

TESTIMONY OF  
PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS  
BEFORE THE  
HOUSE COMMITTEE ON ENERGY AND COMMERCE  
SUBCOMMITTEE ON COMMERCE, TRADE AND CONSUMER  
PROTECTION  
ON  
THE TOXIC CHEMICALS SAFETY ACT, H.R. 5280  
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People for the Ethical Treatment of Animals represents more than two million members and supporters who are concerned about promoting reliable and relevant toxicity testing strategies that protect human health while reducing, and ultimately eliminating, the use of animals in painful laboratory experiments. Our members are especially troubled by instances where validated non-animal methods exist yet animal experiments are still used.

While we appreciate the language in the current version of the Toxic Chemicals Safety Act (H.R. 5820) that it is policy of the U.S. government to reduce, replace, and refine the use of animals in laboratory experiments, unless this sentiment is backed by concrete requirements, it will be no more effective than previous language has been. And because this legislation requires much additional chemical testing, millions more animals suffering in laboratories are at risk.

**In order for the stated policy to reduce animal use in chemical testing to carry weight, the following changes to the current legislation must be included:**

- 1. As in Europe, there must be a *requirement* to use available alternatives to animal testing where they exist.**
- 2. Dedicated appropriations for implementing the non-animal approach must be provided.**
- 3. Any reference to the failed Interagency Committee on the Validation of Alternative Methods must be removed.** The government representatives on ICCVAM do not have expertise in the development and implementation of alternative methods and have become a major obstacle to the implementation of non-animal methods in the United States.

## **BACKGROUND**

It is estimated that more than 15 million animals are killed annually in the name of regulatory testing in the U.S.<sup>1</sup> Regulatory testing is performed to allow chemicals (industrial chemicals, pesticides, and pharmaceuticals) to be sold and traded within the U.S. and internationally. The stated goal of this testing is to provide some indication of the potential toxicity to humans that may result from exposure to a given chemical.

However, the overwhelming majority of toxicity testing is based on science that is decades old and has no relevance in today's evaluation of public or environmental health protection. Awareness of this problem has been increasing for decades, and is now widely recognized by scientists, regulators, and other stakeholders including the animal protection community. Recent highly publicized debacles have emphasized the inadequacies of current regulatory testing paradigms, particularly with respect to pharmaceuticals.<sup>2</sup>

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<sup>1</sup> Because the animals most commonly used in these tests – namely birds, rats, and mice – are excluded from the minimal protections of the U.S. Department of Agriculture's Animal Welfare Act (AWA), no records are required to be kept on their numbers.

<sup>2</sup> One example is the unanticipated risk of cardiovascular complications associated with the arthritis medication Vioxx (<http://www.drugs.com/vioxx.html>) even though the drug was shown to be heart protective in six different animal species. Another example is the dramatic multi-organ failure experienced by volunteers in clinical trials of TG1412 ([http://news.bbc.co.uk/2/hi/uk\\_news/england/london/4807042.stm](http://news.bbc.co.uk/2/hi/uk_news/england/london/4807042.stm)).

Retrospective analyses also suggest a general failure of the current paradigm: a striking example of this is the fact that 94% of all cancer drugs that have been thoroughly tested for efficacy and toxicity in animals fail in clinical trials due to toxicity or lack of therapeutic value in humans (Okie, 2006).

In Europe, some progress has been made in overhauling both regulatory policies and testing methods to take advantage of scientific advances that make regulatory testing more relevant. The trend toward the elimination of animals in regulatory testing and other kinds of experimentation began more than 20 years ago in Europe as a social commitment to the principle of the “3Rs”: the *reduction* and *replacement* of animals used for experimentation, and *refinement* of animal tests to cause less suffering. This principle was first outlined in 1959 (Russell and Burch, 1959) and was written into legislative policy in Europe in 1986: “An experiment shall not be performed if another scientifically satisfactory method of obtaining the results sought, not entailing the use of an animal, is reasonably and practicably available” (*Council Directive 86/609/EEC*).

As “alternative” or non-animal-based methods were developed, scientists also realized that these methods can be more sensitive, reproducible, and relevant to predicting human health effects than the standard animal methods. Consequently, **as a result of its active implementation of the 3Rs, Europe has been making noticeable progress in the realm of effective regulatory policies.**

**However, during this same time period, the U.S. has failed to make any substantive changes to its regulatory testing policies. The result is that, while the U.S. leads the world in cutting-edge science, including the non-animal science that could be applied to regulatory testing, the regulatory situation in the U.S. has been stagnant for decades. A major cause of this discrepancy is a lack of legislative initiative.**

To gain a perspective on this problem, a comparison between legislation in Europe and the U.S. is attached (Appendix A: Regulatory Testing – Why is the U.S. so far behind Europe and Appendix D: Washington Post investigation).

