HESI Emerging Issues Session

Dr. Hal Zenick
(US EPA)
EIC Chair

Dr. Ruth A. Roberts
(AstraZeneca R&D)
EIC Vice Chair

HESI Annual Meeting
11 June 2014
Washington, DC

ILSI Health and
Environmental Sciences
Institute

Today's Session

- Learn about HESI's approach to identifying emerging science priorities.
- Hear about new project areas initiated in 2013-2014 within existing HESI scientific committees.
- Consider four new proposals for possible HESI action.
- Engage in discussion on opportunities for the future.

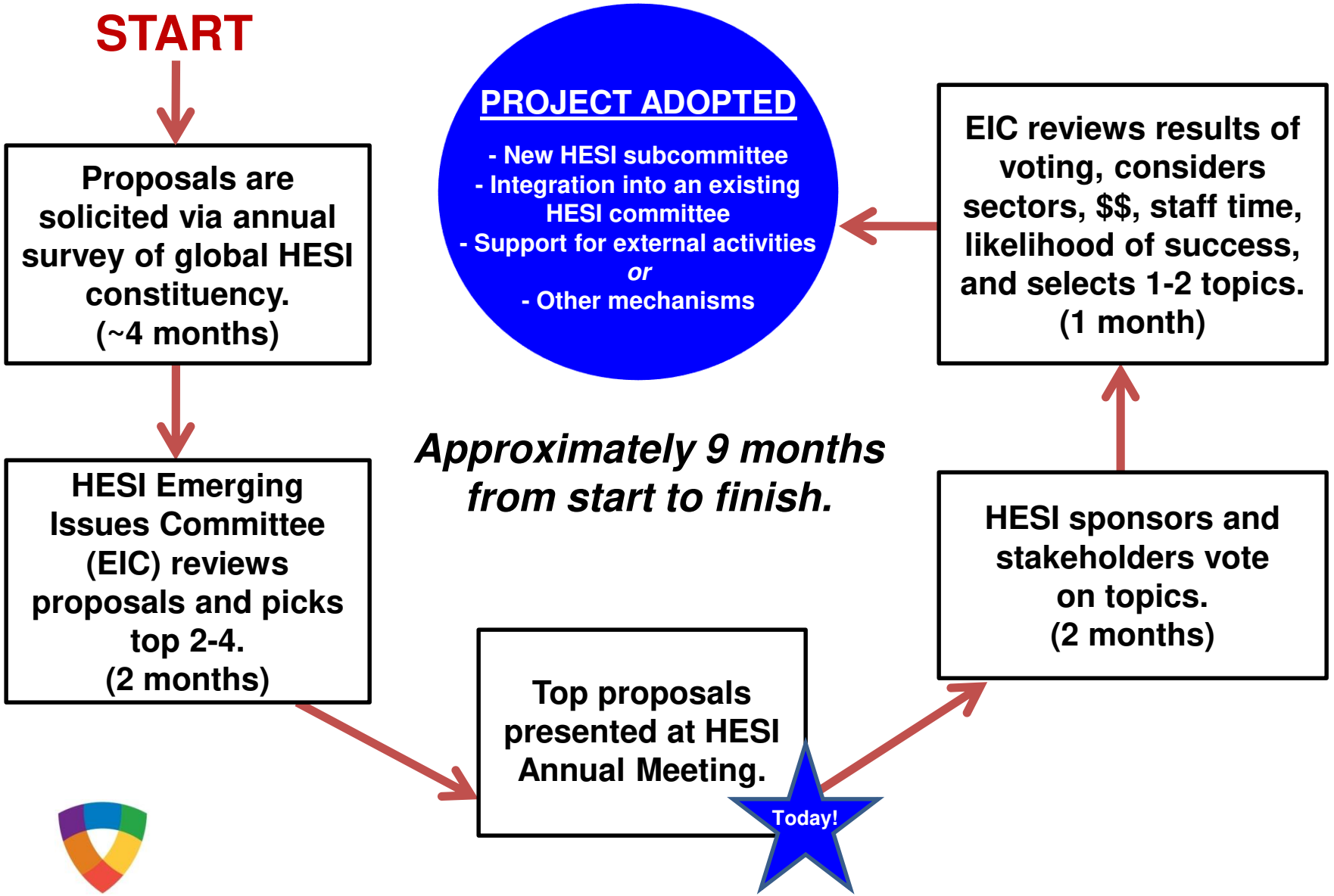
ABOUT THE EIC

What Is the EIC?

- Independent, elected science advisory body that reports to the HESI Board of Trustees.
- Composed of a Chair, Vice Chair, Past Chair, and Science Advisors from the public and private sectors
  - Chair and Vice Chair must be a public/private sector team
- Administers the Emerging Issues (EI) process – HESI's traditional and longest-standing project adoption process.
- Scopes the science landscape for new HESI opportunities in conjunction with the HESI Board Program Strategy and Stewardship Committee (PSSC).

