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MATTEK
A BICO COMPANY

The Honorable Melony Griffith
Chair, Senate Finance Committee
3 East -Miller Senate Office Building
Annapolis, Maryland 21401

February 23, 2023

RE: Support SB 0560

Dear Chair Griffith and honorable members of the Senate Finance Committee:

I am writing on behalf of MatTek Life Sciences to express our strong support for SB 0560, legislation that would help speed up the transition to non-animal research methods by creating a Human-Relevant Research Fund. This fund would provide grants to private or public facilities developing non-animal research techniques.

MatTek has been a leader in reliable in vitro human tissue model innovation. Our skin, ocular, oral, respiratory, and intestinal tissue models are used to assess safety and efficacy throughout the cosmetics, chemical, pharmaceutical, and household product industries. These advanced tissue models empower companies to achieve their goals of non-animal testing while lowering testing costs and providing human-relevant results.

By minimizing animal testing and focusing on the use of faster, cost effective, and more reliable testing methods, companies can save lives, time, and money. Current alternatives can also provide information of equivalent or superior quality and relevance to humans in comparison to animal tests.

We urge your support of SB 0560 to help make Maryland a leader in the advancement of non-animal test methods for research.

Sincerely,

Alex Armento
MatTek President and CEO

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Position: FAV

The Honorable Melony Griffith
Chair, Senate Finance Committee
3 East, Miller Senate Office Building
Annapolis, Maryland 21401

February 22, 2023

RE: Support SB0560

Dear Chair Griffith and honorable members of the Senate Finance Committee:

On behalf of the Institute for In Vitro Sciences (IIVS), I am writing to express our support for SB0560, legislation that would help speed up the transition to non-animal research methods by creating a Human-Relevant Research Fund.

IIVS is a non-profit research and testing laboratory dedicated to the advancement of *in vitro* (non-animal) methods worldwide. Founded in 1997, IIVS is unique in its position as a high-quality testing laboratory, while also offering technical and educational resources to advance the field. Non-animal alternative test methods and strategies can provide more efficient, as well as more predictive, chemical safety assessments. IIVS provides assistance and training to government agencies to help them more efficiently implement these alternative methods and reduce their reliance on animals. In addition, we help industry to choose the appropriate *in vitro* assays needed to inform decision-making.

As a non-profit, we are often ineligible for funding through grants like Small Business Innovation Research (SBIR) that support biotech innovations in the field. We are hopeful that the Human-Relevant Research Fund would provide monetary support accessible by groups like ours to not only assist in the development of new methodologies, but fund the validation work necessary to gain scientific confidence in New Approach Methodologies (NAM)s.

Thank you for your support of SB0560 to make Maryland a leader in advancing non-animal methods in research.

Sincerely,

DocuSigned by:
Amanda K. Ulrey
3B7365D81E5246B...

Amanda Ulrey, RQAP-GLP
President, Institute for In Vitro Sciences, Inc.

Akhtar Flaws human harms.pdf
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Position: FAV

The Flaws and Human Harms of Animal Experimentation

AYSHA AKHTAR

Abstract: Nonhuman animal ("animal") experimentation is typically defended by arguments that it is reliable, that animals provide sufficiently good models of human biology and diseases to yield relevant information, and that, consequently, its use provides major human health benefits. I demonstrate that a growing body of scientific literature critically assessing the validity of animal experimentation generally (and animal modeling specifically) raises important concerns about its reliability and predictive value for human outcomes and for understanding human physiology. The unreliability of animal experimentation across a wide range of areas undermines scientific arguments in favor of the practice. Additionally, I show how animal experimentation often significantly harms humans through misleading safety studies, potential abandonment of effective therapeutics, and direction of resources away from more effective testing methods. The resulting evidence suggests that the collective harms and costs to humans from animal experimentation outweigh potential benefits and that resources would be better invested in developing human-based testing methods.

Keywords: animal research; medical testing; human health; human ethics; drug development; animal ethics

Introduction

Annually, more than 115 million animals are used worldwide in experimentation or to supply the biomedical industry.[1] Nonhuman animal (hereafter "animal") experimentation falls under two categories: basic (i.e., investigation of basic biology and human disease) and applied (i.e., drug research and development and toxicity and safety testing). Regardless of its categorization, animal experimentation is intended to inform human biology and health sciences and to promote the safety and efficacy of potential treatments. Despite its use of immense resources, the animal suffering involved, and its impact on human health, the question of animal experimentation's efficacy has been subjected to little systematic scrutiny.[2]

Although it is widely accepted that medicine should be *evidence based*, animal experimentation as a means of informing human health has generally not been held, in practice, to this standard. This fact makes it surprising that animal experimentation is typically viewed as the default and gold standard of preclinical testing and is generally supported without critical examination of its validity. A survey published in 2008 of anecdotal cases and statements given in support of animal experimentation demonstrates how it has not and could not be validated as a necessary step in biomedical research, and the survey casts doubt on its predictive value.[3]

I am deeply indebted to David DeGrazia, Tom Beauchamp, and John Pippin for their careful review and helpful comments. The opinions expressed here are those of the author and do not represent the official position of the U.S. Food and Drug Administration or the U.S. government.

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Cambridge Quarterly of Healthcare Ethics (2015), **24**, 407–419.

doi:10.1017/S0963180115000079

I show that animal experimentation is poorly predictive of human outcomes,[4] that it is unreliable across a wide category of disease areas,[5] and that existing literature demonstrates the unreliability of animal experimentation, thereby undermining scientific arguments in its favor. I further show that the collective harms that result from an unreliable practice tip the ethical scale of harms and benefits against continuation in much, if not all, of experimentation involving animals.[6]

Problems of Successful Translation to Humans of Data from Animal Experimentation

Although the unreliability and limitations of animal experimentation have increasingly been acknowledged, there remains a general confidence within much of the biomedical community that they can be overcome.[7] However, three major conditions undermine this confidence and explain why animal experimentation, regardless of the disease category studied, fails to reliably inform human health: (1) the effects of the laboratory environment and other variables on study outcomes, (2) disparities between animal models of disease and human diseases, and (3) species differences in physiology and genetics. I argue for the critical importance of each of these conditions.

The Influence of Laboratory Procedures and Environments on Experimental Results

Laboratory procedures and conditions exert influences on animals' physiology and behaviors that are difficult to control and that can ultimately impact research outcomes. Animals in laboratories are involuntarily placed in artificial environments, usually in windowless rooms, for the duration of their lives. Captivity and the common features of biomedical laboratories—such as artificial lighting, human-produced noises, and restricted housing environments—can prevent species-typical behaviors, causing distress and abnormal behaviors among animals.[8] Among the types of laboratory-generated distress is the phenomenon of contagious anxiety.[9] Cortisone levels rise in monkeys watching other monkeys being restrained for blood collection.[10] Blood pressure and heart rates elevate in rats watching other rats being decapitated.[11] Routine laboratory procedures, such as catching an animal and removing him or her from the cage, in addition to the experimental procedures, cause significant and prolonged elevations in animals' stress markers.[12] These stress-related changes in physiological parameters caused by the laboratory procedures and environments can have significant effects on test results.[13] Stressed rats, for example, develop chronic inflammatory conditions and intestinal leakage, which add variables that can confound data.[14]

A variety of conditions in the laboratory cause changes in neurochemistry, genetic expression, and nerve regeneration.[15] In one study, for example, mice were genetically altered to develop aortic defects. Yet, when the mice were housed in larger cages, those defects almost completely disappeared.[16] Providing further examples, typical noise levels in laboratories can damage blood vessels in animals, and even the type of flooring on which animals are tested in spinal cord injury experiments can affect whether a drug shows a benefit.[17]

In order to control for potential confounders, some investigators have called for standardization of laboratory settings and procedures.[18] One notable effort was

made by Crabbe et al. in their investigation of the potential confounding influences of the laboratory environment on six mouse behaviors that are commonly studied in neurobehavioral experiments. Despite their "extraordinary lengths to equate test apparatus, testing protocols, and all possible features of animal husbandry" across three laboratories, there were systematic differences in test results in these labs.[19] Additionally, different mouse strains varied markedly in all behavioral tests, and for some tests the magnitude of genetic differences depended on the specific testing laboratory. The results suggest that there are important influences of environmental conditions and procedures specific to individual laboratories that can be difficult—perhaps even impossible—to eliminate. These influences can confound research results and impede extrapolation to humans.

The Discordance between Human Diseases and Animal Models of Diseases

The lack of sufficient congruence between animal models and human diseases is another significant obstacle to translational reliability. Human diseases are typically artificially induced in animals, but the enormous difficulty of reproducing anything approaching the complexity of human diseases in animal models limits their usefulness.[20] Even if the design and conduct of an animal experiment are sound and standardized, the translation of its results to the clinic may fail because of disparities between the animal experimental model and the human condition.[21]

Stroke research presents one salient example of the difficulties in modeling human diseases in animals. Stroke is relatively well understood in its underlying pathology. Yet accurately modeling the disease in animals has proven to be an exercise in futility. To address the inability to replicate human stroke in animals, many assert the need to use more standardized animal study design protocols. This includes the use of animals who represent both genders and wide age ranges, who have comorbidities and preexisting conditions that occur naturally in humans, and who are consequently given medications that are indicated for human patients.[22] In fact, a set of guidelines, named STAIR, was implemented by a stroke roundtable in 1999 (and updated in 2009) to standardize protocols, limit the discrepancies, and improve the applicability of animal stroke experiments to humans.[23] One of the most promising stroke treatments later to emerge was NXY-059, which proved effective in animal experiments. However, the drug failed in clinical trials, despite the fact that the set of animal experiments on this drug was considered the poster child for the new experimental standards.[24] Despite such vigorous efforts, the development of STAIR and other criteria has yet to make a recognizable impact in clinical translation.[25]

