Fall Newsletter 2016

Mission: To promote the reduction and humane use of animals in toxicology research by encouragement of the development and validation of effective in vitro and alternative methods or models

Welcome from the IVAM Presidents - Past, Present and Future

We're excited about the future of IVAM and especially the role our younger members will play in the future as leaders of SOT and in the development and application of alternative methods that are more informative and efficient than traditional animal toxicity testing approaches. To help launch that future there are exciting opportunities in the upcoming year that we hope all IVAM members will take advantage of.

For our younger members, we have planned a webinar entitled "Career opportunities related to *in vitro* and *in silico* toxicology". The webinar, which is co-sponsored with the GLSC, will provide students with insights into a typical workday of professional researchers (register here). This follows our May 2016 webinar recognizing IVAM's 2016 student and postdoc award winners (webinar recording can be found online).

We are proud of IVAM's accomplishments over the last year. We polled IVAM members for feedback about how SOT can provide maximum value and identified three major areas where IVAM could best help its members: networking, job leads and webinars. We put these poll results into action in the networking session that opened the annual business meeting and have identified future opportunities for networking, training and engagement.

To increase our membership and inform new SOT members about what IVAM has to offer, we wrote to each new 2015 SOT member individually to inform them about IVAM and to invite them to join our specialty section. To better serve our existing members, we have identified workshops, symposia and meetings relevant to IVAM's mission and notified IVAM members about them. To most effectively communicate with our members, we have initiated substantial modernization of the IVAM webpage and logo—stay tuned.

2016-2017 IVAM Officers

President:
Amy Clippinger
AmyJC@PISCLtd.org.uk

Vice President:
Barbara Wetmore
bwetmore723@gmail.com

Vice President-Elect:
Warren Casey
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Past President:
Jack Fowle

Secretary/Treasurer:
Jill Merrill

Councilors:
Kate Willett
Katie Paul Friedman

Student Rep:
Troy Hubbard

Vice Student Rep:
Georgina Harris

Post Doc Rep:
Susanne Ramm

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For information about IVAM see www.toxicology.org/groups/ss/IVSS

At SOT 2016, IVAM officers facilitated table discussions at the Colgate Palmolive In Vitro luncheon, reached out to IVAM past presidents to help identify potential candidates for IVAM leadership positions, endorsed Mel Andersen for 2016 SOT Merit Award, and noting that they were out of date, we updated the IVAM bylaws.

We explored common interests and potential mutually beneficial joint activities with our counterparts in China, and presented a webinar describing the role of Integrated Approaches to Testing and Assessment as well as Adverse Outcome Pathways (AOPs) as more efficient and informative ways to test for and evaluate potential toxicity.

We recently reviewed 31 excellent proposals for presentations at the 2017 SOT meeting—with IVAM tied for second for the most proposals submitted. Of the sessions submitted to IVAM, SOT selected 6 of the 18 symposia, 5 of the 9 workshops, and 3 of the 4 continuing education courses for inclusion in the SOT 2017 program.

It was a busy year and we expect more of the same for the year to come. We look forward to working with and serving you and we hope that you will join us in our efforts.

Sincerely,
Amy Clippinger, President
Barbara Wetmore, Vice President
Warren Casey, Vice President-Elect
Jack Fowle, Immediate Past President

Nominations for new Executive Committee Officers are now being accepted for 2016

Please send your nominations (for yourself or others) by October 5, 2016 to Kate Willett atkwillett@humanesociety.org we will request BioSketches of all nominees, which are due November 30, 2016.

See www.toxicology.org/groups/ss/IVSS/about.htm#officers

Student and Postdoctoral Awards

Every year the IVAM SS recognizes outstanding student and postdoctoral scientists for their work in the field of *In Vitro* Toxicology with ***In Vitro* and Alternative Methods Specialty Section Awards.**

- Winners receive awards of up to $500
- Awards presented at the IVAM luncheon at the SOT 56th Annual Meeting in Baltimore
- Deadline for the upcoming 2017 awards is **January 15, 2017**
- Please send application information to Warren Casey at Warren.Casey@nih.gov
- Additional details at www.toxicology.org/groups/ss/IVSS/awards.asp

MB Research supports annually the **MB Research Award for Distinction in Practical *In Vitro* and Alternative Toxicology Methods**.

