Citizens Petition to the Department of Health and Human Services

SUBMITTED TO

The U.S. Department of Health and Human Services

SUBMITTED BY

People for the Ethical Treatment of Animals

March 15, 2011

The Honorable Kathleen Sebelius, Secretary
Department of Health and Human Services
200 Independence Ave., SW, Room 615-F
Washington, DC 20201

Dear Secretary Sebelius:

People for the Ethical Treatment of Animals and its two million members and supporters ("the petitioners") sponsor this rulemaking petition for consideration and enactment by the Department of Health and Human Services.

I. Introduction and Statutory Authority

Pursuant to the Right to Petition Government Clause contained in the First Amendment of the Constitution, the Administrative Procedure Act ("APA"), 5 U.S.C. §553(e), and the Health and Human Services ("HHS") implementing regulations, the petitioners submit this citizens petition for rulemaking in the interests of protecting the public health and welfare, and furthering the objectives of the statutes cited below that pertain to animal testing.

II. Action Requested

The petitioners request that HHS and its institutes, the National Institutes of Health ("NIH"), the National Institute of Environmental Health Sciences ("NIEHS"), the National Center for Toxicological Research ("NCTR"), and the National Institute for Occupational Safety and Health ("NIOSH"), commence rulemaking concerning cessation of funding for, or animal testing by or for the National Toxicology Program ("NTP") and the NIH, as more fully described below.
III. The NTP’s Host Susceptibility Branch Program to Identify Orthologous Human Genes in Inbred Strains of Mice

The NTP was established in 1978 for the purposes of: 1) coordinating toxicity testing among federal agencies; 2) reinforcing the scientific underpinnings in toxicology; 3) developing, validating, and improving testing methods; and 4) providing data about toxic substances to health, research, medical and scientific stakeholders, as well as to the public.¹ Three federal agencies comprise the nucleus of the NTP, namely the NCTR, the NIEHS, and the NIOSH.

The Host Susceptibility Branch (HSB) of the NTP was initially developed as a new research program in 2007. Its mission is to investigate individual differences in susceptibility to environmental toxicants due to genetic variation within the human population. It is doing this by attempting to identify genes in which variation correlates with susceptibility differences, not in humans but among multiple strains of inbred mice.² The HSB apparently hopes that identification of mouse genes linked to susceptibility may indicate orthologous human genes that can then be further investigated, for example by epidemiology of exposed human populations.³

NIEHS has recently decided to integrate the HSB into the Biomolecular Screening Branch (BSB) of NTP with the stated goal of utilizing the identified genes and pathways to “design more specific and targeted research and testing strategies (both in vitro and in vivo) for NTP scientists to use for predicting the potential toxicity of substances in our environment and their presumptive risk to humans that may differ in disease susceptibility.”⁴ While the reorganization may facilitate the correlation of information from the HSB with that from other initiatives, it does not increase the likelihood that the HSB will provide information that is relevant to humans or other animal species.

HSB’s intended use of multiple mice strains will lead to an exponential increase in the number of animals killed in toxicity testing. To test the utility of its approach, the HSB first conducted an ADME (absorption, distribution, metabolism and elimination) evaluation in 17 inbred strains of mice plus one hybrid strain using orally-administered benzene, a chemical that has been studied extensively in rodents and humans.⁵ At a December, 2009 NTP Board of Scientific Counselors meeting, Dr. John French presented calculations showing that, as a result of using multiple strains, 1,360 mice would be required for planned low dose inhalation exposure studies. The selection of these strains was based upon available resources⁶ and includes 15 inbred strains of mice for which the genomic DNA sequences were recently determined.⁷ The HSB admits that the optimal number of strains for measuring these metabolic parameters is poorly understood and that calculations suggest that 30-50 strains may be required to obtain

¹ History of the National Toxicology Program (NTP), viewed 25 Feb 2011, http://ntp.niehs.nih.gov/?objectid=720163C9-BDB7-CEBA-FE4B970B9E72BF54
sufficient statistical power to identify trait loci and candidate genes. Since many available strains of inbred mice derive from common precursors, genetic variation is limited among them. In its description of the initial genomic DNA sequencing project, the NTP observed that the 15 strains sequenced may not adequately represent the genetic variation existing in nature and suggested that it was therefore “desirable” to create 50-100 newly derived inbred strains from wild mice.