Under closer scrutiny, it is not difficult to surmise why animal stroke experiments fail to successfully translate to humans even with new guidelines. Standard stroke medications will likely affect different species differently. There is little evidence to suggest that a female rat, dog, or monkey sufficiently reproduces the physiology of a human female. Perhaps most importantly, reproducing the preexisting conditions of stroke in animals proves just as difficult as reproducing stroke pathology and outcomes. For example, most animals don't naturally develop significant atherosclerosis, a leading contributor to ischemic stroke. In order to reproduce the effects of atherosclerosis in animals, researchers clamp their blood vessels or artificially insert blood clots. These interventions, however, do not replicate the elaborate pathology of atherosclerosis and its underlying causes. Reproducing human

diseases in animals requires reproducing the *predisposing* diseases, also a formidable challenge. The inability to reproduce the disease in animals so that it is congruent in relevant respects with human stroke has contributed to a high failure rate in drug development. More than 114 potential therapies initially tested in animals failed in human trials.[26]

Further examples of repeated failures based on animal models include drug development in cancer, amyotrophic lateral sclerosis (ALS), traumatic brain injury (TBI), Alzheimer's disease (AD), and inflammatory conditions. Animal cancer models in which tumors are artificially induced have been the basic translational model used to study key physiological and biochemical properties in cancer onset and propagation and to evaluate novel treatments. Nevertheless, significant limitations exist in the models' ability to faithfully mirror the complex process of human carcinogenesis.[27] These limitations are evidenced by the high (among the highest of any disease category) clinical failure rate of cancer drugs.[28] Analyses of common mice ALS models demonstrate significant differences from human ALS.[29] The inability of animal ALS models to predict beneficial effects in humans with ALS is recognized.[30] More than twenty drugs have failed in clinical trials, and the only U.S. Food and Drug Administration (FDA)–approved drug to treat ALS is Riluzole, which shows notably marginal benefit on patient survival.[31] Animal models have also been unable to reproduce the complexities of human TBI.[32] In 2010, Maas et al. reported on 27 large Phase 3 clinical trials and 6 unpublished trials in TBI that all failed to show human benefit after showing benefit in animals.[33] Additionally, even after success in animals, around 172 and 150 drug development failures have been identified in the treatment of human AD[34] and inflammatory diseases,[35] respectively.

The high clinical failure rate in drug development across all disease categories is based, at least in part, on the inability to adequately model human diseases in animals and the poor predictability of animal models.[36] A notable systematic review, published in 2007, compared animal experimentation results with clinical trial findings across interventions aimed at the treatment of head injury, respiratory distress syndrome, osteoporosis, stroke, and hemorrhage.[37] The study found that the human and animal results were in accordance only half of the time. In other words, the animal experiments were no more likely than a flip of the coin to predict whether those interventions would benefit humans.

In 2004, the FDA estimated that 92 percent of drugs that pass preclinical tests, including "pivotal" animal tests, fail to proceed to the market.[38] More recent analysis suggests that, despite efforts to improve the predictability of animal testing, the failure rate has actually increased and is now closer to 96 percent.[39] The main causes of failure are lack of effectiveness and safety problems that were not predicted by animal tests.[40]

Usually, when an animal model is found wanting, various reasons are proffered to explain what went wrong—poor methodology, publication bias, lack of preexisting disease and medications, wrong gender or age, and so on. These factors certainly require consideration, and recognition of each potential difference between the animal model and the human disease motivates renewed efforts to eliminate these differences. As a result, scientific progress is sometimes made by such efforts. However, the high failure rate in drug testing and development, despite attempts to improve animal testing, suggests that these efforts remain insufficient to overcome the obstacles to successful translation that are inherent to the use of animals.

Too often ignored is the well-substantiated idea that these models are, for reasons summarized here, intrinsically lacking in relevance to, and thus highly unlikely to yield useful information about, human diseases.[41]

Interspecies Differences in Physiology and Genetics

Ultimately, even if considerable congruence were shown between an animal model and its corresponding human disease, interspecies differences in physiology, behavior, pharmacokinetics, and genetics would significantly limit the reliability of animal studies, even after a substantial investment to improve such studies. In spinal cord injury, for example, drug testing results vary according to which species and even which strain within a species is used, because of numerous interspecies and interstrain differences in neurophysiology, anatomy, and behavior.[42] The micropathology of spinal cord injury, injury repair mechanisms, and recovery from injury varies greatly among different strains of rats and mice. A systematic review found that even among the most standardized and methodologically superior animal experiments, testing results assessing the effectiveness of methylprednisolone for spinal cord injury treatment varied considerably among species.[43] This suggests that factors inherent to the use of animals account for some of the major differences in results.

Even rats from the same strain but purchased from different suppliers produce different test results.[44] In one study, responses to 12 different behavioral measures of pain sensitivity, which are important markers of spinal cord injury, varied among 11 strains of mice, with no clear-cut patterns that allowed prediction of how each strain would respond.[45] These differences influenced how the animals responded to the injury and to experimental therapies. A drug might be shown to help one strain of mice recover but not another. Despite decades of using animal models, not a single neuroprotective agent that ameliorated spinal cord injury in animal tests has proven efficacious in clinical trials to date.[46]

Further exemplifying the importance of physiological differences among species, a 2013 study reported that the mouse models used extensively to study human inflammatory diseases (in sepsis, burns, infection, and trauma) have been misleading. The study found that mice differ greatly from humans in their responses to inflammatory conditions. Mice differed from humans in what genes were turned on and off and in the timing and duration of gene expression. The mouse models even differed from one another in their responses. The investigators concluded that "our study supports higher priority to focus on the more complex human conditions rather than relying on mouse models to study human inflammatory disease."[47] The different genetic responses between mice and humans are likely responsible, at least in part, for the high drug failure rate. The authors stated that every one of almost 150 clinical trials that tested candidate agents' ability to block inflammatory responses in critically ill patients failed.

Wide differences have also become apparent in the regulation of the same genes, a point that is readily seen when observing differences between human and mouse livers.[48] Consistent phenotypes (observable physical or biochemical characteristics) are rarely obtained by modification of the same gene, even among different strains of mice.[49] Gene regulation can substantially differ among species and may be as important as the presence or absence of a specific gene. Despite the high degree of genome conservation, there are critical differences in the order and function of

genes among species. To use an analogy: as pianos have the same keys, humans and other animals share (largely) the same genes. Where we mostly differ is in the way the genes or keys are expressed. For example, if we play the keys in a certain order, we hear Chopin; in a different order, we hear Ray Charles; and in yet a different order, it's Jerry Lee Lewis. In other words, the same keys or genes are expressed, but their different orders result in markedly different outcomes.

Recognizing the inherent genetic differences among species as a barrier to translation, researches have expressed considerable enthusiasm for genetically modified (GM) animals, including transgenic mice models, wherein human genes are inserted into the mouse genome. However, if a human gene is expressed in mice, it will likely function differently from the way it functions in humans, being affected by physiological mechanisms that are unique in mice. For example, a crucial protein that controls blood sugar in humans is missing in mice.[50] When the human gene that makes this protein was expressed in genetically altered mice, it had the opposite effect from that in humans: it caused *loss* of blood sugar control in mice. Use of GM mice has failed to successfully model human diseases and to translate into clinical benefit across many disease categories.[51] Perhaps the primary reason why GM animals are unlikely to be much more successful than other animal models in translational medicine is the fact that the "humanized" or altered genes are still in nonhuman animals.

In many instances, nonhuman primates (NHPs) are used instead of mice or other animals, with the expectation that NHPs will better mimic human results. However, there have been sufficient failures in translation to undermine this optimism. For example, NHP models have failed to reproduce key features of Parkinson's disease, both in function and in pathology.[52] Several therapies that appeared promising in both NHPs and rat models of Parkinson's disease showed disappointing results in humans.[53] The campaign to prescribe hormone replacement therapy (HRT) in millions of women to prevent cardiovascular disease was based in large part on experiments on NHPs. HRT is now known to *increase* the risk of these diseases in women.[54]

HIV/AIDS vaccine research using NHPs represents one of the most notable failures in animal experimentation translation. Immense resources and decades of time have been devoted to creating NHP (including chimpanzee) models of HIV. Yet all of about 90 HIV vaccines that succeeded in animals failed in humans.[55] After HIV vaccine gp120 failed in clinical trials, despite positive outcomes in chimpanzees, a *BMJ* article commented that important differences between NHPs and humans with HIV misled researchers, taking them down unproductive experimental paths.[56] Gp120 failed to neutralize HIV grown and tested in cell culture. However, because the serum protected chimpanzees from HIV infection, two Phase 3 clinical trials were undertaken[57]—a clear example of how expectations that NHP data are more predictive than data from other (in this case, cell culture) testing methods are unproductive and harmful. Despite the repeated failures, NHPs (though not chimpanzees or other great apes) remain widely used for HIV research.

The implicit assumption that NHP (and indeed any animal) data are reliable has also led to significant and unjustifiable human suffering. For example, clinical trial volunteers for gp120 were placed at unnecessary risk of harm because of unfounded confidence in NHP experiments. Two landmark studies involving thousands of menopausal women being treated with HRT were terminated early because of

increased stroke and breast cancer risk.[58] In 2003, Elan Pharmaceuticals was forced to prematurely terminate a Phase 2 clinical trial when an investigational AD vaccine was found to cause brain swelling in human subjects. No significant adverse effects were detected in GM mice or NHPs.[59]

In another example of human suffering resulting from animal experimentation, six human volunteers were injected with an immunomodulatory drug, TGN 1412, in 2006.[60] Within minutes of receiving the experimental drug, all volunteers suffered a severe adverse reaction resulting from a life-threatening cytokine storm that led to catastrophic systemic organ failure. The compound was designed to dampen the immune system, but it had the *opposite* effect in humans. Prior to this first human trial, TGN 1412 was tested in mice, rabbits, rats, and NHPs with no ill effects. NHPs also underwent repeat-dose toxicity studies and were given 500 times the human dose for at least four consecutive weeks.[61] None of the NHPs manifested the ill effects that humans showed almost immediately after receiving minute amounts of the test drug. Cynomolgus and rhesus monkeys were specifically chosen because their CD28 receptors demonstrated similar affinity to TGN 1412 as human CD28 receptors. Based on such data as these, it was confidently concluded that results obtained from these NHPs would most reliably predict drug responses in humans—a conclusion that proved devastatingly wrong.

