



Corners

CAATfeed

Save the Date: Pan-American Conference for Alternative Methods
April 12-14, 2016
Baltimore, MD

This conference will bring together experts and stakeholders from across the Americas, with a focus on the Six Rs: Replacement, Reduction, Refinement, Read-across, Relevance, and Roadmaps. Although still in the early stages of development, this event promises to fill up quickly, as it will be limited to 300 participants on a first-come, first-served basis. Registration will open soon, and full details may be found at: <http://caat.jhsph.edu/programs/workshops/PanAmerican/index.html>

Please note that there are no fees required to attend this conference. The organizers are currently working on offers for lodging, food, and social events, which will have to be borne by the participants.

Save the Date: CAAT-Europe and Cefic-LRI Workshop 2016: Good Read-across Practices: Making it Work for You!
February 26, 2016
Crowne Plaza Brussels Airport
Hosted by CAAT-Europe, Cefic-LRI, and EUToxRisk

This workshop will present and discuss the new Good Read-across Practice guidance and other current initiatives for the benefit of past and future REACH registrants. Key speakers will include Nick Ball (Dow), Mark Cronin (Liverpool John Moores University), and CAAT's

Thomas Hartung. Topics will cover the 2016 Good Read-across practice guidance, Ambit tool, Seurat-1 case studies, EUToxRisk, and the ECHA Read-across Assessment Framework (RAAF).

Thomas Hartung will present the keynote talk on good read-across practices. Dr Norbert Fedtke from ECHA has joined the roster of speakers for the event.

Registration is free and spaces are limited. Information and registration details may be found at: <http://bit.ly/1NVNs3g>

Save the Date: Symposium on Social Housing of Laboratory Animals
March 17-18, 2016

UC Davis School of Veterinary Medicine, Davis, CA
Co-hosted by USDA, OLAW, UC Davis School of Veterinary Medicine, Division of Veterinary Resources NIH, and CAAT.

Attendee registration closes February 29, 2016.

Details and Registration: http://caat.jhsph.edu/programs/workshops/social_housing.html

CAAT's Lena Smirnova Wins 2015 Lush Young Researcher Prize

Lena Smirnova, Research Associate at CAAT, won the £10,000 Lush Young Researcher Prize for her research on 3D organotypical human *in vitro* brain model development in combination with multi-omics technologies for (developmental) neurotoxicity testing.

The Lush Prize is a major initiative aiming to bring forward the day when safety testing takes place without the use of animals. It focuses pressure on toxicity testing for consumer products and ingredients, in a way which complements the many projects already addressing the use of animals in medical testing.

Two CAAT Researchers Receive 2016 Society of Toxicology (SOT) Awards

David Pamies won the SOT Colgate-Palmolive Grant for Alternative Research award for his project "A 3D *in vitro* BBB-microphysiological system to study cerebrovascular perturbation." The SOT Colgate-Palmolive Grants for Alternative Research are awarded to scientists at any career level to support efforts that promote, develop, refine, or validate scientifically acceptable animal alternative methods to facilitate the safety assessment of new chemicals and formulations. The maximum grant amount is \$40,000, and awardees are allowed to re-apply for funding in subsequent years.

Thomas Luechtefeld won the Syngenta Fellowship Award in Human Health Applications of New Technologies for his project on "Multi-endpoint toxicological models with integrated data." The SOT Syngenta Fellowship Award in Human Health Applications of New Technologies provides research funding to a third-year (or later) graduate student or postdoctoral trainee. The award supports mode-of-action research aimed at characterizing dose-dependent effects of xenobiotics on mammalian systems in such a way that



the causal sequence of key events underlying toxicity is made clearer. The award also includes support to attend the SOT Annual Meeting and ToxExpo, where the recipient will be recognized for the award, and to travel to a Syngenta facility to present the research results.

CAAT-Europe and IVTIP Host “Meet Your Biotech SMEs” at the European Parliament

This half-day event in October, co-organized by CAAT-Europe and IVTIP, was designed to help SMEs become more familiar with the EU instruments and to facilitate interactions with Members of the European Parliament (MEPs) from their respective countries. It was also an opportunity for MEPs to get concrete feedback on EU legislation's impact on the SME's businesses, whether it is the result of the Horizon2020 program, REACH, cosmetics, pharmaceuticals, etc. The event was attended by nearly a dozen MEPs and representatives from eighteen SMEs.

CAAT Director Thomas Hartung at the World Science Forum in Budapest

Thomas Hartung spoke on “Fit for Purpose Global Health Policies” at the 2015 World Science Forum in Budapest on November 6, 2015. The theme for the forum was “The Enabling Power of Science,” reflecting how science opens new paths for the improvement of human life, business innovation and policy making. The World Science Forum brings together over 900 science leaders from 100 countries to call for a more responsible and ethical use of science to address pressing global challenges in environment and health.