In addition to the impracticality of evaluating known and potential toxicants in as many as 100 different strains, even if sufficient statistical power could be achieved, studies which have been able to achieve direct genetic extrapolation from mice to humans are generally lacking. The organization of immune-related genes linked to lupus traits is a case in point. While the signaling lymphocyte activation molecule (SLAM) gene family exhibits considerable homology between mice and humans, the interferon-inducible (Ifi) and immunoglobulin Fc gamma receptor (FCGR) gene families are so diverse in both gene number and position that it is very difficult to determine the human–mouse orthologs even when the actual sequence is examined.

In cases where orthologous human genes can be identified, genetic structure can diverge between species, resulting in considerable differences in gene expression and/or function. A recent investigation of transcriptional regulator binding to promoter regions of orthologous genes found that 41-89% of the orthologous promoters bound by a protein in one species were not bound by the same protein in the other. Further, the location of binding events varied widely between species in ways that could not be predicted from human-mouse sequence alignments alone. Analysis of genomic regions bound by the same factors in both species showed that approximately two-thirds of the binding events are not aligned between the mouse and human genomes. The authors concluded that their findings have implications for the use of mice as model organisms. For example, while HNF1A bound strongly to the SEL1L promoter in human liver, this binding was entirely absent from the corresponding mouse region. Polymorphisms around the SEL1L locus influence the onset of disease in individuals with maturity-onset diabetes caused by haploinsufficiency of HNF1A. The lack of HNF1A binding in the mouse suggests that this susceptibility may be species specific.

The HSB’s approach to identifying genes associated with susceptibility to environmental toxicants in humans runs counter to all efforts to move toward human-relevant methods. In addition to the difficulties common to all animal toxicity testing, such as extrapolating results from one species to another and from high test doses to much lower human exposures, the HSB faces unique obstacles resulting from differences in genetic structure and organization between humans and mice used in laboratories. Further, given the already high cost of animal toxicity testing, it is inconceivable that multiplying that cost up to 100-fold will result in a comparable benefit. A more relevant and efficient approach, similar to that used by the International HapMap Project, would be to screen the human genome using microchip technologies that can provide information on more than 100,000 different polymorphisms. While this approach is currently being used to identify haplotypes associated with susceptibility to disease and

8 NTP, HSB Project 2: Benzene ADME Phenotype and Haplotype Association Analyses.
9 NTP, The NIEHS/NTP-Perlegen Resequencing Project.
13 Rigby et al., 2006. Mice, humans and haplotypes—the hunt for disease genes in SLE. Rheumatology 45(9): 1062-1067.
response to pharmaceuticals, it could also be applied effectively to investigating susceptibility to environmental toxicants.

IV. The NIH’s Funding of the IMPC’s Knockout Experiments in Mice

Knockout experiments in mice, in which a gene is inactivated or removed, are widely used to infer the role of individual genes. The International Mouse Phenotyping Consortium (IMPC) plans to inactivate each of the genes in the mouse genome – thereby creating 20,000 new strains of knockout mice – with the intention of determining the phenotype of each knockout strain. A recent report from the meeting at which the project was announced boasted that it will provide “the ultimate mouse model of human disease.” According to the report, researchers would need only query the IMPC database in order to learn the function of genes associated with human disease. The NIH has already committed $110 million of the $900 million needed.

In fact, examples in which the inactivation of a gene clearly predicts its function are relatively rare. In many cases, a knockout is found to have no effect at all, even when the inactivated gene encodes a protein that is believed to be essential. In other cases, the knockout has a completely unexpected effect. For example, the AP1 transcription factor activates a number of genes, the products of which are known to play important roles in cell division. Several genes coding for the protein subunits that combine to form AP1 have been inactivated but in most cases, the phenotype of the knockout mice is virtually normal.14 The unexpected results of knockout experiments are partly caused by gene redundancy and pleiotropy. An example of gene redundancy, where one gene can compensate for the inactivation of another gene is the mouse gene Uch-L3, which codes for an enzyme involved in breaking down damaged proteins. Knockout mice have no discernable phenotype unless the related gene Uch-L1 is also inactivated, in which case mice develop walking difficulties, paralysis and eventually die early from degeneration of nerve cells in the spinal cord.15 Examples of gene pleiotropy, where one gene can cause many different phenotypes, include genes affecting memory formation in Drosophila that were found to code for enzymes already known to participate in the cAMP signaling pathway16, and the gene for the aryl hydrocarbon receptor which, when inactivated in mice, also causes early mortality along with decreases in the number of white blood cells and in the size of the liver.17