As exemplified by the study of HIV/AIDS, TGN 1412, and other experiences,[62] experiments with NHPs are not necessarily any more predictive of human responses than experiments with other animals. The repeated failures in translation from studies with NHPs belie arguments favoring use of *any* nonhuman species to study human physiology and diseases and to test potential treatments. If experimentation using chimpanzees and other NHPs, our closest genetic cousins, are unreliable, how can we expect research using other animals to be reliable? The bottom line is that animal experiments, no matter the species used or the type of disease research undertaken, are highly unreliable—and they have too little predictive value to justify the resultant risks of harms for humans, for reasons I now explain.

The Collective Harms That Result from Misleading Animal Experiments

As medical research has explored the complexities and subtle nuances of biological systems, problems have arisen because the *differences* among species along these subtler biological dimensions far outweigh the *similarities*, as a growing body of evidence attests. These profoundly important—and often undetected—differences are likely one of the main reasons human clinical trials fail.[63]

"Appreciation of differences" and "caution" about extrapolating results from animals to humans are now almost universally recommended. But, in practice, how does one take into account differences in drug metabolism, genetics, expression of diseases, anatomy, influences of laboratory environments, and species- and strain-specific physiologic mechanisms—and, in view of these differences, discern what is applicable to humans and what is not? If we cannot determine which physiological mechanisms in which species and strains of species are applicable to humans (even setting aside the complicating factors of different caging systems and types of flooring), the usefulness of the experiments must be questioned.

It has been argued that some information obtained from animal experiments is better than no information.[64] This thesis neglects how misleading information can be worse than no information from animal tests. The use of nonpredictive animal

experiments can cause human suffering in at least two ways: (1) by producing misleading safety and efficacy data and (2) by causing potential abandonment of useful medical treatments and misdirecting resources away from more effective testing methods.

Humans are harmed because of misleading animal testing results. Imprecise results from animal experiments may result in clinical trials of biologically faulty or even harmful substances, thereby exposing patients to unnecessary risk and wasting scarce research resources.[65] Animal toxicity studies are poor predictors of toxic effects of drugs in humans.[66] As seen in some of the preceding examples (in particular, stroke, HRT, and TGN1412), humans have been significantly harmed because investigators were misled by the safety and efficacy profile of a new drug based on animal experiments.[67] Clinical trial volunteers are thus provided with raised hopes and a false sense of security because of a misguided confidence in efficacy and safety testing using animals.

An equal if indirect source of human suffering is the opportunity cost of abandoning promising drugs because of misleading animal tests.[68] As candidate drugs generally proceed down the development pipeline and to human testing based largely on successful results in animals[69] (i.e., positive efficacy and negative adverse effects), drugs are sometimes not further developed due to unsuccessful results in animals (i.e., negative efficacy and/or positive adverse effects). Because much pharmaceutical company preclinical data are proprietary and thus publicly unavailable, it is difficult to know the number of missed opportunities due to misleading animal experiments. However, of every 5,000–10,000 potential drugs investigated, only about 5 proceed to Phase 1 clinical trials.[70] Potential therapeutics may be abandoned because of results in animal tests that do not apply to humans.[71] Treatments that fail to work or show some adverse effect in animals because of species-specific influences may be abandoned in preclinical testing even if they may have proved effective and safe in humans if allowed to continue through the drug development pipeline.

An editorial in *Nature Reviews Drug Discovery* describes cases involving two drugs in which animal test results from species-specific influences could have derailed their development. In particular, it describes how tamoxifen, one of the most effective drugs for certain types of breast cancer, "would most certainly have been withdrawn from the pipeline" if its propensity to cause liver tumor in rats had been discovered in preclinical testing rather than after the drug had been on the market for years.[72] Gleevec provides another example of effective drugs that could have been abandoned based on misleading animal tests: this drug, which is used to treat chronic myelogenous leukemia (CML), showed serious adverse effects in at least five species tested, including severe liver damage in dogs. However, liver toxicity was not detected in human cell assays, and clinical trials proceeded, which confirmed the absence of significant liver toxicity in humans.[73] Fortunately for CML patients, Gleevec is a success story of predictive human-based testing. Many useful drugs that have safely been used by humans for decades, such as aspirin and penicillin, may not have been available today if the current animal testing regulatory requirements were in practice during their development.[74]

A further example of near-missed opportunities is provided by experiments on animals that delayed the acceptance of cyclosporine, a drug widely and successfully used to treat autoimmune disorders and prevent organ transplant rejection.[75] Its immunosuppressive effects differed so markedly among species that researchers

judged that the animal results limited any direct inferences that could be made to humans. Providing further examples, PharmaInformatic released a report describing how several blockbuster drugs, including aripiprazole (Abilify) and esomeprazole (Nexium), showed low oral bioavailability in animals. They would likely not be available on the market today if animal tests were solely relied on. Understanding the implications of its findings for drug development in general, PharmaInformatic asked, "Which other blockbuster drugs would be on the market today, if animal trials would have not been used to preselect compounds and drug-candidates for further development?"[76] These near-missed opportunities and the overall 96 percent failure rate in clinical drug testing strongly suggest the unsoundness of animal testing as a precondition of human clinical trials and provide powerful evidence for the need for a new, human-based paradigm in medical research and drug development.

In addition to potentially causing abandonment of useful treatments, use of an invalid animal disease model can lead researchers and the industry in the wrong research direction, wasting time and significant investment.[77] Repeatedly, researchers have been lured down the wrong line of investigation because of information gleaned from animal experiments that later proved to be inaccurate, irrelevant, or discordant with human biology. Some claim that we do not know which benefits animal experiments, particularly in basic research, may provide down the road. Yet human lives remain in the balance, waiting for effective therapies. Funding must be strategically invested in the research areas that offer the most promise.

The opportunity costs of continuing to fund unreliable animal tests may impede development of more accurate testing methods. Human organs grown in the lab, human organs on a chip, cognitive computing technologies, 3D printing of human living tissues, and the Human Toxome Project are examples of new human-based technologies that are garnering widespread enthusiasm. The benefit of using these testing methods in the preclinical setting over animal experiments is that they are based on *human* biology. Thus their use eliminates much of the guesswork required when attempting to extrapolate physiological data from other species to humans. Additionally, these tests offer whole-systems biology, in contrast to traditional in vitro techniques. Although they are gaining momentum, these human-based tests are still in their relative infancy, and funding must be prioritized for their further development. The recent advancements made in the development of more predictive, human-based systems and biological approaches in chemical toxicological testing are an example of how newer and improved tests have been developed because of a shift in prioritization.[78] Apart from toxicology, though, financial investment in the development of human-based technologies generally falls far short of investment in animal experimentation.[79]

Conclusion

The unreliability of applying animal experimental results to human biology and diseases is increasingly recognized. Animals are in many respects biologically and psychologically similar to humans, perhaps most notably in the shared characteristics of pain, fear, and suffering.[80] In contrast, evidence demonstrates that critically important physiological and genetic differences between humans and other animals can invalidate the use of animals to study human diseases, treatments, pharmaceuticals, and the like. In significant measure, animal models specifically,

and animal experimentation generally, are inadequate bases for predicting clinical outcomes in human beings in the great bulk of biomedical science. As a result, humans can be subject to significant and avoidable harm.

The data showing the unreliability of animal experimentation and the resultant harms to humans (and nonhumans) undermine long-standing claims that animal experimentation is necessary to enhance human health and therefore ethically justified. Rather, they demonstrate that animal experimentation poses significant costs and harms to human beings. It is possible—as I have argued elsewhere—that animal research is more costly and harmful, on the whole, than it is beneficial to human health.[81] When considering the ethical justifiability of animal experiments, we should ask if it is ethically acceptable to deprive humans of resources, opportunity, hope, and even their lives by seeking answers in what may be the wrong place. In my view, it would be better to direct resources away from animal experimentation and into developing more accurate, human-based technologies.

Notes

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SB0560_Favorable_AyshaAkhtar_Center for Contempora
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Position: FAV

CENTER FOR CONTEMPORARY SCIENCES

The Honorable Melony Griffith

Chair, Senate Finance Committee

3 East, Miller Senate Office Building

Annapolis, Maryland 21401

Testimony in Support of SB0560

Presented to the Senate Finance Committee

March 2, 2023

By Aysha Akhtar, MD, MPH. Co-founder and CEO, Center for Contemporary Sciences

Dear Chair Griffith and honorable members of the Senate Finance Committee:

Thank you for giving me the opportunity to submit this written testimony on behalf of the Center for Contemporary Sciences, a non-profit organization based in Maryland, and as a personal citizen of Gaithersburg, Maryland. I urge a favorable report of SB0560. This legislation creates a Human-Relevant Research Fund to provide grants to public and private institutions in Maryland to advance the discovery, creation, and use of human-relevant research techniques in the medical sciences.

A Personal Story

One of the hardest things I have had to do as a neurologist is to watch my own aunt, a strong, vibrant woman, deteriorate from Parkinson's disease until she died. I watched helplessly as she slowly lost control of her own body, a truly terrifying experience. Her arms pained continuously from the constant, uncontrollable tremors. Meanwhile, her legs often refused to move. By the end, she was unable to walk, stand, and perform the most basic of movements we expect from our bodies. Perhaps even more devastating, she lost her sense of self and her unique personality, humor and intelligence disappeared, to be replaced with a swirling chaos of

dementia. My uncle, her husband, had to call my family on several occasions to help find my aunt after she walked out of her home and got lost –unable to remember her way home.

I tell you my aunt's story because there is not a single effective treatment for Parkinson's disease. Nor is there an effective treatment for Multiple Sclerosis, dementias, spinal cord injury, most cases of stroke, and just about every neurological disease. At best, we have treatments that help with some of the symptoms, but which do not truly impact the illnesses themselves. I routinely have had to tell patients after I diagnosed them with devastating neurological illness that there is no treatment that will significantly alter the course of their diseases.

A Professional Story

In fact, there is no approved treatment for most diseases, neurological or otherwise.[1] During my decade as a Medical Officer at the Food and Drug Administration (FDA) and in their Office of Counterterrorism and Emerging Threats, I studied the safety and effectiveness of new drugs and saw how promising drug after drug came through the pipeline only to fail in human clinical trials. During my tenure as Deputy Director of the Army's Traumatic Brain Injury Program, I witnessed how despite hundreds of billions of dollars spent on head injury experiments in animals, we had not a single treatment to offer soldiers who suffered from head injuries, other than supportive care. I myself am a US Veteran and have seen the immense suffering experienced by soldiers from traumatic brain injury.

