

Toxicology and Risk Science

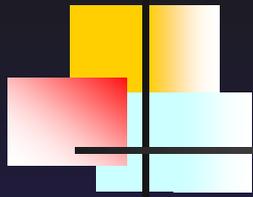
Alan R Boobis

Imperial College London

a.boobis@imperial.ac.uk

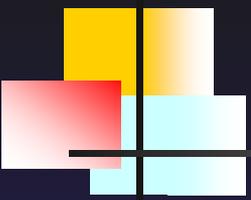
ILSI Annual Meeting
ONE ILSI Strategy

Southampton, Bermuda
17-22 January, 2014



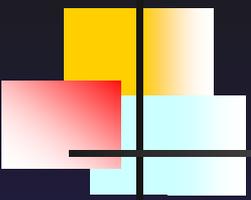
Toxicology and Risk Science

- One of four thematic areas proposed under the ONE ILSI Strategy
- ILSI's very first work in 1978 focused on the toxicology and risk/benefit of food ingredients. Since then, our research and translation of science into practical tools has expanded to all areas of risk science: food and water, pharmaceuticals and consumer products, industrial chemicals, environmental and human health
 - Risk 21
 - TTC and mode of action
 - Nanotech
 - Broad range of toxicology topics (e.g., developmental, neuro, cardiac, genetic, etc.)
 - Risk of risk perception
 - Legacy/history: Lab work on saccharin and ILSI's contribution to delisting



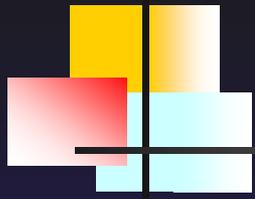
Some contributions of ILSI entities to chemical risk assessment

- Cohen SM, Robinson D and MacDonald J (2001). **Alternative models for carcinogenicity testing**. *Toxicol Sci* **64**:14-19.
- Kroes et al (2000). **Threshold of toxicological concern** for chemical substances present in the diet: a practical tool for assessing the need for toxicity testing. *Food Chem Toxicol* **38**:255-312
- Kroes et al (2004). Structure-based **thresholds of toxicological concern** (TTC): guidance for application to substances present at low levels in the diet. *Food Chem Toxicol* **42**:65-83
- Renwick et al (2003). **Risk characterisation** of chemicals in food and diet. *Food Chem Toxicol* **41**: 1211–1271 [FOSIE]
- Barlow et al (2006). **Risk assessment** of substances that are **both genotoxic and carcinogenic** report of an International Conference organized by EFSA and WHO with support of ILSI Europe. *Food Chem Toxicol* **44**:1636-1650
- Benford D, Bolger PM, Carthew P, Coulet M, DiNovi M, Leblanc JC, Renwick AG, Setzer W, Schlatter J, Smith B, Slob W, Williams G, Wildemann T (2010). Application of the **Margin of Exposure** (MOE) approach to substances in food that are **genotoxic and carcinogenic**. *Food Chem Toxicol* **48** Suppl 1:S2-24



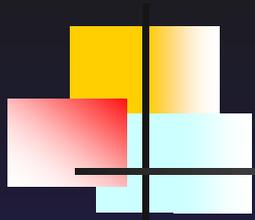
Some contributions of ILSI entities to chemical risk assessment

- Meek ME, Bucher JR, Cohen SM, Dellarco V, Hill RN, Lehman-McKeeman LD, Longfellow DG, Pastoor T, Seed J and Patton DE (2003). A framework for human relevance analysis of information on carcinogenic modes of action. *Crit Rev Toxicol* **33**:591-653
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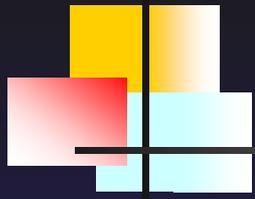
ILSI's mode of operation

- Collaborative research programs
 - Laboratory and desk-based
- Workshops, conferences, and expert panels
- Literature reviews and white papers
- Development and analysis of databases
- Development of accepted test guidelines
- Dissemination of information through journals and other publications.
- Pooling of financial resources



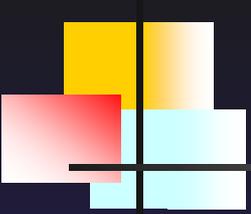
Agricultural Chemical Safety Assessment

- Integrates testing and targets endpoints that will be used for risk assessment
- Avoids generation of data that are not relevant for risk assessment
- Contributes to the reduction and refinement in animal use
- Promotes a dialogue on study relevance
- Reverses trend to guideline proliferation



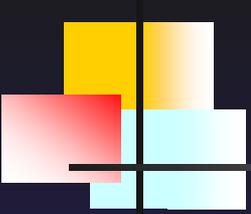
Agricultural Chemical Safety Assessment

- First comprehensive effort to re-design current testing framework for pesticides used by many national authorities
- Cited as the basis for the OECD Guideline for Testing of Chemicals – Extended One-Generation Reproductive Toxicity Study (TG 443)
- Received international attention (e.g. EPA, EFSA, JMPR, OECD): precedent-setting potential in harmonizing data requirements; moves towards a more science-based approach