Knockout experiments can be further confounded by the presence of regions of genetic variability (“passenger” or “flanking” genes) that are transported with the knocked out gene onto the selected genetic background. This is related to the common practice of using embryonic stem cells from the mouse strain 129 to host the new gene sequence. The confounding presence of extraneous genes from the strain 129 host can greatly affect expression and the phenotype of the intended gene knockout. These surrounding regions potentially contain hundreds of genes, any of which can produce an observable phenotype and can have a critical impact on the interpretation of phenotypic data and, obviously, any extrapolation of the results to human genes.18

17 Gonzales et al., 1995. Xenobiotic receptor knockout mice. Toxicology Letters 82-83: 117-121.
Another factor to consider when attempting to relate the results of mice experiments to humans is that consistent phenotypes are rarely obtained by inactivation of the same gene in different strains of mice. One example is the gene for the epidermal growth-factor receptor, inactivation of which causes embryonic death in CF-1 mice while CD-1 mice pups survive for up to three weeks after birth. Another is the retinoblastoma-related p130 gene, inactivation of which causes severe abnormalities and embryonic death in Balb/cJ mice but has no effect in C57BL/6 mice. Studies of genes or gene products in other species along with the mouse have indicated that the two organisms may not always use the same genes to perform the same function. For example, C-tenascin, a protein whose location in the amphibian embryo strongly suggests an active role in controlling the first wave of cell migrations, can be eliminated from the mouse without causing any effects on its development.

It is simplistic to assume that a gene’s function is what is lost when it is inactivated. Similar reasoning might lead to the conclusion that spark plugs are ‘sputter suppressors.’ Instead, a gene’s function must be understood against the background of interacting gene products. The inactivation of one gene may cause a cascade of events with interactions of multiple genes and gene products, sometimes also utilizing compensatory pathways. These pathways often differ between species and even between individuals or strains of the same species. For example, Lesch Nyhan syndrome, an inheritable disorder with symptoms of spasticity and self-mutilation in children, results from inactivation of an enzyme involved in nucleotide biosynthesis (also another example of pleiotropy). Inactivation of the same gene in mice results in no detectable pathology, suggesting that only humans use this metabolic pathway in the central nervous system to an important degree.

Thus far, only a few genes have been identified as causative factors for corresponding disorders in humans and there is little reason to expect that experiments with knockout mice will provide insights into the complex gene interactions that occur in humans. As David F. Horrobin wrote in a Nature opinion piece in 2003: ‘If one mouse gene is so difficult to understand in a mouse context, and if the genome of a different inbred strain of mouse has so much impact on the consequences of that single gene’s expression, how unlikely is it that genetically modified mice are going to provide insights into complex gene interactions in the non-interbred human species?’

Some of the most widely studied diseases and corresponding mouse knock-out or knock-in “models” demonstrate that it is a mistake to assume a one-to-one correlation between mouse genes and those of humans. For example, many genetically modified mouse “models” attempt to replicate the inherited form of Alzheimer’s disease (AD); however, the problem with even the most widely accepted and commonly used of these models is that they still do not duplicate the human condition in many ways. The characterized symptoms for AD include deterioration of intellect, memory, cognition, behavior and even emotion. The histopathology of the affected brain includes two distinctive markers: 1) visible extracellular amyloid plaques due to the aggregation of β-amyloid peptide and 2) intracellular neurofibrillary tangles (NFTs), which are composed of hyper-phosphorylated tau protein. An important

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23 Morange, The Misunderstood Gene:70.
difference between human and mice brain anatomy is that a mouse’s brain is comprised of 70% neurons and 30% glia, whereas humans have the opposite ratio.

Many of the mouse transgenic “models” for AD are those which modify the expression of the amyloid precursor protein (APP). Catabolic cleavage of APP results in various peptides including beta-amyloid protein. One hypothesis of the cause of AD is that an imbalance of these cleavage products and their clearance results in the aggregation and deposition of beta-amyloid outside and around neurons and is associated with the progression of AD. APP transgenic mouse “models” are the result of over-expression of APP five-to-ten-fold over normal, whereas in the human disease, APP expression is only 50% above normal. In addition, the nature of the plaques differs in the transgenic mice – they are far more dense and they dissolve in a detergent solution whereas the human plaques do not. This physical difference also indicates a compositional difference between mice and human plaques. In contrast to the human condition, there is little cell death when the disease is being modeled in the mouse with a single gene mutation. Also, the neuropathological progression of the disease differs strikingly in the mouse models. In mice, cognitive defects precede plaque formation; whereas in humans the opposite is seen. The differences in protein levels, plaque composition, and neurodegenerative progression are so substantial that it raises serious questions about the transferability of data collected on a disease in these mouse models that appears in no way related to the human genetic form of Alzheimer’s.