- Winner receives $500
- Award is presented at the IVAM luncheon at the SOT 56th Annual Meeting in Baltimore
- Deadline for the upcoming 2016 award is **January 15, 2017**
- Please send application information to George DeGeorge at mbinfo@mbresearch.com
- Additional details at www.toxicology.org/groups/ss/IVSS/awards.asp

2016 Award Winners

Congratulations to the 2016 IVAM Specialty Section Award Winners!

1st Place Student — Shih-Yu Chang, University of Washington for "Microphysiological Systems (MPS) to Identify Organ-Organ Interactions in Toxicology: Hepatic Metabolism Enhances Nephrotoxicity of Aristolochic Acid"

2nd Place Student — Leah Norona, University of North Carolina for "Modeling Drug-Induced Hepatic Fibrosis *In Vitro* Using Three-Dimensional Liver Tissue Constructs"

3rd Place Student — Ashley Maiuri, Michigan State University for "A Promising, *In Vitro* Approach to Classify Drugs According to Their Potential to Cause Idiosyncratic, Drug-Induced Liver Injury"

1st Place Postdoctoral — Jenna Currier, US EPA for "Investigating key event-based points of departure for adverse oxidative events in human bronchial epithelial cells exposed to zinc: A systems biology approach"

2nd Place Postdoctoral — Michelle Angrish, US EPA for "Adverse Outcome Pathway (AOP) Network Development for Fatty Liver"

3rd Place Postdoctoral — Sreenivasa Ramaiahgari, US National Institute of Environmental Health Sciences for "Metabolically Competent HepaRG Spheroid Model for *In Vitro* Toxicology Studies"

MB Student Research Award Winner — Katherine Dunnick, West Virginia University for "Assessing DNA damage through direct measurement of double strand breaks"

Colgate-Palmolive Award for Student Research Training in Alternative Methods

The purpose of this award is to enhance graduate student research training using methods that reduce, replace, or refine the use of animals in toxicological research through the use of *in vitro* and *ex vivo* procedures, non-mammalian animal models, computer modeling, and structure-activity relationships. The proposal will include a budget of up to $3,750 to defray travel, per diem, training expenses, and research costs.

Details for how to compete for the Colgate-Palmolive Award for Student Research Training in Alternative Methods can be found at
www.toxicology.org/application/af/awards_details.aspx?id=4

Important Dates to Remember

EVENT	DEADLINE/DATE
Submit a Poster or Platform Session Abstract	Oct 7, 2016
SOT Awards and Sponsored Awards Applications	Oct 9, 2016
SOT Membership Renewal	Dec 15, 2016
MB Research Award Applications	Jan 15, 2017
IVAM SS Student Awards Applications	Jan 15, 2017
SOT Annual Meeting Early Bird Registration	Jan 13, 2017
SOT Annual Meeting Standard Registration	Feb 10, 2017
SOT Annual Meeting in Baltimore, MD	Mar 12 - 16, 2017
IVAM Lunch Reception & Business Meeting at SOT Annual Meeting	Mar 13, 2017

Message from the Student and Postdoctoral Representatives

Greetings IVAM Student and Postdoctoral members,

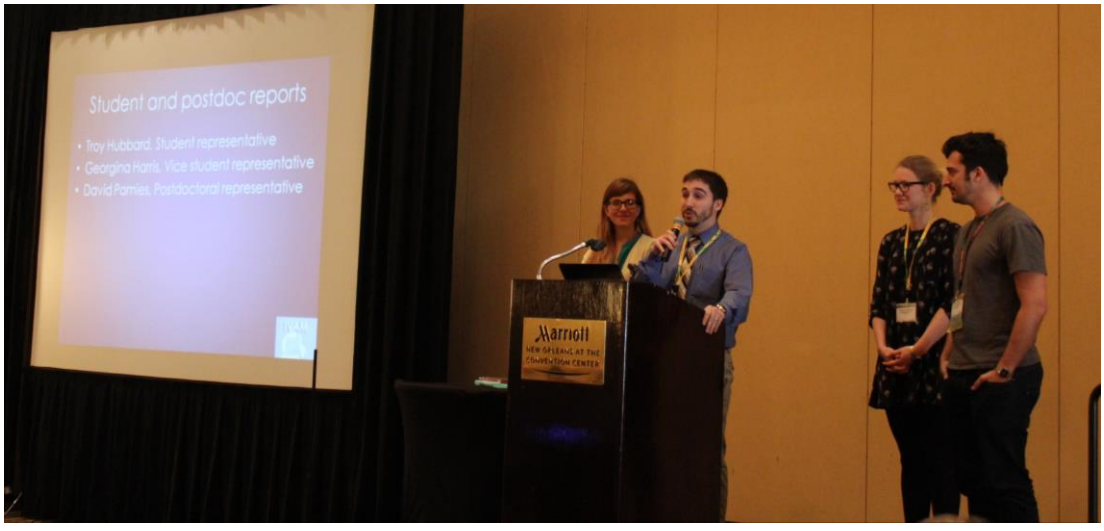
For the past 23 years, the IVAM Specialty Section has been actively promoting the widespread use of in vitro and alternative methods to facilitate reduction and replacement of animal testing in toxicology.

