



HESI NEWS

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Bioinformatics Workshop Draws International Interest

The HESI Protein Allergenicity Technical Committee hosted a successful International Bioinformatics Workshop in Mallorca, Spain, on February 22-24, 2005. Conducting this workshop in Europe provided an excellent opportunity to highlight the global nature of HESI activities and facilitate discussion about the state of the science of human allergenicity by international experts.

More than 40 scientists from industry, government, and academia participated in the workshop. The primary goal was to evaluate current methodologies for identifying similarities to known allergens and toxins, and to examine the state of the science of sequence homology comparisons and bioinformatics evaluations done in the context of a human allergenicity assessment. A clear example of a concept where consensus was achieved as part of the workshop discussions was the inappropriateness of using short (6, 7, or 8) linear amino acid sequences as the basis for a homology comparison. Evaluating the similarity between a novel protein and an allergen, expressed as percent similarity over the complete three-dimensional structure of the protein, was thought to be a more scientifically-defensible approach. In addition, there was broad interest in further exploration of structural motifs as the basis of homology comparisons.

The primary deliverable from this workshop will be a comprehensive manuscript that will summarize discussions and key findings. The manuscript will be submitted for publication in the peer-reviewed, scientific literature. A range of topics will be addressed in the manuscript that are important for sequence homology evaluations, such as structural biology, IgE cross-linking, serum IgE testing, and a review of allergen databases. Each workshop participant will have an opportunity to provide comments on the final manuscript before it is submitted for publication. An editorial board has the overall responsibility for developing the final manuscript. This workshop is part of the Protein Allergenicity Technical Committee's broader objective to advance the scientific understanding of relevant parameters for characterizing the allergenic potential of novel proteins and biotechnology products.

For more information about the outcome of the International Bioinformatics Workshop, contact Mr. Karluss Thomas, Senior Scientific Program Manager, at kthomas@ilsi.org.

Government Scientists Offer Perspectives on HESI Scientific Portfolio

Long-term and unbiased input from government scientists is critical to HESI's success. Recognition of this key component of the HESI "tripartite" approach prompted HESI leadership and staff to organize a government forum at the 2005 annual meeting to elicit perspectives on HESI's scientific portfolio. The first of its kind at a HESI annual meeting, the government forum provided an opportunity to review HESI's existing portfolio and explore new strategic directions. Perspectives collected from the government forum will complement the results of HESI's traditional emerging issues process and the organization's more recent "mapping exercise" (see HESI News, Fall 2004, p. 2).

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Message from the President



Dear Colleagues:

It is with pleasure that I write this message to you today as the new president of the ILSI Health and Environmental Sciences Institute. I follow in the footsteps of individuals who have played critical roles in making this organization the leader in science that it has so clearly become. I want to add my personal thanks to the many accolades already bestowed on Dr. Lewis Smith, my

immediate predecessor. Lewis's contributions to HESI have been many—I cite the “scientific mapping” process and its contribution to the development of HESI's scientific project portfolio as a key component of his legacy as president. I look forward to many more years of contributions to HESI from our esteemed colleague!

We have just completed our annual meeting for 2005, and it was indeed an impressive event—one that highlighted the strengths of this organization. And HESI's strengths are many. Our membership is strong, with some 44 companies representing multiple industrial sectors from Europe, the United States, and Japan, and more companies expressing interest in joining. The scientists from these companies, with our academic and government colleagues, comprise the unique HESI tripartite mechanism that is critical to the strength of our scientific portfolio of projects. The success and strength of these projects become increasingly apparent as they are recognized, acknowledged, and cited—with increasing frequency—by scientific institutions and bodies around the world.

The HESI staff is strong, and under the highly capable leadership of HESI's executive director, Michael Holsapple, is also a critical component of the organization's success. Our finances are strong and sound, with a team of trustees working with the staff to ensure the continued fiscal strength of the organization.

I am excited to serve this organization as its president for the next two years—to help ensure its continued successful contributions to science, to continue its support of the evolving ILSI organization, and to continue to build on the legacies of its previous presidents. I welcome and encourage your suggestions to help achieve these goals.

William T. Robinson, PhD
HESI President
March 2005

Message from the Chair



Dear Colleagues:

I enjoyed seeing many of you at this year's ILSI and HESI annual meeting in New Orleans. I would like to take this opportunity to add my congratulations to the HESI staff and all participants involved in the organization of the meeting. The presentations of HESI's projects and activities during the Assembly of Members meeting, the “State of the Science in HESI”

session, and other sessions provided real information about our scientific portfolio—and made it abundantly clear that ours is an active and vivid institution with broad scientific excellence. HESI brings great value to our members and the scientific community!