This issue is timely and relevant to this bill since revision of TSCA provides an opportunity to rectify this situation. Two pieces of European legislation – the Cosmetics Directive (7th Amendment) and REACH – that involve regulatory testing are coming into effect and both will have a great impact on regulatory testing involved in international trade. At the same time, the U.S. National Research Council (NRC) has released a lengthy report, entitled “Toxicity Testing in the Twenty-first Century: A Vision and a Strategy,” that recommends a shift away from the current animal tests toward more modern approaches that are largely based on non-animal methods (NRC, 2007). In its report, the NRC recognizes that “A revolution is taking place in biology,” and now is the time to capitalize on that revolution.

### **ICCVAM HAS BECOME A MAJOR OBSTACLE TO THE IMPLEMENTATION OF NON-ANIMAL TESTING METHODS IN THE U.S.**

**The U.S has not been implementing available non-animal tests and technology to reduce and eliminate tests on animals, as Congress clearly intended by the ICCVAM Authorization Act of 2000. It has been the experience of the U.S. animal protection community over the past decade that ICCVAM appointees do not have the experience, knowledge, or interest needed to advance the development or implementation of non-animal methods.** The non-profit Physicians Committee for Responsible Medicine (PCRM) filed a Freedom of Information Act lawsuit in an attempt to obtain documents revealing

qualifications of agency representatives and the manner in which they are chosen. After losing a court battle, the National Institute of Environmental Health Sciences provided some documents, but none relevant to these issues. In 2007, an email among ICCVAM officials was leaked to PETA detailing efforts to ‘circle the wagons’ against the implementation of a non-animal methodology (7-27-07 Email correspondence between ICCVAM officials, leaked to PETA 7-30-07).

Even though ICCVAM is responsible for “encourag[ing] the use” of validated methods, ICCVAM has taken years to make recommendations after the reviews are completed, and has no authority to ensure that the recommended methods are used by agencies or by industry.

In addition to the obvious differences in political commitment to the 3Rs between the U.S. and Europe, ICCVAM is clearly not capitalizing on the limited capabilities it does have. For example, one of ICCVAM’s tasks is to facilitate harmonization of international regulatory test methods. Yet, of the over two dozen methods that have been accepted for regulatory purposes in Europe, ICCVAM has reviewed 15, only four of which have been recommended for use by ICCVAM and accepted by U.S. regulatory agencies.

Further, despite the fact that ICCVAM members are on the European Committee for the Validation of Alternative Methods (ECVAM) Scientific Advisory Council and are therefore privy to ECVAM validation proceedings, subsequent ICCVAM review of those methods approved by ECVAM usually results in either an outright rejection of the validation or recommendation of the method only in severely limited applications.

Another aspect of failed harmonization is in validation criteria used by ICCVAM and ECVAM. ICCVAM’s criteria are similar but more stringent than those used by ECVAM (arguably too stringent to be practical in many cases). This results in added difficulties when attempting to harmonize the validation and use of alternative methods. To make matters even worse, the criteria are applied differentially to *in vitro* and *in vivo* methods. An extremely relaxed set of these criteria are applied to *in vivo* methods, if applied at all, and none of the *in vivo* methods currently used by regulatory agencies has ever been validated using the current criteria applied to *in vitro* methods.

Due to a demonstrated lack of progress during its first decade, ICCVAM was charged by the U.S. Congress to draft a five-year plan. The draft was submitted to the public for comment, and was reviewed internally by a working group of ICCVAM’s scientific advisory committee. Interestingly, the criticisms brought forth by the working group were nearly identical to those put forth by the animal protection community. Major gaps identified in the plan included the identification of regulatory endpoints that are ripe for modernization, an organized approach for identifying priority areas, and a plan for the translation of validation to regulatory use.

In response to the criticism received, ICCVAM has consistently responded with excuses or exaggerated claims of progress. ICCVAM claims to have reviewed “over 185 alternative test methods,” and “contributed to 33 methods” but closer inspection of their documented activities demonstrates this to be a gross and unjustified exaggeration (see Appendix B and C).

For example, ICCVAM claims to have reviewed 23 alternatives to the use of animals in “biologics testing.” However, the footnote to that claim states that this “review” consisted of one workshop in which several people were invited to present different approaches to address a single purpose — botulism toxin testing. In this case, it appears that ICCVAM is equating listening to a talk with a “review.” Similarly, 138 of the 185 “methods” are for testing endocrine disruption and are actually variations of the same four methods. Additionally, ICCVAM claims that it has reviewed 95 estrogen receptor (ER) transcriptional activation

methods to assess endocrine disrupting chemicals. Since 95 entirely unique ER transcriptional activation assays do not exist, one can only assume that ICCVAM is using an extremely narrow definition of the word “method” (e.g., changing a minor component of the protocol constitutes a new “method”) in an effort to make it appear as though they have accomplished vastly more than reality would indicate.

The fact of the matter is that, after 10 years, only four methods that have been processed by ICCVAM have received regulatory acceptance by U.S. agencies. This number compares poorly to the more than two dozen methods that have been accepted for regulatory purposes in Europe.