Another case to consider is chronic obstructive pulmonary disease (COPD), which is acquired, progressive, and due to exposure to environmental factors over the course of a human’s life. Much effort has been put into creating COPD models in mice despite the fact that mice have obvious physiological differences related to breathing and processing smoke. Their pulmonary systems lack goblet cells, extensive cilia, and contain few tracheal submucosal glands. Mice are obligate nasal breathers and also are incapable of expectorating sputum. They have less branching of their bronchial trees and filter smoke inefficiently. Molecularly, some of their inflammatory mediators differ. For example, MMP-1 is found in humans, but not in mice and the roles of IL-8 and LTB-4 have not been ascertained in mice. The role of IL-8 in human COPD is an important one and has been shown to correlate with airway bacterial load and blood myeloperoxidase levels. Additionally, the cytokine profile of COPD differs from that seen in other airway diseases. Cytokines are rarely produced individually – they are pleiotropic and redundant. The effect of cytokines on each other and the surrounding tissue may be influenced by the host of cytokines in action. Therefore, the exact cytokine profile found in affected cells determines the activation cascade and subsequent cellular responses. In order to study a disease such as COPD in mice, three alternative approaches are often taken: 1) tracheal instillation of tissue-degrading enzymes typically followed by induction of lesions in the lung parenchyma, 2) inhalation of noxious stimuli such as tobacco smoke, sulfur dioxide, nitrogen dioxide, or oxidants, which may also lead to lesions (depending on mouse strain-specific genetic susceptibility), and 3) over-expression or depletion of a particular gene in transgenic mice together with the tissue damaging methods. These steps often result in mice that appear to have pulmonary disease, yet the mechanism and causes of the phenotype seen in mice differ from those seen in humans and make comparison between the two difficult.

Lastly, an examination of research intended to elucidate the genetic foundations of Parkinson’s disease through use of mice models shows inconsistent and questionable results. Parkinson's disease (PD) is a

26 Balducci, C and Gianluigi, F. ’APP Transgenic Mice: Their Use and Limitations,’ Neumolecular Medicine 2010 Dec 9
28 Chung, K. ’Cytokines in Chronic Obstructive Pulmonary Disease,’ European Respiratory Journal (2001) 34 suppl 50s-59s
degenerative disorder of the central nervous system that impairs motor skills resulting in tremor, rigidity, slowness of movement and postural instability. Non motor symptoms include effects on cognitive processes, autonomic and enteric nervous system dysfunction, and sensory dysfunction such as olfactory loss. Symptoms result from insufficient formation and action of dopamine produced in the dopaminergic neurons of the substantia nigra. Pathologically, the disease is characterized by the accumulation of the α-synuclein protein, which forms cytoplasmic Lewy bodies. Some symptoms can be treated with dopaminergic therapies such as Levodopa and dopamine agonists. Additional motor symptoms such as freezing and balance problems are not responsive to such therapies suggesting that, in common with non-motor symptoms, they are not primarily due to dopaminergic neuron loss. While some cases of PD have been associated with exposure to certain chemicals or a genetic predisposition, the majority are sporadic and of idiopathic origin. Hereditary forms of PD are rare, yet a number of different genes associated with PD have been identified including α-synuclein, ubiquitin carboxy-terminal hydrolase L1, leucine-rich repeat kinase 2 (LRRK2), parkin, PTEN-induced putative kinase 1 (PINK1), DJ-1, and ATPase type 13A2.

Of the several α-synuclein mouse “models” that have been created, mice with the A53T mutation exhibit the spectrum of pathology that most closely resembles the human disease, including α-synuclein aggregation, fibrils, oligomers phosphorylation, ubiquitination and progressive age-dependent neurodegeneration. However, unlike in humans, motor deficits in these mice are caused by a loss of brain stem neurons and anterior horn motor neurons of the spinal cord. These mice do not display the characteristic loss of dopaminergic neurons in the substantia nigra as seen in PD. Neither A53T mutant mice nor another α-synuclein mouse “model,” A30P, demonstrate the cardiac autonomic abnormalities or olfactory dysfunction prevalent in PD. And while both of these “models” display abnormalities in the enteric nervous system, neither one shows the dopaminergic neurotransmitter deficits, Lewy body inclusions or neurodegeneration characteristic of PD. Other mouse “models” are considered representative of the very early stages of PD because they have broad-based but regionally selective accumulation of insoluble α-synuclein and other deficits, such as autonomic dysfunction and early motor and olfaction deficits, yet administration of Levodopa or apomorphine (a dopa agonist) to these mice does not reverse the motor function deficiency. Thus, the lack of many of the fundamental symptoms of PD and responses to known therapies underscores the limited value of these mouse models.