Joint Information Day on Good Cell Culture Practice: Human (Stem) Cells and Organoids

Advances in cell culture techniques and the establishment of *in vitro* test systems in research need to be accompanied by

approaches to standardize processes and documentation. The “Bologna Statement on Good Cell Culture Practice” in 1999 prompted the ECVAM Task Force on Good Cell Culture Practice (GCCP) to produce two seminal guidance documents. Additional refinements were introduced in 2011. With the growing availability of cultured organoids, and the increasing generation and use of pluripotent stem cells and their differentiation progeny, there is a need for revision and update of the GCCP guidelines with these new technologies. This includes quality assurance of supplied biological materials as well as consideration of ethical and legal aspects. This symposium, held on December 3, 2015 in Konstanz, Germany, focused on GCCP in regard to human cells and tissues and the quality assurance of cells obtained by reprogramming.

Video Interview with Thomas Hartung on Chemicals and Mixtures

Watch an interview with CAAT Director Thomas Hartung discussing the importance of studying mixtures of substances for toxicity and the new technologies that will allow us to understand complex chemical interactions. The interview was recorded at the EFSA Expo 2015, held in Milan in October.

Video (streaming): <https://vimeo.com/agtel/review/147036207/63ba1f2105>

News and Upcoming Events from the Evidence-based Toxicology Collaboration (EBTC)

The Evidence-based Toxicology Collaboration (EBTC) is pleased to announce the formation of the Board of Trustees and election of Dr John “Jack” Fowle III as its first President and Dr Rob de Vries as Vice President. The new Board is succeeding the US and European steering committees and is expected to drive the strategy of the EBTC and to support efforts to raise awareness of its programs, events, and fundraising activities.

The formation of the EBTC Board of Trustees is the result of a year-long effort

of the Governance and Work Processes Work Group, which was formed to refine the mission and vision for the EBTC and to develop appropriate supporting governance. Full details may be found in the latest EBTC newsletter, which you can subscribe to at: <http://bit.ly/1Vwu3Lc>

On February 8-10, 2016 the EBTC is giving a talk at the ToxForum Annual Winter Meeting in Washington, DC on: “Translation of Diagnostic Test Accuracy Guidelines to Toxicology Test Method Performance: Zebrafish Embryo Test as a Predictor of Developmental Toxicity.”

On March 16, 2016, the Director of EBTC, Katya Tsaïoun will be co-chairing a workshop at the Society of Toxicology annual meeting in New Orleans, LA. The workshop, “Paradigm Change in Toxicology: What Will It Take to Bring Advances in the Science of Toxicology into Regulatory Use?” is aiming to define a path towards systematic assessment of the criteria for inclusion of new science into regulatory decisions for different industries. The workshop includes presentations from ECHA, US FDA, and chemical, cosmetic, and pharmaceutical industries. The workshop features a presentation on the importance of evidence-based methods in advancing regulatory science by Ellen Silbergeld and Alan Goldberg from the Johns Hopkins Bloomberg School of Public Health and Daniel Mandrioli from Ramazzini Institute.

Recent Publications

- Head, S. A., Shia, W., Zhao, L. et al. (2015). Antifungal drug itraconazole targets VDAC1 to modulate the AMPK/mTOR signaling axis in endothelial cells. *Proc Natl Acad Sci U S A*, Epub ahead of print 2015 Dec 10. <http://dx.doi.org/10.1073/pnas.1512867112>
- Smirnova, L., Harris, G., Delp, J. et al. (2015). A LUHMES 3D dopaminergic neuronal model for neurotoxicity testing allowing long-term exposure and cellular resilience analysis. *Arch Toxicol*, Epub ahead of print 2015 Dec 8. <http://dx.doi.org/10.1007/s00204-015-1637-z>



NTP
National Toxicology Program
U.S. Department of Health and Human Services



NICEATM Director Casey Recognized for Contributions to Animal Welfare

In a December 14 announcement, the Society of Toxicology (SOT) recognized NICEATM Director Warren Casey, PhD, with the 2016 Enhancement of Animal Welfare Award. This award is given for advancing toxicology through the development and application of methods that replace, refine, or reduce the need for experimental animals.

In recognizing the work done by Casey during his three years as NICEATM director, the award specifically noted his efforts to improve the quality of data from traditional animal studies used for the evaluation of new approaches, and his leadership on projects supporting replacement of animal tests with high throughput screening approaches and computational models.

Casey and the other SOT honorees will be presented with their awards in a ceremony during the 2016 SOT Annual Meeting in March in New Orleans.

