



## January Insights 2017 in Review

### Cardiac Safety

The Cardiac Safety Committee launched three new projects in 2017 that will collectively improve our ability to interpret whether ECG signal data or cardiac contractility changes reflect an actual or pending adverse response to a drug. The results of the much anticipated CiPA Myocyte validation study also came to a successful completion. In 2017, the committee published four peer-reviewed journal articles from the Cardiac Biomarkers, ProArrhythmia, and Integrative Strategies Working Groups and started developing another 6 manuscripts.

### Translational Biomarkers of Neurotoxicity

The Translational Biomarkers of Neurotoxicity (NeuTox) Committee completed an *in vivo* rodent pilot study to identify easily accessible, fluidic biomarkers of neurotoxicity and published the first of several planned papers with initial results. The NeuTox Micro-Electrode Array (MEA) Subteam launched a seven-site pilot study to investigate use of MEA technology to predict seizure liability. We are pleased to announce that the NeuTox Committee completed their first HESI Program Stewardship and Strategy Review and was re-chartered for another 3 years to continue this important work.

### RISK21

HESI launched a new phase of this highly successful program with the convening of a public-private RISK21 2.0 Scientific Advisory Board (SAB) composed of leading experts in risk assessment and related disciplines. The SAB is actively developing plans for advanced case studies, new methods and tool development, and training and outreach. The program built on its global outreach success with new trainings and presentations in Milan, Italy, Hangzhou, China, and Buenos Aires, Argentina.

### Animal Alternatives in Environmental Risk Assessment

HESI's Animal Alternatives in Risk Assessment Committee advanced the development of the ecological threshold of toxicological concern (eco-TTC) concept (a means to efficiently evaluate potential hazard to a broad range of species present in aquatic systems) via a 1.5-day expert workshop in Ottawa, Canada. The workshop provided a critical opportunity to gain stakeholder feedback on the innovative web-based tools developed by the committee to support these assessments. This group's work led to a committee publication, "[Mode of Action \(MOA\) Assignment Classifications for Ecotoxicology: An Evaluation of Approaches](#)," by Kienzler et al. The committee also continued its important work in the field of effluent assessment, with the planned publication of a perspectives article highlighting outcomes from a 2016 workshop on "Concepts, Tools, and Strategies for Effluent Assessment."

### Development of Methods for a Tiered Approach to Assess

## Bioaccumulation of Chemicals

This committee further advanced its contributions to OECD global safety standards with the preparation of content in support of two draft Test Guidelines, a Guidance Document, and a report on the committee's experimental ring trial (all materials submitted in support of OECD Project 3.13 on "*In Vitro* Fish Hepatic Metabolism"). It is anticipated that the Test Guidelines will be adopted in spring 2018. The committee has also been asked to provide technical content in support of evolving risk assessment approaches within the European Water Framework Directive (WFD). Peer-reviewed manuscripts detailing the studies and methodologies noted above are in progress.

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## Developmental and Reproductive Toxicology

The Developmental and Reproductive Toxicology (DART) Technical Committee had another very productive year. In 2017, the committee was recognized as **Author of the Year** by the DIA's peer-reviewed journal for the article "[Birth Control in Clinical Trials: Industry Survey of Current Use Practices, Governance, and Monitoring](#)." Additionally, the committee held two workshops ("[Rethinking DevTox](#)" and "[Best Practices in Interpreting DevToxicity Data for Classification and Labeling](#)") and published two manuscripts, while launching two new projects on AGD-areola/nipple retention and thyroid hormone assessment. Links to both publications can be found [here](#).

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## Application of Genomics to Mechanism-Based Risk Assessment

The HESI Genomics Committee is proud to announce major milestones in its work on the first-ever genomic biomarker submitted for FDA qualification. In 2017, the committee received a letter of support from the FDA to encourage its ongoing efforts, published its [research in PNAS](#), and saw its marker incorporated into an online tool via the [NTP website](#). The committee's other impacts included developing novel biomarker approaches via use of microRNA analyses, innovating [genomic analysis](#) of stored tissue samples, and convening global experts via an [international workshop](#) on addressing roadblocks in the use of genomics data in cancer risk assessment.

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## Biomarkers of Nephrotoxicity

This committee is completing research on micro-RNAs that will aid in the ability to localize the site of drug-induced injury in the kidney. A manuscript on best practices for detection of urinary protein biomarkers is in its final stages. The Biomarkers of Nephrotoxicity Committee merged with the Application of Genomics to Mechanism-Based Risk Assessment Committee in late 2017 and will complete its work in partnership with that committee during 2018.

