The American Society of Cellular and Computational Toxicology (ASCCT) is now accepting new members on its website, www.ascctox.org. The ASCCT was formed in 2010 to capitalize on a recent surge in interest in and demand for more human-relevant methods to assess hazards of chemical exposure and to provide a complement to well established in vitro societies in the European Union and other regions.

Increased demands for scrutiny of new and existing chemicals, as well as environmental contaminants, for a wider spectrum of health effects, combined with a decreasing availability of resources for assessing risk, led to the US National Academies publication of Toxicity Testing in the 21st Century: A Vision and a Strategy. This report envisions a human-based hazard assessment process that is quick and cost-effective but offers broader dose range and endpoint coverage and more inherent human relevance than current animal-based tests.

At the same time, public interest in decreasing the use of animals for toxicity testing has led to large investments – mostly by the EU’s cosmetics industry – for in vitro (non-animal) methods. Established scientific societies like ESTIV, EUSAAT (formerly MEGAT), and a host of national societies provide forums where members of the in vitro community can collaborate to speed progress.

The ASCCT was formed in part to inspire collaboration between these two efforts by bringing together disparate industrial sectors – from cosmetics to pesticides to industrial chemicals – to join with scientists and regulatory professionals working in different fields to maximize the effectiveness of efforts and accomplish a true paradigm shift.

This goal is reflected in the selection of the Board of Directors, which comprises President Rodger Curren and Treasurer Erin Hill of the Institute for In Vitro Sciences and Secretary Kristie Sullivan of the Physicians Committee for Responsible Medicine. Thomas Hartung of the Johns Hopkins University and CAAT, Melvin Andersen of The Hammer Institute for Health Sciences, Chihae Yang of Altamira, LLC, and Chad Sandusky of PCRM round out a diverse and dynamic group.

At the 2010 In Vitro Alternatives Forum in Alexandria, Virginia, Drs. Curren and Hartung announced the formation of the ASCCT and encouraged people and organizations to join. In sharing his thoughts on the formation of the ASCCT, Dr. Curren discussed the formation of the Genetic Toxicology Society in 1975 and how its proximity to Washington – and regulators – allowed for the efficient development of in vitro genotoxicity tools.

Individuals can join ASCCT at its website, www.ascctox.org. Memberships are offered for students, individuals, and Founding Member organizations. All members will receive a quarterly e-newsletter, a discounted subscription rate to the journal ALTEX, and discounted registration for ASCCT events. Founding Member organizations will also receive a space for their logo on the ASCCT site and other advertising materials, and one lifetime membership within their organization.

The ASCCT is planning several events for 2011, including an activity in conjunction with the 8th World Congress on Alternatives and Animal Use in the Life Sciences, to be held in Montréal, as well as members-only web seminars to allow members to share their work developing the latest tools and assays. There are plenty of ways to get involved and provide input. Join today to help shape your Society!
CAAT feed

Invitation to the kick-off meeting of the Evidence-based Toxicology (EBT) collaboration
10 March 2011, Washington DC, immediately following the SOT Annual Meeting

A group of toxicologists with backgrounds in industry, government oversight, academia, and animal welfare have created the EBT Collaboration to foster the development of a process, based on the Cochrane Collaboration in Evidence-based Medicine (EBM), for quality assurance of new toxicity tests for the assessment of safety in humans and the environment. To start the collaboration and solicit input from the stakeholder community, the EBT Collaboration steering group is organizing a workshop to take place on 10 March 2011 immediately following the Society of Toxicology Annual Meeting in Washington DC. At the workshop, speakers will present the concept of EBT as it pertains to decision-making about the utility of new toxicity tests and their implementation into the risk assessment process. EBT promises to provide a quality, science-driven approach to assessing the effects of drugs and chemicals on human health and the environment and provides principles of how to incorporate published information into the decision-making process. The methods of EBM, to be applied to EBT, include the systematic review of relevant literature, scoring tools to prioritize published reports, and meta-analysis of data. This transparent process will represent another approach toward evaluation and quality assurance of new testing methodologies.