HESI has continued to strengthen and evolve, as indicated by the presentations at the annual meeting. ILSI has also evolved over the past year. The ILSI Research Foundation has been restructured so that the ILSI Human Nutrition Institute, the ILSI Risk Science Institute, and the ILSI Center for Health Promotion now operate under one Board of Trustees and one Council of Scientific Advisors. ILSI has hired a Chief Development Officer who will assist ILSI and its “entities” in identifying new sources of funding. Furthermore, the ILSI Board “Organizational Development and Effectiveness Committee” is looking at a range of opportunities for evolution of the organization. HESI participates actively on the ILSI Board and its committees.

These evolutionary changes in ILSI will provide opportunities and challenges for HESI and all the members of the ILSI family, as each component continues to strive for scientific excellence. When the goals and emphasis of the restructured Research Foundation are discussed, “food safety and nutrition” are highlighted, of course. However, “risk assessment,” “environmental safety,” and “global activities” are terms also used. Because these are focus areas of historical and primary importance to HESI, there is the potential for duplication in efforts to address these topics, and for competition in fund-raising activities, especially in light of increasing financial restrictions within traditional funding sources. The HESI Board, Executive Director, and staff will monitor and offer input as the broader organization considers new paths, both conceptual and practical, and will consider each of these opportunities and challenges in the context of HESI's own evolution. We look forward to the positive impact these new paths will have on all of ILSI!

Helmut H. Greim, MD
Chair, HESI Board of Trustees
March 2005

Message from the Executive Director



Dear Colleagues:

It is my pleasure to formally and officially introduce the new HESI logo in this issue of HESI News. The logo has been “under construction” since the August 2004 meeting of the HESI Board of Trustees. At that time, the Board requested that logo designs be prepared for its consideration. The Board Communications

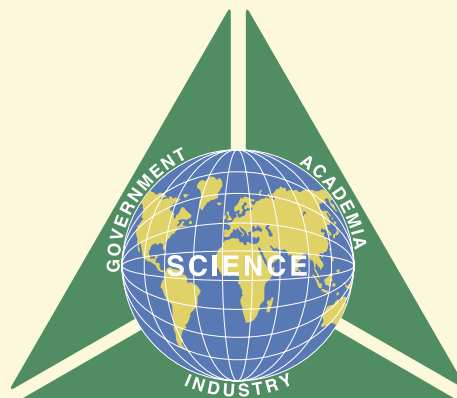
Committee was given oversight of the selection process. Working with the ILSI Press graphic designer, HESI staff developed dozens of potential designs that attempted to capture the key qualities of “HESI” into a simple and recognizable logo. The ultimate design was selected by the Communications Committee with input from the HESI Executive Committee and staff, and was integrated into our 2004 Annual Report. That design was presented to the entire Board of Trustees during the January 2005 annual meeting in New Orleans. With a few minor “tweaks,” the Board unanimously approved the HESI logo.

HESI is first and foremost a scientific organization, and “SCIENCE” appears at the center of our logo. Another important aspect of our identity is that HESI is the global branch of ILSI. Our programs have global impact and our members are multinational corporations. To ensure that all key regions of the world are represented, we have taken some artistic liberties in the depiction of the “globe.” The “tripartite” approach is critical to all HESI activities, and is depicted by the three triangles reflecting “INDUSTRY,” “ACADEMIA,” and “GOVERNMENT,” with

industry providing the base to reflect that HESI is supported primarily by its members. The three triangles are drawn as separate and distinct, but the spaces between them are not large gaps; rather, the spaces converge toward a mutual commitment to engage in tripartite partnerships to address scientific issues with potential global impact.

“ILSI” does not appear in our logo. This decision was a deliberate one for two reasons. First, ILSI has its own logo. To integrate “ILSI” into the HESI design would have effectively made it a new ILSI logo. Second, including “ILSI” in the logo would have perpetuated a recurring situation that provided the impetus for developing a HESI logo. Most of you have been in attendance during a public discussion when a HESI project, activity, published paper, or work product is described as an “ILSI” product. The frequent omission of “HESI” from these important public acknowledgements of our work prompted the HESI leadership to engage in targeted efforts to establishing better name recognition. The decision not to integrate “ILSI” into our logo is an effort to take the “HESI brand” to the next level. Make no mistake, the legal name of our organization is still the “ILSI Health and Environmental Sciences Institute.” The creation of the HESI logo does nothing to change our commitment to remain an active and supportive member of the “ILSI family.” On behalf of the HESI Board of Trustees and staff, I welcome your comments.

