



HESI at 25 Years

A Platform for Science with Impact



Science never appears so beautiful as when applied to the uses of human life. Thomas Jefferson, 1798. Charlottesville, Virginia.

A hand holding a globe of the Earth against a blue sky with white clouds. The globe is painted with green and blue colors, representing land and water. The hand is positioned on the right side of the frame, with the fingers wrapped around the globe. The background is a bright blue sky with scattered white clouds.

Why HESI?

- Established 1989
- Expanded ILSI focus
- The tripartite, partnership forum to improve global health via chemical and drug safety.



1989

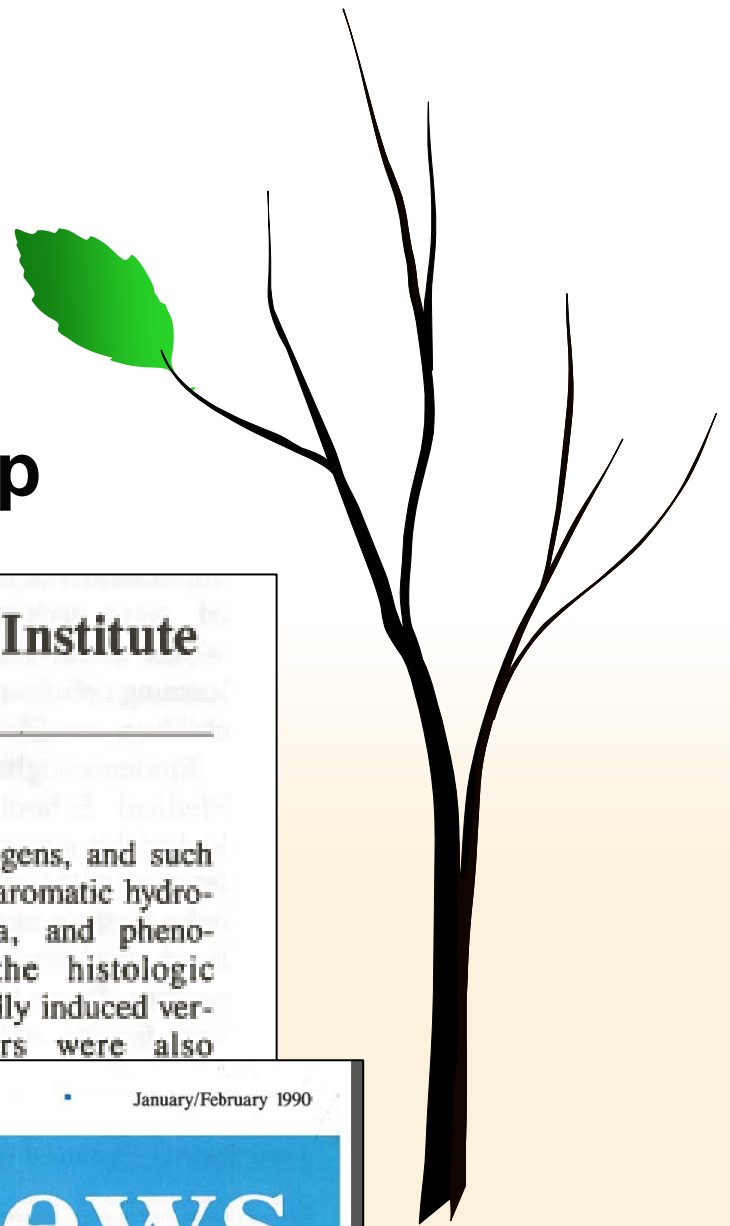
Rodent Liver Tumor Workshop

ILSI Health and Environmental Sciences Institute Hosts Workshop on Mouse Liver Tumors

Future Research Directions Suggested

Fourteen scientists from university, government, and industry laboratories and other facilities described their current research findings on mouse liver tumors at a November 14-15 workshop sponsored by the ILSI Health and Environmental Sciences Institute (HESI). The workshop was the first scientific forum convened by the recently established HESI, was held to

and nongenotoxic carcinogens, and such compounds as polycyclic aromatic hydrocarbons, ethylenethiourea, and phenobarbital. Studies of the histologic characteristics of chemically induced versus spontaneous tumors were also

