Path Forward…

Development and Validation of ED Assays

- US EPA will assess estrogen, androgen and thyroid effects for humans and wildlife
- EDSP will be a two tiered screening and testing program

  - **Tier 1**
    - *in vitro and in vivo screens*
    - *detect potential to interact with the endocrine system*
    - *Data on mechanism*

  - **Tier 2**
    - *multi-generation studies covering a broad range of taxa*
    - *provide data for hazard assessment*

For more information on the EDSP visit
www.epa.gov/scipoly/oscpendo

Initial Chemicals To Be Screened

- The September 27, 2005 Federal Register Notice Vol.70, No., 186 describes the exposure-based approach for selecting the initial 50-100 chemicals to be tested.

- The scope of the chemicals to be tested includes pesticide active ingredients and high production volume (HPV) chemicals used as pesticide inerts.

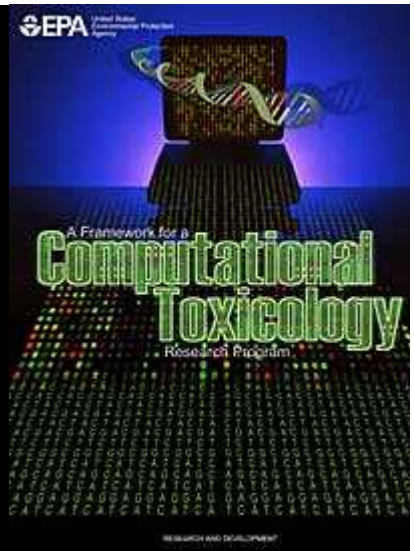
For more information

http://www.epa.gov/fedrgstr/EPA-TOX/2005/September/Day-27/t19260.htm

Initial Chemicals To Be Screened

- Pesticide actives to be selected based on
  - Presence in food
  - Presence in drinking water
  - Residential use
  - Occupational contact
- HPV pesticide inerts to be selected based on
  - Human biological monitoring data
  - Ecological monitoring data
  - Chemicals in drinking water monitoring data
  - Indoor air monitoring data

EPA's Office of Research and Development Computational Toxicology Framework



- The Goal
  - Application of math and computer models for prediction of effect and understanding MOA
- The Objectives
- Characterization of toxicity pathways
  - Provide quantitative structure activity relationships (QSAR) to improve risk assessments and reduce uncertainties
  - Improve quantitative risk assessments
- Measure of Success
  - Enable a paradigm shift to hypothesis-driven hazard assessment

