News from the American Society for Cellular and Computational Toxicology

In the fall of 2012, during and after its first annual meeting, the American Society for Cellular and Computational Toxicology held elections for a new Board of Directors. Rodger Curren and Erin Hill of the Institute for In Vitro Sciences, Thomas Hartung of Johns Hopkins University, and Kristie Sullivan of the Physicians Committee for Responsible Medicine were retained. New members Marilyn Aardema of Marilyn Aardema Consulting, John "Jack" Fowle of the US EPA (retired), and Marianna Gaça of British American Tobacco were elected. Members will serve 2-year terms.

ASCCT members have participated in two member-given webinars since the annual meeting. The first, given by Maureen Bunger of Cellular Dynamics International, discussed the process of reprogramming adult cells to create induced Pluripotent Stem Cells (iPSCs) and subsequent directed differentiation of multiple cell lineages and provided examples of their utility for *in vitro* toxicity testing. Longtime member Erik Janus of Steptoe and Johnson gave a broad and informative overview of the use of non-animal methods in safety testing and risk assessment strategies as well as regulatory considerations and activities in various industry sectors, from pesticides to cosmetics. Webinars are held every other month and are free to members. Non-members can now join any webinar for only $ 25. Keep an eye out at http://www.ascctox.org for new announcements, and contact any board member if you would like to give a webinar or suggest a topic.

Finally ASCCT is pleased to announce its 2nd annual meeting will be held October 31, 2013, in Bethesda, Maryland, USA. *The Future is Here: Practical Applications of Emerging Scientific Tools* will feature a lecture by Dr Donald Ingber from the Wyss Institute for Biologically Inspired Engineering at Harvard University. A second invited lecture, a panel of regulator and industry discussants, a poster session, and lectures selected from submitted abstracts will round out the agenda. Check http://www.ascctox.org for abstract submission guidelines and registration information.

CAAT*feed*

CAAT featured in *Nature* and *Nature Medicine*

CAAT and Director Thomas Hartung have been highlighted in the journals *Nature* and *Nature Medicine* ("The 'Omes Puzzle," *Nature 494*, 419; "Animal Rule for Drug Approval Creates a Jungle of Confusion," *Nature Medicine 19*, 118-119).

In the *Nature* article, Hartung discusses the Human Toxome Project, funded with $ 6 million from the US National Institutes of Health (NIH) over five years, plus extra support from the Environmental Protection Agency (EPA) and the Food and Drug Administration (FDA). "The toxome is very similar to the Human Genome project because it establishes a point of reference," Hartung says, adding that the toxome could help to lay out a series of straightforward cell-based assays that could replace animal tests – and perhaps improve on them.

In *Nature Medicine*, Hartung points out the reality of animal models in pharmaceutical research. "If there was an animal model good enough to substitute for people, we would not have a 92% failure rate in clinical trials," he says. He advocates more predictive *in vitro* systems combining stem cells with microfluidics technologies to create 3D human organ equivalents, i.e., the so-called "human-on-a-chip" approach.

Society of Toxicology Enhancement of Animal Welfare Awarded to Martin L. Stephens

Martin L. Stephens, PhD, was awarded the 2013 Society of Toxicology Enhancement of Animal Welfare Award, becoming the third member of CAAT to receive the honor. Alan Goldberg and Thomas Hartung were earlier recipients. Dr Stephens is a senior research associate at CAAT, where he coordinates the Center's activities on evidence-based toxicology. Prior to joining Hopkins in October 2011, Dr Stephens was vice president for animal research issues at The Humane Society of the United States where he directed the Society's efforts on behalf of animals in laboratories. He served on the National Academy of Sciences committee that wrote *Toxicity Testing in the 21st Century: A Vision and a Strategy*, as well as on program committees for the World Congresses on the Use of Animals and Alternatives in the Life Sciences. He co-founded the Human Toxicology Project Consortium, which seeks to accelerate the implementation of pathway-based toxicity testing. Dr Stephens has received the Doerenkamp-Zbinden Award and the CAAT Recognition Award for his contributions to animal protection and alternative methods.

