

March 8, 2016



ACC Science and Research Highlights

ACC Science & Research at the Society of Toxicology Meeting March 13-17 2016



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Society of Toxicology (SOT) Annual Meeting March 13-17

Next week, close to 7000 scientists from more than 50 countries will participate in the annual meeting of the Society of Toxicology (SOT) in New Orleans. The SOT is the largest professional society of toxicologists in the world. For ACC, the annual SOT meeting, through both scientific sessions and poster presentations, provides a unique opportunity for scientists to communicate their latest research results and to interact with others engaged in related areas of research, testing and assessments. The SOT meeting also provides a great opportunity for networking with leaders in the field and for catalyzing collaborations within and across sectors.

ACC's LRI Research Featured At The Upcoming 2016 SOT Meeting: Presentations by ScitoVation Scientists (Page3)

[ACC's LRI 2015-2019 Research Strategy](#) reflects ACC members' continuing commitment to advance scientific understanding of the potential impacts of chemicals on human health and the environment. The major projects under the ACC LRI program are oriented toward: 1) Further development and use of predictive exposure models; 2) Refinement of tools and approaches that can extrapolate results from in vitro high throughput assays to real-world human exposures; 3) Development of fit-for-purpose assays that are envisioned to provide the means to conduct targeted cellular-based safety assessments. Nineteen presentations by the [ScitoVation](#) scientists leading LRI research investigations are slated for the SOT meeting; these are summarized on page 3. These include presentations in continuing education courses, platform workshop sessions and posters. Selection of these presentations by SOT reflect the importance and credibility of LRI research, the prominence of LRI researchers, and demonstrates LRI's commitment to scientific excellence and public dissemination of research results.

SOT 2016 Merit Award Will Be Presented To Dr. Mel Andersen (Distinguished Research Fellow, ScitoVation LLC)

We congratulate Dr. Andersen on this prestigious and well-deserved [award](#) in recognition of his distinguished contributions to toxicology over the course of his entire career. It's widely recognized that his pioneering research on physiologically-based pharmacokinetic (PBPK) modeling has been transformative in toxicology and risk assessment—it paved the way for more scientifically rigorous and accurate assessments of risks to human health from low, environmentally relevant exposures. After serving on the NAS committee that authored the seminal report "Toxicity Testing in the 21st Century: A Vision and A Strategy," Dr. Andersen has been instrumental in designing, conducting and catalyzing research to experimentally investigate pathway-based safety evaluations. Indeed, much of the progress that has been made over the last 10 years in actualizing the vision articulated in the NAS report is a reflection of Dr. Andersen's dedication, enthusiasm and commitment to improving toxicity testing and risk assessment approaches. In addition, as a principal investigator and scientific team leader, Dr. Andersen's scientific excellence and leadership have been critical driving forces over many years in implementing our ACC LRI program. Dr. Andersen's Merit Award lecture will be at noon on March 14th.

ACC Science and Research Highlights is a publication for ACC members and staff to communicate information on scientific research projects conducted or sponsored by ACC departments
by Richard A. Becker Ph.D., DABT, ACC's Science and Research Division, Regulatory & Technical Affairs Department

ACC's Regulatory & Technical Affairs Department: SOT Presentations to Focus on Risk-Based Approaches Using 21st Century Methods (Page 4). Within ACC's Regulatory and Technical Affairs Department, one area of applied research has focused on integrating exposure information with advanced bioactivity screening methods (such as high throughput ToxCast assays) to enable risk-based prioritization and screening. ACC's work on matching up exposure to ToxCast estrogen-receptor bioactivity results for prioritization for endocrine screening and testing will be presented in a session on using margin of exposure as a risk metric. In addition, a poster developed in collaboration with EPA scientists, will highlight a proposed risk-based prioritization method for substances lacking robust toxicity and exposure data by using the Threshold of Toxicological Concern (in lieu of chemical specific health guidance values (e.g., RfDs)) with EPA's high throughput exposure modeling. A poster will also be presented (led by scientists from ExxonMobil Biomedical Sciences) analyzing the ability of ToxCast assays to reflect the in vivo biology (specific effects vs. nonspecific effects) of chemicals.

