



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.

Why HESI ?

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





1989

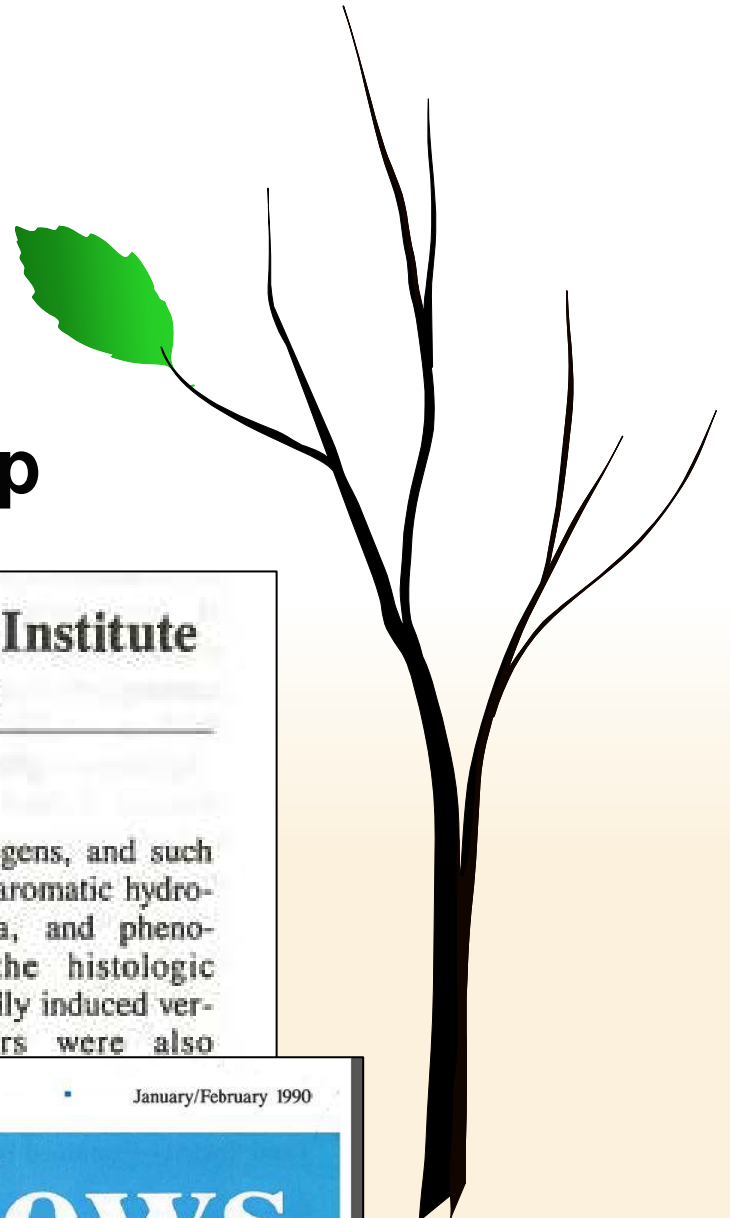
Rodent Liver Tumor Workshop