Michael P. Holsapple, PhD
Executive Director, HESI
March 2005



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Nanomaterial Safety Explored at 2005 Annual Meeting

The HESI Nanomaterial Safety Subcommittee hosted a scientific session titled “Nanomaterial Safety: Unique Chemical Properties and the Associated Implications for Exposure and Risk Assessment” at the 2005 annual meeting. The session was well-attended, and featured speakers from government, industry, and academia. Co-chaired by Drs. Paul Borm (Zuyd University, The Netherlands) and Tim Landry (The Dow Chemical Company), the session focused on the challenges and opportunities associated with conducting a comprehensive risk assessment for engineered nanomaterials. Dr. Landry opened the session by providing an overview of nanotechnology and a summary of the activities of the

HESI Nanomaterial Safety Subcommittee. These activities address the development of data to support risk assessments for nanomaterials, including nanomaterial toxicity, characterization, dissolution, and life-cycle analysis. Dr. Nakissa Sadrieh (US Food and Drug Administration) offered an FDA perspective on nanomaterial-containing products. FDA-regulated products—including drugs, drug-delivery systems, medical devices, vaccines, biotechnology products, cosmetics, and genes and protein delivery systems—will be impacted by nanotechnology. Dr. Borm presented an overview of a nanomaterials screening network known as Nanoscreen. The evaluation and control of nanomaterial exposures in the

workplace was discussed by Dr. Andrew Maynard (CDC National Institute for Occupational Safety and Health). Dr. Edgar Liebold (BASF) summarized work on nanomaterial characterization and testing that is under way in his laboratory. Dr. Liebold’s studies have focused primarily on in vitro studies of dermal toxicity. Finally, Dr. Kevin Dreher (EPA) summarized the current state of the science regarding development of a complete dataset for facilitating comprehensive risk assessment for nanomaterials.

For more information about the HESI Nanomaterial Safety Subcommittee, contact Mr. Karluss Thomas, Senior Scientific Program Manager, at kthomas@ilsa.org.

State of the Science within HESI Featured at 2005 Annual Meeting

At each annual meeting, HESI historically organizes scientific sessions and provides brief updates on committee activities to the Assembly of Members. At the 2005 annual meeting, the HESI Board of Trustees and HESI staff worked together to merge two of these sessions into a scientific program titled “State of the Science within HESI: Improving

Our Approach to Safety and Risk Assessment.” The session featured six mature HESI projects. The objectives of each presentation were to provide a more detailed description of the project than was possible at past annual meetings, and to invite perspectives from HESI’s government colleagues regarding the impact of each featured project.

Juvenile Animal Testing

Dr. Mark Hurtt (Pfizer) presented results of the HESI Developmental and Reproductive Toxicology (DART) Technical Committee’s project addressing the role of juvenile animal studies in assessment of pediatric safety. The project involved a literature review on comparative postnatal development, part of which is ongoing, and a major international workshop conducted in late 2003. The purpose of the workshop was twofold: to determine when juvenile animal studies are necessary and to identify study designs and test strategies. Proceedings of the workshop were published in 2004 (*Birth Defects Res., Part B, Dev. Reprod. Toxicol.* 71:281-288, 2004). A principle finding of the workshop was that decisions to use juvenile animal tests should be made on a case-by-case basis. Dr. David Jones (UK Medicines and Healthcare Products Regulatory Agency), who actively participated in the workshop, described the project’s value in the context of development of the European Union’s “Guideline on the Need for Non-Clinical Testing of Human Pharmaceuticals in Juvenile Animals.” Dr. David Jacobson-Kram (US FDA Center for Drug Evaluation and Research) reviewed FDA’s “Draft Guidance to Industry: Non-clinical Safety Evaluation of



Drs. Ron Hines (Medical College of Wisconsin) and Mark Hurtt (Pfizer) find time for technical debate at the 2005 annual meeting poster session.

Pediatric Drugs,” and discussed design considerations for juvenile animal toxicity studies. FDA scientists developing the guidance have been involved in the DART project from its inception.