At some point, it became clear to me why there are so few effective treatments for human illnesses. We now know that whatever role animal testing may have played in the past, medicine is now exploring the subtle nuances of molecular biology, chemistry, and physiology. Subtle differences between humans and other animals now significantly mislead the results of studies. In fact, evidence now shows that 90—95% of all drugs that are found safe and effective in animal tests are unsafe and/or don't work in humans.[2] I authored a study that showed that one of the most significant reasons why there are so few treatments for most illnesses is because animal tests do not predict human results.[3] There is strong concern that drugs that would have been safe and would have worked—maybe even been cures—in humans were discarded because they didn't work in the animal tests. Perhaps, this, more than anything else, is most alarming.

A Way Forward

Despite the dire situation in drug development, you have a great opportunity before you in SB0560. In 2020, I founded the Center for Contemporary Sciences to help the discovery, development, and use of human-relevant testing methods. We helped the passage of a significant new bill, the FDA Modernization Act 2.0. which was signed into law by President Biden this past December. This new law recognizes the importance of allowing better innovative human-relevant testing methods to be used in place of unreliable animal testing for drug development.

Human-relevant testing methods are the future in medicine. These are methods, such as human body on a chip, bioprinted mini-organs, smart AI, and virtual humans that are rapidly becoming the go-to methods for biomedical research. Not only are these methods so advanced and sophisticated, but they are based on human data and human biology. Thus, unlike tests using different species, these new methods are *human-relevant*. They are already outperforming animal tests in modeling human diseases and predicting human results. But these testing methods need more funding.

Passing SB0560 will showcase Maryland as a true leader in the future of biotechnology and medicine. This is a unique, and important bill. Perhaps my aunt would not have suffered so much had there been more human-relevant testing methods to use for Parkinson's disease research. I and the Center for Contemporary Sciences urge a favorable report of SB0560 that can pave the way for a new frontier in medicine, more effective research tools, and real hope for people suffering from devastating illnesses.

Sincerely,

Aysha Akhtar, MD, MPH
Co-founder, President, and CEO
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9841 Washingtonian Blvd
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SB560-2.pdf
Uploaded by: Beth Wiseman
Position: FAV

TESTIMONY IN FAVOR OF SB 560
Animal Testing and Research - Human-Relevant Research Funding and Animal Testing and Research Licensure

It is so good to see the movement toward animal testing compassion.

I constantly get email information about companies that use animals to test and, of course, I would not buy those products. Seeing what happens to the tested animals and the conditions in which they are kept will upset even those who do not like animals.

Please give this Bill a Favorable vote and show that Maryland cares about animals.

Thank you.

Beth Wiseman
410-484-6866
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SB 560_Favorable_Propagenix Inc.pdf
Uploaded by: Brian Pollok
Position: FAV

propagenix

The Honorable Melony Griffith
Chair, Senate Finance Committee
3 East
Miller Senate Office Building
Annapolis, Maryland 21401

February 20, 2023

RE: Support for SB 560

Dear Chair Griffith and honorable members of the Senate Finance Committee:

My name is Dr. Brian Pollok and I am a Founder, Board Director and past CEO of Propagenix Inc, located in Gaithersburg. MD. I am writing to express our company's support for SB 560, legislation that would help speed up the transition to non-animal research methods by creating a Human-Relevant Research Fund. This fund would provide grants to private or public facilities developing non-animal research techniques.

Propagenix is a biotechnology company engaged in the development and commercialization of human tissue models for use in drug and chemical testing. Our patented cell culture technology enables cost-efficient production of a wide variety of human cell models such as skin, airway, kidney, intestine, eye and bladder tissues that recapitulate the normal structure and function of these tissues. By creating physiologically-relevant in vitro models for a wide range of human barrier tissues, the need for animal testing – and the attendant animal suffering – will be decreased. These human tissue models will also be more predictive of drug and chemical agent actions than mouse/rabbit/rat/dog models, thereby increasing the efficiency of developing new and safe drugs and consumer products.

Maryland has worked hard to position itself as a hub for research and biotechnology and now is the time to lead the way in advancing the development of human-relevant alternatives to animal testing. We believe that this is a very worthy objective for research overall, and our company is poised to assist in that endeavor.

Sincerely,

Brian A. Pollok, Ph.D.
Co-Founder, Board Director, and Principal Investigator
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SB0560_Favorable_Jim Corbett_Emulate.pdf
Uploaded by: Jim Corbett
Position: FAV

emulate

February 27, 2023

Testimony of

Jim Corbett, CEO Emulate, Inc.

Before the Maryland Finance Committee

RE: Animal Testing and Research – Human-Relevant Research Funding and Animal Testing and Research Licensure

Dear Senator Guzzone

On behalf of Emulate, Inc., the leading provider of Organ-on-a-Chip technology, I offer this testimony in support of Maryland Senate Bill 560.

There is no doubt that animal models have contributed to major scientific advancements and to safe and effective drugs making it to market. However, these models have the difficult job of approximating the human body, and sometimes they get it wrong.

A growing body of evidence suggests that animal models are lacking in both sensitivity and specificity when it comes to predicting drug toxicity in humans.[1-3] A 2014 study analyzing the effects of 2,366 drugs in both animals and humans found that "tests on animals (specifically rat, mouse, and rabbit models) are highly inconsistent predictors of toxic responses in humans and are little better than what would result merely by chance."[4] A 2008 review found similar results, concluding that animal models predicting drug toxicity in humans may have sensitivity and specificity values below 70%.[2]

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Boston, MA 02210

The costs of poor specificity and sensitivity are too often passed onto the patient. A review of 578 discontinued and withdrawn drugs in Europe and the United States showed that nearly half halted distribution due to post-approval toxicity.[5] Similarly, a 2012 analysis of 43 post-approval drugs with serious toxicity effects found that only 19% of them showed indications of toxicity in animal studies.[6]

In a recent study published in *Communications Medicine*, part of Nature Portfolio, researchers found the Emulate human Liver-Chip to have an 87% sensitivity and 100% specificity when differentiating hepatotoxic from non-hepatotoxic small molecules.[7] Importantly, all 22 hepatotoxic drugs included in the study had previously been classified as safe due to a lack of toxicity in animal models. Collectively, these compounds resulted in 208 patient fatalities and 10 liver transplants. Had the Emulate human Liver-Chip been used during the preclinical screening of these compounds, it's likely that many of these fatalities could have been avoided.

Animal models have played an undeniably significant role in the evolution of medicine and will continue to do so, but to make the drug development process safer, more efficient, and more humane, we must take a hard look at how we can leverage scientific advancements to continuously improve patient safety.

With the FDA Modernization Act 2.0 being signed into law by President Biden in December 2022, we applaud the state of Maryland for moving quickly to identify creative ways to fund human-relevant research. The collective industries of New Approach Methods, Microphysiological Systems, and Organ-Chips will spur the next-generation of scientific advancements, leading to new education and career opportunities as well as boosting the economy of Maryland.

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Sincerely,

Jim Corbett
Emulate, Inc. CEO

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Position: FAV

WRITTEN STATEMENT

Keith Murphy
Founder, CEO, and Chairman, Viscient Biosciences
Founder, Organovo
Board Member, California Life Sciences

Finance Committee - Bill Hearing
SB 560: Animal Testing and Research – Human–Relevant Research Funding and Animal Testing and Research Licensure

March 2, 2023

Thank you, Chair Griffith and Vice Chair Klausmeier, for the opportunity to submit testimony on SB 560, critical legislation that would advance the use of non-animal testing methods in medical and product research and mark Maryland's commitment to developing safer and more successful drug therapies.

I and those in my field appreciate your efforts and I wanted to provide the perspective of an entrepreneur and innovator working on new non-animal testing methods. I am here to tell you that we are at the cusp of a major technological revolution. The technology exists today to dramatically improve our ability to develop drugs, improve the likelihood of success of drugs in clinical trials, and lower the costs of drug development. For patients, this can mean more new breakthrough therapies and lower priced drugs. But first, the technology needs to be taken up more broadly.

Several companies now are in the early stages of applying more modern technologies, such as 3D bioprinted tissues made from human cells from a patient, to avoid the "species gap" and overreliance on rodent and animal models in pharmaceutical research. I am the Chief Executive Officer of Viscient Biosciences in San Diego, which has a superior model for liver fibrosis made from 3D human cells. Several major big pharma drug programs in this space have failed to reduce fibrosis in patients, and two have been successful. Animal models predicted all of them would work, but our 3D human model shows exactly which two reduce fibrosis and which ones fail to do so. Our human 3D disease model, if available a decade ago, would have avoided wasting hundreds of millions of dollars on failed clinical trials, but more importantly it would have avoided thousands of patients receiving experimental drugs that were doomed to fail and led to new drugs sooner. Our own drug found using this model, unrelated to the others, should be in clinical trials by 2024, and we believe it has a much higher chance of success than the typical drug would.

These models and other technology to do better than animal models exist today and need support to be more broadly used. Our company is one of several, some of which commercially offer their models and their solutions to drug developers. Your efforts through this legislation will yield great benefit in making these models be used sooner with greater impact. The result will be not only beneficial in the sense of less use of animal models, but it will end the ethical tragedy that is using humans in experiments doomed to fail, when the technology exists to avoid such practices.

Some of the world's top 25 drug manufacturers are incorporating alternatives to animal testing in their drug development programs that demonstrate to be more predictive of drug safety, toxicity, and efficacy than traditional models. SB 560 is the right legislation at the right time to further support this field of discovery, enable better treatments for individuals and families, and establish the State as an incubator primed to change the frontier for new and existing drugs and therapeutics.

Organovo is a U.S. company dedicated to developing and utilizing highly customized, bioprinted 3D human tissues as dynamic models of healthy and diseased human biology for drug development. These advances

are enabling complex, multicellular disease models that can be used to develop clinically effective drugs for selected therapeutic areas without relying on animal models. Viscient Biosciences, a company working with Organovo and using Organovo's bioprinting technology under license, has produced a liver model of nonalcoholic steatohepatitis (NASH, commonly known as fatty liver disease) that shows high evidence of disease reproduction. When tested in this model, results for NASH drugs match results obtained in clinical trials.