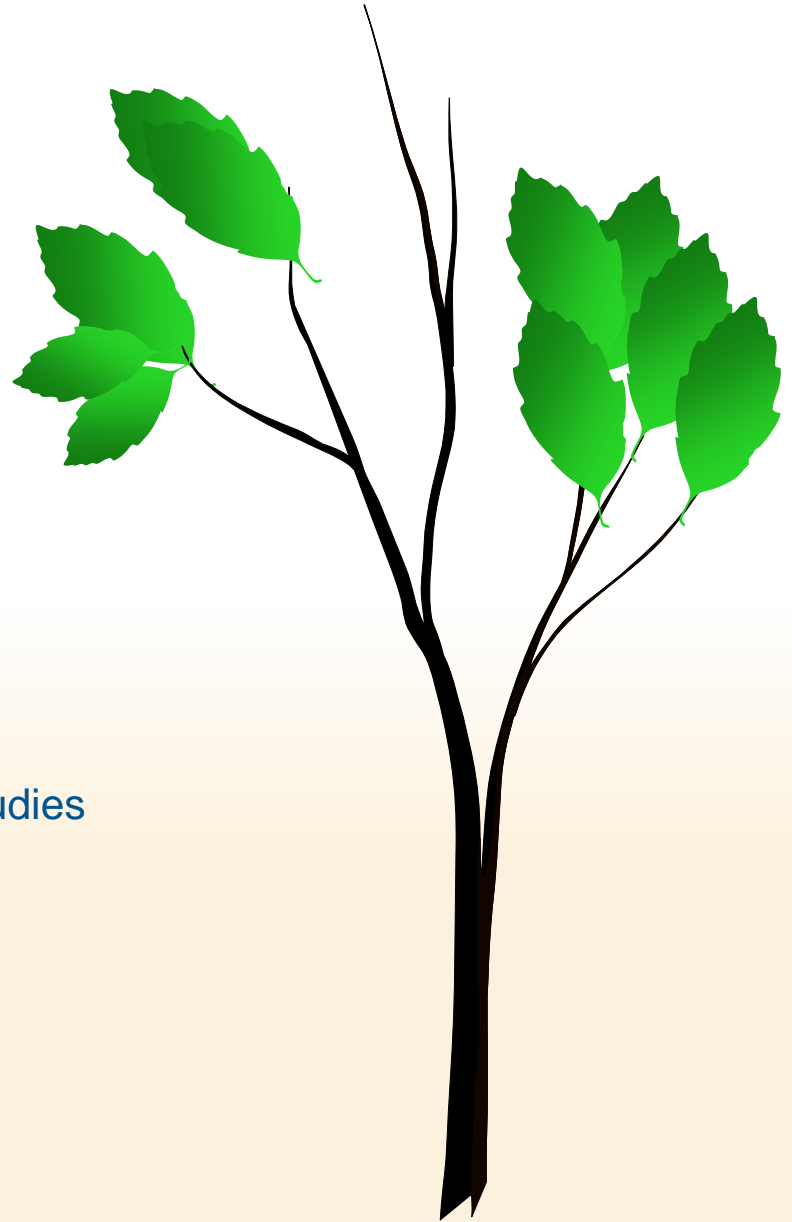




1999

12 Committees, ~20 projects

- Alternatives to Animal Testing for Eye Irritation
- Alternative Methods for Carcinogenicity Testing
- Developmental and Reproductive Toxicology
- Immunotoxicology
- Predictivity of Toxicity in Humans from Animal Studies
- Water Quality
- Aggregate Exposure Assessment
- Insect Resistance Management
- Genomics and Proteomics in Risk Assessment
- Use of Mechanistic Data in Risk Assessment
- Criteria for Evaluation of Epidemiology Studies
- Structure Activity Relationships Database

