THE ILSI® RISK ASSESSMENT PROGRAM

A 30-year history of strengthening the scientific basis for human health risk assessment to improve public health

Scientific Integrity…

founded to serve the scientific community's efforts to protect people and the environment

ILSI develops and shares advanced risk assessment knowledge through worldwide network of experts and collaborators.

- Credited by government health officials and leading scientists around the world as a consistent, credible source of relevant knowledge.
- Risk Science Institute (RSI) funded $4 million in research, conducted by more than 40 researchers, during its first decade.

[ILSI, with support from its member companies, would create]
"…a mechanism for research on the scientific issues underlying risk assessments."

Dr. Frank Press,
President of the National Academy of Sciences,
1983, challenging ILSI to form Risk Science Institute

Focuses attention on sensitive subpopulations.

- RSI expert dialogue and landmark publication provided valuable insight on common practice of extrapolating adult data to children in risk assessment. Influenced National Academy of Sciences (NAS) pivotal work on pesticides in children's diets, which prompted inclusion of child-specific provisions in U.S. Food Quality Protection Act (FQPA), Safe Drinking Water Act (SDWA), and Environmental Protection Agency (EPA) policy guidance.
- Published "Framework for Assessing Risk to Children from Environmental Agents," serving as resource for EPA's framework.
- Health & Environmental Sciences Institute (HESI) published series of papers describing appropriate use of animal studies to evaluate safety of drugs intended for children.

The ILSI Approach for Furthering Scientific Inquiry:

1. Identify critical issues.
2. Convene expert working groups.
3. Publish and disseminate findings.

Leadership…

born of ILSI integrity, flexibility, foresight, and convening ability

Evaluates new and existing experimental systems.

- HESI published results of collaborative research program, "Evaluation of Alternative Methods for Carcinogenicity Testing." Incorporated data from more than 50 laboratories worldwide. Improved understanding of strengths and limitations of animal models used in risk assessment. Led regulatory authorities worldwide to modify pre-clinical study requirements.
- HESI, ILSI Europe, and RSI contributed to updating and improving toxicity testing strategies for chemicals and other agents in fields of agricultural chemicals, chemicals in food, nanomaterials, and manmade fibers.

Enhances risk assessment tools and principles to support work of scientific community.

- Created repositories of chemical agent-specific and pathogenic species-specific hazard and exposure data.
  - HESI compiled chemical-specific data related to carcinogenicity, mutagenicity, dermal sensitization, hepatic toxicity, and safety pharmacology.
  - Published physiological parameters for humans, of value when extrapolating from animal data for human health risk assessments.
- HESI improved approach to generate developmental toxicity data from rodent studies.
- Identified criteria for neurotoxicity evaluation in developing organisms. Informed EPA's guideline development.
- HESI proposed framework for evaluating effects of drugs and chemicals on immune system in developing organisms.

Builds up scientific infrastructure and technical foundations for risk assessment.

- Sponsored basic research for more than two decades to improve understanding of immunologic, pathologic, and physiologic mechanisms of adverse reactions to foods. Stimulated interest in field, fostering opportunities for researchers who later emerged as leaders in food allergy.
- Developed risk assessment frameworks across range of focus areas, such as chemicals in foods, human relevance of animal studies, genotoxic carcinogens, integrating human biomonitoring exposure data into risk assessment, and cancer hazard identification.

Asking the Right Questions:

Are the modes of action through which substances produce adverse effects in rats relevant to humans?

- HESI addressed reliance on experimental animal research to evaluate risk, extrapolating results to humans.
- Saccharin research sponsored by ILSI North America demonstrated that adverse effects in rodents not relevant in humans. Resulted in delisting of saccharin as carcinogen.
- Expert working group developed Human Relevance Framework (HRF) for characterizing modes of toxic action of substances under review. Demonstrated HRF applicability to reproductive, developmental, neurological, and other endpoints.
- Published, presented, and stimulated dialogue among scientists and regulators worldwide regarding findings of more than two decades of research.
- Framework incorporated into EPA and World Health Organization (WHO) cancer risk assessment guidelines.

Global Reach… Local Relevance…

paving a two-way street between international and local efforts and perspectives, facilitating resource sharing around globe

Harvests global experiences to bring relevant solutions to local problems.