As an innovator who has dedicated my career to bringing significant new technologies to market, my assessment is that these and similar case studies reflect that the biomedical community is nearing a tipping point of sufficient data that calls into twofold-question the ethics of continued animal drug testing in light of proven non-animal testing pathways. Recent scientific validation of non-animal research capabilities includes a July 2016 peer-reviewed study[1] using 3D bioengineered liver tissues modeling drug-induced liver injury (DILI) to investigate the effects of *Trovafloxin*, a drug withdrawn from the market due to acute liver failure in patients. The study provided new evidence that 3D bioengineered tissues can better model the effects of chronic drug dosing or conditions that develop over extended periods of time. Additionally, peer-reviewed data presented at the March 2016 Society of Toxicology[2] conference found that 3D human tissue models can identify drug-induced liver toxicity of compounds in a preclinical setting. These models can detect complex and induced toxic events requiring multiple human cell types which, to date, have only been captured in animal models or subsequent clinical trials.

Expanded regulatory avenues to support non-animal testing more directly, like the proposed Human-Relevant Research Fund, would accelerate the development of game-changing treatments, potentially drive down research and experimentation costs, and begin to address ethical concerns involving animal models. The goals and dedicated investments outlined in SB 560 greatly would aid researchers and stakeholders and further incentivize this essential line of medical discovery.

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[1] Nguyen DG, Funk J, Robbins JB, Crogan-Grundy C, Presnell SC, Singer T, et al. (2016) Bioprinted 3D Primary Liver Tissues Allow Assessment of Organ-Level Response to Clinical Drug Induced Toxicity *In Vitro*. PLoS ONE 11(7): e0158674. <https://doi.org/10.1371/journal.pone.0158674>

[2] Norona L, Nguyen DG, Gerber DA, et al. Modeling Drug-Induced Hepatic Fibrosis *In Vitro* Using Three-Dimensional Liver Tissue Constructs. Society of Toxicology Annual Meeting, 2016. Presentation. <https://organovo.com/wp-content/uploads/2019/01/2016-SOT-UNC-Orgnaovo-Drug-Induced-Hepatic-Fibrosis.pdf>

Animal Testing and Research - Human Relevant Resea

Uploaded by: Lisa Radov

Position: FAV

MARYLAND VOTES FOR ANIMALS

PO BOX 10411
BALTIMORE, MD 21209

March 3, 2023

To: Senate Finance Committee
From: Lisa Radov, President and Chair, Maryland Votes for Animals, Inc.
Re: Animal Testing and Research – Human Relevant Research Funding and Animal Testing and Research Licensure – SB 560 - Support

Chair Griffith, Vice Chair Klausmeier, members of the Finance Committee, thank you for the opportunity to testify before you today. My name is Lisa Radov. I am the President and Chair of Maryland Votes for Animals. We champion humane legislation to improve the lives of animals in Maryland. Speaking for Maryland Votes for Animals, our Board of Directors, and our members across Maryland, I respectfully request that the Finance Committee vote favorably for Animal Testing and Research - Human-Relevant Research Funding and Animal Testing and Research Licensure – SB 560.

This bill would establish the Human–Relevant Research Fund. The purpose of the fund is to promote state-funded research through grants and loans to public and private entities in Maryland to develop human-relevant alternatives to using animals in medical and product testing and research.

Laboratory testing on animals is often painful, debilitating, and cruel. A Pew Research Center poll found that 52% of U.S. adults oppose the use of animals in scientific research. The smaller percentage of the population that still accepts animal experimentation often does so only because it believes it to be necessary for medical progress. In an article published in *The Journal of the American Medical Association*, however, researchers found that medical treatments developed on animals often ***do not*** translate to humans. The study also warned patients and physicians to be cautious about extrapolating the findings of prominent animal research to the care of human disease. What we now know is that there are many alternatives to using animals in research.

This is an opportunity for Maryland to invest in an emerging scientific area that will continue to grow. Maryland already has a niche in the biomedical and biotech industries with numerous famous hospitals and universities. This Fund would not only provide jobs for Marylanders utilizing the most advanced scientific models for research, but also it would save animals from unnecessary suffering in tests that have been deemed less reliable than computer simulations and synthetic materials testing.

Let's Make Maryland a Leader in Finding Alternatives to Animals in Research.

Passing this bill is a win-win-win. It is a win for animals, a win for medical research, and a win for Maryland's economy.

In closing, I would like to thank Senator Guzzone for his sponsorship of SB 560 and ask the committee to give this bill a favorable report.

SB 560_mgoldstein_fav 2023.pdf
Uploaded by: Mathew Goldstein
Position: FAV

Secular Maryland secularmaryland@tutanota.com

March 03, 2023

SB 560 - SUPPORT

Animal Testing and Research - Human-Relevant Research Funding and Animal Testing and Research Licensure

Dear Chair Griffith, Vice-Chair Klausmeier, and Members of the Finance Committee,

Secular Maryland supports this bill which would confer better protection for animals against unnecessary reliance on animals for medical and product testing and research. This bill promotes the development and use of alternatives to animal testing. Current state law lacks consideration for the potential of animals to be harmed. Scientific research has revealed that humans are more similar to our non-human animal counterparts than some people may want to believe. The provisions in this bill strike a sensible balance between the potential harms and benefits from medical and product testing and research on animals. One concern with this bill is that information on testing with animals that must be reported may nevertheless need to be kept under wraps because of the potential for researchers to be threatened by extreme animal rights activists acting outside the law in an effort to shut down all animal testing.

Respectfully,
Mathew Goldstein
3838 Early Glow Ln
Bowie, MD

SB 560-SUPPORT-Alternatives Research & Development
Uploaded by: Sue Leary
Position: FAV

Re: Testimony in SUPPORT of S.B. 560, Animal Testing and Research - Human-Relevant Research Funding and Animal Testing and Research Licensure

Dear Chair Griffith, Vice-Chair Klausmeier, and members of the Senate Finance Committee,

Thank you for this opportunity to submit written testimony in support of S.B. 560, which would establish a fund for human-relevant non-animal testing and research methods under the administration of the Maryland Technology Development Corporation. Our organization, the Alternatives Research & Development Foundation (ARDF), is a non-profit funding organization that supports the development of non-animal research methods and models. Through our grant programs and sponsorship of scientific conferences, ARDF supports rigorous and innovative research to advance the development of human-relevant methods and replace the use of animals in research, education, and testing. Non-animal, human-relevant research methods show great promise to advance human health and reduce animal suffering, however, considerable research investment is needed to fully realize this potential. We are writing to enthusiastically urge a favorable report of S.B. 560.

The Funding Needs for Human-Relevant Non-Animal Methods are Significant

ARDF's flagship grant program is our Annual Open grant program, which funds investigator-initiated, one-year projects up to $40,000.[1] Established in 1993, this grant program is one of the longest-running programs of its kind. All applications are reviewed by external experts from across academia, industry, and government, who provide assessments based on our program's review criteria. Due to our budget constraints, we are currently only able to fund approximately six research projects each year, even though we generally receive at least 30 applications. Of these 30 applications, usually at least ten are scored as highly meritorious and "fundable" by our expert reviewers. However, we have no doubt that, each year, innovative and promising proposals are left unfunded due to our own budget limitations. Additional funding targeted to non-animal methods could help close this gap and ensure that we are able to benefit from the most promising research.

Putting Maryland at the Forefront of Biomedical Research

Some of the most promising human-relevant non-animal methods—microphysiological systems (MPS) such as organoids and "organs-on-a-chip", and bioprinting—also happen to currently be some of the most cutting-edge areas in biomedical science.[2,3,4] Researchers have made astounding progress developing these technologies in recent years and we are just beginning to reap some of the exciting scientific rewards. For example, recognizing the promise of MPS for drug development, the National Institutes of Health (NIH) recently announced funding to establish research centers to accelerate the

[1] https://www.ardf-online.org/ardf-grants.html

[2] Low LA, Mummery C, Berridge BR, Austin CP, Tagle DA. Organs-on-chips: into the next decade. Nat Rev Drug Discov. 2021 May;20(5):345-361. doi: 10.1038/s41573-020-0079-3. Epub 2020 Sep 10. PMID: 32913334.

[3] Anderson WA, Bosak A, Hogberg HT, Hartung T, Moore MJ. Advances in 3D neuronal microphysiological systems: towards a functional nervous system on a chip. In Vitro Cell Dev Biol Anim. 2021 Feb;57(2):191-206. doi: 10.1007/s11626-020-00532-8. Epub 2021 Jan 12. PMID: 33438114; PMCID: PMC7802613.

[4] Ingber DE. Human organs-on-chips for disease modelling, drug development and personalized medicine. Nat Rev Genet. 2022 Aug;23(8):467-491. doi: 10.1038/s41576-022-00466-9. Epub 2022 Mar 25. PMID: 35338360; PMCID: PMC8951665.

translational use of this new technology.[5] Additionally, recent federal legislation has cleared the way for the Food and Drug Administration (FDA) to consider new drug applications without requiring animal testing, relying instead on human-relevant, non-animal methods, which again indicates the accelerating importance of these technologies.[6]

It is clear this sector is poised to rapidly expand, and Maryland should benefit from this growth. Investing in human-relevant research technologies would build on the state's already-excellent reputation as a biotechnology hub and center of excellence for biomedical research.

Leverage and Augment Current Resources

As the home of NIH and Johns Hopkins University, Maryland residents include some of the most successful and innovative biomedical researchers in the country. The many biomedical companies along the I-270 biotechnology corridor are a testament to the creativity and entrepreneurial spirit of Maryland's diverse and highly-educated workforce. Many of these companies grew out of prior investments the state of Maryland made to leverage the resources and human capital available due to NIH and Johns Hopkins. The Johns Hopkins University Center for Alternatives to Animal Testing (CAAT) is home to some of the most successful and highly recognized researchers in this sector and could help position the state as a leader in the world.[7] Dedicated, targeted funding focused on human-relevant, non-animal technologies would allow the state to capitalize on these resources and benefit from this new technology sector.