Stakeholders from the regulatory and regulated communities, as well as toxicologists in an academic environment, will benefit from the presentations and ensuing discussions. Speakers will represent different facets of the EBT quality assurance process – representatives from regulatory agencies, the regulated industries (chemical, pharmaceutical, household product), and academia will present the concept of EBM and its application to toxicology and outline ideas for how this process can be utilized to ensure quality assurance for new toxicity tests.

For additional information, please contact Marilyn Principe: mprincip@jhsph.edu or +1 410-614-4989.

Newly redesigned CAAT website launched
In mid-November, CAAT launched its new website, which has been reorganized and redesigned to make all of CAAT’s programs and publications more attractive and easily accessible. CAAT-Europe has been seamlessly integrated into the new site, as has the Altweb news feed and the organization’s growing social networking activities. Please stop by for a visit and let us know what you think: http://caat.jhsph.edu

Joint Appointment
In addition to serving as Director of CAAT and holding the Doerenkamp-Zbinden Chair in Evidence-based Toxicology, Thomas Hartung now has been granted a joint appointment in the Department of Molecular Microbiology & Immunology for the term October 1, 2010 to June 30, 2011. This appointment is given by the authority of the President of the Johns Hopkins University and upon the nomination of the Advisory Board of the Bloomberg School of Public Health.

Upcoming Meetings
March 6-10: SOT Annual Meeting
(Washington DC)
March 6: Tox 21c Implementation Meeting (Washington DC) – in conjunction with SOT
March 10: EBT Collaboration Kick-Off (Washington DC) – see above

Awards
Marcel Leist, Co-Director of CAAT-Europe, received the “Research Award for Alternative Methods to Animal Experiments.” The award of €25,000 was presented on 29 November 2010 by the state government of Baden-Württemberg, Germany and acknowledges a new method to replace animal experimentation in neurodegeneration research.

Maria Moreno-Villanueva and Alexander Bürkle (CAAT-Europe), received the Ursula M. Händel Animal Protection Prize. The award of €25,000 was presented on 24 January 2011 by the German Research Council (DFG) for a new method in genotoxicity testing.

Recent Publications
News from NICEATM and ICCVAM

We are pleased to provide this update on recent and planned activities of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM). ICCVAM is an interagency committee composed of representatives from the 15 U.S. Federal regulatory and research agencies that require, use, or generate toxicological and safety testing information. ICCVAM is charged by law to evaluate the usefulness and limitations of new, revised, and alternative test methods with regulatory applicability, and to provide recommendations on their scientific validity to U.S. Federal agencies. ICCVAM also promotes the scientific validation and regulatory acceptance of safety testing methods that more accurately assess the health hazards of chemicals and products while reducing, refining (decreasing or eliminating pain and distress), and replacing animal use.

NICEATM administers ICCVAM and provides scientific and operational support for ICCVAM-related activities. Consistent with the NTP mission, NICEATM also conducts and coordinates international validation studies on high priority improved safety testing methods. NICEATM and ICCVAM collaborate to evaluate new and improved test methods applicable to the needs of U.S. Federal agencies and work to achieve national and international harmonization of safety testing methods.

U.S. Federal agencies accept ICCVAM-recommended test methods to identify allergic contact dermatitis hazards

In June 2010, ICCVAM provided recommendations to U.S. Federal agencies on the usefulness and limitations of the first two nonradioactive versions of the murine local lymph node assay (LLNA) and on expanded applications of the LLNA for assessing the allergic contact dermatitis hazard potential of chemicals and products. These recommendations have now been accepted or endorsed by the 15 regulatory and research member agencies of ICCVAM. The nonradioisotopic methods are the LLNA: 5-bromo-2-deoxyuridine-ELISA (LLNA:BrdU-ELISA), and the LLNA: Daicel Adenosine Triphosphate (LLNA:DA) test methods. The expanded applications are for pesticide formulations, metals, aqueous solutions, and other products.