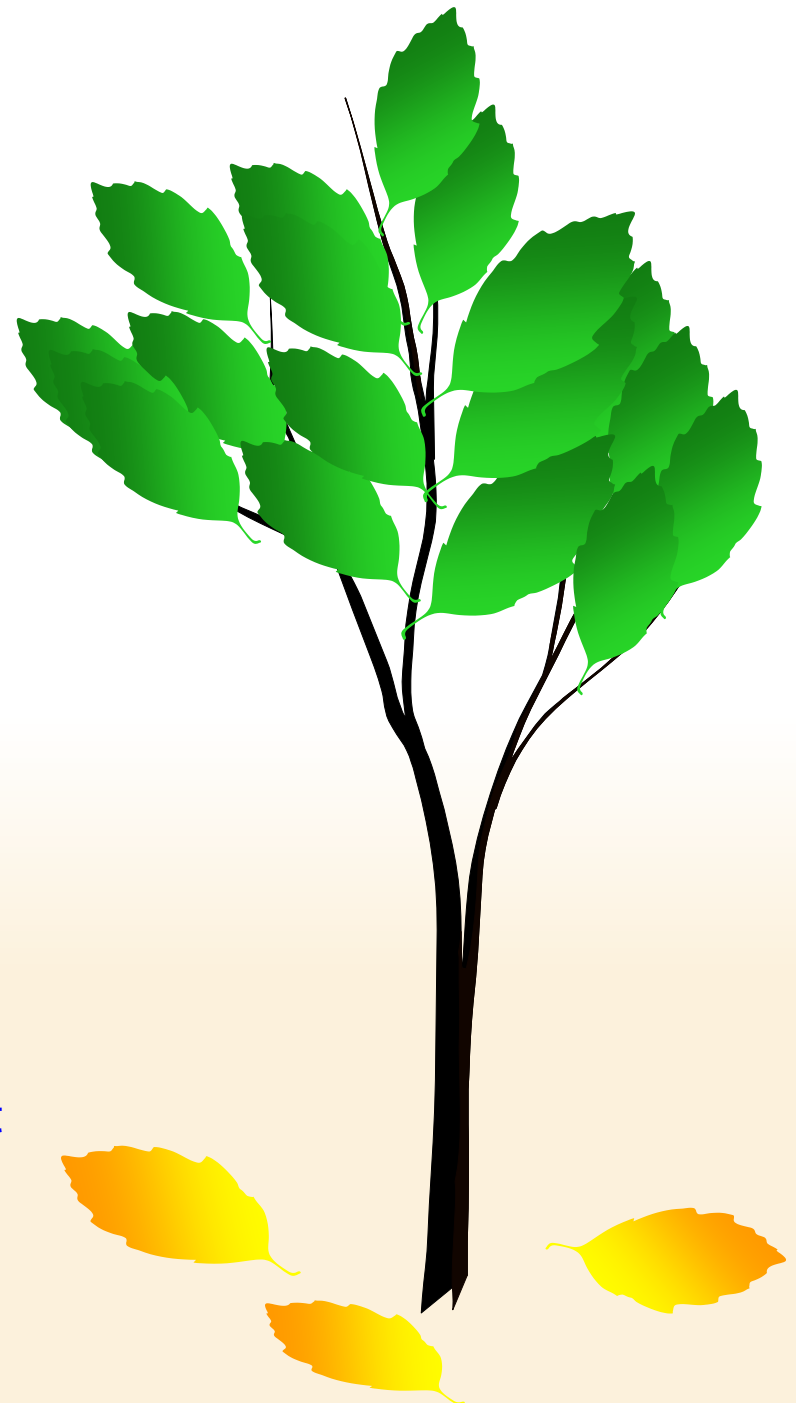




June 2014

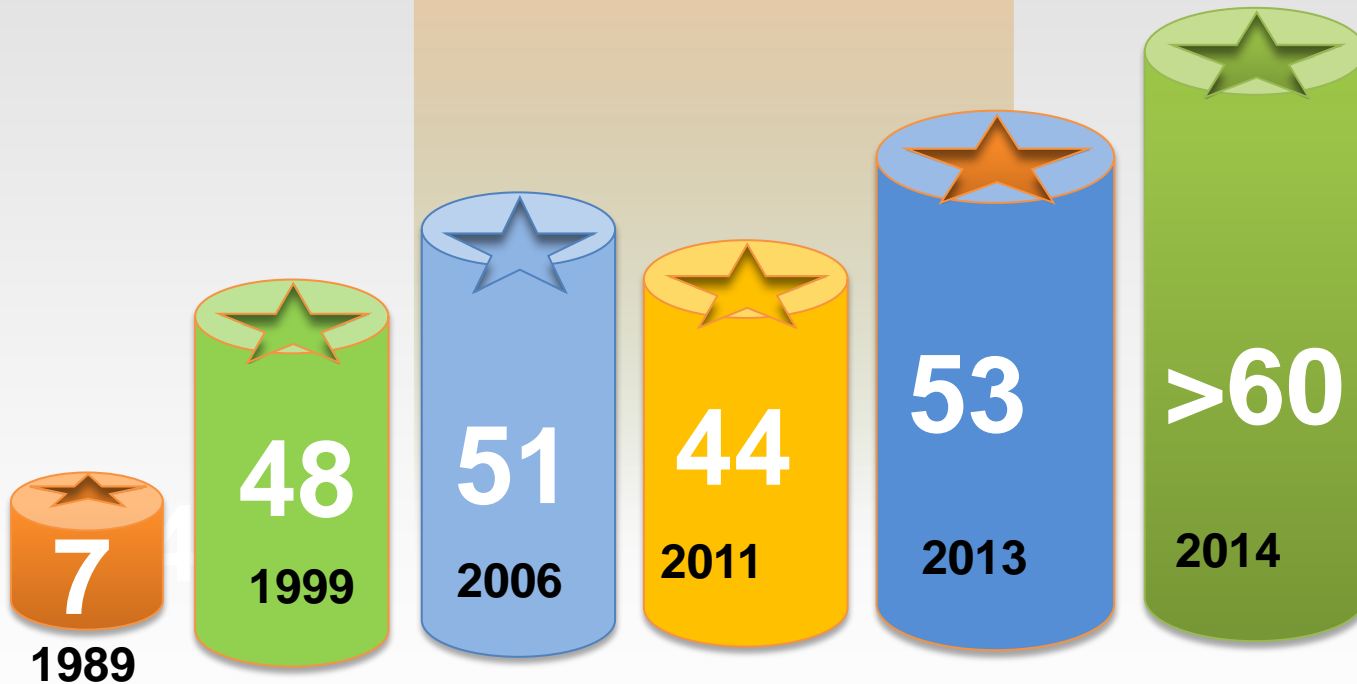
14 Committees, ~80 projects

- ❖ Nephrotoxicity
- ❖ Genetic Toxicology
- ❖ Immunotoxicology
- ❖ Cardiac Safety
- ❖ Developmental and Reproductive Toxicology
- ❖ Neurotoxicity Biomarkers
- ❖ Bioaccumulation
- ❖ Protein Allergenicity
- ❖ Animal Alternatives for Env. Risk Assessment
- ❖ Risk Assessment (RISK21)
- ❖ Sustainable Chemical alternatives
- ❖ Imaging for Safety Assessment
- ❖ Genomics



Number of Sponsor Organizations

Growth in Corporate Membership



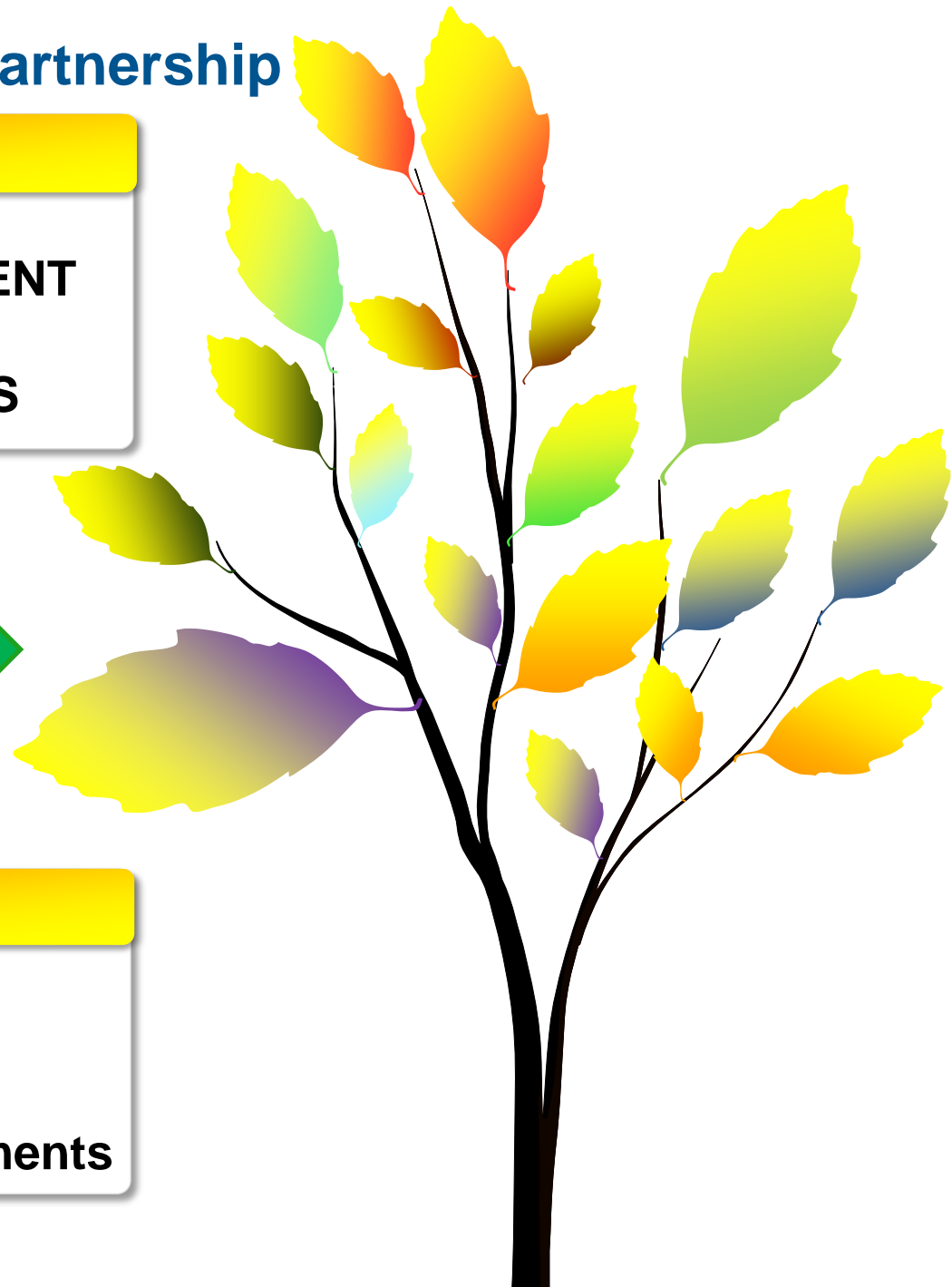
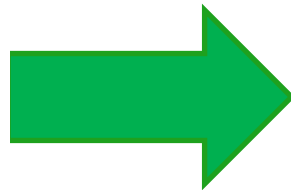
Year