PROJECT MECHANISMS

HESI Emerging Issues Proposal Solicitation Process



Criteria for Identification and Prioritization of Emerging Issues

1. **The issue should be a priority for a broad cross-section (academia, industry, government) of the scientific community and should have current public health significance.**

2. **HESI's efforts to address the issue will have measurable scientific impact.**

3. **Proprietary and product-specific issues will not be considered. Proposals should not include lobbying or advocacy components.**

4. **HESI's efforts to address the issue should not be duplicative of other groups.**

Other HESI Project Mechanisms

- **Resources-at-Initiation (RAI) process**
  - For well-defined and time-sensitize projects.
  - Includes a requirement for dedicated funding up front by project submitters.
  - Requires tripartite engagements.
  - Must fit within HESI's mission.
- **Integration into existing HESI scientific committees**
  - Must be directly relevant to the mission and objectives of the targeted committee.
  - Should augment the current research portfolio of the committee.
  - Must be approved for adoption by the targeted committee.

Three HESI Pillars

KNOWLEDGE TO APPLICATION:
Implementing fit-for-purpose scientific programs, engaging diverse stakeholders and disciplines.

GLOBAL VISION:
Engaging in and supporting global initiatives that recognize that science has no borders.

HESI

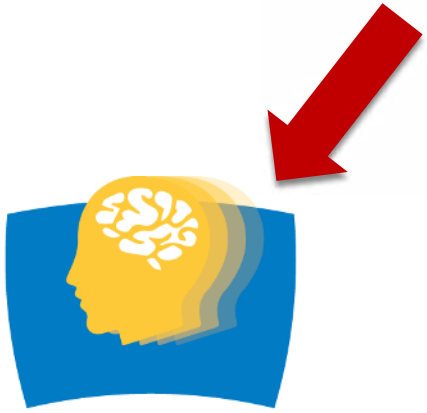
FUTURE LEADERS:
Providing training, awards, and mentorship to foster the skills needed to meet the challenges of modern safety sciences.

PILLAR: Knowledge to application

Implementing fit-for-purpose scientific programs, engaging diverse stakeholders and disciplines.

Emerging Science Scoping Fund

Funds made available to the HESI Emerging Issues Committee for enhancing identification and recruitment of emerging science *(e.g., scoping, identifying players and approaches, supporting external activities).*



Other Mechanisms

- FAST Fund
- Open Access Fund
- CITE outreach and programs

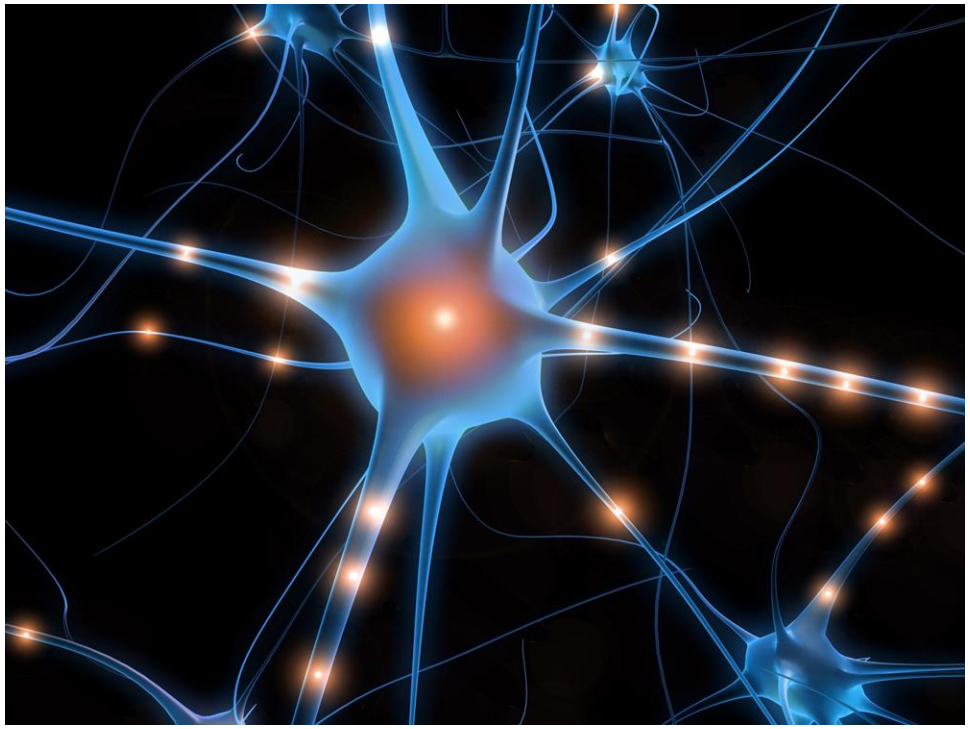
HESI Scoping Exercises 2013-2015

June 2013 HESI Annual Meeting – Breakout groups at last year's Emerging Issues Session resulted in formation of scoping teams on the following issues:

- **Framework for intelligent non-animal alternative methods for safety assessment** *(**Status**: EI proposal submitted; will hear more today)*
- **A new exposure science emerging from new demands, technology, and big data** *(**Status**: EI proposal submitted; will hear more today)*
- **Evaluation of diseased animal models in nonclinical safety assessments** *(**Status**: Pharma companies continue to scope)*
- **Workshop: Incorporating an ecosystem services perspective into the Cumulative Effects Assessment process** *(**Status**: EIC leadership and staff to scope this summer)*