ACC's Regulatory & Technical Affairs Department: SOT Presentations to Focus on Quantifying Uncertainty and Improving Systematic Review Approaches in Risk Assessments (Page 4). ACC has been a leader over many years in working towards improving the science and methods used in risk assessments. Accordingly, as part of an SOT workshop co-chaired by an ACC Reg Tech scientist, an ACC-supported researcher will present a talk on application of Bayesian methods for uncertainty factors in risk assessment. This talk reflects ACC's work to actualize a recommendation made by the NAS in a recent review of EPA's IRIS assessment methodologies. Furthermore, improving the approach to identifying, reviewing and integrating studies for comprehensive chemical risk assessments is also a core element of [ACC's Risk Principles](#). As improvements proceed, it's become apparent that designing the protocol that specifies the methods and procedures that will be followed to gather, evaluate and integrate relevant and reliable scientific evidence is a critical activity. Working with a team of scientists supported in part by ACC's ARASP, an ACC Reg Tech scientist collaborated in developing a poster which highlights and discusses the challenges in developing a systematic review protocol.

ACC's Chemical Products & Technology Division (CPTD): SOT Presentations to Focus on Understanding and Incorporating Mode of Action (MOA) in Chemical Risk Assessments (Page 4).

- **ACC's Alkanolamines Panel** has sponsored a poster that organizes and presents the evidence that diethanolamine(DEA)-induced liver tumors in mice are caused by choline deficiency—a dose-dependent threshold mode of action. The poster presents an analysis of the weight of evidence for DEA-induced liver tumors, and makes the case that this response in mice is of little relevance to humans. Such an understanding of the MOA can be applied in support of a nonlinear, threshold approach for low-dose extrapolation to evaluate potential risks to humans.
- **ACC's FluoroCouncil** will present a poster summarizing results of the weight of evidence analysis of potential effects of perfluorohexanoic Acid (PFHxA) on endocrine systems. PFHxA is a potential degradation product of 6:2 fluorotelomer compounds used to manufacture fluorotelomer-based products. This poster will presents results of a detailed analysis showing PFHxA is not a selective reproductive or thyroid toxicant, is not carcinogenic and does not produce adverse effects on, or via, endocrine systems and therefore, cannot be considered an endocrine disruptor according to the 2002 definition of the World Health Organization.
- One of the activities **ACC's Center for Advancing Risk Assessment Science and Policy (ARASP)** has focused on is catalyzing improvements in the risk assessment methods used for environmental substances that are also naturally present in the body. Consequently, ARASP proposed a session, which was accepted and will be held at the SOT meeting, on improving the scientific approaches for conducting risk assessments of endogenously produced chemicals. This workshop session, to be co-chaired by a CPTD scientist, will feature speakers from research institutions, academia and state government. A key focus will be on how to integrate exogenous exposures in a risk assessment with knowledge of the biological processes that have evolved to safely handle typical levels of internal endogenous exposures.
- **ACC's North American Flame Retardant Alliance** sponsored an analysis to evaluate the relevance to humans of adenocarcinomas of the uterus found in some TBBPA high dose animal studies; a workshop presentation will discuss the likely MOA. Researchers will report that the MOA, although of some relevance, is unlikely to occur in humans based on 1) differences in the kinetic and dynamic factors between lab animals and humans; and 2) doses of TBBPA in the animal studies were some 1,000,000 times greater than estimated human exposures. The Alliance will also present a poster on the kinetics of plasma concentrations of TBBPA after repeat dosing; results indicate the doses associated with uterine tumors cause a decrease in TBBPA sulfation, thus supporting the likely MOA (increased estradiol bioavailability via inhibition of estradiol sulfation).

Best Paper Published in 2015 in the Category of Advancing the Science of Risk Assessment (Page 4): A committee of SOT's Risk Assessment Specialty Section selected the publication "Increasing Scientific Confidence in Adverse Outcome Pathways: Application of Tailored Bradford-Hill Considerations for Evaluating Weight of Evidence" ([Reg Tox Pharm 72:514-537](#); lead author ACC's R. A. Becker, for this award. In this publication, tailored Bradford Hill causality considerations were applied to AOP case examples, demonstrating and documenting how to assign levels of confidence to Key Events and promoting use of causality evaluation in AOPs. Coauthors that collaborated on the analyses and paper included scientists from ACC, EPA, Health & Environment Canada, EC's Joint Research Council, University of Ottawa, University of Bern, US Army Corps of Engineers, BioDetection Systems BV and Japan's NIES.