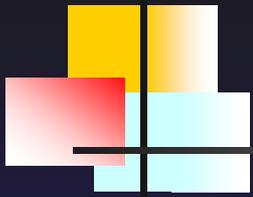
Global change in risk assessment landscape

- High-throughput technologies, computational toxicology, systems biology and bioinformatics
- Genomics and epigenetics
- Need to understand cumulative risk
- New regulatory schemes that will provides reams of data
- Issues of international importance
 - Biofuels
 - Nanotechnology
 - Climate change
- Finding solutions to issues of international importance will require a talented workforce, conducting integrated, multi-disciplinary research



Importance of global collaboration to advance risk assessment

- Lack of toxicity/exposure information on chemicals in commerce
 - 100,000+ chemical on market <1981
 - 4,000+ chemicals >1981
 - No basic tox data for 86% of HPV chemicals (>1,000 tons/yr)
 - Previous risk assessment/management completed for 39 of 141 HPV chemicals
- Slow chemical risk assessment, burden on government
- No incentives for developing/implementing safer substitutes
- Increasing evidence of health effects
- Lack of integrated and comprehensive approach to chemicals management
- Therefore, global collaboration is important to advance risk assessment both within US as well as in countries/institutions around the world



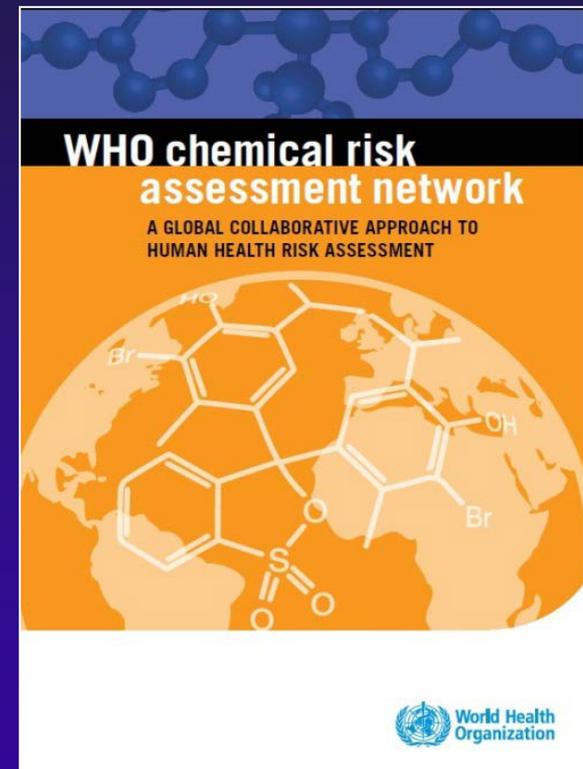
Challenges to ILSI

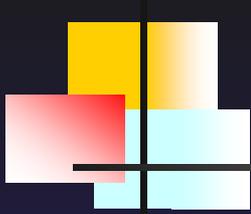
- Need to capitalize more on global reach of organization
 - Greater collaboration between entities both to benefit from expertise and to provide solutions where they are most needed
- Improve multi-stakeholder and multi-sector interactions
- Work with external organizations, not necessarily always as lead but ensure recognition for ILSI's contribution

Goal of the WHO Risk Assessment Network

Network Launch 1 July 2013

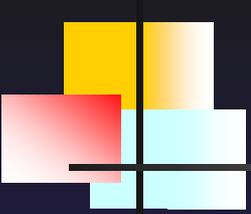
- To improve chemical risk assessment globally through fostering and facilitating sustainable interaction between institutions on chemical risk assessment issues and activities





Objectives of Network

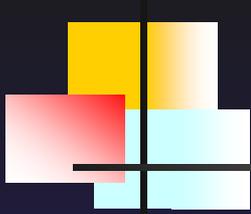
- Provide a forum for scientific and technical exchange
- Facilitate and contribute to capacity building
- Promote best practices and encourage harmonization of methodologies
- Assist in the identification of research needs and promote the application of new science in risk assessment practice
- Assist in the identification of emerging risks to human health from chemicals
- Share information about work programmes to avoid duplication of effort
- Upon request, assist WHO in the development of training and other materials in support of the above



Structure of WHO Risk Assessment Network

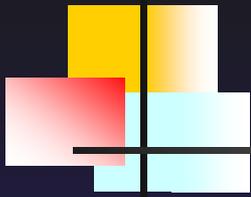
- Global scope; all WHO regions and all economic strata
 - Comprised of participants from institutions such as:
 - Government and public health institutions
 - Intergovernmental organizations
 - Professional societies
 - WHO Collaborating Centres
 - Non-governmental organizations in official relations with WHO
 - Other non-profit entities with relevant expertise
- Contributions from Network Participants may be in form of financial support, in-kind input to projects, technical expertise or sharing of information