ICCVAM developed the recommendations following a comprehensive evaluation of available data supporting the scientific validity of the new LLNA versions and applications, which included independent scientific peer review by a panel of international experts. Regulatory agencies’ acceptance of these recommendations is expected to reduce the number of animals required to identify potential allergic contact dermatitis hazards and virtually eliminate any pain or discomfort for those animals used for such testing.

The ICCVAM evaluation of the LLNA: BrdU-ELISA and LLNA: DA test method protocols also formed the basis for two new test guidelines adopted by the Organisation for Economic Co-operation and Development (OECD) in July 2010. These test guidelines will allow use of these methods by the 33 member countries of OECD. The guidelines are expected to support global reduction and refinement of animal use for allergic contact dermatitis hazard testing. The nonradioisotopic versions of the LLNA also are safer for laboratory personnel and provide an environmental “green” advantage by avoiding the generation of radioactive laboratory waste.


NICEATM and ICCVAM agencies present at international meeting on alternative methods for vaccine potency testing

Dr. William Stokes, Director of NICEATM, and several scientists from U.S. regulatory agencies presented papers at the recent international meeting entitled “Potency Testing of Veterinary Vaccines: The Way From In Vivo to In Vitro.” The meeting was held on December 1-3, 2010 at the Paul Ehrlich Institute in Langen, Germany and was co-sponsored by the German government, the European Directorate for the Quality of Medicines, and the International Association of Biologicals.

Dr. Stokes spoke on “Recent Progress and Future Directions for the 3Rs in Vaccine Potency and Safety Testing: Conclusions and Recommendations from the 2010 U.S. International Workshop.” The presentation summarized the September 2010 NICEATM-ICCVAM workshop at which nearly 200 scientists from 13 countries gathered to discuss the state of the science of alternative methods development for both human and veterinary vaccine potency and safety testing.

In his presentation, Dr. Stokes summarized the priorities recommended for future research and development efforts needed to advance new methods and approaches for vaccine potency and safety testing. By applying new technology and scientific knowledge, improved methods that also reduce, refine, and replace animal methods are anticipated. Examples include in vitro protective antigen quantification assays, serological assays combined with in vitro antibody quantification, incorporation of earlier more humane endpoints while challenge testing is still necessary, and iden-

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tification and avoidance of experimental variables that can further reduce animal use. ICCVAM workshop recommendations to accelerate global progress in development and implementation of alternatives for human and veterinary vaccine testing included: improved accessibility of information on new initiatives, documents, and guidelines; increased international harmonization of validation principles for new vaccine safety and potency test methods; harmonized tests for protective antigens; accelerated product-specific validation of available alternative methods by vaccine manufacturers; and increased support for research and development into new alternative methods.

Other scientists affiliated with ICCVAM or ICCVAM member agencies who presented at the Langen meeting included:

- Dr. Jodie Kulpa-Eddy, Senior Staff Scientist at the U.S. Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) and Acting Chair of ICCVAM. Dr. Kulpa-Eddy’s presentation was entitled, “Successful Development and Validation of In Vitro Replacment Assays for Veterinary Vaccine Potency Tests – Lessons Learned: An Authority’s Point of View.”

- Dr. Donna Gatewood, Section Leader of the Virology Section of the USDA/APHIS Center for Veterinary Biologics. Dr. Gatewood presented on “Testing of Vaccines Against Rabies: Replacement of Challenge by In Vitro Tests – Considerations for Development of the Test.” She also served as a session chair.

- Dr. Juan Arciniega, Research Microbiologist at the Center for Biologics Evaluation and Research (CBER) of the U.S. Food and Drug Administration (FDA), and member of the ICCVAM Interagency Biologics Working Group. Dr. Arciniega’s presentation was entitled “Potential Application of the Consistency Approach for Vaccine Potency Testing.”

- Dr. Karen Brown, President of Pair O’docs Enterprises, on “Approach to In Vitro Potency Testing When Developing a New Vaccine; Is a Parallel In Vivo Potency Test Necessary? (Important Issue in R&D)” Dr. Brown is a member of ICCVAM’s advisory committee, the Scientific Advisory Committee on Alternative Toxicological Methods.