Maryland has an impressive track record of recognizing the importance of new technologies and benefiting from wise investments in these areas. By supporting S.B. 560, Maryland could once again demonstrate its foresight and create a welcoming environment for cutting-edge research.

Sincerely,

Sue A. Leary

Sue A. Leary
President
Alternatives Research & Development Foundation
Jenkintown, Pennsylvania
www.ardf-online.org

[5] https://grants.nih.gov/grants/guide/rfa-files/RFA-TR-23-001.html

[6] Wadman, M. FDA no longer has to require animal testing for new drugs. Science. 2023 Jan 13; 379(6628):127-128. https://doi.org/10.1126/science.adg6276

[7] https://publichealth.jhu.edu/2021/caat-director-thomas-hartung-honored-with-eurotox-merit-award

SB 560_FAVORABLE_HSUS.pdf
Uploaded by: Vicki Katrinak
Position: FAV

THE HUMANE SOCIETY OF THE UNITED STATES

Testimony in Support of SB 560
Presented to the Senate Finance Committee
March 3, 2023
By Vicki Katrinak, Director, Animal Research and Testing
The Humane Society of the United States

Dear Chair Griffith, Vice-Chair Klausmeier, and members of the Senate Finance Committee,

I appreciate the opportunity to submit this written testimony on behalf of the Humane Society of the United States (HSUS) and our Maryland members and supporters urging a favorable report of SB 560. This legislation creates a Human Relevant Research Fund to provide grants to public and private institutions in the state of Maryland to advance non-animal research techniques. The funding for SB 560 is achieved through a mandatory contribution by institutions using animals for research and testing (as amended). This important legislation will provide a necessary investment in 21st century science and will speed the transition from traditional animal methods toward research and development of modern technologies that are based on human biology.

The promise of human relevant research

The world is continuously moving toward a future dominated by sophisticated methods that use human cells, tissues and organs, 3D printing, robotics, computer models and other technologies to create experiments that do not rely on animals. While animal experiments were developed decades ago and will always have severe limitations, advanced non-animal methods represent the very latest techniques that science has to offer, provide countless possibilities to improve our understanding and treatment of human diseases and will only continue to improve over time. Non-animal methods also have several advantages over outdated animal experiments: they more closely mimic how the human body responds to drugs, chemicals and treatments; they are more efficient and often less expensive; and they are more humane. Ultimately, moving away from animal experiments is better for both humans and animals.

Passage of SB 560 would demonstrate that Maryland is making a concerted effort to shift funding and technological development toward more non-animal alternatives. Examples of alternative approaches include:

- "Organs-on-chips" are tiny 3D chips created from human cells that look and function like miniature human organs. Organs-on-chips are used to determine how human systems respond to different drugs or chemicals and to find out exactly what happens during infection or disease. Several organs, representing heart, liver, lungs or kidneys, for example, can be linked together through a "microfluidic" circulatory system to create an integrated "human-on-a-chip" model that lets researchers assess multi-organ responses.
- Sophisticated computer models use existing information to predict how a drug or chemical might affect a human.
- Cells from a cancer patient's tumor are used to test different drugs and dosages to get exactly the right treatment for that specific individual, rather than testing the drugs on animals.
- Specialized computers use human cells to print 3D tissues that are used to test drugs.

- Skin cells from patients, such as those with Alzheimer's disease, are turned into other types of cells (brain, heart, lung, etc.) in the laboratory and used to test new treatments.
- Sophisticated computer programming, combined with 3D imaging, is used to develop highly accurate 3D models of human organs, such as the heart. Researchers then input real-world data from healthy people and those with heart disease to make the model hearts "beat" and test how they might respond to new drugs.
- Human cells or synthetic alternatives can replace horseshoe crab blood in tests to determine whether bacterial contaminants are present in vaccines or injectable drugs.

Limitations of animal testing

The continued use of animal models for human disease or to assess the possible impact of substances on the human body carries serious scientific limitations. Different species can respond differently when exposed to the same drugs or chemicals. Consequently, results from animal tests may not be relevant to humans, under- or over-estimating real world health hazards. It should not be surprising, therefore that more than 90% of human drugs fail during clinical trials[1] after having completed extensive animal studies. These failures are due to unexpected toxicity in human patients or lack of efficacy, sometimes resulting in hospitalizations or even death. In addition, animals do not always develop the same diseases as humans, or the impact of the disease varies greatly by species. Often treatments that seem incredibly promising in animal models turn out to not be effective in treating human diseases.

Animal tests are not only inaccurate, but also incredibly cruel. In traditional animal tests, dogs, rabbits, non-human primates, mice and rats have substances forced down their throats or into their lungs, dripped into their eyes, or smeared onto their skin. Thousands of animals may be used for a single test, and they can suffer for months or years before being killed. Mice, rats, and birds who have been purpose-bred for research make up the majority of animals used in research and testing, and yet they are excluded from even the most minimal protections of the Animal Welfare Act.

Impact of laws and regulatory agency actions

In 2016, Congress revised the Toxic Substances Control Act, which included a provision directing the Environmental Protection Agency (EPA) to reduce and replace the use of animals in chemical testing. Since that time, EPA has been at the forefront of efforts to assess modern non-animal test methods for chemical and pesticide safety including the creation of a New Approach Methods Workplan that was updated in 2021, where the agency declared that "reducing the use of vertebrate animals for toxicity testing is a priority."[2] This forward-thinking workplan provides an updated roadmap for ensuring the agency's success in this reduction goal.

The Food and Drug Administration has also indicated a need to prioritize the development and acceptance of non-animal methods to assess the safety of products regulated by the agency including drugs, vaccines, medical devices, and food ingredients. As part of the federal omnibus signed into law at the end of 2022, Congress appropriated $5,000,000 to *Reduce Animal Testing through Alternative*

[1] National Center for Advancing Translational Sciences. *About New Therapeutic Uses.* (n.d.). Retrieved from: https://ncats.nih.gov/ntu/about

[2] U.S. Environmental Protection Agency. *New Approach Methods Work Plan*. (2021, December). Retrieved from: https://www.epa.gov/system/files/documents/2021-11/nams-work-plan_11_15_21_508-tagged.pdf

Methods, a full funding of the agency request submitted as part of President Biden's budget.[3] The agency requested this money in part to create of a cross-agency New Alternatives Methods Program in the Commissioner's office. In 2021, FDA launched its Innovative Science and Technology Approaches for New Drugs (ISTAND) Pilot Program with the goal of assuring qualification of drug development tools such as tissue chips and novel toxicology assays.[4]

The National Institutes of Health (NIH), the largest funder of animal research in the world, has also proclaimed the value of non-animal approaches for testing and research. The National Center for Advancing Translational Sciences (NCATS) — one of 27 Institutes and Centers at NIH — was established by Congress in 2011 with its stated mission to "support the creation of innovative methods and technologies to speed the development, testing and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions."[5] One of NCATS first projects was developing a Tissue Chip for Drug Screening initiative in conjunction with FDA and Defense Advanced Research Projects Agency (DARPA).[6] While this NIH investment in human-relevant science is important, it represents just a small fraction of the total research rewards given by the agency.

In addition to efforts from Congress and federal agencies, states have also taken actions recently to address the need to end unnecessary animal testing. Since 2018, ten states (including Maryland) have passed laws to prohibit the sale of cosmetics that have been newly tested on animals. There are currently 42 countries that have passed laws to help bring about an end to animal testing for cosmetics and Congress has considered legislation in recent years to do the same throughout the United States. Even China, which once required animal testing for all cosmetics, has begun to accept non-animal test methods for these products.[7]

The message being sent is clear: science is moving away from outdated animal methods and toward human relevant approaches. **Maryland could become a leader in this biotechnological space by passing SB 560.**

Strong public support for investing in non-animal research methods

In a poll of Maryland voters in February 2023, seventy-nine percent of respondents supported investing in research and development techniques that don't require animal testing, with only 13 percent opposed. In addition, seventy-two percent support banning animal testing to determine product toxicity. Passage of SB 560 would align with the sentiment of Maryland voters.

---

[3] U.S. Food and Drug Administration. *FDA Seeks $8.4 Billion to Further Investments in Critical Public Health Modernization, Core Food and Medical Product Safety Programs.* (2022, March 28). Retrieved from: https://www.fda.gov/news-events/press-announcements/fda-seeks-84-billion-further-investments-critical-public-health-modernization-core-food-and-medical

[4] U.S. Food and Drug Administration. *Innovative Science and Technology Approaches for New Drugs (ISTAND) Pilot Program.* (2021, February 10). Retrieved from: https://www.fda.gov/drugs/drug-development-tool-ddt-qualification-programs/innovative-science-and-technology-approaches-new-drugs-istand-pilot-program

[5] National Center for Advancing Translational Sciences. *NCATS History.* (2022, November 8). Retrieved from: https://ncats.nih.gov/about/center/history

[6] National Center for Advancing Translational Sciences. *About Tissue Chip.* (2022, September 15). Retrieved from: https://ncats.nih.gov/tissuechip/about

[7] Institute for In Vitro Sciences. *China's Acceptance of Certain Non-Animal Testing Methods for the Regulation of Cosmetics.* (2019, April 3). Retrieved from: https://iivs.org/2019/04/03/china-accepts-new-alternative-methods-for-cosmetics/

Importance of dedicated funding

HSUS appreciates the willingness of research institutions in Maryland to work with us on amendment language all parties can agree to. We support the agreement thus far, which would create a mandatory annual contribution by institutions using animals into the Human Relevant Research Fund.

As regulatory agencies and state, federal, and international law continue to push for the use of non-animal methods and the public opposition to the continued use of animals grows, Maryland should take the opportunity to invest in the development of the new technologies that will be used by the chemical, cosmetics, and drug industries to evaluate their products. Maryland, a leader in research and biotechnology, should be aligned with this global shift away from animal use and encourage further innovation and development of modern non-animal approaches. This will also provide young scientists in Maryland with opportunities in this sector, creating a foundation for the future. HSUS urges a favorable report of SB 560 to help advance human relevant alternatives to animal testing in Maryland.