25 Years of Diversifying Partnership



25 Years of Diversifying Partnership

ACADEMIA **GOVERNMENT**
INDUSTRY **NGOs**
FOUNDATIONS **HOSPITALS**



**In-kind, \$\$ support
for HESI science
from all sectors +
Formal collaborative agreements**



A Broad Reach Across Human and Environmental Health

**Accurate
and Efficient
Chemical
Risk
Assessment**

**Safe and
Effective
Medicines**

**Environmental
Quality and
Sustainability**

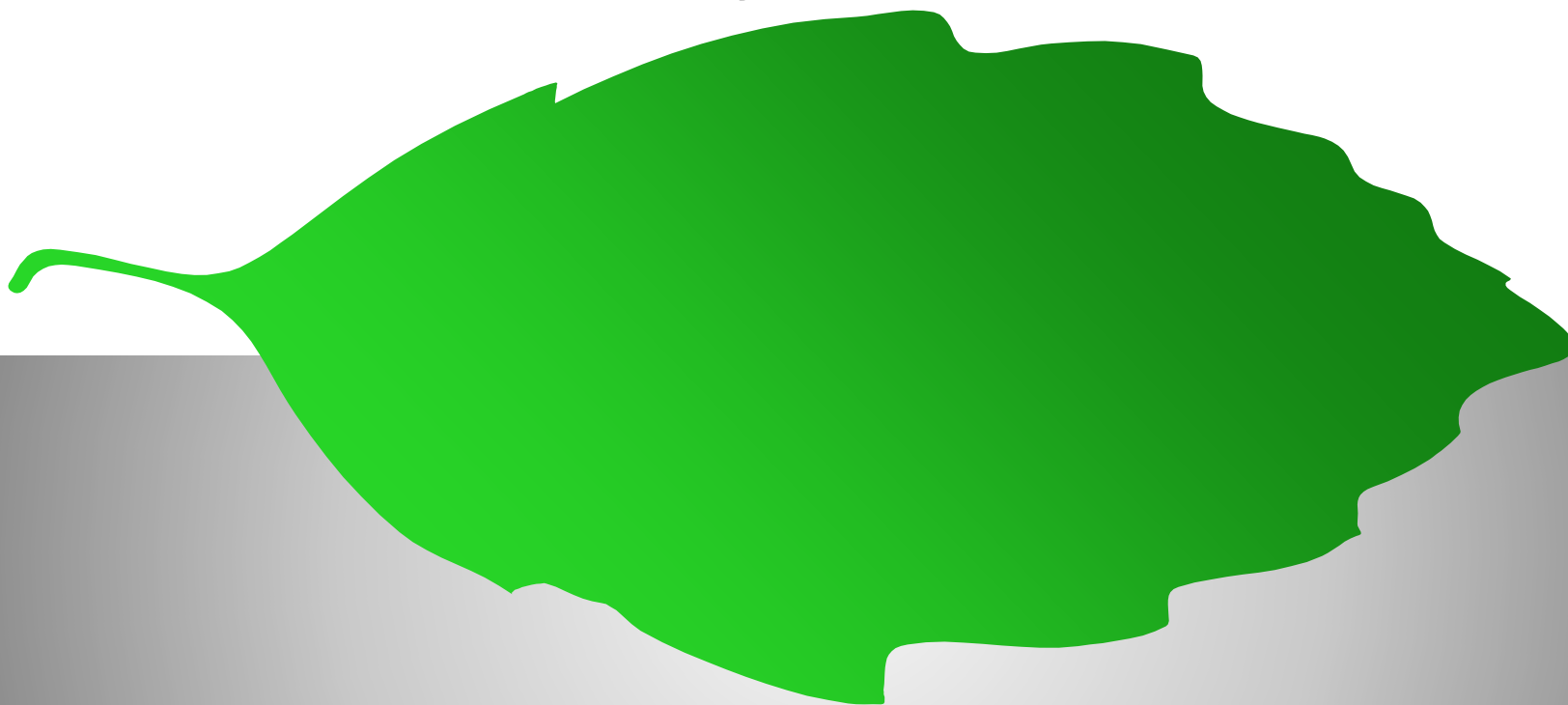
Food Safety





HESI's 25 Years of Success is ...

**More than just the
ability to produce
quality science...**





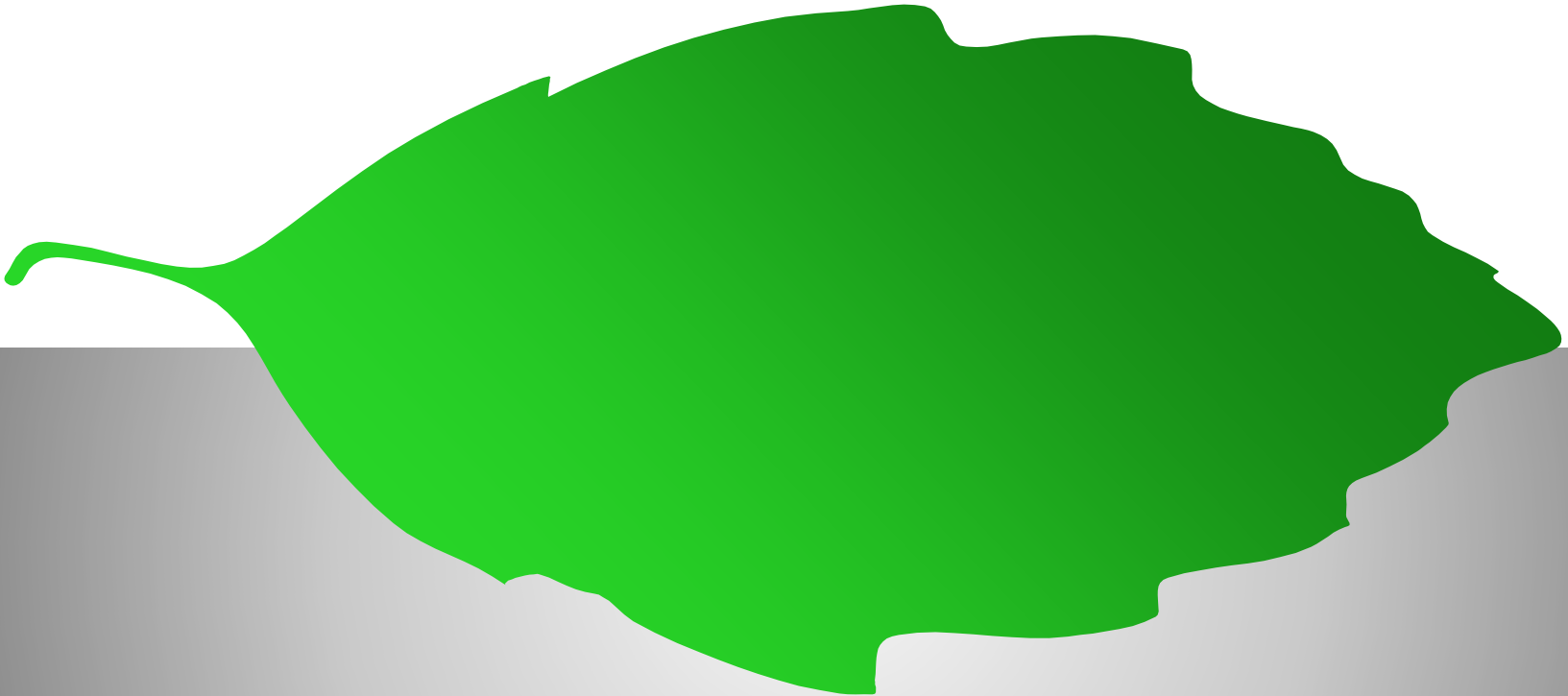
HESI's 25 Years of Success is...