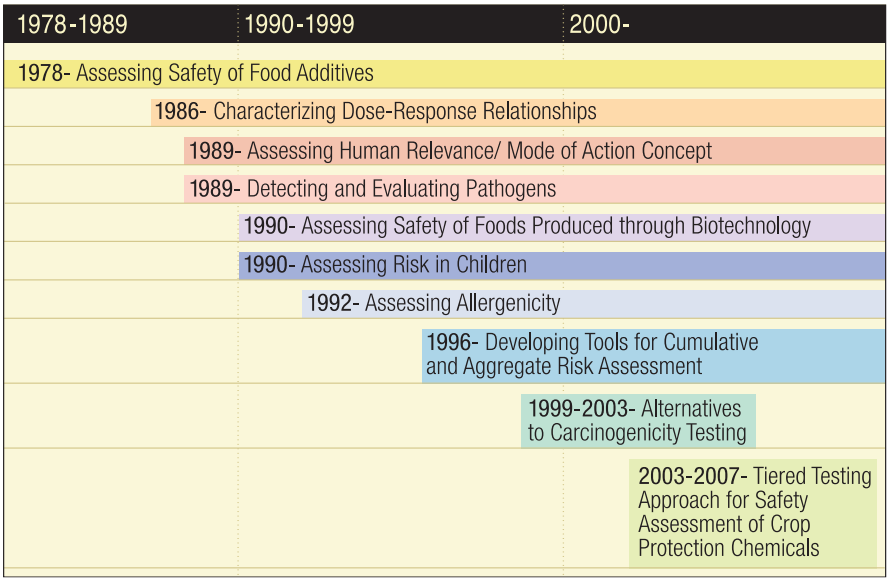
- Developed approaches to collect country- and region-specific food consumption information. "Local" data sets would provide officials with ability to conduct locally-relevant assessment of food pathogens, chemicals/contaminants, and/or nutrients.
- Described need for capacity-building in developing countries and systematic process to collect data on microbial contamination of food and water and associated diseases.
- Pilot project initiated by ILSI Europe, in collaboration with Swiss food retailer, to explore novel way to generate food intake data. Enhanced cooperation with government efforts through communicating findings to European Food Safety Authority's (EFSA) Scientific Committee and Additives and Food Contaminants Panel. Initiated comparison of results to probabilistic modeling.

Convenes scientists, health professionals, educators, and government officials to provide dialogue, information sharing, and training opportunities related to timely issues.

- Conducted risk assessment training workshops as part of the Food and Agriculture Organization (FAO)/ILSI Framework:
  - Microbiological Risk Assessment Workshop hosted by ILSI Brasil and ILSI Focal Point in China. Provided information and manpower training as China initiated nationwide microbial foodborne illness monitoring program.
  - General Risk Assessment Workshops hosted by ILSI Argentina, RSI, and ILSI North America.
- ILSI South Africa provided outreach to developing nations, addressing risk analysis in food regulatory decision-making.
- ILSI India hosted 2003 Workshop on Risk Assessment of Pesticide Residues in Water and Food. Organized quickly and conducted effectively in shadow of then-current controversies.
- ILSI North America hosted December 2001 Bioterrorism Workshop. Attended by high-profile officials. Provided previously unavailable synopsis of food bioterrorism issue.
- Addressed impact of pesticide residues in foods through series of workshops co-organized by HESI and ILSI Argentina.
- Improved assessment of potential allergenicity of products of biotechnology through two separate workshop series hosted by HESI and ILSI Argentina and by HESI and ILSI Brasil.

Develops practical solutions to real-world problems through research.

Bringing Standardization to Risk Assessment Worldwide



- Provided scientific evidence to support water disinfection through ILSI Brasil-hosted International Symposium on Cholera in the American Continent and subsequent ILSI water safety meetings in Argentina and USA.
- RSI developed framework for assessing human health risk following exposure to waterborne pathogens.
- ILSI India facilitated water quality management conference, and symposium on pesticide residues in water and food.
- Japan Center for Health Promotion developed operational models to supply clean water and improve hygiene and sanitation practices in Vietnam.

Partnerships…

strategically formed to enhance ILSI research capabilities, dissemination capacity, and local relevance

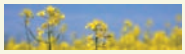
Builds sustainable partnerships that create cumulative scientific benefit to society over time.

- ILSI Southeast Asia (SEA) Region and food safety regulatory bodies of 10 countries in the Association of Southeast Asian Nations (ASEAN) organized Food Safety Standards Harmonization Workshop series, with support from ILSI/ FAO framework.
- ILSI SEA Region nominated to develop and host ASEAN Food Safety Standard Database for online access, providing ongoing updates to the initiative's progress.
- Plays pivotal role in ASEAN science capacity-building efforts.
- With FAO and WHO, organized more than 50 capacity-building workshops to help developing country regulators learn how to use risk assessment in their daily work.

Extends dissemination of information and resources to local levels through appropriate local partnerships.

Advancing Research in Critical Health Risk Arenas

Agricultural Biotechnology



HESI and regional branches pioneered approach to safety assessment and nutritional evaluation of agricultural biotechnology products.

