Year 2008 Annual Report for Registration Number: 57-R-000. Attachments to APHIS Form 7023

| 081-2007Y | Regulation of Motor Function in Parkinson's Disease:<br>Effects of Cannabinoid Antagonists in the MPTP<br>Primate Model of Parkinson's Disease | 8 rhesus macaques                   |
|-----------|--|-------------------------------------|
| 094-2007Y | Neuropsychology of Primate Social Cognition  | 8 rhesus macaques and 10 chimpanzee |

B. In the study of Alzheimer-like disease, animal will be studied following injections of lentiviral constructs in the brain following craniotomy. The safety and efficacy of immunizations also will be evaluated. Single or protected contact housing is required after surgery for 6 to 16 weeks to evaluate behavior or other clinical complications.

| Protocol # | Title   | # Species          |
|------------|---|--------------------|
| 066-2007Y  | Alzheimers Immunotherapy in Primate Model of<br>Cerebral Amyloid Angiopathy | 7 squirrel monkeys |
| 255-2008Y  | Focal Alzheimer transgene expression in rhesus monkeys                      | 4 rhesus macaques  |

C. Infectious disease vaccine development studies may require single housing to prevent disease agent transmission. Some of the studies described here involve the development of a SIV/HIV vaccine, investigation of the role of host immune response in protecting against or contributing to the appearance of immune system damage following AIDS infection, evaluation of the function of the thymus during infection with SIV, evaluation of the development and pathogenicity of mutant viruses that develop over time in chronically infected animals, the effect of opiate dependency on the progression of AIDS, and the testing of the immunogenicity and efficacy of different AIDS vaccines and treatment regimens. Single housing is required after exposure to the virus to prevent transmission of virus from animal to animal. In addition, the animals need to be accessed frequently for blood draws. The experimental design requires that the efficacy of vaccines will be assessed after a single exposure and without the possible confound of exposure to mutant viruses. Infected animals in an experimental group will be housed together after approximately one month. In some experiments, animals are singly housed one month prior to inoculation to allow sufficient time for acclimatization to the new housing arrangement so that the stress of separation doesn't influence susceptibility to or course of infection.

A study testing the effects of T cell depleting antibodies in SIV-infected mangabeys requires frequent antibody infusions and blood draws during the first 3 weeks of the treatment (animals are assessed up to 4 times per week), followed by weekly blood draws for the remainder of the study, which lasts 2 months. Because these animals will be frequently handled for testing, animals are housed in protected contact housing.

RECEIVE Malaria studies are being done to develop a vaccine and to provide antigens for serologic and molecular studies, genomic libraries, antibody production, and gametocytes for infection of mosquitoes. It is necessary to house the animals indoors to

BY.

prevent contact with the local mosquito population. Following blood collections and treatment of the malaria infection, the animals are returned to their normal housing environment. Protected-contact housing is utilized in other malaria vaccine studies in monkeys due to the requirement of daily heel or ear sticks (as well as blood collection and immunization), as well to avoid frequent reunions following stressful procedures Dengue is one of the most important mosquito-borne viral diseases affecting humans, with over half of the world's population living in Dengue endemic areas. A wide spectrum of clinical manifestations has been noted which range from asymptomatic, mild febrile (dengue fever, DF) to dengue hemorrhagic fever (DHF)/dengue shock syndrome (DSS), and a severe form associated with a life-threatening illness. The incidence rate of the latter disease form is 1-5% and predominantly occurs in children under the age of 15. The pathological hallmarks that determine disease severity and distinguish DHF from DF and other viral hemorrhagic fevers are plasma leakage resulting from increased vascular permeability and abnormal blood clotting.

The objectives of this pilot proposal are to generate sufficient data to further pursue for the more completed underlying mechanisms triggering DHF/DSS and to better define and understand the initial target cells infected by dengue virus, which may correlate with hematopoietic suppression. The proposed study, therefore, may potentially provide a new insight and shed a new light on human immunology in response to dengue virus infection.

| Protocol # | Title  | # Species                             |
|------------|--|---------------------------------------|
| 013-2008Y  | Evaluation of infection, viral dissemination and immune responses to the gamma human retrovirus XMRV in rhesus macaques  | 3 rhesus macaques                     |
| 088-2007Y  | Evaluation of anti-HIV Interventions for the prevention of SHIV Transmission in Pig-tailed Macaques  | 28 pigtail macaques                   |
| 198-2008Y  | Non-human Primate Models of Malarial Anemia  | 18 rhesus macaques                    |
| 247-2007Y  | Early Innate Immune Response in Dengue Virus Infection   | 3 rhesus macaques                     |
| 142-2008Y  | Innate Immunity and affects of Macrophage Depletion in SIV-Infected Non-Human Primates   | 3 rhesus macaques                     |
| 256-2008Y  | Molecular Evolution of Multiply Deleted SIV in Vivo  | 23 rhesus macaques                    |
| 261-2008Y  | Vaccination Against mucosal HIV Clade C<br>Transmission  | 71 rhesus macaques                    |
| 010-2006Y  | Infant Immunoprophylaxis Against a Primate<br>Lentivirus   | 21 rhesus macaques                    |
| 061-2007Y  | SHIV Transmission Through Oral versus Other Mucosae  | 22 rhesus macaques                    |
| 030-2007Y  | Role of virus specific immunity in primate AIDS;<br>CD4 T cell activation in SIV+ disease resistant<br>mangabeys; Role of CTL in indian macaques with<br>live attenuated deglycoslated SIV | 6 mangabeys and<br>20 rhesus macaques |
| 259-2007Y  | Molecular Analysis of Antigenic Variation in Malaria   | 18 rhesus macaques                    |

cursor to a target on a video screen. During these tasks, these monkeys are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory.

Animals assigned to studies to distinguish different types of cognition or memory may be tested in homecages, specifically designed rooms or using physical restraint.

To motivate the animals to work effectively, the first feeding of the day may be reduced or delayed. However, water or food is provided during and immediately after the testing session to meet the daily ration. The total intake of the restricted material, food or water, is recorded daily and the animal's body weight is checked and recorded at least twice weekly to ensure that are being well maintained.

1. Food and/or water restricted, but provided during and after laboratory

| testing    | /  | # Species  |
|------------|--|--|
| Protocol # | Title  | ALL DE STATE OF THE STATE OF TH |
| 004-2006Y  | Effects of Viewing Distance on Eye Growth and          | 11 rhesus macaques   |
|            | Refractive Development                                 |  |
| 264-2007Y  | Binocular Coordination of Eye Movements; Surgical      | 11 rhesus macaques   |
|            | Treatment of Strabismus in Juvenile Monkeys            |  |
| 087-2007Y  | Cellular Mechanisms Underlying the Therapeutic Benefit | 2 rhesus macaques  |
|            | of High-Frequency Stimulation of the Subthalamic       |  |
|            | Nucleus for Parkison's Disease                         | ( 1  |
| 091-2005Y  | Episodic Memory in Rhesus Monkeys: Spatial and         | 6 rhesus macaques  |
|            | Temporal Contexts                                      | 0.1  |
| 124-2008Y  | Laminar Specific Neural Mechanisms for Memory in the   | 2 rhesus macaques  |
|            | Entorhinal Cortex                                      | 2.1  |
| 178-2008Y  | Local Field Potentials in the Basal Ganglia            | 2 rhesus macaques  |
| 040-2007Y  | Transgenic Monkey: Inherited Neurodegenerative         | 45 rhesus macaques   |
|            | Disease  | l  |
| 204-2008Y  | Hippocampal-Cortical Interaction and Memory            | 4 rhesus macaques  |
|            | Formation  | 4.1  |
| 173-2008Y  | Neural Control of Visual-Vestibular Behavior           | 4 rhesus macaques  |
| 204-2008Y  | Hippocampal-Cortical Interaction and Memory            | 4 rhesus macaques  |
|            | Formation  | 1.5  |
| 242-2007Y  | The neurology of memory in the nonhuman primate        | 15 cynomolgus  |
|            |  | macaques   |
| 003-2006Y  | Imaging Medial Temporal Lobe Activity Related to       | 2 rhesus macaques  |
|            | Memory and Emotion in Awake, Behaving Primates         | ļ  |
| 249-2005Y  | Cocaine Use and Monoamine Function in Nonhuman         | 44 squirrel monkeys  |
|            | Primates   |  |

2. Short-term physical restraint only:

| Protocol # | Title  | # Species          |
|------------|--|--------------------|
| 264-2007Y  | Binocular Coordination of Eye Movements; Surgical<br>Treatment of Strabismus in Juvenile Monkeys   | 11 rhesus macaques |
| 003-2006Y  | Imaging Medial Temporal Lobe Activity Related to<br>Memory and Emotion in Awake, Behaving Primates | 2 rhesus macaques  |
| 087-2007Y  | Cellular Mechanisms Underlying the Therapeutic Benefit   | 2 rhesus macaques  |

See reverse side for additional information. Interagency Report Control No 0180-DOA-AN

#### UNITED STATES DEPARTMENT OF AGRICULTURE ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. CERTIFICATE NUMBER: 57-R-0003

CUSTOMER NUMBER: 896

FORM APPROVED OMB NO. 0579-0036

### ANNUAL REPORT OF RESEARCH FACILITY (TYPE OR PRINT)

**Emory University** 1599 Clifton Rd NE, 1599-001-1BE Atlanta, GA 30322

Telephone: (404) 727-3889

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, or experimentation or held for these purposes. Attach additional sheets if necessary)

#### FACILITY LOCATIONS (Sites) - See Attached Listing

| A.  Animals Covered By The Animal Weifare Regulations | B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes. | C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs. | D. Number of animal upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used. | E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report) | F.  TOTAL NUMBER OF ANIMALS  (COLUMNS C+D+E) |
|---|---|---|--|--|--|
| 4. Dogs   | 0   | 3   | 27   | 0  | 30   |
| 5. Cats   | 0   | 0   | 17   | 0  | 17   |
| 6. Guinea Pigs  | 0   | 8   | 43   | 88   | 139  |
| 7. Hamsters   | 0   | 0   | 0  | 0  | 0  |
| 8. Rabbits  | 1   | 40  | 253  | 0  | 293  |
| 9. Non-human Primates                                 | 1664  | 400   | 1778   | 17   | 2195   |
| 10. Sheep   | 0   | 0   | 27   | 10   | 37   |
| 11. Pigs  | 0   | 0   | 294  | 0  | 294  |
| 12. Other Farm Animals                                | 0   | 0   | . 0  | 0  | 0  |
| 13. Other Animals                                     |   |   |  |  |  |
| VOLES   | 156   | 1054  | 135  | 124  | 1313   |
| GERBILS   | 0   | 8   | 12   | 0  | 20   |
|   |   |   | 1  |  |  |

#### **ASSURANCE STATEMENTS**

- 1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.
- 2) Each principal investigator has considered alternatives to painful procedures.