A breakthrough in the development of a human-relevant model was recently described in the March 2011 issue of Cell Stem Cell: pluripotent stem cells induced from cells isolated from a PD patient were differentiated into dopaminergic (DA) neurons. These DA neurons carry the p.G2019S mutation, a key mutation for the genetic form of Parkinson’s disease, and show increased expression of oxidative stress-response genes and α-synuclein protein, both of which are important mediators of human PD. The mutant neurons were also more sensitive to caspase-3 activation and cell death caused by exposure to stress agents, similar to the increased sensitivity seen in early stages of PD. This represents the first

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human-based model of PD and will be used to identify novel therapies for degenerating neurons of PD patients.\textsuperscript{34}

There are significant differences in the physiologies of rodents and humans that are likely responsible for the differences seen in the phenotypes of mice and humans harboring the same mutations. In addition rodent “models” that rely on knock-in or knockout mutations do not take into account other genetic subtleties, such as varied penetrance and the influence of other genetic and environmental factors. It wastes time and resources to focus on mouse models when few, if any, of them accurately and reliably represent the human condition. Devotion of significant resources to the systematic knock-out of every mouse gene is unlikely to provide insight into the function of the analogous human genes and is a gross waste of money and other resources as well as animal lives.

V. Policies and Attitudes Surrounding the Use of Animals in Regulatory Testing

On the legislative side, Congress expresses the voice of the citizenry in the statutes it enacts. There are several laws that relate to the care, use, and welfare of animals used for testing including the Animal Welfare Act of 1966\textsuperscript{35} (7 U.S.C. §2131 \textit{et seq.}), the National Institutes of Health Revitalization Act of 1993 (42 U.S.C. §283e), and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) Authorization Act of 2000 (42 U.S.C. §285l \textit{et seq.})\textsuperscript{36}

\textbf{The Animal Welfare Act} provides minimum standards for the care of animals used in laboratory research and experiments. However, the Animal Welfare Act is exceedingly limited in its protections since it specifically excludes mice, rats and birds, even though those species represent between 98-99\% of the animals used in testing.

\textbf{The NIH Revitalization Act} directs the NIH to conduct or support research into methods that “do not require the use of animals,” “reduce the number of animals used in such research,” encourage the “acceptance by the scientific community” of alternative methods, and train “scientists in the use of such methods.” It is clear from the language of the statute that Congress intended HHS to be an active contributor to the development and implementation of the above-mentioned plan since NIH is an operating institute within HHS. These provisions clearly demonstrate Congressional intent with respect to advancing the reduction, refinement, and ultimate replacement of animal testing.

\textbf{The ICCVAM Authorization Act’s} central objective is to promote and advance the reduction and replacement of animal testing, and to search diligently for alternatives. In establishing the ICCVAM as a permanent entity, Congress signaled its firm commitment to replacing live animal testing with \textit{in vitro} methods.

Each of the above-referenced Acts expresses Congressional intent with respect to the reduction, refinement, and ultimate replacement of animal use in testing. Despite the foregoing, the use of animals in various forms of testing has increased. According the USDA, in 2006, 1,012,713 animals were used in regulated animal testing in registered labs in the United States – a number which does not include mice, mice, mice.

\begin{footnotesize}

\textsuperscript{35} The Animal Welfare Act has been amended four times in 1970, 1976, 1985 and 1990.

\textsuperscript{36} See http://www.hsus.org/web-files/PDF/legislation/CRS-07-animal-protection-fed-statutes.pdf for a comprehensive listing of statutes relating to animals.
\end{footnotesize}
rats and birds – the overwhelming majority of animals used in toxicity testing. It has been estimated that for mice alone, some 100 million are used each year. These numbers reflect an enormous increase in the use of live animals in testing and research over the past two decades. This trend stands in stark contrast to the laws cited above.