Type of presentation	Title	Day	Time	Room	Abstract #	Authors
ScitoVation (presentations at 2016 SOT of ACC LRI research projects)						
Continuing Education	Strategies to Quantitate Chemical-Specific Toxicokinetic Variability Due to Genetics and Other Factors	Sun, Mar 13	1:15 - 5:00	CC Second Floor	PM10	B. Wetmore
Workshop	Overview: Moving Beyond Prioritization towards True In Vitro-Based Safety Assessment	Mon, Mar 14	2:00 - 2:10	208	1711	R. A. Clewell
Workshop	Addressing Metabolism and Kinetics In Vitro—Not Just for Dose Extrapolation	Mon, Mar 14	2:10 - 2:45	208	1712	M. Yoon
Workshop	Development of Fit-for-Purpose Assays: Adverse Outcome Pathway and Toxicity Pathway Approaches to Defining In Vitro Assays Sufficient for Safety Assessment	Mon, Mar 14	4:01 - 4:30	Great Hall A	1730	R. A. Clewell
Poster	Developing an In Vitro Assay to Measure Key Signaling Events in Estrogen-Initiated Pathways and Guide Risk Assessment	Tues, Mar 15	9:30a - 12:45p	CC Exhibit Hall	1867	M. M. Miller, D. L. Doheny, P. Balbuena, S. M. Ross, C. Deisenroth, R. A. Clewell.
Poster	Isolation, Culture and Characterization of Human Uterine Cells for Comparison to Current Estrogen Screening Assays	Tues, Mar 15	9:30a - 12:45p	CC Exhibit Hall	1871	P. Balbuena, S. M. Ross, S. Rowley, M. Miller, B. Foley, R. A. Clewell.
Poster	Validation of a High Content Imaging Assay for Steatosis and Phospholipidosis in a Micropatterned Human Hepatocyte Co-Culture Model	Tues, Mar 15	9:30a - 12:45p	CC Exhibit Hall	2005	C. Deisenroth, K. Wolf, J. Trask, E. LeCluyse, R. Clewell, M. Andersen.
Poster	The Influence of System-Specific Factors on In Vitro Kinetics in 3D Flow-Based Liver Bioreactors	Tues, Mar 15	9:30a - 12:45p	CC Exhibit Hall	2014	M. Yoon, J. M. Pedersen, E. L. LeCluyse, J. M. Macdonald, M. E. Andersen, H. J. Clewell
Poster	Application of an In Vitro High Content Imaging Assay for Quantitative Assessment of Rat, Mouse, and Human Primary Hepatocyte Proliferation	Tues, Mar 15	9:30a - 12:45p	CC Exhibit Hall	2018	V. Soldatow, R. Pepper, D. Cowie, K. Lichti-Kaiser, R. Clewell, M. Andersen, E. LeCluyse, C. Deisenroth
Poster	Application of Gene Set Enrichment Analysis for Identification of Critical Gene Expression Networks for Application in Human Health Risk Assessment	Tues, Mar 15	9:30a - 12:45p	CC Exhibit Hall	2164	J. Dean, B. Hawkins, M. Black, R. Thomas, S. Wesselkamper
