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May 13, 2026

Amy Bany Adams, Ph.D.
Acting Director
Office of the Director
National Institute of Neurological Disorders and Stroke

Via email: adamsamy@mail.nih.gov

Dear Dr. Adams:

I am writing on behalf of People for the Ethical Treatment of Animals, Inc. (PETA) to request that the National Institute of Neurological Disorders and Stroke (NINDS) immediately suspend—and, if warranted, terminate—financial support for grants awarded to Principal Investigator Heather Gray-Edwards at the University of Massachusetts Chan Medical School (UMass-Chan).

This request is based on extensive whistleblower disclosures documenting systemic animal welfare violations at UMass-Chan, including chronic veterinary understaffing, inadequate pain management, delayed or withheld treatment, unsafe housing conditions, and repeated failures to implement humane endpoints. These concerns have already been reported to the U.S. Department of Agriculture (USDA), the NIH Office of Laboratory Animal Welfare (OLAW), and the Massachusetts Department of Public Health. Given the severity of the reported risks to both animal well-being and research data integrity, immediate administrative action from NINDS is warranted.

Systemic Animal Welfare Failures at UMass-Chan

Documented failures at UMass-Chan to provide minimum animal welfare standards include:

- **Critically inadequate veterinary staffing and oversight**, with only two veterinarians responsible for tens of thousands of animals across multiple species for more than 16 months.
- **Widespread deficiencies in pain management and postoperative care**, including the use of invasive and repeated survival surgeries without adequate analgesia, failure to escalate pain control when animals exhibited clear signs of suffering, and failure to stock required pain medications even after federal inspections cited these deficiencies.
- **Repeated delays or failures in diagnosis and treatment**, resulting in prolonged and preventable suffering from untreated injuries, infections, seromas, gastrointestinal obstructions, necrosis, hypothermia, and severe weight loss

Entities
- PETA Asia
- PETA India
- PETA France
- PETA Australia
- PETA Germany
- PETA Switzerland
- PETA Netherlands
- PETA Foundation (U.K.)

- **Failure to implement humane endpoints or timely euthanasia**, allowing animals to deteriorate for days or weeks, including animals found dead in their cages after prolonged visible distress
- **Unsafe housing conditions and environmental management** that facilitated ingestion of foreign materials, irritation and injury from bedding, and housing arrangements that created chronic stress (e.g., prey species housed adjacent to barking dogs)
- **Intentional underfeeding of animals to avoid regulatory housing requirements**, resulting in chronic hunger, emaciation, food aggression, and injuries from fighting
- **IACUC and institutional oversight failures**, including approval of protocols lacking adequate safeguards for pain, distress, and foreseeable complications, and in the failure to intervene decisively when patterns of animal suffering became evident

Taken together, these pervasive deficiencies call into serious question both the ethical foundation and scientific reliability of *any* animal-based experimentation conducted at UMass-Chan.

NINDS-Funded Projects Led by Heather Gray-Edwards

The following NINDS-funded projects described below involve experimental designs that inherently impose severe and prolonged animal suffering—burdens that are likely compounded by the facility-wide deficiencies described above.

R01NS145295: Evaluating the Efficiency of In Vivo Gene Transfer to Correct the Molecular Neuropathology Causing Psychiatric Disease in MSUD

Project Goal:
Develop and evaluate AAV-based gene therapy approaches for Maple Syrup Urine Disease (MSUD) that not only correct peripheral metabolic abnormalities but also address the persistent neurological dysfunction that remains despite current standard-of-care treatments. Using a naturally occurring large-animal model (calf) of MSUD, the study aims to determine whether targeted gene therapy can improve central nervous system outcomes while maintaining long-term biochemical control.

Project End Date: May 31, 2030

Animal Welfare Concerns:
Calves with MSUD typically develop symptoms shortly after birth, beginning with lethargy, weakness, poor suckling, and failure to thrive. As the disease progresses, neurologic signs become prominent and include tremors, unsteady or abnormal gait, difficulty standing, and worsening coordination, often progressing to recumbency. Affected calves may display altered behavior, diminished responsiveness, episodes of confusion, seizures, and progressive loss of consciousness as toxic metabolites accumulate in the brain. In non-research settings, calves born with MSUD typically die within days of birth and are euthanized to prevent the prolonged and severe suffering associated with the condition.