There has never been a more exciting time to work in the field of in vitro and alternative methods than right now. The ways cells are being cultured in the lab are changing fundamentally due to new developments, such as 3D cell systems, dynamic cultures in bioreactors, and the co-culturing of different cell types. Furthermore, organ-on-a-chip technologies aim to mimic the complex interplay between cells of different organs in order to render cell culture more reliable and predictive of in vivo systems. Even the long discussion about limited availability and reproducibility of primary human cells seems to have found an answer: induced pluripotent stem cells might soon be used to generate a sufficient supply of human cells for toxicity testing. Finally, the in vitro and alternative methods community was among the first to embrace not just high-throughput screening methods, but also computer-based in silico approaches. The integration of toxicological bench work and computational analysis are now used to make sense of the vast amounts of generated data and develop predictive models or Adverse Outcome Pathways which can explain how a chain of molecular effects could lead to a toxic response.

This excitement is reflected by a rise in student membership during the last years to

Calling All Students!

Students are essential to the maintenance and growth of the IVAM SS. Many student members of SOT – or their mentors! - do not realize that their SOT membership entitles them to a free specialty section membership. The Executive Committee encourages students to join IVAM and participate as an officer and/or submission of an abstract for the Student/Postdoc Awards. The students of today will be tomorrow's leaders of toxicology organizations and laboratories. We hope that students by participating in IVAM will form a lasting bond with our organization as has been the case for many of the leaders of IVAM.



account for 21% of IVAM's approximately 500 members. We welcome all students interested in joining or learning more about the IVAM specialty section. Contributions and participation by student and postdoctoral members are vital to the success of IVAM educational programs, networking events, and training workshops. Abstract submission for the upcoming SOT Annual meeting and ToxExpo in Baltimore, MD is open until Friday, Oct 7, 2016. The IVAM specialty section recognizes significant research contributions to the field of In vitro and alternative methods and provides a number of awards to graduate and postdoctoral researchers. Be sure to apply for these awards by the dates indicated below. We want to thank all student and postdoctoral members for their participation in our most recent poll. When asked what would improve the specialty section as a whole, you suggested increased opportunities for career education and networking. An upcoming seminar titled "Career opportunities related to in vitro and in silico toxicology", will be hosted by IVAM and the Graduate Student Leadership Council (GSLC) on Oct 11th at 1pm. If you want to know how to prepare for such a career from industry experts, register and listen in to learn more about career opportunities within the field of alternatives to animal testing that are available to graduate students and postdoctoral scholars. Please stop by the annual IVAM Luncheon at the upcoming SOT annual conference for wonderful networking opportunities and to learn more about the mission of IVAM SS.

We would also like to make you aware of Toxchange, this self-service portal for SOT has been extensively improved for easier navigation. Visit www.toxchange.toxicology.org to log in. This platform allows you to search for members, contact information, updates on articles, and specialty section/interest groups. Under member search click communities to visit regional chapters and student resources. We advise you try to join your regional chapter and special interest groups as it likely they provide further graduate funding opportunities.

If you have any questions about how to get involved with the IVAM specialty section, please contact us. We look forward to hearing from you!

2015 – 2016 Student Representatives at David Pamies and Troy Hubbard and Postdoc Representative Susanne Ramm at the 2016 IVAM luncheon.

Student Representatives,
Troy Hubbard (tdh176@psu.edu)
Georgina Harris (gharri27@jhu.edu)
Postdoctoral Representative
Susanne Ramm
(Susanne_Ramm@hms.harvard.edu)

OECD updates

Below are a few OECD updates. For more details on OECD projects, please check out the OECD Guidelines for the testing of chemicals:
www.oecd.org/chemicalsafety/testing/oecdguidelinesforthetestingofchemicals.htm

Test Guidelines

The OECD has published several new test guidelines—including the h-CLAT for skin sensitization testing (OECD TG 442E) and an *in vitro* human androgen receptor transcriptional activation assay (OECD TG 458)—which can be found here: www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788

