Science Advancement & Outreach
A DIVISION OF PETA

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Request for Information: Inviting Input on NIDA's Strategic Plan for 2027-2031

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Please comment on proposed Priority Area 1: Support Basic Research to Understand the Mechanisms Contributing to Drug Use and Addiction and their Impacts on Brain, Behavior, and Health.

For NIDA to advance understanding of the biological mechanisms underlying drug use and addiction, the effects of drugs on the human body and brain, and their impacts on behavior and health across the lifespan, the upcoming strategic plan must commit to ending experiments that use animals to study substance use and addiction and instead prioritize human-based methods and data. That transition must include a deliberate end to funding and conducting animal experimentation—not simply increasing non-animal funding alongside continued animal experimentation.

Despite the prevalence of substance use disorder research conducted on animals, there are only limited treatment options available for individuals addicted to opioids, nicotine, and alcohol, and no approved treatments for marijuana, stimulant, or polysubstance use disorders (https://www.drugdiscoverynews.com/developing-new-drugs-to-treat-addiction-16033). Moreover, most addiction and relapse prevention drugs that have shown promise in animals have either failed in human trials or were not well tolerated (https://doi.org/10.1111/add.14764).

These failures reflect fundamental limitations of using animals to study the biological mechanisms, drug effects, and behavioral processes underlying substance use and addiction. First, drug use and dependence in humans are complex experiences that have been impossible to mimic using animals in a laboratory setting (https://doi.org/10.1517/17460441.2014.948415). Experiments on animals cannot capture important aspects of human brain disorders, which often arise from genetic, developmental, and environmental factors, compounded by interspecies differences in neurological systems (https://doi.org/10.1016/j.dmpk.2024.101036). Key diagnostic criteria for substance use disorders—including subjective cravings, taking a substance in greater amounts or for longer than intended, and wanting to stop using a substance but being unable to do so—also cannot be assessed in animals (https://doi.org/10.1111/add.14764).

Second, drug pharmacokinetics can differ substantially among species. For example, MDMA is metabolized more slowly in humans than in rats or monkeys, which may help explain why neurotoxicity has been observed in rodents but not in humans (https://doi.org/10.1111/j.1476-

5381.2011.01819.x). Such differences can obscure how drugs are absorbed, distributed, and metabolized, and how they exert their effects in humans, preventing animal experiments from informing understanding of drug mechanisms and therapeutic potential.

Third, animals used in substance use experiments typically do not choose to consume the addictive substance they are provided. Instead, they are forced to consume it or given a less appealing alternative. Studies have found that most animals, when given an alternative reward such as sugar, will choose sugar over the drug (https://doi.org/10.1016/j.neubiorev.2010.04.005). For alcohol use disorder, researchers have described their "consistent failure to replicate the volitional consumption of ethanol to the point of physical dependency" in experiments using animals (https://doi.org/10.1002/jhbs.21715). Thus, experiments on animals cannot adequately recapitulate a defining feature of substance use disorders in humans: voluntary substance use and the complex behavioral and psychological factors that contribute to it.

Given these limitations, NIDA should move away from experiments on animals for substance use and addiction research and instead prioritize non-invasive human and human biology-based methods that can directly investigate the biological mechanisms of drug effects and addiction in humans while capturing the genetic, developmental, environmental, behavioral, and experiential factors that shape substance use disorders across the lifespan.

Please comment on proposed Priority Area 2: Improve Interventions for Substance Use Disorders (SUDs) and Substance Use-Related Problems, from Preventing Drug Use to Supporting Recovery from Addiction.

Ending the funding and conduct of substance use experiments on animals would free funding and research resources for approaches directly focused on preventing substance use disorders, reducing overdose, and supporting recovery. Given that preventing overdose and other adverse consequences of substance use is a major priority for NIDA, redirecting resources from ineffective animal experiments toward prevention could allow NIDA to expand strategies with demonstrated relevance to affected communities.

For example, the HEALing Communities Study (https://hcs.rti.org/about.html), discussed in the previous strategic plan, partnered researchers with community members over four years to implement and test the Communities That HEAL intervention (https://hcs.rti.org/communities-that-heal-intervention.html), which is "a set of evidence-based interventions and approaches for reducing overdose deaths in communities highly impacted by the opioid crisis." With renewed funding, this work could be repeated to further evaluate effective overdose prevention strategies or support implementation of the Communities That HEAL program in additional communities where it is needed.

The NIDA strategic plan should therefore include a clear commitment to redirecting funding and resources from ineffective animal experiments toward prevention, treatment, and recovery support programs for substance use disorders.

Please comment on proposed Priority Area 3: Develop Novel Interventions to Prevent, Diagnose, and Treat Overdose and other Harms from Substance Use.

As discussed above, research focused on developing novel interventions to prevent, diagnose, and treat overdose and other harms from substance use should use solely human-based approaches and data. Human-based methods can address questions that experiments on other animals are fundamentally unable to answer and can provide information directly relevant to human health.

For example, a multi-omics study conducted by a team of researchers across the U.S. as part of the Million Veteran Program used systems biology to identify key genetic targets for new drugs to treat opioid use disorder (https://doi.org/10.1016/j.biopsych.2024.11.013). Hesperos Inc. developed a human multi-organ microphysiological model of acute opioid drug overdose that can be used to investigate the efficacy of new overdose treatments (https://doi.org/10.1016/j.crtox.2024.100209). Researchers at the University of Washington developed algorithms that convert a smartphone into a short-range active sonar capable of detecting changes in respiration that precede opioid overdose (https://doi.org/10.1126/scitranslmed.aau8914).