SIGNATURE OF C.E.O OR INSTITUTIONAL OFFICIAL

- 3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). A summary of all such exceptions is attached to this annual report. In addition to identifying the IACUC-approved exceptions. this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.
- 4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL (Chief Executive Officer or Legally Responsible Institutional Official) I certify that the above is true, correct, and complete (7 U.S.C Section 2143)

NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL (Type or Print)

DATE SIGNED

(b)(6), (b)(7)c

11/25/2008

APHIS FORM 7023 (AUG 91)

(Replaces VS FORM 18-23 (OCT 88), which is obsolete)

PART 1 - HEADQUARTERS

Thirty "stimulus" prairie voles pups were used to test maternal behavior. In order to test the appropriate behavioral response, the adult subjects must establish physical contact with the pups and the pups need to be awake, warm and emit all stimuli that normally trigger the attention of the subjects. Replacement of pups by objects or anesthetized pups would not trigger the appropriate maternal responses from the adult subjects. In order to reduce the number of pups, they are reuse at different ages 2, 3, 4, and 5 days. The risk of the mother attacking the pups cannot be avoided in any maternal behavior test. The animals are under continuous observation during the test. The major goal of this study is understanding variability in the response to pups within and across species that ranges from spontaneous caring activities to neglecting or infanticidal behavior.

Finally, seventy voles were used in the tail suspension test and forced swim tests. These tests are designed to assess active versus passive behavior when challenged by either tail suspension or forced swimming. The tail suspension and forced swim test are well-described and currently accepted assays for depressive-like behavior in rodents. Each test is brief and does not produce long term distress in the animal. Since the main question is how these animals respond to the mildly stressful situations, distress relieving measures cannot be used.

| Protocol # | Title  | # Species |
|------------|--|-----------|
| 025-2006Y  | Neuropeptide Basis of Social Loss and Depression | 94 voles  |
| 060-2007Y  | Oxytocin and Social Attachment                   | 30 voles  |

Disorders affecting dopamine transmission, such as Parkinson's Disease, are associated with disrupted sleep patterns and arousal. Rhesus monkeys are used in this study to investigate the cellular mechanism of these sleep disorders and how medications act and can be better used to manage them. Nonhuman primates given the neurotoxin MPTP are used as a model of parkinsonianism. Induction of parkinsoniansim with MPTP causes impaired movement, blunted motivation, apathy and drowsiness that may be distressful. This condition cannot be relieved with pain-relieving drugs. In fact, analgesics, anesthetics and tranquilizers are medically contraindicated for the condition potentially enhancing drowsiness and creating risk of aspiration or respiratory distress. Although the federal reporting requirements only considers the use of anesthetics, analgesics and tranquilizers to relieve pain or distress, it should be noted that dopaminomimetic agents, a more specific and appropriate intervention, may be used to reverse acute signs of MPTP intoxication in animals on this study. The five animals reported with this work were carried-over from 2007 and do not represent new acquisitions.

| Protocol # | Title  | # Species         |
|------------|--|-------------------|
| 072-2008   | Modulation of the sleep/wake state by dopamine | 5 Rhesus Macaques |

Human patients with a wide range of illnesses may exhibit a high rate of depression mediated by activation of the immune system and the release of cytokines. The latter can exert effects upon the brain leading to altered behavior. For example, about 50% of humans given the cytokine IFN-alpha therapeutically develop depression. In these studies, the administration of IFN-alpha causes chronic immune activation and a behavioral syndrome in macaques similar to depression in humans. Monkeys given the cytokine are used to study how it disrupts brain neurochemistry and to develop treatment interventions. The syndrome may also be characterized by apathy, poor motivation and sleepiness. Potentially animals may also experience heightened sensitivity to painful stimuli and other neurological abnormalities. Pain relieving drugs, except during and immediately following surgery, cannot be used because of the potential confounding effects upon the neurological effects of the model as well as increasing the risk of sleepiness, respiratory

a chair and typically spend 4-6 hours per daily session in the laboratory. Animals assigned to studies to distinguish different types of cognition or memory may be tested in homecages, specifically designed rooms or using physical restraint.

To motivate the animals to work effectively, the first feeding of the day may be reduced or delayed. However, water or food is provided during and immediately after the testing session to meet the daily ration. The total intake of the restricted material, food or water, is recorded daily and the animal's body weight is checked and recorded at least twice weekly to ensure that are being well maintained.

1. Food and/or water restricted, but provided during and after laboratory

| testing    |  | # Species  |
|------------|--|--|
| Protocol # | Title  | THE RESERVE THE PARTY OF THE PA |
| 004-2006Y  | Effects of Viewing Distance on Eye Growth and          | 11 rhesus macaques   |
|            | Refractive Development                                 |  |
| 264-2007Y  | Binocular Coordination of Eye Movements; Surgical      | 11 rhesus macaques   |
|            | Treatment of Strabismus in Juvenile Monkeys            |  |
| 087-2007Y  | Cellular Mechanisms Underlying the Therapeutic Benefit | 2 rhesus macaques  |
|            | of High-Frequency Stimulation of the Subthalamic       |  |
|            | Nucleus for Parkison's Disease                         |  |
| 091-2005Y  | Episodic Memory in Rhesus Monkeys: Spatial and         | 6 rhesus macaques  |
|            | Temporal Contexts                                      |  |
| 124-2008Y  | Laminar Specific Neural Mechanisms for Memory in the   | 2 rhesus macaques  |
|            | Entorhinal Cortex                                      |  |
| 178-2008Y  | Local Field Potentials in the Basal Ganglia            | 2 rhesus macaques  |
| 040-2007Y  | Transgenic Monkey: Inherited Neurodegenerative         | 45 rhesus macaques   |
|            | Disease  |  |
| 204-2008Y  | Hippocampal-Cortical Interaction and Memory            | 4 rhesus macaques  |
|            | Formation  |  |
| 173-2008Y  | Neural Control of Visual-Vestibular Behavior           | 4 rhesus macaques  |
| 204-2008Y  | Hippocampal-Cortical Interaction and Memory            | 4 rhesus macaques  |
|            | Formation  | <u> </u>   |
| 242-2007Y  | The neurology of memory in the nonhuman primate        | 15 cynomolgus  |
|            |  | macaques   |
| 003-2006Y  | Imaging Medial Temporal Lobe Activity Related to       | 2 rhesus macaques  |
|            | Memory and Emotion in Awake, Behaving Primates         |  |
| 249-2005Y  | Cocaine Use and Monoamine Function in Nonhuman         | 44 squirrel monkeys  |
|            | Primates   |  |

2. Short-term physical restraint only:

| Protocol #  | Title   | # Species          |
|---|---|--------------------|
| 264-2007Y Binocular Coordination of Eye Movements; Surgical Treatment of Strabismus in Juvenile Monkeys |   | 11 rhesus macaques |
| 003-2006Y   | Imaging Medial Temporal Lobe Activity Related to<br>Memory and Emotion in Awake, Behaving Primates      | 2 rhesus macaques  |
| 087-2007Y   | Cellular Mechanisms Underlying the Therapeutic Benefit of High-Frequency Stimulation of the Subthalamic | 2 rhesus macaques  |

| egistration Num | ber: 57-R-0003 Attachments to APHIS Form 7023  |                        |
|-----------------|--|------------------------|
|                 | Nucleus for Parkison's Disease   |                        |
| 095-2008Y       | Development of a Reversible Deactivation, via Cooling<br>Technique of Study Higher Cognitive Function in<br>Monkeys                    | 2 rhesus macaques      |
| 134-2008Y       | Development of a Focal Transgenic Model of<br>Huntington's Disease   | 1 rhesus macaque       |
| 112-2006Y       | Glutamate Receptors: Novel Targets for Parkinson's Disease Therapy   | 11 rhesus macaques     |
| 178-2008Y       | Local Field Potential in the Basal Ganglia   | 2 rhesus macaques      |
| 187-2006Y       | Evolution of Aging and Dementia in Female Primates,<br>Cores A-D and Projects 1-3  | 25 rhesus macaques     |
| 195-2008Y       | Visual Processing and Smooth Eye Movements & Novel Immunotoxin and IGF Therapy for Strabismus  | 18 rhesus macaques     |
| 217-2006Y       | Function of Dopamine in the Primate Substantia Nigra   | 2 rhesus macaques      |
| 031-2006Y       | Maintenance of Yerkes Primate Center Animal Colony   | 148 rhesus macaques    |
| 012-2008Y       | Transition States of Drug Addiction in Non-human<br>Primates   | 16 rhesus macaques     |
| 070-2006Y       | Behavioral, neural and endocrine effects of differential rearing history in rhesus monkeys (Macaca mulatta)                            | 70 rhesus macaques     |
| 079-2007Y       | PET Neuroimaging and Cocaine Neuropharmacology in Monkeys; PET in conscious monkeys  | 39 rhesus macaques     |
| 112-2007Y       | Orbitofrontal-limbic ontogeny and early dysfunction;<br>The integration of multisensory social cues and its neural<br>basis in monkeys | 18 rhesus macaques     |
| 076-2007Y       | Development of Reversible Inactivation Technique for<br>the Study of Higher Cognitive Functions in Monkeys                             | 2 rhesus macaques      |
| 144-2007Y       | Development of Medial Temporal Lobe Function   | 22 rhesus macaques     |
| 124-2008Y       | Laminar Specific Neural Mechanisms for Memory in the Entorhinal Cortex   | 2 rhesus macaques      |
| 173-2008Y       | Neural Control of Visual-Vestibular Behavior   | 4 rhesus macaques      |
| 040-2007Y       | Transgenic Monkey: Inherited Neurodegenerative Disease   | 48 rhesus macaques     |
| 242-2007Y       | The neurology of memory in the nonhuman primate  | 15 cynomolgus macaques |
| 249-2005Y       | Cocaine Use and Monoamine Function in Nonhuman Primates  | 44 squirrel monkeys    |

### Summary of Studies (Animal) Listed in Column E

Animals are used to study the effect of social deprivation during infancy in the prairie vole, to model maternal neglect, which occurs in humans. Pups are separated from their mother and placed in a warm incubator. Since the aim is to study the effects of the stress of maternal separation on the pups, drugs or other procedures cannot be used to alleviate the stress. The pups do not experience pain but only the psychosocial stress of being without their mother.

