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IIVS UPDATE

A Quarterly Newsletter for Friends of the Institute for In Vitro Sciences

Revising the Toxics Substances Control Act (TSCA):

An opportunity to improve the science behind risk assessment

IIVS would like to thank Catherine Willett, PhD, Science Policy Advisor, Regulatory Testing Division, PETA, for contributing this article

In April, bills were introduced into both Houses of Congress to update the 1976 Toxics Substances Control Act.[1,2] Both bills are very similar in that they would fundamentally change US legislation and would, like the Registration, Evaluation, Authorization, and Restriction of Chemicals (REACH) legislation in the European Union[3], require industry to provide hazard and exposure information for all chemicals. If passed, the proposed revisions to TSCA would result in a significant increase in testing and animal use in the near term.

There has been much discussion about how many animals will be used to satisfy REACH requirements. Regardless of the estimate, what is clear is that not only would the cost - in both dollars and animal lives - be enormous, but it would also be logistically infeasible to perform all of the proposed hazard testing for every chemical. This will also be true for the proposed US legislation. In addition, chemical testing on animals has proven shortcomings with respect to providing information that is useful in risk assessment, which led to the now famous NRC report, Toxicity Testing in the 21st Century: A Vision and a Strategy[4] which EPA has largely embraced in its current Strategic Plan[5]. All things considered, there is an immediate need to incorporate the application of alternatives to testing and the use of animals into all modern legislation, including TSCA reform.

With this in mind, PETA and others began lobbying Congress long before the current bills were introduced, and were happy to see that both versions of the bill incorporate a number of animal protection measures that we advocated, including:

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1 US Senate, Committee on Environment and Public Works. Senate bill S. 3209, the "Safe Chemicals Act of 2010". Available at http://thomas.loc.gov/cgi-bin/bdquery/z?d111:S.3209 (accessed 6 July 2010).

2 US House of Representatives, Energy and Commerce Committee. Discussion Draft: Toxic Chemicals Safety Act of 2010. Available at: http://energycommerce.house.gov/Press_111/20100415/TCSA.Discussion.Draft.pdf (accessed 6 July 2010).

3 European Commission, Environment Directorate. Registration, Evaluation, Authorisation and Restriction of Chemical substances, 1 June 2007. Background available at: http://ec.europa.eu/environment/chemicals/reach/reach_intro.htm (accessed 6 July 2010).

4 National Research Council, Committee on Toxicity Testing and Assessment of Environmental Agents. 2007. Toxicity Testing in the 21st Century: A Vision and a Strategy. National Academies Press, Washington, DC. Available at: http://www.nap.edu/catalog.php?record_id+11970 (accessed 6 July 2010).

5 U.S. Environmental Protection Agency. Strategic Plan for Evaluating the Toxicity of Chemicals. 2009. Office of the Science Advisor Science Policy Council, Washington, DC. Available at: http://www.epa.gov/spc/toxicitytesting/docs/toxtest_strategy_032309.pdf (accessed 6 July 2010).

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Bits and Pieces

Dr. R. Clothier is the recipient of The Björn Ekwall Memorial Award in recognition of his outstanding contribution in the field of *in vitro* toxicology, in particular to the development, implementation and validation of alternative toxicity test methods, and for his substantial contribution to the FRAME Research Programme.

The Dieter Lütticken Award will be awarded to Dr. A.W. Tucker, University of Cambridge, for the development of an *in vitro* air interface respiratory tract organ culture model for investigation of bovine respiratory diseases. The award is sponsored by Intervet/Schering-Plough Animal Health.

ACuteTox web address has changed to: www.acutetox.eu.

InVitroJobs: a new online resource for scientists and students seeking employment in non-animal research www.invitrojobs.com.

Upcoming Events

Animals, Research, and Alternatives: Measuring Progress 50 Years Later, August 26-27. Washington, DC

LINZ and ESTIV 2010, September 2-4. University of LINZ, Austria.

In Vitro Alternatives Forum, October 18-19th. Alexandria VA
www.iivs.org
Early Bird Registration ends Aug. 15th

Accelerating Implementation of the NRC Vision for Toxicity Testing in the 21st Century
Nov. 9-10
http://htpconsortium.wordpress.com/

IIVS Institute for In Vitro Sciences
Advancing Science & Animal Welfare Together

Workshop Report: Mutagenicity/ Genotoxicity Testing without Animals?