Current status of WHO Risk Assessment Network



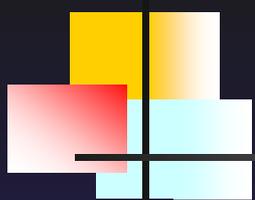
WHO Chemical Risk Assessment Network





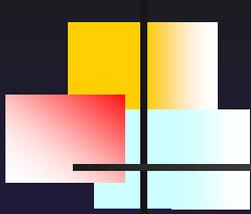
Training Database

- An online database is being developed to provide access to information regarding human health chemical risk assessment training courses worldwide
- Database will allow for searching for in-person and online post- and undergraduate, continuing education and society-sponsored training courses, of a non-profit nature
- Relevant details and contact information would be provided
- Examples of topic areas to be included: basic & complex assessments, environmental & occupational health, hazard identification & characterization, toxicology, epidemiology, predictive methods, exposure assessment, risk characterization, bioinformatics, etc.



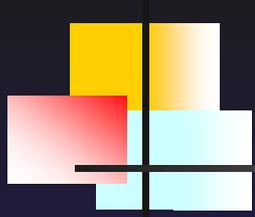
Training Database

- November 2013
- ILSI HESI finalized a collaborative agreement with the World Health Organization to jointly develop and maintain a freely-available on-line database of chemical risk assessment training courses
- WHO will provide regular input and guidance on the overall database project activities
- HESI will provide financial and in-kind support for development and implementation of this collaborative resource



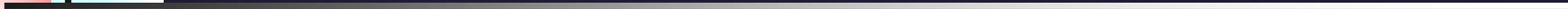
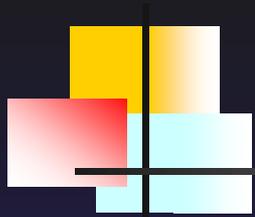
Mode of Action

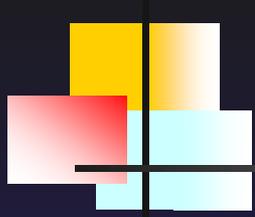
- WHO MOA Steering Group provides a forum for coordination and collaboration on international activities on Mode of Action.
- Current areas (and lead organizations):
 - Update of the WHO MOA Framework Guidance (Meek et al, 2013) (WHO)
 - Development of case studies (WHO)
 - Implementation of MOA in category approaches (OECD)
 - Development of a MOA/AOP database (JRC, USEPA, OECD)
- ECETOC/WHO Workshop held in February 2013 in Vienna to present the guidance and obtain feedback on communicating the framework and enhancing its implementation



WHO Network and One ILSI

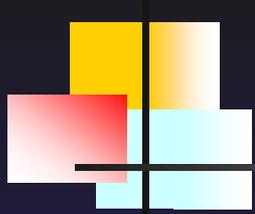
Potential opportunity to utilize ILSI's involvement in the WHO Chemical Risk Assessment Network to better coordinate amongst branches





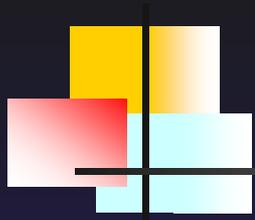
Anticipated network outcomes

- Enhanced collaboration between institutions on RA issues
- Increased capacity to conduct high quality RA
- Incorporation of harmonized methodologies and emerging science
- Efficient and timely knowledge transfer



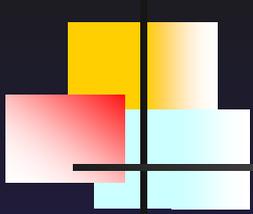
Agricultural Chemical Safety Assessment

- Base Set (Tier 1)
 - Integrated approach to evaluating systemic toxicity
 - Pivotal 28-day rat study
 - Dosing based on kinetics and physiology
 - Evaluation of relative sensitivity of rat v. dog
 - Full utilization of animals in each study via thorough analysis of clinical chemistry, histopath, etc.
 - Reduces/refines animal usage
 - Concentration on effects of concern
- Tier 2
 - Testing focused on endpoints identified in Tier 1
 - Flexible study designs
 - Mechanistic data explored



ILSI: Making a difference

- Primary research
- Improved methodologies
- Anticipation of emerging issues
- Global collaboration
- Solutions with tangible health outcomes



Some current network activities

Activities underway include:

- Development of an on-line database of risk assessment training courses
- Update of the WHO Framework on Mode of Action
- WHO publication on identifying important life stages for monitoring and assessing risks from exposure to environmental contaminants
- WHO guidance on characterizing uncertainties and variability in hazard assessment
- A review of research needs identified in past WHO risk assessment documents