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

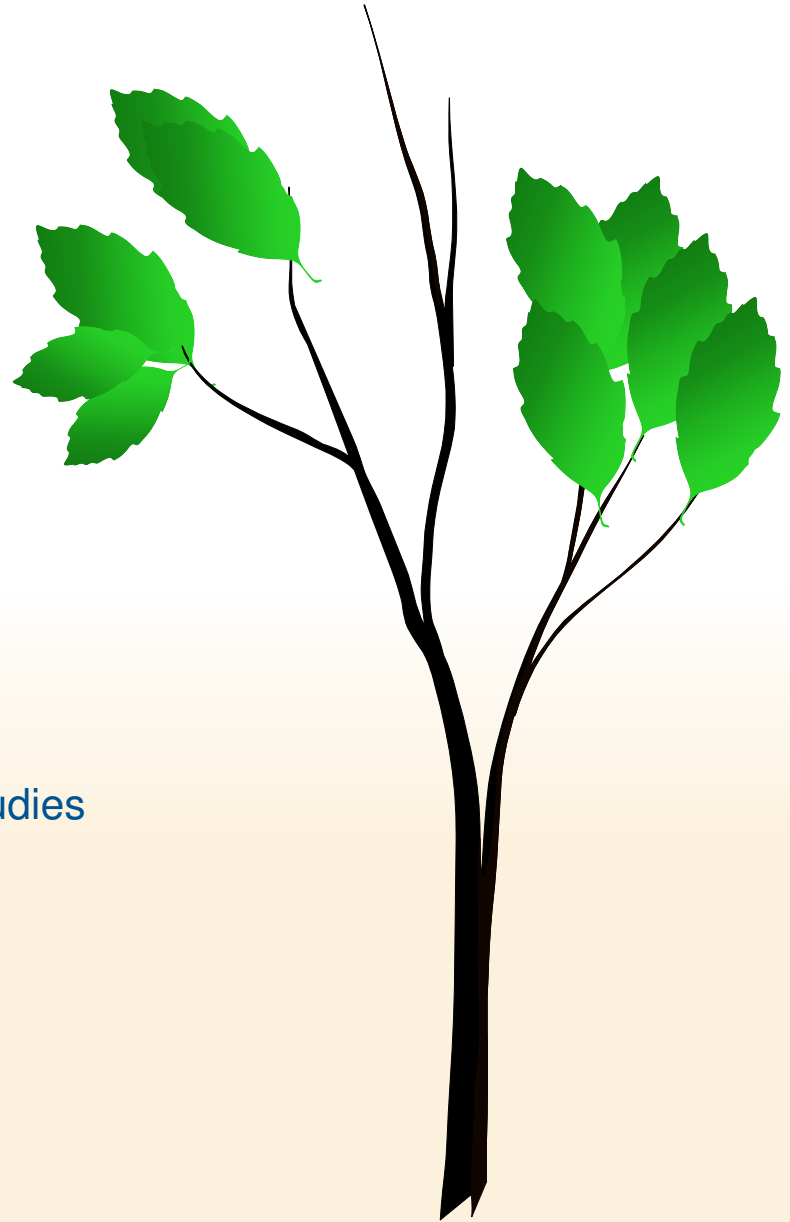




1999

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

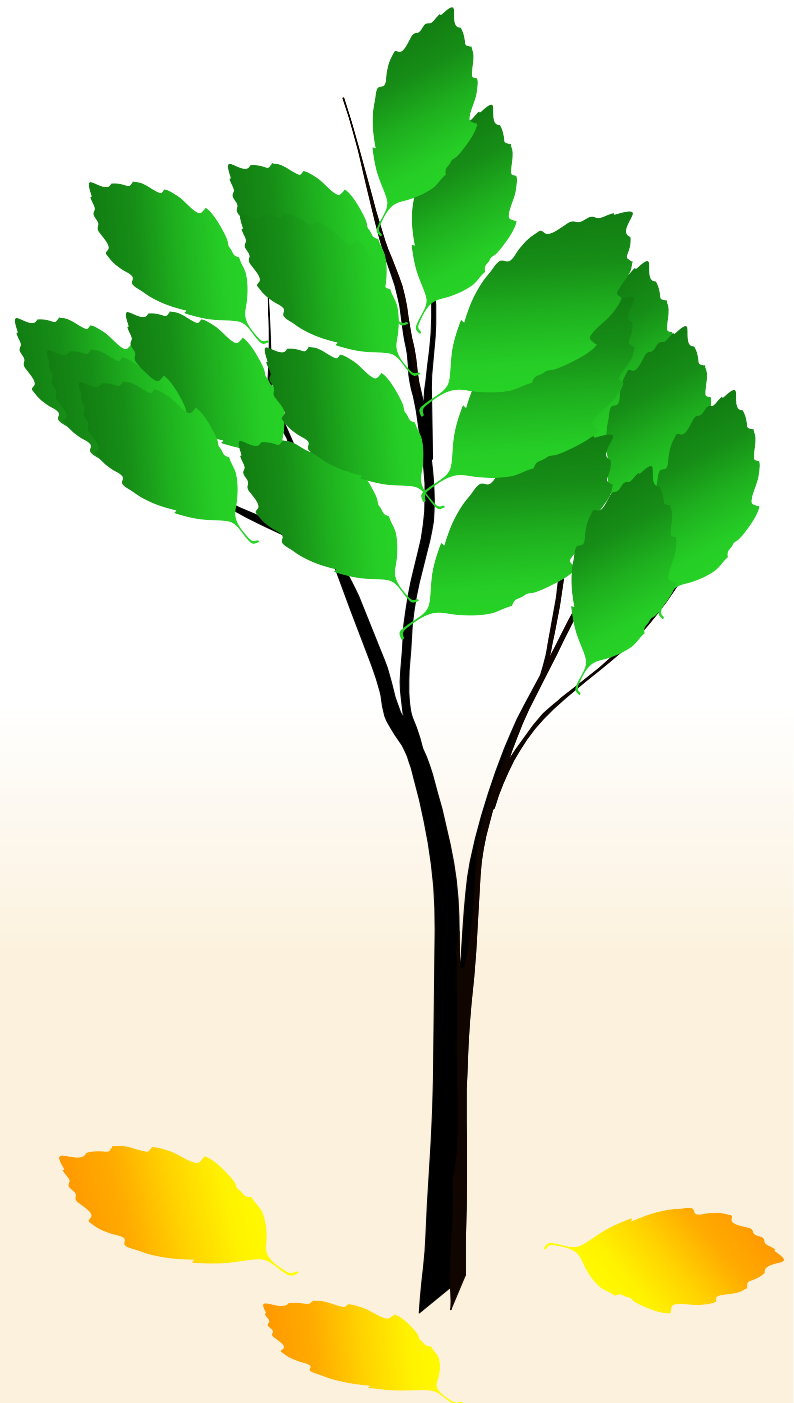