CAAT 2013-2014 Research Grants

CAAT grants, although relatively small, often provide critical seed money for researchers hoping to develop new in vitro methods. We have a stringent, peer-reviewed process for selecting the recipients of these grants. This process consists of sending each application to at least four experts in the field from academic, industrial, and government institutions. These reviewers evaluate the applications with regard to scientific merit, budget appropriateness, relatedness to CAAT's mission, and expertise of the investigators. They also assign a priority score based on the scoring system used by the NIH.

- **Sabra Klein:** Differentiated human respiratory epithelial cell cultures as a surrogate system for assessing the effects of estrogenic compounds on pulmonary disease pathogenesis
- **Yusuke Marikawa:** Novel axial elongation morphogenesis systems using embryonic stem cells to investigate teratogenic factors
- **Jeffery Morgan:** A new 3D *in vitro* model of chemical transport across the human placenta
- **Walter Petroll:** A novel anterior corneal construct for ocular toxicity testing *in vitro*
- **Nicole zur Nieden:** Skeletal teratogenicity of environmental chemicals predicted with human induced pluripotent stem cells *in vitro*

CAAT at the Society of Toxicology Annual Meeting

CAAT organized a satellite meeting at the 2013 Society of Toxicology Meeting in San Antonio, Texas on March 14: *Updates on 21st Century Toxicology Activities and Related Efforts: Invited Presentations and Open Microphone*. Thomas Hartung and Martin Stephens presented, as well as representatives from EPA, NIEHS, and the Hamner Institutes for Biomedical Science. Also at the conference, Lena Smirnova, CAAT Research Associate, presented a poster on our current work elucidating effects of developmental toxicants on microRNA expression during differentiation of LUHMES neuronal progenitor cells. The poster described the different differentiation conditions: 2D vs 3D, as well as expression of neural specific microRNA in course of LUHMES differentiation, and effects of two well-known developmental neurotoxicants, lead chloride and valproate, on miRNA expression during neuronal differentiation of LUHMES cells. Helena Hogberg, CAAT research associate, presented the FDA funded project "DNTox-21c: Identification of pathways of developmental neurotoxicity for high throughput testing by metabolomics" in platform session "Validation and Application of Neurotoxicology In Vitro Methods."

Lessons Learned, Challenges, and Opportunities: The US Endocrine Disruptor Screening Program April 23-24, 2013, Research Triangle Park, NC

This workshop brings together multiple stakeholders, including CAAT as co-organizer, in an open forum for the opportunity to review and discuss the challenges and lessons learned from the initial experiences with Tier 1 screening assays. Such an open meeting with all stakeholders – including Federal Regulatory Agencies, NGOs, industry, contract laboratory scientists, and academic researchers – is critical and timely – to best use this collective experience for potential improvements in Tier 1 assays and to further advance our ability to assess endocrine disruption. All stakeholders and interested parties are invited to participate.
More information is available at:
http://www.tera.org/peer/EDSP

Developing Microphysiological Systems for Use as Regulatory Tools – Challenges and Opportunities May 10, 2013, Silver Spring, MD

CAAT, along with The Food and Drug Administration (FDA), National Institutes of Health, National Institute for Environmental Health Sciences (NIEHS), National Center for Advancing Translational Science (NCATS), and the International Consortium for Innovation and Quality in Pharmaceutical Development (IQ) are collaborating to present this workshop. CAAT Director Thomas Hartung will chair a session on "Inventing Microphysiological Systems: Cell Types, Tissues, and How to Apply Them" and speak on good cell cultures and quality control.

The workshop's goal is to provide a forum for academia, industry, and regulatory agencies to address two objectives: 1) discuss essential elements needed to develop microphysiological systems as regulatory tools, and 2) discuss pathways to qualification as regulatory tools.

The FDA has invited CAAT Director Thomas Hartung to chair a session and present at the workshop.