HESI conducted research and developed database to facilitate characterization of allergenic responses to novel proteins.

Chemicals in Packaging and Agriculture

HESI advanced consensus regarding approaches to chemical safety evaluation: facilitated multi-sector evaluation of agricultural chemical safety assessment; characterized dose-dependent transitions in mechanisms of chemical toxicity.

ILSI Europe initiated expert collaboration to develop guidelines for assessing exposure to chemicals in food packaging materials.

Chemical Substances in Food

ILSI North America supported toxicological studies to refine understanding of fumonisin's biological effects. Funded U.S. Department of Agriculture research in Guatemala and Uruguay comparing effects of corn processing techniques on fumonisin content.

ILSI Europe, ILSI North America, and RSI collaborated to respond rapidly and effectively to acrylamide controversy through working groups, expert consultations, publications, and providing resources to critical authorities (FDA and JECFA).

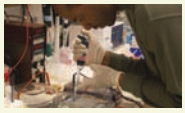
ILSI Europe contributed significantly to European and international harmonization of risk assessment practices for chemicals in foods.

Food Allergens

Funded basic research including: identification and treatment of allergen-sensitive individuals; elucidated immune mechanisms in gastrointestinal response to adverse food reactions; demonstrated cross-reactivity among several allergens; provided unequivocal evidence of pathogenesis of food hypersensitivity in subset of people with asthma; informed understanding of predictors of oral tolerance in children.

ILSI Europe, HESI, ILSI North America, and Research Foundation initiated work on framework for assessing allergenic potential of foods, and for regulatory decision-making on low-dose exposures.

Genomics



HESI conducted extensive, multi-laboratory research contributing to understanding of applicability of genomics.

Evaluated experimental methodologies for measuring alterations in gene expression.

Initiated dialogue regarding integration of genomics into regulatory context.

Pathogens

RSI and ILSI North America collaborated to update science base for *Listeria monocytogenes* risk assessment. Published and shared with Codex Committee on Food Hygiene.

Assessed antibiotic resistance and risk of farming practices to human health.

Developed model systems to filter microbial pathogens from agricultural run-off water.

ILSI Europe published extensive series of reports on pathogens related to foods.

- Formed European network to consider risk assessment realities and needs through three-year European Commission Concerted Action. Led to ILSI Europe work on Benefit and Risk Analysis for Foods (BRAFO).
- HESI collaborated with European Bioinformatics Institute to develop publicly available database of experimental design, toxicology, and microarray data. Developed second database on baseline gene expression in untreated laboratory rodents.
- HESI collaborated with European Chemicals Bureau (ECB) to improve assessment of bioaccumulation of chemicals.

Dialogue…

a neutral ground for fruitful discussions and meaningful consensus among industry, government, academia, and public interest/public health communities

Builds consensus on best practices for risk assessment of food constituents, chemicals, and pharmaceuticals.

- Developed tiered testing framework, through multi-year HESI program, to facilitate safety assessment of agricultural chemicals. Supported and undertaken by international scientists from regulatory agencies, academia, and private sector. EPA working with Organization for Economic Cooperation and Development (OECD) to adapt parts of the tiered testing approach into guidelines.
- Convened allergy experts to develop guidelines for conduct of double-blind, placebo-controlled food challenges to test for food allergic reactions in humans. Guidelines currently utilized worldwide.

- ILSI Europe convened expert group to initiate work on Threshold of Toxicological Concern (TTC) principle. Decision tree for application of principle developed. Joint Expert Committee on Food Additives (JECFA) and EFSA applying TTC to food flavors evaluation and considering other uses.

Provides international forum to advance state of science related to human health, toxicology, risk assessment, and environment.

- Convened expert group of ILSI Europe to develop risk assessment framework for genotoxic carcinogens in food. Evaluated current data and challenges to characterization of the carcinogens. Disseminated findings at international conference co-hosted by EFSA and WHO.
- International expert group convened by RSI to develop principles for selection of doses in long-term animal studies. Incorporated into OECD guidance.

FORWARD FOCUS

Building on three decades of experience, ILSI, the Research Foundation, and the ILSI branches are poised to make significant contributions toward risk assessment for the public good. ILSI focus going forward will be to:

- Develop general principles for adequate characterization of dose-effect relationships.
- Develop improved data and tools that support concomitant assessment of risks and benefits of food components.
- Extend and strengthen application of mode of action in risk assessment.
- Determine if current data and risk assessment tools can be applied to establishing thresholds for food allergens.
- Expand risk assessment training for local partners of the branches.
- Continue to build and recognize science leadership.

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