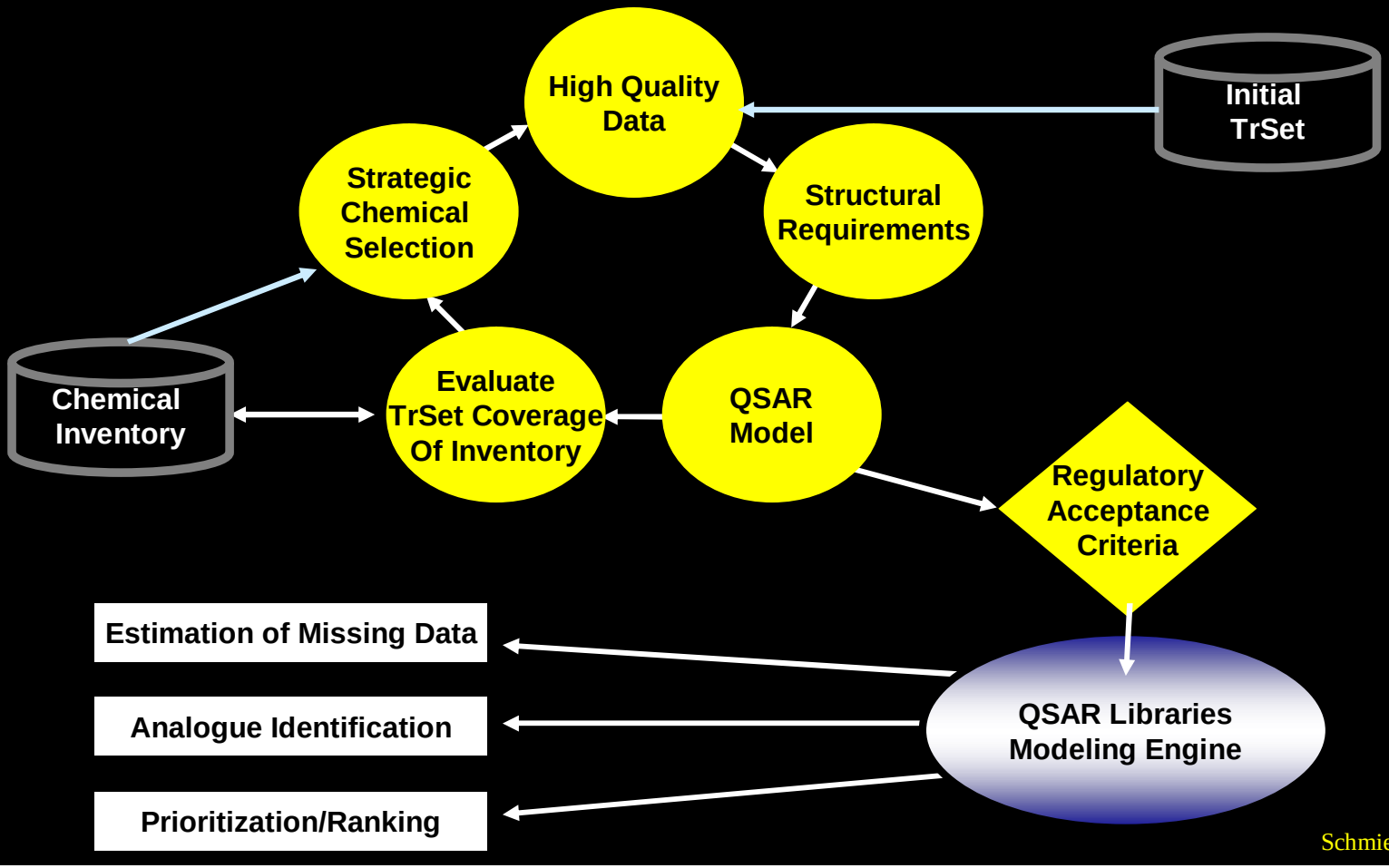
http://www.epa.gov/comptox

Prioritizing EDC Risk Assessment Questions within Large Chemical Inventories

Developing Predictive Models is an Iterative Process

Elucidate Toxicity Pathway
(e.g., ER binding
initiated pathway)

Evaluate Inerts and Antimicrobials
For Ability to Initiate Pathway
(e.g., ER binding training set (TrSet))

