Science Advancement & Outreach
A DIVISION OF PETA

1536 16th St. N.W., Washington, DC 20036

June 16, 2026

Dear Interagency Pain Research Coordinating Committee members:

On behalf of Science Advancement and Outreach, the biomedical science policy division of People for the Ethical Treatment of Animals, I am writing to request that the Committee prioritize and support pain research that uses solely human-based approaches and advise the Department of Health and Human Services (HHS) to end the conduct and funding of pain research that uses other animals.

Weighed together, the following principles support our request:

1. The biological and experiential differences between animal subjects and human pain patients, as well as the confounds built into laboratory settings.
2. The inherently high level of harm inflicted on animals used in pain experiments, compared to the low level of potential benefit for human patients, and the need for these harms and benefits to be weighed.

Why pain research should not use other species

Animals are being used in experiments to study human pain despite substantial biological and environmental differences between human patients and animals confined in laboratories. Animals used in pain experiments are typically young, healthy, and genetically homogeneous, whereas patients experiencing chronic pain are often older adults with diverse genetic backgrounds, multiple comorbidities, and complex treatment histories. Human pain is also shaped by psychological, social, environmental, and cultural factors that cannot be replicated in animals. Moreover, pain cannot be directly measured in animals. Researchers must infer pain from behavioral responses, which serve only as indirect proxies and cannot capture the subjective experience that defines pain in humans.[1]

Significant biological differences between species prevent translation of findings, including differences in pain sensitivity,[2] ion channel function,[3,4,5,6] immune responses,[7,8] and responses to analgesic drugs.[9,10,11]

Finally, recent scholarship has revealed that being confined in a laboratory amplifies animals' pain before any procedure is even performed. Standard laboratory housing, which is barren compared to animals' natural environments, disables "multiple endogenous analgesic mechanisms, while simultaneously activating several neurobiological pathways that intensify nociceptive signaling and delay healing."[12] Experts note that, for research, "pain models built on

barren laboratory housing may not accurately reflect drug efficacy or clinical relevance."[13] Animals used in experiments are confined in environments that are not biologically neutral; the laboratory setting intensifies pain, alters physiological responses, and impairs recovery. As a result, data generated under these conditions are inherently confounded by captivity itself, further undermining their reliability and relevance to human health.

Human-based tools are available for pain research

Given these limitations, pain research should be conducted using methods that reflect human physiology, neurobiology, and disease, meaning human-based research methods should be the focus. Advances in this area include a human spinal organoid-on-a-chip system that models nociceptive circuitry[14] and human neuronal platforms that investigate the molecular mechanisms underlying pain signaling in peripheral nerves.[15] These approaches offer opportunities to study human pain directly rather than attempting to translate results from other species.

Harm-benefit analyses should be applied to pain research

In many jurisdictions globally, harm-benefit analyses are required to be conducted before experiments on animals can proceed. In the U.S., oversight bodies claim to assess harms and benefits,[16,17] but these evaluations are fragmented. Institutional Animal Care and Use Committees review animal welfare concerns, while funding bodies assess scientific merit, with zero coordination or communication between the two. As a result, no single body systematically weighs animal suffering against the anticipated benefits of the research. Without such an assessment, it is impossible to determine whether the supposed benefits of a study justify the pain and distress imposed on animals. Retrospective analyses have demonstrated that they often do not, and that existing regulations are failing "to safeguard animals from severe suffering or to ensure that only beneficial, scientifically rigorous research"[18] is conducted.

Until animal experimentation in pain research is ended, a system for assessing a "risk threshold" or "upper limit" for harm, similar to that employed in research on humans, should be implemented.[19] Additionally, any assessment of harm should account not only for experimental procedures but also for the cumulative impacts of laboratory confinement (including its amplification of pain) and the inability of animals to engage in species-typical behaviors.

Considering that pain research inherently involves a high level of harm, as well as the above-mentioned scientific limitations of human pain research using animals, this Committee has an increased ethical responsibility to ensure that harm-benefit analyses are rigorously applied to any animal experimentation conducted or funded under its purview.

In summary, prioritizing human-based approaches and implementing harm-benefit analyses are necessary to improve the scientific translatability and ethical accountability of pain research. The Committee must take this into account in its advisement of HHS and in setting our nation's pain research agenda.

These and related recommendations, which align with NIH's mission to prioritize human-based approaches,[20] are expanded in our policy roadmap, Research Modernization NOW.

Thank you for considering these recommendations.