The proceedings of the ICCVAM workshop will be published as a dedicated issue of *Procedia in Vaccinology* in 2011. The ICCVAM Interagency Biologics Working Group currently is addressing implementation of the recommendations from the 2010 ICCVAM workshop. Presentation slides and more information about the ICCVAM workshop are available on the NICEATM-ICCVAM website at: http://iccvam.niehs.nih.gov/meetings/BiologicsWksp-2010/BiologicsWksp.htm

ICCVAM workshops on Best Practices for Regulatory Safety Testing

NICEATM and ICCVAM convened two workshops on “Best Practices for Regulatory Safety Testing” in January 2011. The workshops, “Assessing the Potential for Chemically Induced Eye Injuries” and “Assessing the Potential for Chemically Induced Allergic Contact Dermatitis” took place on January 19 and 20, 2011, respectively, and were co-sponsored by the Society of Toxicology and the Society for Risk Analysis. The workshops were open to the public with no admission charge.

These one-day workshops helped participants gain a practical understanding of the theory and application of available methods that can be used to evaluate the hazard potential of chemicals and products while minimizing animal use and avoiding pain and distress. Participants learned about the strengths and weaknesses of available alternative test methods, became familiar with the types of data they provide, and learned how to use these data for regulatory safety decisions.

The program included summaries of U.S. requirements for the consideration of available alternatives, current regulatory requirements for ocular and allergic contact dermatitis safety testing, and acceptance status of applicable alternative methods. Background information on the scientific basis of the test methods and discussion of the current validation status of the test methods was provided. Discussions of case studies in breakout groups provided practical instruction on application of the test methods, including selection of appropriate methods and data interpretation. Each day’s program concluded with presentations on new models currently being evaluated in ongoing validation studies. A poster session highlighted new methods and technologies applicable to ocular or allergic contact dermatitis safety assessment.

Topics discussed during these workshops were of particular interest to those involved in conducting safety tests for chemically induced eye injuries and/or chemically induced allergic contact dermatitis, those responsible for reviewing study protocols prior to testing, and regulators who will review data generated by the tests.

These and future workshops are free and open to the public with attendance limited only by the space available. More information on the workshop, a draft agenda, and presentations are available on the NICEATM-ICCVAM website at: http://iccvam.niehs.nih.gov/meetings/Implement-2011/ImplmntnWksp.htm

ICCVAM international peer review panel meeting to review in vitro test method for identification of potential endocrine disruptor activity

NICEATM and ICCVAM will convene a meeting of an international independent peer review panel on March 29-30,
2011. The Panel will review data from a NICETAM-sponsored validation study to assess the accuracy and reliability of an in vitro estrogen receptor (ER) transcriptional activation (TA) test method, the BG1Luc4E2 ER TA, for the qualitative detection of substances with in vitro ER agonist or antagonist activity. The Panel will also consider ICCVAM draft test method recommendations on the usefulness and limitations of this test method for identifying potential ER agonists or antagonists.

Endocrine disruptors (EDs) are substances that interfere with the normal function of hormones in the endocrine system. These interferences can lead to abnormal growth, development, or reproduction. A number of studies have been published indicating that animal populations exposed to high levels of these substances have an increased incidence of reproductive and developmental abnormalities. Exposure of humans to EDs also has been linked to adverse health outcomes.

NICETAM coordinated an international interlaboratory validation study of the BG1Luc4E2 ER TA test method following development and standardization of the assay (LUMI-CELL) by XDS, Inc as part of a Small Business Innovation Research grant from the National Institute of Environmental Health Sciences. The international validation study included participating laboratories located in Italy, the U.S., and Japan, and it was the first validation study sponsored jointly by NICETAM-ICCVAM, the European Centre for the Validation of Alternative Methods, and the Japanese Center for the Validation of Alternative Methods.