Sincerely,

Vicki Katrinak
Director, Animal Research and Testing
The Humane Society of the United States
700 Professional Dr.
Gaithersburg, MD 20879

NABR MD SB560.pdf
Uploaded by: Brandon Morton
Position: FWA

National Association *for* Biomedical Research

March 3, 2023

The Honorable Senator Melony Griffith
Chair, Senate Finance Committee
3 East Miller Senate Office Building
11 Bladen Street
Annapolis, MD 21401

Dear Senator Griffith:

The National Association for Biomedical Research (NABR) encourages that SB560- Animal Testing and Research – Human-Relevant Research Funding and Animal Testing and Research Licensure be reported favorably out of committee with amendments.

This bill will establish the Human-Relevant Research Fund to distribute grants to researchers working to develop alternatives to animal testing. It also includes licensing and reporting provisions, as well as criminal penalties.

For over 43 years, NABR has been the nation's only organization solely dedicated to advocating for sound public policy in support of ethical and essential laboratory animal research and the lifesaving discoveries they produce. NABR's diverse and unified membership includes more than 330 universities, medical and veterinary schools, teaching hospitals, pharmaceutical and biotechnology companies, patient groups and academic and professional societies that rely on humane and responsible use of research animals to advance global human and animal health.

Animal research remains vital to our mission to understand disease, discover targeted therapies, alleviate suffering, and improve and increase the quality of life. Biomedical research projects involving animals, governed by a strict structure of laws, regulations, and guidelines, continue to yield invaluable data in the process of discovering new therapies to treat, cure, and prevent disease. Cancer therapies, immunizations, organ transplants, reconstructive surgeries, and many other innovations have been brought to fruition through research conducted at our member institutions.

Certain provisions in this bill, as written, could deter life-saving research and negatively impact scientific innovation. Therefore, we encourage the committee to favorably report Senate Bill 560 with the amendments below.

Sincerely,

Matthew R. Bailey
President

1100 Vermont Avenue NW, Suite 1100, Washington, DC 20005 • 202.857.0540 • www.nabr.org • info@nabr.org

National Association *for* Biomedical Research

NABR supports the following amendments:

1. The term "animal" should be defined in the bill. Leaving the term undefined opens up to insects, fish, and other species that are difficult, if not impossible, to count. Given that the proposed contribution structure relies on the number of animals held, it is important to clarify which species the bill contemplates, and it must be possible to count the individual animals each facility holds. Fortunately, the federal Animal Welfare Act already defines "animal in a way that is workable and widely accepted. The definition in this bill should, therefore, align with 7 USC Ch. 54, §2132(g), which states: "The term "animal" means any live or dead dog, cat, monkey (nonhuman primate mammal), guinea pig, hamster, rabbit, or such other warm-blooded animal, as the Secretary may determine is being used, or is intended for use, for research, testing, experimentation, or exhibition purposes, or as a pet; but such term excludes (1) birds, rats of the genus Rattus, and mice of the genus Mus, bred for use in research, (2) horses not used for research purposes, and (3) other farm animals, such as, but not limited to livestock or poultry, used or intended for use as food or fiber, or livestock or poultry used or intended for use for improving animal nutrition, breeding, management, or production efficiency, or for improving the quality of food or fiber. With respect to a dog, the term means all dogs including those used for hunting, security, or breeding purposes."

2. As explained above, the licensing requirement, beginning on page 6 through the top of page 9 of the bill, should be removed in its entirety. Testing facilities are already required to obtain a license from at least one federal agency and the Maryland Department of Natural Resources Wildlife and Heritage Service for use of animals caught in captivity or bred for research purposes. Adding a State-level license requirement will be burdensome and duplicative.

3. The corresponding reporting requirements are unnecessary and duplicative as well. Testing facilities are already required to report annually to the USDA on the covered species they hold. These reports are publicly available online. Therefore, the reporting requirements should be removed from the bill.

4. If the licensing provisions are removed from the bill, a new mechanism would need to be developed for the testing facilities to contribute to the Fund. Therefore, the licensing fee should be removed, and a contribution structure inserted in its place. We propose a contribution structure, based on the number of animals held, maxing out at $75,000.

5. As discussed above, the use of animals in scientific research is both heavily regulated and yield benefits to society. Therefore, the criminal penalty provisions in the bill send the wrong signal about the role of research in society.

National Association *for* Biomedical Research

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SB560 - Johns Hopkins - Support with Amendments.pd
Uploaded by: Michael Huber
Position: FWA

JOHNS HOPKINS
UNIVERSITY & MEDICINE
Government and Community Affairs

SB560
Favorable

TO: The Honorable Melony Griffith, Chair
Senate Finance Committee

FROM: Michael Huber, Director, State Affairs,
Johns Hopkins University & Medicine

DATE: March 3, 2023

RE: SB560 – Animal Testing and Research – Human-Relevant Research Funding and Animal Testing and Research Licensure

Johns Hopkins University and Medicine urges a favorable report with amendments on **SB560 – Animal Testing and Research – Human-Relevant Research Funding and Animal Testing and Research Licensure.**

This bill will establish the Human-Relevant Research Fund to distribute grants to researchers working to develop alternatives to animal testing. It also includes licensing and reporting provisions, as well as criminal penalties.

As the leading research institution in the State, Johns Hopkins takes seriously its mission to improve the health of the community and the world by setting the standard of excellence in medical education, research and clinical care. The use of animals is critical to the success of our mission.

Johns Hopkins shares this legislation's goal of continuing to develop alternatives to animal testing. Progress in this area of research has been impressive and inspirational, but at present biomedical research could not continue to provide the breakthroughs in our understanding of human disease and treatments without the use of animals. Use of animals in research is subject to considerable oversight by multiple federal agencies, including the National Institute of Health and the U.S. Department of Agriculture. Federal guidance serves as a benchmark in our efforts to optimize animal care and animal welfare in Hopkins facilities.

Almost every medical advance – from polio vaccines, insulin therapy for diabetes, medical treatments for cardiovascular disease, and cancer therapy to organ transplants and heart surgery – are the direct result of research performed in animals. Simply put, modern medicine, as we understand it today, would not exist without research performed on animals.

For example, The State of Maryland played a key role in the development of COVID-19 vaccines. Starting 3 years ago, as COVID initially spread world-wide, institutions, including Johns Hopkins and the University of Maryland, and private companies, rapidly ramped up research to develop new ways to treat and prevent COVID-19. The vaccines and therapeutics developed by biomedical researchers during

this time were tested on animals before human trials as an integral part of development. Many different kinds of institutions and facilities contributed to this effort, leading to widely available COVID-19 vaccines in an unexpectedly short time. These efforts were central to containing the COVID pandemic.

While cutting-edge scientific research often involves the use of animals, Johns Hopkins is a major supporter of alternatives to animal testing. In fact, Johns Hopkins is home to the Center for Alternatives to Animal Testing (CAAT). Housed in the Bloomberg School of Public Health and founded in 1981, CAAT supports the creation, development, validation, and use of alternatives to animals in research, product safety testing, and education. Researchers at Johns Hopkins have led the way in developing alternatives to animal testing.

Johns Hopkins recognizes and adheres to our ethical and legal obligations relating to the use of animals in medical research. We follow strict policies designed to assure that laboratory animals receive the highest quality care as well and adhere to the highest standards to protect the health and safety of people who work with and around animals. We take seriously our obligations to implement the Three Rs principle:

- **Replacement:** Wherever possible, use alternatives to animals, including computer models and animal-derived tissue and organs.
- **Reduction:** Employ methods that reduce the number of animals used as much as possible without sacrificing the integrity of the research.
- **Refinement:** Use approaches that minimize or eliminate the animals' pain and distress.

We are subject to extensive oversight by multiple federal agencies and are committed to complying with all federal laws that govern the use of animals in research -- and there are many. We voluntarily seek accreditation of our facilities from AAALAC International, the benchmark for assessing institutional animal care and use policies and practices, and we are proud of our several decades of uninterrupted AAALAC accreditation. Our facilities are subject to unannounced inspections by the United States Department of Agriculture, and our programs are designed to assure compliance with the Animal Welfare Act and the "Public Health Service Policy on Humane Care and Use of Laboratory Animals." Policies and protocols are in place, and strictly adhered to, that address animal housing and care, veterinary medical care, facilities management, training, and occupational health. Additionally, the Johns Hopkins Animal Care Program is voluntarily accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International ("AAALAC"). AAALAC is the primary accrediting body for animal research programs in the United States and elsewhere.

In summary, we simultaneously are using animals in research where necessary while also advancing alternatives to the use of animals. Given our extensive experience on both fronts, we assert it is still critically necessary to use various animal models in many research settings and, thus, grossly scientifically premature to do anything that would penalize the valid, approved use of animals in research. Thus, although we strongly share the bill's intent and motivation, the licensing, reporting, and criminal penalty provisions of the bill are inappropriate, counterproductive, and outright unfair because they would have the effect of chilling critical research.

We propose the following amendments, on which we have worked closely with the Humane Society:

1. The term "animal" should be defined in the bill. Leaving the term undefined opens up to insects, fish, and other species that are difficult, if not impossible, to count. Given that the proposed contribution structure relies on the number of animals held, it is important to clarify which species the bill contemplates, and it must be possible to count the individual animals each facility holds. Fortunately, the federal Animal Welfare Act already defines "animal in a way that is workable and widely accepted. The definition in this bill should, therefore, align with 7 USC Ch. 54, §2132(g), which states: "The term "animal" means any live or dead dog, cat, monkey (nonhuman primate mammal), guinea pig, hamster, rabbit, or such other warm-blooded animal, as the Secretary may determine is being used, or is intended for use, for research, testing, experimentation, or exhibition purposes, or as a pet; but such term excludes (1) birds, rats of the genus Rattus, and mice of the genus Mus, bred for use in research, (2) horses not used for research purposes, and (3) other farm animals, such as, but not limited to livestock or poultry, used or intended for use as food or fiber, or livestock or poultry used or intended for use for improving animal nutrition, breeding, management, or production efficiency, or for improving the quality of food or fiber. With respect to a dog, the term means all dogs including those used for hunting, security, or breeding purposes."