K. Recent studies have shown that a molecule called Programmed Death-1 (PD-1) is highly expressed by killer CD8 T cells during lymphochorio meningitis virus (LCMV) infection and that the binding of PD-1 with its counter part PD-L1 on cells that present the viral protein (antigen presenting cell) results in the loss of killing ability of killer T cells. Blocking the binding between PD-1 and PD-L1 in mice by injecting anti-PD-1 antibody recovered the killing ability of killer CD8 T cells and improved the control the of LCMV infection. Recent studies have extended these observations to killer CD8 T cells in individuals infected with human immunodeficiency virus (HIV). These studies show that these killer CD8 T cells express high levels of PD-1 and this expression is higher in individuals with high viral burden. Blocking binding between PD-1 and PD-1 ligand (PD-L1) in the laboratory in culture dish recovered the function of these killer CD8 T cells. Data from our laboratory also show that rhesus monkey killer T cells express high levels of PD-1 following infection with a simian immunodeficiency virus (SIV, virus that causes AIDS in monkeys) and blocking binding between PD-1 and PD-L1 in culture dish recovers the killing function of SIV-specific T cells. Collectively, these results strongly suggest that blocking the binding between PD-1 and PD-L1 in SIV-infected monkeys by injecting anti-PD-1 or anti-PD-L1 antibody (in vivo blockade) may recover the function of anti-viral killer cells and lower the levels of SIV in blood. Thus, in vivo blockade of PD-1 or PD-L1 may represent a novel therapeutic approach for HIV/AIDS.

| Protocol # | Title                                     | # Species          |
|------------|---|--------------------|
| 149-2007Y  | PD-1 Blockade as Therapy for SIV/AIDS     | 26 rhesus macaques |
| 260-2007Y  | PD-1 Ligand Blockade as a Therapy for SIV | 22 rhesus macaques |

# Physical Restraint, Exemptions from Social Housing, and Food or Water Restriction of Nonhuman Primates

Nonhuman primates used under these conditions are in motion disorder studies or studies of brain function. Most of the animals are used to research the cause and treatment of Parkinson's Disease (PD) because of the great similarity of brain function and that Parkinson's-like disease can be induced in them by giving the neurotoxic chemical – MPTP. Monkeys in these studies usually are given MPTP by intracarotid injection, so that only one side of the brain is affected. These monkeys have only slight deficits in precise control of movements on one side of the body and have no substantial movement problems. In general, isolation housing is only done for a 3 day period immediately after administration of MPTP during the time of excretion of the neurotoxin in the feces and urine. Otherwise, monkeys in these studies are housed within sight and sound of other animals of the species and permitting physical contact with a compatible conspecific.

Monkeys in studies requiring food or water restriction are provided *ad libitum* food and water on weekends according to standard husbandry practices. During weekdays, food or water is restricted overnight and in the morning (12-15 hours total) and then food or water is provided to satiety during morning or afternoon test sessions as an inducement to perform video-based tasks. Single housing is necessary to facilitate food or water restriction — otherwise a conspecific would be subjected to unnecessary restriction or food sharing might occur. Monkeys are trained using food or water as an inducement to perform simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. These monkeys, except as indicated, are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory. During these periods, the monkeys with head appliances may also undergo short-term fixed head

restraint to access the appliances for neurophysiologic recording and microdialysis. Water or food is provided during and immediately after the testing session to meet the daily ration. The total intake of the restricted material, food or water, is recorded daily and the animal's body weight is checked and recorded at least twice weekly to ensure that are being well maintained.

In eye movement studies, animals must be awake, alert and comfortably seated. The tasks involve following a smoothly moving or jumping target spot that is rear-projected on a tangent screen. First the animals are fitted with a collar that it will always wear. It is made of a soft nylon material. Animals are then adapted to pole handling and using a primate chair. It takes most animals 4 weeks to reach proficiency. Animals are trained 5 days per week for time periods of 15 minutes to 3 hours.

A study to develop a transgenic model of Huntington's Disease uses the primate chair during semen collections and, again, during cognitive testing procedures for offspring produced. In these tests, the monkeys are habituated to the use of a chair over a one to two week period before performing the task for preferential looking while sitting with free movement of arms and legs.

In cocaine abuse studies, cocaine is scheduled as the consequent event and is sufficiently reinforcing that food and water restrictions are not necessary. However, for self-administration experiments, subjects are trained to sit quietly in standard primate chairs over a 2-4 week period. The pole-and-collar system for handling and training nonhuman primates will facilitate immobilization. Initially, subjects will be immobilized for approximately 20-30 minutes per training session, but over the course of several weeks, the amount of time will increase to from 1 to 4 hours per session. Each subject will be immobilized at least twice per week for 6 weeks. In a related study, changes in sensitivity to the CNS effects of cocaine are assessed after the monoamine neurotransmitter is manipulated pharmacologically. The animals are trained to be seated in a loosely fitting chair during daily (Mon. – Fri.) sessions. The chair is designed to provide minimal skin contact with the animal, and is limited primarily to the waist and buttocks. Typically, experiments are conducted so as to require no more than one hour per day in the apparatus. This minimal restraint provides protection of indwelling catheters used for drug administration and contact with a localized area of the tail for electrical stimulation.

Startle reflex testing is done in one study after each monkey is habituated to chair restraint. The sessions are 2-3 times per week for 60 minutes each session. The tests continue for 2 weeks. These tests may be repeated every 3-4 months to monitor potential developmental changes in emotionality.

Some of the animals used under these conditions are in oculomotor, visual disorders, and visual cortex studies. Monkeys are used because they are capable of the same range of eye movements as humans. Infant monkeys are swaddled in a blanket. Older animals have a chair adjusted for comfort. The chair includes a standard design that allows the animal to sit in a natural position. The animal is allowed to sit in the chair for 5-15 minutes on the first occasion, during which time treats (apple slices, applesauce, etc) are offered to make the chair session a positive experience. Head movements in the animals during visual testing are restricted by an implanted stainless steel receptacle (SSR) on the head. In other studies, head movement is restricted with a custom-fit helmet.

In these studies with transiently-induced movement disorders or studies of midbrain function, monkeys are trained to do simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. During these tasks, these monkeys are loosely restrained in

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> our rhesus monkeys, reduce the numbers of euthanasia due to these conditions, and improve animal welfare.

| Protocol # | Title   | # Species         |
|------------|---|-------------------|
| 067-2008Y  | Does CRH Receptor Antagonism Reduce Self-<br>Injurious Behavior and Improve Gastrointestinal<br>Health in Rhesus Macaques | 3 rhesus macaques |

I. Studies of pancreas, kidney, and bone marrow transplants as well as arterial grafts are investigating the ability of costimulation blockade to protect the organs from rejection. For experiments involving bone marrow transplantation, single housing is required for the first 75-100 days following the transplant due to the potential complications including immunosuppression, anemia, leukopenia and thrombocytopenia. After that time, the animals may be paired with same sex and age animals. In the pancreatic islet cell transplant model, daily monitoring of urine and stool output are necessary to diagnose steatorrhea, polyuria and ketoacidosis. In addition, pancreatic enzyme replacement and Rapamycin are administered orally in a treat and it is essential that the amount consumed by each animal is recorded. Following renal transplantation, animals will require protected housing so that an accurate assessment of daily food/water intake and urine/feces production be accounted. Prior to surgery, animals may be pair-housed. With immunosuppressive therapy, healing can be delayed. A study using nonhuman (mouse) stem cells involves inoculation of the cells in the nonhuman primate model to evaluate survival of the cells and effects on the recipients.

| Protocol # | Title   | # Species          |
|------------|---|--------------------|
| 005-2008Y  | Transplant Tolerance in Nonhuman Primates   | 82 rhesus macaques |
| 098-2008Y  | Pre-Clinical Non-human Primate Islet Allotransplantation Model for Tolerance Induction Testing with CTLA-4-Ig (Abatacept), LFA-3-Ig (Alefacept), and Sirolimus; Improving the Efficacy of Costimulation Blockade by Targeting T Cell Memory | 3 rhesus macaques  |
| 192-2007Y  | Creating a non-human primate model of graft-versus host<br>disease: Determining Mechanism and Assessing Novel<br>Therapeutics   | 17 rhesus macaques |
| 240-2008Y  | Immune Function and Biodefense in Children, Elderly and Immunocompromised Populations: Project 3  | 29 rhesus macaques |
| 208-2007Y  | Non-human Primate Renal Transplantation as a<br>Preclinical Model for Testing Genzyme 29155 for<br>Allospecific Tolerance Induction   | 20 rhesus macaques |

J. The following project investigates the alterations in behavioral, neuroendocrine and neuroanatomical development of rhesus macaque infants who are physically abused (examples of abuse: infant dragging, throwing) or neglected by their mothers, from birth through adulthood. Specifically, we intend to investigate possible long-term changes in social behavior, emotional regulation and reactivity to stress induced by early abuse and the neural and neuroendocrine mechanisms underlying these changes. Because infant abuse in monkeys and humans share several important characteristics, this study could enhance our understanding of the consequences of child abuse as well as make an important contribution to the prevention and treatment of this phenomenon.

Protocol# Title # Species 107-2007Y Developmental Consequences of Infant Abuse in 39 rhesus macaques Primates NOV 9 6 2008 stainless-steel receptacle is implanted. It is sometimes necessary to house animals in protected housing when they have surgical implants. This is to protect the animal from any injury due to aggressive behavior of other animals. Animals also sometimes wear goggles which may be removed during paired housing.

| Protocol# | Title  | # Species          |
|-----------|--|--------------------|
| 173-2008Y | Neural Control of Visual Vestibular Behavior   | 4 rhesus macaques  |
| 195-2008Y | Visual Processing and Smooth Eye Movements & Novel Immunotoxin and IGF Therapy for Strabismus    | 18 rhesus macaques |
| 264-2007Y | Binocular Coordination of Eye Movements; Surgical<br>Treatment of Strabismus in Juvenile Monkeys | 11 rhesus macaques |

G. Neuroreceptor imaging studies in postpartum women have provided preliminary support for several mechanisms that may contribute to the maternal behavior and mood changes observed in postpartum depression. First, based on neuroimaging studies there are significant alterations in serotonin-1A (5HT1A) receptor binding in limbic regions of the brain involved in emotionality and in dopamine-2 (D2) receptor binding in striatal regions of the brain associated with emotion and reward in healthy control postpartum relative to healthy control non-postpartum women. These results converge with animal models to suggest a process of perinatal neuroplasticity in the service of maternal behavior that occurs in recently delivered mothers compared to non-postpartum women. Second, postpartum depressed women had significant 5HT1A and D2 receptor binding alterations relative to postpartum healthy control women. These changes are consistent with the literature that describes monoamine deficits in major depressive disorder, anxiety disorders, and social stress. These cumulative findings suggest three potential mechanisms of perinatal mood disorder: pre-existing neurobiological vulnerability to mood disorder that persists perinatally, a failure of optimal perinatal neuroplasticity in susceptible women, or both processes.