**A unique ability to
bring together a
diverse set of
stakeholders &
perspectives...**



HESI's 25 Years of Success is...

**Framing technical questions
and executing initiatives to
that meet the need**



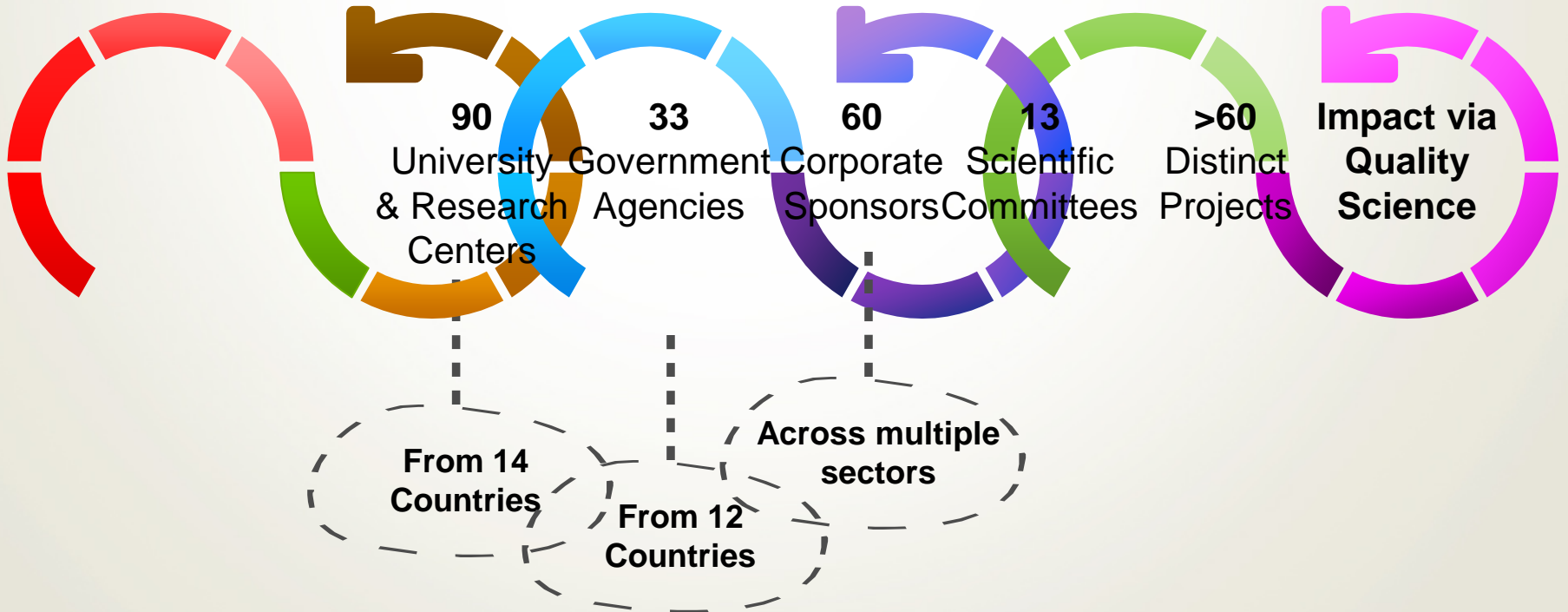


HESI's 25 Years of Success is...

Efficiently generating
the **RIGHT SCIENCE**
to improve
shared health & safety
challenges

In a survey of 150 HESI participants, **90%** said their experience with HESI has led them to a more positive view of the value of working in a collaborative team.

**25
Years**



4,625

Number of
times HESI
Publications
were cited
between 1994
& June 2013.

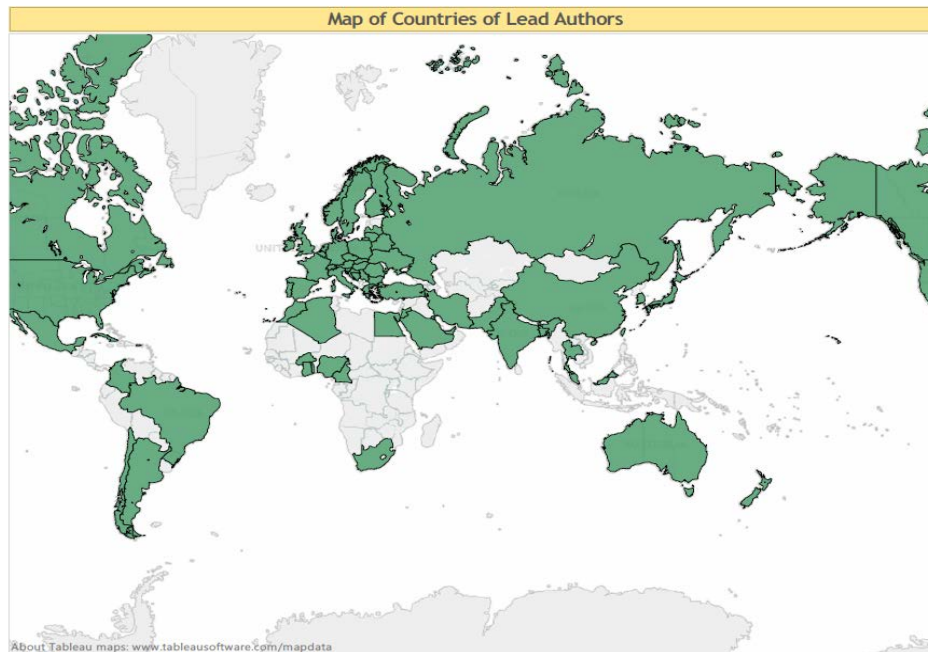
21.1
Average #
of times
each HESI
paper is
cited.