Further, of these methods only one is a non-animal method originating in the U.S. (Corrositex for skin corrosion). Three of these methods still use animals (Up/Down for acute toxicity, LLNA for skin sensitization) or animal derivatives (BCOP/ICE for eye corrosion), including one that still involves poisoning animals until they die (Up/Down for acute toxicity).

**ICCVAM’S REMIT IS FOR METHODS WITH INTERAGENCY APPLICABILITY. WHILE NOT ADEQUATELY FULFILLING ITS MANDATE, ICCVAM ALSO WORKS OUTSIDE ITS PURVIEW AND AGAINST THE ACCEPTANCE OF ALTERNATIVE METHODS.**

The ICCVAM Act of 2000 clearly states “*ICCVAM shall facilitate appropriate interagency and international harmonization of acute or chronic toxicological test protocols that encourage the reduction, refinement, or replacement of animal test methods.*” Even though it does not fulfill its interagency mandate, ICCVAM is now also working to scuttle non-animal methods in which individual agencies are interested.

For example, a consortium of manufacturers of antimicrobial cleaning products (AMCP) and the Institute for In Vitro Sciences (IIVS) worked for several years to develop and evaluate a completely non-animal method to assign ocular hazard categories required for EPA registration of AMCPs, an activity that was agency-specific and not applicable for interagency use. Nonetheless the consortium agreed to an ICCVAM review and ***kept ICCVAM apprised of its activities from very early in the process.*** ICCVAM had agreed to an expedited review, yet ICCVAM held a full peer review meeting at which the consortium-proposed *in vitro* approach was rejected. While the promise of an expedited review does not assure a positive outcome, ICCVAM had opportunity to make suggestions and requests throughout the process. Apparently, the U.S. Environmental Protection Agency did not share ICCVAM’s negative view of this method, and has initiated a pilot project requesting companies to submit data using this approach.

According to the ICCVAM Authorization Act, ICCVAM’s purpose is to:

- (1) increase the efficiency and effectiveness of Federal agency test method review;
- (2) eliminate unnecessary duplicative efforts and share experiences between Federal regulatory agencies;
- (3) optimize utilization of scientific expertise outside the Federal Government;
- (4) ensure that new and revised test methods are validated to meet the needs of Federal agencies; and
- (5) reduce, refine, or replace the use of animals in testing where feasible.

The Director of ICCVAM has been lobbying agencies to prevent the acceptance of the Globally Harmonized System of labeling, an internationally agreed upon labeling system that would reduce redundancy in animal testing, and offer better worker and consumer protection by harmonizing labeling requirements and standards

around the world. Labeling is a risk determination, and is thus clearly within the purview of the regulatory agencies and not under ICCVAM, whose purpose is to review and make recommendations regarding specific test methods.

Yet ICCVAM is claiming authority to review or recommend regulatory safety decisions, including classification frameworks, and its rejection of GHS labeling is in direct contradiction to purposes 1, 2 and 5 above, as well as of the duty (also arising from the ICCVAM Authorization Act) to “[f]acilitate appropriate interagency and international harmonization of acute or chronic toxicological test protocols that encourage the reduction, refinement, or replacement of animal test methods.”

### **THE SELECTION PROCESS FOR BOTH ICCVAM AND ICCVAM’S SCIENTIFIC ADVISORY COMMITTEE (SACATM) LACK TRANSPARENCY.**

NIEHS requests nominations annually for open spaces on its science advisory board, SACATM. In 2007, 2008, and 2009, animal protection groups either jointly or individually nominated several well-qualified individuals from state government, the business community, and non-governmental organizations. All were extremely familiar with the development or implementation of non-animal methods and the use of animals—and the “3Rs”—in toxicology testing; some worked on these issues on a daily basis. In three years not a single one was selected to serve on the SACATM.

Despite repeated efforts, we have been unable to obtain specifics of ICCVAM’s selection process for SACATM members or, indeed, for agency selection of ICCVAM representatives, the vast majority of whom lack any expertise in the development or implementation of non-animal methods.

### **THE SOLUTION**

**Legislative mandates, such as those that exist in Europe to use existing non-animal methods, are needed to provide the incentive for regulatory agencies to progress and the Toxic Chemicals Safety Act is the opportune place to provide that incentive, both with legislative language and dedicated appropriations. Any reference to ICCVAM must be deleted in favor of either no review board (since EPA already has in place procedures for creating ad hoc Scientific Advisory Panels to review its regulatory processes) or a public review board whose members have demonstrated expertise in the development and implementation of non-animal testing methods.**

Thank you for your consideration of these comments.

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## **ENCLOSURES**

APPENDIX A: REGULATORY TESTING – WHY IS THE U.S. SO FAR BEHIND EUROPE

APPENDIX B: RESPONSE TO ICCVAM CLAIMS

APPENDIX C: ANALYSIS OF ICCVAM'S METHOD REVIEW

APPENDIX D: WASHINGTON POST INVESTIGATION OF ICCVAM