Humane and Existing Alternatives in Research and Testing Sciences [HEARTS] Act. H.R. 4101

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 are also increasingly better at predicting human response and are therefore likely to result in the development of cheaper, safer and more effective solutions for human conditions, more quickly.

Currently, the NIH spends at least $12 billion a year on animal testing, but research shows that the return on investment is often low, and the results irrelevant because of their inability to accurately predict human reactions. NIH reports that approximately 90 percent of promising medications have failed in human clinical studies despite having passed pre-clinical studies, including animal tests. **Prioritizing the use of non-animal methods in taxpayer-funded research 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 needles pain, suffering and death.**

Nearly everyone can agree that whenever non-animal methods are available for replacing the use of animals in research protocols they should be used. A 2019 SurveyUSA nationwide poll revealed high levels of support among voters for non-animal alternatives. When it comes to spending taxpayer funds on medical research, 79 percent said that the National Institutes of Health (NIH) should prioritize research proposals that utilize scientifically valid alternatives to animal testing. Similarly, 80 percent said that medical researchers seeking funding for animal tests should first be required to show that an alternative is not available.

The HEARTS Act includes specific steps to achieve these goals and fill gaps in the existing system of oversight that can lead to funding painful, wasteful, and replaceable animal tests even when scientifically valid non-animal methods exist. If enacted, this legislation would require:

- the establishment of incentives for investigators to use available non-animal methods,
- that investigators fully evaluate available non-animal methods using standardized guidelines,
- that research proposals are reviewed by at least one person with expertise in non-animal research methods
- that proposal reviewers have access to a reference librarian with expertise in evaluating the adequacy of the search methods used for alternatives.

FAQ:

<u>What are some alternatives to animal use research?</u> Non-animal methods, which include epidemiological and clinical studies, cell-based methods, computer modeling and simulation, human tissue studies, 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 brain imaging technologies, such as fMRI, and more invasive techniques such as electrocorticography and single-unit recordings can replace tests on non-human primates[i].
- Human tissues and cell cultures (including 3D cultures and organoids) can replace animals in biomedical research. For example, 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"[ii] are small silicone chips lined with living human cells that can accurately mimic the heart, kidney, lungs, gut, and other organs.[iii] These innovative devices can be used to study biological disease processes, as well as drug metabolism.
- Sophisticated computer models of human organs, such as the heart, lungs and kidneys, can be used to conduct virtual experiments based on existing information and mathematical data.
- Studies for nutrition, drug addiction and pain can be carried out on consenting human volunteers in the interest of advancing medical science. These studies come with the advantage that people can explain how they are feeling, which is something animals cannot do.
- Microdosing can also be used in human volunteers to measure how very small doses of potential new drugs behave in the body.

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 and 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 opinions 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*[iv]*."*

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.[v] 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 alternatives to painful

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

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

Despite the increasing recognition that animal experiments are deeply flawed and the increasing 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."*[viii]

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."*[ix]

Other common barriers to the widespread use of non-animal alternatives include the lack of central and national funding for the development of alternatives, bureaucratic delays between method validation and regulatory acceptance, lack of enforcement, and general fear that these novel methods will not be accepted by regulators, funding agencies or for publication in scientific journals.

The continued use of animals is also likely related at least in in part to failure to thoroughly research and consider alternatives and simple adherence to older more familiar methods. Indeed, while federal regulations and guidelines stipulate that researchers proposing animal-based research should consider methods that can avoid or minimize animal use, reports show that failure to search for alternatives to painful procedures and to document the availability of non-animal methods is a common shortcoming. Those who have served on laboratory oversight committees have echoed concern that researchers often fail to perform adequate searches for alternatives to the use of animals or are unfamiliar with the efficacy of these critical research methods.

---

[i] Bailey, 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

[ii] 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

[iii] 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

[iv] Gluck, J.P 2016, *Voracious Science and Vulnerable Animals: A primate scientist's ethical journey*. University of Chicago Press.

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

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

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

[viii] 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

[ix] 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