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AMERICAN BAR ASSOCIATION

ADOPTED BY THE HOUSE OF DELEGATES

2024 MIDYEAR MEETING
LOUISVILLE, KENTUCKY
FEBRUARY 5, 2024

RESOLUTION

RESOLVED, That the American Bar Association urges national governments, the U.S. Congress, and U.S. federal agencies to promote the development and use of methods that aim to replace, reduce, and refine the use of animal models in research and testing; and

FURTHER RESOLVED, That the American Bar Association urges national governments, the U.S. Congress, and U.S. federal agencies to remove barriers to, and create incentives for, the use of non-animal model research and testing methods in regulatory testing and federally sponsored research.

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REPORT

Introduction

This Resolution is based on the scientific principle of the Three Rs—Replacement, Reduction, and Refinement—which have been the foundation of better science and of improved conditions for animals used in research for over 60 years and which underpin laws worldwide, including in Europe and the United States.[1] Further, this Resolution is consistent with a bi-partisan federal legislative initiative (the HEARTS Act, discussed below)[2] that seeks to further implement the Three Rs with particular emphasis on the 1st R, by accelerating the development and use of non-animal alternatives ("replacement alternatives") to replace the use of animals.[3] In short, this Resolution provides a balanced approach to advance science, promote human health, protect the environment, and spare animals' lives.

The Three Rs were first described by William Russell and Rex Burch in 1959 in *The Principles of Humane Experimental Technique.*[4] Russell and Burch advocated using scientific ingenuity to replace (avoid using animals), reduce (use as few animals as possible), and refine (cause as little suffering to animals as possible wherever feasible) to support science.[5] This Resolution focuses on the first R, replacement, which was intended by Russell and Burch to be given the highest priority in the framework, followed by reduction and refinement, respectively. Today's ever-evolving science and technology is creating opportunities to move closer to the goal of replacing animals in biomedical

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[1] In 1986 the European Union enacted European Directive 86/609/EEC, which put much of the Three Rs in practice (without mentioning the approach explicitly). In 2010, this Directive was updated and replaced by European Parliament and Council Directive 2010/63/EU of the European Parliament and of the Council on the Protection of Animals Used for Scientific Purposes, https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32010L0063, which specifically mentions the Three Rs in the preamble and the body of the legislation. *See* Robert Hubrecht & Elizabeth Carter, *The 3Rs and Humane Experimental Technique: Implementing Change*, 9(10) ANIMALS 754 (Sept. 30, 2019), https://www.mdpi.com/2076-2615/9/10/754. In the United States, the principles behind the Three Rs were introduced in 1985 is an amendment to the Animal Welfare Act (AWA). Food Security Act, Pub. L. No. 99-198 (1985). Further, the Three Rs are contained in the *Guide for the Care and Use of Laboratory Animals*. THE NATIONAL RESEARCH COUNCIL, COMMITTEE FOR THE UPDATE OF THE GUIDE FOR THE CARE AND USE OF LABORATORY ANIMALS, GUIDE FOR THE CARE AND USE OF LABORATORY ANIMALS (8th ed. 2011), https://grants.nih.gov/grants/olaw/guide-for-the-care-and-use-of-laboratory-animals.pdf [hereinafter NATIONAL RESEARCH COUNCIL GUIDE]. *See* Courtney G. Lee, *The Animal Welfare Act at Fifty: Problems and Possibilities in Animal Testing Regulation*, 95 NEB. L. REV. 194 (2016), https://digitalcommons.unl.edu/nlr/vol95/iss1/6; Gilly Griffin & Paul Locke, *Comparison of the Canadian and US Laws, Regulations, Policies, and Systems of Oversight for Animals in Research*, 57(3) ILAR J. 271 (2016), https://doi.org/10.1093/ilar/ilw037.

[2] The Humane and Existing Alternatives to Animals in Research and Sciences (HEARTS) Act, H.R. 1024 118th Cong. (2023-2024).

[3] *See* NATIONAL RESEARCH COUNCIL GUIDE, *supra* note 1, at 1.

[4] Hubrecht & Carter, *supra* note 1, at 754–55.

[5] Martin Stephens & Nina Mak, *History of the 3Rs in Toxicity Testing: From Russell and Burch to 21st Century Toxicology*, 19 REDUCING, REFINING AND REPLACING THE USE OF ANIMALS IN TOXICITY TESTING 1 (2013), https://www.wellbeingintlstudiesrepository.org/cgi/viewcontent.cgi?article=1000&context=humsmov.

research and regulatory testing. Modern and more human-relevant methods include sophisticated two- and three-dimensional cell-based methods, microphysiological systems (also called "organs on a chip"), computer modeling and simulation, and human tissue studies. These options can advance science and spare animal lives while more effectively protecting human health, the environment, and the economy.

Although U.S. law is based on the principles of the Three Rs,[6] there is no legal obligation to apply any of them.[7] There are also barriers that act as obstacles to achieving the 1st R (replacement), including lack of funding, shortcomings in existing law governing how research projects are funded, and outdated regulatory requirements have been cited as obstacles to achieving the 1st R (replacement).[8] Moreover, the current legal regime in some cases may discourage replacement—if not prevent it—where regulations may require the use of animal methods even when more effective replacement alternatives exist. 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.[9]

The human health and environmental advantages of moving toward replacement of animal tests have been acknowledged by U.S. institutions and agencies. In 2007, the National Academies called for the Environmental Protection Agency (EPA) to shift from animal testing to alternatives:[10] "Today, toxicological evaluation of chemicals is poised to take advantage of the on-going revolution in biology and biotechnology. This revolution is making it increasingly possible to study the effects of chemicals using cells, cellular components, and tissues—preferably of human origin—rather than whole animals."[11] In 2020, the EPA announced that it was committed to fully ending all requirements for, and funding of, testing on mammals by 2035—with a 30 percent reduction of both by 2025.[12]

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[6] Health Research Extension Act, Pub. L. No. 99-158 (1985) (codified at 42 U.S.C. §289d) (administered by the US Department of Health and Human Services and directed at facilities using live vertebrate animals in research funded by the U.S. National Institutes of Health and Public Health Service).

[7] *Id*.; *see generally* Griffin & Locke, *supra* note 1.

[8] 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.

[9] 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.

[10] Cheryl Hogue & Jeff Johnson, *Animal Testing Alternatives: Studies Should Focus on Cells, National Research Council Says,* CHEMICAL AND ENGINEERING NEWS (June 18, 2007), https://cen.acs.org/articles/85/i25/Animal-Testing-Alternatives.html.

[11] THE NATIONAL ACADEMIES, TOXICITY TESTING IN THE 21ST CENTURY: A VISION AND STRATEGY (2007) (Report in brief prepared by the National Research Council based on the committee's report), https://nap.nationalacademies.org/resource/11970/Toxicity_Testing_final.pdf.