A panel of expert scientists from seven countries will review a draft background review document (BRD) detailing the study results. The Panel also will consider the extent to which the BRD supports draft ICCVAM test method recommendations on the usefulness and limitations of the BG1Luc4E2 ER TA test method, a recommended protocol, future studies to further characterize the test method, and performance standards. The draft documents to be reviewed by the panel will be made available on the NICETAM-ICCVAM website for public review and comment at least 45 days prior to the meeting. Visit the NICETAM-ICCVAM website at http://iccvam.niehs.nih.gov/methods/endocrine/end_eval.htm.

The Panel will meet on March 29-30, 2011 at the Natcher Conference Center on the main campus of the National Institutes of Health, Bethesda, Maryland, USA. The meeting of the peer review panel is open to the public with no registration charge. More information on the Panel meeting, a draft agenda, and a link to an online registration form will be available in February on the NICETAM-ICCVAM website at: http://iccvam.niehs.nih.gov/methods/endocrine/end_eval.htm.

NICEATM-ICCVAM requests nominations and submissions of test methods with potential regulatory applications

NICEATM and ICCVAM welcome nominations and submissions from the public for new or revised alternative safety testing methods with the potential to improve the accuracy of safety assessments and the potential to reduce, refine, or replace the use of animals. Test methods that incorporate advances in science and technology are especially encouraged.

– Nominations can be submitted for proposed test method validation studies, specific test method or validation issues, or requests for test method evaluations. Such nominations typically are addressed with international validation studies, workshops, conferences, or test method independent scientific peer review meetings.

– When validation studies for a test method have been completed that adequately characterize its usefulness and limitations for a specific proposed regulatory requirement or application, a submission can be sent to ICCVAM for review and technical evaluation of the test method. ICCVAM then develops a test method evaluation report and formal recommendations that are forwarded to U.S. Federal agencies for acceptance consideration.

Organizations or individuals that wish to propose nominations or submissions of promising test methods are encouraged to contact NICEATM for information and guidance on preparing proposals. Submission and nomination guidelines also are available on the NICETAM-ICCVAM website at http://iccvam.niehs.nih.gov/SuppDocs/submission.htm

For More Information

Questions about NICEATM and ICCVAM activities are welcomed and can be directed to Dr. William S. Stokes, Director, NICEATM, at niceatm@niehs.nih.gov; phone: +1 919 541 2384; fax: +1 919 541 0947. Copies of documents mentioned in this update can also be obtained by contacting NICEATM.

Information on the availability of NICEATM and ICCVAM draft documents, requests for nominations of experts to participate at workshops and on peer review panels, and specific information about NICEATM-ICCVAM meetings are communicated via the ICCVAM-all e-mail list and in notices posted in the U.S. Federal Register.

Subscribers to the ICCVAM-all e-mail list are notified directly of NICEATM-ICCVAM activities. Subscribers receive e-mail notification of NICEATM-ICCVAM Federal Register notices, availability of NICEATM-ICCVAM reports, notices of upcoming meetings, requests for public comments or data, and other events of interest to our stakeholders. If you would like to subscribe to the ICCVAM-all list, or for more information, please visit the NICEATM-ICCVAM website at http://iccvam.niehs.nih.gov/contact/ni_list.htm
IIVS update

Skin sensitization: Moving towards a predictive in vitro approach

Determination of skin sensitization potential is a critical toxicological endpoint in the development and evaluation of both the ingredients used in consumer and industrial products and the final products themselves. With the European Union regulatory deadline (7th Amendment to the Cosmetics Directive) to ban animal testing of cosmetic ingredients for skin sensitization quickly approaching and many companies proactively choosing to eliminate animal and human clinical testing due to ethical considerations, alternative methods are urgently needed to replace the existing animal tests. The development of many promising in vitro methods to evaluate skin sensitization is encouraging, and these efforts are moving forward steadily with contributions from the fragrance, cosmetic, and personal care industries, as well as regulatory agencies, contract research laboratories, and animal welfare groups.

