

March 9, 2001

Mr. Ken Cook, President  
Environmental Working Group  
1718 Connecticut Avenue NW, Suite 600  
Washington DC 20009



**PETA**

**PEOPLE FOR THE ETHICAL  
TREATMENT OF ANIMALS**

**HEADQUARTERS**  
501 FRONT STREET  
NORFOLK, VA 23510  
TEL 757-622-PETA  
FAX 757-622-0457

Dear Mr. Cook:

People for the Ethical Treatment of Animals (PETA) is the largest animal rights organization in the world. We have 700,000 members who are concerned about the protection of animals and the environment. We are writing to ascertain your organization's position on an issue of critical importance to the animal protection community – the use of large numbers of animals in chemical-testing programs initiated by the U.S. Environmental Protection Agency (EPA).

You may be aware that PETA led a coalition of animal protection organizations that opposed the EPA's high production volume (HPV) chemical testing program announced in late 1998. That coalition consisted of almost every national animal protection organization in the U.S. and represented more than 10 million Americans. As you will see from the enclosed issue paper, the animal protection community has serious concerns about the EPA's current approach to risk assessment, which (1) subjects enormous numbers of animals to painful toxicity tests, (2) is based on test methods that are of dubious scientific validity, and (3) does not result in concrete protections for human health or the environment. We believe that our organizations have a number of areas of mutual interest on these issues, not the least of which is the goal of properly labeling and informing the public about hazardous substances and ultimately removing toxic substances from the environment.

Many PETA members are also members of various environmental organizations and we routinely receive inquiries regarding the position that other organizations take on animal testing in general and EPA animal-testing programs in particular. So that we may better inform our members – as well as members of other animal protection organizations – regarding the Environmental Working Group's position on these matters, we would greatly appreciate it if you would send us a copy of your organization's policy on animal testing. In addition, we ask that you consider the attached issue paper and either endorse or reject the attached statement on validation of test methods and funding of non-animal test development.

Should you wish to discuss these matters further, please feel free to contact me or our federal agency liaison, Jessica Sandler. I look forward to hearing from you on this important matter.

Yours truly,

A handwritten signature in black ink, appearing to read "Ingrid Newkirk".

Ingrid E. Newkirk  
President

Enclosures

## THE EPA'S ANIMAL TESTING PROGRAMS ~ INHUMANE AND INEFFECTIVE ~

### High Production Volume (HPV) Chemical-Testing Program

The HPV chemical-testing program was established by the Environmental Defense Fund, the EPA, and the Chemical Manufacturers Association to gather baseline toxicity data on 2,800 high production volume chemicals. Under the HPV chemical-testing program, chemical manufacturers "volunteer" to evaluate various industrial chemicals. They have pledged to review all existing data prior to conducting new animal tests. However, because of slipshod reviews and the failure of the EPA to require such a data review, many companies are proposing to simply repeat uninformative tests on animals.

Under the HPV chemical-testing program, companies and consortia that have agreed to "sponsor" a chemical submit test plans that are posted on the EPA's web site for a 120-day comment period. To date, the animal protection community is the only stakeholder to review and comment on the proposed test plans. Examples of wholly unnecessary and meaningless tests that industry has proposed include the Chemical Manufacturers Association (CMA) plan to kill animals in acute toxicity studies of the already well-characterized substance butadiene. Moreover, the levels to which the CMA proposed to expose animals in these lethal poisoning tests were, literally, explosive. The American Petroleum Institute has proposed – and the EPA has encouraged – large numbers of animal tests on such well-characterized substances as butane, propane, and ethane. Many companies have submitted poorly researched test plans that make *no* use of existing data, calling instead for the HPV chemical-testing program's notorious "checklist" battery of animal tests.<sup>1</sup>

### Voluntary Children's Chemical Evaluation Program (VCCEP)

The VCCEP proposes to use crude animal-based tests to establish levels of toxic contaminants that children should be expected to tolerate. Exposure assessment studies indicate that all of the chemicals proposed for testing under the VCCEP are present in detectable concentrations in human tissues, and include such already well-characterized – and known hazardous – substances as benzene, toluene, and trichloroethylene. The EPA has ignored the animal protection community's call for a more sensible plan of action to implement strategies that prevent or reduce children's exposure to these chemicals. Instead, the EPA plans to spend years and millions of dollars subjecting more animals to painful toxicity tests rather than taking regulatory action.

### Endocrine Disruptor Screening Program (EDSP)

The EDSP is by far the largest animal-testing program ever conceived. According to the EPA's web site on this program, as many as 80,000 chemicals will be tested. Scientific estimates of animal usage are that between 600,000 and 1.2 million animals will be used to test each 1,000 chemicals.<sup>2</sup> This enormous program is moving ahead despite widespread criticism from the scientific, regulatory, and even some within the environmental community.