June 2014

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





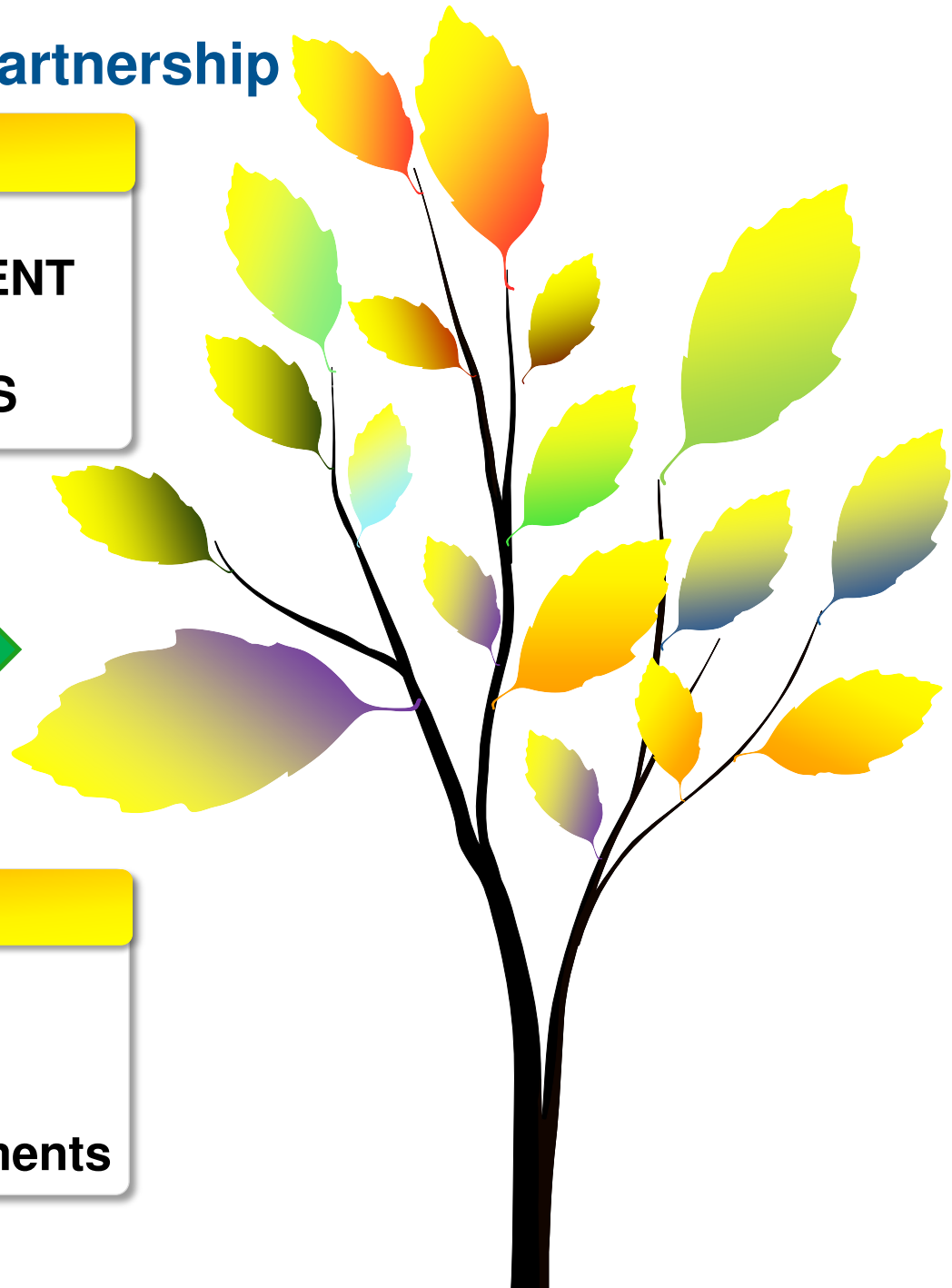
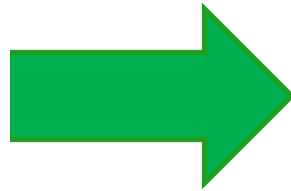
25 Years of Diversifying Partnership



