



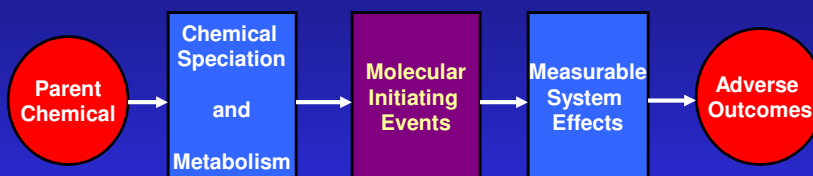
Toxicity Pathways as an Organizing Concept

Gilman Veith

McKim Conference on Predictive Toxicology

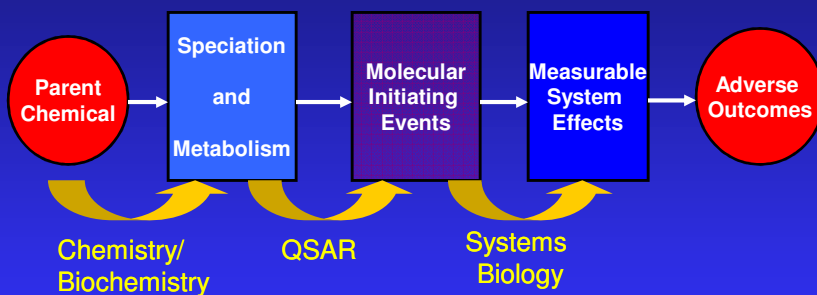
The Inn of Lake Superior
Duluth, Minnesota
September 25-27, 2007

Conceptual Framework



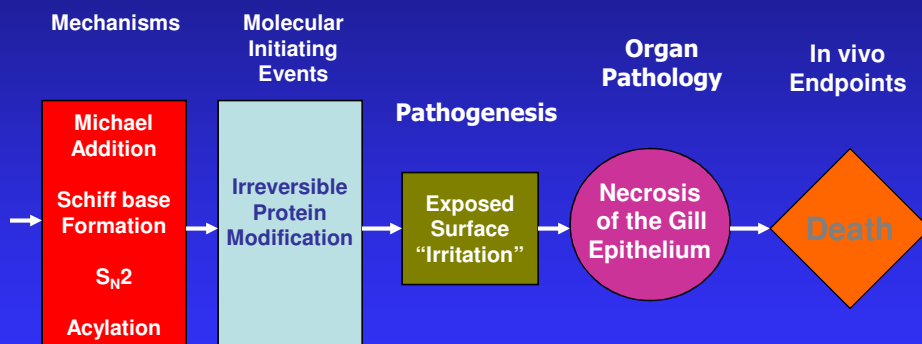
Rather than developing statistical models of complex endpoints, key molecular initiating events become the "well-defined" endpoints for QSAR.

IQF Framework for QSAR

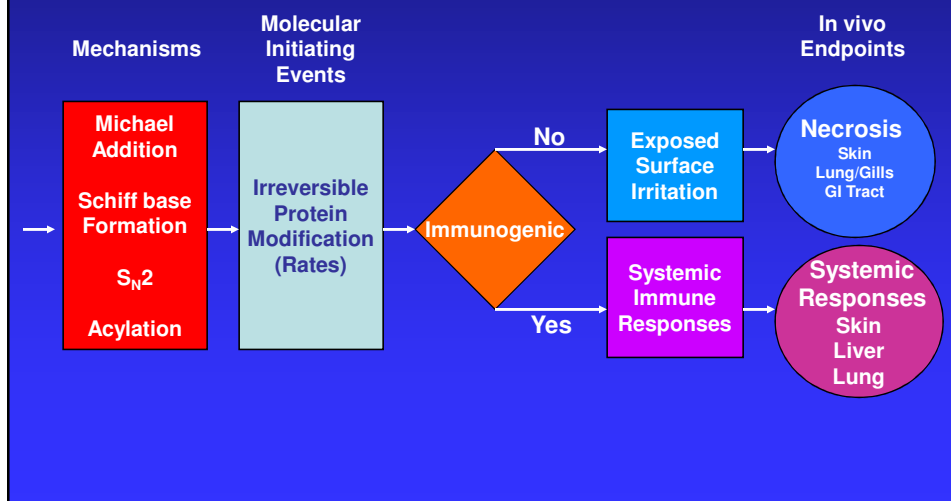


1. Identify Plausible Molecular Initiating Events
2. Design Database for Abiotic Binding Affinity/Rates
3. Explore Linkages in Pathways to Downstream Effects
4. Develop QSARs to Predict Initiating Event from Structure

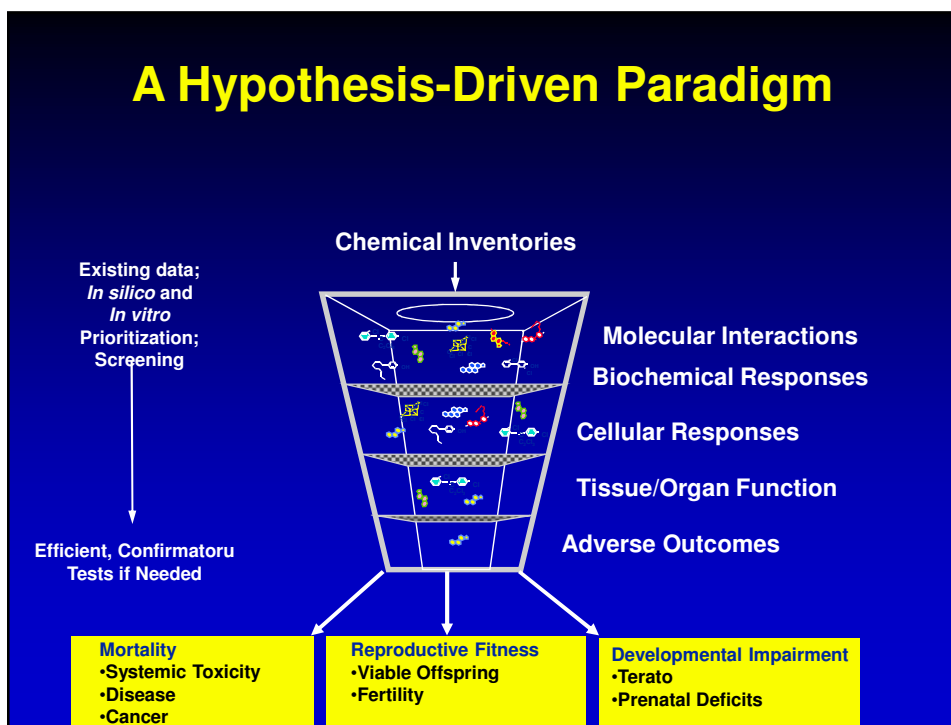
Major Pathway for Reactive Toxicants To Fish



Primary Pathways for Reactive Toxicity from Soft Electrophiles



A Hypothesis-Driven Paradigm



Current Paradigm

- Risk Managers Focus on Potential Adverse Outcomes



- Current toxicology testing paradigm generates *In Vivo* animal data for all possible outcomes to determine which are relevant

Example: Receptor-Mediated Pathways

Linkage Across Levels of Biological Organization