Peripartum rhesus monkeys represent an ideal model to begin to better understand how changes in monoamine systems emerge during pregnancy that may predict what females may be more likely to exhibit PPD symptomatology. This proposal represents a pilot study to show the feasibility of using microPET neuroimaging to quantify changes in 5HT1A and D2 receptor binding during late pregnancy and the early post partum period.

| Protocol # | Title                                     | # Species            |
|------------|---|----------------------|
| 062-2008Y  | Peripartum Changes in Monoamine Activity  | 2 rhesus macaques    |
| 139-2005Y  | Genetics of Neuropathogenic SIV Infection | 6 pigtailed macaques |

H. Evaluates the efficacy of a corticotropin releasing hormone type 1 (CRH<sub>1</sub>) receptor antagonist in reducing chronic diarrhea and self-injurious behavior (SIB) in captive housed rhesus macaques. Chronic diarrhea in the absence of identifiable pathogens and SIB are two of the most troublesome clinical conditions in rhesus monkeys housed in biomedical research facilities, for which current treatment methods are often ineffective. Chronic exposure to psychosocial stress is thought to play a role in these conditions. Emerging data indicate that corticotropin releasing hormone (CRH) mediates stress-induced anxiety and depression, and that these emotional problems are corrected by treatment with specific CRH<sub>1</sub> receptor antagonists. Furthermore, this treatment also attenuates stress-induced gut motility and the incidence of diarrhea. We aim to determine whether treatment with a CRH<sub>1</sub> receptor antagonist can ameliorate chronic diarrhea in the absence of enteric pathogens and/or reduce SIB in rhesus macaques.
Data obtained from this study has the potential to greatly impact the clinical health of

that occur. Single cage housing will be required for post surgical events until healing has occurred. Implants may require single cage housing to prevent damage to implants in incompatible animals.

One of the primary brain structures coordinating emotional responses is the amygdala. Much of our understanding of how the amygdala coordinates our behavior has come from whole animal research. However, the amygdala is not a simple structure in that it consists of at least 15 subdivisions, and contains at least 5 types of neurons. If we are to understand how the amygdala helps to coordinate our behavior, we must first understand the functional properties of the individual subdivisions and the properties of the neurons contained therein. Despite the importance of the amygdala as a structure, there is still relatively little information available concerning the properties of amygdala neurons. It is now possible to keep thin sections of the brain "alive" for several hours in an artificial environment. This "slice" preparation gives us direct access to the individual neurons from which we can record their electrical activity in response to drug application. Moreover, by stimulating input pathways to these neurons we can begin to construct a

simple model of how the neurons in the amyodala may be connected.

| Protocol #         | Title  | # Species                                  |
|--------------------|--|--|
| 012-2008Y          | Transitional States of Drug Addiction in Non-human Primates  | 16 rhesus macaques                         |
| 076-2007Y          | Development of Reversible Inactivation Technique<br>for the Study of Higher Cognitive Functions in<br>monkeys                          | 2 rhesus macaques                          |
| 079-200 <b>7</b> Y | PET Neuroimaging and Cocaine Neuropharmacology in Monkeys; PET in conscious monkeys  | 39 rhesus macaques                         |
| 203-2007Y          | Development of a Monkey Dystonia Model   | 3 rhesus macaques                          |
| 249-2005Y          | Cocaine use and Monoamine Function in Nonhuman Primates  | 44 squirrel monkeys                        |
| 254-2007Y          | Studies of the natural SIV infection of sooty mangabeys  | 2 sooty mangabeys and<br>5 rhesus macaques |
| 139-2005Y          | Genetics of Neuropathogenic SIV Infection  | 6 pigtailed macaques                       |
| 224-2007Y          | Modulating HIV Immunity with Dendritic Cells   | 52 rhesus macaques                         |
| 102-2006Y          | Functional Neuroanatomy of the Basolateral<br>Amygdala   | 3 rhesus macaques                          |
| 112-2007Y          | Orbitofrontal-limbic ontogeny and early dysfunction;<br>The integration of multisensory social cues and its<br>neural basis in monkeys | 18 rhesus macaques                         |
| 163-2007Y          | Imaging Estrogen Receptors with PET  | 4 rhesus macaques                          |
| 126-2008Y          | Analysis of the Neuronal Microcircuitry of the Basal<br>Ganglia  | 2 rhesus macaques                          |

F. Visual, vestibular and oculomotor systems must work together for normal visual function. Various disease processes or injuries can compromise the normal interaction of these systems. Research in this area will provide a basic science foundation for understanding eye movement control in humans. Primates are used since they exhibit the same set of eye movements as humans. To facilitate the research, sclera search-coils are implanted to precisely measure eye movement. In addition, head movements need to be restricted during visual testing to allow accurate tracking of visual targets. Therefore, a

| 031-2006Y | Maintenance of Yerkes Primate Center Animal<br>Colony                 | 148 rhesus macaques |
|-----------|---|---------------------|
| 142-2007Y | Project 3: Attenuated Listeria Vectors as an AIDS Vaccine in Macaques | 10 rhesus macaques  |
| 177-2006Y | Poxvirus Immunity and DNA/MVA HIV Vaccines                            | 4 rhesus macaques   |
| 077-2007Y | Therapeutic DNA/MVA Vaccines for HIV                                  | 18 rhesus macaques  |
| 176-2007Y | Determinants of Vaccine-Induced Memory T-Cell Development             | 24 rhesus macaques  |
| 224-2007Y | Modulating HIV Immunity with Dendritic Cells                          | 52 rhesus macaques  |
| 062-2007Y | Virus Turnover and T Cell Responses During SIV<br>Infection           | 10 rhesus macaques  |

D. Studies of dose and delivery vehicle in non-human primates have become a critical step to prepare for human clinical trials in lumbar fusion studies. Spine fusion surgery will be performed on animals followed by administration of different bone growth factors. Then animals will be in protected contact housing to prevent possible trauma to the surgical wound.

| Protocol # | Title  | # Species         |
|------------|--|-------------------|
| 069-2007Y  | Use of Osteoinductive Factors (BMP) to Enhance<br>Spine Fusion | 9 rhesus macaques |

E. The integration of functional MRI (fMRI) technology with proven utility will significantly advance research efforts in biomedical and behavioral sciences. One proposal is directed towards brain activation studies during cocaine use. This may help to determine the brain structures and neural circuits that underlie the addictive properties of cocaine. In studies on cocaine and drug abuse, animals will be used for pharmacological and neurochemistry experiments involving the placement of an indwelling venous catheter for drug delivery during daily sessions lasting 1-2 hours. Some animals also have in dwelling guide cannulae. The catheters and guide cannulae must be protected from contact by other animals. If contact is allowed, the preparations can be compromised with the risk of physical injury and infection. Protected contact housing reduces the risk since both animals can control proximity to others. The animals may require single housing if they persistently place themselves at risk to damage their indwelling venous catheters or guide cannulae, or that demonstrate a proclivity to damage another animal's catheter.

Determining the relationship between prefrontal cortical circuitry and components of dopaminergic neurotransmission is the focus of one research study that will enhance understanding of the cognitive processes subserved by the prefrontal cortex. This will hopefully shed light on human disease states, notably schizophrenia. In order to identify particular neural connections in the prefrontal cortex of macaques, axonal tracers will be injected intracerebrally. Following stereotaxic surgery, craniotomies will be made over the prefrontal cortex. Subjects must be in protected contact housing to protect craniotomy sites and sutures.

Assessment of specific roles of separate neuronal structures are performed on monkeys to evaluate the brain's response to damage at different ages. Studies will provide detailed descriptions of loss of memory functions, and other developmental disorders

population. Following blood collections and treatment of the malaria infection, the animals are returned to their normal housing environment. Protected-contact housing is utilized in other malaria vaccine studies in monkeys due to the requirement of daily heel or ear sticks (as well as blood collection and immunization), as well to avoid frequent reunions following stressful procedures. During the period to evaluate viral load and safety testing of gene therapy in a hepatitis C study, it is necessary to maintain the animals in metabolism cages. This is due to frequent blood collections and surgical interventions during the initial 4—6 weeks on study.

Dengue is one of the most important mosquito-borne viral diseases affecting humans, with over half of the world's population living in Dengue endemic areas. A wide spectrum of clinical manifestations has been noted which range from asymptomatic, mild febrile (dengue fever, DF) to dengue hemorrhagic fever (DHF)/dengue shock syndrome (DSS), and a severe form associated with a life-threatening illness. The incidence rate of the latter disease form is 1-5% and predominantly occurs in children under the age of 15. The pathological hallmarks that determine disease severity and distinguish DHF from DF and other viral hemorrhagic fevers are plasma leakage resulting from increased vascular permeability and abnormal blood clotting.