[12] Memorandum from EPA Administrator Andrew Wheeler on Directive to Prioritize Efforts to Reduce Animal Testing (Sept. 10, 2019), https://www.epa.gov/sites/default/files/2019-09/documents/image2019-09-09-231249.pdf [hereinafter Wheeler Memorandum]. In a 2021 update, the EPA removed mentions of the

In writing about organ-on-a-chip technologies,[13] Dr. Francis Collins, former Director of the National Institutes of Health (NIH), said, "What makes advances like this especially important is that only 1 in 10 drug candidates entering human clinical trials ultimately receives approval from the Food and Drug Administration (FDA). Often, drug candidates fail because they prove toxic to the human brain, liver, kidneys, or other organs in ways that preclinical studies in animals didn't predict." Dr. Collins has postulated that organ-on-a-chip technologies will soon, "mostly replace animal testing for drug toxicity . . . giving results that are more accurate, at lower cost and with higher throughput."[14]

Promoting ABA Goals

This Resolution urges the ABA to join the institutions that have recognized the human health and environmental benefits of replacement alternatives and that have urged Congress to prioritize and invest in the development and use of methods that replace the use of animals in research and testing and to remove barriers to, and create incentives for, the use of non-animal research and testing methods in regulatory decision-making and federally sponsored research. In doing so, this Resolution promotes ABA Goal IV to "advance the rule of law" by "work[ing] for just laws."[15] Further, the Resolution furthers ABA Goal I, which includes "promot[ing] members' . . . quality of life." The Resolution also furthers one of the ABA's constitutional purposes, "to apply the knowledge and experience of the profession to the promotion of the public good."[16]

Encouraging the replacement of animal-based research and testing with scientifically suitable, cost-effective, and humane non-animal methods promotes just laws and the public good. The congressional findings on the 1985 amendment to the Animal Welfare Act (AWA) stated in part:

> (2) methods of testing that do not use animals are being and continue to be developed which are faster, less expensive, and more accurate than traditional animal experiments for some purposes and further opportunities exist for the development of these methods of testing; (3) measures which

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deadlines set by Wheeler but reiterated that reducing animal testing is an important goal. The update also expanded test species covered to include all vertebrates. *See EPA New Approach Methods Work Plan: Reducing the Use of Vertebrate Animals in Chemical Testing*, U.S. ENVIRONMENTAL PROTECTION AGENCY, https://www.epa.gov/chemical-research/epa-new-approach-methods-work-plan-reducing-use-vertebrate-animals-chemical (last updated Apr. 12, 2023).

[13] Oliver Wainwright, *The End of Animal Testing? Human-Organs-on-Chips Win Design of the Year,* GUARDIAN (June 22, 2015), https://www.theguardian.com/artanddesign/2015/jun/22/the-end-of-animal-testing-human-organs-on-chips-win-design-of-the-year.

[14] Hearing on FY2017 National Institutes of Health Budget Request before the S. Comm. on Appropriations (Apr. 7, 2016) (Statement of Francis Collins), https://www.appropriations.senate.gov/hearings/hearing-on-fy2017-national-institutes-of-health-budget-request.

[15] *ABA Mission and Goals*, AMERICAN BAR ASSOC, https://www.americanbar.org/about_the_aba/aba-mission-goals/#:~:text=Objectives%3A,service%20by%20the%20legal%20profession.

[16] American Bar Association, *Constitution and Bylaws: Rules of Procedure House of Delegates* (2022), *available at* https://www.americanbar.org/groups/leadership/house_of_delegates/aba-constitution-and-bylaws/.

> eliminate or minimize the unnecessary duplication of experiments on animals can result in more productive use of Federal funds; and (4) measures which help meet the public concern for laboratory animal care and treatment are important in assuring that research will continue to progress.[17]

The report sets out below a brief overview of the benefits of an increased focus on human-relevant replacement alternatives to public health, the environment, and animal wellbeing, and the need for this Resolution given the shortcomings of existing laws and regulations to promote the development and use of replacement alternatives.

Advancing Human Health, the Environment, and Animal Wellbeing

Now, perhaps more than ever, it is vital for humanity to consider the quality and ethical basis of science and prioritize the development of progressive replacement alternatives that benefit human health, the environment, and animal wellbeing.

Twenty-first century scientific and technological advancements have made the goal of replacement a possibility. Modern human-based approaches promise to deliver new medicines, vaccines, and safer chemicals that can better protect human health and the environment and minimize harm to animals.[18]

Replacement alternatives are revolutionizing science through an innovative and diverse array of ground-breaking technology in all areas of research. Examples include:

- Product safety: While skin allergy tests in guinea pigs only predict human reactions 72% of the time, a combination of chemistry and cell-based alternative methods has been shown to accurately predict human reactions 90% of the time.[19]
- Chemical safety: Carcinogenicity tests on animals are notoriously unreliable with an estimated prediction of human cancers of only 42%.[20] But a combination of human cell-based tests can detect 90-95% of human carcinogens.[21]

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[17] Food Security Act of 1985, Pub. L. 99–198, §1751, 99 Stat. 1645 (Dec. 23, 1985).
[18] Kathrin Herrmann, *Refinement on the Way Towards Replacement: Are We Doing What We Can?, in* ANIMAL EXPERIMENTATION, *supra* note 8, at 3–64.
[19] Caroline Bauch et al., *Intralaboratory Validation of Four In Vitro Assays for the Prediction of the Skin Sensitizing Potential of Chemicals*, 25 TOXICOLOGY IN VITRO 1162 (2011), https://pubmed.ncbi.nlm.nih.gov/21669280/.
[20] Andrew Knight et al., *For and Against Which Drugs Cause Cancer?* BMJ, 5, 477 (2005) https://www.wellbeingintlstudiesrepository.org/cgi/viewcontent.cgi?article=1002&context=acwp_arte.
[21] Paule Vasseur,& Claude Lasne OECD Detailed Review Paper (DRP) number 31 on *Cell Transformation Assays for Detection of Chemical Carcinogens": Main Results and Conclusions, Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, Vol. 744, Issue 1, 11 April (2012), pp. 8–11:https://www.sciencedirect.com/science/article/abs/pii/S1383571811003408?via%3Dihub; Romualdo Benigni et al., *In Vitro Cell Transformation Assays for an Integrated, Alternative Assessment of Carcinogenicity: A Data-Based Analysis, Mutagenesis*, Volume 28, Issue 1, Jan. 2013, Pages 107–116, https://academic.oup.com/mutage/article/28/1/107/1265414.