2. As explained above, the licensing requirement, beginning on page 6 through the top of page 9 of the bill, should be removed in its entirety. Testing facilities are already required to obtain a license from at least one federal agency and the Maryland Department of Natural Resources Wildlife and Heritage Service for use of animals caught in captivity or bred for research purposes. Adding a State-level license requirement will be burdensome and duplicative.

3. The corresponding reporting requirements are unnecessary and duplicative as well. Testing facilities are already required to report annually to the USDA on the covered species they hold. These reports are publicly available online. Therefore, the reporting requirements should be removed from the bill.

4. If the licensing provisions are removed from the bill, a new mechanism would need to be developed for the testing facilities to contribute to the Fund. Therefore, the licensing fee should be removed, and a contribution structure inserted in its place. We propose a contribution structure, based on the number of animals held, maxing out at $75,000.

5. As discussed above, the use of animals in scientific research is both heavily regulated and yield benefits to society. Therefore, the criminal penalty provisions in the bill send the wrong signal about the role of research in society.

Johns Hopkins stands ready to support this effort, but for the reasons stated above, is concerned that some provisions of the bill will prematurely move researchers away from important, society-benefitting research and would be redundant to our already strict adherence to federal guidance on the care and use of animals. We look forward to continued collaboration with advocates and the sponsor on amendments that will fulfill the intent of the legislation while also recognizing practices and requirements already in place that support the continued development of alternative methods to the use of animals in research. Therefore, we urge a favorable report *with amendments* on **Senate Bill 560**.

SB 560 Animal Testing Written Testimony 3.3.23.pdf
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Position: FWA

SB 560 – Animal Testing and Research-Human-Relevant Research Funding and Animal Testing and Research Licensure
Senate Finance Committee

March 3, 2023

Good Afternoon Chair Griffith, Vice Chair Klausmeier and members of the Finance Committee,

My name is Pam Lanford, Director of Animal Research Compliance for the University of Maryland, College Park (UMCP). As amended, we support the overall concept of establishing the Human-Relevant Research Fund to provide additional resources to develop alternatives to using nonhuman animals in medical and product testing and research.

While animal-based research is necessary for the development of lifesaving and life altering treatments for people and animals, UMB and UMCP holds firm to the belief that we have an ethical and moral responsibility to provide quality, compassionate and humane treatment of all our animals. We also recognize that our responsibility to our animals does not end when a research project concludes.

All laboratory animal work at UMB and UMCP must be approved by the Institutional Animal Care and Use Committee (IACUC) in accordance with the Animal Welfare Act, *The Guide for the Care and Use of Laboratory Animals*, and other federal regulations. Researchers consider all alternatives to procedures by employing appropriate, protocol specific search strategies, regardless of species. They are guided by the approach of the Three Rs which represents a practical method for implementation referring to replacement, refinement, and reduction when deciding to use animals in research and in designing humane animal research studies. In terms of justifying the use of an animal model, the principal investigator must submit to the IACUC whether other alternatives (e.g. cell culture, computer/modeling/simulation) to animal usage exist and why they are not feasible for this particular research protocol.

We adhere to all federal regulations, are inspected once a year, have internal protocol measures and oversight in place and provide an annual report to the USDA as a registered research facility.

It is important to remember that animal-based research has resulted in groundbreaking discoveries that have helped to save or improve the lives of countless individuals in the United States and throughout the world. UMB has carried out major life saving medical research using animal models including the development of aromatase inhibitors for the treatment of breast

cancer. In addition, animal-based research carried out by our own Shock Trauma has led to major advances in life saving procedures such as the use of hypothermia to improve the survival of non-trauma cardiac arrest patients. Last year, University of Maryland School of Medicine (UMSOM) faculty at the University of Maryland Medical Center (UMMC), together known as the University of Maryland Medicine were able to successfully transplant a modified pig heart into an adult human with end-stage heart disease. Recently, UMCP's researchers were able to develop an inhalable coronavirus vaccine making it safe for children and the immunocompromised after conducting animal trials. More broadly, animal-based research has resulted in treatments for asthma, dementia, epilepsy, diabetes, high blood pressure, and numerous other medical conditions. We continue to see the benefits of animal-based research in our everyday lives and the lives of animals.

SB560 - FIN hearing - Animal Testing - TEDCO_writ
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Position: FWA

TESTIMONY PRESENTED TO THE SENATE FINANCE COMMITTEE

SENATE BILL 560 - ANIMAL TESTING AND RESEARCH – HUMAN–RELEVANT RESEARCH FUNDING AND ANIMAL TESTING AND RESEARCH LICENSURE

MARCH 3, 2023
POSITION STATEMENT

The Maryland Technology Development Corporation (TEDCO) is dedicated to economic growth through the fostering of an inclusive entrepreneurial and innovation ecosystem. TEDCO discovers, invests in, and helps build great Maryland-based, technology companies.

As drafted, SB 560 - Animal Testing and Research – Human–Relevant Research Funding and Animal Testing and Research Licensure requires TEDCO to establish a grant and loan program for State–funded, human–relevant animal testing alternatives research. The legislation also requires TEDCO to contract with an independent scientific review board composed of recognized scientific experts in the field of human–relevant animal testing alternatives to act as the human–relevant research review board.

TEDCO appreciates being considered as the implementing agency for the Human-Relevant Research Funding program and appreciates the support of the bill sponsor. TEDCO recognizes that the program like the one established by SB 560, is not a part of TEDCO's current strategic plan, and would require adequate planning time for TEDCO to collaborate with key entities in the ecosystem to effectively develop and advance the related program. Importantly, alternatives must be accepted by NIH and FDA to meet federally established standards.

For example, the U.S. Food and Drug Administration (FDA) has established standards and requirements for approving medical devices, biologics, and new drugs. These standards and requirements currently drive much of the testing in animal models in companies and universities developing products for improving human health and advancing the field of life sciences and bioscience. For research and development to be accepted and/or approved by these agencies, it must comply with the related standards and requirements. Additionally, animal research is highly regulated by organizations like the National Institutes of Health (NIH). Protocols for research involving animals must be approved through an Institutional Animal Care and Use Committee (IACUC), which reviews the humane treatment of animals used in research. Institutions receiving grants from the NIH and other agencies must adhere to the requirements of IACUC approval of all research involving the use of animals.

As reflected in the policy and fiscal note for SB 560, TEDCO would need to expand our staffing resources to adequately support, develop, and launch an effective, successful program. While it is unclear at this time, the related staffing and funding needs the program would require, at a minimum, TEDCO assumes the program will require a program manager and a coordinator. TEDCO estimates $300,000 in annual costs for the two positions, including salary and benefits, plus $162,000 annually for overhead and indirect expenses including office space, auditing, IT, marketing, etc. Based on these assumptions, TEDCO estimates that it will cost about $440,000 annually or $2,200,000 over five years.

TEDCO appreciates the opportunity to provide a position statement on this legislation.

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Uploaded by: Laura Bogley
Position: UNF

Opposition Statement SB560/HB626
Animal Testing and Research – Human-Relevant Research Funding
Laura Bogley, JD
Director of Legislation, Maryland Right to Life

We Oppose SB560/HB626 As Written

On behalf of our 200,000 followers across the state, we respectfully oppose HB626/SB560 to the extent that it may commit public funding to the unethical use of human embryonic cells or fetal tissue for the purpose of medical or even commercial research. "Human-Relevant" testing methods are largely undefined and will continue to expand with additional public funding. The state of Maryland should not adopt a definition of "human-relevant" testing that includes the destruction of human embryos or procurement of fetal human body parts.

Human Embryo Testing is Unethical

Embryonic stem-cell research is routinely touted by supporters as having the potential to cure a number of diseases and medical conditions. However, the procedure for obtaining embryonic stem cells is fraught with ethical and scientific pitfalls and, importantly, such research has yet to yield an effective treatment for any disease or condition.

Living human beings in embryonic stage are destroyed in embryonic stem-cell research and human cloning. Specifically, embryonic stem-cell research is done by taking a days-old embryo that has grown to the several hundred-cell stage, breaking it apart, and taking the cells from the embryo's inner mass. These unspecialized cells are then grown and used for research.

More than 15 years after the first isolation of embryonic stem cells, there is not a single disease that these cells can cure, regardless of whether the embryonic cells are created through the fusion of a human sperm and egg or through cloning. In fact, Geron Corporation, the company that received governmental approval for the first clinical trials using stem cells derived from human embryos, discontinued "further stem cell work" after "a strategic review of the costs… timelines and clinical, manufacturing and regulatory complexities associated with the company's research and clinical-stage assets."[1]

Embryonic Testing is Unsuccessful

Conversely, there are proven, ethical alternatives to research using stem cells from human embryos. One important source is umbilical cord blood—a very rich source of stem cells. Another is adult stem cells, which can be obtained from various organs. For example, researchers know that bone marrow cells can form into fat, cartilage, and bone tissue. A third promising source is neural stem cells. These

[1] *See* M. Smith, *Geron Move Shows Embryonic Stem Cell Research Not Successful*, LifeNews (Nov. 15, 2011), *available at* http://www.lifenews.com/2011/11/15/geron-move-shows-embryonic-stem-cell-research-not-successful/ (last visited June 26, 2017).

stem cells have been successfully isolated and cultured from living human neural tissue and even from adult cadavers.

Moreover, since 2007, research breakthroughs are opening the door for the "reprogramming" of adult stem cells into the embryonic state—without the use or destruction of human embryos.

In sum, any alleged "therapeutic" purposes for destructive embryo research have proven to be speculative, while simultaneously crossing ethical boundaries and taking human life. As such, states should prohibit this ethically problematic research that has proven completely unnecessary.

For legislators and policy makers, it is vitally important that careful attention be exercised to avoid some types of research (especially in the area of cloning) that are ineffective or that create incentives for researchers to destroy preborn human life and increase the demand for aborted fetal tissue including late term, fully developed human organs.

For these reasons we urge your amendment to ensure that any testing methods licensed or funded by the State of Maryland are ethical and prohibit the use of cells or tissues obtained from embryonic or fetal human beings. The state instead should encourage the development of ethical alternatives.