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Column E Explanations

1. Registration Number: 31-R-0014/216
2. Species of animals used in the study: Rabbits
3. Number of animals used in this study: 60
4. Explain the procedure producing pain and/or distress:

   The goal of the study is to develop new treatment paradigms for osteomyelitis. Some antibacterial drugs being evaluated have potential side effects such as severe diarrhea or other forms of gastrointestinal disruption that may result in significant loss of weight and signs of lack of well-being.

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.

   Supportive measures are used to minimize antibiotic side effects; however, significant weight loss (20%) is still observed. Since the treatment of bacterial osteomyelitis requires the use of antibiotics at relatively high levels and durations of treatment, the use of antibiotics in spite of side effects is scientifically justified if the gastrointestinal distress can be controlled via supportive therapy.

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Column E Explanations

1. Registration Number: 31-R-0014/216
2. Species of animals used in the study: Hamsters
3. Number of animals used in this study: 15
4. Explain the procedure producing pain and/or distress:

   Adult hamsters are subjected to 18 hours of sleep deprivation using an established disk-over-water method. Potential distress could be caused by exposure to water in addition to the sleep deprivation.

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.

   One goal of the study is to examine how immune function following sleep deprivation is affected by season. Sleep deprivation is an integral part of the research goal. Other non-water means of sleep deprivation were considered, but these methods induce the animals to move and therefore exert energy. Because the amount of locomotor activity from these types of manipulations could potentially bias the results in this experiment, these methods cannot be/were not used. Possible adverse effects to exposure to water are minimized since animals will be monitored continuously by video and water levels have been lowered such that it would be impossible for the animal to aspirate water. The water is also warmed to prevent hypothermia. Animals will be removed from the experiment if signs of behavioral stress are observed/documented such as shivering lasting over a minute, a rapid decrease or increase in respiration rate, or seizure.

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Column E Explanations

1. Registration Number: 31-R-0014/216
2. Species of animals used in the study: Pigs
3. Number of animals used in this study: 12
4. Explain the procedure producing pain and/or distress:

   This study uses a spinal muscular atrophy (SMA) pig model that exhibits symptoms of progressive limb paresis in order to test gene therapy efficacy. The limb weakness reduced ability to ambulate normally may cause distress.

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.

   In order to determine if gene therapy is successful, the progression of muscle weakness is monitored over time in affected animals using clinical observations and physiologic function monitoring. Animals which exhibit rear limb weakness or paralysis will not be removed from the study if there is no significant progression to the forelimbs. Supportive care is provided to animals exhibiting clinical signs to ensure the distress is minimized as much as possible. A lack of disease progression indicates the gene therapy is effective, and further characterization of the duration of the effectiveness is essential to understanding of this treatment and its potential application to human patients.

   If the front limbs become weak or there is a clear indication of denervation according to the electromyography, then the treatment will be deemed ineffective, and the animal will be removed from the study and humanely euthanized.

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**IACUC Approved Exception to standards and regulations under the Animal Welfare Act**

Registration Number: 31-R-0014/216

Approved by IACUC:

Space Requirements §3.128: Piglets and calves are used in gnotobiotic studies, which require that they are maintained in primary enclosures that allow animals to make postural adjustments without impedance during the initial stage of the study, but that result in the touching of enclosures during normal postural adjustments during the final stage of the study. Since the use of gnotobiotic chambers is necessary for conducting this type of research, the IACUC has approved this enclosure size exception. Piglets are in the cages from birth up to 69 days old and calves are in the cages from birth up to 45 days. This exception involved 21 calves and 245 piglets during this reporting period.

Lighting Requirements §3.26 (c): Hamsters are subject to constant light conditions for up to 8 weeks in order to study impacts of light on physiology and behavior of ovariectomized hamsters. Conditions consist of up to 16 hours of dim light (10 lux) with 8 hours of bright light (120 Lux) or constant bright light at 120 lux for the entire period. During this reporting period, this exception involved up to 200 hamsters under 16:8 hrs of dim: bright lights. No hamsters were subject to the constant bright light conditions.