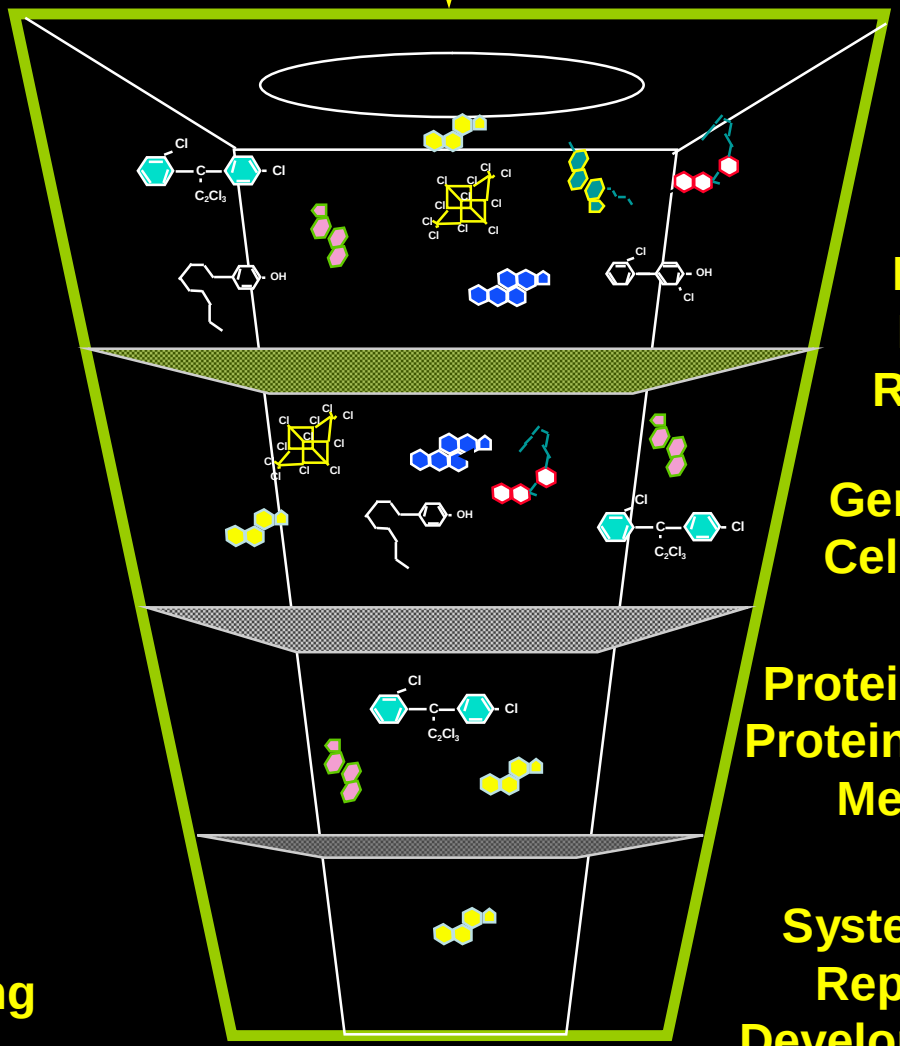


Schmieder, 2004

Goal: Identifying Toxicological Potential

Chemical Inventories (pesticide actives, inerts, antimicrobials, high production volume chemicals,etc)

Non-Animal Ranking & Prioritization; Screening



Efficient Animal Testing

Partitioning; Electrophilicity; Redox Cycling; Receptor Binding

Gene Activation; Cellular Function

Protein Inhibition; Protein Production; Metabolism

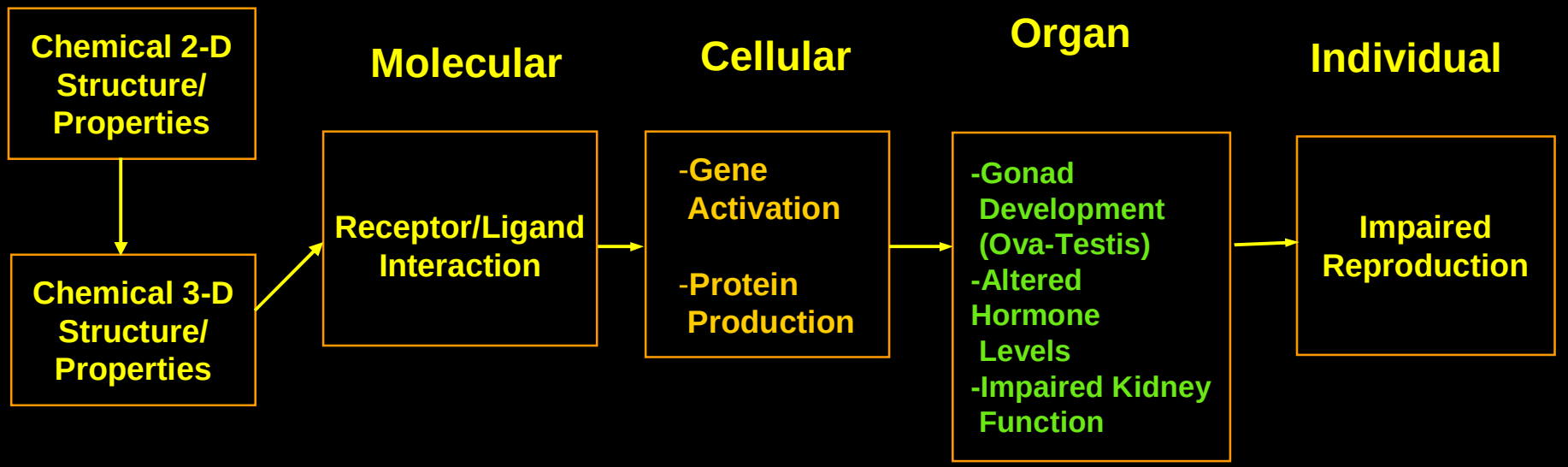
Systemic effects, Reproduction, Development, Cancer