- Drug development: "Organs-on-a-chip"[22] accurately mimic human heart, kidney, lungs, and gut.[23]

- Neuroscience: Advances in functional magnetic resonance imaging (fMRI) and neuronal activity recording techniques, such as electrocorticography and single-unit recordings, can replace tests on non-human primates.[24] These offer significant welfare advantages over non-human primate neuroscience experiments which can involve many invasive and stressful methods, including intracranial electrodes, various restraint and training techniques, and water deprivation.[25]

- Alzheimer's research: Despite years of attempting to mimic Alzheimer's symptoms in animals, no animal experiment has been able to reflect all the features of this complex human condition and most Alzheimer's disease drugs fail in human trials despite promising results reported in the preceding animal tests. A recent review found the overall failure rate for 244 drugs in 413 trials in the decade between 2002 and 2012 was 99.6%.[26] Non-animal approaches could lead to better results. Computer models using a combination of already available data, mathematical modelling, and system analysis can be used to study the origin and progression of Alzheimer's disease. Researchers at Weill Cornell Medical College have developed a computer program that can help predict how dementia spreads through the brain to predict patterns and determine whether a potential therapy is effective.[27]

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[22] Theodor Wilson, *Scientists Create 'Human on a Chip' Using Miniature Organs as a Cutting-Edge Way to Test Latest Drugs*, MIRROR (July 7, 2016, 4:09 PM), http://www.mirror.co.uk/tech/scientists-create-human-chip-using-8364231.

[23] *Airway-on-a-Chip: Speeding Up COVID-19 Treatment Testing*, NIH COVID-19 RES. (Oct. 15, 2021), https://covid19.nih.gov/news-and-stories/airway-on-a-chip; Wainwright, *supra* note 13.

[24] Jarrod Bailey & Katy Taylor, *Non-Human Primates in Neuroscience Research: The Case Against Its Scientific Necessity*, 44 ATLA 43 (2016), https://crueltyfreeinternational.org/sites/default/files/2021-10/Bailey_Taylor_primate%20neuroscience_ATLA_2016.pdf; Duke Univ. Med. Cntr, *Alzheimer's Plaques in PET Brain Scans Identify Future Cognitive Decline*, SCIENCE DAILY (July 11, 2012), https://www.sciencedaily.com/releases/2012/07/120711210100.htm.

[25] John Pickard et al., REVIEW OF THE ASSESSMENT OF CUMULATIVE SEVERITY AND LIFETIME EXPERIENCE IN NON-HUMAN PRIMATES USED IN NEUROSCIENCE RSCH. (2013), https://www.researchgate.net/publication/271726082_Review_of_the_assessment_of_cumulative_severity_and_lifetime_experience_in_non-human_primates_used_in_neuroscience_research.

[26] Jeffrey L. Cummings et al., *Alzheimer's Disease Drug-Development Pipeline: Few Candidates, Frequent Failures*, 6 ALZHEIMER'S RES. & THER. 37 (2014), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4095696/; Enrica Alteri & Lorenzo Guizzaro, *Be Open About Drug Failures to Speed Up Research,* 13 NATURE (2018), https://www.nature.com/articles/d41586-018-07352-7.

[27] Weill Cornell Medicine, *Computer Model of Spread of Dementia Can Predict Future Disease Patterns Years Before They Occur in a Patient*, CORNELL (Mar. 21, 2012), https://news.weill.cornell.edu/news/2012/03/computer-model-of-spread-of-dementia-can-predict-future-disease-patterns-years-before-they-occur-in.

Human Health

There is growing awareness of the artificiality of animal models of human diseases[28] and the limitations of animal models to make reliable predictions for humans due to differences among species,[29] even between other primates and humans.[30] Analyses indicate that animal studies are often poorly designed[31] and irreproducible[32] and that published findings are frequently exaggerated in the media.[33] A few statistics that illustrate the magnitude of the human/animal translation problem include:

- A review of 101 high impact basic science discoveries based on animal experiments found that only 5% resulted in approved treatments within 20 years.[34]
- 92% of drug candidates fail in clinical trials despite showing promise in pre-clinical tests, including in animal experiments.[35] As previously noted, the failure rate for Alzheimer's drugs is estimated to be higher than 99% as previously noted.[36]
- Other areas with low success rates include urology drugs (only 3.6% approved after entering clinical trials), heart drugs (4.8% success rate), cancer drugs (5.3% success rate), and neurology drugs (5.9% success rate).[37]

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[28] Aysha Akhtar, *The Flaws and Human Harms of Animal Experimentation*, 24 CAMBRIDGE Q. HEALTHCARE ETHICS 407 (2015), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4594046/.

[29] 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/.

[30] Jarrod Bailey, *Monkey-Based Research on Human Disease: The Implications of Genetic Differences*, 42 ALT. LAB'Y. ANIMAL 287 (2014), https://pubmed.ncbi.nlm.nih.gov/25413291/; Bailey & Taylor, *supra* note 24; Bailey et al., *supra* note 29.

[31] Malcom R. Macleod et al., *Risk of Bias in Reports of In Vivo Research*, PLOS BIOLOGY (Oct. 13, 2015), https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1002273.

[32] Bernhard Voelkl et al., Reproducibility of Animal Research in Light of Biological Variation, NATURE REVIEWS NEUROSCIENCE, 21(7), 384–393, (2020), https://www.nature.com/articles/s41583-020-0313-3; Francis S. Collins & Lawrence A. Tabak, *Policy: NIH Plans to Enhance Reproducibility*, 505 NATURE 7485 (2014), https://pubmed.ncbi.nlm.nih.gov/24482835/; John P. A. Loannidis, *Extrapolating from Animals to Humans*, 4 Sci. TRANSLATIONAL MED. 151 (2012), http://stm.sciencemag.org/content/4/151/151ps15.full; Pound & Bracken, *supra* note 29; Eric Brock. *Much Biomedical Research is Wasted Argues Bracken,* NIH RECORD*,* https://nihrecord.nih.gov/2016/07/01/much-biomedical-research-wasted-argues-bracken.

[33] R.J. Wall & M. Shani, *Are Animal Models as Good as We Think?*, 69 THERIOGENOLOGY 2 (2008), https://pubmed.ncbi.nlm.nih.gov/17988725/; Petroc Sumner et al., *The Association Between Exaggeration in Health-Related Science News and Academic Press Releases*, 349 BMJ 7015 (2014), https://www.bmj.com/content/349/bmj.g7015.

[34] Despina G. Contopoulous-Ioannidis et al., *Translation of Highly Promising Basic Research into Clinical Applications*, 114 AM. J. OF MED. 477 (2003), https://pubmed.ncbi.nlm.nih.gov/12731504/.

[35] Biotechnology Innovation Organization, *Clinical Development Success Rates and Contributing Factors 2011–2020*, https://go.bio.org/rs/490-EHZ-999/images/ClinicalDevelopmentSuccessRates2011_2020.pdf.

