Thinking about the future of ‘toxicology’

HESI Presentation to the National Toxicology Program
February 2019

Syril D Pettit, HESI Executive Director

Health and Environmental Sciences Institute

International, non-profit leader in convening scientists from academe, government, NGOs, foundations, clinic, industry, and other scientific sectors seeking build a safer, more sustainable world

Safe & Effective Medicines

Cell Reports

RESOURCE | VOLUME 24, ISSUE 13, P3582-3592, SEPTEMBER 25, 2018

International Multisite Study of Human-Induced Pluripotent Stem Cell-Derived Cardiomyocytes for Drug Proarrhythmic Potential Assessment

Ksenia Blinova [24] • Qianyu Dang • Daniel Millard • ... Norman Stockbridge • David G. Strauss • Gary Gintant • Show all authors • Show footnotes

Food Safety

Akkerdaas et al. Clin Transl Allergy (2018) 8:30
https://doi.org/10.1186/s13601-018-0216-9

Clinical and Translational Allergy

RESEARCH Open Access

Protease resistance of food proteins: a mixed picture for predicting allergenicity but a useful tool for assessing exposure

Jaap Akkerdaas[1], Muriel Totis[2], Brian Barnett[3], Erin Bell[4], Tom Davis[5], Thomas Edrington[4], Kevin Glenn[4], Gerson Graser[6], Rod Herman[7], Andre Knulst[8], Gregory Ladics[9], Scott McClain[6], Lars K. Poulsen[10], Rakesh Ranjan[11], Jean-Baptiste Rascle[2], Hector Serrano[11], Dave Speijer[12], Rong Wang[4], Lucilia Pereira Mouriès[13], Annabelle Capt[2] and Ronald van Ree[1,14*]

ORIGINAL RESEARCH ARTICLE

WILEY Birth Defects Research

Rethinking developmental toxicity testing: Evolution or revolution?

Anthony R. Scialli[1] | George Daston[2] | Connie Chen[3] | Prägati S. Coder[4] | Susan Y. Euling[5] | Jennifer Foreman[6] | Alan M. Hoberman[7] | Julia Hui[8] | Thomas Knudsen[9] | Susan L. Makris[10] | LaRonda | Dinesh Stanislaus[13] | Kary E. Thompson[14]

Risk Assessment Methodologies and Enabling Technologies

OXFORD SOT Society of Toxicology www.toxsci.oxfordjournals.org ToxSci 20 Years

TOXICOLOGICAL SCIENCES, 164(2), 2018, 563–575

doi: 10.1093/toxsci/kfy113
Advance Access Publication Date: May 14, 2018
Research Article

Reliability of *In Vitro* Methods Used to Measure Intrinsic Clearance of Hydrophobic Organic Chemicals by Rainbow Trout: Results of an International Ring Trial

John Nichols,* Kellie Fay,[†,‡] Mary Jo Bernhard,[§] Ina Bischof,[¶] John Davis,[‖] Marlies Halder,[|||] Jing Hu,[‖] Karla Johanning,[|||] Heike Laue,[#] Diane Nabb,[**] Christian Schlechtriem,[¶] Helmut Segner,[††] Joe Sw… Michelle Embry[c,1]

Environmental Quality & Sustainability

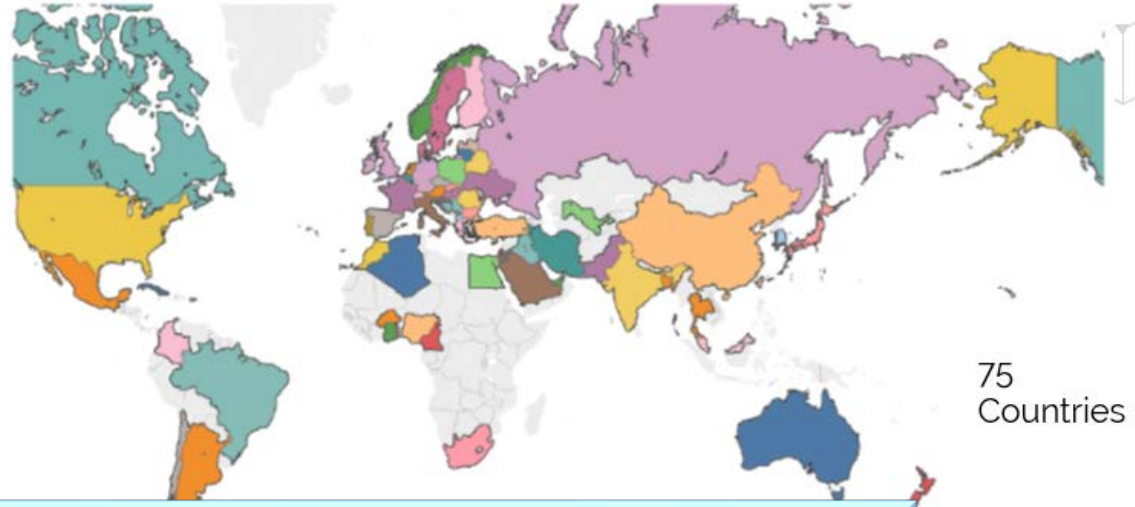
Demodifying RNA for Transcriptomic Analyses of Archival Formalin-Fixed Paraffin-Embedded Samples