UPDATE:
Emerging Issues Subcommittee on Translational Biomarkers of Neurotoxicity

Dr. Ruth A. Roberts (AstraZeneca, R&D)



Subcommittee on Translational Biomarkers of Neurotoxicity

Co-Chairs:

Dr. Ruth Roberts, AstraZeneca
Dr. Merle Paule, FDA
Dr. David Calligaro, Lilly

HESI Staff:

Ms. Jennifer Pierson, Program Manager
Mr. Alex Keller, Program Associate
Mr. Kyle Brunette, Program Associate

Mission and Scope

- To identify biomarkers for improving the prediction of neurotoxicity
- Neurotoxicant of interest: Trimethyl tin
- Metrics may include imaging, histopathology, electrophysiology (e.g., EEG), behavioral analyses.
- Biomarkers of interest:
  - Fluidic biomarkers (from serum, urine, CSF)
  - microRNAs
  - Metabolome
  - Cytokines and chemokines
  - Isoprostanes
  - Proteomic screening of serum

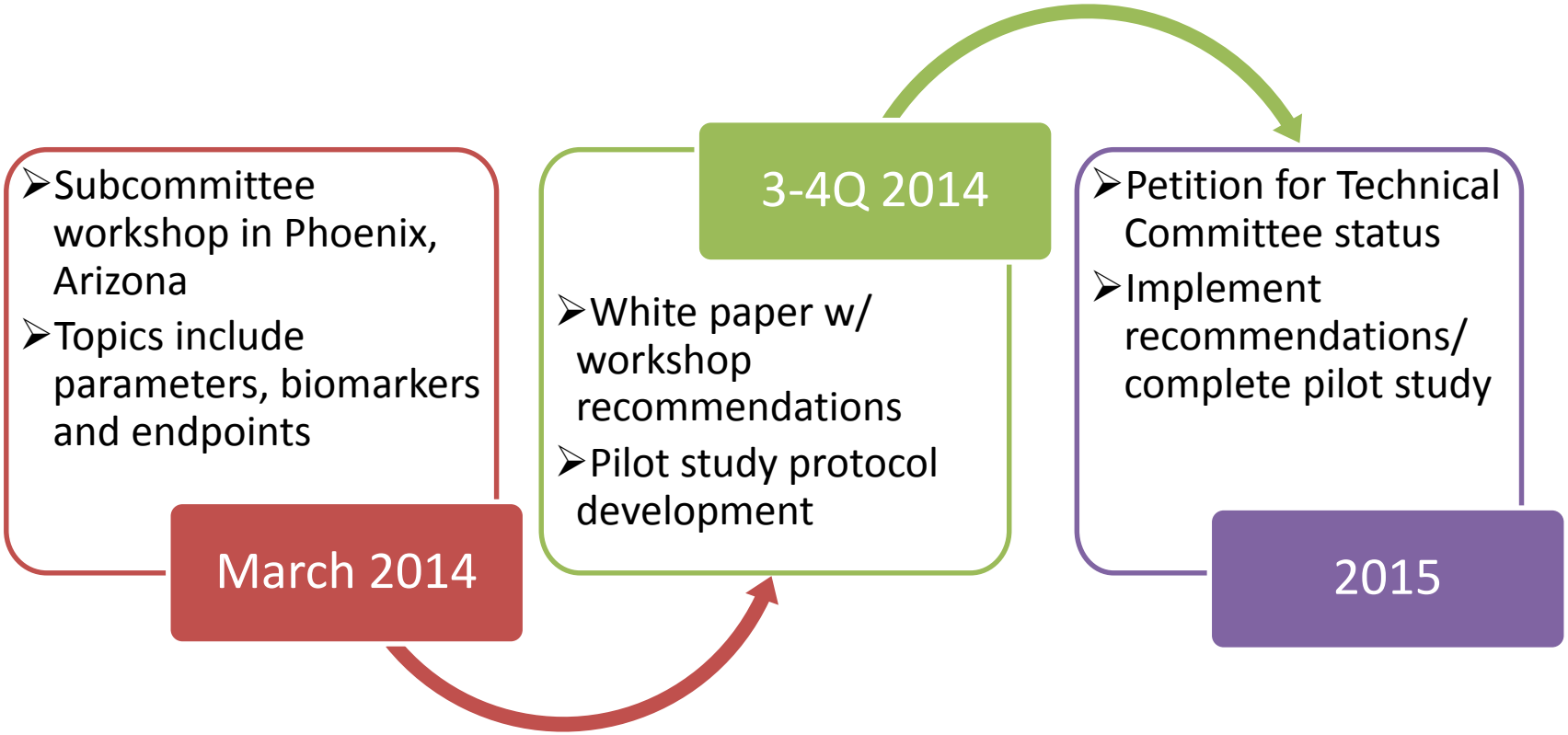
Activities

- Initial in-person meeting held March 2013.
- Regular monthly webinars with informative state-of-the-science presentations.
- Workshop convened March 2014.
- White paper under development.
- Pilot study protocol initiated.
- EUROTOX 2014 session proposal accepted.
- JSOT 2014 abstract submitted.