[36] Cummings et al., *supra* note 26.

[37] Biotechnology Innovation Organization. *supra* note 35.

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In its most recent five-year strategic plan, the NIH stated: "Petri dish and animal models often fail to provide good ways to mimic disease or predict how drugs will work in humans, resulting in much wasted time and money while patients wait for therapies."[38] The NIH has also noted that "[a]pproximately 30 percent of promising medications have failed in human clinical trials because they are determined to be toxic—despite promising pre-clinical studies in animal and cell models."[39] It has been estimated that adverse drug reactions (ADR) kill more than 100,000 people in the United States each year—making ADRs the 4th leading cause of death, ahead of pulmonary disease, diabetes, AIDS, pneumonia, accidents, and automobile deaths.[40] A recent analysis found that, out of 93 ADRs, only 19% could have been predicted by animal tests.[41]

Even more troubling is the likelihood that many drugs abandoned based on animal tests may have worked effectively in humans. Candidate drugs generally proceed down the development pipeline to human testing based primarily on successful results in animals.[42] Of every 5,000–10,000 potential drugs investigated, only about five proceed to Phase 1 clinical trials.[43] It has been demonstrated that animal tests can be unsuccessful in modelling human diseases adequately and can provide highly misleading information. For example, cyclosporine, a drug widely and successfully used to treat autoimmune disorders and prevent organ transplant rejection, was delayed because of animal tests.[44]

Shortcomings of animal tests have long been recognized by the pharmaceutical industry, which has responded by increasing research and investment in new human-relevant technologies in recent years. A recent review, *"Animal Testing and Its Alternatives—The Most Important Omics Is Economics,"* reports that, "an economy of alternative approaches has developed that is outperforming traditional animal testing."[45] Ensuring that cutting-edge technologies that can replace animal tests and better predict human response are accepted and used whenever available will allow companies to realize a

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[38] NIH-WIDE STRATEGIC PLAN: FISCAL YEARS 2016-2020: TURNING DISCOVERY INTO HEALTH, NATIONAL INST. OF HEALTH (2015), https://www.nih.gov/sites/default/files/about-nih/strategic-plan-fy2016-2020-508.pdf.
[39] *Tissue Chip for Drug Screening*, NATIONAL INST. OF HEALTH, https://ncats.nih.gov/tissuechip.
[40] *Preventable Adverse Drug Reactions: A Focus on Drug Interactions. ADRs: Prevalence and incidence*, FOOD AND DRUG ADMIN. (2019), https://www.fda.gov/drugs/drug-interactions-labeling/preventable-adverse-drug-reactions-focus-drug-interactions#ADRs:%20Prevalence%20and%20Incidence.
[41] Peter van Meer et al., *The Ability of Animal Studies to Detect Serious Post Marketing Adverse Events is Limited*, 64 REGULATORY TOXICOLOGY & PHARMACOLOGY, 345–49 (Dec. 2012).
[42] Ingrid Torjesen, *Drug Development: The Journey of a Medicine from Lab to Shelf.* THE PHARMACEUTICAL JOURNAL (May 12, 2015) https://www.pharmaceutical-journal.com/publications/tomorrows-pharmacist/drug-development-the-journey-of-a-medicine-from-lab-to-shelf/20068196.article?firstPass=false
[43] Sandra Kraljevic et al., *Accelerating Drug Discovery*, 5(9) EMBO REP. 837-42 (Sep. 2004); Jesse A. Berlin et al. *Adverse Event Detection in Drug Development: Recommendations and Obligations Beyond Phase 3.* 98(8) AMERICAN JOURNAL OF PUBLIC HEALTH 1366-1371 (Aug. 2008): https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2446471/.
[44] Akhtar, *supra* note 28.
[45] Lucy Meigs, et al., *Animal Testing and Its Alternatives—The Most Important Omics is Economics*, 35 ALTEX 275, 280 (2018), https://www.altex.org/index.php/altex/article/view/1134/1131.

return on their investment and deliver safer, more effective medicines—saving both human and animal lives.

Finally, the use of animal tests may not only waste time but also money. On average, it takes 10-15 years to develop a new drug.[46] The cost to bring a new drug to market is $1 to $6 billion, which is passed on to consumers in the form of high prices.[47] The unreliability of animal tests results in many of these drugs ultimately failing. In sum, the shortcomings in animal testing contribute to human suffering by failing to predict serious adverse events in humans, creating missed opportunities in treatments, increasing the wastage of time, money, and other resources, and further elevating already high drug costs.

The Environment

The need for ethical, accurate, and economical safety assessment procedures grows in parallel with the number of new chemicals introduced yearly into our environment by the pharmaceutical, cosmetics, and chemical industries. Global chemical production is expected to double by 2030.[48] In order to keep pace and limit adverse impacts, faster and more reliable toxicity tests are needed. Indeed, as Andrew Wheeler, former Administrator of the EPA, stated in his 2019 memo to the agency:

> Animal testing is expensive and time-consuming. The agency must develop more accurate, quicker, and more cost-effective test methods if it is to meet the 21st century commitments. We must make that investment now. Through scientific innovation and strategic partnerships, we can protect human health and the environment by using cutting-edge, ethically sound science in our decision-making that efficiently and cost effectively evaluates potential effects without animal testing.[49]

There is broad agreement in the public, private, and non-profit sectors on the importance of accelerating the development non-animal testing methods for hazard risk assessments.[50] The application of vetted, low-cost, high throughput non-animal methods can strengthen environmental protections by allowing for more rapid assessment of new and existing chemicals and chemical mixtures and can allow for faster removal of

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[46] S. Marchetti & JHM Schellens, *The Impact of FDA and EMEA Guidelines on Drug Development in Relation to Phase 0 Trials.* BR J CANCER, 97(5): 577581 (2007). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2360360/.

[47] Jonathan Gardner, *New Estimate Puts Cost to Develop a New Drug at $1B, Adding to Long-running Debate*, BIOPHARMADIVE (Mar. 3, 2020), https://www.biopharmadive.com/news/new-drug-cost-research-development-market-jama-study/573381/.

[48] U.N. ENVIRONMENTAL PROGRAMME, GLOBAL CHEMICALS OUTLOOK II: FROM LEGACIES TO INNOVATIVE SOLUTIONS (Mar. 11, 2019), https://www.unep.org/resources/report/global-chemicals-outlook-ii-legacies-innovative-solutions.

[49] Wheeler Memorandum, *supra* note 12.