See this link for more information: http://bit.ly/YSq7Xy

Fourth International Conference on Alternatives for Developmental Neurotoxicity Testing (DNT) May 12-14, 2014, Philadelphia, PA

TestSmart DNT 4:
Developmental Toxicity
Registration information not yet available
http://caat.jhsph.edu/dnt4

Call for Abstracts: Submission Deadline: December 31, 2013

You are invited to submit an abstract on the following DNT topics:
- Development and use of alternative testing methods and strategies
- Automation of test methods
- Models of chemical-induced neurological deficits
- The impact of international legislation on chemical testing and data interpretation
- Toxicity pathways: Linking molecular events to adversity (AOP and PoT)
- Predictive molecular and cellular biomarkers of DNT
- Modeling gene/environment interactions that impact neurodevelopment
- Epigenetic changes and neural development

Scientific Roadmap for the Future of Animal-free Systemic Toxicity Testing May 30-31, 2013, Maryland

Organized by CAAT and hosted by FDA, with more than twelve co-sponsoring organizations, this workshop will be held at the FDA Wiley Building in College Park, Maryland. Discussions and presentations will address the roadmap outlined in "*A roadmap for the development of alternative (non-animal) methods for systemic toxicity testing*," by Basketter et al. in ALTEX 29, 5-91. This stakeholder forum will be modeled on the one held in Brussels in March, 2012, co-organized by numerous organizations and attended by some 150 experts.
For details contact Marilyn Principe: mprincip@jhsph.edu

In Vitro Medical Device Testing December 10-11, 2013, Baltimore, MD

This symposium, hosted by CAAT, will examine how *Toxicity Testing in the 21st Century* can be applied to Medical Devices. The program will examine current requirements and testing approaches, followed by an examination of *in vitro* assays useful in medical device testing.
For more information contact:
Marilyn Principe (mprincip@jhsph.edu)
or Alan Goldberg (goldberg@jhsph.edu)

2014 CAAT Science-based Refinement Awards Call for Proposals

Attention veterinarians, lab technicians, animal technicians, and all who work with laboratory animals: CAAT now is accepting proposals for the 2014 Science-based Refinement Awards (formerly the Animal Welfare Enhancement Awards).

The focus of these awards is to elicit scientific evidence to support the enhancement of the housing, handling and/or experimental situations for laboratory animals. Deadline for submissions is September 30, 2013.

Details: http://caat.jhsph.edu/programs/awards/AWE/2014/index.html

CAAT at EU Parliament

At the European Parliament, during the *EU Science: Global Sciences and Global Collaboration* meeting, CAAT organized two events to raise awareness and chart progress on the implementation of the 3Rs and discuss new developments in toxicology testing.

MEP Chris Davies (ALDE) chaired a discussion on the *Worldwide implementation of the 3Rs for laboratory animals used for scientific purposes*. Presentations were offered by an international group of scholars in humane science, and explained the situation in North America, where the focus is largely on Refinement; South America, where efforts are in the developmental and early planning stages, with a new center established in Brazil (Brazilian Centre for the Validation of Alternative Test Methods); and the diverse approaches and cultures of Asia (China, India, South Korea, Japan, Thailand, Cambodia) that predominantly focus on reduction and refinement and integrate not only science but also religious and cultural influences. Australia has recently established an alternatives research unit at The John Curtin School of Medical Research (ANU, Canberra) with an evolving emphasis on developing replacement alternatives. As a wrap-up, all the speakers agreed that the European Union was a leader in many areas of regulation and policy on the use of laboratory animals for scientific purposes (Directive 2010/63 EU).

A second workshop, chaired by MEP Vittorio Prodi (S&D), took place the same day and focused on how and why to integrate *Systems toxicology in regulatory science*. The panelists' representations covered the main actors in the field: regulators (e.g., FDA, SCAHT), harmonization bodies (OECD), industries (CEFIC), NGOs (HSI), and academia (CAAT, INSERM). One of the key messages of the session was the strong commitment of newly appointed Director of the US FDA's European office in Brussels, Dara Corrigan, to promote "fit-for-purpose" regulatory toxicology. Thomas Hartung suggested that coordination should be central to achieving harmonization and a steering committee or the creation of an agency could be a solution.

ecopa

The ecopa board meeting will be held in Denmark on September 24, prior to the Scandinavian Society of Cell Toxicity meeting in Vilvorde on September 25-28.

The ecopa general assembly will take place on October 23 from 1 pm to 4 pm in Mainz, Germany. This will be followed by a symposium on high content imaging (HCI) systems in safety sciences on October 24 from 9 am to 5 pm. The co-hosts are ecopa, set foundation, CAAT-Europe, IVTIP, and ESTIV. ECOPA is also the co-host of the workshop on the same topic which will take place on October 21-23.

