

Georgia State University
58 Edgewood Avenue NE
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Registration Number: 57-R-0012
Customer ID Number: 907

Explanation of and reason why pain and distress could not be relieved for **Category E Hamsters:**
Species: Syrian Hamsters

1. The study involves behavioral tests that model depression and Post-Traumatic Stress Disorder (PTSD) and brief exposure to aggressive conspecifics to induce conditioned defeat. The purpose of the work is to determine how social defeat alters the brain and subsequent behavior. Giving a drug to alleviate the stress would alter the natural responses to this social stressor and thus defeat the purpose of the research. This behavior is naturally produced and of a brief duration. This study was approved by the IACUC, and humane endpoints were developed and applied to minimize animal pain or distress.

Number of Animals Affected: 1,664

2. The study involves brief exposure to aggressive conspecifics and restraint stress. The purpose of the work is to determine how aggression and stress alters the brain and subsequent behavior. Giving a drug to alleviate the stress would alter the natural responses to this social stressor and thus defeat the purpose of the research. The researcher studies behavior that these animals naturally produce and that it is relatively mild and of a short duration. This study was approved by the IACUC, and humane endpoints were developed and applied to minimize animal pain or distress.

Number of Animals Affected: 69

Explanation of and reason why pain and distress could not be relieved for **Category E Hamsters:**
Species: Roborovski Dwarf Hamsters

1. The study involves exposure to SARS-CoV-2 infection. The purpose of the work is to study viral pathogenesis and evaluate efficacy of novel broad-spectrum antiviral drug candidates for prevention and improved case management of SARS-CoV-2 infections. Once infected, these animals have experienced piloerection, weight loss, hypothermia, and respiratory distress. Providing pharmacologic agents for pain relief will confound the model due to anti-inflammatory effects of the analgesics, impairing the host antiviral response. Interventions must be kept to an absolute minimum for a rigorous assessment of the therapeutic benefit resulting from administration of the candidate drugs compared to vehicle-treated control animals. (PMID:16764216) This study was approved by the IACUC, and humane endpoints were developed and applied to minimize animal pain or distress.

Number of Animals Affected: 644

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Explanation of and reason why pain and distress could not be relieved for **Category E**
Species: Domestic Ferret (*Mustela putorius furo*):

1. One study will involve exposure to Influenza virus infection. Once infected, these animals have experienced airway mucus production, lethargy, loss of body weight, and increased body temperature. Providing pharmacologic agents for pain relieve will confound the model due to interference with the host immune response. Therefore, interventions need to be kept to an absolute minimum for a rigorous assessment of the benefit resulting from treatment with the drug candidates compared to vehicle-only treatment. This study was approved by the IACUC and humane endpoints were developed and applied to minimize animal pain or distress."

Number of Animals Affected: 15

2. In the ferret model, CDV infection results in lethargy, loss of bodyweight, fever, vomiting, paralyzes, diarrhea, rash and possibly seizures. Providing pharmacologic agents for pain relieve will confound the model due to interference with the host immune response (<https://www.ncbi.nlm.nih.gov/pubmed/16764216>). Although, buprenorphine has been shown to exhibit less immunosuppressive effects on host immune response in comparison to other opioids, it has still been shown to be capable of modulating the humoral immune response (<https://www.ncbi.nlm.nih.gov/pubmed/29197801>) and should not be used as an analgesic. Therefore, interventions need to be kept to an absolute minimum for a rigorous assessment of the benefit resulting from treatment with the drug candidates compared to vehicle-only treatment. This study was approved by the IACUC and humane endpoints were developed and applied to minimize animal pain or distress."

Number of Animals Affected: 23

3. In the ferret model, SARS-CoV-2 infection reportedly leads to increased body temperature, lethargy, sneezing/nasal discharge, and conjunctivitis. Providing pharmacologic agents for pain relieve will confound the model due to interference with the host antiviral response. Although effects vary by drug and buprenorphine, for instance, has been shown to exhibit less immunosuppressive effects, it is still reportedly capable of modulating humoral and cell-mediated immune pathways (PMID: 29197801). Therefore, interventions must be kept to an absolute minimum for a rigorous assessment of the therapeutic benefit resulting from administration of the candidate drugs compared to vehicle-treated control animals. This study was approved by the IACUC and humane endpoints were developed and applied to minimize animal pain or distress."

Number of Animals Affected: 158

4. The study involves exposure to Influenza virus infection for the development of influenza vaccines that confer effective cross-protection. Once infected these animals have experienced discomfort, sickness including pain or distress, lethargy, and anorexia. ferrets. Providing

pharmacologic agents for pain relief may adversely affect the results of the studies by interfering with the immune system or by adding confounding variables to the data. Therefore, symptoms of infection in the ferrets cannot be alleviated because they are important measures of the success or failure of the vaccine candidates being testing. This study was approved by the IACUC, and humane endpoints were developed and applied to minimize animal pain or distress.

Number of Animals Affected: 18