The objectives of this pilot proposal are to generate sufficient data to further pursue for the more completed underlying mechanisms triggering DHF/DSS and to better define and understand the initial target cells infected by dengue virus, which may correlate with hematopoietic suppression. The proposed study, therefore, may potentially provide a new insight and shed a new light on human immunology in response to dengue virus infection.

| Protocol # | Title  | # Species                             |
|------------|--|---------------------------------------|
| 013-2008Y  | Evaluation of infection, viral dissemination and immune responses to the gamma human retrovirus XMRV in rhesus macaques  | 3 rhesus macaques                     |
| 088-2007Y  | Evaluation of anti-HIV Interventions for the prevention of SHIV Transmission in Pig-tailed Macaques  | 28 pigtail macaques                   |
| 198-2008Y  | Non-human Primate Models of Malarial Anemia  | 18 rhesus macaques                    |
| 247-2007Y  | Early Innate Immune Response in Dengue Virus Infection   | 3 rhesus macaques                     |
| 142-2008Y  | Innate Immunity and affects of Macrophage Depletion in SIV-Infected Non-Human Primates   | 3 rhesus macaques                     |
| 256-2008Y  | Molecular Evolution of Multiply Deleted SIV in Vivo  | 23 rhesus macaques                    |
| 261-2008Y  | Vaccination Against mucosal HIV Clade C<br>Transmission  | 71 rhesus macaques                    |
| 010-2006Y  | Infant Immunoprophylaxis Against a Primate Lentivirus  | 21 rhesus macaques                    |
| 061-2007Y  | SHIV Transmission Through Oral versus Other<br>Mucosae   | 22 rhesus macaques                    |
| 030-2007Y  | Role of virus specific immunity in primate AIDS;<br>CD4 T cell activation in SIV+ disease resistant<br>mangabeys; Role of CTL in indian macaques with<br>live attenuated deglycoslated SIV | 6 mangabeys and<br>20 rhesus macaques |
| 259-2007Y  | Molecular Analysis of Antigenic Variation in Malaria   | 18 rhesus macaques                    |

| 081-2007Y | Regulation of Motor Function in Parkinson's Disease:<br>Effects of Cannabinoid Antagonists in the MPTP<br>Primate Model of Parkinson's Disease | 8 rhesus macaques                      |
|-----------|--|--|
| 094-2007Y | Neuropsychology of Primate Social Cognition  | 8 rhesus macaques and<br>10 chimpanzee |

B. In the study of Alzheimer-like disease, animal will be studied following injections of lentiviral constructs in the brain following craniotomy. The safety and efficacy of immunizations also will be evaluated. Single or protected contact housing is required after surgery for 6 to 16 weeks to evaluate behavior or other clinical complications.

| Protocol # | Title   | # Species          |
|------------|---|--------------------|
| 066-2007Y  | Alzheimers Immunotherapy in Primate Model of<br>Cerebral Amyloid Angiopathy                                   | 7 squirrel monkeys |
| 255-2008Y  | Focal Alzheimer transgene expression in rhesus monkeys  | 4 rhesus macaques  |
| 068-2007Y  | Relationship between Serum and CSF Drug Levels<br>and Central D2 Occupancy for Two Atypical<br>Antipsychotics | 5 rhesus macaques  |

C. Infectious disease vaccine development studies may require single housing to prevent disease agent transmission. Some of the studies described here involve the development of a SIV/HIV vaccine, investigation of the role of host immune response in protecting against or contributing to the appearance of immune system damage following AIDS infection, evaluation of the function of the thymus during infection with SIV, evaluation of the development and pathogenicity of mutant viruses that develop over time in chronically infected animals, the effect of opiate dependency on the progression of AIDS, and the testing of the immunogenicity and efficacy of different AIDS vaccines and treatment regimens. Single housing is required after exposure to the virus to prevent transmission of virus from animal to animal. In addition, the animals need to be accessed frequently for blood draws. The experimental design requires that the efficacy of vaccines will be assessed after a single exposure and without the possible confound of exposure to mutant viruses. Infected animals in an experimental group will be housed together after approximately one month. In some experiments, animals are singly housed one month prior to inoculation to allow sufficient time for acclimatization to the new housing arrangement so that the stress of separation doesn't influence susceptibility to or course of infection.

A study testing the effects of T cell depleting antibodies in SIV-infected mangabeys requires frequent antibody infusions and blood draws during the first 3 weeks of the treatment (animals are assessed up to 4 times per week), followed by weekly blood draws for the remainder of the study, which lasts 2 months. Because these animals will be frequently handled for testing, animals are housed in protected contact housing.

Malaria studies are being done to develop a vaccine and to provide antigens for serologic and molecular studies, genomic libraries, antibody production, and gametocytes for infection of mosquitoes. Chimpanzees infected with malaria are housed individually in metabolism cages. This is usually required for a period of 1-2 months. It is also necessary to house the animals indoors to prevent contact with the local mosquito

### **Exceptions to Regulations and Standards**

Physical Restraint and Exemptions from Social Enrichment for Nonhuman Primates: Social Isolation

There are a variety of human diseases (Parkinson's Disease, Huntington's Disease, progressive supranuclear palsy, narcolepsy, and periodic leg movements during sleep) that are associated with uncontrolled movements in sleep that cause injury. Studies described here are on monkeys with Parkinsonism induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Monkeys given MPTP are kept in social isolation for periods of three days after drug administration while MPTP and its toxic metabolites are excreted. On a scheduled basis afterwards, these animals are placed in a cage specially designed for behavioral testing and telemetric recording in a room separated from the other monkeys. Individual monkeys may be maintained in the observation and recording room for a maximum of 14 days and are then returned to their home cage in a colony with other monkeys of the same species for at least 7 days before repetition. Isolation from other monkeys is necessary in order to permit sleep undisturbed by commotion caused by other monkeys or human traffic in and out of the room. Monkeys under study are instrumented with backpack transmitters which telemeter their EEG, EOG and EMG signals. This telemetric approach allows studying sleep behavior in monkeys that are unrestrained. In addition, physical restraint in a chair is done up to 8 times per month for 6-10 hours per session. This is done either to facilitate brain mapping, intracerebral recording, and neurochemical microdialysis or for fearpotential startle testing.

Protocol # Title # Species

072-2008 Modulation of the sleep/wake state by dopamine 5 rhesus monkeys.

182-2006 Cytokine-induced depression: A rhesus monkey model 12 rhesus monkeys

Exemptions from Social Enrichment for Nonhuman Primates: Social Isolation

The male capuchin monkeys on census have repeatedly injured each other when paired or given protected contact housing opportunities. For their safety and well-being, they have been exempted from social housing. These animals are no longer used experimentally and are awaiting donation to a sanctuary.

| Protocol # | Title  | # Species          |
|------------|--|--------------------|
| 072-2008   | Modulation of the sleep/wake state by dopamine | 2 capuchin monkeys |

Physical Restraint of Swine

Pigs are used in studies of reperfusion injury – that injury to the myocardium that occurs in patients after the blockage of a coronary artery is relieved and blood flow to poorly perfused tissue is restored. At one week following surgical implantation of an occluding device on the left anterior descending coronary artery, pigs are sedated with midzolam, provided intravenous fluids, and restrained in a porcine sling. The occluder is inflated to obstruct coronary artery blood flow for one hour simulating a myocardial infarction and microspheres are injected at the beginning and end of the procedure. The occluder is then deflated and the heart reperfused with or without pharmacologic intervention and the pig is removed from the sling and recovered from sedation.

| Protocol # | Title   | # Species |
|------------|---|-----------|
| 225-2006   | Consortium to investigate myocardial protection strategies to reduce infarct size | 8 swine   |

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#### Physical Restraint of Sheep

Sheep are used in studies of the effect of gene therapy or pharmacologic agents (including inhaled) upon the pulmonary epithelium and general physiology. These studies are intended to better understand the pathophysiology and improvement treatment of conditions such as pulmonary hypertension, acute lung injury, and ARDS. In the conduct of the research procedures, sheep are loosely restrained in small ruminant stanchions for up to five hours to enable hemodynamic and pulmonary physiology measurements while under continuous observation.

| Protocol # | Title                                     | # Species |  |
|------------|---|-----------|--|
| 080-2007   | C/EBPbeta regulation of lung inflammation | 10 sheep  |  |

Physical Restraint and Exemptions from Social Enrichment for Nonhuman Primates: Single-housing In Sight and Sound of Conspecifics:

Included in this section are primates that were housed in any condition other than group or pair housing for any significant period of time. For example, study subjects discussed below include those that were housed continuously in protected-contact housing, and those housed in protected-contact and/or group or pair housing for a significant portion, but not the entirety, of the period covered in this report.

A. Some animals used under these conditions are in studies of normal control of movement or motion disorders induced by MPTP. Monkeys given MPTP may be kept in social isolation for periods of three days after drug administration and while MPTP and its toxic metabolites are excreted. Before and after MPTP administration, monkeys in these studies are trained to do simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. During these tasks, these monkeys are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory. During these periods, monkeys with head appliances may also undergo short-term fixed head restraint to access the appliances for neurophysiologic recording and microdialysis. Additionally, the administration of the neurotoxin MPTP to induce Parkinson's Disease (PD) in macaques causes physical impairments that put such animals at risk of plummeting in the social order and wounding and fight injury from a cage mate. Consequently, animals given MPTP are generally housed singly, but in colony rooms within sight, sound and close physical proximity of other animals of the same species. Likewise, to prevent damage to expensive and sensitive surgically-implanted devices by a conspecific, monkeys may be housed singly, but otherwise within sight and sound of conspecifics.

Species Protocol# Title 2 rhesus macaques Analysis of the Neuronal Microcircuitry of the Basal 126-2008Y 4 rhesus macaques Glutamate and GABA Related Therapies in 037-2005Y Parkinson's Disease 2 rhesus macaques Local Field Potentials in the Basal Ganglia 178-2008Y Glutamate receptors: Novel targets for Parkinson's 11 rhesus macaques 112-2006Y Disease Therapy The Thalamostrital System as a Target for Tourette's 2 rhesus macaques 213-2006Y Syndrome Function of Dopamine in the Primate Substantia nigra 2 rhesus macaques 217-2006Y 212-2006Y GABA-B Receptors and Parkinson's Disease 1 rhesus macaque

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depression and aspiration. The 12 animals reported with this study were carried-over from the 2007 census and do not represent new acquisitions.

| Protocol # | Title  | # Species          |
|------------|--|--------------------|
| 182-2006   | Cytokine-Induced Depression: A Rhesus Monkey Model | 12 Rhesus Macaques |

Inflammatory diseases of the lung cause respiratory dysfunction, may involve infectious agents and often with a septic component, and may cause high mortality. To simulate sepsis and associated pulmonary pathology in a controlled and self-limiting fashion, sheep are administered endotoxin by intravenous injection. The host response to the endotoxin elicits a cascade of events resulting in hypoxemia, pulmonary hypertension, pulmonary inflammation and edema, and respiratory distress lasting for several hours. Additionally, sheep experience transient fever, malaise and other flu-like symptoms lasting 12-15 hours before restoration to normal health. The administration of pain relieving agents, both narcotics and nonsteroidal anti-inflammatory drugs, may alter inflammatory effect, immune response and, if tranquilizing, respiratory function. Such would confound the interpretation of scientific data making the use of anesthetics, analgesics or tranquilizers contraindicated in the model. All 10 of these sheep were new acquisitions.

| Protocol # | Title                                     | # Species |  |
|------------|---|-----------|--|
| 080-2007   | C/EBPbeta regulation of lung inflammation | 10 Sheep  |  |