1096

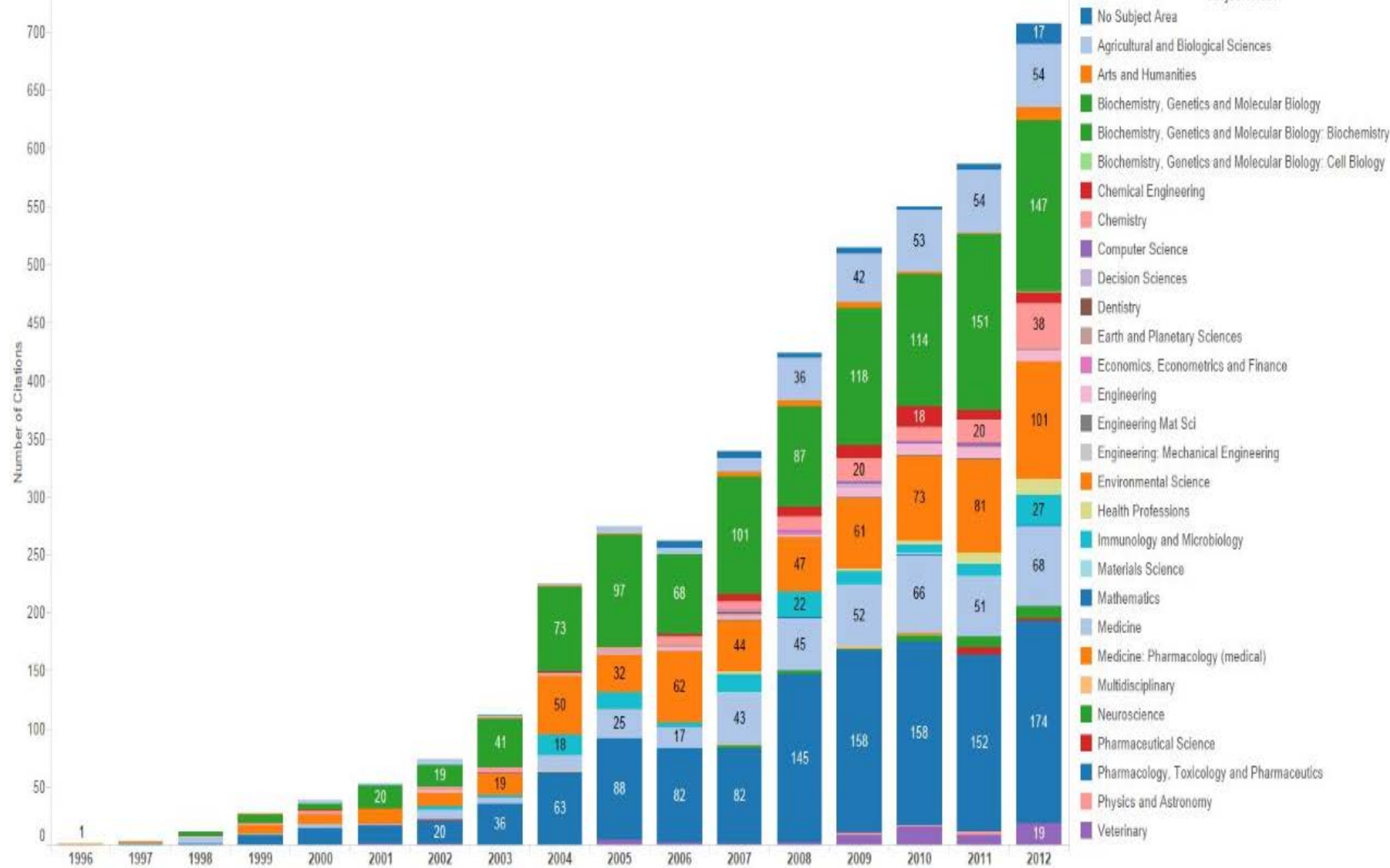
Number of journals citing
HESI publications

1373

Number of
different author
organizations that
cited HESI
papers



Subject Areas



Source: SCOPUS, 2013

Generating Relevant & Rigorous Science **For Stakeholders**



In a survey of 150 HESI participants...

HESI's scientific programs and publications have..

*Influenced their approach to safety or risk assessment
decision-making; **70%***

*Influenced their level of confidence in the use of
particular technologies, markers, endpoints, or analysis
approaches; **80%***



How?

A few examples..



*Creating frameworks to
integrate data and
decision-making*



**Prioritize risks,
Protect
ecosystems and
their inhabitants**



TOXICOLOGICAL SCIENCES **89**(1), 51–56 (2006)
doi:10.1093/toxsci/kfj001
Advance Access publication October 12, 2005

FORUM

Mode of Action in Relevance of Rodent Liver Tumors to Human Cancer Risk

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Timothy Pastoor,|| Vicki L. Dellarco,||| and Yvonne P. Dragan|||

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Articles

Toxicologic Pathology, 37: 714-732, 2009
Copyright © 2009 by The Author(s)
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DOI: 10.1177/0192623309343779

A Data-Based Assessment of Alternative Strategies for Identification of Potential Human Cancer Hazards

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⁶Private Consultant, Tairua, New Zealand

⁷BASF Corporation, Research Triangle Park, NC, 27709 USA

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¹¹Syngenta, Jealotts Hill, United Kingdom

ABSTRACT

The two-year cancer bioassay in rodents remains the primary testing strategy for in-life screening of compounds that might pose a potential cancer

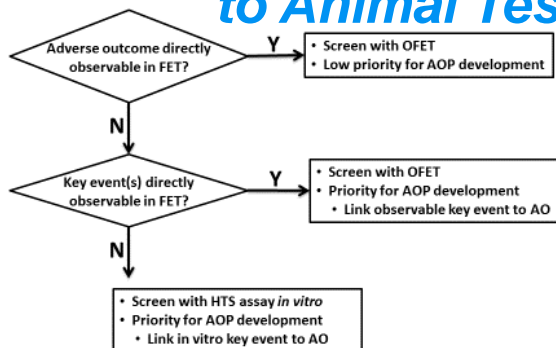
From HESI's First Program...

“The recommendations from these early HESI-EPA workshops **provided a foundation upon which to develop a mode of action (MOA) framework.** The IPCS defined the criteria for accepting a MOA as adequate for evaluating a specific tumor type in animals...subsequent work ...determined how MOA studies can be **used to establish the relevance of rodent tumors to humans.**”



Figure 3.