25 Years of Diversifying Partnership

ACADEMIA
INDUSTRY
FOUNDATIONS

GOVERNMENT
NGOs
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**

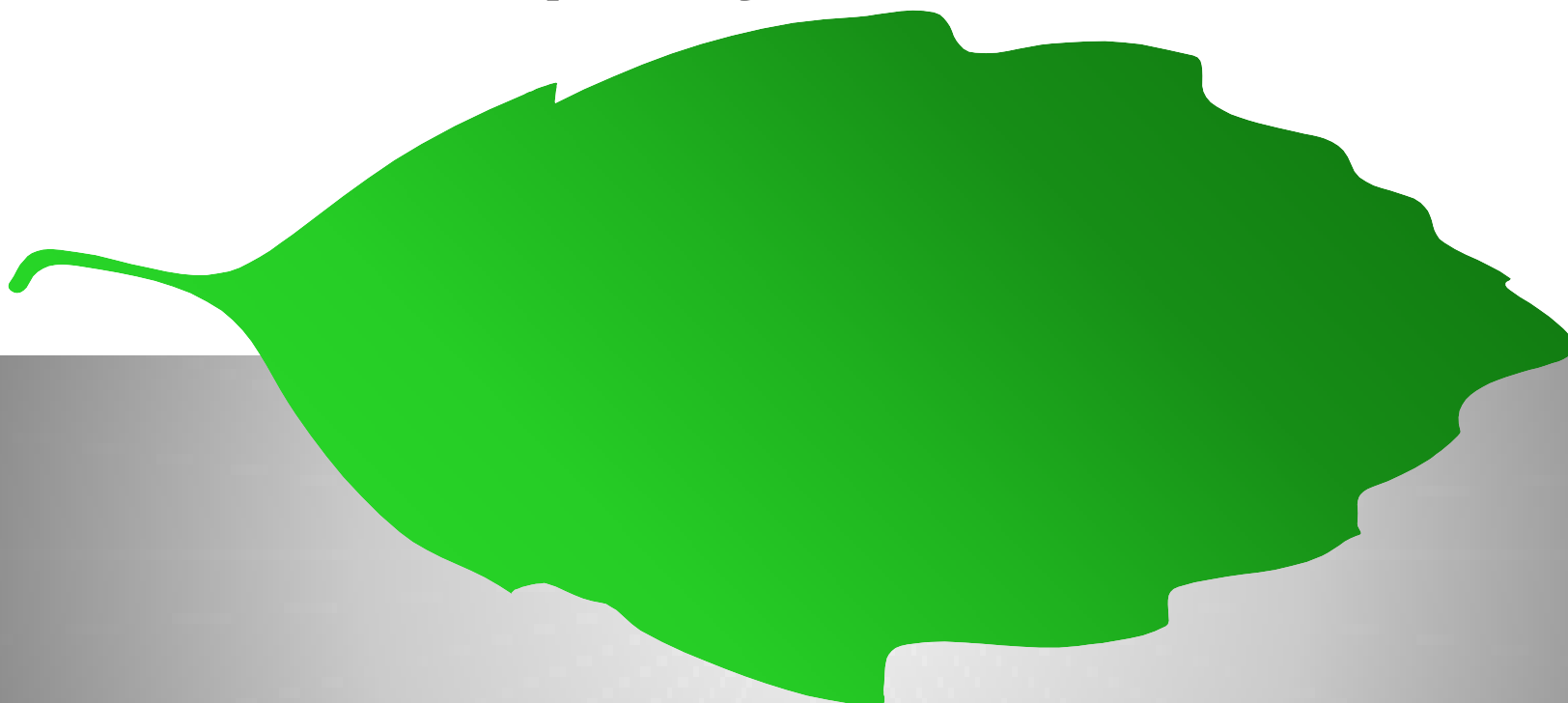
**Environmental
Quality and
Sustainability**

Food Safety



HESI's 25 Years of Success is ...

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





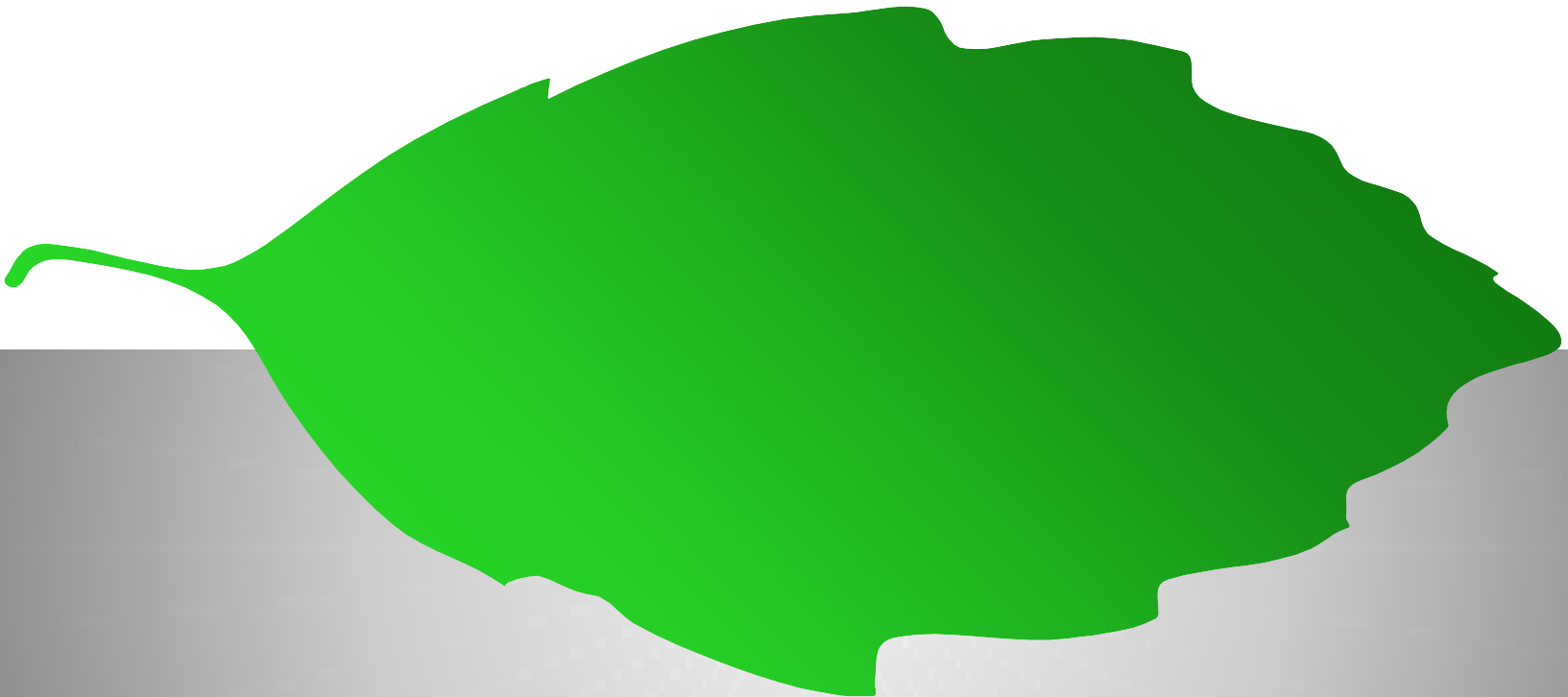
HESI's 25 Years of Success is...