Leah C Wehmas ✉, Charles E Wood, Remi Gagne, Andrew Williams, Carole Yauk, Mark M Gosink, Deidre Dalmas, Ruixin Hao, Raegan O'Lone, Susan Hester Author Notes

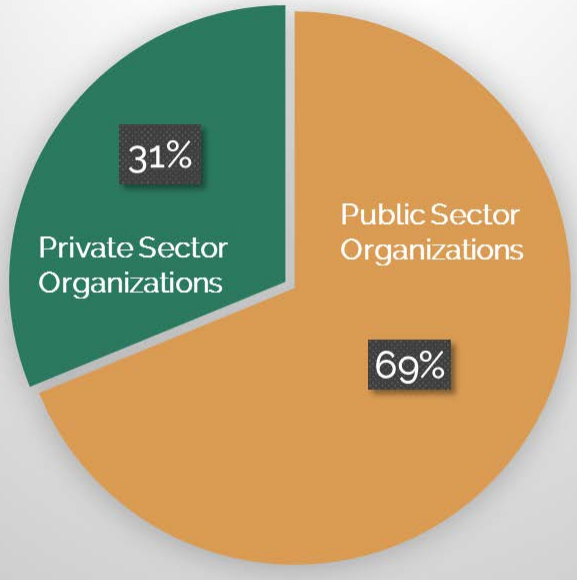
Toxicological Sciences, Volume 162, Issue 2, 1 April 2018, Pages 535–547, https://doi.org/10.1093/toxsci/kfx278

- Diverse Science
- Human & Env Health & Safety

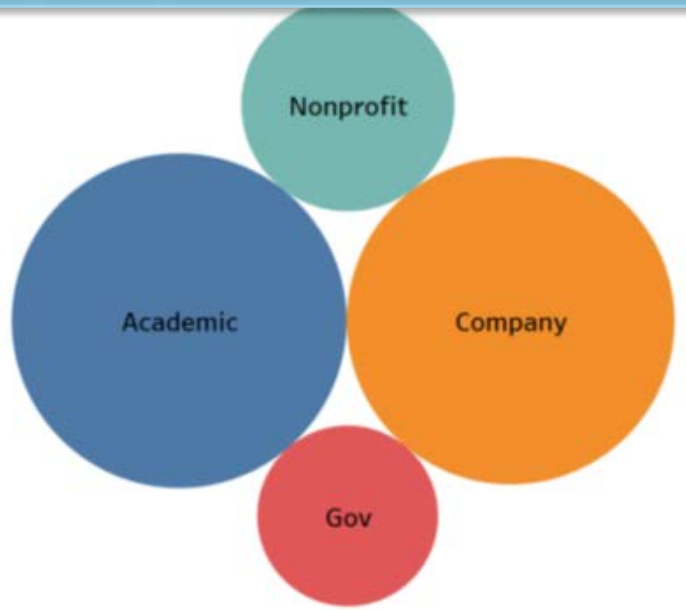
Geographical Distribution of Lead Citing Authors