VI. Failure of HHS and Its Institutes, the NIH and the NTP, To Discharge their Mandate of the NIH Revitalization Act of 1993 or the ICCVAM Authorization Act By Funding and Supporting Irrelevant and Irresponsible Animal Testing and Gene Manipulations

The fact that the use of animals has caused serious delays in protecting humans or failed to protect them altogether has been recognized by the National Academy of Sciences, the NIH, and the Environmental Protection Agency (EPA).

With respect to toxicity testing, two significant events occurred in 2007 and 2008 that signify a shift in attitude among scientists and regulators about the usefulness of animal studies in human safety assessments. In June 2007, the National Research Council of the National Academy of Sciences issued a report prepared by an expert panel entitled “Toxicity Testing in the Twenty-first Century: A Vision and a Strategy” (the "Strategy Report")

The Strategy Report notes that animal-based toxicity testing is deeply entrenched but that its relevance to humans is questionable. The report also underscores the need to take a progressive approach to testing the safety of chemicals, pesticides and other compounds that focuses on in vitro instead of animal studies.

As the Strategy Report recognizes in its opening pages:

Change often involves a pivotal event that builds on previous history and opens the door to a new era. Toxicity testing is approaching such a scientific pivot point. It is poised to take advantage of the revolutions in biology and biotechnology. Advances in toxicogenomics, bioinformatics, systems biology, epigenetics, and computational toxicology could transform toxicity testing from a system based on whole-animal testing to one founded primarily on in vitro methods that evaluate changes in biologic processes using cells, cell lines, or cellular components, preferably of human origin. This report … envisions a major campaign in the scientific community to advance the science of toxicity testing and put it on a forward-looking footing.

A second important event was the issuance in February 2008 of a Memorandum of Understanding (MOU) between the NIH and the EPA. Pursuant to the MOU, high-speed, automated screening robots will be used to test suspected toxic compounds that may pose a risk to human health and the environment. These tests will utilize cells and isolated molecular targets instead of animal models. The collaboration between the EPA and the NIH is expected to increase the number of chemicals tested, reduce the costs and time required by animal based testing, and produce data that is far more relevant to humans. The MOU and the Strategy Report point toward a future in which toxicity testing will rely on in vitro methods, and unreliable and irrelevant animal-based testing will be obsolete.

38 The upward trend can only be expected to continue with the increase in production of genetically engineered animals and the huge national and international initiatives aimed at toxicity testing such as the High Production Volume Chemical Challenge and the Endocrine Disruptor Screening Program in the United States and the Registration, Evaluation and Authorization of Chemicals in the European Union. See A. Knight, ‘Systematic Reviews of Animal Experiments Demonstrate Poor Human Clinical and Toxicological Utility,’ ATLA 35 (2007):641-659.
Even the U.S. Food and Drug Administration (FDA), the agency tasked with ensuring the safety and quality of the nation’s food and medical products, has recently issued a call for change. Dr. Margaret Hamburg, Commissioner of FDA, states in the journal *Science*, that FDA “is working to eventually replace animal testing with a combination of *in silico* and *in vitro* approaches. The inherent complexity of the vertebrate reproductive system represents a major challenge to developing such technologies that replace whole-animal tests, and advanced regulatory science is needed to address this challenge.”

All of the above – the legislation, initiatives, understandings, and reports – signal a future in science that no longer looks at animal models for answers to human conditions. The HHS must embrace a 21st Century mindset in its approach to its mission and its mandate. That mindset should consist of sound scientific principles that are relevant to the human species.

V. CONCLUSION

This rulemaking petition furthers the interests of sound science, human health, animal welfare, and principles of significant ethical concern. The HHS can advance each of those interests by enacting rulemaking that requires all NTP and NIH testing to adhere to the scientifically valid standards of reliability, reproducibility, and relevance to human biology. We urge the Agency to commence rulemaking to effect the cessation of funding for, or animal testing by or for the NTP and the NIH as detailed above.

Without a serious re-evaluation of the reliance on animal testing at all levels in agencies and the government, American citizens will continue to bear the double burdens associated with such testing. First, taxpayers will bear the financial burden of underwriting this unenlightened and unfruitful method of research. And second, Americans will pay the price in reduced scientific advancements in cures for disease and human health issues generally. To improve the nation’s health, the government should only fund testing that is scientifically justified. The search for orthologous human genes in inbred strains of mice, and related knock-out experiments in mice cannot satisfy that standard.

Respectfully submitted,

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