Government of the Netherlands

Netherlands Knowledge Centre on Alternatives to Animal Use (NKCA)

The Netherlands Knowledge Centre on Alternatives to Animal Use (NKCA) promotes the application of the 3R alternatives – *replacement, reduction and refinement* – in the Netherlands. The Centre, which is a collaboration between the RIVM and the University of Utrecht, was established by the Ministry of Health, Welfare and Sport and has been operational since January 2010. The dossier on "animal testing and 3R-alternatives" was transferred to the Ministry of Economic Affairs in January 2013.

- NKCA promotes the use of 3R-alternatives through coordinated activities in the following areas:
- Knowledge and information management
- Communication management (professionals and public)
- Education (including extra training)
- Advising professionals on policy and practice

Knowledge and information management

Finding suitable 3R-alternatives for animal testing is a complex business as it is not always a question of simply replacing an animal test. More and more often it is like solving a puzzle: applying a well thought-out trial or test strategy using a combination of the 3R-methods to minimize the use of animals in testing. NKCA will promote this is in 2013 by promoting the sharing of knowledge and experience as well as actual collaboration between professionals operating in the national and international arena. NKCA aims to strengthen its role as "3R-information broker" and build upon the framework and resources developed over the past few years. We must persuade professionals that NKCA is the place to bring and collect their 3R-knowledge and hands on experience.

Communication management

NKCA invested in a comprehensive website for professionals in 2012, in response to requests from within the field. This website will continue to develop in 2013. NKCA is currently exploring the possibilities of social media, such as twitter, facebook and linkedin for professional use. "Network gatherings" are also organized by the Centre, because networking invariably results in good teamwork and collaboration. In 2013, NKCA will focus considerable attention on corporate partners and collaboration within the entire research chain. This is a recommendation from the workshop organized by the NCKA, TNO and the University of Utrecht in 2012 on obstacles and barriers preventing regulatory acceptance. Collaboration with industry in the Utrecht region has produced some positive results through the project "Smarter from Innovation to Man" (SLIM). NKCA will launch a public communication initiative in 2013, the preparations for which started in 2012.

Education

In accordance with Articles 9 and 14 of the Experiments on Animals Act, NKCA organizes the "animal testing alternatives" module as part of the postgraduate

training for professionals. Animal testing regulations are relatively unknown in secondary schools. In an effort to prohibit animal testing in secondary schools, NKCA contacted the education body responsible for teacher training. NKCA advises teachers on the animal-free testing models available for secondary schools, and recommends animal-testing alternatives as a potential subject for student projects. The new Law on Animal Testing, which will take effect in 2013, marks a change in education for everyone involved in animal testing. NKCA will be in a key position to provide advice on how to implement the new regulations within the education system.

Policy advice

The number of laboratory animals used for testing in the Netherlands appears to have stabilized at around 600,000 over the past few years. In 2012, upon request of the Ministry of Health Welfare and Sport, NKCA produced a report advising on data storage and monitoring. This advisory report includes an evaluation of the currently available data on animal testing in the Netherlands, in accordance with a request from stakeholders. Preventing duplication of animal tests and an efficient centralized registration are just two of the issues raised in this report. NKCA is also exploring the value of a monitoring system that will provide an insight into developments in the Replacement, Reduction and Refinement (3R) methods. The report describes which data or combinations of data (both new and existing) are reliable indicators. The Ministry of Economic Affairs is currently considering how best to implement this advice.

News from NICEATM and ICCVAM

Environmental Health Perspectives Editorial: "Reinventing ICCVAM"

A recent editorial by National Institute of Environmental Health Sciences (NIEHS) and National Toxicology Program Director Linda Birnbaum discussed the current status and future direction of ICCVAM. In the editorial, entitled "15 Years Out: Reinventing ICCVAM," Dr Birnbaum summarizes the history and purpose of ICCVAM and notes that concerns have been raised about the lack of implementation of ICCVAM-recommended methods. She goes on to state that NIEHS is beginning to move forward with an approach that will allow ICCVAM's activities to be driven by the partner regulatory agencies. At the same time, NICEATM will expand its scope and begin to provide bioinformatic and computational toxicology support to NIEHS Tox21 projects, with the goal of better positioning ICCVAM to address how data from high-throughput assays can be integrated into the regulatory framework.