German Federal Institute for Risk Assessment (BfR)
June 24 – 25, Berlin, Germany

Since March 2009, the 7th Amendment to the EU Cosmetics Directive (76/768/EEC) has banned the marketing of cosmetics or ingredients that have been tested *in vivo* after this date for acute toxic effects. For the assessment of genotoxic/ mutagenic effects, a battery of well-established and regulatory accepted *in vitro* assays are available. However, long experience with these *in vitro* assays has revealed low specificity of the methods resulting in a high percentage of false positive results. Combining the *in vitro* assays in a battery approach increases the overall sensitivity while the specificity is even further reduced. Thus various regulations accept negative results from the battery as a valid predictor of the absence of a genotoxic/mutagenic hazard, while positive outcomes in any of the assays in the battery generally require confirmatory *in vivo* testing.

Rodger Curren, IIVS President, was invited to participate in a BfR Expert Meeting focused on identification of the current status of development or prevalidation of new, complex *in vitro* models (e.g. human 3D epidermal or full thickness skin models, embryonated hen's egg test, etc.) for genotoxicity. Models like these are believed not only to better model biokinetic aspects of barrier and metabolism, but to exhibit more normal DNA repair systems. The participants also considered whether modifications of existing tests, their test data interpretation procedures, or modifications of testing strategies might result in better predictions of the risk of genotoxic events *in vivo*. The general conclusion was that several of the scientific solutions proposed will eventually allow us to make adequate predictions of genotoxic risk without the use of animals. A consensus document of the proceedings of the workshop is expected to be published before the end of the year. For more information on the BfR and its activities, please visit www.bfr.bund.de.

IIVS Receives First Ethical Science Award

In recognition of its leadership in the optimization, validation and routine use of non-animal testing methods, IIVS has been awarded the first Mark Twain Ethical Science Award. This honor, presented by PETA, recognizes IIVS for its successes in helping hundreds of companies world wide utilize testing strategies that minimize the use of animals, while at the same time maintaining or improving the current level of safety for the public.

"We are honored to be the first recipient of this prestigious award from PETA," says Rodger Curren, President of IIVS. "Their continued support of our work to expand the application of non-animal methods for products testing has been significant for many of our successes." A recent example of such collaboration was the partial funding provided by PETA for IIVS to participate in an international study for non-animal methods to detect skin irritants. This resulted in the EU accepting certain reconstructed human skin models for regulatory submissions. The award is named for Mark Twain in recognition of his staunch opposition to the abuse of animals in laboratory experiments. PETA recently sponsored Twain's hometown museum exhibit and hailed the author as America's first animal advocate.

In Vitro OECD Test Guideline for Skin Irritation

In another major advance for *in vitro* methods, OECD Draft Test Guideline 439 (TG439) - *In Vitro* Skin Irritation: Reconstructed Human Epidermis Test Method, was approved by the Working Group of National Coordinators (WNT) on 23-25 March 2010. The TG is expected to be adopted by the Council in July and subsequently published for use by the international toxicology community. TG439 allows any of three reconstructed human epidermis models (EpiSkin™, EpiDerm™ SIT (EPI-200), and the SkinEthic™ RHE) to be used to classify materials as either GHS 2 or non-irritant (UN GHS No Category). The WNT also agreed to develop a Guidance Document on Skin Irritation/Corrosion. This project will start with an Expert Meeting to review the different types of tools that can be used in a testing strategy and their applicability. Hans Raabe, VP and Director of Laboratory Services at IIVS, will participate in the Expert Meeting scheduled in October at the German Federal Institute for Risk Assessment (BfR) in Berlin, Germany.

American Society for Cellular and Computational Toxicology (ASCCT)

IIVS and PCRM encourage your support for the newly established scientific society, ASCCT, dedicated to the advancement of *in vitro, in silico*, and other toxicological testing methods, especially as replacements for animal-based tests. A key goal of the society is to provide regular meetings during which experts can share their knowledge of such methods with those seeking to implement non-animal testing strategies. It is hoped that these meetings will also provide an opportunity for scientists from industry and the regulatory community to discuss the best practice of these methods as they are applied to regulatory toxicology situations. An open information session about the goals of the Society will be held during the 2010 In Vitro Alternatives Forum (see article on the right). If you are interested in participating in the Society or learning more about proposed activities, please visit www.ascctox.org or contact Erin Hill at ehill@iivs.org or Kristie Sullivan at ksullivan@pcrm.org.

SAVE THE DATE

2011 Practical Methods for In Vitro Toxicology Training Workshop

January 18-20th, 2011
Gaithersburg, Maryland

The annual IIVS training course has been moved from June to January! Please contact Amanda Ulrey at aulrey@iivs.org or visit www.iivs.org if you are interested in registering. Limited space is available.

