

The Humane and Existing Alternatives in Research and Testing Sciences [HEARTS] Act of 2023

For scientific, ethical, and economic reasons, cell-based, computational, and other non-animal study methods are being increasingly developed and replacing the use of animals in many areas of research. Modern non-animal methods not only spare animals from pain and death, but they have more predictive value and specificity to human conditions than do animal tests due to differences among species.¹

Yet, there are some barriers that limit the full realization of these benefits. Lack of overall funding, shortcomings in existing law governing how research projects are funded and outdated requirements have been cited as obstacles capitalizing on alternatives.²

The HEARTS act will modernize the National Institutes of Health to ensure that humane and human-relevant methods are at the heart of its science investment.

About Prioritizing the Use and Development of Humane Alternatives through the NIH

Today the NIH spends at least \$12 billion a year on animal testing. However, there is a growing awareness of the limitations of animal research and its inability to make reliable predictions for humans, as a result the return on investment is often low. The NIH reports that approximately 90 percent of promising medications have failed in human clinical studies despite having passed pre-clinical studies, including animal tests.³

Nearly everyone can agree that whenever non-animal methods are available for replacing the use of animals in research protocols they should be used. According to a 2019 SurveyUSA nationwide poll, 79 percent of voters said that the NIH should prioritize research proposals that utilize scientifically valid alternatives to animal testing and 80 percent said that medical researchers seeking funding for animal tests should first be required to show that an alternative is not available⁴. Unfortunately, this is not always the case. Office of Inspector General reports have repeatedly note repeated failures to search for alternatives to painful procedures and to document the availability of alternatives in research proposals.⁵ A system of active incentives is needed to encourage researchers to develop and utilize humane, cost-effective, and scientifically suitable non-animal methods based on human biology.

In 2019, the United States Government Accountability Office (GAO) recommended that federal agencies better monitor and report on their efforts to develop and promote replacement alternatives and decrease animal use.⁶ Moreover, under the National Institutes of Health Revitalization Act of 1993

¹ Thomas Hartung, *Look Back in Anger—What Clinical Studies Tell Us About Preclinical Work*, 30 ALTEX 275 (2013), <https://pubmed.ncbi.nlm.nih.gov/23861075/>; Pandora Pound & Michael B. Bracken, *Is Animal Research Sufficiently Evidence Based to be a Cornerstone of Biomedical Research?*, 348 BMJ 3387 (2013), <https://pubmed.ncbi.nlm.nih.gov/24879816/>; Jarrod Bailey et al., *Predicting Human Drug Toxicity and Safety via Animal Tests*, 43 ALT. LAB ANIMAL 393 (2015), <https://pubmed.ncbi.nlm.nih.gov/26753942/>; Isabella WY Mak et al., *Lost in Translation: Animal Models and Clinical Trials in Cancer Treatment*, 6 AM. J. TRANSLATIONAL RSCH. 114 (2014), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3902221/>.

² Katy Taylor, *Recent Developments in Alternatives to Animal Testing in ANIMAL EXPERIMENTATION: WORKING TOWARDS A PARADIGM CHANGE* (Kathrin Herrmann & Jayne Kimberley, eds. 2019) [hereinafter ANIMAL EXPERIMENTATION]; Gary E. Marchant, *Law—Not Science—Impedes Shift to Non-Animal Safety Testing*, BLOOMBERG L. (July 18, 2021), <https://news.bloomberglaw.com/environment-and-energy/law-not-science-impedes-shift-to-non-animal-safety-testing>; Lee, *supra* note 1.

³National Institutes of Health, NCATS: The Tissue Chip for Drug Screening <https://ncats.nih.gov/tissuechip#:~:text=Why%20Tissue%20Chips%20Matter,based%20approach%20to%20this%20challenge>

⁴Cruelty Free Int'l, *Ending Medical Testing on Animals in the USA: A Nationwide Poll of 1,000 Adults by SurveyUSA* (Aug. 2019), <https://crueltyfreeinternational.org/sites/default/files/2021-11/Medical%20testing%20-%20USA%20polling.pdf>

⁵ *Audit Report APHIS Animal Care Program Inspection and Enforcement Activities*, USDA OFF. INSPECTOR GENERAL (2005), https://www.animallaw.info/sites/default/files/awa_enforcement_2005.pdf

⁶ U.S. GENERAL ACCOUNTABILITY OFF., GAO-19-629, ANIMAL USE IN RESEARCH: FEDERAL AGENCIES SHOULD ASSESS AND REPORT ON THEIR EFFORTS TO DEVELOP AND PROMOTE ALTERNATIVES (Sep. 2019), <https://www.gao.gov/assets/gao-19-629.pdf>.

