## **Category E Explanation**

Cattle. Two (2) cows were used to study pulmonary hypertension (PH). The main aspect of our experimental procedures with potential to cause pain or distress is housing in hypoxia. We recognize that exposure in the hypoxic chamber causes PH and that there are physiological changes that occur in the hypoxic chamber exposure that may result in distress. Removal from the hypoxic chamber to alleviate the distress would negate the model. However, while cardiovascular and respiratory changes are certainly occurring, most animals may display tachypnea and lethargy. Animals are monitored daily by study veterinarians throughout the experiment for signs of distress that would indicate removal from hypoxia, or humane euthanasia.

Ferret. Fifteen (15) ferrrets were used as controls (unvaccinated) for a rabies vaccine study. The ferrets were observed twice daily for clinical signs associated with rabies virus such as altered behavior, dysphagia, or other neurologic signs, at which time they were euthanized. Analgesics will not be used as they will likely alter disease progression, confound interpretation of the study, and unlikely relieve the distress due to rabies virus infection.