Poster	Development of an In Vitro Pharmacokinetic Model to Describe Nicotine Kinetics in a Multi-organ Culture System	Tues, Mar 15	1:15 - 4:30	CC Exhibit Hall	2188	Y. Zhao, M. Yoon, M. D. Gaca, G. Phillips, H. Clewell, M. E. Andersen, J. M. McKim.
Poster	In Vitro to In Vivo Extrapolation for Estrogenic Activity of Environmental Chemicals	Tues, Mar 15	1:15 - 4:30	CC Exhibit Hall	2224	X. Chang, N. Kleinstreuer, P. Ceger, N. Choksi, J. Hsieh, B. A. Wetmore, S. Ferguson, M. DeVito, D. Allen, W. Casey
Poster	Computational Models to Estimate In Vivo Activity Concentrations from Tox21 HTS Data	Weds, Mar 16	9:30a - 12:45p	CC Exhibit Hall	2604	N. S. Sipes, J. F. Wambaugh, R. Pearce, B. A. Wetmore, M. J. DeVito, S. S. Ferguson
Poster	Assessing Bioactivities and Exposure Profiles of Fruit and Vegetable Juices	Weds, Mar 16	1:15 - 4:30	CC Exhibit Hall	3017	B. A. Wetmore, M. J. DeVito, M. Xia, B. Parks, R. Huang, K. Houck, R. R. Tice, R. Judson, R. S. Thomas, M. E. Andersen
Poster	Dose Response Studies Supporting In Vitro-Based Safety Assessments for Chemicals Inducing Oxidative Stress	Weds, Mar 16	1:15 - 4:30	CC Exhibit Hall	3071	B. Huang, S. M. Ross, S. Rowley, A. Efremenko, S. Pendse, L. Pluta, P. Xue, J. Pi, P. L. Carmichael, A. White, R. A. Clewell
Poster	High Throughput Determination of Critical Human Dosing Parameters	Thurs, Mar 17	9:30a - 12:45p	CC Exhibit Hall	3437	C. I. Nicolas, B. L. Ingle, M. Bacolod, J. Gilbert, B. A. Wetmore, C. L. Ring, R. W. Setzer, R. Tornero-Velez, M. T. Martin, J. F. Wambaugh
Poster	Metabolite Profile Identification Using Alginate Supported 3D Culture of Primary Hepatocytes	Thurs, Mar 17	9:30a - 12:45p	CC Exhibit Hall	3464	J. M. Pedersen, J. Shim, E. L. LeCluyse, J. M. Macdonald, M. E. Andersen, H. J. Clewell, M. Yoon
Poster	Quantitative Bias Analysis for Epidemiological Associations of Perfluoroalkyl Substance Serum Concentrations and Early Onset of Menopause	Thurs, Mar 17	9:30a-12:45p	Great Hall A	3619	C. D. Ruark, G. Song, G., M. Yoon, M. A. Verner, M. E. Andersen, H. J. Clewell, III, M. P. Longnecker
Poster	Quantitative Bias Analysis of a Reported Association between Perfluorooctanoic Acid and Early Onset of Menopause	Weds, Mar 16	1:15 - 4:30	CC Exhibit Hall	2975	G. Ngueta, M. Yoon, H. Clewell, M. Andersen, M. Longnecker, M. Verner.
Awards Lecture	Forty-Five Years Modeling Dose-Response Relationships: An Unanticipated Career!	Mon, Mar 14	12:30 - 1:20	R08	AWL-01	M. E. Andersen