Agricultural Chemical Safety Assessment (ACSA)

On behalf of the HESI Technical Committee on Agricultural Chemical Safety Assessment, Dr. Neil Carmichael (Bayer CropScience) described an improved tiered testing approach for assessing the safety of crop protection chemicals. Developed by an international group of government, academic, and industry scientists, the results of the multi-year HESI project include integration of metabolic and kinetic data into the safety assessment process; a hierarchy of study types, end points, and triggers to cover vulnerable life stages; a tiered testing framework for end points such as neurotoxicity, carcinogenicity, and chronic toxicity; and evaluation of the range of relevant human exposure situations in the context of experimental study design. Dr. Vicki Dellarco (US EPA Office of Pesticide Programs) emphasized the scientific value and timeliness of the ACSA proposal in the context of EPA's proposed revisions to pesticide data requirements. Dr. Canice Nolan (European Commission) praised the merits of the ACSA tiered testing proposal, as well as the consensus approach taken in its development.

Cardiovascular Safety Assessment

Dr. Peter Siegl (Merck Pharmaceuticals) gave an overview of a study recently completed by the HESI Cardiovascular Safety Assessment Project Committee. In the study, performed by Quintiles, the utility of selected non-clinical approaches for assessing QT prolongation was compared using a panel of drugs with extensive clinical data on their propensity to elicit QT prolongation and proarrhythmia in humans. Twelve compounds with well-characterized effects were evaluated with respect to whether they caused QT prolongation in humans. The specific test systems included two in vitro assays (a HERG potassium ion channel assay and an assay to record changes in action



Drs. Sam Cohen (University of Nebraska Medical Center) and Jim MacDonald (Schering-Plough Research Institute) share scientific views at the 2005 annual meeting poster session.

potentials from dog-isolated cardiac Purkinje fibers) and one in vivo technique (use of conscious, telemetered dogs to monitor changes in ECG and blood pressure subsequent to exposure to the 12 test compounds). Data from this study suggest that compounds that may pose a proarrhythmia risk for patients can be distinguished from safe compounds by using the integrated results of three assays: HERG, Purkinje repolarization, and the in vivo QT studies in dogs. The findings from the study also suggest that, taken collectively, non-clinical and early clinical results could be integrated to develop an accurate risk assessment.

Application of Genomics to Mechanism-based Risk Assessment

Dr. Cynthia Afshari (Amgen) presented outcomes from the HESI Technical Committee on the Application of Genomics to Mechanism-based Risk Assessment. The presentation detailed the design and results of the first phase of the Committee's toxicogenomic experimental program (2000–2003). The Committee's extensive microarray studies indicated highly consistent detection of affected biological pathways across inter- and intra-laboratory replicates, although gene-by-gene comparisons across replicates remained challenging. New research programs to be executed by the committee membership in 2005 include a survey of current and future practices in toxicogenomics across sectors, de novo research on the utility of microarrays for

mechanistic toxicology, and compilation of a pilot database of control animal genomic data. In response to Dr. Afshari's presentation, Dr. Jean-Marc Vidal (EMEA) confirmed the unique value of the HESI Genomics Committee as a multi-sector forum for discussion and resolution of the many pending issues around the appropriate use of toxicogenomics for risk assessment.

A Proposed Testing Framework for Developmental Immunotoxicology

Dr. Leigh Ann Burns-Naas (Pfizer) described a proposed testing framework for developmental immunotoxicology, which was developed during a HESI workshop organized by the Immunotoxicology Technical Committee. The framework was recently published (*Toxicol. Sci.*, 83:18–24, 2005). The key conclusions of the workshop included the following: the rat is the preferred model; end points should be based on current validated assays; the framework should be incorporated into existing protocols to the extent possible (rather than stand alone); the approach should be similar for chemicals and drugs, but the design should be flexible enough to answer specific questions; and triggers for the framework include SAR, intended use, and/or anticipated exposure in juveniles or neonates. Dr. Michael Luster (CDC National Institute for Occupational Safety and Health) reviewed epidemiological and experimental evidence for

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HESI welcomed the following distinguished government scientists from the United States and Europe as panel participants at the forum:

- Dr. John Bucher (NIEHS National Toxicology Program)
- Dr. David Jacobson-Kram (US FDA Center for Drug Evaluation and Research)
- Dr. David Jones (UK Medicines and Healthcare Products Regulatory Agency)
- Dr. Michael Luster (CDC National Institute for Occupational Safety and Health)
- Dr. Canice Nolan (European Commission – Agriculture, Fisheries, Food Safety and Consumer Affairs Section)
- Dr. William Slikker (US FDA National Center for Toxicological Research)
- Dr. Jean-Marc Vidal (European Medicines Evaluation Agency)
- Dr. Doug Weed (NIH National Cancer Institute)
- Dr. Harold Zenick (US EPA National Health and Environmental Effects Research Laboratory)

Due to travel schedules, Drs. William Farland (US EPA Office of the Science Advisor and Office of Research and Development) and Vicki Dellarco (US EPA Office of Pesticide Programs) were unable to join the panel. However, their input was integrated into panel remarks by Dr. Zenick, who served as the moderator of the government forum.