Infection with the arenavirus of Lassa fever causes a potentially lethal human hemorrhagic disease where it is endemic in West Africa. Unlike Lassa fever, the infection of guinea pigs with the related Pichinde arenavirus does not pose a human health hazard, but is an important model in the study of the pathogenesis and possible treatments or vaccines for diseases caused by arenaviruses. Guinea pigs infected with Pichinde virus develop Lassa fever-like symptoms of fever progressing to hypothermia and weight loss. The regular administration of pain-relieving drugs during the clinical course might inhibit fever (nonsteroidal inflammatory agents) and can alter immune function (opioids) and their use is contraindicated in this model. Instead, the guinea pigs are humanely euthanatized when they show a combination of weight loss and hypothermia or any signs of hemorrhage, dyspnea, or distress.

| Protocol # | Title  | # Species      |
|------------|--|----------------|
| 204-2007   | Pichinde virus infection of guinea pigs as an animal model for Lassa fever | 88 guinea pigs |

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FORM APPROVED OMB NO. 0579-0036

U.S DEPARTMENT OF AGRICULTURE ANIMAL AND PLANT HEALTH INSPECTION SERVICE

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| X Award X Contract X Grant Loan   | Individual  |
| 9. IF INDIVIDUAL, IDENTIFY EACH OWNER, IF PARTNERSHIP IDENTIFY EACH<br>FOR RESEARCH FACILITIES INCLUDE THE INSTIT | PARTNER OR OFFICER, IF CORPORATION, IDENTIFY PRINCIPAL OFFICERS UTIONAL OFFICIAL (Use separate sheet if needed)                 |
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|   | ICATION er under the Animal Welfare Act 7 U.S.C. 2131 et seq. I certify that the information                                    |

provided herein is true and correct to the best of my knowledge. I hereby acknowledge receipt of and agree to comply with all the regulations and standards in CFR, Subpart A, Parts 1, 2 and 3. I certify that all listed persons are 18 years of age or older.

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920 Main Campus Drive Suite 200 Raleigh, NC 27606

Tel No. 919-855-7100 Fax No. 919-855-7123 March 24, 2009

The following protocols were reviewed because they involve exceptions to the standards and the description of the protocols was not clear on the 2008 annual report. All of the protocols in question have an exception request found under the primary heading "Physical restraint and Exemptions from Social Enrichment for Non Human Primates: Single Housing in Sight and Sound of Conspecifics" which starts on page 2 of the document. Sections A-K(pages 2-9) all fall under this heading.

Protocol 247-2007Y

Early Innate Immune Response in Dengue Virus Infection

A review of this protocol revealed that originally three rhesus would be used in the study. An approved modification requested three more rhesus due to an unexpected but localized skin coagulopathy developing in the original three animals. It was determined that the exception involved social housing/enrichment. Since the study involves three animals, one animal would need to be singly housed and not in a social group or paired housing. On my visit there for inspection, I did observe a singly housed rhesus in the dengue lab. The staff had placed a large mirror across from the animal so that it could see its reflection and it was on an enrichment schedule.

Protocol 107-2007Y
Developmental Consequences of Infant Abuse in Primates

A review of this protocol revealed that the infant rhesus involved are the offspring of mothers who are less than attentive. The exception requested is for social housing and enrichment. The infants may need to be separated from the mothers if the mother becomes too abusive and/or the life of the infant becomes threatened.

Protocol 198-2008Y
Non human Primate Models of Malarial Anemia

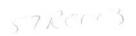
A review of this protocol revealed that a total of 30 rhesus macaques per year would be used for a total of 90 animals, not chimps as stated in the annual report. The exception requested is for social housing and enrichment. The animals will need to be singly housed or in protected contact housing.

Tami L Howard, DVM



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| 75 Y         |   |  |      |  |
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July 30, 2009

Elizabeth Goldentyer, DVM USDA-APHIS 920 Main Campus Drive Suite 200, Unit 3040 Raleigh, NC 27606

RE: 2008 Annual Report - Facility 57-R-0003

Dear Dr. Goldentyer:

Emory University submitted their 2008 USDA annual report on November 25, 2008. Attached are revised pages of the 2008 annual report that rectify several errors listed in the version originally submitted. The changes are in the text on page 3, the top of page 4, and at the top of page 11. We have included red-lined versions of the pages, as well as clean copies. The first error involves a protocol that was included in the report in error. The second error was brought to our attention by Dr. Tami Howard with the USDA, and we have corrected it in this revised version. The third change is editorial as to spacing of a sentence. We respectfully request that these pages replace the similarly numbered pages from our 2008 USDA annual report.

We understand that the USDA may be placing the Annual Reports from registered research facilities on the USDA Freedom of Information Act Web Page. We also request that the clean copy version of the corrected pages be used when this information is posted on the web. We appreciate your cooperation in these matters.

Sincerely,

(b)(6), (b)(7)c

JY'

JUN 0 1 2009

### DEPARTMENT OF HEALTH & HUMAN SERVICES



PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:
Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive - MSC 7982
Bethesda, Maryland 20892-7982
Home Page: http://grants.nih.gov/grants/olaw/olaw.htm

FOR EXPRESS MAIL:
Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 402-2803

May 26, 2009

(b)(6), (b)(7)c

Emory University
(b)(2)High, (b)(7)f
Atlanta, GA 30322

Dear (b)(6), (b)(7)c

On behalf of the Office of Laboratory Animal Welfare (OLAW), I would like to thank you and your staff for the hospitality extended to me and Ms. Eileen Morgan during our May 19, 2009 mutual site visit conducted with USDA representatives at Emory University/Yerkes National Primate Research Center (EU/YNPRC). We appreciated personally meeting with you, Dr. James Else, Dr. Sam Speck, David Knight, Dr. Stuart Zola, Casey Brinsfield, Dr. Joyce Cohen, Dr. Mark Wilson, Mark Sharpless, Dr. Mollie Bloomsmith, Dr. Elizabeth Strobert, Sunday Buge, Rachel Fest, Dr. Michael Huerkamp, Dr. Deborah Mook, Dr. Douglas Taylor, Dr. Ben Basile, Dr. Lisa Parr, and the other members of the investigative and animal program staff who explained their research activities and showed us around the facilities.

Our assessment of the EU/YNPRC is that of a well maintained facility housing healthy well kept chimpanzees and other nonhuman primates. We recognize the efforts of a dedicated competent staff and a knowledgeable and engaged veterinary staff operating an animal care and use program in compliance with the provisions of the PHS Policy on Humane Care and Use of Laboratory Animals. We found the Institutional Animal Care and Use Committee (IACUC) records, animal health records, standard operating procedures, and other documentation to be comprehensive and conveniently maintained in electronic format.

We found the Field Station demonstration of the clicker method to control and separate individual primates from the colony very impressive and effective. Also, we were pleased to see that the chimpanzees housed at the Field Station were able to exhibit natural behaviors by extracting food treats with sticks and that the animals appeared calm and well adjusted.

As noted in our discussions, the following items should be further addressed by the IACUC:

- Animal housing areas that are investigator maintained would benefit from additional post approval monitoring by the IACUC, veterinary staff, and compliance staff.
- In addition to the description in the protocol, training of nonhuman primates to pole and collar restraint should be addressed by standard operating procedure and initial training and subsequent chairing of animals should be monitored by veterinarians and IACUC members.

- Cleaning and care of primate head caps needs to be adjusted to clinical presentation (i.e., animals
  exhibiting serosanguinous discharge require more frequent cleaning or other care).
- Additional efforts should be taken to pair or group house as many primates as possible when not contraindicated by IACUC approved scientific justification or for clinical or behavioral reasons. Animals that cannot be socially housed due to concerns of contagion during portions of a study should be separated only during times when scientifically necessary. The animal records are to clearly reflect the clinical or behavioral reasons for exemption from social housing.

Please update OLAW in the next Annual Report on the status of the items noted above.

Finally, we would like to commend you as Institutional Official on your personal involvement in and commitment to the success of the animal care and use program and in establishing an overall culture of compliance.

Sincerely,

Axel Wolff, M.S., D.V.M.

Director

Division of Compliance Oversight

axel Way, ms, a

Sincerely,

Eileen M. Morgan

Director

Division of Assurances

cc:

(b)(6), (b)(7)c

Elizabeth Goldentyer, D.V.M., Director Eastern Sector, USDA-APHIS-AC

| SENDER: COMPLETE THIS SECTION  | COMPLETE THIS SECTION ON DELIVERY  |                    |  |  |
|--|--|--------------------|--|--|
| <ul> <li>Complete items 1, 2, and 3. Also complete item 4 if Restricted Delivery is desired.</li> <li>Print your name and address on the reverse so that we see a true and address on the reverse</li> </ul> | A. Signature   | ☐ Agent ☐ Addresse |  |  |
| so that we can return the card to you.  Attach this card to the back of the mailpiece, or on the front if space permits.   | B. Received by ( Printed Name)   | C. Date of Deliver |  |  |
| 1. Article Addressed to:  Emory University  (b)(2)High, (b)(7)f  | D. Is delivery address different from item 1? Yes If YES, enter delivery address below: No  SEP 0 8 2008 |                    |  |  |
| Atlanta, GA 30322  | 3. Service Apel NIVERSITY MAI  Certified Mail  | L SERVICES         |  |  |
|  | 4. Restricted Delivery? (Extra Fee)  | ☐ Yes              |  |  |
| 2. Article Number (Transfer from service label) 7008 1300  | 0001 2214 8203   |                    |  |  |



**United States** Department of Agriculture

January 22, 2008

Marketing and Regulatory **Programs** 

**Emory University** 

**Animal and Plant Health Inspection**  Pffoce of Research Administration

Services

Mailstop 1599/001/1BE 1599 Clifton Road NE Atlanta, GA 30322

(b)(6), (b)(7)c

Animal Care

920 Main Campus Drive Suite 200 Raleigh, NC 27606

Dear (b)(6), (b)(7)c

Tel No. 919-855-7100 Fax No. 919-855-7123 Thank you for your letters of January 4, 2008 reporting corrective action taken in connection with incidences of non compliance involving a ferret on September 17, 2007 and a rhesus macaque in June 2006 at Emory University. This information will be helpful to USDA, APHIS, Animal Care. Please convey our thanks to the IACUC and the Animal Care staff.

Sincerely,

Elizabeth Goldentyer, DVM Eastern Regional Director

Animal Care

Cc:

A. Bartholomew

G. Gaj

57-R-0003

Animal Care is a part of the Department of Agriculture's Animal and Plant Health Inspection Service

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An Equal Opportunity Provider and Employer



January 4, 2008

Elizabeth Goldentyer, D.V.M. USDA – APHIS 920 Main Campus Drive Suite 200, Unit 3040 Raleigh, NC 27606

Dear Dr. Goldentyer:

As Institutional Official for Emory University Institutional Animal Care and Use Committee (IACUC), and in accordance with applicable regulatory requirements, I am writing to update you regarding the anesthestic death of a rhesus macaque at the Yerkes National Primate Research Center (Yerkes) in June 2006. Following the recommendations of the Emory IACUC, Yerkes has implemented the following corrective procedures and new equipment.