Number of Participating Organizations in 2018



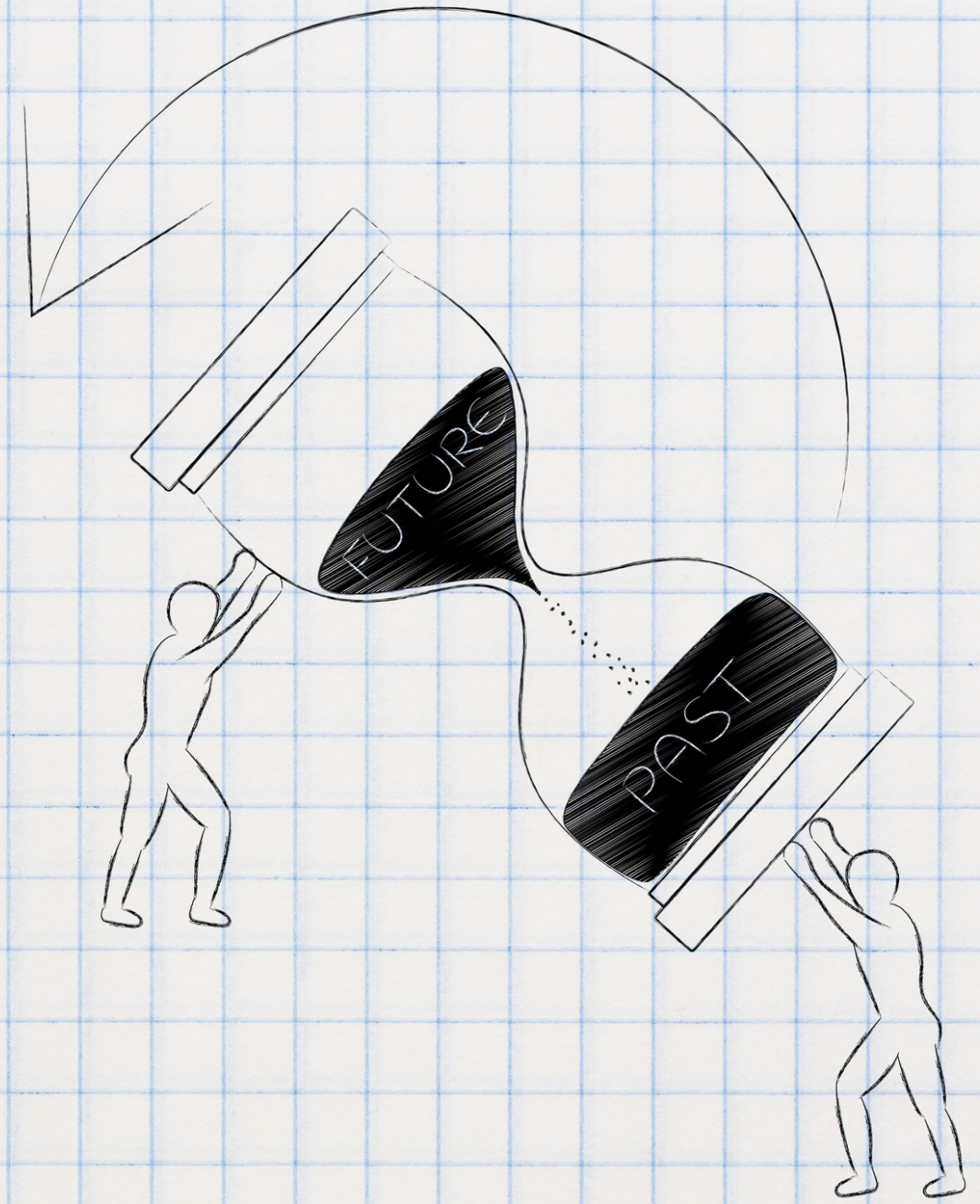
20,000 Citations of HESI's
300+ Peer-Reviewed Publications,
Around Globe, Across Sectors



OECD
BETTER POLICIES FOR BETTER LIVES

ICH
harmonisation for better health

- Global Reach
- Multi-Sector Scientific Impact
- Multi-Sector Participation
- Science for OECD & ICH