TSCA

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- Encouraging the use of scientifically acceptable non-animal methods
- Maximizing the use of existing data
- Avoiding explicit mention of specific animal-based tests, thus allowing for flexibility as science and new technologies advance
- Supporting and funding the development of new non-animal methods

While these bills are headed in the right direction, further elements need to be strengthened or clarified to ensure that animal use is minimized and eventually eliminated. A major improvement would be to *require* the use of non-animal methods where they exist, along the lines of the European Council Directive 86/609/EEC, enacted in 1986, which states that "an experiment shall not be performed if another scientifically satisfactory method of obtaining the result sought, not entailing the use of an animal, is reasonably and practically available."[6] The REACH legislation also states that animal testing should be performed "only as a last resort" and provides guidance for implementing alternatives and reducing the use of animals.[7] Based on these precedents, which have spurred the development and use of non-animal methods in the EU, the US legislation should incorporate similar language. The bill should also include stronger language requiring, rather than allowing, the use of integrated strategies.

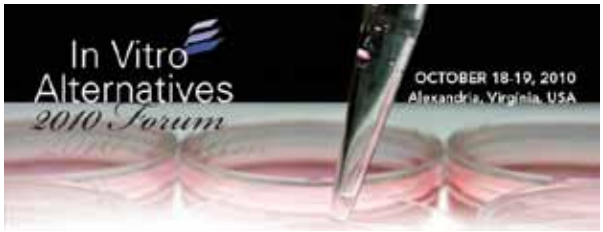
Encouragingly, the bills direct EPA to develop non-animal methods; however, the final bill should also provide dedicated appropriations. In addition, the safety standard in this bill, "reasonable certainty of no harm," has been borrowed from the Food Quality Protection Act (FQPA). This safety standard may not be appropriate for all chemicals as attempting to adhere to it in situations of low risk could result in much more testing than is necessary for regulation. The bill also currently provides a Scientific Advisory Board to oversee development and implementation of alternative methods; however, the proposed membership is inappropriate, and should include experts in alternative methods and members of the public. Their oversite of peer review should also be removed.

The House bill was introduced as a discussion draft, and a number of stakeholder meetings were held to discuss various sections of the bill. We provided detailed comments to the Committee including the points mentioned above. It's not clear what the outcome of the discussions will be, but PETA will continue to lobby for the best possible science as well as the best animal protection measure. We feel that inclusion of these considerations will not only reduce the numbers of animals killed in this new testing program but also vastly increase the EPA's ability to protect human health and the environment.

6 European Commission, Environment Directorate. Council Directive 86/609/EEC on the protection of animals used for experimental and other scientific purposes. Background available at: Council adopted Directive 86/609/EEC on the protection of animals used for experimental and other scientific purposes (accessed 6 July 2010). This Directive is currently under revision. http://ec.europa.eu/environment/chemicals/lab_animals/nextsteps_en.htm.
7 European Chemicals Agency. Practical Guide 10: How to avoid unnecessary testing on animals http://echa.europa.eu/doc/publications/practical_guides/pg_10_avoid_animal_testing_en.pdf (accessed 6 July 2010).

2010 In Vitro Alternatives Forum

October 18 & 19 Hotel Monaco - Old Town Alexandria, VA



The beautiful Hotel Monaco in historic Old Town Alexandria provides a superb setting to learn about the factors driving the increased need for alternative test methods and the international activities designed to promote their use and acceptance. The program includes overview and commentary on the reauthorization of TSCA, advancements in the area of 21st Century Toxicity Testing, approaches to identify skin sensitizers, utilization of 3D tissue models and more. Speakers include international experts from industry, regulatory agencies and the animal protection community. **Register soon at www.iivs.org. Early Bird Registration ends August 15.**

IIVS Update

2010 IIVS Science Advisory Panel

Corporate Members

Daniel Bagley
Colgate-Palmolive

Joel Burdick
Beauty Avenues

Brian Jones
Mary Kay

Frank Jones
S.C. Johnson & Son

Mark Lafranconi
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Mary Kay

PETA

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POM Wonderful

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BASF Now Offers Equipment for the BCOP Assay

OECD Test Guideline 437 describes the BCOP test as a method that can be used to classify substances as ocular corrosives and severe irritants as defined by the EPA (Category 1), the EU (Category R41) and the GHS (Category 1). During the in-house validation of the BCOP assay, BASF experienced difficulty in obtaining reliable, state-of the-art, and commercially available equipment. Therefore they designed and optimized instrumentation for the BCOP which they now offer commercially. The BASF BCOP Opacitometer Kit includes an opacitometer with certified light meter, PC interface with data transfer program, corneal holder set for 8 test substances, glass filter with holder for calibration, validation data set and instruction manual. The complete Opacitometer Kit is available for 9900€. Individual components may be purchased separately. A lead time of approximately 6 weeks is required. To receive a brochure please contact info@iivs.org or ToxOffice@basf.com.

The opacitometer, calibration chamber, and calibration inserts manufactured by BASF for use in the Bovine Corneal Opacity and Permeability Assay.