[50] Melvin E. Andersen et al., *Developing Context Appropriate Toxicity Testing Approaches Using New Alternative Methods (NAMs)*, 36 ALTEX 523–34 (2019).

hazardous chemicals from the market and prevent new ones from reaching the market in the first place.[51]

Moreover, animal research itself has direct negative environmental impacts. For example, a 2014 study catalogued the environmental harms of use of animals in research, including pollution and toxins from the incineration and disposal of animal carcasses and tissues, resources used for maintaining animals (e.g., specialized ventilation and bedding), and chemicals used for maintaining animals (e.g., cleaning). The study also noted the harmful biodiversity impacts of illegal capture of wild animals; for example, the long-tailed macaque—one of the most used primates in research—is declining in the wild.[52]

Animal Wellbeing

Every year an estimated 192.1 million animals are used in experiments around the world, with the United States estimated to be among the world's largest users.[53] According to an analysis of U.S. Department of Agriculture (USDA) data, a total of 712,683 animals were used in U.S. research in 2021, including 71,921 primates, 44,847 dogs, and 12,595 cats—a 6% *increase* in total animals used compared to 2020. Moreover, 70,161 (10%) of those animals were used in experiments for which no pain relief was provided.[54]

These USDA statistics, reported under the AWA, do not account for every animal used in research and testing because birds, rats, and mice who are bred for research purposes are not included in the definition of "animal" under the AWA.[55] As a result, the true number of animals used annually in U.S. laboratories is unknown, with estimates ranging from at least 14 million[56] to over 100 million.[57]

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[51] *NIH Collaborates with EPA to Improve the Safety Testing of Chemicals*: *New Strategy Aims to Reduce Reliance on Animal Testing,* NATIONAL INSTITUTES OF HEALTH https://www.nih.gov/news-events/news-releases/nih-collaborates-epa-improve-safety-testing-chemicals (February 14 2008); Andreas O. Stucki et al*., Use of New Approach Methodologies (NAMs) to Meet Regulatory Requirements for the Assessment of Industrial Chemicals and Pesticides for Effects on Human Health*, 4 FRONT TOXICOL. (Sept.1, 2022).

[52] Katherine Groff et al., *Review of Evidence of Environmental Impacts of Animal Research and Testing*, 1 ENV'T 14 (2014); *see also* Phoebe Weston, *$20,000 Monkeys: Inside the Booming Illicit Trade for Lab Animals*, GUARDIAN (Dec. 7, 2023), https://www.theguardian.com/environment/2023/dec/07/how-the-demand-for-lab-monkeys-is-driving-trade-in-endangered-macaques-aoe.

[53] Katy Taylor & Laura Rego Alvarez, *An Estimate of the Number of Animals Used for Scientific Purposes Worldwide in 2015*, 47 ATLA196 (2019), https://journals.sagepub.com/doi/pdf/10.1177/0261192919899853.

[54] *Number of Animals Used in Experiments in the U.S. in 2021 Rises by 6%.* Cruelty Free International https://crueltyfreeinternational.org/USDA (Feb 24, 2023);U.S. Dept. Of Agriculture, Research Facility Annual Summary Archive Reports, https://www.aphis.usda.gov/aphis/ourfocus/animalwelfare/sa_obtain_research_facility_annual_report/ct_research_facility_annual_summary_reports (last modified Oct. 25, 2022).

[55] 7 U.S.C. § 2132(g).

[56] Taylor & Alvarez, *supra* note 53.

[57] Larry Carbone, *Estimating Mouse and Rat Use in American Laboratories by Extrapolation from Animal Welfare Act-Regulated Species,* SCIENTIFIC REPORT 493 (2021), https://doi.org/10.1038/s41598-020-79961-0 (estimating that 111.5 million mice and rats are used in research and testing annually in the United States.).

Animals used in a laboratory setting experience stress and distress due to their confinement in environments that restrict or limit their natural behavior as well as from experiment or testing protocols.[58] Animals used in research or testing will, in most cases, experience fear, pain, disease, or surgery, and will be killed.[59]

Federal Requirements Impacting the Use of Animals in Research and Testing

There are three general types of federal requirements that impact the use of animals in regulatory testing and research and, by extension, the use or exclusion of replacement alternatives: 1) laws (or acts), 2) regulations, and 3) agency policies or guidelines.[60]

The AWA[61] and the Health Research Extension Act of 1985 (HREA)[62] together provide the bulk of regulatory coverage of vertebrate non-human animals used in research. The AWA gives authority to the USDA to promulgate regulations, inspect facilities, and enforce noncompliance. The HREA (an amendment to the Public Health Services Act) applies to any institution receiving monies from the Public Health Service.[63]

Regulatory agencies such as the EPA and the FDA also impact the use of animals in research and testing because they have animal testing requirements incorporated into their regulations, which have the force of law.[64] Guidance documents issued by agencies are non-binding but can be impactful because they signal testing expectations to regulated entities.[65]

The Need for Legislative and Regulatory Action to Advance Replacement Alternatives

The existing legal framework does not adequately encourage the use of replacement alternatives. At the statutory level, the AWA and the Public Health Services Act (through the HREA) establish Institutional Animal Care and Use Committees (IACUCs), i.e., committees at research facilities responsible for ensuring compliance with the AWA, the *Guide for the Care and Use of Laboratory Animals*, and the *Public Health Service Policy on Humane Care and Use of Laboratory Animals* (the *PHS policy*).[66] IACUCs are tasked

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[58] Jarrod Bailey, *Does the Stress of Laboratory Life and Experimentation on Animals Adversely Affect Research Data? A Critical Review*, 46 ALTA 291 (2018), https://pubmed.ncbi.nlm.nih.gov/30488713/.
[59] Bernard E. Rollin, *Animal Research: A Moral Science. Talking Point on the Use of Animals in Scientific Research*, 8(6) EMBO REPTS. 521–25 (2007), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2002540/.
[60] Mary Ann Vasbinder & Paul Locke, *Introduction: Global Laws, Regulations, and Standards for Animals in Research*, ILAR JOURNAL, Volume 57, Issue 3, 2016, pp. 261–65, https://doi.org/10.1093/ilar/ilw039.
[61] The Animal Welfare Act (US Code, title 7, chapter 54) of 1966 as amended in 1970, 1976, 1985, 1990.
[62] The Health Research Extension Act of 1985 (HREA) (Public Law 99-158) amended the Public Health Service Act (42 USC 201) and calls for the proper care and treatment of animals (including proper veterinary medical support and nursing care); and the organization and operation of animal care and use committees. The HREA covers the use of *all* live vertebrates and delegates oversight to the Office of Laboratory Animal Welfare, National Institutes of Health.
[63] Vasbinder and Locke, *supra* note 60.
[64] Marchant, *supra* note 8.
[65] FOOD AND DRUG ADMINISTRATION; GUIDANCES (Jan. 24, 2022), https://www.fda.gov/industry/fda-basics-industry/guidances.
[66] 9 CFR § 2.31 - Institutional Animal Care and Use Committee (IACUC).