FUTURE
PAST

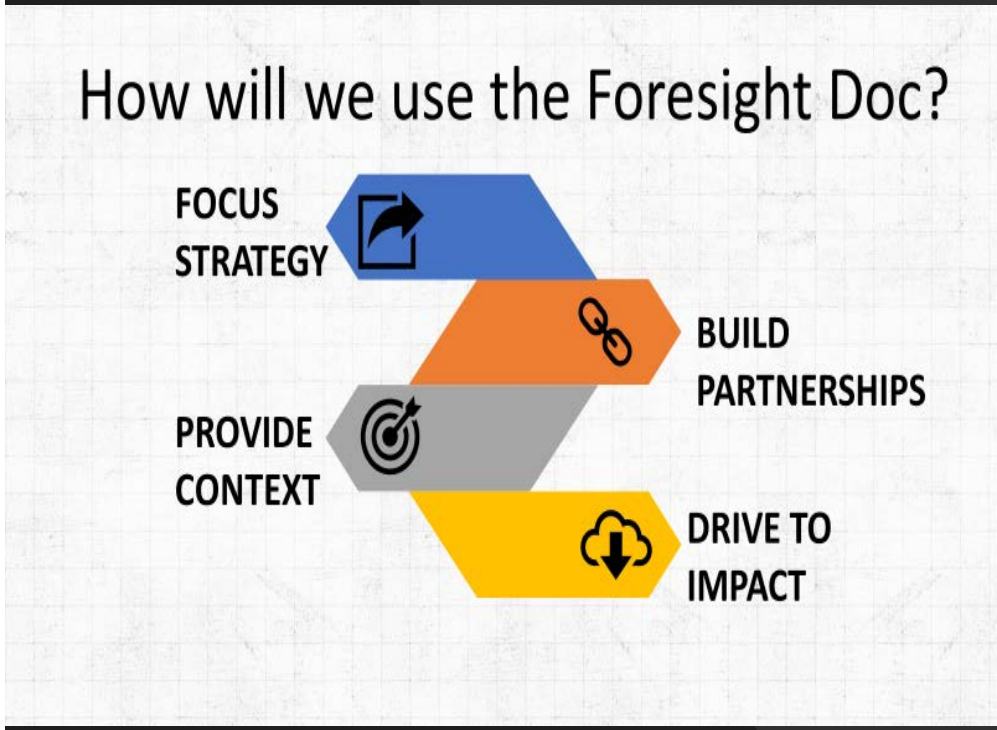
SCIENCE FORESIGHT

PERSPECTIVES FOR 2017-2020

HESI

Objective

Create a broad picture of widely identified global and/or national science and health priorities and align those with priorities identified by our own diverse stakeholder base.



What is coming/ growing and should be a focus for resources and effort?

National Health and/ or Environment Organizations

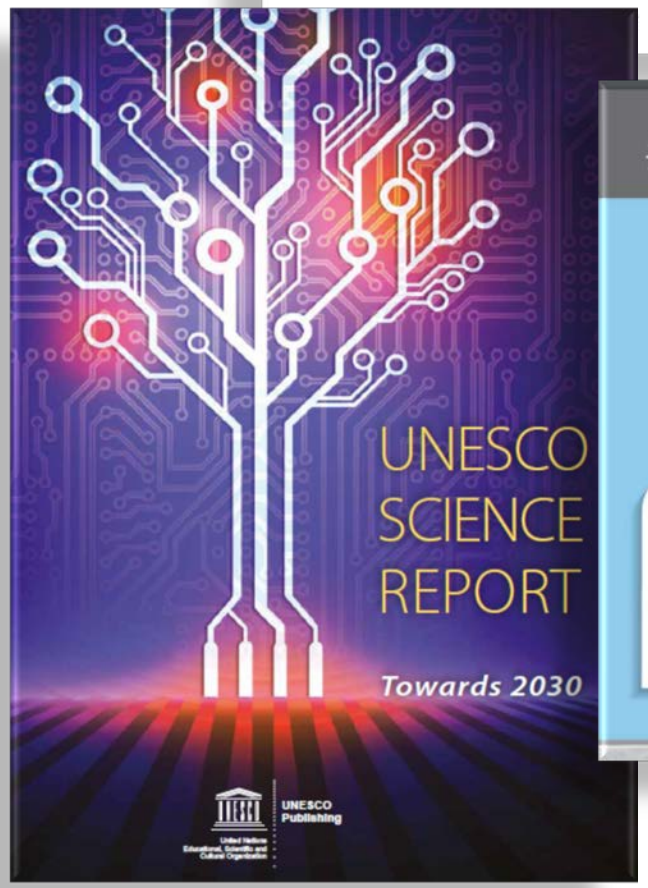
International Health and/or Environment Organizations