Integrating Alternatives to Animal Testing for Ecotox



Globally recognized HESI roadmaps to guide integration of data and decisions.

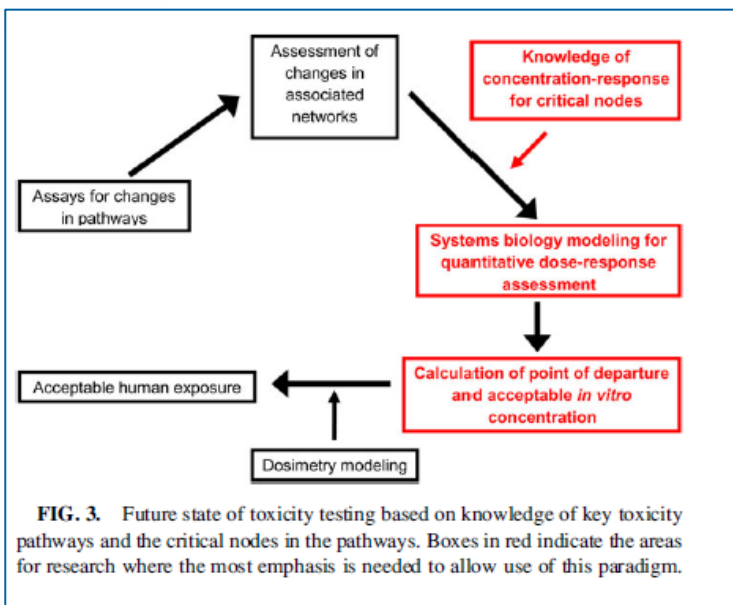
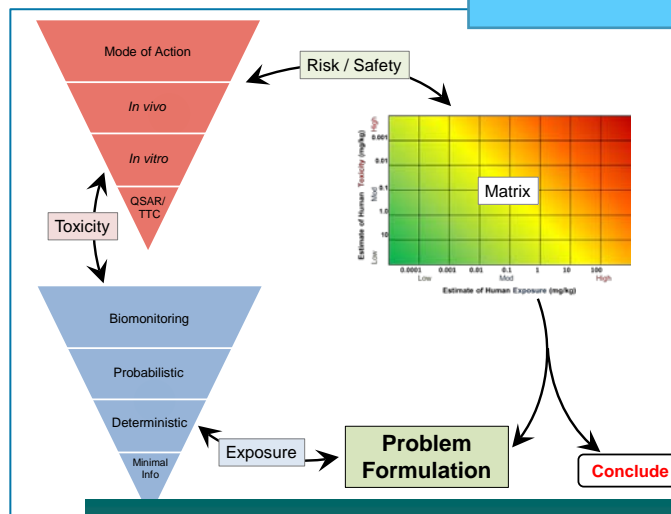
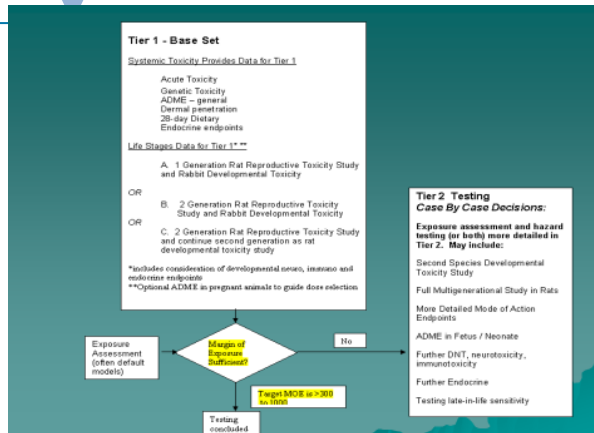


FIG. 3. Future state of toxicity testing based on knowledge of key toxicity pathways and the critical nodes in the pathways. Boxes in red indicate the areas for research where the most emphasis is needed to allow use of this paradigm.

Assessing Adverse vs Adaptive Transitions in Toxicity Pathways



Innovating Chemical Risk Assessment



Enhancing AgChem Safety



A spotlight on one of

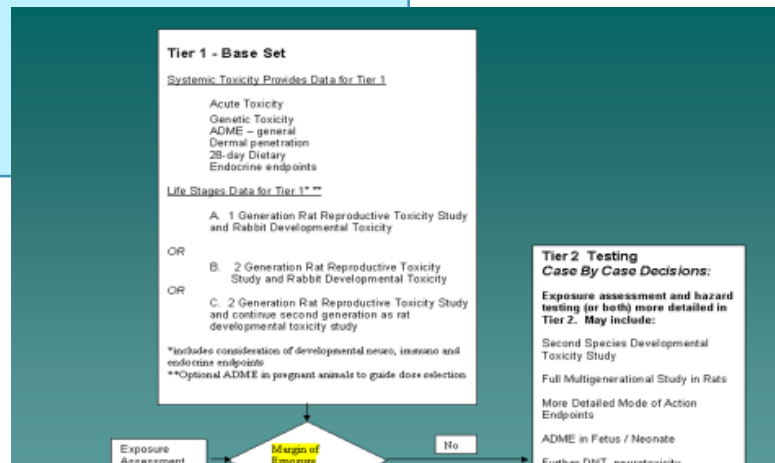
many...

US EPA Scientific and Technological Achievement Award (Honorable Mention)

UK National Center for the Replacement, Refinement, and Reduction of Animals in Research “Highly Commended Prize”

Impact cited in 2 National Academy reports

- Basis for OECD Guideline for Testing of Chemicals (443): Extended One-Generation Reproductive Toxicity Study
- Canine study requirement dropped in EPA Pesticide guidelines;
- Increased use of ADME to enhance dose selection



