



The American Physiological Society

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The Honorable Ken Calvert
2205 Rayburn House Office Building
Washington, DC 20515

Dear Representative Calvert:

I am writing on behalf of the American Physiological Society to express our opposition to H.R. 816, the Federal Accountability in Chemical Testing (FACT) Act. I urge you to reconsider your support for this legislation because it is seriously flawed.

The FACT Act would require agencies that are part of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) to report their progress towards the development, validation, acceptance, and utilization of alternative test methods. They would also have to report animal usage by species, number, and test type for all toxicology testing conducted, supported, required by, or submitted to these agencies. However, tracking the number of animal toxicology studies is a poor measure of progress towards the adoption of alternatives. In addition, this bill would pose significant burdens on government, academia, and industry.

This legislation would hamper efforts to assess the safety and effectiveness of new drugs not only when companies submit these compounds for regulatory approval, but even at the earliest stages of drug discovery when such research is typically funded by the National Institutes of Health. Collecting the information required by this bill would be burdensome both to federal agencies and to the private sector. Furthermore, it will not provide useful information about progress towards the adoption of alternatives. Rather, the bill would reduce a complex issue to a misleading metric: Did the number of animals in toxicology studies rise or fall?

ICCVAM consists of more than a dozen federal agencies responsible for human and animal health and the environment. The ICCVAM authorization (PL-106-545), states that its purpose is "to establish, wherever feasible, guidelines, recommendations, and regulations that promote the regulatory acceptance of new or revised scientifically valid toxicological tests that protect human and animal health and the environment while reducing, refining, or replacing animal tests and ensuring human safety and product

effectiveness." ICCVAM's legislative charter uses the well-accepted definition of an "alternative test method" as one that

- (A) includes any new or revised test method; and
- (B) (i) reduces the number of animals required;
 - (ii) refines procedures to lessen or eliminate pain or distress to animals, or enhances animal well-being; or
 - (iii) replaces animals with non-animal systems or one animal species with a phylogenetically lower animal species, such as replacing a mammal with an invertebrate.

This definition is based upon *Principles of Humane Experimental Technique*, a book by W.M.S. Russell and R. L Burch and the basis for all U.S. animal welfare laws and policies. Russell and Burch defined alternatives broadly as measures that reduce animals' experience of pain or distress. Replacing animals with non-animal testing methods is one kind of alternative, but it is not the only one. Pain and distress are also reduced when mammals are replaced with invertebrates; when procedures are refined; or when valid test data can be obtained by replacing some animal tests with non-animal alternatives or by applying statistical methods that require fewer animals.

Supporters of this legislation claim that all animal-based toxicology testing can be safely replaced with non-animal alternatives. Not only is this a false assertion, it is also an incorrect understanding of what alternatives are available. In order to be considered as a valid alternative, non-animal tests must be at least as accurate as current tests in their ability to assess a compound's impact on human and animal health and the environment. Some non-animal tests have been validated as complete replacements for animal tests, while others are partial replacements. Partial replacements can eliminate some animal tests by screening out compounds with obvious corrosive or toxic effects. However, animal tests are still essential to determine whether there are other, less obvious toxic effects.

Because alternatives include refinements as well as replacements, animal numbers alone cannot provide a reliable metric of progress. Moreover, other factors also influence the number of toxicology studies performed in a given year, including:

- Budgets and priorities of federal agencies, industry, and other research sponsors such as health charities may drive the number of compounds that need to be screened
- Availability of validated non-animal tests to screen these compounds
- Health or environmental crises such as emerging diseases like Zika or lead contamination of the Flint, MI water supply

Recently the National Institutes of Health (NIH) accelerated its efforts to ensure scientific rigor in research. These efforts include studying how treatments affect both male and female animals and making sure that studies use *enough* animals to produce valid findings. This legislation would put pressure on agencies to reduce the number of animals in toxicology studies. If there are too few animals to reach valid conclusions about whether drugs and compounds are safe, people, animals, and the environment all will be at risk.

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The information to be collected under this legislation will not promote improved animal welfare because the Animal Welfare Act and the rules for conducting federally-funded vertebrate animal research already state that such studies may not be approved unless the Principal Investigator has considered whether the use of alternatives is appropriate. Nevertheless, this bill would require a massive and burdensome data collection effort. Federal agencies would have to compile reports of their progress towards the development, validation, acceptance, and utilization of alternative test methods. They would also have to collect animal usage numbers by species, number, and test type not only for their own intramural toxicology studies, but also for drug studies they fund through grants and contracts and from companies seeking regulatory approval for new drugs or other chemicals.

Last year the House and Senate overwhelmingly approved the 21st Century Cures Act. This bipartisan legislation includes a provision directing NIH, USDA, and FDA to review their regulations and policies for the care of laboratory animals and “make revisions, as appropriate, to reduce administrative burden on investigators while maintaining the integrity and credibility of research findings and protection of research animals.” The FACT Act runs completely contrary to the goals of 21st Century Cures by calling for costly, burdensome, and unnecessary reporting.

In sum, the FACT Act will not promote animal welfare because researchers are already required to consider whether animal tests can be replaced by alternatives that involve less pain and distress. The data collection required by the bill would be burdensome to government, academia, and industry. We therefore urge you to withdraw your support for H.R. 816.

Sincerely,

A handwritten signature in blue ink that reads "Dennis Brown".

Dennis Brown, Ph.D.
President

The American Physiological Society (APS) was founded in 1887 to advance physiological research. Our membership consists of nearly 11,000 research scientists who study biological processes that sustain life. Our U.S. members work in academia, industry, and government where they seek to understand human and animal diseases as well as biological traits that enable animals and humans to adapt to their environment. Physiologists combine different research techniques depending upon the scientific questions they seek to answer. Answers to some questions may be found by studying genes, proteins, or isolated cells, tissues or organs. Other answers may be found through computer modeling of biological processes. However, due to the complexity of biological processes, in many cases it is also necessary to study living animals. Physiologists recognize that animal welfare is an essential component of sound science, and we are committed to the humane treatment of animals.