- All anesthetic monitoring equipment in the MRI suite is located in the anteroom and color coded tubing transports the anesthetic gases from clearly labeled gas cylinders located in the hallway.
- An SOP for monitoring procedures and equipment use has been developed and is posted in the MRI prep room as a reference for all personnel responsible for anesthesia.
- Training has been and will continue to be conducted and documented for the personnel responsible for anesthesia in imaging procedures.
- Yerkes has instituted the use of electrocardiography during MRI procedures. Monitoring
  parameters and equipment that are available include: continuous monitoring of pulse rate, pulse
  oximetry, respiratory rate, respiratory wave form, body temperature, ECG, EtCO2, end-tidal gas
  anesthesia, non-invasive blood pressure and direct observation of the animal approximately
  every 30 minutes. All monitored parameters will be recorded at least every 15 minutes.
  Monitoring standards will be dependent on animal species, animal size, method of ventilation, or
  use of paralytic (neuromuscular blocking agent).
- Nonhuman primates and cats that receive a neuromuscular blocking agent will be monitored with all available parameters, as listed above. Particular attention will be given to the use of end-tidal anesthesia monitoring, as mandated by the IACUC Committee.

It is the opinion of the Emory IACUC that the corrective actions taken by Yerkes are appropriate and will prevent the reoccurrence of the events that occurred in June 2006. Please feel free to contact me or (b)(6), (b)(7)c if you would like further information regarding this matter.

Sincerely,

(b)(6), (b)(7)c



#### Office of Research Administration

January 4, 2008

Elizabeth Goldentyer, D.V.M. USDA – APHIS 920 Main Campus Drive Suite 200, Unit 3040 Raleigh, NC 27606

Dear Dr. Goldentyer:

As Institutional Official for Emory University Institutional Animal Care and Use Committee (IACUC), and in accordance with applicable regulatory requirements, I am writing to report certain protocol violations and the corrective action taken with regard to the following study.

Protocol Title: MRI of Animals (mice, rats, ferrets)

IACUC Protocol Number: 091-2007 Sponsor: Departmental Funds

Principal Investigator:

(b)(6), (b)(7)c

It was brought to the attention of the committee that there was a possible non-compliance issue associated with the above protocol. A subcommittee from the Emory IACUC and Georgia State University IACUC was formed to investigate this issue. The subcommittee found a significant deficiency in the animal care provided as part of (b)(6), (b)(7)c protocol whereby a scanning procedure was allowed to be performed with equipment that was known to be malfunctioning. As a result, a ferret scanned as part of a NSF funded study from Georgia State University received third degree burns to isolated abdominal regions(b)(6), (b)(7)©luntarily discontinued work pending the results of the IACUC's inquiry and satisfactory completion of the required corrective action.

The corrective action recommended by the IACUC and implemented b(b)(6), (b)(7) avolved additional training of the personnel involved in the imaging procedures and monitoring of the anesthesia during imaging. A new SOP and checklist was developed in conjunction with veterinarians from the Emory Division of Animal Resources to ensure that anesthesia will be performed and monitored properly by qualified individual (b)(6), (b)(7) also ordered and has in place a new heat pump and heating pads for maintaining the normal physiological parameters of the animals being studied.

It is the opinion of the Emory IACUC that the corrective actions taken in the above occurrence of non-compliance is appropriate and will prevent the reoccurrence of such activities by the investigators. Please feel free to contact me or (b)(6), (b)(7)c if you would like further information regarding this matter.

Sincerely,

(b)(6), (b)(7)c

CC:

(b)(6), (b)(7)c

Emory University Mailstop 1599/001/1BE 1599 Clifton Road NE, 4th Floor Atlanta, Georgia 30322

An equal opportunity, affirmative action university

Tel 404.727.3889 Fax 404.727.1094



OCT 2 0 2009

### United States Department of Agriculture Animal and Plant Health Inspection Service

cnichols 388306 insp\_id

### Inspection Report

**EMORY UNIVERSITY** 

Customer ID: 896

Certificate: 57-R-0003

Site: 003

YERKES REGIONAL PRIMATE RESEARCH CENTER

(b)(2)High, (b)(7)f

Type: ROUTINE INSPECTION

Date: Sep-17-2009

ATLANTA, GA 30322

Prepared By:

CHRISTOPHER E NICHOLS

USDA, APHIS, Animal Care

Date:

Title:

VETERINARY MEDICAL OFFICER Inspector 6007

Sep-17-2009

Received By:

(b)(6), (b)(7)c

Date:

Title:

Sep-17-2009

<sup>\*\*\*</sup> Focused inspection in response to complaint of animal death.

Reviewed documents: Internal memos and statements, employee training logs, corrective action documentation, IACUC Protocol for animal, IACUC meeting minutes regarding incident, OLAW Report.

<sup>\*\*\*</sup>No noncompliance items noted at the time of the documentation review or during the conclusion of this inspection



JUN 0 8 2009 140091524270230

insp\_id

### Inspection Report

**EMORY UNIVERSITY** 

Customer ID: 896

Certificate: 57-R-0003

(b)(2)High, (b)(7)f

Site: 001

(b)(2)High, (b)(7)f

Type: ROUTINE INSPECTION

Date: May-20-2009

ATLANTA, GA 30322

All items are in compliance at this inspection.

Inspection was conducted May 19-May 20, 2009. This inspection included all site 001 facilities and a review of IACUC records for all sites. The inspection and exit interview was conducted with the Director, Division of Animal Resources.

Records reviewed:

- 1) Medical records
- 2) Protocols(146-2007, 023-2009, 204-2007, 072-2008, 057-2007, 023-2007, 182-2006)
- 3)Current IACUC Roster
- 4)Standard Operating Procedures for regulated species
- 5)Post Approval Monitoring records for 204-2007
- 6)Semi-Annual Program Reviews and Facility Inspections
- 7)IACUC Meeting Minutes

This is an amended report for the inspection report # 140091500260248 of May 20, 2009.

Prepared By:

TAMI L HOWARD, D V M

USDA, APHIS, Animal Care

Date:

Title:

VETERINARY MEDICAL OFFICER Inspector 1065

May-20-2009

Received By:

(b)(6), (b)(7)c

Date:

Title:

May-20-2009

Page 1 of 1



JUN 0 8 2009 140091500260248 insp\_id

### Inspection Report

**EMORY UNIVERSITY** 

Customer ID: 896

Certificate: 57-R-0003

Site: 001

(b)(2)High, (b)(7)f

(b)(2)High, (b)(7)f

Type: ROUTINE INSPECTION

Date: May-20-2009

ATLANTA, GA 30322

All items are in compliance at this inspection.

The inspection and exit interview was conducted with the Director, Division of Animal Resources.

Prepared By:

USDA, APHIS, Animal Care

Date:

Title:

VETERINARY MEDICAL OFFICER Inspector 1065

May-20-2009

Received By:

(b)(6), (b)(7)c

Date:

Title:

May-20-2009

Page 1 of 1



78091704060399 insp\_id

### Inspection Report

EMORY UNIVERSITY

Customer ID: 896

Certificate: 57-R-0003

Site: 003

APR 0 6 2009

RECEIVED

(b)(2)High, (b)(7)f

YERKES REGIONAL PRIMATE

Type: ROUTINE INSPECTION

Date: Mar-17-2009

ATLANTA, GA 30322

3.84 (c)

CLEANING, SANITIZATION, HOUSEKEEPING, AND PEST CONTROL.

(c) Housekeeping for premises. Premises (buildings, equipment and grounds) must be kept clean and in good repair in order to protect the nonhuman primates from injury and to facilitate the husbandry practices required in this subpart.

In(b)(2)High, (b)(7)f there is an NHP refrigerator with a soiled bottom. Refrigerators used for non human primate food or drugs should be kept clean to facilitate the husbandry practices required by the Act.

Corrected immediately.

In (b)(2)High, (b)(7)f there is a fume hood in this lab that needs to be cleaned. Equipment should be maintained and kept clean in order to facilitate the husbandry practices required by the Act.

Corrected immediately.

The complete site inspection was conducted March 17-18, 2009.

Prepared By:

TAMI L HOWARD, D V M

USDA, APHIS, Animal Care

Date:

Title:

VETERINARY MEDICAL OFFICER Inspector 1065

Mar-19-2009

Received By:

(b)(6), (b)(7)c

Date:

Title:

Mar-20-2009

Page 1 of 1



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insp\_id

### Inspection Report

**EMORY UNIVERSITY** 

Customer ID: 896

APR 0 6 2009

ECEIVED

(b)(2)High, (b)(7)f

Certificate: 57-R-0003

BY:\_

Site: 002

YERKES PRIMATE CENTER/FIELD

Type: ROUTINE INSPECTION

Date: Mar-19-2009

ATLANTA, GA 30322

3.75 (c)

HOUSING FACILITIES, GENERAL.

(c) Surfaces--(1) General requirements. The surfaces of housing facilities or areas for non human primates must be constructed in a manner and made of materials that allow them to be readily cleaned and sanitized.

In the (b)(2)High, (b)(7)f the first non human primate testing room to the right has a floor which exhibits several 3-4 inch linear and crescent shaped cracks in the flooring. These cracks in the flooring should be repaired. The cracks do not allow for proper cleaning and sanitization of the room. Areas used for housing or testing of regulated species should be kept in good repair to allow for proper cleaning and sanitization.

Correct by July 19, 2009.

3.84 (d)

CLEANING, SANITIZATION, HOUSEKEEPING, AND PEST CONTROL.

(d) Pest control. An effective program for control of insects, external parasites affecting nonhuman primates, and birds and mammals that are pests, must be established and maintained so as to promote the health and well-being of the animals and reduce contamination by pests in animal areas.

In(b)(2)High, (b)(7)there are dead roaches present in all of the light fixtures. In(b)(2)High, (b)(7)f there are dead roaches present in some of the light fixtures. Some live roaches were seen on the floor of S7-8 as well.

In (b)(2)High, (b)(7)f testing there are rodent droppings present. While the institution does have a pest control program in place, the areas cited need special attention and /or adjustments to the pest control measures currently being done. This is necessary to ensure the health and well being of the regulated species, namely non human primates.