**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**



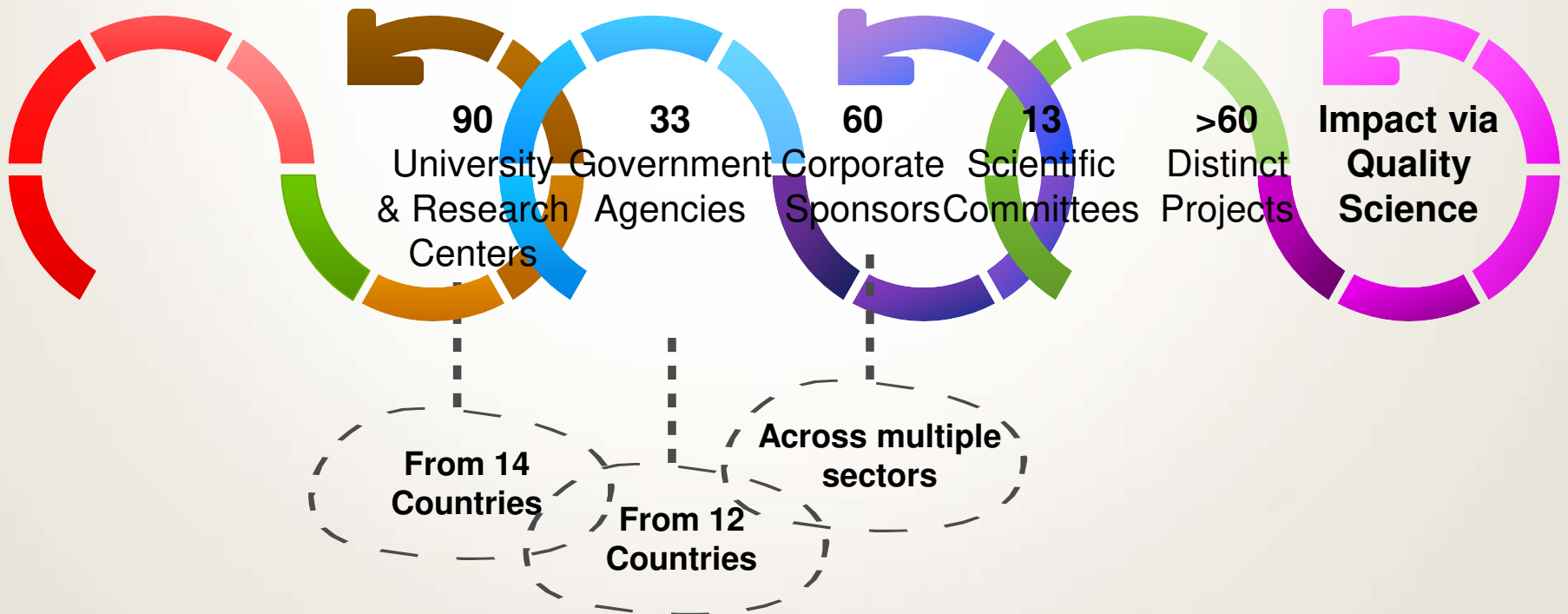


HESI's 25 Years of Success is...

**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

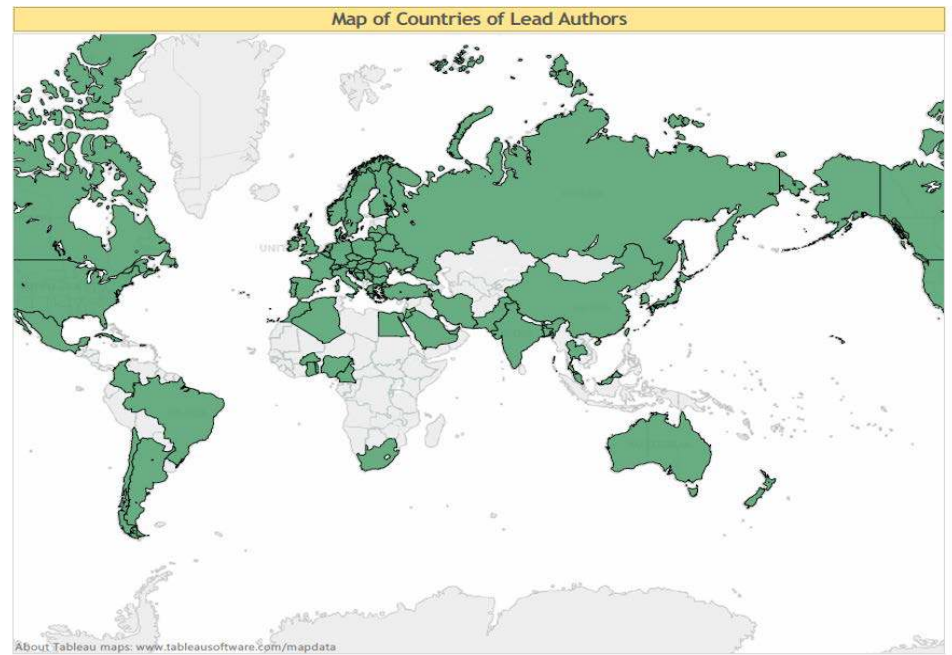
Average #
of times
each HESI
paper is
cited.

