

2. Explanation of the E pain category procedures producing pain and distress and reasons pain relieving agents cannot be used.

Four rabbits were exposed to halogen gas (chlorine or bromine). This caused some discomfort (manifested by labored breathing) and tissue damage (as shown by the development of arterial hypoxemia and damage to the airways). Similar discomfort is experienced by patients with COPD or other chronic lung diseases. Buprenorphine will be administered to Bromine exposed animals, but due to pain and or distress animals are listed in category E.

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This Diabetic Retinopathy (DR) pilot study used ten Tree Shrews in pain category E. Unfortunately, there is no alternative to the use of Tree Shrew in the studies proposed in this pilot study to validate the Tree Shrew as a potential model for DR, which could resemble human pathology closely, but cannot be performed by cell culture. To create the DR, acute hyperglycemia will be induced using streptozotocin causing distress to animal that cannot be relieved without interfering with the disease study. Insulin will be injected to support animal health and avoid hyperglycemia hyperosmolar coma.

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There are two Chronic Obstructive Pulmonary Disease (COPD) studies. One study used 48 ferrets and another used 36 ferrets. All animals were exposed to cigarette smoke, and no theoretical alternatives exist that can replace in vivo modeling of COPD. Exposure of cigarette smoke is expected to cause some amount of discomfort that is well tolerated. Since, the whole study involves several episodes of smoke exposure and to keep physiologically relevant anesthesia cannot be administered during smoke exposure.