Draft Test Guidelines

Draft TG on *In Vitro* Skin Sensitization: IL-8 Luc assay (deadline for public comments, 19 Sept)

Draft TG on *In Vitro* Skin Sensitization: U937 Skin Sensitization Test (U-SENS™) (deadline for public comment, 19 Sept)

See here for more:
www.oecd.org/env/ehs/testing/chemicalstestingdraftoecdguidelinesforthetestingofchemicals-sections1-5.htm

Guidance Documents

Guidance Document on Considerations for Waiving or Bridging of Mammalian Acute Toxicity Tests Series on Testing & Assessment No. 237 can be found here www.oecd.org/env/ehs/testing/mono%202016%2032.pdf

See here for more: www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Updated Version of the OECD QSAR Toolbox

In July 2016, the OECD released Version 3.4 of the QSAR Toolbox. It contains many new features, including inclusion of new databases (acute oral toxicity (ChemIDPlus), ZEBET database, and keratinocyte gene expression LuSens); one new profiler (DNA alerts for chromosomal aberration and micronucleus tests); and one new metabolic simulator (*in vivo* rat metabolism). It also contains updates of databases, profilers, and metabolic simulators, as well as other usability improvements. See www.oecd.org/env/ehs/risk-assessment/oecd-qsar-toolbox.htm

AOPs

The OECD also recently published a new series of documents on adverse outcome pathways (AOPs) for regulatory risk assessment. In addition to a handbook which supplements the guidance document for developing and assessing AOPs, four new AOPs were published and can be found here: www.oecd-ilibrary.org/environment/oecd-series-on-adverse-outcome-pathways_2415170x;jsessionid=8ud7lduqr22tl.x-oecd-live-03.

TSCA Brief

The Toxic Substances Control Act (TSCA) that instructs the Environmental Protection Agency (EPA) on dealing with industrial chemicals was originally passed in 1976. Over the past decade, desire to update this law has been expressed by several stakeholders. Finally after many years of negotiations and no small miracles of bipartisan agreement, on June 22 of this year, the Frank R. Lautenberg Chemical Safety for the 21st Century Act was signed into law by President Obama and came into force. This amendment to TSCA increases the authority of the Environmental Protection Agency to obtain information on both new and existing industrial chemicals and includes the following: a mandatory requirement for the EPA to evaluate existing chemicals with clear and enforceable deadlines; a new risk-based safety standard; increased public transparency for chemical information; and provides a consistent source of funding for EPA to carry out the responsibilities under the new law.

Of special importance to members of IVAM, in addition to requiring the use of the "best available science," the amendment also includes a section requiring both EPA (and any other person developing information under the Act) to reduce and replace vertebrate testing "to the extent practicable, scientifically justified, and consistent with the policies of this title." This section of the bill also requires EPA to "promote the development and timely incorporation" of non-vertebrate animal methods by developing a strategic plan to do so and to publish and update regularly a list of acceptable methods and approaches. Under the amended TSCA, existing chemicals will be subject to prioritization via a risk-based screening process into high and low priority chemicals. High priority chemicals ("those that may present an unreasonable risk" or for which there is insufficient information to make a determination) must undergo a risk evaluation. New chemicals will all be subject to review, and if EPA cannot make a determination regarding safe use with the information they are given, may ask for additional information. The amended Act is therefore likely to require the generation of massive amounts of new information on both existing and new industrial chemicals; at the same time there is pressure to reduce vertebrate testing, creating an immediate need for increased implementation of non-vertebrate evaluation tools. Such rapid development and implementation will require strongly coordinated efforts between industry, agency scientists and regulators and other stakeholders to leverage exiting approaches from other sectors and expand available methods and approaches, and provides a unique and immediate opportunity for scientists of all stripes to develop new, robust, non-animal evaluation tools, including in silico models, high-throughput screening, and systems biology models that integrate multiple types of information.

Councilor, Kate Willett

Organize your own SOT CCT Meeting

SOT sponsors two types of meetings outside of the SOT Annual Meeting: Contemporary Concepts in Toxicology (CCT) and Non-SOT meetings. CCT meetings are one- to two-day focused, open registration, scientific meetings in contemporary and rapidly progressing areas of toxicological sciences. Non-SOT meetings are sponsored by other not-for-profit organizations and SOT will either endorse or provide sponsorship money to toxicology-related meetings.

The Society will underwrite all the liabilities of the CCT meeting with the expectation that the meeting will at least break even financially. The goal of providing $25,000 seed funds is to stimulate the creation of CCT meeting proposals.