The EPA has virtually ignored the use of non-animal (high throughput) screens, which should be used as a first step in any such program, and it is obvious from EPA comments that the Agency fears an industry outcry over "product de-selection" as a result of such screens. Furthermore, the EPA spends none of its \$500 million annual research and development budget on non-animal tests that are frequently faster, cheaper and more predictive of human effects.

The EPA is going to great lengths to circumvent the established process for the validation of test methods for new endpoints and for test methods that have cross-agency application – through the Interagency Coordinating Committee for the Validation of Alternative Methods (ICCVAM). Pursuant to the *ICCVAM Authorization Act of 2000*, every federal agency carrying out a program that prescribes or recommends toxicological testing is required to “ensure that any new or revised acute or chronic toxicity test method, including animal test methods and alternatives, is determined to be valid for its proposed use prior to requiring, recommending, or encouraging the application of such test method.”

Objecting to the EPA’s double standard on test method validation, the Advisory Committee on Alternative Toxicological Methods (ACATM) of the National Toxicology Program passed the following unanimous motion in November 2000:

The ACATM expresses grave concern at the bifurcated approach being taken with review of methods for evaluation of endocrine disruption activity, with ICCVAM considering the *in vitro* methods and with the U.S. EPA proposing to review *in vivo* methods using an ICCVAM-like approach. The Committee’s primary concern is that both *in vitro* and *in vivo* methods be subject to the same rigorous peer review and validation process to ensure the highest likelihood of acceptance by regulatory agencies, the scientific community and the public.<sup>3</sup>

These sentiments were reiterated by Professor Michael Balls, head of the European Centre for the Validation of Alternative Methods (a European Union-funded government entity), who has written with respect to the EPA program:

It has even been said that the validation phase of the new test development and acceptance sequence should be applied flexibly ... How can there possibly be flexibility about whether or not methods are reliable and relevant and about what they should be used for? What would be the value of the data such tests would provide, and with what confidence could they be applied in making decisions?<sup>4</sup>

## Test Method Validation

Validation is “the process by which the reliability and relevance of a procedure are established for a specific purpose.”<sup>5</sup> In its animal welfare factsheet, the EPA states: “Scientific validation is an essential step in determining the adequacy of new alternative test methods.” Why is rigorous validation so important to the EPA for non-animal tests, yet so unnecessary for animal tests?

A case in point is the EPA’s developmental neurotoxicity test (DNT). This test uses 1,200 to 2,500 animals *per test*, and is currently being required by the EPA in the assessment of certain pesticides, and may also be used in the VCCEP. However, the DNT is so far from being validated that the EPA asks companies to submit the protocol they used along with their test results, even though standardization of protocol is a key element in the validation process. At the 18<sup>th</sup> International Neurotoxicology Conference, a panel of experts on the DNT – including three EPA officials – acknowledged that they did not know how to interpret the results of the test. They also agreed with a National Research Council report that questioned whether the rat was the correct “model” for the DNT. One EPA official even stated that the agency’s reliance on the rat model was “like being in a bad marriage – you know you should get out but you don’t because there is so much history there.”<sup>6</sup>

Clearly, *all* test methods intended for regulatory risk assessment purposes – whether animal or non-animal – should be subject to the same rigorous standards of scientific validation to ensure their relevance, reliability and reproducibility. Anything short of this results in the proverbial “garbage in, garbage out.”

Out of frustration with government inaction, many environmental organizations repeatedly call for more and more animal-testing. Yet the following examples illustrate the futility of this approach:

- ◆ The Multicenter Evaluation of *In-Vitro* Cytotoxicity (MEIC) study examined rat and mouse lethal dose data for 50 chemicals and found that these tests were able to predict toxicity in humans with only 65 percent accuracy.<sup>7</sup> In fact, scientists at a recent international conference on alternatives to acute toxicity testing held in Washington D.C.<sup>8</sup> stated that they are uncertain as to whether the rat LD-50 is even able to predict lethality in rats! (By contrast, the MEIC study found that a “battery” of four non-animal tests using human cells was able to predict human toxicity with 84 percent accuracy.)
- ◆ The causal link between benzene and human leukemia was established in 1928. However, subsequent animal studies were unable to replicate this effect<sup>9</sup> and the EPA is still calling for more testing on benzene. Even when evidence from human epidemiological studies implicates a chemical, the results are ignored by the EPA for the sake of conducting more and more animal studies. For years, population studies have shown that arsenic in drinking water causes cancer in humans. Yet the EPA dragged its feet for more than 20 years while thousands of animals were killed in tests that attempted to reproduce the effects already seen in humans. The EPA has finally proposed new standards for arsenic exposure in drinking water, but refused to restrict the poison to the lowest level feasible. Having failed to learn their lesson from lead, EPA scientists (with input from industry) decided to set a supposedly “safe level” of arsenic contamination in drinking water based largely on the results of animal-feeding studies.
- ◆ This familiar scenario is currently repeating itself with phthalates and the pesticide atrazine. In both of these cases, companies have successfully argued that cancers that develop in animals exposed to these chemicals would not occur in humans. These chemicals remain on the market and in widespread use.