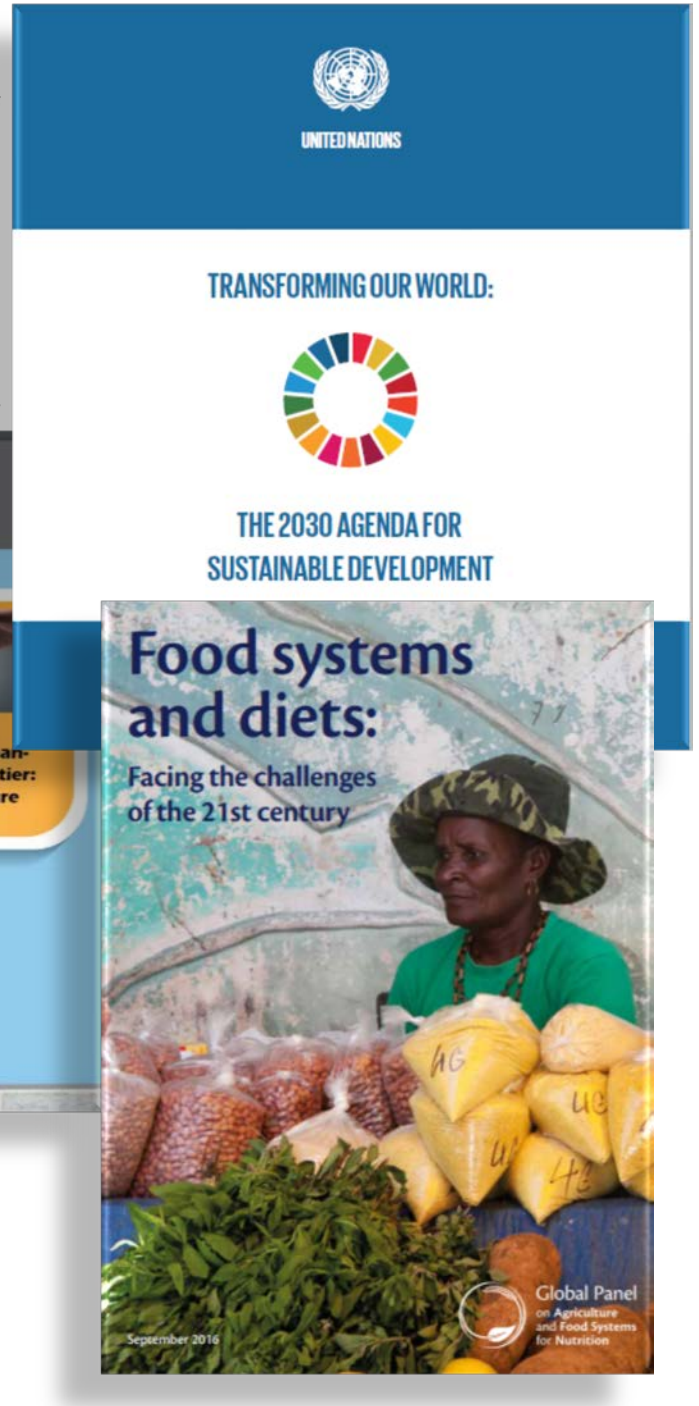
SCIENCE AND HEALTH PRIORITIES AND PREDICTIONS

Global Health View

21 Issues for the 21st Century -- Result of the UNEP Foresight Process on Emerging Environmental Issues

UNEP, 2012

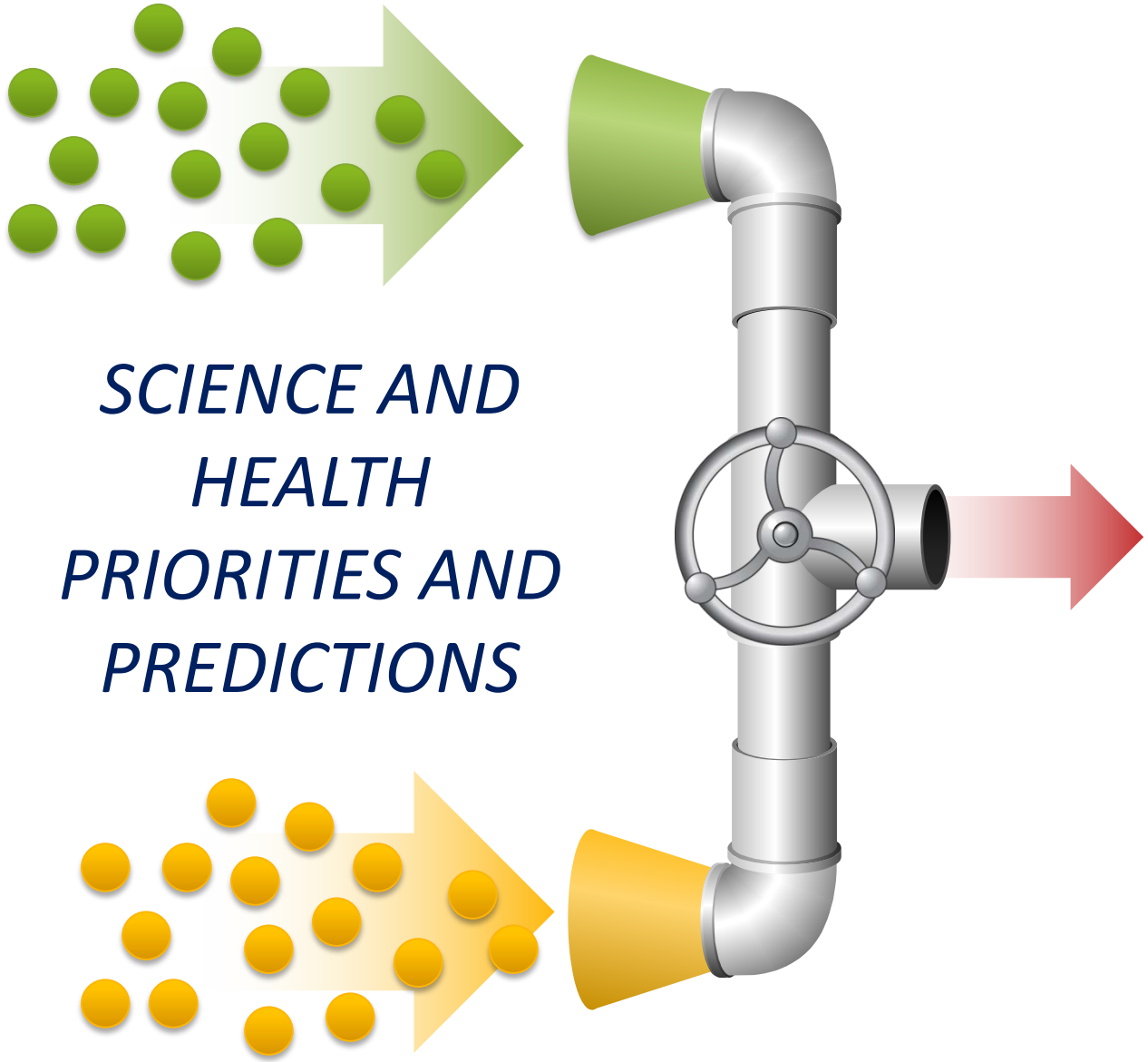




A SAMPLING…

What is coming/ growing and should be a focus for resources and effort?

HESI Governance & Leadership Perspective



SCIENCE AND HEALTH PRIORITIES AND PREDICTIONS

HESI Stakeholder View

HESI Scientific Committee Perspective

SCIENCE FORESIGHT

PERSPECTIVES FOR 2017-2020

HESI

http://hesiglobal.org/scienceforesight/

PLANETARY PRESSURES

EXTERNAL VIEW

- Climate Change
- Ability to sustain natural resources (water, air, minerals)
- Population growth
- Waste management

HESI VIEW

- Climate change impact on human and environmental health
- Environmental exposures and human/eco health outcomes
- Chemical substitutions and sustainability

TECHNOLOGY

EXTERNAL VIEW

- High density data
- Sensory technologies & tracking
- Regenerative medicine
- Genome editing
- 3D Printing
- Robotics
- Nanotech

HESI VIEW

- Cell, immune, and gene therapy
- Personal monitoring data & role in health, disease, exposure
- Organ chips
- 3D printing