with reviewing proposed animal experiments to ensure that researchers *consider* alternatives to animal use in painful procedures and that they do not unnecessarily duplicate previous experiments.[67] Investigators and IACUCs use literature searches on alternatives to document and demonstrate that alternatives to procedures that cause more than momentary pain or distress have been considered.[68] However, Office of Inspector General reports note repeated failures to search for alternatives to painful procedures and to document the availability of alternatives in research proposals.[69] Some who have served on laboratory oversight committees have echoed concern that researchers often fail to perform adequate searches for replacement alternatives or are unfamiliar with their efficacy.[70]

One reason for these failures is that the AWA merely requires that researchers *consider* alternatives and only for procedures that induce pain.[71] 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.[72] These provisions have been identified as critical shortcomings in the law.[73] As Matthew Scully, former literary editor of National Review and senior speechwriter to President George W. Bush, observed:

> We would all like laws telling us what we must "consider" doing, but it doesn't work that way. The law makes a clear finding of fact and on that basis determines the standard of acceptable practice. Here, the fact is real and conscious pain by animal subjects. And here the standard—not the option—must be utter necessity and nothing less.[74]

Despite available replacement alternatives, the continued use of animals appears to be related not only to a failure to thoroughly search for alternatives but also an adherence to older, more familiar methods. A 2020 National Academies of Sciences study about the use of dogs in research at the U.S. Department of Veterans Affairs concluded that many investigators cited their experience using dogs and the historical data available in dog models as justification for using dogs in further testing. The study noted, however, that

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[67] *Id.*

[68] *Literature Searching: How to Find Animal Use Alternatives*, USDA NATIONAL AGRICULTURAL LIB., https://www.nal.usda.gov/legacy/awic/alternatives-literature-searching.

[69] *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; *Animal and Plant Health Inspection Service Oversight of Research Facilities*, USDA OFF. INSPECTOR GENERAL (2014), https://www.peta.org/wp-content/uploads/2022/07/2014-USDA-OIG-Audit-of-APHIS-Enforcement-of-AWA.pdf.

[70] JOHN P. GLUCK, VORACIOUS SCIENCE AND VULNERABLE ANIMALS: A PRIMATE SCIENTIST'S ETHICAL JOURNEY (2016).

[71] 7 U.S.C. § 2143(a)(3)(B); 9 C.F.R. § 2.31 (d).

[72] *Literature Searching: How to Find Animal Use Alternatives*, *supra* note 68.

[73] *See generally* Lee, *supra* note 1; GLUCK, *supra* note 70.

[74] MATTHEW SCULLY, DOMINION: THE POWER OF MAN, THE SUFFERING OF ANIMALS, AND THE CALL TO MERCY (2003).

such justifications, "are insufficient alone and constitute a form of circular reasoning that perpetuates the use of laboratory dogs without adequate examination of alternatives."[75]

Legislative efforts have attempted to remedy these shortcomings at least partially. For example, the bipartisan Humane and Existing Alternatives in Research and Testing Sciences (HEARTS) Act (H.R. 1024, 118th Cong.) targets specific shortcomings in existing law that govern NIH-funded research proposals.[76] The HEARTS Act would help advance replacement alternatives by amending the HREA and directing the NIH to provide incentives to researchers to use replacement alternatives whenever feasible and applicable. Further, it would require: (1) the NIH to "establish and maintain research proposal guidelines for conducting thorough searches for non-animal alternatives to the use of animals for biomedical and behavioral research"; (2) that proposal reviewers have access to a reference librarian with expertise in evaluating the adequacy of the search methods described in the protocol; and (3) that proposals be reviewed by at least one person with expertise in non-animal research methods.[77]

Additionally, the HEARTS Act aims to accelerate the use of replacement alternatives in science by providing additional funding for the research and development of new replacement alternatives. [78] The Act would establish the "National Center for Alternatives to Animal Research and Testing" within the NIH.[79] It would also require federal agencies or departments and federally funded research entities using animals for research and testing to report the number of animals that they use to the Center and to develop plans to reduce the use of animals in their activities.[80]

A majority of the public agree that replacement alternatives should be used whenever available. According to a 2019 nationwide poll, 79% of voters said that "the NIH should prioritize funding research proposals that use scientifically valid alternatives to animal testing" and 80% said that medical researchers seeking funding for animal tests should first be required to show that an alternative is not available.[81]

Prioritizing the use of replacement alternatives in federally funded research as well as establishing new funding to further develop alternatives could improve the cost efficacy of federal research investment and foster innovation in science—leading to better therapies to treat human conditions and sparing animal lives.

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[75] COMMITTEE ON ASSESSMENT OF THE USE AND CARE OF DOGS IN BIOMEDICAL RESEARCH, NECESSITY, USE, AND CARE OF LABORATORY DOGS AT THE U.S. DEPARTMENT OF VETERANS AFFAIRS (National Academies of Sciences, Engineering, and Medicine, 2020), https://www.nap.edu/read/25772/chapter/2.

[76] HEARTS Act, H.R. 1024 118th Cong. (2023–2024).

[77] *Id.*

[78] *Id.*

[79] *Id.*

[80] *Id.*

[81] Cruelty Free International, *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.

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At the regulatory level, replacement alternatives could be advanced by updating regulations and guidance documents to eliminate the requirement of animal tests where possible and to make clear that replacement alternatives can and should be used when possible. Otherwise, regulated entities may either be required to conduct unnecessary animal tests or may voluntarily conduct them because the tests are viewed as the most secure route to approval.[82] To achieve this, the FDA should update its existing regulations and accompanying guidance documents to make clear that regulated entities may utilize modern technologies that better mimic human response.

Drug approval procedures may require preclinical animal testing, yet animal tests often fail to predict safety and efficacy in humans.[83] Better human-centered testing would save much time and money for patients and industry alike. As an example, in 2019, Vanda Pharmaceuticals filed suit against the FDA arguing that the FDA's request for chronic non-rodent toxicity data and decision to impose a partial clinical hold on tradipitant, a drug being studied as a treatment for idiopathic and diabetic gastroparesis, lacked an articulated scientific basis.[84] In an open letter, the company pointed out:

> It is striking that over the past two decades, advances in technology have revolutionized drug development, but the FDA has not revisited its approach to animal toxicity studies. The toxicity studies required by the FDA are the same in 2019 as they were in 1997 and the FDA's stated basis for its policy is an analysis published in 1999, which did not reach any conclusion as to the potential human significance of any toxicological findings identified in longer-term studies.[85]

To remain a competitive global leader in science research and innovation, deliver safer products and treatments, and confront twenty-first century challenges, the use, funding, and development of human-specific, replacement alternatives must be prioritized. The scientific literature is now replete with calls to transition to more predictive and more human-relevant approaches as a matter of urgency.[86]

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[82] Marchant, *supra* note 8; Lee, *supra* note 1.

