Attachment to APHIS FORM 7023
Explanation of Column E Procedures
Oklahoma Medical Research Foundation73-R-0002
Fiscal Year 2010

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.

C0131: *Protective Immunity to Influenza-Pilot Projects*
Species Used: Ferret
Numbers Used: 12

Explain the procedure producing pain and/or distress:

The objective of the experiment is to define the antibody properties necessary for protective immunity to influenza. Under anesthesia, the ferrets will receive viral particles (either 10^6, 10^7, 10^8) of the H1N1influenza virus (Solomon Islands) suspended in 0.5ml of PBS via intra-tracheal delivery. Post infection, the ferrets are weighed each day, observed for clinical signs (such as sneezing, nasal discharge, and disinterest in play), and nasal washes will be collected. All animals will be euthanized on day fourteen (14) post infection, and tissues will be collected for analysis.

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.):

No pain will occur as a consequence of the influenza infection and based on the human experience with seasonal influenza, we anticipate that the animals will experience only mild to moderate distress. In humans, symptoms of influenza infection (i.e. fever and body aches) are most commonly treated with acetaminophen or NSAIDs. However, the overall goal of these experiments is to determine the ability of an anti-influenza antibody to reduce clinical disease (fever, weight loss, and disinterest in play) and lung pathology. Therefore, the withholding of medications, such as NSAIDs, is justified because they will suppress the key clinical endpoints of the therapeutic intervention and interfere with the interpretation of the data.

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 protocols involve 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.

JAN 31 2011

K0131: *Effects of HPN-07 on Acute Acoustic Trauma (ATT)*
Species: Chinchilla
Numbers Used: 4

K0132: *Mechanisms and treatment of ongoing deterioration of cochlear structure and function after acute noise injury*
Species Used: Chinchilla
Numbers Used: 76

F0100: *Pre-Clinical Study of Combination Oral Treatment for ATT*
Species Used: Chinchilla
Numbers Used: 13

Explain the procedure producing pain and/or distress:

The objective of the experiments 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 thresholds 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*