- Computational modeling

PRACTICE OF SCIENCE

EXTERNAL VIEW

- New disciplines merging with biology
- Interdisciplinary science

HESI VIEW

- Epidemiology data & use
- 'Alternative' testing methods
- Data sharing and data access
- Predictive signatures & epigenetics
- Exposure in risk assessment

POPULATION & INDIVIDUAL SENSITIVITY

EXTERNAL VIEW

- Increased aging population
- Microbial resistance & disease
- Rates of NCDs in population
- Novel disease pathogens

HESI VIEW

- Aging related disorders
- Neurological illness/safety
- Drug-drug interactions
- Safety of novel cancer therapies
- Impact of combined exposure

SOCIETAL INFLUENCES

EXTERNAL VIEW

- Science in period of political, economic Instability
- Public skepticism of science
- Culture of open access

HESI VIEW

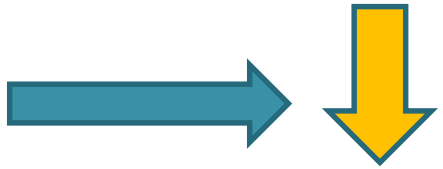
- Global regulatory standards
- Role of social media in information collection and exchange
- Public perception of risk v hazard
- Reduced research $$s

For today – not focusing on specific project concepts

Will share an over-arching theme

Moving Toxicology from Defense to Offense

CURRENT

Tox on Defense  **Toxicity = Avoid Harms/ ‘De-Risk’**

CURRENT

Tox on Defense → ↓ Toxicity = Avoid Harms/ ‘De-Risk’