Prior to the forum, panelists were asked to assess the importance and potential impact of projects within HESI's current scientific portfolio. Dr. Zenick presented the results of this informal survey. Results indicated a substantial divergence of opinion.

While triggering some initial surprise, it was agreed on closer examination that the disparity reflected the multi-sector government representation on the panel, as well as the broad-based, international composition of the HESI membership with whom these panelists work. In fact, the panelists suggested that a far more surprising outcome would have been survey results that demonstrated a convergence of opinions. Such an unlikely conclusion would indicate that these very diverse agencies share common priorities and concerns on a project-by-project basis, which is rarely the case.

Panelists shared perspectives on those science-based safety and risk assessment issues that are the highest priorities for their respective agencies. Recommendations were offered regarding how these priorities could be addressed by HESI. The most critical observations focused on the need for HESI to better emphasize the impact of its projects on public health and to translate science to address more societal concerns. The panel agreed that HESI plays an important, and sometimes unique, role in improving the science associated with approaches to safety and risk assessment through its "tripartite" approach.

There was strong agreement among all who attended the government forum that the session provided a good opportunity for meaningful dialogue. Initial feedback from those who attended the forum indicates that the session should be repeated at future HESI annual meetings. HESI solicits input on the session and welcomes suggestions on improvements to the format. To provide feedback or request information, contact Mr. J. David Sandler, Senior Branch Administrator and Scientific Program Manager, at dsandler@ils.org.

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developmental immunotoxicology and the challenges inherent in identifying effects in children. He concluded that, based on existing data, a consensus developmental immunotoxicology screening protocol is warranted and that testing in children, while not easy, is possible.

Human Relevance of Rodent Liver Tumors

Dr. Jim Klaunig (Indiana University School of Medicine) presented the outcome of a May 2004 HESI workshop held at EPA facilities in Research Triangle Park, NC. The human relevance of rodent liver tumors (RLTs), while not a current focus of a standing HESI committee, was developed as a "special project" to build on previous HESI efforts. Concern about the issue is based on a recognition that RLTs are the most common neoplasm observed following

chronic chemical exposure. The HESI workshop extended the mode-of-action (MOA) framework for the human relevance of RLTs to include the following MOAs: cytotoxicity, phenobarbital-like compounds, hormonal/receptor-mediated events, metal overload, and porphyria. Dr. Vicki Dellarco (US EPA Office of Pesticide Programs) provided perspectives on the significance of this project. She noted that a manuscript is being prepared that will identify those rodent liver MOAs common among chemicals and define both the key events (what is known) and the remaining issues (what needs to be done). Dr. David Jacobson-Kram (US FDA Center for Drug Evaluation and Research) provided FDA perspectives on RLTs. He emphasized that carcinogenicity is seldom a "drug approvability" issue; that the highest concern is for genotoxic carcinogens because

nongenotoxic carcinogens are thought to have thresholds; and that most tumors result from exaggerated pharmacologic responses, hormonal imbalance, or immune suppression.

Participant feedback from the HESI State-of-the-Science session was overwhelmingly positive. The Board of Trustees and staff will continue to feature the scientific accomplishments of mature HESI committees, as well as government perspectives on these programs, at future annual meetings. For more information about the State-of-the-Science session at the 2005 HESI Annual Meeting, contact Mr. J. David Sandler, Senior Branch Administrator and Scientific Program Manager, at dsandler@ils.org.

HESI Emerging Issues for 2005

The HESI Emerging Issues process provides a mechanism by which new scientific programs related to human health and environmental safety can be identified. In the fall of 2004, HESI surveyed its corporate membership and key contacts in academia, government, and the public sector to identify emerging scientific issues of public health concern and interest to the chemical, agrochemical, petrochemical, pharmaceutical, biotechnology, and consumer products industries. Suggested topics were chosen by the Emerging Issues Steering Committee (EISC) using the following criteria:

- Basic science issues related to safety assessment
- Emerging methods and technologies with applications to safety assessment
- Regulatory initiatives, current industry concerns, and/or significant public health issues with opportunity for scientific input

The EISC culled down a list of over 30 proposals, and selected the following topics for potential exploration in 2005. These topics were presented at the HESI emerging issues meeting during the January 2005 HESI annual meeting in New Orleans:

- Assessing and Addressing Health Risk: Attributable Risk as a Complement to Risk Assessment

