Attachment to APHIS FORM 7023
Explanation of Column E Procedures
Oklahoma Medical Research Foundation73-R-0002
Fiscal Year 2011

1. The following protocol involves experiments reported in Column E. Experiments were approved by the Oklahoma Medical Research Foundation (OMRF) Institutional Animal Care and Use Committee (IACUC) after their determination of scientific justification.

L0074: Validation of extracellular histones as biomarker and therapeutic target in sepsis
Species Used: Baboon
Numbers Used: 6

Explain the procedure producing pain and/or distress:

The objective of the experiment is to investigate the survival and organ-protective effects of histone inhibition during the 2 different phases of sepsis, early inflammatory response manifested within the first 4 hours after onset of infection in this animal model and ischemia reperfusion starting 8 hours after onset of infection. Animals will be anesthetized and brachial and saphenous veins cannulated. One of the IV catheters will be used for infusion of bacteria to induce the septic state and another one for administration of antibody or histone neutralizing peptide. A third catheter is in place for blood collection and/or saline administration. After an 8 hour anesthesia the catheters are removed and the animals are closely monitored for up to 7 days post-infection.

Provide scientific justification for why pain and/or distress could not be relieved. State methods used to determine that pain and/or distress relief would interfere with test results. (For federally-mandated testing, see next response.):

Sepsis is a major medical problem responsible for approximately 750,000 ICU admissions and 225,000 deaths in the US annually. Animals will receive supportive care and opioids to minimize pain and distress. However, since sepsis is such a fulminant disease often associated with organ failure and death negative effects on the wellbeing of the animals need to be anticipated. The administration of narcotic drugs will put the animals in a sedated state and therefore minimize those effects but not totally exclude.

What, if any, federal regulations require this procedure? Cite agency, the Code of Federal Regulations (CFR) title number and the specific section number (e.g. APHIS, 9CFR 113.102):
Agency: *Not Applicable* CFR: *Not Applicable*

2. The following protocol involves experiments reported in Column E. Experiments were approved by the Oklahoma Medical Research Foundation (OMRF) Institutional Animal Care and Use Committee (IACUC) after their determination of scientific justification.

K0132: *Mechanisms and treatment of ongoing deterioration of cochlear structure and function after acute noise injury*
Species Used: Chinchilla
Numbers Used: 91

F0100
10-21: *Preclinical Study of Combination Oral Treatment of ATT*
Species Used: Chinchilla
Numbers Used: 23

Explain the procedure producing pain and/or distress:

The objective of the experiment is to reveal the underlying mechanisms related to long term hearing disorders and early auditory aging, in an effort to prevent accelerated aging of the cochlea. Chinchillas will be exposed to a speaker which is suspended directly above the cages. Steady state noise exposure will be digitally generated and passed through a real-time attenuator, filtered, and amplified. Each animal will be exposed to the noise level of 105 dB SPL at 4 kHz octave band noise for 6 hours. All animals will be conditioned to handling and then acclimated to the small wire cages and the sound booth prior to the noise exposure. During the noise exposure the animals will be restrained by a breeding collar and tether system secured in small wire animal cages with free access to water. This system will secure the chinchilla in a comfortable position while preventing the animal from assuming a position that will shield either of its ears.

Provide scientific justification for why pain and/or distress could not be relieved. State methods used to determine that pain and/or distress relief would interfere with test results. (For federally-mandated testing, see next response.):

Generalized anesthesia for a six-hour duration would be medically complicated and in itself lead to a distressful recovery period. Animal models without anesthesia mimic human subjects under noise exposure better than the anesthetized animal. Noise exposure should try to replicate the real world as much as possible; we typically are not exposed to noise in an anesthetized state. The administration of drugs to sound exposed animals effects several important aspects of sound transduction in the inner ear and electrophysiological measurements of inner ear function. Because these confounded results from animals cannot be extended to human models, these models are not used in hearing research. Noise exposure in normal animals always results in significant variations in threshold shifts. These variations may result from a variety of factors overactive middle ear muscles, efferent feedback, and state of the animal. Now there may be evidence that an animal gives larger and more consistent threshold shifts because of elimination of the aforementioned variables. Sodium pentobarbital has been shown to have a significant effect on total middle ear impedance and on the shape of the tympanograms. The use of ketamine causes significant increases in distortion-product otoacoustic emissions. This result indicates that tonic activity levels in the cochlear efferents are reduced by the anesthetic effects

which could lead to greater damage due to loud sound exposure. Isoflurane significantly attenuates auditory steady state response (which is a response of the brain to auditory stimuli) in a dose dependents matter.

What, if any, federal regulations require this procedure? Cite agency, the Code of Federal Regulations (CFR) title number and the specific section number (e.g. APHIS, 9CFR 113.102):
Agency: *Not Applicable* CFR: *Not Applicable*