Given the ease with which companies can challenge results from animal-based tests and thus thwart regulatory efforts, it is no wonder that, despite killing hundreds of thousands of animals, the EPA has not banned a *single* toxic industrial chemical under the *Toxic Substances Control Act* in the past decade. It is unclear, given these facts, why some environmental organizations depend so heavily on animal-based toxicity tests whose results are so subject to manipulation by industry. Clearly, a better approach is needed, and other environmental organizations have recognized the predictive value of non-animal test methods.

In 1980, Dr. Joshua Lederberg, Nobel Laureate in Medicine, wrote: “It is simply not possible with all the animals in the world to go through chemicals in the blind way we have at the present time, and reach credible conclusions about the hazards to human health.” Twenty years later, millions of animals are still dying in agonizing chemical toxicity tests and we are no closer to getting dangerous chemicals out of our environment.

In its recent report, *In Harm's Way*, Physicians for Social Responsibility wrote:

Our snail's pace approach to regulation clearly sets children in a minefield of uncertainty and potential harm, where the full extent of current hazards will be unknown for the foreseeable future. Even when there is substantial evidence of hazard, chemicals continue to be inflicted on the unsuspecting public for decades ... Rigid adherence to an inflexible standard for justifying action prevents timely regulatory response to public health threats ... We should not need to identify with certainty exactly how much and through what mechanism a neurotoxic chemical impairs brain development before coming to the conclusion that public health is not protected when the urine of virtually every child in this country contains the residues of these chemicals ... Animal studies of lead, mercury, and PCB's each underestimated the levels of exposures that cause effects in human by 100 to 100,000-fold. Regulatory decisions that rely largely on toxicity testing in genetically similar animals under controlled laboratory conditions will continue to fail to reflect threats to the capacities and complexity of the human brain as well as important gene-environment interactions.

The solution must lie in reducing emissions, minimizing exposures, adopting reliable test methods, and forcing the EPA to take action on well-documented, known hazards. By asking for ever-more animal testing, it appears that some environmental organizations are falling into the EPA's own trap of believing that there is never enough information to take action.

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- <sup>1</sup> A complete set of the animal protection community's comments on each HPV test plan may be viewed on-line at:  
<http://www.epa.gov/chemrtk/viewsrch.html>
- <sup>2</sup> Purchase I. Ethical review of regulatory toxicology guidelines involving experiments on animals: the example of endocrine disrupters. *Toxicological Sciences* 1999; 52: 141-147.
- <sup>3</sup> Minutes of the 28 November 2000 Meeting of the NTP Advisory Committee on Alternative Toxicological Methods, National Library of Medicine, Bethesda, Maryland.
- <sup>4</sup> Balls M. The precautionary principle should be used with caution and should be applied to animal experimentation and genetic manipulation, not merely to protection of the environment. *Alternatives to Laboratory Animals* 1999; 27: 1-5.
- <sup>5</sup> Interagency Coordinating Committee on the Validation of Alternative Methods. *Validation and Regulatory Acceptance of Toxicological Test Methods*. NIH Publication No: 97-3981. National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.
- <sup>6</sup> Rice D. Children's Health and the Environment 2000 – 18<sup>th</sup> International Neurotoxicology Conference. Colorado Springs, Colorado, 23-26<sup>th</sup> September 2000.
- <sup>7</sup> US National Toxicology Program Interagency Centre for the Evaluation of Alternative Toxicological Methods (NICEATM). *The Multicentre Evaluation of In Vitro Cytotoxicity (MEIC) – Summary*. September 2000.
- <sup>8</sup> Bruner L. Presentation at the International Workshop on *In Vitro* Methods for Assessing Acute Systemic Toxicity, 17-20<sup>th</sup> October 2000, Arlington, Virginia.
- <sup>9</sup> Huff JE, Haseman JK, DeMarini DM, Eustis S, Maronpot RR, Peters AC & Persing RL, Chrisp CE & Jacobs AC. Multiple-site carcinogenicity of benzene in Fischer 344 rats and B6C3F1 mice. *Environmental Health Perspectives* 1989; 82: 125-63.