Science Advancement & Outreach
A DIVISION OF PETA

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Request for Information: Inviting Comments and Suggestions on the NIH Minority Health and Health Disparities Strategic Plan, 2026-2030 (NOT-MD-25-002)

Submitted by email to NIMHDPlanningandReporting@nih.gov **on December 17, 2024**

We are writing on behalf of Science Advancement and Outreach, a division of People for the Ethical Treatment of Animals—PETA entities have more than 9 million members and supporters globally, and PETA U.S. is the largest animal rights organization in the world—to provide suggestions for improving the NIH Minority Health and Health Disparities (NIMHD) Strategic Plan for 2026-2030, building on the 2021-2025 plan.

The NIMHD's Strategic Plan for Research (2021-2025) included many important goals, such as proposing strategies to understand and improve the health of racial and ethnic minority populations; for example: "examine health determinants that underlie resilience or susceptibility to diseases and conditions experienced by minority populations" (1.1). The NIMHD should retain this strategy and provide additional information on its progress. However, several sections throughout the strategic plan could be improved, particularly in the institute's approach to basic and translational research that relies on ineffective animal-based models.

There are numerous documented issues with using animal models to understand human conditions, including failures in translation, validity, and reproducibility. Furthermore, Congress has repeatedly called for the reduction and replacement of animal use in biomedical research funded by the NIH. In recent years, public support for animal use in biomedical research has significantly declined.

We strongly urge the NIMHD to modernize its plans for 2026-2030 by participating in new agency initiatives, such as the Common Fund's Complement-ARIE program. The NIMHD should embrace advancements in human-relevant research and adhere to agency directives to "conduct or support research into…methods of biomedical research and experimentation that do not require the use of animals [and]…methods of such research and experimentation that reduce the number of animals used in such research."[1]

Our recommendation for the NIMHD's strategic plan for 2026-2030 is to conduct and fund basic research using human biology-based systems exclusively and move away from research that uses other species. Below, we expand on specific recommendations for the basic research the NIMHD should support moving forward.

[1] 42 U.S.C. § 283e(a)(1)(A)-(C)

We would also like to share our Research Modernization Deal, a comprehensive plan with detailed recommendations for advancing biomedical research in the U.S. across various research domains with minority disparities, such as cardiovascular disease, cancer, diabetes, and stroke. This plan is available at https://www.peta.org/wp-content/uploads/2023/01/peta-research-modernization-deal.pdf.

In order for the NIMHD to "improve minority health and reduce health disparities through enhanced research activities," it needs to prioritize the most translatable research. To effectively "promote research to understand and to improve the health of racial/ethnic minority populations; advance scientific understanding of the causes of health disparities, develop and test interventions to reduce health disparities, [and] create and improve scientific methods, metrics, measures, and tools that support health disparities research," the NIMHD must focus on innovative, non-animal, human-relevant research. The 2026-2030 strategic plan should clearly state that it will prioritize basic biological research based in human biology to improve translatability and achieve its goals.

In the 2021-2025 strategic plan, NIMHD's strategy 4.3 aimed to "apply complex systems modeling approaches, including biological models, to identify and predict relationships between health determinants and health disparity outcome measures." We commend NIMHD for emphasizing the development of computational methods in this area. However, we want to ensure that, regarding biological models, the focus is on human-based models, not animal models.

Some of the health disparities noted in the strategic plan 2021-2025 were increased rates of cardiovascular disease (CVD), cancer, diabetes, and stroke. Key aspects of these conditions do not occur in other species or occur in different ways compared to humans. A review of 121 studies using animals for human CVD found that 79% failed to be replicated in human trials.[2] While CVD can occur in other species, the etiology and pathology in animals differ significantly from that in humans due to differences in cardiovascular functions and structural parameters such as resting heart rate, action potentials, protein isoforms, contraction, and force-frequency response.[3,4,5]

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[2] Vyas MV, Gros R, Hackam DG. Translation of Cardiovascular Animal Models to Human Randomized Trials. *Am J Cardiol*. 2020;137:141. doi:10.1016/j.amjcard.2020.10.027

[3] Gintant G, Sager PT, Stockbridge N. Evolution of strategies to improve preclinical cardiac safety testing. *Nat Rev Drug Discov*. 2016;15(7):457-471. doi:10.1038/nrd.2015.34

[4] Milani-Nejad N, Janssen PM. Small and large animal models in cardiac contraction research: advantages and disadvantages. *Pharmacol Ther*. 2014;141(3):235-249. doi:10.1016/j.pharmthera.2013.10.007

[5] Janssen PML, Elnakish MT. Modeling heart failure in animal models for novel drug discovery and development. *Expert Opin Drug Discov*. 2019;14(4):355-363. doi:10.1080/17460441.2019.1582636