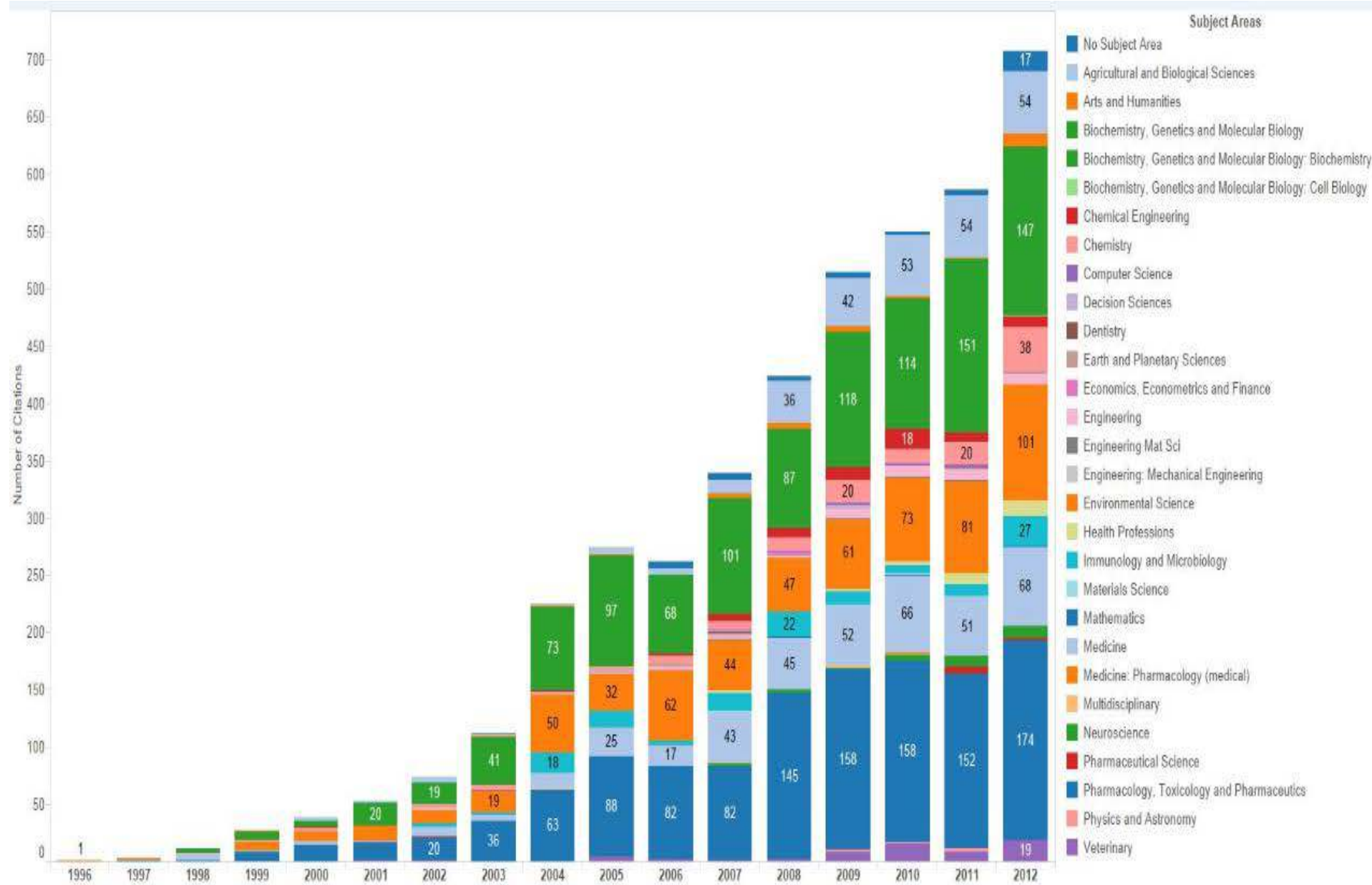
1096

Number of journals citing
HESI publications

1373

Number of
different author
organizations that
cited HESI
papers





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

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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

“The recommendations from these early HESI-EPA workshops **provided a foundation upon which to develop a mode of action (MOA) framework.**

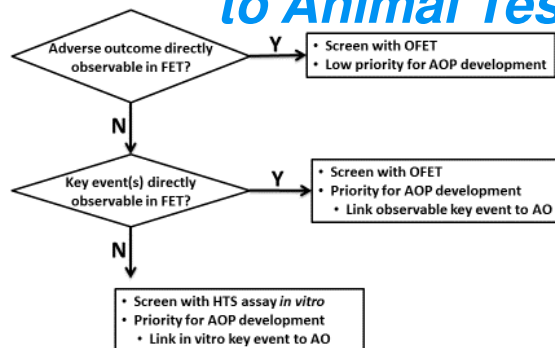
The IPCS defined the criteria for accepting a MOA as adequate for evaluating a specific tumor type in animals...subsequent work ...determined how MOA studies can be **used to establish the relevance of rodent tumors to humans.**”