(Public Law 103–43), the NIH is supposed to outline a plan for reducing the use of animals in research and is supposed to conduct or support research methods of biomedical research and experimentation that do not require the use of animals. A dedicated center that provides resources, funding, and training to encourage researchers to utilize humane, cost-effective, and scientifically suitable non-animal methods based on human biology will complete the vision that Congress set out in the Act and will result in more progress toward understanding human diseases and their treatments and cures.

The HEARTS Act will prioritize the use of alternatives by amending the Public Health Services Act to

(1) establish incentives for investigators to use available non-animal methods whenever feasible and applicable.

(2) create guidelines for biomedical and behavioral research to ensure that animal testing alternatives are utilized whenever available and appropriate in proposals.

(3) ensure that proposal reviewers have access to a reference librarian with expertise in evaluating the adequacy of the search methods for alternatives described in the protocol.

(4) require that proposals be reviewed by at least one person with expertise in non-animal research methods.

(5) establish a center within the NIH to train and support scientists in the development and use of human-centered methods and to develop a plan for reducing the number of animals used in federally funded research.

In addition, the bill updates the definition of “animal” to include cephalopods (octopuses etc.) to ensure that these animals will receive the minimum protections afforded to other animals used in NIH-funded research. This change is consistent with regulations in the EU and UK.

To remain a global leader in science, research, and development, the U.S. must create frameworks to develop and incentivize the use of modern human-relevant methods. Prioritizing the development and use of non-animal methods in taxpayer-funded research at the NIH could improve the cost efficacy of our federal research investment and foster innovation in science which would in turn lead to better therapies for human conditions while sparing millions of animals from needless suffering.

FAQ:

What are some alternatives to animal use research? Non-animal methods, which include epidemiological and clinical studies, *in vitro* methods, computer modeling and simulation, human tissue studies, microfluidics methods, microdosing, and other approaches have more predictive value and specificity to the human conditions than do animal methods, which rely on different species with different anatomies and physiologies. Examples include:

- In the area of neuroscience, the increasing power of human-specific methods, including advances in fMRI and invasive techniques such as electrocorticography and single-unit recordings can replace tests on non-human primates.⁷
- The use of human tissues and cell cultures (including 3D cultures and organoids) for biomedical research purposes e.g. post-mortem brain tissue has provided important leads to understanding brain regeneration and the effects of Multiple Sclerosis and Parkinson's disease, while cell cultures have been central to key developments in areas such as cancer, sepsis, kidney disease and AIDS.
- "Organs-on-a-chip"⁸ - small silicone chips lined with living human cells that accurately mimic the heart, kidney, lungs, and gut.⁹
- Studies for nutrition, drug addiction and pain can be carried out on consenting human volunteers in the interest of advancing medical science.

How is animal use in research currently monitored? In 1985 amendments to the Animal Welfare Act established Institutional Animal Care and Use Committees (IACUC(s) – self-monitoring committees at research facilities responsible for ensuring compliance with the AWA and the *Public Health Service Policy on Humane Care and Use of Laboratory Animals* (the PHS policy). IACUCs are charged with reviewing proposed animal experiments to ensure that researchers *consider* alternatives to animal use or painful procedures and that they do not unnecessarily duplicate previous experiments. However, there is no uniform standard for what constitutes "consideration" of alternatives and each IACUC develops its own protocol for what constitutes a "literature search" for alternatives. The NIH will not fund research that uses animals if the IACUC has not given its approval to the proposed study. This can place increased pressure on the IACUC to approve research protocols that serve the financial interest of the researchers and the facility.