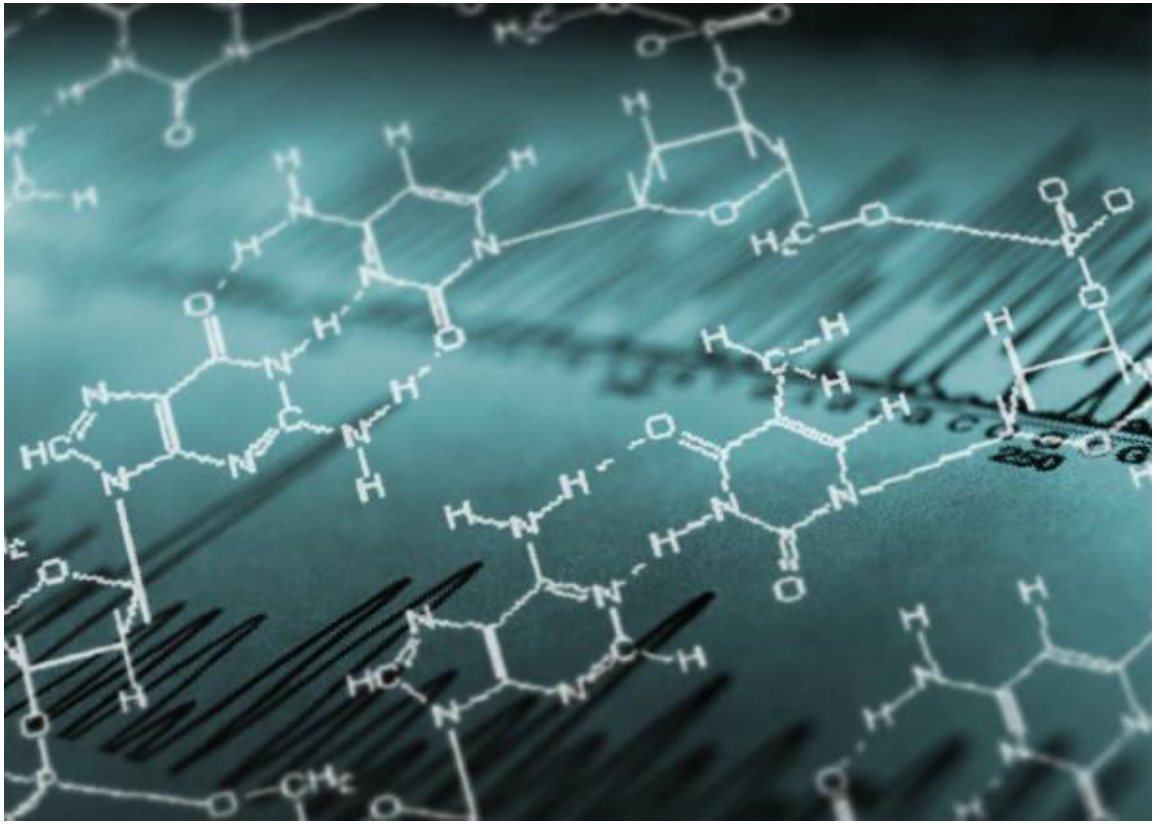
EUROTOX SYMPOSIUM

EUROTOX Symposium Speakers	Session Title
Neurotoxicity in drug discovery: importance & assessment	Ruth Roberts, AstraZeneca
Fluid-based biomarkers of neurotoxicity	Andreas Jeromin, Quanterix
Neurobehavioural assessment of neurotoxicity	Will Redfern, AstraZeneca
Magnetic resonance histology	Al Johnson, Duke University
Neuropathology as an endpoint	Alys Bradley, UK Consultant Pathologist

Next Steps for Translational Biomarkers of Neurotoxicity Subcommittee



ENHANCEMENT OF THE HESI SCIENTIFIC PORTFOLIO



New Science at HESI: 2013-2014

New science also arises from work taken on by HESI's 13 committees.

2014 HESI Scientific Portfolio

Technical Committees

- Animal alternatives in environmental risk assessment
- Application of genomics to mechanism-based risk assessment
- Biomarkers of nephrotoxicity
- Cardiac safety
- Developmental and reproductive toxicology (DART)
- Development of methods for a tiered approach to assess bioaccumulation of chemicals
- Genetic toxicology
- Immunotoxicology
- Protein allergenicity
- Risk assessment in the 21st century (RISK21)
- Sustainable chemical alternatives
- Use of imaging for translational safety assessment

Emerging Issues Subcommittees

- Translational biomarkers of neurotoxicity

New Science at HESI

A high-level visualization of the landscape of HESI's new science across existing committees from 2013 to 2014.