These few examples illustrate the range of questions surrounding prevention, diagnosis, and treatment that can be addressed using human-based data and approaches. Rather than continuing to invest in experiments on animals that cannot reproduce human substance use disorders, NIDA should prioritize non-animal approaches for developing and evaluating novel interventions for overdose and other harms from substance use.

Please comment on proposed Priority Area 5: Advance our National Capacity to Conduct Cutting-Edge Research on Drug Use and Addiction.

To advance our national capacity to conduct cutting-edge research on drug use and addiction, researchers using non-animal, human-based methods need greater funding, training, and institutional support. Federally funded researchers still predominantly receive training in animal-based methods and have limited or no exposure to advanced human-based technologies applicable to substance use disorder research. Transitioning to these approaches can be time- and resource-intensive, requiring retraining, new laboratory equipment, and access to interdisciplinary expertise.

The NIH has committed to prioritizing human-based research technologies and reducing animal use in research (https://www.nih.gov/news-events/news-releases/nih-prioritize-human-based-research-technologies) and has begun investing in human-based, non-animal approaches (https://www.nih.gov/news-events/news-releases/nih-invests-150-million-human-based-research-reduce-use-animal-models). NIDA should join this effort by providing greater support for researchers transitioning away from animal use. Specifically, NIDA should create funding mechanisms to help laboratories transition from animal use to animal-free technologies; develop fellowships, career development awards, and career transition awards for individuals focused on animal-free methodologies; and partner with research institutions to establish institutional awards supporting predoctoral and postdoctoral training programs in non-animal methods.

The NIDA strategic plan should incorporate these recommendations and commit to ending investment in animal-based research infrastructure while expanding investment in non-animal research infrastructure across both its intramural and extramural programs. Redirecting resources toward human-based research tools for studying substance use disorders would support scientific innovation, build expertise in emerging research methods, improve research efficiency, and advance public health.

Please comment on proposed Priority Area 7: Foster a Culture of Transparency, Collaboration, and Good Stewardship.

To foster a culture of transparency and good stewardship, NIDA's strategic plan must include a clear commitment to quantitatively track and publicly report: 1) the number of animals used in NIDA-supported research and the purposes for which they are used; 2) how NIDA funding is allocated between research using animals and human-based approaches; and 3) systematic evaluations of NIDA's research portfolio to inform funding decisions.

In its 2019 report on animal use in research (https://www.gao.gov/products/gao-19-629), the Government Accountability Office recommended that federal agencies track metrics to monitor their progress in reducing animal use and report this progress to the public. By tracking the number of animals used in NIDA-supported research, the institute would be able to measure progress toward adopting new methods, assess how resources are being allocated, and guide funding toward approaches that improve reproducibility and cost-effectiveness. Transparent reporting would also strengthen NIDA's ability to evaluate its research portfolio in a data-driven manner.

In NIH's April 2025 announcement to prioritize human-based methods and reduce animal use, the agency stated that it would "publicly report on research spending annually to measure progress toward reduction of funding for animal studies and an increase in funding for human-based approaches." While NIH has not publicly announced progress on this commitment since then, NIDA could establish its own transparent system by incorporating a requirement to track

and publicly report research spending on animal and non-animal approaches in its strategic plan. Doing so would provide NIDA with a publicly available measure of its progress toward modernizing substance use disorder research and could establish a model for other NIH institutes and centers to follow.

NIDA should also conduct or commission systematic reviews of the experiments on animals it uses and funds for substance use disorder research. As discussed above, there are unsurmountable limitations in modeling substance use disorders in other animals and doings so has not produced adequate treatment options. Systematic reviews can identify experiments that fail to recapitulate the human condition and should be discontinued, while also helping prevent unnecessary duplication and poorly designed studies from receiving continued funding and wasting taxpayer dollars (https://doi.org/10.1093/ilar/ilu042; https://brill.com/edcollbook-oa/title/35072). The NIH provides resources on conducting these reviews here: https://www.nihlibrary.nih.gov/services/evidence-synthesis.

Transparent tracking of animal use and research spending, combined with systematic evaluation of NIDA's research portfolio, would provide the accountability and evidence needed to reduce and ultimately eliminate experiments on animals and redirect resources toward innovative human-based approaches. These measures would help NIDA demonstrate good stewardship and ensure that its research investments advance science and improve substance use disorder research in ways that best serve the public.

Please share any additional comments not covered above.

As discussed above, NIDA's strategic plan should commit to ending the funding and conduct of experiments on animals. Until animal experimentation has ended, however, NIDA should establish a framework for evaluating the harms and anticipated benefits of the animal experiments it funds, including a "risk threshold" or "upper limit" for harm similar to that employed in research involving humans. While NIDA does not oversee IACUC determinations, it can incorporate harm-benefit considerations into its own funding decisions by requiring an independent evaluation of the expected scientific and public health benefits of proposed animal experiments, the harms inflicted on animals, and evidence related to their human relevance.

These evaluations should consider the lifelong harms inflicted on animals, the anticipated benefits of the proposed research, and the history of failures associated with similar methods. NIDA could use this information, together with findings from systematic reviews, to determine which animal experiments should be discontinued immediately. Such analyses should serve as an interim safeguard while NIDA works toward ending animal experimentation, not as a means of justifying its continuation.

Considering the significant ethical concerns surrounding animal use, NIDA should require clear, prospective evidence of human relevance and realistic anticipated clinical benefit as a condition of funding for any research involving animals until such funding has ended.