- Environmental Risk Assessment of Pharmaceuticals: Development of Science-Based Strategies to Assess Environmental Risk
- Development of Methods for a Tiered Approach to Assess the Bioaccumulation of Chemicals
- State of the Art of Hepatotoxicity Testing
- Relevance and Follow-up of Positive Results in In Vitro Genetic Toxicology Testing

These five topics were then prioritized by the EISC on February 28, 2005. Based on survey results and member interest, the following new projects will be addressed by HESI in 2005:

- Development of Methods for a Tiered Approach to Assess the Bioaccumulation of Chemicals
- Relevance and Follow-up of Positive Results in In Vitro Genetic Toxicology Testing

For further information about the emerging issues process or the selected topics for 2005, contact Dr. Michael Holsapple, HESI Executive Director, at mholsapple@ils.org.

2004 HESI Annual Report Available on HESI Website

HESI's 2004 Annual Report is available online. This resource includes comprehensive information about HESI's structure, membership, board of trustees, technical committees, project committees, subcommittees, programs, activities, publications, meetings, and external scientific presentations in 2004. The HESI Annual Report can be viewed and downloaded at http://hesi.ils.org/file/heis_ar04.pdf, or may be accessed on the HESI home page at <http://hesi.ils.org>.

2005 HESI Annual Meeting Posters Online

At the January 2005 HESI Annual Meeting in New Orleans, HESI presented 17 posters, detailing the activities and accomplishments of HESI technical committees, project committees, and subcommittees. The HESI posters can be viewed and downloaded at <http://hesi.ils.org/info/infolist.cfm?infolist=104>.

HESI to Host European Workshop on Risk Assessment Framework Approaches

On November 14–16, 2005, HESI will hold a public workshop on framework approaches to risk assessment at Le Meridien Hotel in Nice, France. The objective of this 3-day meeting is to demonstrate how science-based safety assessment is advanced through cooperative government, academic, and industry partnerships. This model, routinely employed by HESI, is the basis for three HESI project areas to be addressed at the workshop: Biological Significance of DNA Adducts, Rodent Liver Tumors as Predictors of Human Cancer Risk?, and Agricultural Chemical Safety Assessment. Each session will feature an overview of HESI's activities on the topic, pre-

sentations from international experts, and panel discussions that include government, academic, and industry scientists from the United States and Europe. Participants may opt to register for one, two, or all three sessions. The meeting is open to participants from industry, academia, and government worldwide. The workshop program will be of interest across sectors, and diverse perspectives will be offered. HESI encourages participation from HESI colleagues, as well as those interested in learning more about HESI programs. For registration information, contact Ms. Candice Hamilton-Parker, Senior Program Assistant, at chamilton@ils.org.

HESI Communicates Science

Publications

Akerman, GS, Rosenzweig, BA, Domon, OE, McGarrity, LJ, Blankenship, LR, Tsai, CA, Culp, SJ, MacGregor, JT, Sistare, FD, Chen, JJ, and Morris, SM. 2004. Gene expression profiles and genetic damage in benzo(a)pyrene diol epoxide-exposed TK6 cells. *Mutat. Res.* 549, 43-64.

Brent, RL. 2004. Utilization of juvenile animal studies to determine the human effects and risks of environmental toxicants during postnatal developmental stages. *Birth Defects Res., Part B, Dev. Reprod. Toxicol.* 71, 303-320.

Collins, JJ, Bukowski, JA, Weed, DL, Brent, RL, Klein, P, Boerstoele-Streefland, M, Sprafka, M, Lavin, AL, Murphy, PA, and Anderson, SA. 2004. Evaluating emerging issues in epidemiology. *Environ. Health Perspect.* Submitted.

Dickinson, DA, Warnes, GR, Quievryn, G, Messer, J, Zhitkovich, A, Rubitski, E, and Aubrecht, J. 2004. Differentiation of DNA reactive and non-reactive genotoxic mechanisms using gene expression profile analysis. *Mutat. Res.* 549, 29-41.

Doerr, NG, and Holsapple, MP. 2004. Integration of biomonitoring exposure data into the risk assessment process. *Risk Policy Report*, December 4, 2004, Vol. 11, Number 12, pp. 33-35.

Holsapple, M, Burns-Naas, LA, Hastings, K, Ladics, GS, Lavin, AL, Makris, S, Yang, Y, and Luster, M. 2005. A proposed testing framework for developmental immunotoxicology (DIT). *Toxicol. Sci.* 83, 18-24.