Dr Birnbaum concludes the editorial by noting recent leadership changes at NICEATM. Dr William Stokes, who has served as the director of NICEATM since its inception, retired from the Public Health Service in December 2012. Dr Warren Casey, who has served as Deputy Director of NICEATM, is now acting director of NICEATM.

The full editorial, published in the Feb. 1 issue of *Environmental Health Perspectives*, can be read at: http://ehp.niehs.nih.gov/2013/02/1206292/

New OECD Test Guidelines available for Eye Safety Testing

The Organisation for Economic Co-operation and Development (OECD) has officially adopted two test guidelines for identification of substances with the potential to cause eye injury. One of these, an updated test guideline for the traditional rabbit eye test, incorporates specific procedures to avoid or minimize animal pain and distress when it is necessary to use animals to identify substances with the potential to cause eye injuries. The other test guideline provides a new method to identify substances that may cause serious eye injuries without using animals.

The updated OECD Test Guideline 405 incorporates recommendations made by ICCVAM to U.S. Federal agencies in 2010. After an evaluation of the use of anesthetics, analgesics, and humane endpoints in eye safety testing, ICCVAM recommended that these pain management procedures should *always* be used when it is determined necessary to use the rabbit eye test for regulatory safety assessments. The ICCVAM recommendations were accepted or endorsed by U.S. Federal agencies in 2011. The adoption of the updated OECD Test Guideline 405 means that these procedures may now be used in the 34 member countries of the OECD.

The new Test Guideline 460 describes the fluorescein leakage test method, which can be used to identify ocular corrosives and severe irritants. While it is not a complete replacement for the rabbit eye test, the fluorescein leakage test method can be used as an initial step in a testing strategy to identify water-soluble substances and mixtures that are potential corrosives or severe irritants.

The new test guidelines are available on the ICCVAM website:

OECD Test Guideline 405: Acute Eye Irritation/Corrosion is available at: http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG405-2012-508.pdf

OECD Test Guideline 460: Fluorescein Leakage Test Method for Identifying Ocular Corrosives and Severe Irritants is available at: http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG460-508.pdf

New Test Guidelines available for Endocrine Disruptor Testing

OECD has also officially adopted two test guidelines for test methods to identify substances with the potential to affect the function of the endocrine system. Both test guidelines describe *in vitro* methods that do not use animals, and the tests are appropriate for use in the U.S. Environmental Protection Agency (EPA) Endocrine Disruptor Screening Program.

Test Guideline 457 describes the BG1Luc estrogen receptor (ER) transactivation (TA) assays to detect ER agonists and antagonists and provides performance standards for each assay. The test guideline was based on data from an international validation study that was coordinated by NICEATM in conjunction with the European Union Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM) and the Japanese Center for the Validation of Alternative Methods (JaCVAM) and that included laboratories in the United States, Japan, and Italy.

NICEATM worked closely with the EPA to usher this method through the OECD nomination and adoption process. The adoption of Test Guideline 457 means that these methods may now be used in the 34 member countries of the OECD. In July 2012, the EPA announced its acceptance of the BG1 method as an alternative to the HeLa-9903 TA assay in response to a recommendation by ICCVAM.

Test Guideline 455 has been updated to include both the BG1 and HeLa-9903 methods, and now describes general characteristics of stably transfected transactivation *in vitro* assays to detect ER agonists. This performance-based test guideline also provides standards that will support more efficient validation of new test methods of this type. These standards include a harmonized list of reference chemicals that should be tested during assay development, as well as performance standards that should be met by successful assays.

The new test guidelines are available on the ICCVAM website:

OECD Test Guideline 457: BG1Luc Estrogen Receptor Transactivation Test Method for Identifying Estrogen Receptor Agonists and Antagonists is available at: http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG457-508.pdf

OECD Test Guideline 455: Performance-Based Test Guideline for Stably Transfected Transactivation *In Vitro* Assays to Detect Estrogen Receptor Agonists is available at: http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG455-2012-508.pdf

Acting NICEATM Director meets with international experts to assess Endocrine Disruptor Testing

Acting NICEATM Director Dr Warren Casey participated in two expert meetings in November that considered *in vitro* methods for detecting substances that might interfere with normal hormone function. Casey attended the annual meeting of the Validation Management Group for Non-Animal Testing (VMG-NA) on November 29 and 30. He also attended the first meeting of the Thyroid Scoping Effort Expert Group on November 28. Both meetings were sponsored by OECD and took place at OECD Headquarters in Paris.

