

Welcome to June *Insights*. Inside this edition: Annual Meeting wrap-up, OECD test guideline approval, and more!



June Insights

2018 HESI Annual Meeting Wrap-Up



(Left to right) Ernie Harpur, Syril Pettit and Tim Pastoor at the HESI 2018 Annual Meeting

HESI recently convened their [2018 Annual Meeting](#) in Washington, D.C. More than 100 scientists from across the globe attended to hear presentations on the meeting's theme, *The Science of Implementation*. Speakers discussed both ongoing research and emerging issues that could benefit from public-private collaboration towards effective scientific solutions. In addition to HESI Committee project updates, speakers also presented work related to implementation of the [HESI RISK21](#) tool in Indonesia and Ghana, as well as topics on natural language processing methods and using wearable technology to predict health outcomes. The meeting concluded with presentations from the [HESI THRIVE](#) Grantees, who are conducting research towards improving cancer patient outcomes.



Tim Pastoor addresses attendees at the HESI 2018 Annual Meeting

In Vitro Rainbow Trout Hepatic Metabolism Test Guidelines and Guidance Document Approved by OECD

Two OECD test guidelines (“Determination of *in vitro* intrinsic clearance using cryopreserved rainbow trout hepatocytes” and “Determination of *in vitro* intrinsic clearance using rainbow trout liver S9 sub-cellular fractions”) and an accompanying Guidance Document were **approved in April 2018 at the OECD Meeting of the Working Group of National Coordinators (WNT)**. The approaches use substrate depletion methods to determine the rate at which the *in vitro* test systems (S9 fractions and cryopreserved hepatocytes) metabolize test chemicals. This information can then be extrapolated to the whole liver to provide a direct basis for comparison, which can then be extrapolated to whole organism bioaccumulation. The Guidance Document provides detailed information on how to conduct the tests as well as how to apply the measured *in vitro* biotransformation rates to predict bioconcentration factors (BCFs). In addition, the document also covers guidance on the selection of the assay system (e.g., primary hepatocytes versus liver S9 fractions), specific considerations for testing chemicals, use of negative and positive controls, BCF extrapolation models, and application of the two test methods beyond BCF prediction.

These methodologies were the result of many years of work by the HESI Bioaccumulation Committee and other stakeholders, supported by a multilaboratory ring trial that involved seven laboratories in Europe and North America. The ring-trial study report by Nichols et al. was also accepted for publication in *Toxicological Sciences* and is currently in press (available [here](#)).

For more information, please contact Michelle Embry (membry@hesiglobal.org).

Cardiac Safety Committee Meetings

The Cardiac Safety Committee recently convened a workshop to discuss updating their mission to focus on mechanism-based assays. Workshop participants heard presentations on the current state of cardiovascular safety liabilities, new technologies to potentially assess these, as well as some existing committee projects and new possible partnerships. Participants also broke out into groups to discuss the state of the science and ways HESI can contribute to help better understand cardiovascular safety risk assessments. The committee plans to further map this problem by developing a manuscript based on the workshop and is currently discussing next steps.

In addition, a CiPA Update meeting co-sponsored by the Cardiac Safety Research Consortium (CSRC), the FDA, and HESI, was held 21–22 May 2018 in Washington, DC. The large audience of more than

150 attendees heard presentations from all four CiPA workstreams, including protocols and the latest data. This meeting marks a turning point in the CiPA process, whereby all workstreams have presented data. The next step is to seek to reopen the ICH S7B Discussion Group. Presentations are now available on the [CSRC website](#).

For more information on the Cardiac Safety Committee, contact Jennifer Pierson (jpierson@hesiglobal.org) or Stan Parish (sparish@hesiglobal.org).

Bioaccumulation Course in Rome

A course on “The Application of Emerging Tools for Bioaccumulation Assessment: Integration of Biotransformation” was held on 13 May 2018 in Rome, Italy. The course was attended by 25 government and industry scientists and was co-sponsored by the HESI Bioaccumulation Committee and CEFIC-LRI.