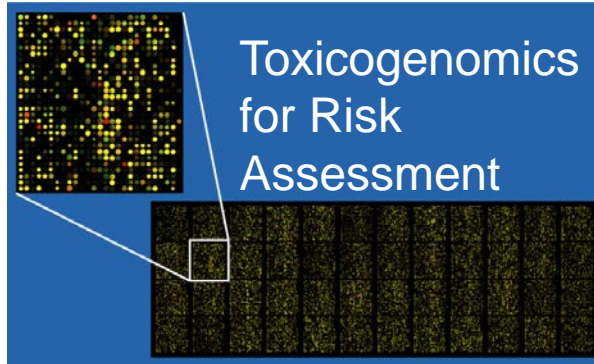


*Enhancing the
predictive relevance of
experimental studies*



**Safer medicines for
patients,
safer products for the
public & environment**

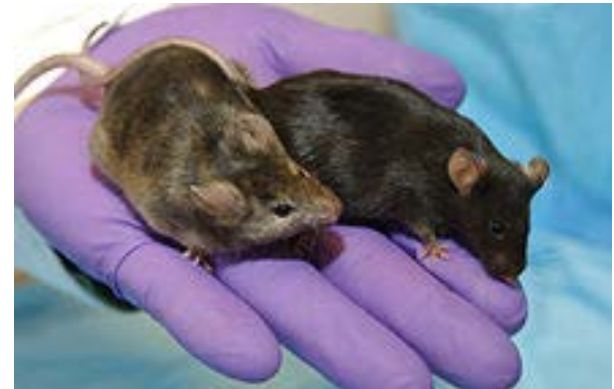
Informing discovery & decision-making with new technologies



- First large scale TGx experimental program, first public array/tox dbase
- Led to adoption of data standards, genomic biomarkers
- Resource for strengths & limitations of TgX use for safety

- \$33M collaborative effort
- Critical data on predictivity of available transgenic models
- Data underpins current guidelines on alternatives to 2 year mouse bioassay
- Improved prediction of safety

Transgenic Models for Cancer Risk Assessment





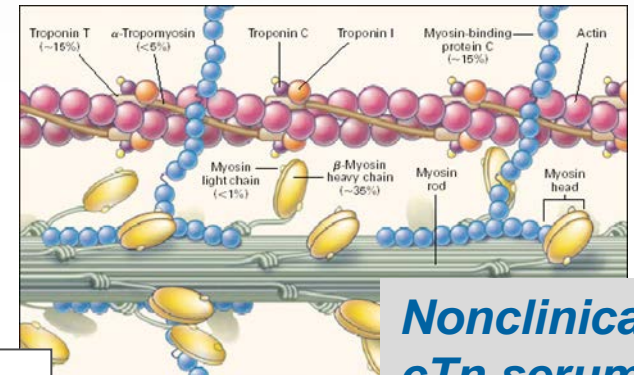
Translating from animal to human, and back to improve relevance

HESI Approach to Biomarkers

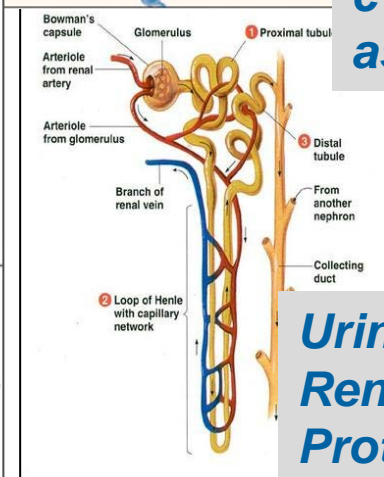
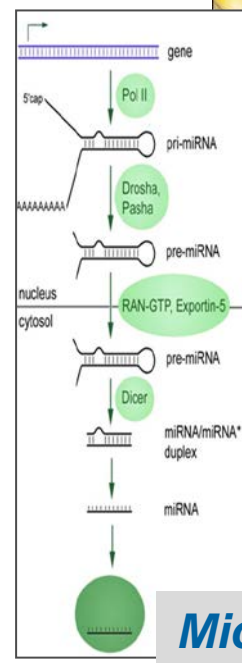
- Consensus on Safety or Translational Need
- Experimental Data
- Analysis & Publication
- Integration of Data & Context of Use

Non-clinical Inhibin Assays

EIA Kits



Nonclinical cTn serum assays



Urinary Renal Protein Biomarkers

MicroRNAs as translation tox markers

A spotlight on one of many...

Heart safe medicine and HESI linking nonclinical data & known clinical outcomes

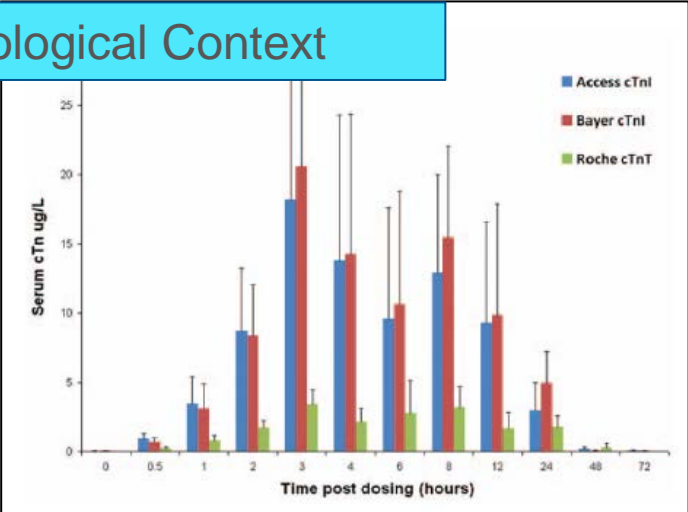
1. Technical Evaluation

Clinical Chemistry 54:12
1982-1989 (2008) Animal Clinical Chemistry

Analytical Characteristics of Commercial Cardiac Troponin I and T Immunoassays in Serum from Rats, Dogs, and Monkeys with Induced Acute Myocardial Injury

Fred S. Apple,^{1*} MaryAnn M. Murakami,¹ Ranka Ler,¹ Dana Walker,² and Malcolm York,³ for the HESI Technical Committee of Biomarkers Working Group on Cardiac Troponins^{4†}

2. Biological Context



3. Translation

A translational approach to detecting drug-induced cardiac injury with cardiac troponins: Consensus and recommendations from the Cardiac Troponins Biomarker Working Group of the Health and Environmental Sciences Institute

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4. Context of Use – Regulatory Approval & Enhanced Acceptance and Utilization

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

February 23, 2012

ATTN: PJ O'Brien (University College, Dublin, Ire)
WJ Reagan (Pfizer Inc, Groton, CT, USA)
MJ York (GlaxoSmithKline, Ware, Herts, UK)
MC Jacobsen (AstraZeneca, Macclesfield, UK)

The list goes on...

**Enhancing
developmental and
reproductive health**



**Supporting ecological
and human safety of
food resources**



**Predicting and
Protecting Against
Adverse Effects
from Chronic
Exposures**



**Established
Credibility
& Rigor**



**Positive
Impact on
Health via
Improved Science**

**Ever-Growing
Partner Base**



Thank you

"The HESI approach to bringing together experts from academia, government, and the private sector to address focused scientific topics in an unbiased, unconstrained way works.

Simple as that."