The November VMG-NA meeting considered additional methods currently under evaluation for this purpose by the EPA and groups in Europe and Japan. Casey serves on the study management teams for these projects, and he commented on their progress and addressed questions about selection of reference chemicals and evaluation methods. Participants at this meeting also considered the development of medium and high throughput screening methods for endocrine disruptors. Casey presented recent work on the adaptation of the BG1Luc ER TA methods (see preceding article) to a high throughput platform, which was one of several case studies discussed at the meeting.

Casey also attended the first meeting of the Thyroid Scoping Effort Expert Group. The purpose of this meeting was to identify available assays for the detection of potential thyroid disruptors and assess their suitability for regulatory use or potential future test guideline development. Recommendations from this meeting will be submitted to the National Coordinators of the OECD Test Guidelines Programme, who will consider it at their 2013 meeting this spring. Approval of the recommendations will provide direction for future development of test methods to identify potential thyroid disruptors.

Summary available of Workshop on Alternatives for Pertussis Vaccine Safety Test

A summary is now available of the November 2012 "International Workshop on Alternatives to the Murine Histamine Sensitization Test (HIST) for Acellular Pertussis Vaccines." This workshop brought together over 40 scientific experts from 10 different countries representing government, industry, and academia to review and discuss the usefulness and limitations of *in vitro* alternatives to the HIST.

Participants reviewed and discussed data generated in a 12-laboratory international study to evaluate the performance of *in vitro* assays using both a single pertussis toxin (PTx) standard and common sets of seven vaccines from three manufacturers. Participants agreed that

the current mouse HIST should be replaced with a suitable *in vitro* alternative test(s) and that any proposed replacement method(s) must ensure that the vaccine contains safe levels of PTx. Advantages and disadvantages of the alternatives were recognized. Participants recommended further development and optimization of specific methods and to move forward with an international collaborative study for calibration of the pertussis toxin standard using a standardized CHO cell assay in 2013.

The workshop was held at the headquarters of the U.S. National Institutes of Health in Bethesda, Maryland. NICEATM organized the workshop in collaboration with ICCVAM and partner organizations in the International Cooperation on Alternative Test Methods.

The workshop summary is available on the ICCVAM website at: http://iccvam.niehs.nih.gov/meetings/HISTWksp-2012/HISTWksp.htm

The final workshop program and a link to slides presented at the workshop are also available on this page. A report of the workshop will be published in 2013 in the journal Biologicals.

U.S. Consumer Product Safety Commission publishes New Rules on Animal Testing Policy

A rule published in December 2012 by the U.S. Consumer Product Safety Commission (CPSC) codifies the statement of policy on animal testing that provides guidance for manufacturers of products subject to the Federal Hazardous Substances Act (FHSA) regarding replacement, reduction, and refinement of animals. Codification of this policy is intended to make CPSC's animal testing policy and test methods recommended by ICCVAM and accepted by CPSC more transparent and accessible to interested parties. The rule includes comments received on the proposal and CPSC responses to the comments. The rule also includes the relevant amendments made to the text of 16 CFR part 1500. The statement of policy took effect in January 2013.

The rule is available on the ICCVAM website at: http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/CPSC/CPSC-FR-2012-29260.pdf or http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/CPSC/CPSC-FR-2012-29260.htm

In a related notice, the CPSC announced amendments to its regulations on the CPSC's animal testing methods under the FHSA. The announcement, also published in December 2012, includes comments received on the proposed rule and CPSC responses to the comments. The rule also includes revisions to animal testing regulations and explanations of the rationale for the revisions. The rule took effect in January 2013.

The rule is available on the ICCVAM website at: http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/CPSC/CPSC-FR-2012-29258.pdf or http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/CPSC/CPSC-FR-2012-29258.htm

The FHSA (15 U.S.C. 1261-1278) requires appropriate cautionary labeling to alert consumers to the potential hazards that certain hazardous household products may present. These include products that are toxic, corrosive, irritants, flammable, combustible, or strong sensitizers. The changes to the FHSA announced in December clarify the criteria used for classification of substances as "highly toxic," "toxic," "corrosive," "irritant," "primary irritant," and "eye irritant." The changes emphasize that the use of *in vitro* and other alternative test methods, including a weight-of-evidence approach, and prior human experience are recommended over *in vivo* animal tests wherever possible. Furthermore, the CPSC reiterates its preference for reliable human experience over animal test data.