Kleinstreuer Appointed NICEATM Deputy Director

Nicole Kleinstreuer, PhD, has been named deputy director of NICEATM. Kleinstreuer most recently worked for

ILS, the NICEATM support contractor, where she led the NICEATM computational toxicology group. In her new role as NICEATM deputy director she will continue to lead NICEATM computational toxicology projects, as well as interacting with NICEATM's U.S. and international partners and stakeholders.

Kleinstreuer's research focuses on mathematical and computational modeling of biological systems and those systems' susceptibility to perturbations that result in adverse health outcomes. She received her PhD in biomedical engineering from the University of Canterbury in Christchurch, New Zealand, and B.S. degrees in mathematics and biomedical engineering from the University of North Carolina at Chapel Hill. Prior to joining ILS, she completed postdoctoral training at the U.S. Environmental Protection Agency (EPA) National Center for Computational Toxicology.

NICEATM and ICCVAM to Hold Forum at SOT

Casey and ICCVAM Co-chair Anna Lowit, PhD (EPA), will lead a discussion forum during the 2016 SOT Annual Meeting. Casey and Lowit will begin the forum with summaries of recent ICCVAM and NICEATM activities, focusing on efforts to reduce animal use for acute

systemic toxicity and the EPA "six-pack" tests, efforts towards international harmonization of non-animal test methods, and best practices for *in vitro* to *in vivo* extrapolation. There will then be an open discussion focusing on challenges and opportunities to replace current regulatory requirements using animals. Participants are encouraged to bring forward specific examples of challenges to the implementation of alternatives within their organizations.

The forum will be held Monday, March 14, from 5:00-6:00 p.m. in the Belle Chasse room of the Hilton New Orleans Riverside in New Orleans. The forum is being co-sponsored by the Physicians Committee for Responsible Medicine, the PETA International Science Consortium, and the Human Toxicology Project Consortium.

A full list of NICEATM and ICCVAM activities at the 2016 SOT Annual Meeting is available at <http://ntp.niehs.nih.gov/go/niceatm-sot16>.

NICEATM Activities at FutureTox III Meeting

Scientists from NICEATM and other National Toxicology Program (NTP) offices joined about 300 other researchers at a Nov. 19-20 meeting in Arlington, Virginia, to assess how high throughput



laboratory methods and big-data analysis techniques could be applied to chemical safety testing. FutureTox III: Bridges for Translation focused on the theme “Transforming 21st Century Science Into Risk Assessment and Regulatory Decision-making.” The meeting was the third in a series organized by SOT to bring together stakeholders from diverse sectors to consider how new technologies can be applied to protect human health and the environment.

NTP scientists co-authored 15 of the over 80 posters presented at the meeting’s poster session. Of these, five focused on NICEATM projects to develop alternative methods for identifying potential endocrine disruptors and skin sensitizers. Other posters presented by members of the NTP Biomolecular Screening Branch and NTP Toxicology Branch described how high throughput assays and computational approaches can be used for a variety of applications, such as prioritization for future testing or identification of substances likely to cause DNA damage or birth defects.

Speakers and moderators at the meeting will co-author a report for publication in 2016. Information about the meeting can be found on the SOT website at <https://www.toxicology.org/events/shm/cct/futureToxIII.asp>. NICEATM posters presented at the meeting are available at <http://ntp.niehs.nih.gov/go/765658>.

ICCVAM Presents Webinar on QSAR and Read-across

ICCVAM presents its second Communities of Practice webinar on January 26. These annual webinars provide opportunities for detailed consideration of a current topic relevant to alternative test method development. The January webinar, Fundamentals of Using Quantitative Structure-Activity Relationship Models and Read-across Techniques in Predictive Toxicology, will feature presentations by Alex Tropsha, PhD, University of North Carolina at Chapel Hill, and Louis (Gino) Scarano, PhD, of the EPA Office of Pollution Prevention and Tox-

ics. Slides from the January webinar will be available at <http://ntp.niehs.nih.gov/go/commprac-2016>.

Workshop on IVIVE

NICEATM and EPA are co-organizing a workshop on In Vitro to In Vivo Extrapolation for High Throughput Prioritization and Decision Making, to be held February 17-18, 2016, at EPA in Research Triangle Park, North Carolina. The workshop aims to address the capabilities and the limitations of *in vitro* to *in vivo* extrapolation (IVIVE) within the context of risk decision making. Workshop participants will (1) review the state of the science to form recommendations on the best practices for using IVIVE in chemical screening and risk decision making, (2) identify areas that require additional data and/or research, and (3) highlight examples of how best to apply IVIVE in a tiered risk decision-making strategy.

