

**Supplement to  
Citizens Petition to the  
Department of Health and  
Human Services  
to Adopt Modern Toxicity  
Testing Standards**



**PETA**

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TREATMENT OF ANIMALS

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July 14, 2008

**SUBMITTED TO**

The U.S. Department of Health and Human Services

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**SUBMITTED BY**

*People for the Ethical Treatment of Animals*  
Jessica Sandler, Director, Regulatory Testing Division

*Physicians Committee for Responsible Medicine*  
Daniel Kinburn, General Counsel

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July 14, 2008

U.S. Department of Health and Human Services  
 Michael O. Leavitt, Secretary  
 200 Independence Avenue, S.W.  
 Washington, D.C. 20201



Re: Supplement to Petition for Rulemaking to the Department of Health and Human Services to Adopt Modern Toxicity Testing Standards

Dear Mr. Leavitt:

This Supplement to Citizens Petition to Adopt Modern Toxicity Testing Standards is submitted jointly by People for the Ethical Treatment of Animals (“PETA”) and the Physicians Committee for Responsible Medicine (“PCRM”). PETA and PCRM have a combined membership exceeding two million supporters.

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***I Background***

PETA submitted a rulemaking petition to the U.S. Department of Health and Human Services (“HHS”) dated April 4, 2008. That petition sought rulemaking concerning animal testing. Specifically, the petition requested that HHS and its institutes, the National Institutes of Health (“NIH”), the National Institute of Environmental Health Sciences, the National Center for Toxicological Research, and the National Institute for Occupational Safety and Health (“NIOSH”), commence rulemaking concerning animal testing by or for the National Toxicology Program (“NTP”) requiring that the following criteria be satisfied:

1. There must be a showing that no alternatives to the proposed tests involving animals are available or will be available within the reasonably foreseeable future;
2. There must be a showing that there is, or are, no existing studies, research or data on the subject of interest, or studies, research or data which are closely related to the subject of interest and can be extrapolated thereto (i.e. route-to-route extrapolation, QSAR Toolbox, *Medline*, *Scopus* and similar resources). Compounds and substances which are already known to be hazardous to

human health or to the environment are presumptively unsuitable for testing on animals;

3. There must be a showing to a reasonable degree of scientific certainty that the adverse effects caused to the animals are significantly outweighed by the expected benefits to be gained from the research<sup>1</sup>;
4. There must be a showing that there are no existing human data and that any proposed animal tests have relevance to human health effects, and that the results of such tests will be predictive of human outcomes; and
5. There must be a sworn affidavit executed by the principal investigator certifying to compliance with the foregoing under penalty of perjury.

By letter dated May 20, 2008, HHS, through its acting Director Samuel H. Wilson, M.D., denied PETA's rulemaking petition. The reason for the denial was that the criteria requested for animal testing "are redundant to existing federal mandates that already apply to research before the NTP..." The denial goes on to cite the following laws and guidances as examples of the petition's redundancy:

- Public Health Service Act,
- U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training,
- Policy on Humane Care and Use of Laboratory Animals,
- Guide for the Care and Use of Laboratory Animals, and
- Animal Welfare Act.

## ***II. HHS' Initial Response to the Petition Simply Misses the Point***

### **A. HHS Ignored the Thrust of the Petition**

The Petition describes, at great length, the overwhelming evidence that NTP, while paying lip service to the concept of the replacement, refinement and reduction of animals in research (the "3Rs"), in fact ignores the laws, regulations and procedures designed to implement the 3Rs. Petitioners concede that there are laws and structures in place which, if fully and faithfully implemented, would constitute a good faith starting point for the 3Rs. At the same time, the current laws and structures are no substitute for the relief sought in the Petition since the current system does not mandate the use of alternatives, nor even a complete and meaningful search to rule out the existence of studies and data which render the proposed animal study duplicative. Most critically, there is nothing in the current system which requires a balancing

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<sup>1</sup> *Guidance on the Operation of the Animals (Scientific Procedures) Act 1986*, Section 5(4). 2000. Available at <http://www.archive.official-documents.co.uk/document/hoc/321/321-xa.htm>.

between the harm to the animals and the expected benefits allegedly to be gained by the animal experimentation.

Furthermore, looking past the current structure which HHS claims is sufficient and considering the unnecessary and cruel experiments HHS actually conducts, the reality is undeniable. As noted at greater length in the Petition, there is no possible justification for conducting cruel experiments on animals when the substances being studied have been fully characterized through human exposure. In the cases of artificial butter flavoring and asbestos, there is no scientific dispute that the toxic effects of these substances on humans is well characterized, and that further animal based data cannot add meaningful additional information which would justify the suffering and cruelty of such testing.

HHS needs to address why there is ongoing animal testing of substances whose human effects are well characterized, not just with respect to the specific toxins referenced in the Petition, but with respect to hundreds of chemicals and substances. We note that this problem is not limited to HHS, but endemic throughout the federal government. However, HHS needs to justify its own actions and explain why stronger, mandatory animal protection standards are not necessary to carry out the will of Congress and the American people. HHS' weak initial response to the Petition utterly fails to do so.