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## Immunotoxicology

In April 2017, the Immunotoxicology Technical Committee (ITC) held a highly successful public training course on "T Cell Biology and Immunopharmacology and Immunotoxicology." Given the high demand for the course, the ITC will hold a repeat session in Germany in 2018. The diverse scientific portfolio progressed actively via seven distinct research teams focused on improving our ability to predict and prevent adverse immune reactions to drugs as well as chemicals.

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## Framework for Intelligent Non-Animal Methods

The Framework for Intelligent Non-Animal Methods Subcommittee focused on completing a manuscript that will provide critical guidance on criteria, considerations, and resources for evaluating potential non-animal alternative methods for risk or safety assessment (as well as case studies to illustrate the application of the framework). The subcommittee also initiated preparations for 2018 workshops to further demonstrate and improve the frameworks relevance.

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## Genetic Toxicology

The Genetic Toxicology Technical Committee (GTTC) held a workshop on mode of action in conjunction with

the Genetic Toxicology Association in 2017. In addition, the GTTC's eight subgroups have continued to make progress, publishing multiple manuscripts and planning upcoming workshops in 2018 in conjunction with the European Environmental Mutagen and Genomics Society.

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## Cell Therapy-TRacking, Circulation & Safety

In its second full year, the Cell Therapy-TRacking, Circulation & Safety (CT-TRACS) subcommittee refined its focus with the formation of two focused subteams. The Point of Administration/Biodistribution subteam examines methodologies for tracking cells after administration and evaluating biodistribution *in vivo*, while the Tumorigenicity subteam examines methodologies for tumorigenicity assessment of human cell-based therapeutic products. A survey, "Assessing the Needs for Cell-Based Therapies Translation," was distributed to stakeholders with experience in developing and/or evaluating cell therapies. Results are currently being analyzed and will serve as the basis for two CT-TRACS manuscripts. Subcommittee members participated in six outreach events, including a [scientific session](#) at the [International Society of Cellular Therapy](#) (ISCT) meeting in May 2017, the World Stem Cells Summit, and the 16th Congress of the Japanese Society of Regenerative Medicine. The committee is preparing a proposal to transition from an Emerging Issues Subcommittee to a HESI Technical Committee.

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## COMprehensive Protein Allergen REsource (COMPARE)

In early 2017, HESI released the COMprehensive Protein Allergen REsource (COMPARE) 2017 database, a new comprehensive repository of protein sequences of known or putative allergens, as a resource available to the public ([www.comparedatabase.org](http://www.comparedatabase.org)). The process included the creation and implementation of a novel approach, based on an automated bioinformatic "rule-based" sorting algorithm, for sequence sorting and identification of candidate allergen sequences. In spring 2017, the COMPARE steering team made available a step-by-step description of the process development online, explaining transparently the rigorous database build processes, carefully designed to meet the needs for allergy safety assessment. Members presented the database at several outreach events throughout the year (and the world!), including the 2017 European Academy of Allergy and Clinical Immunology Congress (Helsinki); the 2017 HESI Annual Meeting (Dublin); events coordinated jointly with ILSI China, ILSI Argentina, and ILSI Japan; and last but not least, a dedicated COMPARE session at the Joint Institute for Food Safety and Applied Nutrition (JIFSAN) workshop titled "FoodRisk.org – Risk Analysis Tools and Data, A Guided Tour by Tool Creators" (Greenbelt, MD).

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## Protein Allergenicity

In 2017, the Protein Allergenicity Technical Committee (PATC) expanded its portfolio with the launch of two new research projects to explore the impact of food matrices on the digestibility of proteins as well as the impact of amino acid replacement on IgE binding and allergenicity. Additionally, the committee released the first iteration of a new public COMPARE database (as described above), completed experimental work on *in vitro* gastrointestinal digestion protocols for allergenicity assessment (manuscript in preparation), and completed preliminary work on functional classification of protein toxins ([Negi et al. 2017, Scientific Reports](#)). Committee members also participated in five international outreach events in Beijing, Dublin, Helsinki, Buenos Aires, and Tokyo in 2017.

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## Microbiome

The Microbiome subcommittee launched in early 2017 and quickly formed a steering team and five different working groups focused on identifying the state of the science and research gaps in drug efficacy and xenobiotic toxicity. A workshop is planned for late June 2018, with a goal of identifying avenues of research. More information on the workshop can be found [online](#).

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