CPSC has also established a page on its website regarding ICCVAM recommendations and new developments in test methods that avoid or further reduce or refine animal testing. The page is located at: http://www.cpsc.gov/en/Business--Manufacturing/Third-Party-Testing/Recommended-Procedures-Regarding-the-CPSCs-Policy-on-Animal-Testing/

According to the ICCVAM Authorization Act, ICCVAM member agencies should promote and encourage the development and use of alternatives to animal test methods for regulatory purposes. Since the establishment of ICCVAM, the CPSC has approved, where applicable, recommendations made by ICCVAM to reduce and refine animal testing applicable to test methods under the FHSA. A table summarizing U.S. and international regulatory acceptance of alternative test methods, which includes methods recommended by ICCVAM applicable to testing under the FHSA, is available on the ICCVAM website at: http://iccvam.niehs.nih.gov/about/accept.htm

Institute for In Vitro Sciences
Advancing Science & Animal Welfare Together

IIVS News & Views

EPAA and IIVS sign memorandum of understanding

In an effort to ensure stronger international cooperation on advancing non-animal testing methods, the European Partnership for Alternative Approaches to Animal Testing (EPAA) and IIVS have agreed to establish a strategic partnership dedicated to the international dissemination of alternative techniques for safety evaluation. EPAA will provide sponsorship of up to € 100,000 over the next two years to IIVS to support training activities in key regions, including China and Brazil.

IIVS shares Poster Award at EPAA meeting

The 2012 Poster Recognition Award, restricted to industry applicants, was given to a poster co-authored by IIVS entitled: *Pre-validation of the Reconstructed 3D Human Skin Micronucleus and Comet Assays*. Eight organizations cooperated in these studies, financed primarily by Cosmetics Europe, to develop genotoxicity assays that would assist in addressing the EU ban on the animal testing of cosmetics products or ingredients, or the marketing of animal-tested cosmetics products.

IIVS wins the first LUSH Cosmetics Prize for Training

Designed to accelerate the date when products and chemicals are no longer tested on animals, the LUSH prize recognizes individuals or organizations who have excelled in establishing training programs to make scientists aware of the range of available non-animal testing methods. IIVS received the first annual Lush Training Prize during an award ceremony in London on November 15, 2012. The prize is a joint project between the global handmade cosmetics company and Ethical Consumer magazine. "At IIVS we believe the change to non-animal testing methods will be hastened through education and training. Seeing, touching, using these methods firsthand and understanding the results will change perceptions and practices," said Erin Hill, Vice President of IIVS, during the awards ceremony in London. "Our trainings change the fuzzy image of 'alternatives' into the reality of better science and the removal of animal pain and suffering." IIVS shares the award with InterNICHE; an international network focusing on animal use and alternatives within biological sciences, medical, and veterinary medical education.

COLAMA 2012: 1st Latin American Congress on Alternative Methods for Use of Animals in Education, Research and Industry

Styled after the World Congress on Alternatives and Animal Use in the Life Sciences, COLAMA provided a forum for Latin American countries interested in alternative methods. The host country, Brazil, recently created the Brazilian Center for the Validation of Alternative Methods (BraCVAM) through cooperation between the Oswaldo Cruz Foundation (FIOCRUZ), the National Health Surveillance Agency (ANVISA) and the National Network of Alternative Methods (RENAMA). The COLAMA conference was organized in Niteroi (RJ) and was attended by almost 200 people including over 40 speakers and 12 supporting organizations. IIVS was proud to give a lecture and to be recognized as a Bronze Supporter of the meeting.

While in Brazil, IIVS participated in the Humane Society International's regulatory science workshop titled *Current and Future Prospects of Alternatives for Cosmetics Testing*. IIVS also presented during a meeting of ANVISA, ABIHPEC, and ITEHPEC titled *Harmonization of Techniques for Safety Evaluation of Cosmetics and their Ingredients*.