[83] Gary Michelson and Aysha Akhtar, *Finding Cures Faster: Bring The FDA into the 21st Century with Advanced Testing,* STAT (Mar. 4, 2022), https://www.statnews.com/2022/03/04/fda-animal-testing-rule-needs-update/#:~:text=The%201938%20Federal%20Food%2C%20Drug,have%20been%20developed%20since%20then.%20%20%20.

[84] Alex Gangitano, *Drugmaker Challenges FDA on Animal Testing*, THE HILL (June 27, 2019), https://thehill.com/regulation/court-battles/450551-drugmaker-challenges-fda-on-animal-testing.

[85] Open Letter from Vanda Pharm. to the Food and Drug Admin., Vanda Pharmaceuticals Takes a Stand Against Unnecessary Animal Research, https://mma.prnewswire.com/media/818251/open_letter.pdf.

[86] ANIMAL EXPERIMENTATION, *supra* note 8; Paul Locke & D. Bruce Myers, *A Replacement-First Approach to Toxicity Testing Is Necessary to Successfully Reauthorize TSCA*, 28(4) ALTEX - ALTERNATIVES TO ANIMAL EXPERIMENTATION 266 (2011), https://www.altex.org/index.php/altex/article/view/487.

Lessons from Covid-19

The Covid-19 pandemic has highlighted how crucial human-relevant methods are to producing safe and effective medicines as quickly as possible. As scientists struggled to generate data with animals who do not manifest Covid-19 the way humans do, major vaccine companies did not wait for animal efficacy studies to be completed before moving to human trials.[87] Meanwhile, U.S. scientists found the first direct evidence that coronavirus could infect the human brain and replicate inside its cells using miniature human brain-like structures (cerebral organoids) grown in vitro from human stem cells.[88] And, in a promising step forward, the National Centre for Clinical and Translational Sciences began supporting the work of the Wyss Institute for Biologically Inspired Engineering at Harvard University to develop a human airway chip for testing new Covid-19 treatments.[89] Similarly, the FDA entered into a partnership with Emulate, Inc., to evaluate the safety and efficacy of Covid-19 vaccines using a human lung chip.[90]

Global Leadership

To remain a global leader in science, research, and development, the United States must create frameworks to develop and incentivize the use of modern replacement alternatives that prove meaningful for the protection of humans and the environment. Global market forecasts suggest significant business opportunities abound in the development and utilization of replacement alternatives. Global market forecasts project stem cell technologies to reach $25.68 billion by 2028,[91] organs-on-a-chip to reach $1.6 billion by 2030,[92] in vitro toxicity testing to reach $18.6 billion by 2027,[93] and cell-based assays to reach $22 billion by 2025.[94]

Other countries have acknowledged the importance of moving away from animal-based testing. For example, in 2016, the Dutch government announced its plan to phase out

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[87] Eric Boodman, *Researchers Rush to Test Coronavirus Vaccine in People Without Knowing How Well It Works in Animals*, STAT (Mar. 11, 2020), https://www.statnews.com/2020/03/11/researchers-rush-to-start-moderna-coronavirus-vaccine-trial-without-usual-animal-testing/.

[88] Clive Cookson, *Coronavirus Could Infect Human Brain and Replicate, US Study Shows,* FINANCIAL TIMES (June 15, 2020), https://www.ft.com/content/e5f20455-4422-4eea-9c51-b083040a0878.

[89] *Airway-on-a-Chip*, *supra* note 23.

[90] *Emulate Signs Collaborative Agreement with the FDA to Apply Lung-Chip to Evaluate Safety of COVID-19 Vaccines and Protective Immunity Against SARS-CoV-2,* EMULATE, https://emulatebio.com/press/fda-organ-chip-crada-2020/.

[91] STEM CELLS MARKET - GLOBAL INDUSTRY ANALYSIS, SIZE, SHARE, GROWTH, TRENDS, AND FORECAST, 2021-2028, TRANSPARENCY MARKET RESEARCH, https://www.transparencymarketresearch.com/stem-cells-market.html.

[92] ORGAN ON CHIP MARKET BY TYPE; GLOBAL OPPORTUNITY ANALYSIS AND INDUSTRY FORECAST, 2020-2030, ALLIED MARKET RESEARCH (Mar. 2022), https://www.alliedmarketresearch.com/organ-on-chip-market#:~:text=The%20global%20organ%2Don%2Dchip,31.1%25%20from%202021%20to%202030.

[93] IN VITRO TOXICOLOGY TESTING MARKET BY PRODUCT - GLOBAL FORECAST TO 2027, MARKETS AND MARKETS (June 2022), https://www.marketsandmarkets.com/Market-Reports/in-vitro-toxicology-testing-market-209577065.html.

[94] CELL-BASED ASSAYS MARKET BY PRODUCT & SERVICE - GLOBAL FORECAST TO (2022 - 2025), MARKETS AND MARKETS (Mar. 2021), https://www.marketsandmarkets.com/Market-Reports/cell-based-assays-market-119917269.html.

toxicology tests on animals for chemicals, food ingredients, pesticides, veterinary medicines, and vaccines by 2025,[95] and in 2021 the European Parliament passed a resolution to accelerate the transition from the use of animals in research and testing to human-relevant science across the European Union.[96]

If the United States prioritizes innovation in humane and human-relevant technology and provides sufficient resources to support the development and implementation of sophisticated replacement alternatives, it could become the global leader in safe chemical production and in drug development, which would in turn incentivise production in the United States.

Conclusion

Replacing the use of animals in research and testing is an enduring goal dating back at least sixty years.[97] Today, scientific innovation is rapidly offering new research and testing strategies to achieve this goal. Replacement alternatives increasingly have more predictive value and specificity to human conditions than do animal methods, which rely on different species with different anatomies and physiologies. Prioritizing the use of human-relevant replacement alternatives and adequately investing in them will foster innovation in science—which will, in turn, lead to safer products, better-quality medicines, and new tools for confronting future challenges and unexpected emergencies like the COVID-19 pandemic.[98] Encouraging replacement of animal models with modern, human-relevant research and testing methods advances the ABA's mission to work for just laws and to promote members' quality of life.

Respectfully submitted,

Loren D. Podwill, Chair
Tort Trial & Insurance Practice Section

David A. Schwartz, Chair
International Law Section

February 2024

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[95] NCAD OPINION: TRANSITION TO NON-ANIMAL RESEARCH, NETHERLANDS NATIONAL COMMITTEE FOR THE PROTECTION OF ANIMALS USED FOR SCIENTIFIC PURPOSES (Dec. 15, 2016), https://www.ncadierproevenbeleid.nl/documenten/rapport/2016/12/15/ncad-opinion-transition-to-non-animal-research.