Hu, T, Gibson, DP, Carr, GJ, Torontali, SM, Tiesman, JP, Chaney, JG, and Aardema, MJ. 2004. Identification of a gene expression profile that discriminates indirect-acting genotoxins from direct-acting genotoxins. *Mutat. Res.* 549, 5-27.

Hurt, ME, Daston, G, Davis-Bruno, K, Feuston, M, Silva Lima, B, Makris, S, McNERNEY, ME, Sandler, JD, Whitby, K, Wier, P, and Cappon, GD. 2004. Juvenile animal studies: testing strategies and design. *Birth Defects Res., Part B, Dev. Reprod. Toxicol.* 71, 281-288.

Müller, A, Boitier, E, Le Fèvre, AC, Hu, T, Carr, GJ, Marchandeaude, JP, Flor, M, Jefferson, F, Aardema, MJ, and Thybaud, T. 2004. Intra- and inter-laboratory variability does not preclude identification of hydroxyurea molecular signature. *Environ. Mol. Mutagen.* In press.

Slikker, W, Jr, Andersen, ME, Bogdanffy, MS, Bus, JS, Cohen, SD, Conolly, RB, David, RM, Doerr, NG, Dorman, DC, Gaylor, DW, Hattis, D, Rogers, JM, Setzer, RW, Swenberg, JA, and Wallace, K. 2004a. Dose-dependent transitions in mechanisms of toxicity. *Toxicol. Appl. Pharmacol.* 201, 203-225.

Slikker, W, Jr, Andersen, ME, Bogdanffy, MS, Bus, JS, Cohen, SD, Conolly, RB, David, RM, Doerr, NG, Dorman, DC, Gaylor, DW, Hattis, D, Rogers, JM, Setzer, RW, Swenberg, JA, and Wallace, K. 2004b. Dose-dependent transitions in mechanisms of toxicity: case studies. *Toxicol. Appl. Pharmacol.* 201, 226-294.

Weaver, JL, Chapdelaine, JM, Descotes, J, Germolec, D, Holsapple, MP, House, R, Lebec, H, Meade, J, Pieters, R, Hastings, KL, and Dean, JH. 2005. Evaluation of a lymph node proliferation assay for its ability to detect pharmaceuticals with potential to cause immune-mediated drug reactions. *J. Immunotoxicol.* In press.

Presentations

Dellarco, V (EPA Office of Pesticide Programs), January 31, 2005. An Improved Testing Paradigm for Pesticide Chemicals—An Overview of the HESI Agricultural Chemical Safety Assessment (ACSA) Proposal. Side Meeting to the OECD Workshop to Advance Worksharing of Agricultural Pesticide Reviews, Washington Hilton Hotel, Washington, DC.

Doerr, NG (HESI), February 24, 2005. Activities of the HESI Technical Committee on Integration of Biomonitoring Exposure Data into the Risk Assessment Process. Meeting of the Strategic Science Team of the American Chemistry Council Long-Range Research Initiative, Arlington, VA.

Holsapple, MP (HESI), March 15, 2005. ILSI HESI Perspective on Innovative Drug Safety Evaluation in 2015. Symposium on "Innovative Drug Safety Evaluation." Inauguration of the new Johnson & Johnson PRD Drug Safety Evaluation Center, Beerse, Belgium.

Holsapple, MP (HESI), March 16, 2005. ILSI HESI Activities on Non-Clinical / Clinical Safety Correlations. EC/EFPIA Workshop on "Improved Predictivity of Safety Evaluation—Predictive Toxicology," Brussels, Belgium.

Robison, SH (Procter & Gamble Company), March 21-22, 2005. The HESI Technical Committee on Integration of Biomonitoring Exposure Data into the Risk Assessment Process. First Meeting of the NAS National Research Council (NRC) Committee on Human Biomonitoring for Environmental Toxicants, Washington, DC.

Slikker, W, Jr (FDA National Center for Toxicological Research), David, RM (Eastman Kodak Company), Doerr, NG (HESI), February 9, 2005. Dose-Dependent Transitions in Mechanisms of Toxicity. Monthly Teleconference of the Society of Toxicology Risk Assessment Specialty Section.

Workshops, Roundtables, Symposia

HESI Immunotoxicology Technical Committee, February 9, 2005. Clinical Immunotoxicity Testing Workshop. Wilmington, DE.

HESI Protein Allergenicity Technical Committee, February 22-24, 2005. International Bioinformatics Workshop. Mallorca, Spain.