The course objectives were to

1. Provide an overview of the newly developed rainbow trout liver S9 fraction and cryopreserved trout hepatocyte substrate depletion assays for the evaluation of xenobiotic biotransformation in fish;
2. Highlight and discuss recent advances for *in silico* predictions of biotransformation;
3. Provide an introduction and overview of the Bioaccumulation Assessment Tool (BAT); and
4. Demonstrate the application of BAT using illustrative hands-on case examples.



Bioaccumulation Course Attendees

The course instructors were Jon Arnot (ARC), Michelle Embry (HESI), Karla Johanning (KJ Scientific), Heike Laue (Givaudan), Ester Papa (University of Insubria), Alessandro Sangion (University of Insubria), James Armitage (AES), Liisa Toose (ARC), and Karen Foster (KFER). A follow-up course is being planned, potentially in coordination with the November 2018 SETAC North America Meeting.

For more information, please contact Michelle Embry (membry@hesiglobal.org).

Upcoming Events

Registration Closing Soon: Gut Microbiome Workshop

The HESI Microbiome Subcommittee is proud to announce “**The Gut Microbiome: Markers of Human Health, Drug Efficacy and Xenobiotic Toxicity Workshop**,” which will be held in Alexandria, Virginia, on **25–26 June 2018**. The workshop will focus on:

- current science on the gut microbiome and identification of areas of interest regarding its role in human health
- our understanding of how xenobiotic toxicity affects the microbiome
- discussion of biomarkers of disease or organ damage due to alterations of microbiome structure or endogenous microbial metabolites



Visit our webpage [here](#) for the full agenda and to register!

Recent Publications

Nichols J, Fay K, Bernhard MJ, Bischof I, Davis J, Halder M, Hu J, Johanning K, Laue H, Nabb D, Schlechtriem C, Segner H, Swintek J, Weeks J, Embry M (2018) Reliability of *in vitro* methods used to measure intrinsic clearance of hydrophobic organic chemicals by rainbow trout: results of an international ring trial. *Toxicological Sciences*. In press. [Read More](#)

Scialli AR, Daston G, Chen C, Coder PS, Euling SY, Foreman J, Hoberman AM, Hui J, Knudsen T, Makris SL, Morford L, Piersma AH, Stanislaus D, Thompson KE (2018) Rethinking developmental toxicity testing: evolution or revolution? *Birth Defects Research*. 10:840–850. [Read More](#)

From the Leadership

HESI's annual meeting in June was a showcase of impressive science and proposals for moving forward. Under the new model adopted two years ago this was also the occasion for transition of the roles of both the HESI President and the Chair of the Board of Trustees. Transitions are part of a journey, like a single frame is part of a movie. We have had many of those single frames in the recent journey of HESI, and we are grateful, as we transition to past-president and past-chair, to have been part of the frame-by-frame development of the HESI movie. Since its inception, HESI has been continuously evolving for the better and over the past few years there have been important changes. With the energetic leadership of Cyril and her indefatigable staff we helped with the development of a clear strategy, the Science Forward initiative, the evolving role of the EIC and PSSC, governance changes that consolidate our structure as a true public-private partnership at all levels of the organization and most recently and momentously, our exit from the ILSI umbrella. We are eager to see the next frames develop in HESI's storyline, including Lois Lehman McKeeman and Charlene McQueen taking on the mantle of leadership, more clearly defining the roles of the EIC and PSSC, and the inclusion of new and impactful projects that will solidify HESI's growing reputation as the place where public/private collaboration finds solutions to difficult scientific challenges. Transitions can be difficult, emblematic, joyous, or epic. But ultimately, they are the still frames that make up the tapestry of our collective cinematic journey. We are so very thankful that we have had, and continue to have, the opportunity to contribute to such an impactful organization.



Tim Pastoor
HESI President



Ernie Harpur
Chair, HESI Board of Trustees

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