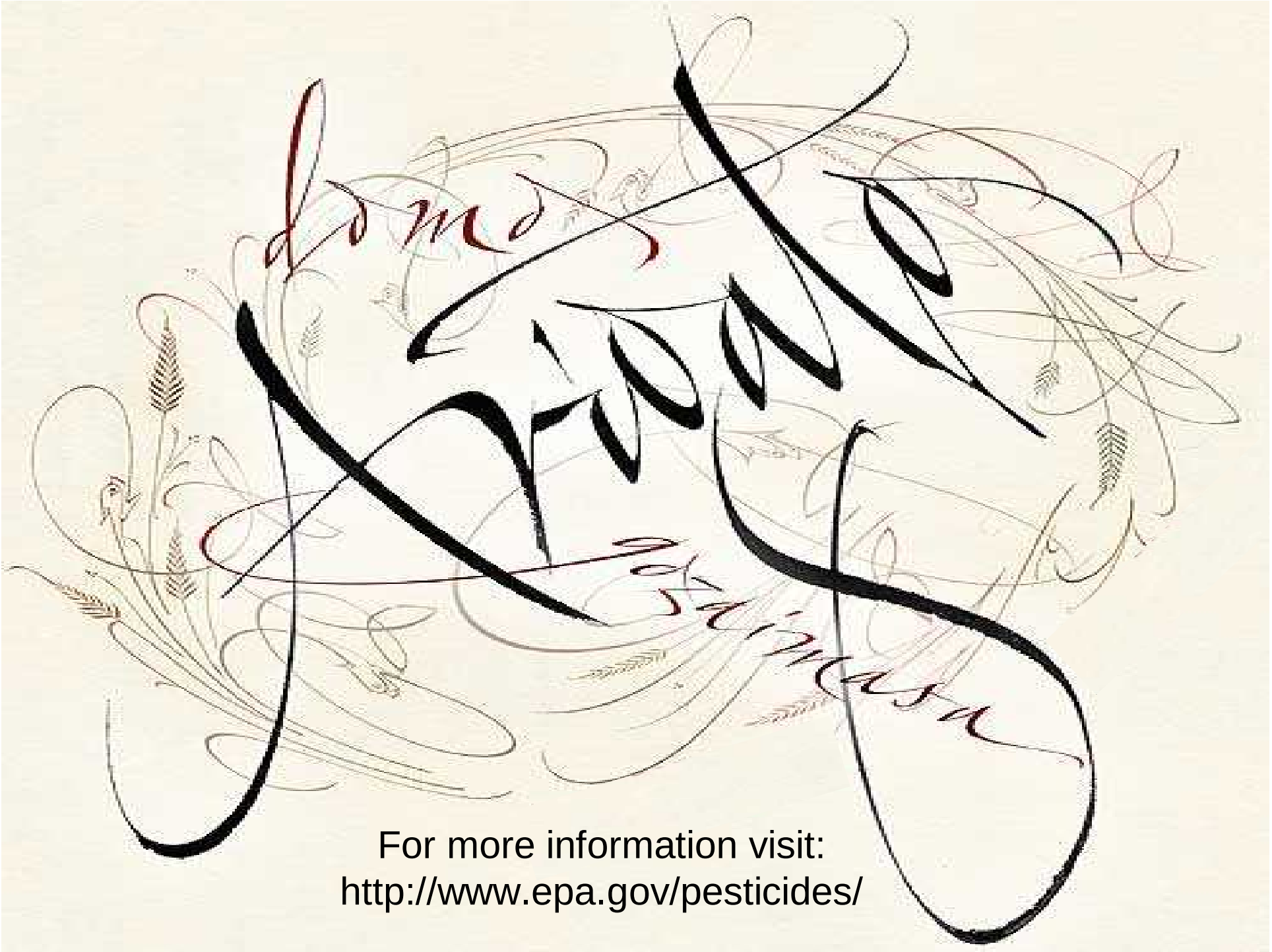
Existing Data and Models

Chemical Risk Assessments

Links Across Levels of Biological Organization

Receptor-Mediated Pathways




Thank You
For more information visit:
http://www.epa.gov/pesticides/