The European Centre for the Validation of Alternative Methods (ECVAM) has initiated formal prevalidation of the human cell line activation test (h-CLAT), the myeloid U937 skin sensitization test (MUSST), and the direct peptide reactivity assay (DPRA). At the In Vitro Alternatives 2010 Forum, Dr. David Basketter reported that each of these assays has entered the practical phase but full results are not expected until next year. The primary goal of the prevalidation trial is to assess the transferability and reproducibility (inter- and intralaboratory) of the test methods when challenged with a set of coded chemicals, with a secondary goal of performing a preliminary assessment of the ability of the test methods to discriminate sensitizing chemicals from non-sensitizing chemicals and categorize the skin sensitizing chemicals into GHS sub-categories 1A and 1B.

Additional methodologies, such as the KeratinoSens assay, a novel test method developed by Givaudan, are undergoing ring trials in preparation for subsequent ECVAM review. Results of the KeratinoSens ring trial were presented at the poster session of the 2010 Forum. Participating laboratories, including Givaudan, BASF, Procter & Gamble, Beiersdorf, and the Institute for In Vitro Sciences, evaluated the KeratinoSens assay, a cell-based reporter gene assay that can be used to screen substances with a full dose-response assessment with 28 coded chemicals. The results of the ring trial indicate that the KeratinoSens assay is easily transferable between laboratories, and that the predictive capacity is similar between laboratories. In addition, the quantitative dose-response data were very similar in the different laboratories. The full results of this KeratinoSens ring trial are being submitted to ECVAM for prevalidation/validation. For a copy of the poster of the ring trial presented at the Alternatives Forum, please visit www.iivs.org under “What’s New” or contact IIVS Study Director, Dr. Kimberly Norman, at knorman@iivs.org.

IIVS is now on Twitter, LinkedIn, and Facebook

Follow the IIVS feeds on Twitter, LinkedIn, and Facebook for the latest news about the Institute and the field of in vitro testing. By following IIVS, you will receive news and event updates as they happen. Social media provide a wonderful opportunity for IIVS to provide information to and interact with a wide variety of stakeholders. It also allows our followers to interact with IIVS and other stakeholders by writing replies, “liking” our Facebook posts, or directly sending specific questions and comments. The websites below link to our pages on Twitter, Facebook, and LinkedIn. Please visit and follow us to help create a vibrant, informative discussion about IIVS and in vitro testing.

http://twitter.com/#!/the_iivs
http://www.facebook.com/#!/pages/The-Institute-for-In-Vitro-Sciences-Inc/153611251343473
OECD Guidance Document for In Vitro Skin Irritation/Corrosion

Following approval of OECD Test Guideline 439 (In Vitro Skin Irritation: Reconstructed Human Epidermis Test Method) earlier this year, the Working Group of National Coordinators (WNT) agreed to develop a Guidance Document on Skin Irritation and Corrosion. The first step of this process was to convene an Experts Meeting at the German Federal Institute for Risk Assessment (BfR) in Berlin, Germany. Hans Raabe, Vice President of IIVS, attended the Expert Meeting, which reviewed the applicability of different tools to various testing strategies and discussed a proposed integrated testing strategy to utilize in vitro and in silico methods. IIVS will continue to participate with the OECD to refine and finalize the Guidance Document.

IIVS joins IVTIP

The in Vitro Testing Industrial Platform (IVTIP) is an interactive scientific forum of companies with a genuine and active interest in in vitro testing for regulatory, safety, and efficacy testing. IVTIP actively contributes to promoting the dissemination of progress, knowledge, and transfer of state-of-the-art technologies related to the 3Rs. The platform offers its membership an informal atmosphere that fosters one-on-one contact that promotes networking opportunities for Small and Medium Enterprises (SME), contract research organizations, and larger industrial companies. The platform holds one closed membership meeting per year and one open meeting, which focuses on discussions of current regulatory and testing themes, which are subsequently are published as white papers. The publicly available IVTIP website also offers its members exclusive access to numerous OECD, EU, and other documents related to the 3Rs through a secure portal. IIVS looks forward to participating with IVTIP member companies and furthering the goals of the platform. To learn about IVTIP activities and membership opportunities, please visit www.ivtip.org.

Erin Hill, IIVS