[96] *MEPs Demand EU Action Plan to End the Use of Animals in Research and Testing*, NYHETER (Sept. 16, 2021), https://www.europarl.europa.eu/news/sv/press-room/20210910IPR11926/meps-demand-eu-action-plan-to-end-the-use-of-animals-in-research-and-testing.

[97] *See* Hubrecht & Carter, *supra* note 1, at 754–55.

[98] Francois Busquet, et al., *Harnessing the Power of Novel Animal-Free Test Methods for the Development of COVID-19 Drugs and Vaccines*, 94(6) ARCH. TOXICOL. 2263 (May 23, 2020), https://pubmed.ncbi.nlm.nih.gov/32447523/.

GENERAL INFORMATION FORM

Submitting Entities:
Tort Trial & Insurance Practice Section (TIPS)
International Law Section (ILS)
Co-Sponsor: Section of Environment, Energy, and Resources (SEER)

Submitted By: Daina Bray, TIPS Delegate

1. Summary of the Resolution(s).

   This Resolution urges national governments, the U.S. Congress, and U.S. federal agencies to prioritize and invest in the development and use of methods that replace the use of animals in research and testing and to remove barriers to, and create incentives for, the use of non-animal research and testing methods in regulatory decision-making and federally sponsored research.

2. Indicate which of the ABA's Four goals the Resolution seeks to advance (1-Serve our Members; 2-Improve our Profession; 3-Eliminate Bias and Enhance Diversity; 4-Advance the Rule of Law) and provide an explanation on how it accomplishes this.

   This Resolution promotes ABA Goal IV to "advance the rule of law" by "work[ing] for just laws." By this Resolution, the ABA would join the institutions that have recognized the human health, environmental, and animal welfare benefits of replacement alternatives for the use of animals in research and testing.

   The Resolution advances ABA Goal I, which includes "promot[ing] members' . . . quality of life." The Resolution also furthers one of the ABA's constitutional purposes, "to apply the knowledge and experience of the profession to the promotion of the public good." Encouraging the replacement of animal-based research and testing with scientifically suitable, cost-effective, environmentally-friendly, and humane non-animal methods promotes just laws and the public good.

3. Approval by Submitting Entity.

   TIPS Council voted to approve this Resolution at its meeting held on October 12, 2023, and ILS Council voted to approve it at its meeting held on November 6, 2023. The SEER Executive Committee voted to co-sponsor the Resolution at its meeting held on December 15, 2023.

4. Has this or a similar Resolution been submitted to the House or Board previously?

   No.

5. What existing Association policies are relevant to this Resolution and how would they be affected by its adoption?

   None.

6. If this is a late report, what urgency exists which requires action at this meeting of the House?

   N/A

7. Status of Legislation. (If applicable)

   This Resolution is consistent with the bipartisan Humane and Existing Alternatives in Research and Testing Sciences (HEARTS) Act (H.R. 1024, 118th Cong.), which addresses specific shortcomings in existing law that governs research proposals funded by the National Institutes of Health (NIH).

   The Fiscal Year 2023 Department of Labor, Health and Human Services, and Education and Related Agencies appropriations bill included report language directing the NIH to establish incentives to encourage investigators to utilize non-animal methods whenever appropriate for the research question and to establish standardized guidelines for peer review evaluation of the justification for research with animals.

   The Fiscal Year 2022 Department of Labor, Health and Human Services, and Education and Related Agencies appropriations bill included report language directing the NIH to appoint a working group to make recommendations for encouraging the use of non-animal models where appropriate in NIH intramural and extramural research, including epidemiological and clinical studies, cell-based methods, computer modeling and simulation, and human tissue studies, with consideration for complexity of the biomedical research area, and the current applicability and translatability of the non-animal model. In response, the NIH has convened an “Advisory Council to the Director Working Group on Catalyzing the Development and Use of Novel Alternative Methods to Advance Biomedical Research.”

8. Brief explanation regarding plans for implementation of the policy, if adopted by the House of Delegates.

   The Sections could work with the ABA Governmental Affairs Office to ensure that the Resolution supports the above-mentioned policy efforts by lobbying Congress and other national governments to accelerate the transition to non-

animal testing methods and increase investment in these technologies, and with non-governmental organizations working on this issue in the United States and around the world.

9. Cost to the Association. (Both direct and indirect costs)

   None.

10. Disclosure of Interest. (If applicable)

    None.

11. Referrals.

    Health Law Section
    Science & Technology Law Section
    Young Lawyers Division
    Solo, Small Firm and General Practice Division
    Section of State and Local Government Law

12. Name and Contact Information (Prior to the Meeting. Please include name, telephone number and e-mail address.) *Be aware that this information will be available to anyone who views the House of Delegates agenda online*.)

    Alex Cerussi
    alexcerussi1@gmail.com
    (631) 479-9005

13. Name and Contact Information. (Who will present the Resolution with Report to the House?) Please include best contact information to use when on-site at the meeting. *Be aware that this information will be available to anyone who views the House of Delegates agenda online*.

    Daina Bray
    daina.bray@yale.edu
    (713) 492-6219

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EXECUTIVE SUMMARY

1. Summary of the Resolution.

   This Resolution urges national governments, the U.S. Congress, and U.S. federal agencies to prioritize and invest in the development and use of methods that replace the use of animals in research and testing and to remove barriers to, and create incentives for, the use of non-animal research and testing methods in regulatory decision-making and federally sponsored research.

2. Summary of the issue that the Resolution addresses.

   The Three Rs—Replacement, Reduction, and Refinement—have been the foundation of better science and of improved conditions for animals used in research for over sixty years and underpin laws worldwide, including in Europe and the United States. Today's ever-evolving science and technology is creating opportunities to advance the 1st R by replacing the use of animals in research and testing while benefiting human health, the environment, and the economy.

   The toolbox of non-animal testing models is growing and shows the potential to enhance our understanding of diseases and accelerate the discovery of effective treatments. This toolbox includes, for example, new organ-on-chip technology, sophisticated computer simulations, 3-D cultures of human cells for drug testing, and other modern models and technologies.

   Although U.S. law is based on the principles of the Three Rs, lack of overall funding, shortcomings in existing law governing how research projects are funded, and outdated regulatory requirements limit the full realization of the benefits of replacement alternatives.

3. Please explain how the proposed policy position will address the issue.

   This Resolution is intended to encourage national governments, including the U.S. federal government and agencies, to prioritize the use and further development of replacement alternatives. This will advance animal-wellbeing, foster innovation, protect the environment, and improve the cost efficacy of taxpayer-funded research investments leading to safer products, better-quality medicines, and new tools for confronting future challenges and unexpected emergencies like the COVID-19 pandemic.

4. Summary of any minority views or opposition internal and/or external to the ABA which have been identified.

   None.