each day of a study will be maintained that will include recording observations and animal disposition, including the date (day and time) and personnel initials. Using the guidelines associated with the IACUC 'Pain and Discomfort' (document 013) and 'Humane Endpoints' (document 008) protocols, any animal that appears to be moribund will be immediately removed from the study and euthanized.
Explanation with reason(s) for why anesthetics, analgesics and tranquilizers could not be used:
Most of the test articles that will be evaluated in this model are new investigational compounds and possible drug interactions have not been fully determined. If another drug is used to relieve pain and/or distress, this may interfere with the possible therapeutic/prophylactic efficacy a test article may have in this model. For example, buprenorphine (analgesic) is metabolized by the cytochrome 450-3A4 (CYP450-3A4) pathway. This same metabolic pathway interacts with 3 different antibiotic classes that include macrolides (clarithromycin), rifamycins (rifampin), and fluoroquinolones (ciprofloxacin). Interactions of these drugs in this pathway have been shown to alter the pharmacokinetics of each drug, which can directly impact their efficacy within the host (animal or human). Additionally, several nonsteroidal anti-inflammatory drugs (NSAIDS) are metabolized by the cytochrome 450-2C9 (CYP450-2C9) pathway, which also metabolically interacts with the antibiotics metronidazole and rifampin. As is the case with buprenorphine, the interaction of NSAIDS and other drugs in the CYP450-2C9 pathway can impact the efficacy of each drug by altering their metabolism and pharmacokinetics in the host. In addition to metabolic interference, NSAID use has been shown to clinically aggravate colitis caused by intestinal infections. Given these facts about documented drug interactions within critical metabolic pathways and how these interactions can interfere with drug efficacy or disease outcome in the host (Burton ME et al., Granowitz EV et al., Hogenauer C et al.), it is imperative that non-study associated

drugs used to relieve pain and/or distress not be administered in animals associated with this model so that the therapeutic and/or prophylactic efficacy of a new investigational compound can be accurately evaluated. If a new compound is efficacious in this animal model, then these results would be critical to its development for treating life-threatening Clostridium difficile-associated diarrhea (CDAD) in humans.

References:

Burton ME, Applied Pharmacokinetics & Pharmacodynamics: Priniciples of Therapeutic Drug Monitoring. Lippincott Williams & Wilkins, 2006, ISBN 9780781744317.

Granowitz E.V., and R.B. Brown. Antibiotic Adverse Reactions and Drug Interactions. Crit Care Clin, 2008 Apr;24: 421-442.