The workshop was preceded by four webinars that were presented between October 2015 and January 2016. Slides from the webinars and more information on the workshop are available on the NICEATM website at <http://ntp.niehs.nih.gov/go/ivive-wksp-2016>.

USDA Issues Guidance for Reducing Animal Use for Vaccine Testing

The U.S. Department of Agriculture (USDA) Center for Veterinary Biologics (CVB) recently issued CVB Notice 15-13, Option to Remove Back-titration Hamsters from In Vivo Potency Tests for *Leptospira* Serogroups Canicola and Icterohaemorrhagiae. The notice describes an exemption from the titration requirement in vaccination-challenge potency assays for *Leptospira* Serogroups Canicola and Icterohaemorrhagiae. Removal of the back-titration hamsters could reduce animal use by 50% for potency testing on these two fractions. The policy took effect October 8. CVB Notice 15-13 is available on the USDA website at <http://go.usa.gov/3Srsh>.

National Academy of Sciences to Examine Low-dose Toxicity

A new committee of the National Academy of Sciences will examine whether current EPA toxicity testing practices adequately consider adverse human health effects of low doses of endocrine-active chemicals. Committee activities will include convening a scientific workshop to support systematic reviews of human and animal toxicology data for chemicals that affect the estrogen or androgen system. The committee will also consider how to use adverse outcome pathway or other mechanistic data, including high-throughput data and pharmacokinetic information, to elucidate under what circumstances human and animal data may be concordant or discordant.

The committee held meetings on October 13 and November 17; the next meeting will be on February 3 in Washington, D.C. Information on the committee, including links to information about upcoming meetings and a list of committee members, is available at <http://www8.nationalacademies.org/cp/projectview.aspx?key=49716>.

Recent NICEATM Publications

NICEATM scientists contributed to two recent publications describing integrated approaches to testing and assessment for identification of potential skin sensitizers: Strickland, J., Zang, Q., Kleinstreuer, N. et al. (in print). Integrated decision strategies for skin sensitization hazard. *J Appl Toxicol*.

Jaworska, J. S., Natsch, A., Ryan, C. et al. (2015). Bayesian integrated testing strategy (ITS) for skin sensitization potency assessment: a decision support system for quantitative weight of evidence and adaptive testing strategy. *Arch Toxicol* 89, 2355-2383. <http://dx.doi.org/10.1007/s00204-015-1634-2>



Institute for In Vitro Sciences

Advancing Science & Animal Welfare Together

IIVS Training in China

IIVS continues its work to help China reduce its reliance on animals for the registration and testing of cosmetics through its training of Chinese scientists. In October 2015, as part of its MOU with China's National Institute of Food and Drug Control (NIFDC), IIVS scientists conducted a one-week training at the Zhejiang IFDC. The hands-on training focused on methods for eye irritation and skin sensitization while lectures addressed integrated testing approaches, discussion of alternative endpoints for skin corrosion/irritation, ocular irritation, skin sensitization and product stewardship.

EPA Updates its Policy on an Important "Six-Pack" Endpoint Following Collaboration with IIVS and Industry

A multi-year project between IIVS, Industry and the EPA has resulted in an updated policy for the use of an alternative testing framework for classification of eye irritation potential of EPA pesticide

products. Pending final approval, the new testing framework is based on three non-animal methods (*in vitro/ex vivo*), which can be used in place of the rabbit test to determine the eye irritation potential of commonly used household cleaning products with anti-microbial claims.

The EPA is also finalizing the Process for Establishing & Implementing Alternative Approaches to Traditional In Vivo Acute Toxicity Studies, which was open to public comments early in 2015. Several validated *in vitro* assays are available through OECD test guidelines and could offer alternatives for moving even further away from the *in vivo* testing strategy of the "six-pack" pending analysis of their capacity to address US EPA hazard categories.

IIVS to Host April 2016 Workshop – In Vitro Exposure Systems and Dosimetry Assessment Tools for Inhaled Tobacco Products

In support of its Respiratory Toxicology Program, IIVS will host a three-day workshop April 4-6 that promotes the use

of *in vitro* models in testing and assessing the potential toxicity of pulmonary toxicants. Presenters from industry, government, academia, and non-profits will explore topics such as:

- Tobacco smoke and e-cigarette aerosols
- Air-liquid interface – *in vitro* exposure systems
- Dosimetry approaches for particles and vapors
- *In vitro* dosimetry determinations
- Exposure microenvironment/physiology of cells

This workshop is the third workshop of its kind with the first held in December 2014 followed by a second in June 2015. For registration information, a preliminary agenda and information about submitting a poster, go to <http://conta.cc/1NizKPW>.

For the latest IIVS news and information, visit our website at <http://www.iivs.org> or contact us via <http://http://subdomain.iivs.org/contact/>.