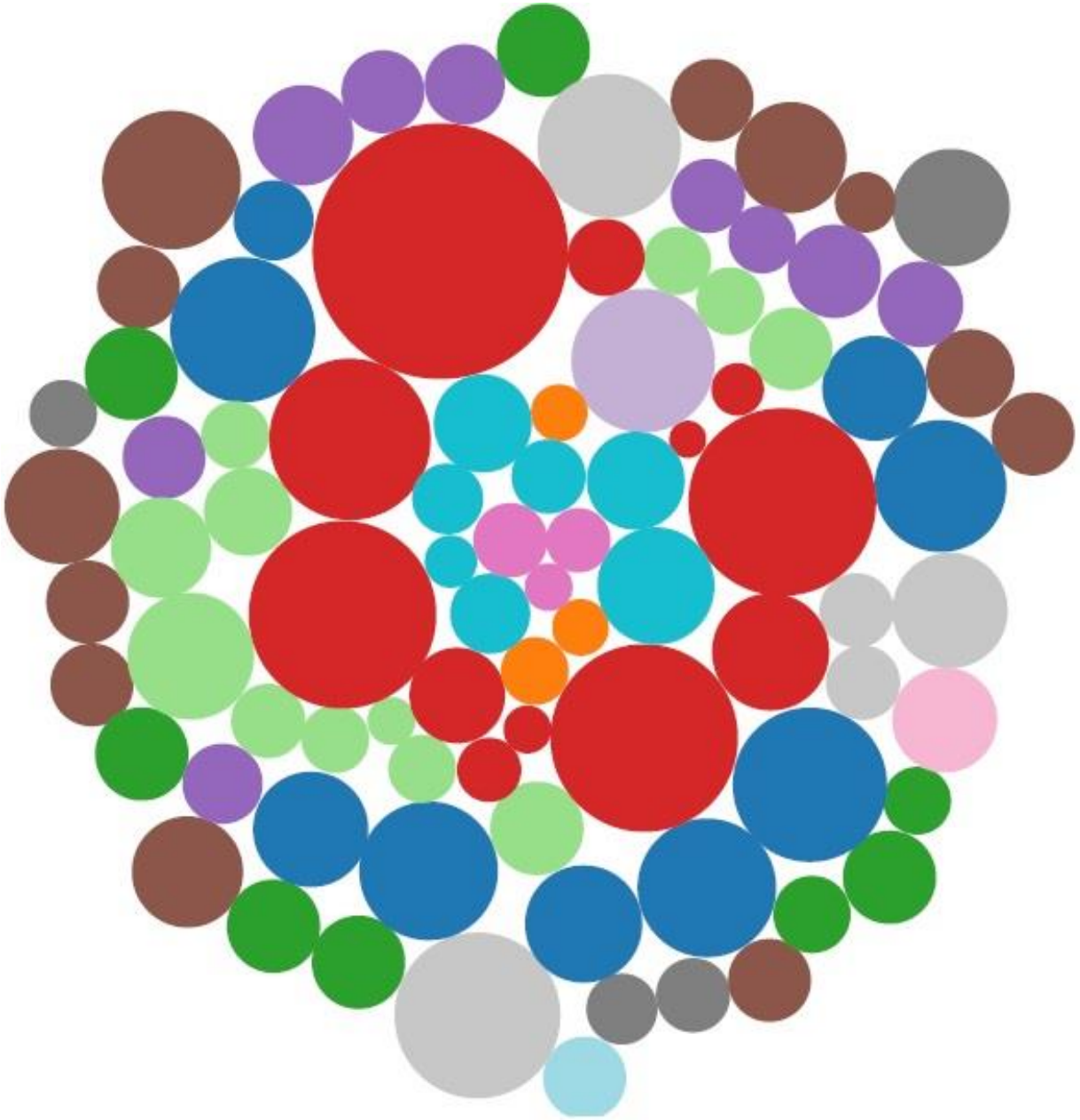
A few examples on the next few slides:

- Used Tableau software
- Key words
- Group size
- Color-coded by committee

Now that preliminary data are entered in the software, HESI can use this tool to:

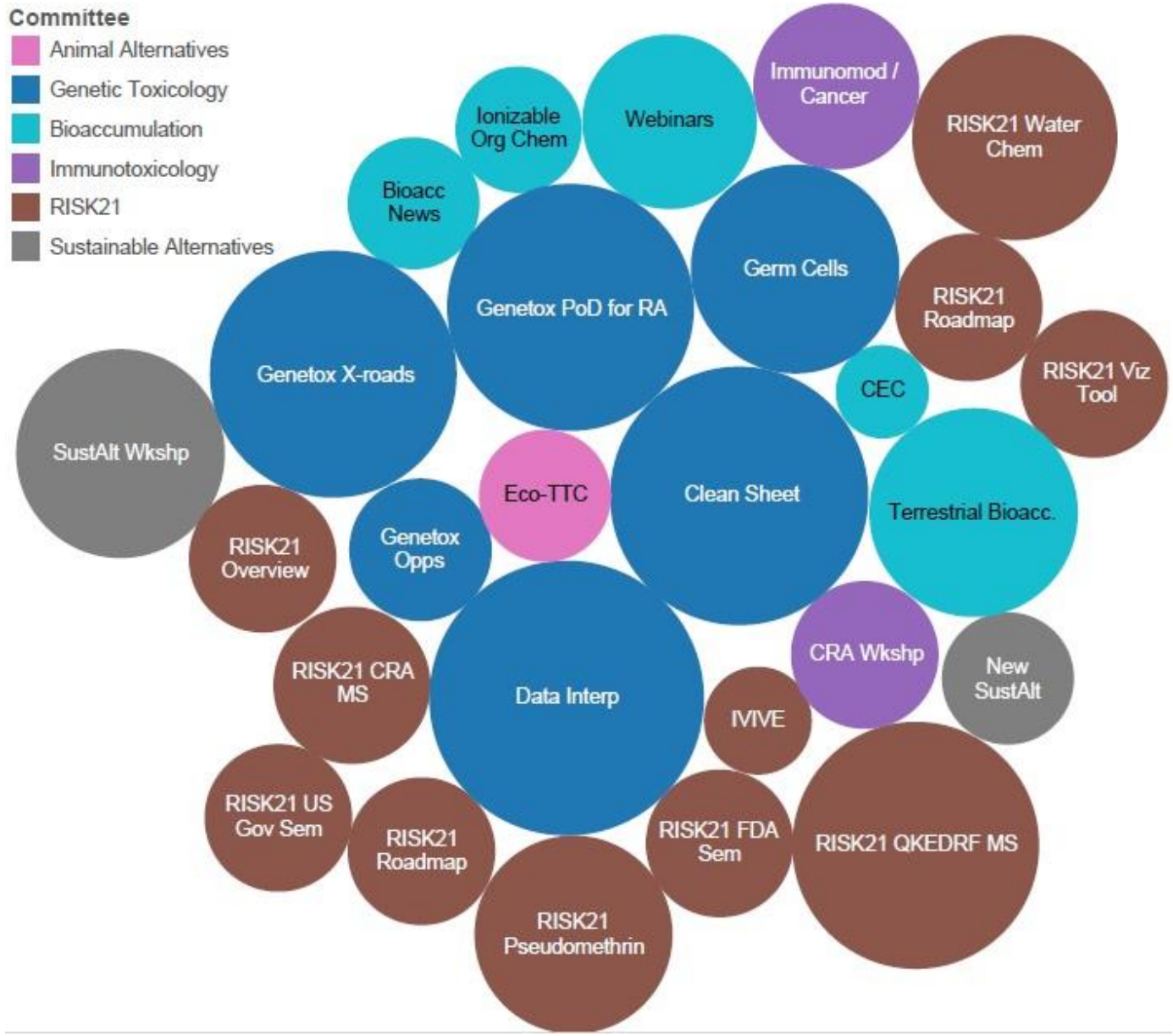
- Track projects and project types over time.
- Determine scientific portfolio priorities and needs.
- Many other possible uses!

2013 – 2014: All new projects *(more than 80!)*



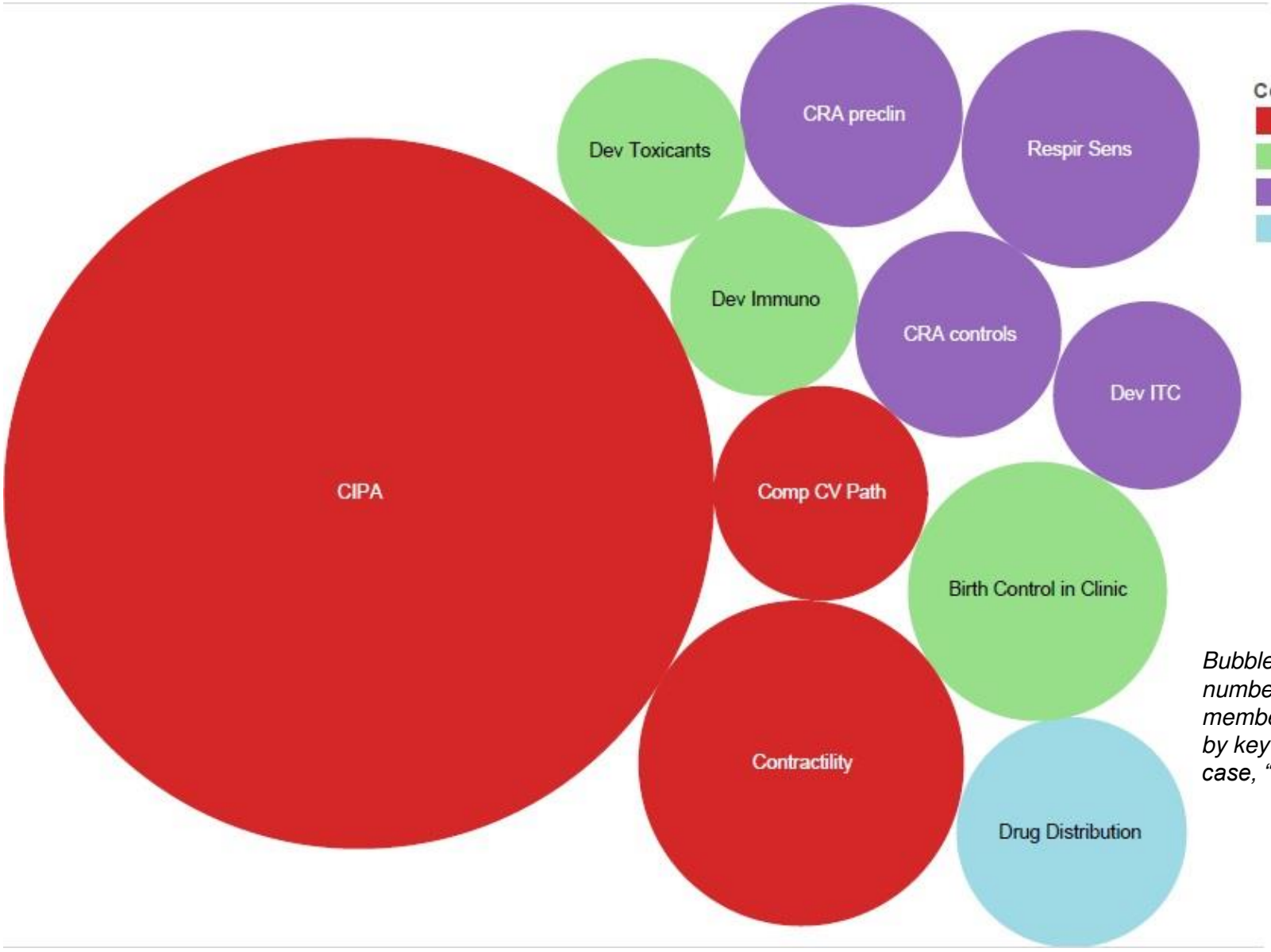
Bubble size reflects number of project members.