For more information about CCT meetings, please visit the SOT Web site

Vote for the new IVAM logo!!

Follow this link (XXX) and e-mail your top three choices to:
kwillett@humanesociety.org

Upcoming Webinars

Date: Tuesday, October 11, 2016
Time: 1pm Eastern Time
Registration link: https://aim-hq.webex.com/aim-hq/onstage/g.php?MTID=e1b449e39554a54d451075c0efe9d615b

Speakers:

Dr. Rhiannon Hardwick, Scientist I, Tissue Applications, Organovo. Organovo develops functional, three dimensional human tissue for medical research and therapeutic applications.

Mr. Brent Gilbert, Director of Business Development, Personal Care and Chemicals, Cyprotex. Cyprotex specializes in *in vitro* and *in silico* testing support for the pharmaceutical, biotech, cosmetics, personal care, and chemical industry, as well as academia and non-profit organizations.

Summary:
Many graduate students are interested in furthering the field of alternatives to animal testing, but do not know what career options are available to them or how to prepare for such a career. With this in mind, the *In Vitro* and Alternative Methods Specialty Section and Graduate Student Leadership Committee are teaming up to provide this information to students interested in pursuing a career focused on alternatives to animal testing.

The speakers will use their experiences as an example to highlight:

- What degree and experience are needed to qualify for specific jobs? Is a post doc required?
- What different types of positions are available (e.g., bench research, marketing or sales)?
- Are there opportunities for graduate students to obtain experience while working on their degrees (e.g., internships)?
- What is a typical day like?
- What are key similarities and differences to working in academia or other industries?
- Who do you regularly collaborate with (e.g., other scientists, business development or engineers)?
- What is the most important advice you can offer to potential career seekers?

Webinar attendees will have an opportunity to ask the speakers questions following the webinar.

We welcome any topic suggestions for future webinars.

Select Publications of Interest

Reconstructed tissues, organoid and organ-on-a-chip models:

1. ***Breast:***
   Williams KE, Lemieux GA, Hassis ME, Olshen AB, Fisher SJ, Werb Z. Quantitative proteomic analyses of mammary organoids reveals distinct signatures after exposure to environmental chemicals. Proc Natl Acad Sci U S A. 2016 Mar 8;113(10):E1343-51. PMID: 26903627
2. ***Intestine:***
   Schweinlin M, Wilhelm S, Schwedhelm I, Hansmann J, Rietscher R, Jurowich C, Walles H, Metzger M. Development of an advanced primary human in vitro model of the small intestine. Tissue Eng Part C Methods. 2016 Aug 1. PMID: 27481569
3. ***Liver:***
   Schepers A, Li C, Chhabra A, Seney BT, Bhatia S. Engineering a perfusable 3D human liver platform from iPS cells. Lab Chip. 2016 Jul 5;16(14):2644-53. PMID: 27296616

   Rennert K, Steinborn S, Gröger M, Ungerböck B, Jank AM, (…), Huber O, Mosig AS. A microfluidically perfused three dimensional human liver model. Biomaterials. 2015 Dec;71:119-31. PMID: 26322723
4. ***Kidney:***
   Morizane R, Lam AQ, Freedman BS, Kishi S, Valerius MT, Bonventre JV. Nephron organoids derived from human pluripotent stem cells model kidney development and injury. Nat Biotechnol. 2015 Nov;33(11):1193-200. PMID: 26458176

   Chang SY, Weber EJ, Van Ness KP, Eaton DL, Kelly EJ. Liver and Kidney on Chips: Microphysiological Models to Understand Transporter Function. Clin Pharmacol Ther. 2016 Jul 22. doi: 10.1002/cpt.436. PMID: 27448090

5. ***Sensitization:***

   Coleman K. P., McNamara L. R., Grailer T. P., Willoughby J. A. Sr., Keller D. J., Patel P., Thomas S., & Dilworth C. Evaluation of an *in vitro* human dermal sensitization test for use with medical device extracts. *Applied In Vitro Toxicol 2015* 1(2): 118-130. Available here: http://online.liebertpub.com/doi/pdf/10.1089/aivt.2015.0007

6. ***Neurotoxicity***

   Schwartz, M.P., Hou, Z., Propson, N.E., et al. Human pluripotent stem cell-derived neural constructs for predicting neural toxicity. *PNAS* 2015 112: 12516-12521. PMID: 26392547

High-throughput/Predictive methods:

1. ***Liver toxicity***
   Sison-Young RL, Lauschke VM, Johann E, Alexandre E, Antherieu S,(…), Hewitt PG,

Ingelman-Sundberg M, Goldring CE, Park BK. A multicenter assessment of single-cell models aligned to standard measures of cell health for prediction of acute hepatotoxicity. Arch Toxicol. 2016 Jun 25. PMID: 27344343

2. ***Neurotoxicity:***
Schmidt BZ, Lehmann M, Gutbier S, Nembo E, Noel S, Smirnova L, Forsby A, Hescheler J, Avci HX, Hartung T, Leist M, Kobolák J, Dinnyés A. In vitro acute and developmental neurotoxicity screening: an overview of cellular platforms and high-throughput technical possibilities. Arch Toxicol. 2016 Aug 4. PMID: 27492622

3. ***Kidney toxicity***
Adler M, Ramm S, Hafner M, Muhlich JL, Gottwald EM, Weber E, Jaklic A, Ajay AK, Svoboda D, Auerbach S, Kelly EJ, Himmelfarb J, Vaidya VS. A Quantitative Approach to Screen for Nephrotoxic Compounds In Vitro. J Am Soc Nephrol. 2016 Apr;27(4):1015-28. PMID: 26260164

4. ***Cardiac toxicity***
Cummins Lancaster M, Sobie EA. Improved prediction of drug-induced Torsades de Pointes through simulations of dynamics and machine learning algorithms. Clin Pharmacol Ther. 2016 Mar 7. PMID: 26950176

AOPs:

1. ***Building AOPs:***

Vietti G, Lison D, van den Brule S. Mechanisms of lung fibrosis induced by carbon nanotubes: towards an Adverse Outcome Pathway (AOP). Part Fibre Toxicol. 2016 Feb 29;13:11. PMID: 26926090

Yauk CL, Lambert IB, Meek ME, Douglas GR, Marchetti F. Development of the adverse outcome pathway "alkylation of DNA in male premeiotic germ cells leading to heritable mutations" using the OECD's users' handbook supplement. Environ Mol Mutagen. 2015 Dec;56(9):724-50. PMID: 26010389.

2. ***Example of applying AOPs in predictive toxicology:***

Perkins EJ, Antczak P, Burgoon L, Falciani F, Garcia-Reyero N, Gutsell S, Hodges G, Kienzler A, Knapen D, McBride M, Willett C. Adverse Outcome Pathways for Regulatory Applications: Examination of Four Case Studies With Different Degrees of Completeness and Scientific Confidence. Toxicol Sci. 2015 Nov;148(1):14-25. doi: 10.1093/toxsci/kfv181. PMID: 26500288

3. ***Beyond AOPs – what's the next step to make testing strategies even better:***

Leontaridou M, Gabbert S, Van Ierland EC, Worth AP, Landsiedel R. Evaluation of non-animal methods for assessing skin sensitisation hazard: A Bayesian Value-of-Information analysis. Altern Lab Anim. 2016 Jul;44(3):255-269. PMID: 27494625

Bal-Price A, Lein PJ, Keil KP, Sethi S, Shafer T, Barenys M, Fritsche E, Sachana M, Meek ME. Developing and applying the adverse outcome pathway concept for understanding and predicting neurotoxicity. Neurotoxicology. 2016 May 17. pii: S0161-813X(16)30088-2. doi: 10.1016/j.neuro.2016.05.010. PMID: 27212452

El-Masri H, Kleinstreuer N, Hines RN, Adams L, Tal T, Isaacs K, Wetmore BA, Tan YM. Integration of Life-Stage Physiologically Based Pharmacokinetic Models with Adverse Outcome Pathways and Environmental Exposure Models to Screen for Environmental Hazards. Toxicol Sci. 2016 Jul;152(1):230-43. doi: 10.1093/toxsci/kfw082. PMID: 27208077

Strickland J, Zang Q, Kleinstreuer N, Paris M, Lehmann DM, Choksi N, Matheson J, Jacobs A, Lowit A, Allen D, Casey W. Integrated decision strategies for skin sensitization hazard. J Appl Toxicol. 2016 Sep; 36(9): 1150-62. doi: 10.1002/jat.3281. PMID: 26851134

Calling All Volunteers!

The IVAM executive committee is creating a volunteer list of those individuals who would be willing to assist throughout the year, on tasks ranging from reviewing award applications, session proposals, or organizing upcoming events. If interested, please email Barbara Wetmore at bwetmore723@gmail.com.