Calves used in this project are subjected to intensive experimental procedures within days of birth following identification of naturally occurring MSUD. Per the study design, calves receive high-dose intravenous administration of an adeno-associated virus (AAV) gene therapy vector and, in some experimental groups, additional direct cerebrospinal fluid delivery via intracerebroventricular and intrathecal routes. These interventions require repeated sedation or anesthesia and invasive vascular and spinal access. Longitudinal

follow-up includes frequent blood draws, cerebrospinal fluid sampling, serial neurological examinations, and repeated MRI and MR spectroscopy.

Throughout the study, calves are deliberately maintained on protocol while experiencing ongoing and progressive neurological disease characteristic of MSUD, including **worsening motor dysfunction, brain swelling, impaired coordination, seizures, cognitive deterioration, and difficulty swallowing**. Treated animals are followed for months to years to permit long-term imaging, electrophysiologic testing, tissue sampling, and endpoint characterization rather than being euthanized at early stages of severe disease.

According to documents obtained from the veterinary facility housing MSUD-affected cattle (Tufts University, Cummings School of Veterinary Medicine), **animals used in these experiments are classified as USDA Category E, indicating that severe or prolonged pain and neurologic distress are anticipated and that palliative or comfort-directed care is intentionally withheld to permit observation of advanced disease endpoints.**

These anticipated outcomes are of particular concern in light of broader whistleblower-reported deficiencies in veterinary staffing, clinical oversight, and IACUC function at UMass-Chan, which raise additional questions about the institution's capacity to adequately monitor or respond to the significant animal welfare burdens inherent in this protocol.

Scientific Concerns:
Although calves experience many of the same severe MSUD symptoms as humans, they lack key features of the human form of the disease that will impede translation to human patients. Notably, calves with MSUD do not recapitulate the neurologic course or the neuropsychiatric symptoms observed in humans — two specific areas of symptoms this project aims to address.

The neurological and neuropsychiatric manifestations of MSUD in humans, including cognitive impairment, executive dysfunction, anxiety and mood disorders, panic, attention-deficit symptoms, compulsive behaviors, and other psychiatric sequelae, are intrinsically difficult to model in nonhuman animals, as they depend on higher-order cognitive processes, complex emotional states, and subjective experiences that cannot be directly assessed in these animals. Many of these symptoms emerge over years following metabolic stabilization, are shaped by human-specific neurodevelopmental trajectories, and reflect disruptions in neurotransmitter systems, myelination, and large-scale neural network function that manifest behaviorally in ways that lack clear animal analogues. Consequently, data from calves with MSUD are fundamentally limited in their capacity to capture the chronic neuropsychiatric burden that defines long-term disease severity and quality-of-life outcomes in human patients.

Moreover, the animal welfare deficiencies documented at this facility, including inadequate pain management, chronic stress, nutritional restriction, delayed treatment of complications, and inconsistent veterinary oversight, will directly compromise the validity of this study's data, in which metabolic, neurochemical, and neuroimaging endpoints are central to evaluating therapeutic efficacy. Stress and unmanaged illness are known to alter branched-chain amino acid metabolism, glutamate levels, neuroinflammatory signaling, and white-matter integrity, all of which are key outcome measures in this project. As a result, observed biochemical or neurological changes may reflect uncontrolled physiological distress rather than true treatment effects, undermining both mechanistic interpretation and confidence in the translational relevance of any findings.

R01NS139268: AAV Gene Therapy for Sialidosis: from Mice to IND

Project Goal:
Develop and translate an AAV-based gene therapy for sialidosis by restoring NEU1 function, using dose-finding, safety, and efficacy studies in both mouse and large-animal (sheep) models to support IND-enabling development and future clinical trials.

Project End Date: May 31, 2029

Animal Welfare Concerns:
Animals used in this protocol will be genetically engineered to carry loss-of-function mutations in the *NEU1* gene, including *NEU1*-deficient mice generated through germline disruption and CRISPR-edited sheep created via genome editing of embryos implanted into surrogate ewes. In both species, *NEU1* deficiency results in a progressive, multisystem lysosomal storage disorder characterized by widespread intracellular vacuolization, neuroinflammation, and degeneration affecting the central and peripheral nervous systems and multiple peripheral organs.

