Science Advancement & Outreach
A DIVISION OF PETA

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Request for Information (RFI) to inform development of the FY 2026-2030 NIH Strategic Plan for HIV and HIV-Related Research

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A division of People for the Ethical Treatment of Animals

Goal 1: Enhance discovery and advance HIV science through fundamental research.

Description: Fundamental research seeks to expand understanding of the biological, physiological, interpersonal, and social-structural mechanisms of HIV—i.e., how it operates as a virus and as an infectious disease pandemic—at the molecular, cellular, individual, community, and population level. This understanding provides the foundation for the development of safe, effective, and scalable tools to prevent, treat, and ultimately cure HIV infection, as well as reduce the risk and impact of comorbid conditions and co-occurring infections. Fundamental research includes theoretical, pre-clinical, and methodological research across scientific disciplines.

To better support fundamental research on HIV, the Office of AIDS Research must embrace human biology-based basic research instead of attempting to understand this human-specific disease by using other species. HIV—the "H" standing for human—is a human-specific virus. HIV can infect and multiply in some other species of primates, but only causes AIDS in humans. Certain biological differences between humans and other species account for this specificity and include the human-specific structure of CD4 and other immune cell receptors, the species-specific varieties of leukocyte antigen genes, and differences in the genes that code for important retrovirus restriction factors (https://doi.org/10.1128%2FJVI.02176-12; https://doi.org/10.1097%2FCOH.0000000000000290; https://doi.org/10.1128/jvi.79.7.3930-3937.2005). Experimenters have attempted to study HIV using a simian version, SIV, but face translational hurdles, including that SIV is a relative of a less pathogenic version of HIV, the low genetic homology between the viruses, and the differences between surface proteins and other molecular markers (https://doi.org/10.1002%2Feji.200939576; https://doi.org/10.1016/j.vaccine.2014.12.004). The use of other primates has not solved these fundamental problems and neither has the use of "humanized" mice, who are limited in their duration and longevity with the disease and retain murine major histocompatibility complex antigens, which confound interpretations of immune response data.

Goal 2: Advance the development and assessment of novel interventions for HIV prevention, treatment, and cure.

Description: Knowledge gleaned from fundamental, pre-clinical, and translational research to inform clinical trials and other intervention studies to test the most promising products, tools,

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or strategies for HIV prevention, treatment, and cure and management of its complications. Rigorous randomized control trials, observational studies, and other methodologies assess biological, behavioral, and social outcomes of novel interventions, as well as their feasibility, acceptability, effectiveness, and scalability in differing populations and across the lifespan.

To reliably inform HIV clinical trials, the basic, preclinical, and translational data used in decision making must be species relevant. An area of stark failure has been the search for an HIV vaccine. A 2008 review of preclinical and clinical data revealed that of 85 candidate vaccines that were tested in 197 clinical trials, some drugs increased the risk of HIV infections, and zero trials were successful (https://doi.org/10.1177/026119290803600403). This is still the case 16 years later. PETA recently funded a systematic review on the use of non-human primates to examine HIV vaccine efficacy. We look forward to sharing the results with OAR. Researchers must first gain a comprehensive understanding of human HIV infection before they are able develop effective interventions, drugs, and vaccines. These therapeutics and prophylactics must then be tested against human biology. Human cell-based models provide promise for both endeavors. Some recent examples of non-animal HIV research involve the use of human T-cells derived from HIV-infected and healthy donors, human brain organoids to study HIV's neurological effects and understand why the brain represents a key reservoir for HIV in the human body, as well as the use of bioinformatics, novel imaging techniques, and in silico simulations.

Goal 3: Optimize public health impact of HIV discoveries through translation, dissemination, and implementation of research findings.

Description: As HIV prevention, treatment, and cure interventions are shown to be efficacious, their findings must be translated to inform practice and to connect with communities and the general public in order to maximize their public health impact. Implementation research can identify how best to facilitate effective adaptation, uptake, integration, and scale-up of evidence-based HIV interventions. Information-sharing through community partnerships, research collaborations, and dissemination activities can amplify the impact of research and promote health equity.

According to OAR's data hub (https://oar.nih.gov/nih-hiv-research-program/data-hub/research-topic), only 17.8% of NIH HIV awards in FY2022 were granted for the purpose of reducing HIV incidence, while 51% were granted for research and therapeutic development. Like most of NIH, OAR does not break down the percentage of grants awarded for experiments on animals, but 64 of these awards mention experiments on non-human primates or mice in their titles. Instead of continuing to support the use of unsuccessful animal models, and in addition to increasing funding for animal-free technologies in the research and therapeutics categories, OAR should also direct more funding toward HIV prevention. As the CDC reports, an estimated 158,500 cases of HIV remained undiagnosed at the end of 2019 (https://www.cdc.gov/hiv/statistics/overview/index.html), representing a major need to identify ways to increase testing. As OAR moves toward human-relevant disease models and increases its translational progress, practitioners and the public will gain greater trust in its portfolio and be more likely to implement those findings. Redirecting funding toward research that involves human subjects and community intervention will also better support scientists from underrepresented communities, who are more likely to propose these kinds of research projects (https://doi.org/10.1126/sciadv.aaw7238) and who are also more affected by HIV.

Goal 4: Build research workforce and infrastructure capacity to enhance sustainability of HIV scientific discovery.

Description: Continued progress in HIV science and its application requires robust support for research tools, computational resources, instrumentation, data and physical infrastructure, and workforce development, particularly in institutions that serve underrepresented or high HIV burden populations or

that historically have been underfunded in the United States and globally. Such enhanced capacity-strengthening efforts will promote diversity and inclusion in the HIV research workforce.

The scientific community is experiencing a sea change as new technologies for animal-free research have become available and are demonstrating their worth. Still, many academic HIV research programs are still heavily animal-based, despite the well-known problems with translation and replicability of animal research in this area. Many HIV researchers whose formative experiences were in the use of animal models lack the time, funding, or institutional support to receive training in emerging, human-relevant research methods. Graduate education and postdoctoral training periods are ideal times to allow early career researchers to familiarize themselves with new and/or unfamiliar technologies and are critical junctures at which to begin building an innovative and sustainable research workforce for the future of HIV research. OAR should work with other institutes to develop and offer institutional training grants, continuing education grants, and early independence awards for the explicit purpose of allowing early career researchers to gain confidence in and further develop non-animal research methods which are applicable to HIV. Additional funding streams should be made available for established HIV researchers to train in these newer methods and the agency should provide support for individuals who wish to transition their laboratories toward animal-free technologies.