The success rate for oncology drugs is lower than 10%, and a meta-analysis showed that cancer experiments on animals have smaller effect sizes and lack reproducibility.[6,7] This is due to significant genetic, molecular, immunologic, and cellular differences between humans and other animals.[8] In addition, the induction of cancer in animals–whether through xenotransplantation, transgenesis, or other means–often relies on artificial manipulation that is difficult to control, preventing accurate replication of the sporadic nature of tumor development and hindering the assessment of cancer treatments for humans.[9,10,11]

Diabetes research using animals has technical and biological limitations due to differences in anatomy, physiology, and exposure that make it difficult to translate this research into effective treatments for humans.[12,13,14,15] Despite testing over a thousand neuroprotective drugs in animals for stroke, none have proven effective in humans.[16] It is clear that new treatments for health disparity-related conditions in humans, developed from basic animal experimentation, overwhelmingly fail to translate–without even considering the effects of race and ethnicity on disease outcomes. Therefore, the NIMHD should shift its focus to human biology-based systems, as species differences present an additional hurdle that the NIMHD should not have to overcome in order to achieve its goal of reducing health disparities.

The strategic plan for 2021-2025 also includes the goal to "bring curative genetic therapies for sickle cell disease (SCD) into first-in-human clinical trials within five years." While this is an important goal, it is critical to note that these therapies should not be first investigated in animals as there are documented translational problems with sickle cell anemia research using animals. These include differences in disease progression, limited phenotypic complexity, and species-specific physiological dissimilarities.[17,18]

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[6] Wong CH, Siah KW, Lo AW. Estimation of clinical trial success rates and related parameters [published correction appears in Biostatistics. 2019 Apr 1;20(2):366. doi: 10.1093/biostatistics/kxy072]. *Biostatistics*. 2019;20(2):273-286. doi:10.1093/biostatistics/kxx069

[7] Errington TM, Mathur M, Soderberg CK, et al. Investigating the replicability of preclinical cancer biology. *Elife*. 2021;10:e71601. doi:10.7554/eLife.71601

[8] Mak IW, Evaniew N, Ghert M. Lost in translation: animal models and clinical trials in cancer treatment. *Am J Transl Res*. 2014;6(2):114-118.

[9] Ormandy EH, Dale J, Griffin G. Genetic engineering of animals: ethical issues, including welfare concerns. *Can Vet J*. 2011;52(5):544-550.

[10] Ben-David U, Ha G, Tseng YY, et al. Patient-derived xenografts undergo mouse-specific tumor evolution. *Nat Genet*. 2017;49(11):1567-1575. doi:10.1038/ng.3967

[11] Cheon DJ, Orsulic S. Mouse models of cancer. *Annu Rev Pathol*. 2011;6:95-119. doi:10.1146/annurev.pathol.3.121806.154244

[12] Pandey S, Chmelir T, Chottova Dvorakova M. Animal Models in Diabetic Research-History, Presence, and Future Perspectives. *Biomedicines*. 2023;11(10):2852. doi:10.3390/biomedicines11102852

[13]Kottaisamy CPD, Raj DS, Prasanth Kumar V, Sankaran U. Experimental animal models for diabetes and its related complications-a review. *Lab Anim Res*. 2021;37(1):23. doi:10.1186/s42826-021-00101-4

[14] Bunner AE, Chandrasekera PC, Barnard ND. Knockout mouse models of insulin signaling: Relevance past and future. *World J Diabetes*. 2014;5(2):146-159. doi:10.4239/wjd.v5.i2.146

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[17] Lutz B, Meiler SE, Bekker A, Tao YX. Updated Mechanisms of Sickle Cell Disease-Associated Chronic pain. *Transl Perioper Pain Med*. 2015;2(2):8-17.

[18] Kamimura S, Smith M, Vogel S, Almeida LEF, Thein SL, Quezado ZMN. Mouse models of sickle cell disease: Imperfect and yet very informative. *Blood Cells Mol Dis*. 2024;104:102776. doi:10.1016/j.bcmd.2023.102776

There is a growing awareness of the limited translatability of using animals to study human conditions such as sickle cell. Advancements in human biology-based models are driving a paradigm shift in how we study this condition. Some examples include techniques involving organ-on-a-chip,[19] microfluidic platforms,[20,21] genomic technology,[22,23] and *in silico* models.[24,25]

The same reasoning applies to other goals found in the 2021-2025 strategic plan, such as the ones that seek to "promote research that increases pharmacological curative treatment of hepatitis C infection among American Indian and Alaska Natives by 50 percent by 2030," and "characterize and understand how adverse environmental exposure profiles that occur during early life stages may enhance vulnerability to diseases of adulthood disproportionately in health disparity populations." Moving forward, the NIMHD's Strategic Plan for Research, 2026-2030 should avoid encouraging approaches that seek answers for minority health disparities using other animals and instead focus on supporting non-animal, human research.

We would be happy to meet or provide resources on the topics covered in this response. You may reach us at info@scienceadvancement.org.

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