FUTURE

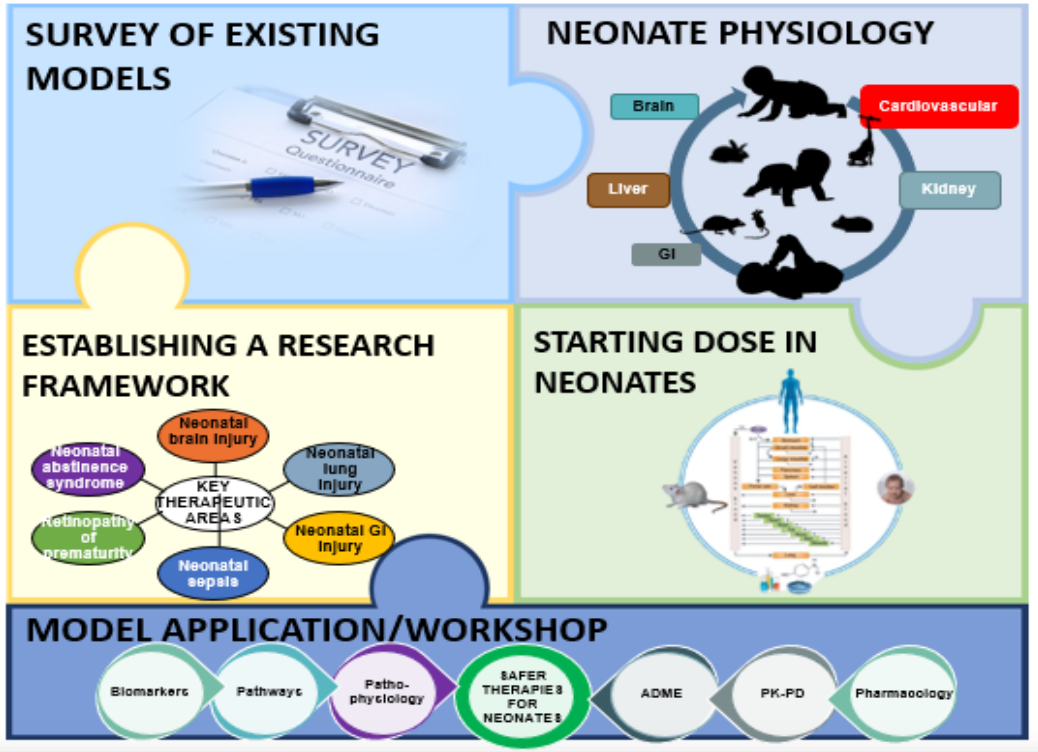
Offense → ↓ Toxicity = ↑ Quality of Life, Public Health

BIDEN CANCER INITIATIVE

- ***Neonatal abstinence syndrome***
- ***Retinopathy of prematurity***
- ***Neonatal brain, GI, lung injury***
- ***Neonatal Sepsis***

Nonclinical models of Neonatal Pediatric Drug Development

Use nonclinical models to fill and inform gaps in neonatal pediatric drug development & use.



Tox Role in Health PROMOTION

EDITORIAL

PATIENT ADVOCACY

Enhancing quality of life as a goal for anticancer therapeutics

Syril D. Pettit is the Executive Director of the ILSI, Health and Environmental Sciences Institute (HESI), Washington, DC 20005, USA. Email: spettit@hesiglobal.org

THE GLOBAL BIOMEDICAL COMMUNITY'S SUCCESSES IN CANCER THERAPY OVER THE past 30 years and particularly in the last 5 years have made many cancers survivable diseases (*1*). The U.S. National Academy of Medicine's 2013 Quality Cancer Care report estimates 18 million survivors in the United States by 2018 and 1.5 million new cancer diagnoses per year. The increase in treatment options and survival progress for many cancer types brings into sharper focus the responsibility to also prioritize continued improvements in the quality of life throughout disease-directed treatment and the full continuum of care for both cancer patients and survivors.

In the weeks, years, and decades after treatment, many survivors experience a significantly higher incidence of serious and even life-threatening chronic conditions—often unintended

Pettit and Kirch *Cardio-Oncology* (2018) 4:5
https://doi.org/10.1186/s40959-018-0031-4

Cardio-Oncology

REVIEW Open Access

Do current approaches to assessing therapy related adverse events align with the needs of long-term cancer patients and survivors?

Syril D. Pettit[1,2*] and Rebecca Kirch[3]

ASPET | DRUG METABOLISM AND DISPOSITION

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Research Article | Minireview

Physiology of the neonatal gastrointestinal system relevant to the disposition of orally administered medications

April Neal-Kluever, Jeffrey Fisher, Lawrence Grylack, Satoko Kakiuchi-Kiyota, and Wendy Halpern

Drug Metabolism and Disposition December 19, 2018, dmd.118.084418; DOI: https://doi.org/10.1124/dmd.118.084418

More on 'Offense' From the Foresight Map

Increasing Rates of Non-communicable Disease in the population

- Understanding mechanisms of toxicity to promote enhanced health.

Role of Microbiome and Microbial Health

- Opportunities to enhance drug efficacy, nutritional quality, ecological resilience and human and environmental health status

Natural Resource Limitations

- Informing new practices to preserve and extend natural or 'engineered' resources.

Why Apply this Concept ACROSS the Traditional Toxicology Portfolio?