HESI a Visible Scientific Presence at 2005 SOT Annual Meeting

The March 2005 Annual Meeting of the Society of Toxicology (SOT) in New Orleans presented HESI with an ideal venue to broadly communicate its scientific accomplishments, work products, and consensus views. At the HESI/ILSI booth at the SOT ToxExpo, Board members and staff talked with colleagues from government, academia, and industry. More formal mechanisms for communication at the SOT meeting included the following HESI-sponsored events:

Continuing Education Courses (sponsored by HESI Technical Committee on Development and Application of Biomarkers):

- “Something Old, Something New: Traditional and Novel Biomarkers of Renal Injury.” PM11. Co-chaired by S. Emeigh Hart (AstraZeneca) and C. Faherty (HESI).
- “Cardiac Drug Toxicity in Pharmaceutical Discovery and Development.” AM06 and PM12.

Workshop (sponsored by HESI Technical Committee on Development and Application of Biomarkers): “The Development and Application of Biomarkers of Toxicity.” Co-chaired by C. Faherty (HESI) and J. Dean (sanofi-aventis).

Risk Assessment Specialty Section Panel Discussion (HESI Project Committee on Dose-Dependent Transitions in Mechanisms of Toxicity): “Dose-Dependent Transitions in Mechanisms of Toxicity.”

Sunset Session. “Developmental Toxicology Evaluations: Issues with Including Neurotoxicology and Immunotoxicology Assessments.” M.P. Holsapple (HESI)—member of panel.

Workshop (organized by the Steering Committee of the HESI Rodent Liver Tumor Workshop): “Mode of Action in Relevance of Rodent Liver Tumors to Human Cancer Risk.” Co-chaired by Y. Dragan (FDA/NCTR) and M.P. Holsapple (HESI).

Poster Presentation (HESI Technical Committee on Integration of Biomonitoring Exposure Data into the Risk Assessment Process.): “Integration of Biomonitoring Exposure Data into the Risk Assessment Process” (Abstract #1291).

Poster Presentation (HESI Protein Allergenicity Technical Committee): “Evaluation of IP Mouse Models for Assessing the Allergenic Potential of Proteins” (Abstract #1307).

Luncheon Roundtable (sponsored by HESI Nanomaterial Safety Subcommittee): “Conducting a Comprehensive Toxicological and Safety Evaluation of Nanomaterials: Current Challenges and Data Needs.” Co-chaired by W. Farland (EPA) and M.P. Holsapple (HESI).

HESI Board Member Achievements

Members of the HESI Board of Trustees are leaders in the scientific community. We are pleased to share with you their latest achievements.

Dr. Jay I. Goodman (Michigan State University) was invited to present the John Barnes Award Lecture at the March 2005 British Toxicology Society meeting at the University of Warwick, Coventry, UK.

Dr. Nobuyuki Ito (Nagoya City University Medical School), former HESI Board member, received the Education Award from the Society of Toxicology at its March 2005 Annual Meeting in New Orleans, LA.

HESI Staff News

Dr. Michael P. Holsapple has been elected Councilor to the Society of Toxicology Council for the period 2005-2007. Enjoy, Mike!

In November 2004, **Dr. Amy L. Lavin** left HESI to join her husband in Stuttgart, Germany. A fond farewell and best of luck to Amy and her family!



HESI is pleased to welcome its newest staff member. **Dr. Ciaran J. Faherty** earned a bachelors degree in biochemistry and a doctoral degree in pharmacology at the University of Galway, Ireland. At St. Jude Children's Research Hospital in Memphis, TN, Ciaran investigated modes of cell death in models of neurodegeneration, including Parkinson's disease. More recently, Ciaran returned to the UK to obtain an MBA degree at the University of Leicester. Ciaran joined HESI as a scientific program manager in January 2005. He can be reached at cfaherty@ilsa.org.

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The ILSI Health and Environmental Sciences Institute (HESI) provides an international forum for understanding scientific issues related to human health, toxicology, risk assessment, and the environment. HESI is a non-profit organization, established in 1989 as a global branch of the International Life Sciences Institute (ILSI). HESI is independently chartered from ILSI, with its own Board of Trustees. Worldwide membership is drawn from the chemical, agrochemical, petrochemical, pharmaceutical, biotechnology, and consumer products industries, with member companies based in the United States, Europe, and Japan. HESI provides an objective forum for initiating dialogue among industry, government, and academic scientists with different perspectives and expertise. Industry members provide primary financial support for HESI programs, but HESI also receives financial and in-kind support from a variety of US and international government agencies.

The mission of HESI is to stimulate and support scientific research and educational programs that contribute to the identification and resolution of health and environmental issues of concern to the public, scientific community, government agencies, and industry. For more information about HESI, consult <http://hesi.ilsilsi.org>.