As disease advances, affected animals experience **progressive neurologic deterioration, including motor dysfunction, impaired coordination, abnormal gait, tremors, seizures, and visual impairment, alongside worsening organ pathology and reduced survival**. Animals are intentionally maintained on protocol for longitudinal study through escalating neurological impairment in order to characterize disease progression, imaging and electrophysiologic correlates, survival, and histopathology rather than to mitigate suffering.

Both mice and sheep undergo systemic administration of adeno-associated virus (AAV) gene therapy vectors via intravenous routes and, in many cases, direct central nervous system delivery, requiring repeated sedation or general anesthesia. The experimental design includes dose-escalation, efficacy, and toxicology studies, beginning at the highest feasible doses and escalating to determine maximum tolerated dose thresholds, including doses exceeding those currently used in human clinical trials. Known and anticipated risks include hepatic toxicity, hematologic abnormalities such as thrombocytopenia and thrombotic microangiopathy, and dorsal root ganglia neurotoxicity.

Sheep, in particular, will undergo repeated invasive procedures while living with progressive neurodegenerative disease, including multiple cerebrospinal fluid access routes (bilateral intracerebroventricular, cisterna magna, and intrathecal injections), serial craniotomies and dural punctures, repeated organ biopsies, and frequent MRI, EEG, EMG, visual, and neurological assessments over many months. Due to their size and lifespan, these animals will endure prolonged in-life experimentation spanning the period of most severe disease expression.

Throughout the study, animals are subjected to cumulative surgical trauma, repeated handling, and escalating physiological stress while neurologic and systemic disease progress. The study design prioritizes endpoint characterization and toxicity tolerance over symptom relief or palliative intervention, and animals are killed and subjected to full necropsy at study conclusion.

These burdens are further exacerbated by reported deficiencies in veterinary staffing, clinical responsiveness, and IACUC oversight at UMass-Chan. In the context of a protocol already involving sustained neurodegenerative disease, repeated invasive procedures, and prolonged observation to late-stage endpoints, lapses in animal care infrastructure and oversight may delay recognition of clinical decline and intensify both the severity and duration of animal suffering.

Scientific Concerns:
While animal models of sialidosis, including NEU1-deficient mice and genetically engineered sheep, have provided some insight into the disease's biochemical pathways and gross neurological decline, they have

significant limitations as models for the full human disease. Many clinically consequential features—including complex seizure phenomenology, progressive cognitive impairment, myoclonus severity, visual processing deficits, and quality-of-life impacts—are difficult or impossible to assess in nonhuman animals. Differences in neurodevelopmental timing, cortical organization, lifespan, and behavioral repertoire further limit extrapolation to human patients, particularly for type I disease, which unfolds over decades.

Although sheep models mitigate some translational gaps, they introduce others, including ethical and welfare constraints inherent to longitudinal experimentation involving progressive, untreatable neurologic disease. In both rodents and sheep, study designs prioritize measurable endpoints—such as biochemical correction, imaging changes, or survival—over subjective neurologic experience. Consequently, observed improvements in animal models may not reliably predict meaningful neurological or functional benefit in human patients, nor fully reflect their disease burdens, thereby carrying inherent translational uncertainty.

Moreover, the presence of significant animal welfare deficiencies and the above model limitations further undermine confidence that any observed treatment effect will be reliable, reproducible, or meaningfully predictive of human benefit.

Requested Actions

Given the documented animal welfare failures, the severity of animal suffering inherent in these protocols, and the resulting risks to data validity and translational relevance, I respectfully urge NINDS to:

- **Immediately suspend funding** for Projects 5R01NS139268 and R01NS145295 pending completion of OLAW's investigation into animal welfare violations at UMass-Chan;
- **Consult with OLAW** regarding the findings of that investigation and determine whether funding should be reinstated or terminated; and
- **Review all NINDS-funded research involving nonhuman animals** at UMass-Chan to assess whether non-animal alternatives are available, and whether welfare deficiencies compromise data integrity.

As a developmental neuroscientist who spent decades working with children affected by rare genetic and developmental disorders, I am deeply aware of the profound suffering these children endure and the anguish experienced by their families. I fully appreciate the urgent need for effective gene therapies; however, it is precisely because of this commitment that I am concerned the animal experiments and facility at issue may be impeding, rather than advancing, that goal.

I am available to provide additional documentation or discuss this matter further. Thank you for your attention.

Sincerely,

Katherine V. Roe, Ph.D.
Chief Scientist
Laboratory Investigations Department
People for the Ethical Treatment of Animals