Sincerely,

Gabby Vidaurre, Ph.D.
Research Associate

[1] Anke Tappe-Theodor A, Sena ES, Rittner HL, Soliman N. Animal models for translational pain research. International Association for the Study of Pain. January 17, 2022. Accessed June 9, 2026. https://www.iasp-pain.org/resources/fact-sheets/animal-models-for-translational-pain-research/

[2] Park TJ, Lu Y, Jüttner R, et al. Selective inflammatory pain insensitivity in the African naked mole-rat (Heterocephalus glaber). *PLoS Biol*. 2008;6(1):e13. doi:10.1371/journal.pbio.0060013

[3] Jordt SE, Julius D. Molecular basis for species-specific sensitivity to "hot" chili peppers. *Cell*. 2002;108(3):421-430. doi:10.1016/s0092-8674(02)00637-2

[4] Chen J, Kym PR. TRPA1: the species difference. *J Gen Physiol*. 2009;133(6):623-625. doi:10.1085/jgp.200910246

[5] Chen J, Kang D, Xu J, et al. Species differences and molecular determinant of TRPA1 cold sensitivity. *Nat Commun*. 2013;4:2501. doi:10.1038/ncomms3501

[6] Han C, Estacion M, Huang J, et al. Human Na(v)1.8: enhanced persistent and ramp currents contribute to distinct firing properties of human DRG neurons. *J Neurophysiol*. 2015;113(9):3172-3185. doi:10.1152/jn.00113.2015

[7] Mestas J, Hughes CC. Of mice and not men: differences between mouse and human immunology. *J Immunol*. 2004;172(5):2731-2738. doi:10.4049/jimmunol.172.5.2731

[8] Smith AM, Dragunow M. The human side of microglia. *Trends Neurosci*. 2014;37(3):125-135. doi:10.1016/j.tins.2013.12.001

[9] Pelissier T, Bustamante D, Saavedra H, Tampier L, Vergara V, Paeile C. New differences between the Wistar rat and Octodon degus, a putative laboratory animal resistant to morphine. *Comp Biochem Physiol C Comp Pharmacol Toxicol*. 1989;93(2):359-366. doi:10.1016/0742-8413(89)90248-x

[10] Puget A, Cros J, Meunier JC. The natural tolerance of the afghan pika (Ochotona rufescens) to morphine. *Eur J Pharmacol*. 1979;53(4):343-349. doi:10.1016/0014-2999(79)90458-8

[11] Mogil JS. The translatability of pain across species. *Philos Trans R Soc Lond B Biol Sci*. 2019;374(1785):20190286. doi:10.1098/rstb.2019.0286

[12] Schuck-Paim C, Alonso WJ, Hartcher K, et al. The pain echo chamber: how barren environments amplify pain in captive animals. *Front Anim Sci*. 2026;(7):1736142. doi: 10.3389/fanim.2026.1736142

[13] *Ibid*.

[14] Ao Z, Cai H, Wu Z, et al. Human spinal organoid-on-a-chip to model nociceptive circuitry for pain therapeutics discovery. *Anal Chem*. 2022;94(2):1365-1372. doi:10.1021/acs.analchem.1c04641

[15] McMillan H, Lundy FT, Dunne OM, et al. Endogenous Mas-related G-protein-coupled receptor X1 activates and sensitizes TRPA1 in a human model of peripheral nerves. *FASEB J*. 2021;35(5):e21492. doi:10.1096/fj.202001667RR

[16] National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals. *Guide for the Care and Use of Laboratory Animals*. 8th ed. National Academies Press; 2011. https://grants.nih.gov/grants/olaw/guide-for-the-care-and-use-of-laboratory-animals.pdf

[17] American Association for Laboratory Animal Science. AALAS position statement on the humane care and use of laboratory animals. *Comp Med.* 2007;57(4):413.

[18] Pound P, Nicol CJ. Retrospective harm benefit analysis of pre-clinical animal research for six treatment interventions. *PLoS One*. 2018;13(3):e0193758. doi:10.1371/journal.pone.0193758

[19] Ferdowsian H, Johnson LSM, Johnson J, Fenton A, Shriver A, Gluck J. A belmont report for animals?. *Camb Q Healthc Ethics*. 2020;29(1):19-37. doi:10.1017/S0963180119000732

[20] National Institutes of Health. NIH to prioritize human-based research technologies. April 29, 2025. Accessed June 9, 2026. https://www.nih.gov/news-events/news-releases/nih-prioritize-human-based-research-technologies