Type of presentation	Title	Day	Time	Room	Abstract #	Authors
ACC Science & Research at 2016 SOT						
Poster	Weight of Evidence (WoE) Assessment of the Potential Effects of PFHxA on Endocrine Systems	Tues, Mar 15	9:30-12:15	CC Exhibit Hall	1862	R. Jung ¹ , N. Wang ² , I. Gaou ² , W. Buxton ⁴ , S. Seiji ³ and A. Lynch ⁵ . 1Archroma, Reinach, Switzerland; 2Arkema, Paris, France; 3Asahi Glass Company, Ltd, Osaka, Japan; 4Chemours Company, Wilmington, DE and 5ACC FluoroCouncil, Washington, DC.
Poster	Challenges in Developing a Systematic Review Protocol for Environmental Contaminants	Tues, Mar 15	9:30-12:45	CC Exhibit Hall	2166	T. Greene ³ , A. Franzen ³ , L. Yost ² , N. Beck ¹ , R. Fensterheim ⁴ , and R. Gentry ³ . 1 American Chemistry Council, Washington, DC; 2 Environ Ramboll, Chicago, IL; 3 Environ Ramboll, Monroe, LA; and 4 RegNet Environmental Services, Washington, DC
Workshop	Presentation entitled "An Exposure: Activity Profiling Method for Interpreting High-Throughput Screening Data for Estrogenic Activity"	Tues, Mar 15	10:05	CC Great Hall B	1768	R. Becker. American Chemistry Council, Washington, DC.
Poster	Evaluating the Ability of High-Throughput Screening (HTS) Assays to Capture the Biological Activity of Industrial Chemicals	Tues, Mar 15	1:15-4:30	CC Exhibit Hall	2468	K. O. Goyak ² , R. Alyea ² , R. A. Becker ¹ , L. M. Plunkett ³ and J. B. Plunkett ³ . 1American Chemistry Council, Washington, DC; 2ExxonMobil Biomedical Sciences, Inc., Annanda
Poster	Evaluation of Chemically-Induced Choline Deficiency as the Mode of Action (MOA) for Diethanolamine-Induced Mouse Liver Tumors	Tues, Mar 15	1:15-4:30	CC Exhibit Hall	2478	B.J. Hughes ¹ , J. Reichard ² , L.T. Haber ² , J. E.Klaunig ³ , P.A. Fenner-Crisp ⁴ , and J. Busch ⁵ 1The Dow Chemical Company, 2TERA Center, University of Cincinnati, 3Indiana University, Bloomington, 4Independent Consultant, 5American Chemistry Council
Workshop	Read-Across: Building Scientific Confidence in the Development and Evaluation of ReadAcross for Regulatory Purposes Using Tox21 Approaches	Tues, Mar 15	2:00-4:45	CC Room 220	2524	Chaired by R. A. Becker (ACC) and G. Patlewicz (EPA ORD)
Poster	Integrating the Threshold of Toxicological Concern (TTC) with High Throughput Exposure Assessment for Risk-Based Screening of Several Thousand Commodity Chemicals	Wed, Mar 16	9:30-12:45	CC Exhibit Hall	2677	R. Becker ¹ , J. Wambaugh ⁴ , G. Patlewicz ⁴ , S. Felter ² and T. Simon ³ . 1American Chemistry Council, Washington, DC; 2Procter & Gamble Company, Mason, OH; 3Ted Simon LLC, Winston, GA and 4NCCT, US EPA, RTP
Award	Best Paper Published in 2015 in the Category of Advancing the Science of Risk Assessment - presented to lead author R. Becker by SOT Risk Assessment Specialty Section at RASS meeting	Wed, Mar 16	6:00-7:30 PM	Hilton Riverside Ballroom B		Becker RA, Ankley GT, Edwards SW, Kennedy SW, Linkov I, Meek B, Sachana M, Segner H, Van Der Burg B, Villeneuve DL, Watanabe H, Barton-Maclaren TS
Workshop	Beyond Benchmark Dose: Advancing Probabilistic and Bayesian Approaches in Hazard Characterization	Thurs, Mar 17	9:30-12:15	CC Room R02	3361a	Chaired by Nancy Beck (ACC) and Annie Jarabek (EPA ORD)
Workshop	Presentation entitled "Bayesian Methods for Uncertainty Factor (UF) Application: Proof-of-Concept and Pitfalls"	Thurs, Mar 17	10:00	CC Room R02	3362	T. W. Simon. Ted Simon LLC, Winston, GA
Poster	Tetrabromobisphenol A (TBBPA); Dose- And Time-dependent Changes in Plasma TBBPA and Its Conjugates Over 28 Days of Administration	Thurs, Mar 17	9:30-12:45	CC Exhibit Hall	3445	S. Borghoff ² , D. Wikoff ¹ , J. E. Rager ¹ and L. C. Haws ¹ . 1ToxStrategies, Austin, TX and 2ToxStrategies, Cary, NC.
Workshop	Bringing More Science into the Process of Risk Assessment for Endogenous Chemicals with Exogenous Exposures	Thurs, Mar 17	9:30-12:15	CC Room220	3367a	Chaired by William Farland (Colorado State) and A. Lynch (ACC)
Workshop	Presentation entitled "Human Relevance Assessment Of Tetrabromobisphenol-A (TBBPA) Induced Uterine Adenocarcinomas: Mode Of Action Dependent On High Dose Molecular Initiating Event (MIE)"	Thurs, Mar 17	10:30	CC Great Hall B	3407	D. Wikoff ¹ , S. Borghoff ² , J. E. Rager ¹ and L. C. Haws ¹ . 1ToxStrategies, Austin, TX and 2ToxStrategies, Cary, NC