*From HESI's First
Program...*

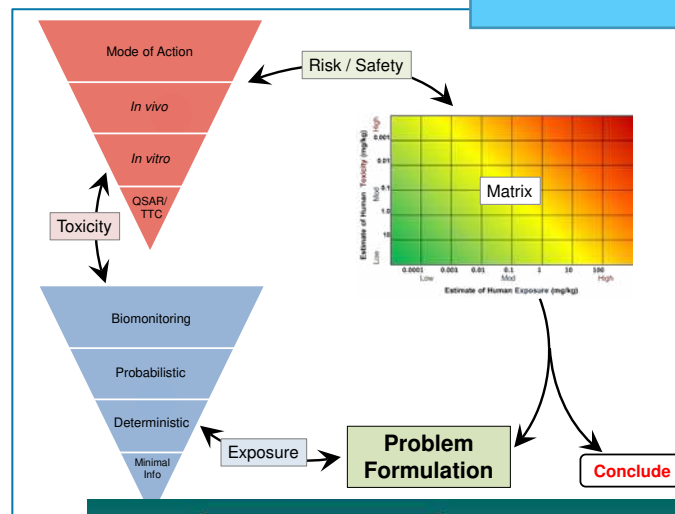
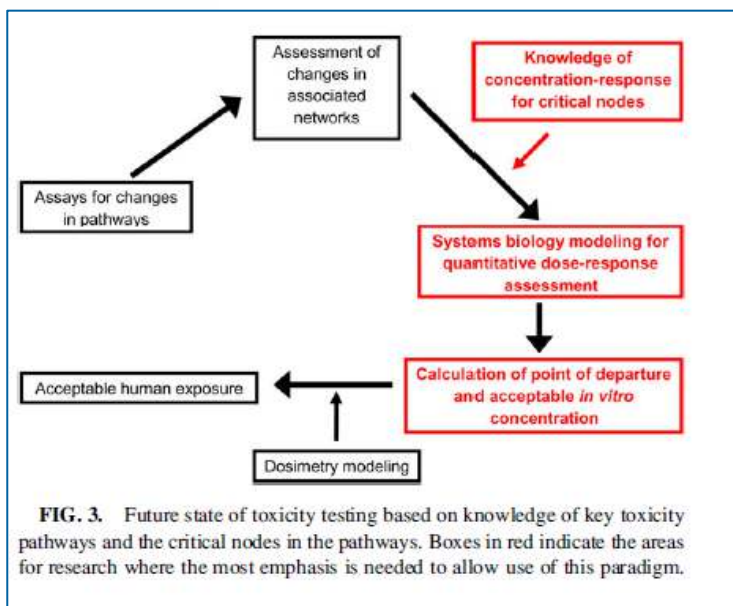


Figure 3.

Integrating Alternatives to Animal Testing for Ecotox

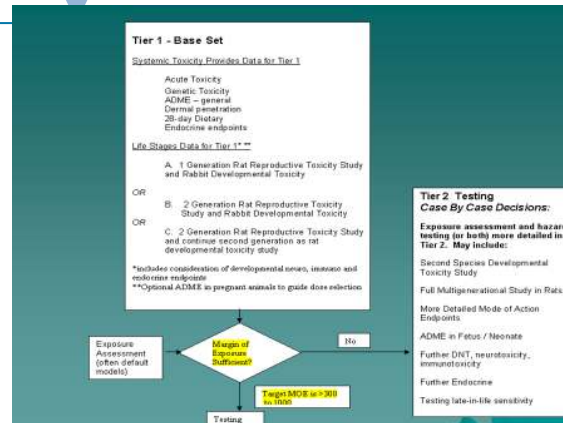


Globally recognized HESI roadmaps to guide integration of data and decisions.



Innovating Chemical Risk Assessment

Assessing Adverse vs Adaptive Transitions in Toxicity Pathways



Enhancing AgChem Safety



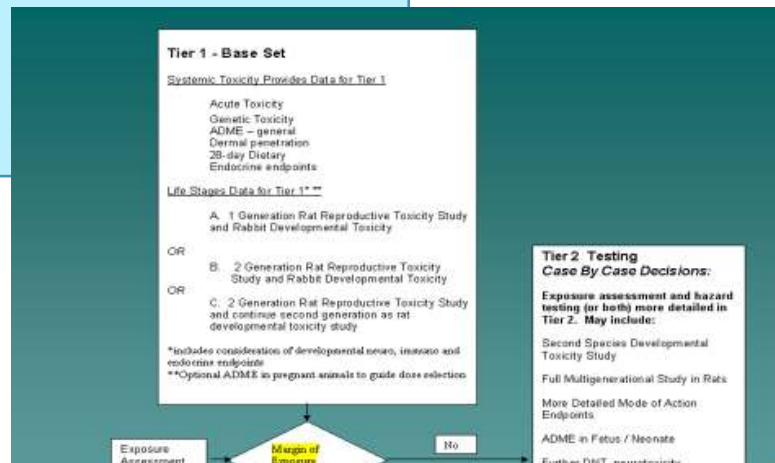
A spotlight on one of many...