Correct by September 19, 2009.

Prepared By:

TAMI L HOWARD, D V M

USDA, APHIS, Animal Care

Date:

Title:

VETERINARY MEDICAL OFFICER Inspector 1065

Mar-19-2009

Received By:

(b)(6), (b)(7)c

Date:

Title:

Mar-20-2009

Page 1 of 1

SUM, VINDO



896 cust 1d 25523 insp id 7800 site\_id

INSPECTION REPORT

EMORY UNIVERSITY

ATLANTA, GA 30344

Customer ID: 896

Certificate: 57-R-0003

Site: 001

**EMORY UNIVERSITY** 

(b)(2)High, (b)(7)f

Inspection

Type: ROUTINE INSPECTION

Date: JUN-02-2008

3.131 (c)

SANITATION.

(c) Housekeeping. Premises (buildings and grounds) shall be kept clean and in good repair in order to protect the animals from injury and to facilitate the prescribed husbandry practices set forth in this subpart.

used for animal holding/receiving contains a cloth-seat chair that cannot be adequately cleaned and sanitized. Furniture in animal rooms must be readily sanitizable to facilitate proper husbandry practices. Correct by: 06 Jun 08.

\*\*\*Inspection conducted 29-30 May 2008 and 02 June 2008 includes all site 001 facilities and complete review of IACUC records for all sites under this registrant\*\*\*

- 1.) IACUC Minutes (07 May 08, 16 Apr 08, 05 Mar 08, 20 Feb 08, 16 Jna 08, 19 Nov 07, 17 Oct 07, 19 Sep 07, 15 Aug 07, 18 Jul 07, 20 Jun 07, 16 May 07)
- 2.) IACUC Program Reviews and Facility Semi-Annual Inspections (Aug 2007 throough Jan 2008)
- 3.) Reports to Institutional Official (09 May 08, 20 Nov 07, 27 Sep 07)
- 4.) Protocol Post-approval Monitoring Records (2007-2008)
- Training records applicable to protocol 82-2006
- 6.) Standard Operating Procedure for Significant Deficiencies
- 7.) Current IACUC Roster, IACUC Attendance Records
- 8.) Protocols (009-2007, 166-2007, 005-2008, 009-2008, 015-2008, 061-2007, 068-2008, 069-2007, 165-2007, 215-2005)

This is an amended report correcting inspection report ( cust id 896, inspection id 200810, site id 42877) by adding the certificate number to the inspection report.

Prepared By:

GREGORY GAJ, D V M , USDA, APHIS, Animal Care

Date:

Title:

SUPERVISORY ANIMAL CARE SPECIALIST, Inspector ID:

SEP-04-2008

Received By:

SENT BY CERTIFIED MAIL

Date:

Title:

SEP-04-2008

U.S. Postal Service CERTIFIED MAIL RECEIPT (Domestic Mail Only; No Insurance Coverage Provided) 8203 ATLANTA GA 30322 무도크리 0708 \$0.42 \$ Postage \$2.70 Certified Fee 7000 00ET Return Receipt Fee (Endorsement Required) \$2.20 Restricted Delivery Fee (Endorsement Required) \$0.00 09/04/2008 \$5.32 Total Postage & Fees \$ 7008 Emory University, (b)(2)High, (b)(7)for PO Box No. 1440 Clifton Rd NE Street, Apt. No.; or PO Box No. Atlanta 30323 See Reverse for Instruct



INSPECTION REPORT

896 cust id JUN 0 9 2008200810 insp\_id

ABARTHOLOMEW

42877 site id 57-R-0003

**EMORY UNIVERSITY** 

Customer ID: 896 Certificate: --

Site: 001

**EMORY UNIVERSITY** 

(b)(2)High, (b)(7)f ATLANTA, GA 30322

Inspection Type: ROUTINE INSPECTION

Date: JUN-02-2008

3.131 (c)

SANITATION.

(c) Housekeeping. Premises (buildings and grounds) shall be kept clean and in good repair in order to protect the animals from injury and to facilitate the prescribed husbandry practices set forth in this subpart.

used for animal holding/receiving contains a cloth-seat chair that cannot be adequately cleaned and (b)(2)High, (b)(7)f sanitized. Furniture in animal rooms must be readily sanitizable to facilitate proper husbandy practices. Correct by: 06 Jun

\*\*\*INSPECTION CONDUCTED 29-30 MAY 2008 AND 02 JUNE 2008 INCLUDES ALL SITE 001 FACILITIES AND COMPLETE REVIEW OF IACUC RECORDS FOR ALL SITES UNDER THIS REGISTRANT\*\*\*

Reviewed:

- 1.) IACUC Minutes (07 May 08, 16 Apr 08, 05 Mar 08, 20 Feb 08, 16 Jan 08, 19 Nov 07, 17 Oct 07, 19 Sep 07, 15 Aug 07, 18 Jul 07, 20 Jun 07, 16 May 07)
- 2.) IACUC Program Reviews and Facility Semi-Annual Inspections (Aug 2007 through Jan 2008)
- 3.) Reports to Institutional Official (09 May 08, 20 Nov 07, 27 Sep 07)
- 4.) Protocol Post-Approval Monitoring Records (2007-2008)
- 5.) Training Records applicable to protocol 82-2006
- 6.) Standard Operating Procedure for Significant Deficiencies
- 7.) Current IACUC Roster, IACUC Attendance Records
- 8.) Protocols (009-2007, 166-2007, 005-2008, 009-2008, 015-2008, 061-2007, 068-2008, 069-2007, 165-2007, 215-2005)

Prepared By:

AMY BARTHOLOMEW, D V M, USDA, APHIS, Animal Care

Date:

Title: VETERMARY MEDICAL OFFICER Inspector ID: 1051

JUN-02-2008

Received By:

(b)(6), (b)(7)c

Date:

Title:

JUN-02-2008



MAR 0 3 2008

896 cust\_id

ABARTHOLOMEW

200758 insp\_id 7802 site id

### INSPECTION REPORT

**EMORY UNIVERSITY** 

Customer ID: 896

Certificate: 57-R-0003

Site: 003

**EMORY UNIVERSITY** 

Inspection

Type: ROUTINE INSPECTION

Date: FEB-12-2008

ATLANTA, GA 30322

2.32 (b)

#### PERSONNEL QUALIFICATIONS.

(b)(2)High, (b)(7)f

(a) It shall be the responsibility of the research facility to ensure that all scientists, research technicians, animal technicians, and other personnel involved in animal care, treatment, and use are qualified to perform their duties. This responsibility shall be fulfilled in part through the provision of training and instruction to those personnel.

\*\*\*15 animals are temporarily housed in tranport boxes in th(b)(2)High, (b)(7)fluring room cleaning. These boxes are designed for employee safety during short-term (room-to-room) transfer as they have ventilatory openings on only the front and 1 side of the box. The 15 boxes are positioned in a manner that obstructs the ventilatory openings. Boxes nearest to the wall are in contact with a wall bumper that obstructs the upper half of the ventilatory openings on the side. On some boxes, the projection rims on the box front/rear overlap, allowing the front ventilatory openings to be obstructed by adjacent boxes. Training and instruction appropriate personnel in transport box handling must be provided to ensure that ventilation is not compromised. Correct by: 28 Feb 08.

3.75 (a)

3.75 (c)

3.75 (e)

### HOUSING FACILITIES, GENERAL.

(a) Structure: construction. Housing facilities for nonhuman primates must be designed and constructed so that they are structurally sound for the species of nonhuman primates housed in them. They must be kept in good repair...

\*\*\*There is an area in ID2 where the ceiling is bowing downward. This is a linear area approximately 5 feet in length near enclosures for RVs3 and RKq4. Facilities must be maintained in good repair for human and animal safety. This area must be assessed for structural integrity. Correct by: 15 Mar 08.

(c) Surfaces

(1) General requirements. The surfaces of housing facilities -- including perches, shelves, swings, boxes, houses, dens, and other furniture-type fixtures or objects within the facility -- must be constructed in a manner and made of materials that allow them to be readily cleaned and sanitized, or removed or replaced when worn or soiled.

(b)(2)High, (b)(7)there is an area of peeling paint approx. 12 inches in diameter on the wall behind enclosure containing RFd8. This inhibits proper cleaning and sanitization of the surface. Surfaces of housing facilities must be maintained so that they can be readily cleaned and sanitized. Correct by: 15 Mar 08.

Prepared By:

AMY BARTHOLOMEW, DVM, USDA, APHIS, Animal Care

Date:

Title: VETERINARY MEDICAL OFFICER, Inspector ID: 1051

FEB-12-2008

Received By:

(b)(6), (b)(7)c

Date:

Title:

FEB-15-2008



### INSPECTION REPORT

896 cust id

ABARTHOLOMEW

MAR 0 3 2000 insp\_id

\*\*\*Animal test boxes ir(b)(2)High, (b)(7)fare in disrepair. Several box doors are cracked/chipped on the interior aspect, exposing underlying particle board. This surface cannot be properly cleaned and sanitized. Surfaces of housing facilities must be maintained so that they can be readily cleaned and sanitized. Correct by: 15 Mar 08.

\*\*\*There is damage to drywall on rear wall of(b)(2)High, (b)(7)f This surface cannot be properly cleaned and sanitized. Surfaces of housing facilities must be maintained so that they can be readily cleaned and sanitized. Correct by: 15 Mar 08.

(e) Storage. Supplies of food and bedding must be stored in a manner that protects the supplies from spoilage, contamination, and vermin infestation. The supplies must be stored off the floor and away from the walls, to allow cleaning underneath and around the supplies. Food requiring refrigeration must be stored accordingly, and all food must be stored in a manner that prevents contamination and deterioration of its nutritive value.

\*\*\*The dry feed storage area adjacent to the Great Ape Wing has sustained ceiling damage. There is a linear brown discoloration of the ceiling. Approx. 1 foot of this area (near the wall) has large pieces of damaged ceiling hanging down. There is brown discoloration on the wall, indicative of a moisture problem in this area. This area must be assessed for structural integrity and repaired. Correct by: 29 Feb 08.

\*\*\*COMPLETE SITE INSPECTION CONDUCTED 11-12 FEBRUARY 2008\*\*\*

Prepared By:

AMY BARTHOLOMEW, DVM, USDA, APHIS, Animal Care

Title: VETERINARY MEDICAL OFFICER, Inspector ID: 1051

FEB-12-2008

Received By:

(b)(6), (b)(7)c

Date:

Date:

Title:

FEB-15-2008

Page 2 of 2