Enhances and illustrates impact

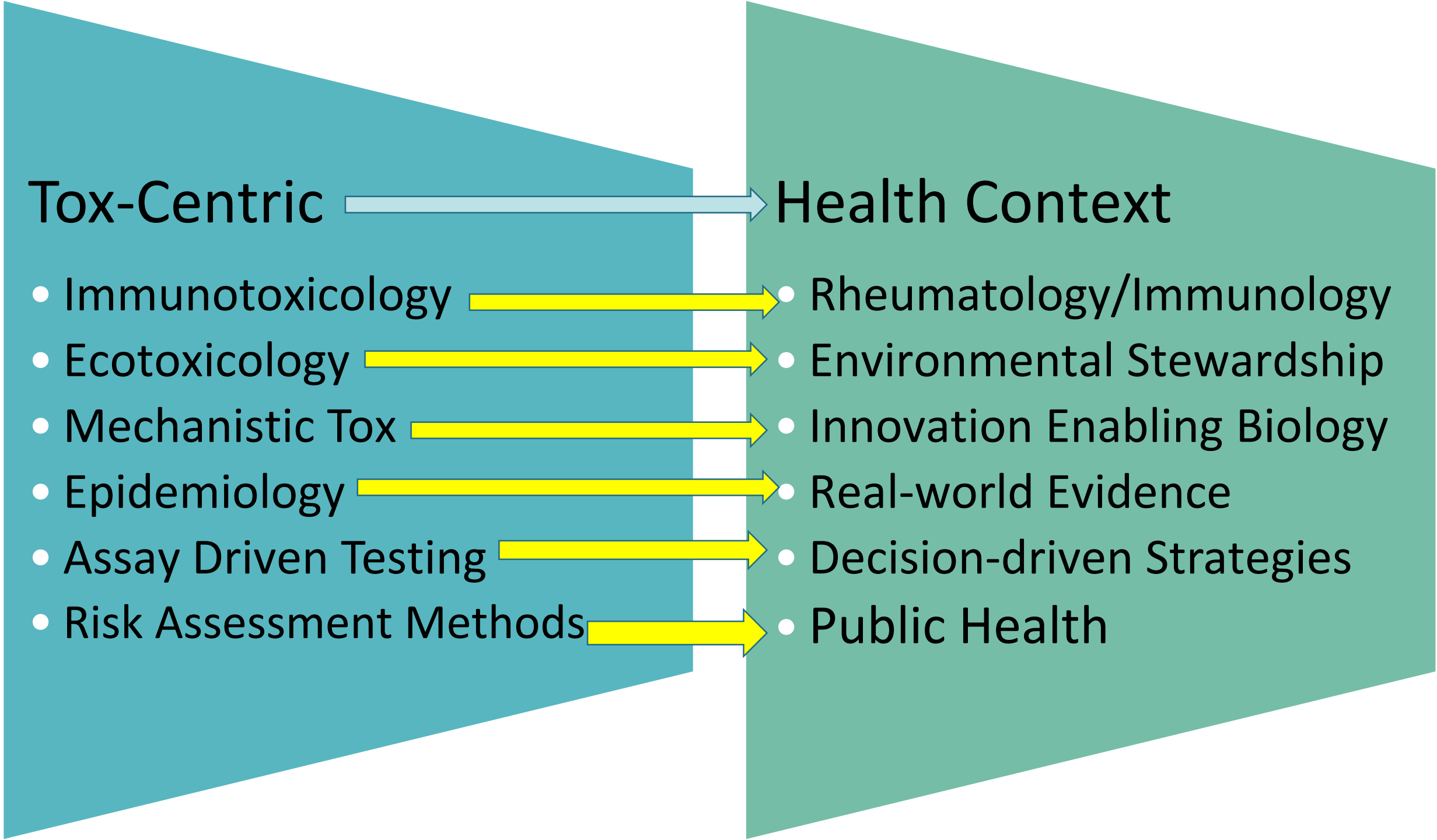
Increases efficiency through cross-purposing effort

Enhances potential partner and resource base

Acknowledges historical progress in managing risk…

Adheres to collaborative and multidisciplinary mission goals

What could that look like?


Tox-Centric
Immunotoxicology
Ecotoxicology
Mechanistic Tox
Epidemiology
Assay Driven Testing
Risk Assessment Methods
Health Context
Rheumatology/Immunology
Environmental Stewardship
Innovation Enabling Biology
Real-world Evidence
Decision-driven Strategies
Public Health

HESI is moving in this direction…looking forward to watching how/if others migrate as well!

Tox-Centric	Health Context
• Immunotoxicology	• Rheumatology/Immunology
• Ecotoxicology	• Environmental Stewardship
• Mechanistic Tox	• Innovation Enabling Biology
• Epidemiology	• Real-world Evidence
• Assay Driven Testing	• Decision-driven Strategies
• Risk Assessment Methods	• Public Health

Thanks for your attention

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