It is not only the animals who are harmed by HHS' willingness to ignore the 3Rs. As long as HHS is continuing to collect animal "data" on various toxins and chemicals, the Federal agencies (which includes HHS sub-agencies such as FDA) charged with regulating those substances can delay issuing regulations on the basis that they are waiting for the "best available science." The "best available science" with respect to human effects from foods, drugs and chemicals is never going to come from animal models, rather, it will come from studies of prior or ongoing human exposure and from scientifically validated non-animal alternatives. Americans are exposed every day to foods, drugs and chemicals whose toxic effects have been shown in humans, and yet the Federal government delays regulating its friends in the business community while it "studies" the problem. People are getting sick and dying every day while HHS does testing which it knows will ultimately play no role in the regulation of the substances being studied.

#### **B. The Laws and Guidances Cited by HHS in its Response Do Not Address the Issues in a Meaningful and Mandatory Way**

Most of the sources cited by HHS in its response address the care and use of animals in testing, not the establishment of sound criteria designed to make testing more scientific, more human-relevant, less duplicative, more thoroughly screened, and more ethical.

Specifically, HHS references the following:

1) Public Health Service Act ("PHS"). We assume this refers specifically to 42 U.S.C. § 289d regarding Animals in Research. This deals solely with animal welfare issues.

2) U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training. None of these are relevant to the Petition except the following two Principles:

II. Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.

III. The animals selected for a procedure should be of an appropriate species and quality and the minimum number required to obtain valid results. Methods such as mathematical models, computer simulation, and in vitro biological systems should be considered.

There are several reasons why these two Principles do not substitute for the mandatory rulemaking that the Petition proposes. First, there is no mechanism for putting these Principles into action. Second, there is no person or organization charged with monitoring the implementation of these Principles, nor is there any penalty or consequence for violating them. The most critical problem of course is that NTP violates each of these Principles on a regular basis, and specifically violated these Principles with respect to the chemicals and toxins listed in the Petition. We note that HHS does not deny it violated each of these Principles in approving the testing detailed in the Petition. The remaining Principles deal solely with animal welfare issues, which are not the subject of the Petition.

3) PHS Policy on Humane Care and Use of Laboratory Animals. This document, in and of itself, deals solely with animal welfare issues. It is relevant to the Petition only to the extent it incorporates by reference the Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act (“AWA”). Each is discussed separately below.

4) Guide for the Care and Use of Laboratory Animals (“Guide”). This lengthy document deals almost exclusively with animal welfare issues. The only portions relevant to the Petition are as follows:

#### **Animal Care and Use Protocols**

The following topics should be considered in the preparation and review of animal care and use protocols:

- Rationale and purpose of the proposed use of animals.

\* \* \*

- Unnecessary duplication of experiments.

While the Guide goes on at great length to discuss issues such as restraints, surgery, personnel, OSHA issues, etc., these two bullet points are all that are devoted to preventing animal experimentation that will have no predictive value for humans, or to prevent animal experiments

on toxins which have been fully characterized in humans. There is no guidance offered as to what these topics mean, how they should be applied, what rationale and purpose are sufficient to justify animal experimentation, what constitutes duplication (e.g., is it duplicative if the toxin is fully characterized in humans, but not in the species being tested?) or indeed any standards the Institutional Animal Care and Use Committee (“IACUC”) should apply in deciding which animal experiments are justifiable and which are not. It seems obvious that so little attention is paid to these issues because they are not considered important by HHS. Only by making these standards mandatory will these issues get the attention that Congress and the American people saw fit to give them.

5) Animal Welfare Act. As an initial matter, this statute by regulation excludes mice, rats, and birds.<sup>2</sup> Since approximately 97% of the animals experimented on are mice, rats and birds,<sup>3</sup> the AWA has no application to 97% of the experiments HHS conducts or funds or to the more than 100 million birds, rats, and mice who are used each year.

Further, there is no meaningful enforcement of the AWA, as it applies to the issues raised by the Petition. For example, with respect to the use of alternatives, the United States Department of Agriculture (“USDA”), the agency charged with enforcing the AWA, has stated:

APHIS believes that [the relevant provision of the AWA] only requires that the principal investigator consider alternatives, and that there is no requirement that an alternative be used after having been considered.

*See*, August 16, 2007 letter from USDA Office of General Counsel to Dr. Pippin at PCRM. Further, USDA relies upon the IACUC to determine whether the experiment duplicates existing data or research, and has never, to our knowledge, challenged such a determination. Without: 1) meaningful enforcement; 2) any requirement to use alternatives; 3) a meaningful and complete search for existing data or research; or 4) any requirement to balance the interests of the animals against the alleged expected benefits, the AWA does not, in reality and on the ground at HHS, prevent animal experimentation which has no predictive effect for humans, or which duplicates existed data or research.