IIVS International Training Programs: IIVS Industry Council for the Advancement of Regulatory Acceptance of Alternatives (ICARAA): Training at Reshine Biotech

At the end of October 2012, IIVS scientists traveled to China to provide training to Chinese researchers through IIVS' Industry Council for the Advancement of Regulatory Acceptance of Alternatives (ICARAA). The team visited Shaanxi Reshine Biotech in Xi'an to instruct their staff on three OECD accepted *in vitro* methods. The program consisted of lectures on the Bovine Cornea Opacity and Permeability (BCOP), 3T3 Neutral Red Uptake Phototoxicity (3T3 NRU PT) and the Skin Irritation Test (SIT) assays followed by hands-on laboratory training in these methods. Nearly 30 scientists attended these instructional sessions including representatives from the Chinese sFDA and AQSIQ.

Although this training provided the Chinese scientists with their first exposure to these methods, their local efforts clearly assisted the program. Importantly, the bovine corneas used in the training were obtained locally and the skin tissue models were generated on-site at Shaanxi Reshine.

A key component of IIVS' mission is to assist *in vitro* test method developers to optimize and validate their products for use by industry and the regulatory community. Realizing the need for 3D skin constructs and the limitation on importation of such models into China, IIVS views Shaanxi Reshine as a viable option for the production of skin models for safety testing within China. With further training and development, it is expected that Shaanxi Reshine can provide tissue constructs for use in regulatory submissions, once they are accepted by Chinese authorities. They could also become a training center to help in the evaluation and validation of *in vitro* methods in China, and potentially provide safety testing to companies for product development and regulatory submissions.

ICARAA was created through the support of companies dedicated to providing technical assistance to companies, universities, and governments with the goal of regulatory acceptance of non-animal methods in countries which still rely on animal models for the safety evaluation of ingredients and products.

IIVS International Outreach Program (IOP): Training at Beijing Technology and Business University

IIVS staff traveled to Beijing to provide training at Beijing Technology and Business University (BTBU). BTBU is the leading Chinese university in cosmetic science having undergraduate and graduate level training in cosmetic formulation, efficacy and safety. BTBU also has had a close connection to the sFDA in understanding *in vitro* methods for safety and efficacy. IIVS scientists provided lectures and a hands-on laboratory demonstration for the BCOP assay. The BCOP assay was conducted using high-quality, locally-sourced bovine corneas. Over 25 students and faculty attended the lectures and demonstration. This was the first step in establishing BTBU as a fully functional *in vitro* laboratory for evaluating the safety and efficacy of cosmetic ingredients and formulations.

This training was funded through support of IIVS and our International Outreach Program (IOP). Additional support was provided by BASF, through donations of opacitometers for BCOP and by PETA for support to the BTBU lab with equipment necessary for conducting accurate *in vitro* assessments. With this funding IIVS was able to provide quality training at BTBU and has been asked to return to China to provide further guidance and training. Further training at these laboratories, as well as at additional sites in China, is being planned for 2013.

52nd Annual Meeting of the Society of Toxicology

IIVS staff attended the annual SOT meeting in San Antonio, Texas. Hans Raabe was a speaker for a well-received continuing education class on non-animal corrosivity and irritation testing for REACH purposes. Listed below are titles of the IIVS posters presented during SOT. For copies of the posters or for more information on any of the poster topics, please visit and contact us through our website: http://www.iivs.org

- Application of a Modified Keratino-Sens Assay to Predict Sensitization Hazard for Botanical Extracts
- Validation of In Vitro and Clinical Safety Assessment of Behentrimonium Chloride-Containing Leave-on Body Lotions Using Post-marketing Adverse Event Data
- The Inter-laboratory Reproducibility of the STE Test for Assessing Eye Irritation of Cosmetic Products
- Choosing the Appropriate Solvent for Solid Materials Tested in the Bovine Corneal Opacity and Permeability (BCOP) In Vitro Assay
- In Vitro Ocular Irritation Testing Strategy for Prototype Cleaning Products
- Surfactant Responses in the Bovine Corneal Opacity and Permeability Assay: Points to Consider for In Vitro Eye Irritation Testing
- Screening of Cosmetics Ingredients for Phototoxic Potential Using the In Vitro 3T3 Neutral Red Uptake Phototoxicity Test