2013 – 2014: New risk assessment projects



Bubble size reflects number of project members. Data filtered by key words (in this case, "risk assessment").

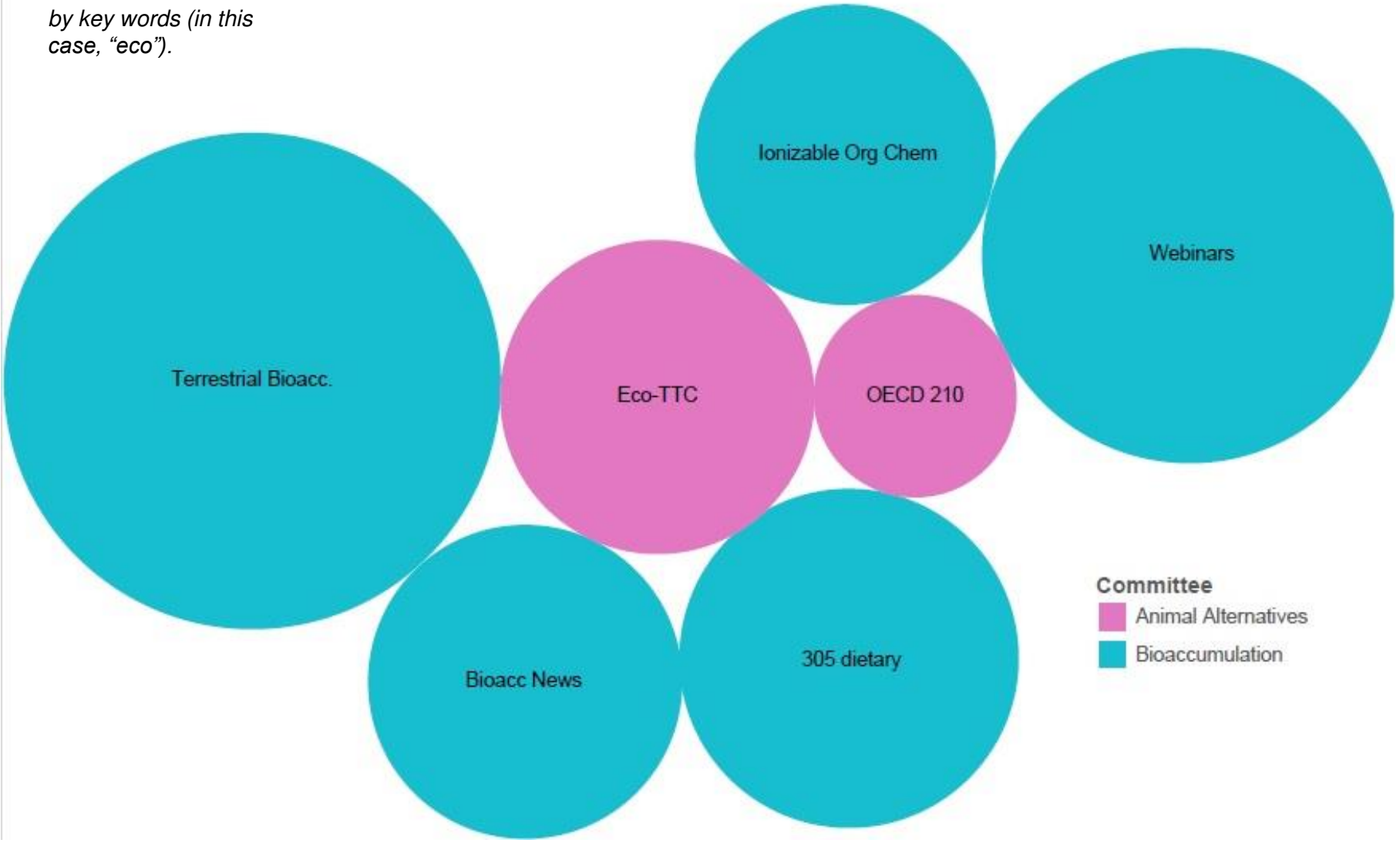
2013 – 2014: New projects engaged in translational work



Bubble size reflects number of project members. Data filtered by key words (in this case, "translational").