**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
AgChem
Safety**

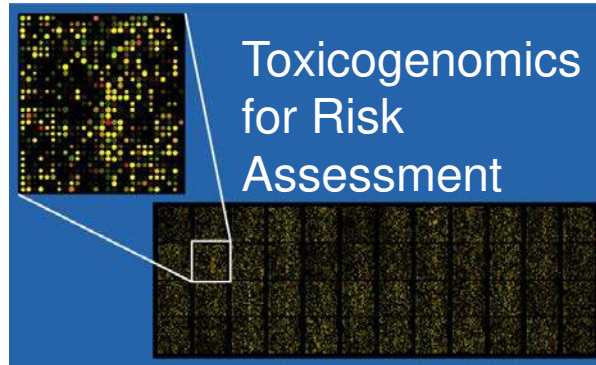


*Enhancing the
predictive relevance of
experimental studies*



**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





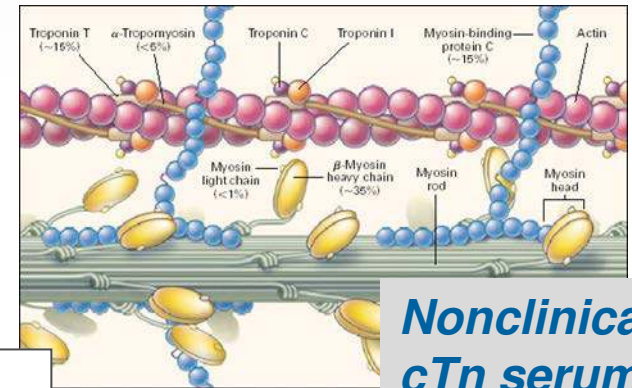
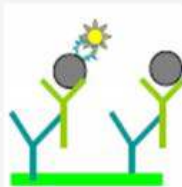
Translating from animal to human, and back to improve relevance

HESI Approach to Biomarkers

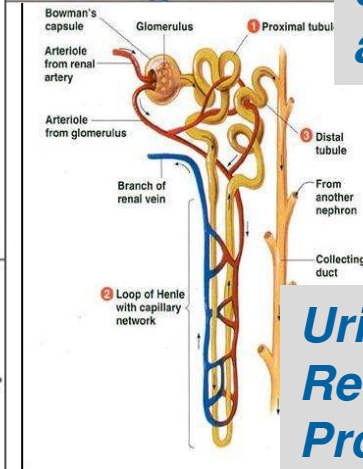
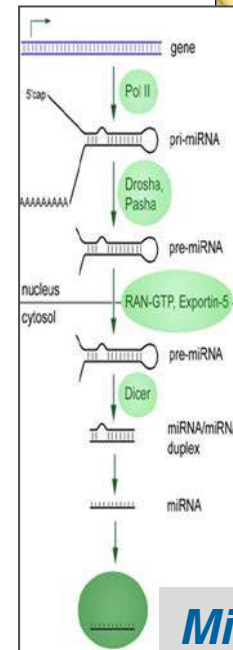
- Consensus on Safety or Translational Need
- Experimental Data
- Analysis & Publication
- Integration of Data & Context of Use

**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

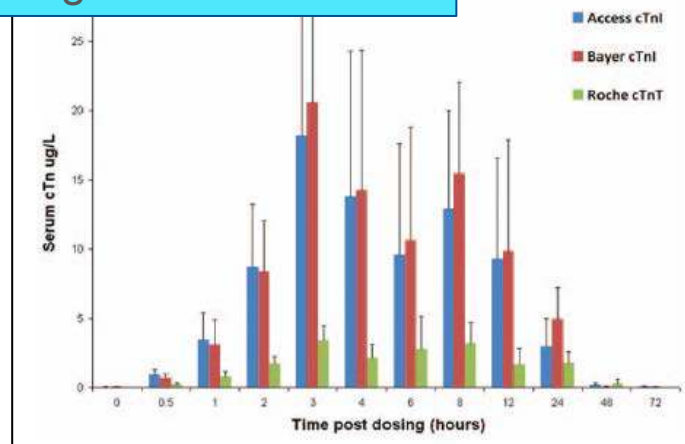
Fred S. Apple,^{1*} MaryAnn M. Murakami,¹ Ranka Ler,¹ Dana Walker,² and Malcolm York,³ for the HESI Technical Committee of Biomarkers Working Group on Cardiac Troponins^{4†}

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

Brian R. Berridge, DVM, PhD,^a Syril Pettit, MS,^b Dana B. Walker, DVM, PhD,^c Alan S. Jaffe, MD,^d Albert E. Schultze, DVM, PhD,^e Eugene Herman, PhD,^f William J. Reagan, DVM, PhD,^g Steven E. Lipshultz, MD,^h Fred S. Apple, PhD,ⁱ and Malcolm J. York, MPhil^j *Research Triangle Park, NC; Washington, DC; East Syracuse, Rochester, and Minneapolis, MN; Indianapolis, IN; Silver Spring, MD; Groton, CT; Miami, FL; and Hertfordshire,*

2. Biological Context



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.”