### ***III. NTP Continues to Conduct Unnecessary Animal Testing***

There are three very recent examples illustrating that NTP is supporting research that would not have passed the criteria this rulemaking petition seeks to establish. NTP has recommended additional animal tests for the following substances:

- bisphenol A
- 2-ethylhexyl p-methoxycinnamate, and
- vanadium tetravalent and pentavalent forms.

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<sup>2</sup> See Code of Federal Regulations, Title 9, Chapter 1, Subchapter A.

<sup>3</sup> Foundation for Biomedical Research. *The Essential Need for Animals in Biomedical Research*. 2004. Available at <http://www.fbresearch.org/Education/pdf/RatsAndMice.pdf>.

PETA submitted comments dated May 23, 2008 on the NTP's draft brief on bisphenol A. (Exh. A.) Bisphenol A is used to make plastics such as food and beverage packages, water and infant bottles, compact discs, and medical devices. As we summarized on page three of those comments, an extensive body of literature on the toxicity of bisphenol A exists, previously conducted animal studies have not been reproducible, and further duplicative and irrelevant animal tests are no substitute for stringent product regulation. On June 11, a NTP expert panel agreed, voting to drop the levels of concern stated in the brief from "some concern" to "minimal concern" for two controversial endpoints and calling instead for better human exposure information. Bisphenol A would not continue to be eligible for animal testing if the criteria set forth in PETA's rulemaking petition were enacted.

PETA also submitted comments dated May 23, 2008 to NTP's recommendation for additional animal studies on vanadium compounds and 2-ethylhexyl p-methoxycinnamate ("OMC"). (Exh. B.)

OMC is a common ingredient in sunscreen products. It was nominated by the National Cancer Institute ("NCI") for toxicological characterization including carcinogenicity, developmental toxicity studies, and photodecomposition. In summarizing the reasons why OMC is an inappropriate substance for animal studies, PETA observed that

[I]n nominating OMC to the NTP, NCI failed to convey the extent to which the toxicological properties of this compound have already been studied. NCI also failed to acknowledge the applicability of *in vitro* methods specifically devised to test topically applied UV filters and human epidemiological studies to risk assessment of OMC. These methods hold much more promise for resolving existing discrepancies between toxicological effect in animals and in humans than simply repeating animal studies.

Again, NTP panelists echoed PETA's comments, noting that the material supporting this nomination was out-of-date and that a lot of work needed to be done before entering into a large-scale animal testing program. Again, OMC would not continue to be eligible for animal testing if the criteria set forth in PETA's rulemaking petition were enacted.

Vanadium is a drinking water contaminant and used in nutritional supplements. Vanadium has been nominated by the NIEHS for comprehensive toxicological characterization including chronic toxicity, carcinogenicity, and multigenerational reproductive toxicity testing. As summarized in PETA's comments, "vanadium is poorly absorbed and exhibits generally low toxicity by the oral exposure route," ... "typical exposures are well below levels that might reasonably cause concern," ... and "there is an existing literature of short-term and subchronic studies in human volunteers." These factors alone would disqualify vanadium for further animal studies under the standards proposed in the rulemaking petition.

Lastly, and perhaps most notably, the National Center for Research Resources recently published its Strategic Plan which exalts, highlights, and promotes continued reliance on animal based testing.<sup>4</sup> The Strategic Plan characterizes animal models as "indispensable for developing effective biodefense strategies and many other emerging health issues." It continues by

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<sup>4</sup> [http://www.ncrr.nih.gov/strategic\\_plan/index.asp](http://www.ncrr.nih.gov/strategic_plan/index.asp).



emphasizing support for "research and research resources that develop and enhance access to a broad range of nonhuman animal models, including primates ..."

There are seven "Strategies" outlined in the Strategic Plans, among which are commitments to the following:

- Provide sustained support for valued traditional and non-traditional animal models,
- Support continued access and availability of the highest quality range of animal models, and
- Modulate the size and output of breeding colonies (including nonhuman primates) to match the demand for specific animal models.

Although some of the Strategies nod in the direction of improved animal welfare, shared databases, and *in vitro* methods, the overwhelming thrust of the Strategic Plan is the institutionalized advancement and continuation of live animals in research. A more blatant affront to efforts at reducing, refining and replacing animal based testing would be difficult to conjure.

## CONCLUSION

This supplement to the rulemaking petition dated April 4, 2008 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 that all NTP testing adhere to the standards set forth above.

We urge the Agency to commence rulemaking in accordance with the original petition of April 4, 2008 as supplemented by this letter.

Respectfully submitted,



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Jessica Sandler  
Director, Regulatory Testing Division  
PETA



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Daniel Kinburn  
General Counsel  
PCRM



**EXHIBIT A:**

***PETA COMMENTS  
ON  
NTP'S DRAFT BRIEF ON BISPHENOL A  
(MAY 23, 2008)***

**EXHIBIT B:**

***PETA COMMENTS  
ON  
NTP'S RECOMMENDATION FOR ADDITIONAL ANIMAL STUDIES  
ON  
VANADIUM COMPOUNDS AND  
2-ETHYLHEXYL P-METHOXYCINNAMATE ("OMC")  
(MAY 23, 2008)***