2013 – 2014: New projects engaged in eco work

Bubble size reflects number of project members. Data filtered by key words (in this case, "eco").



PROPOSALS

Proposals for HESI Consideration

Framework for intelligent non-animal alternative methods for safety assessment
Dr. Craig Rowlands, Dow Chemical Company
Prof. Alan Boobis, Imperial College London

Strategies to integrate exposure, PBPK models and data on metabolism to predict plasma levels of compounds and their metabolites that are directly comparable to in vitro toxicology results
Dr. Timothy Pastoor, Syngenta

A new exposure science emerging from new demands, technology, and big data
Dr. Rosemary Zaleski, ExxonMobil Biomedical Sciences

Environmental chemicals and low-dose non-monotonic dose-responses: Is there an impact on risk assessment based study design and interpretation?
Dr. Sue Yi, Syngenta
Dr. Rita Schoeny, US EPA

Next Steps

In early fall 2014, the HESI Emerging Issues Committee will select one or two topics for HESI action based on your prioritizations. *(Depends on budget and staffing resources.)*

ACTION: A prioritization form is in your Program Book. Please return the form to HESI staff today *OR* return the form to HESI by email or fax by 11 July 2014.

The prioritization form will be distributed electronically to all HESI stakeholders next week.

SCOPING THE SCIENTIFIC LANDSCAPE

Open Discussion

Ideas Submitted from Recent PSSC-EIC Survey

1. **Drug-induced liver toxicity (DILI)** – manifested in Phase II or III testing; not anticipated based on preclinical testing
2. **Energy** – sources (e.g., biofuels, fracking); risks; data for decision-making
3. **Ecosystem services**
4. **Sustainability** – dynamics / tradeoffs between environmental, economic and societal (health) factors
5. **Epigenetic changes during prenatal period**
6. **Is the 10x default safety factor for individual human sensitivity outdated?**
7. **Metabolic syndrome** – contribution and mechanism of genetics and the environment
8. **In vitro correlates to in vivo toxicity compendium**
9. **Exposure to low doses**
10. **Risk assessment of chemical mixtures in aquatic environments**
11. **Genomic assessment of microbes**
12. **dsRNA safety assessment**

EIC LEADERSHIP AND SCIENCE ADVISORS

2014-2015 EIC Leadership

(elected by the HESI Assembly on 10 June 2014)

CHAIR:

Ruth A. Roberts, PhD, FBTS, ATS, ERT, FRCPath

AstraZeneca R&D (term expires June 2016)

VICE CHAIR:

José Manautou, PhD, ATS Fellow

University of Connecticut (term ends June 2017)

PAST CHAIR:

Hal Zenick, PhD

US Environmental Protection Agency (term expires 2015)

2014-2015 EIC Public Sector Science Advisors

Newly elected Advisors

(terms end 2017)

Suzanne C. Fitzpatrick, PhD, DABT
US Food and Drug Administration

Timothy Gant, PhD
CRCE, Public Health England

George Gray, PhD
George Washington University
(re-elected)

Ronald N. Hines, PhD
US Environmental Protection Agency

Continuing Advisors

Toshihisa Ishikawa, PhD
NPO Personalized Medicine & Healthcare *(term ends 2015)*

James E. Klaunig, PhD, ATS
Indiana University
(term ends 2016)

Derek C.G. Muir, PhD
Environment Canada
(term ends 2016)

Dr. Flavio A.D. Zambrone
University of Taubaté / Planitox (Brazil)
(terms ends 2016)

2014-2015 EIC Private Sector Science Advisors

Newly elected Advisors
(terms end 2017)

Matthew S. Bogdanffy, PhD, DABT, ATS
Boehringer-Ingelheim

Jon C. Cook, PhD, DABT
Pfizer, Inc.

Andrew Glickman, PhD
Chevron Energy Technology Company

Continuing Advisors

Robert A. Barter, PhD
ExxonMobil Biomedical Sciences
(term ends 2015)

Ann M. Blacker, PhD, DABT
Bayer CropScience
(term ends 2016)

Daniel A. Goldstein, MD
Monsanto Company
(term ends 2015)

Michael Graziano, PhD, DABT
Bristol-Myers Squibb
(term ends 2016)

Kathleen A. Shelton, PhD
DuPont Haskell Global Centers for Health and Environmental Sciences
(term ends 2016)

Outgoing EIC Participants

(terms ending June 2014)

Thanks to all!

Dr. Stephen J. Newsholme ***(Past Chair)***
GlaxoSmithKline

Dr. Darlene Dixon
NIEHS

Dr. Jesse L. Goodman
Georgetown University Medical Center

Dr. Cynthia A. Afshari
Amgen Inc.

Dr. Patrick D. Guiney
SC Johnson & Son, Inc.

Thank you!