

Column E Explanations

1. Registration Number: **31-R-0014/216**
2. Number of animals used in this study: **13**
3. Species of animals used in the study: **Pig**
4. Procedure producing pain and/or distress:
 - a. Brief description of procedure
 - b. Explain Animal Experience

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

5. Explanation with the reason why anesthetics, analgesics and tranquilizers could not be used:

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 are not be removed from the study if there is no significant progression to the forelimbs. Supportive care was 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.