Do IACUCs require researchers to use available alternatives? Both the AWA the PHS policy ask experimenters to *consider* alternatives to using animals but use of available alternatives is not required. This sets a low standard that allows researchers to take a "check box" approach rather than earnestly searching for alternatives. As observed by former IACUC member Dr. John P. Gluck, *"Even though we now have vast searchable information resources, few researchers take the time to perform even cursory searches of the relevant databases."* He further opines that, *"Requiring researchers to indicate in their protocols the terms they used in their searches is a meaningless exercise unless the IACUC has access to expertise like that of a reference librarian to is capable of determining the adequacy of the methods."*

The USDA has long documented problems with the implementation and effectiveness of IACUCs. In 2000, a USDA survey on the effectiveness of IACUC regulations found that some IACUCs did not ensure that unnecessary or repetitive experiments would not be performed on laboratory animals.ⁱ The survey concluded that *"IACUCs seem to be doing well at functions related to setting up the administrative structure and developing the process but not as well at monitoring and follow through."* In 2005 and 2014, USDA's Office of Inspector General found that failure to search for

⁷Bailey, J. and Taylor, K. (2016). Non-human Primates in Neuroscience Research: The Case Against its Scientific Necessity. *ATLA* 44, 43-69 https://www.crueltyfreeinternational.org/sites/default/files/Bailey_Taylor_primate%20neuroscience_ATLA_2016.pdf

⁸ Wilson, T. (2016). Scientists create 'human on a chip' using miniature organs as a cutting-edge way to test latest drugs. *Mirror*. <http://www.mirror.co.uk/tech/scientists-create-human-chip-using-8364231>

⁹ The end of animal testing? Human-organs-on-chips win Design of the Year. (2015) *The Guardian*

<https://www.theguardian.com/artanddesign/2015/jun/22/the-end-of-animal-testing-human-organs-on-chips-win-design-of-the-year>

alternatives to painful procedures and to document the availability of alternatives were among the most common violations [of the AWA] by research facilities.ⁱ ⁱⁱⁱ

Why would researchers continue to use animals instead of available alternatives?

Despite the increasing recognition that animal experiments are deeply flawed and the increased availability of modern alternatives, animal use remains entrenched in many areas of research and testing. The reasons why animal testing persists are often not scientific. Instead, it can be due to conservatism within the scientific establishment – it is easier and more comfortable to simply do what has always been done. Test results on animals can be easily compared to earlier tests on animals to give confidence to scientists.

A 2020 National Academies of Sciences study about the use of dogs in research at the U.S. Department of Veterans Affairs concluded that although many investigators cited their experience using dogs and the historical data available in dog models as justification for using dogs in further testing, the *“justifications are insufficient alone and constitute a form of circular reasoning that perpetuates the use of laboratory dogs without adequate examination of alternatives.”^{iv}*

In his 2002 book, Mathew Scully former literary editor of National Review and senior speechwriter to President George W. Bush, proffered an explanation for the persistence of animal experiments, *“Every profession and institution knows the pull of simple inertia, refusing to shake off old assumptions and part with settled ways. Often too, the old ways no matter how needless or unreasonable take on a dynamic of their own, with financial interests dependent upon their preservation. There is no reason to believe medical science is any different. And there is every reason to believe that government can act that way. Where alternatives to animal testing and experimentation can indeed serve the purpose, then in each and every case changes must no longer be delayed.”^v*

The continued use of animals is likely related at least in part to failure to thoroughly research and consider alternatives and simple adherence to older more familiar methods.

ⁱ 2000, USDA Employee Survey on the Effectiveness of IACUC Regulations https://www.aphis.usda.gov/animal_welfare/downloads/iacuc/iacucaugust.pdf

ⁱⁱ 2005, OIG Audit Report APHIS Animal Care Program Inspection and Enforcement Programs <https://www.usda.gov/oig/webdocs/33002-03-SF.pdf>

ⁱⁱⁱ 2014, OIG Audit Report APHIS Oversight of Research Facilities <https://www.usda.gov/oig/webdocs/33601-0001-41.pdf>

^{iv} National Academies of Sciences, Engineering, and Medicine Necessity, Use, and Care of Laboratory Dogs at the U.S. Department of Veterans Affairs (2020) The National Academies Press, <https://www.nap.edu/read/25772/chapter/2>

^v Scully, M. (2002). *Dominion: The power of man, the suffering of animals, and the call to mercy*. New York, N.Y: St. Martin's Press