



Integration of Epidemiology along with Other Scientific Evidence into Human Health Risk Assessment

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Introduction

- Office of Pesticide Programs is a licensing program regulating pesticide products in the U.S.
 - ▣ Federal Insecticide, Fungicide & Rodenticide Act (FIFRA)
 - Requires registration of new products and uses
 - Requires review of older pesticides
 - Includes ability to issue data call-ins
 - Regulates the manufacture, composition, sale, labeling, use and disposal
 - Worker protection, certification and training
 - ▣ Federal Food, Drug and Cosmetic Act (FFDCA): Requires establishing tolerances (maximum residue limits) for pesticides on food and feed
 - ▣ Food Quality Protection Act of 1996 (FQPA)
 - Amended both FIFRA & FFDCA
 - Requires aggregate exposure (multi-pathway, single chemical) & cumulative exposure (multi-pathway, multi-chemical for those sharing common mechanism of action)
 - Additional 10X Safety Factor for the protection of children

Experimental Toxicology & Epidemiology



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	Experimental Toxicology	Epidemiology
Subjects	Non-human, homogenous populations, sample sizes limited	Humans, diverse populations, sample sizes vary
Experimental Design/Exposure	Control of experimental factors Exposure well characterized: single, pure active ingredient but high doses & short durations	Observation of associations Exposure difficult (often poor) characterized multiple compound exposures, low exposure, durations vary
Outcomes	Observable & measurable	Observable, measurable, or self-reported
Key challenges	Extrapolation: species, high to low dose, duration	Attribution to chemical(s) of interest

Adapted from Boyes et al, (2007)



Draft FW for Incorporating Epidemiology

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- *Draft Framework for Incorporating Human Epidemiologic & Incident Data in Health Risk Assessment*
 - Reviewed favorably by the FIFRA SAP (Feb, 2010)
- Concepts in the Draft Framework are based on peer-reviewed, robust principles & tools
 - Standard practice in epidemiology, toxicology & risk assessment
 - Flexibility to incorporate information from different sources
 - Transparent tool for organizing, reviewing & interpreting complex information
- Improvements based on recommendations from
 - NRC 2007: Toxicity Testing in the 21st Century
 - NRC 2009: Science & Decisions: Advancing Risk Assessment
- Two major components: Problem formulation & Modified Bradford Hill Criteria as in the Mode of Action Framework



Problem formulation

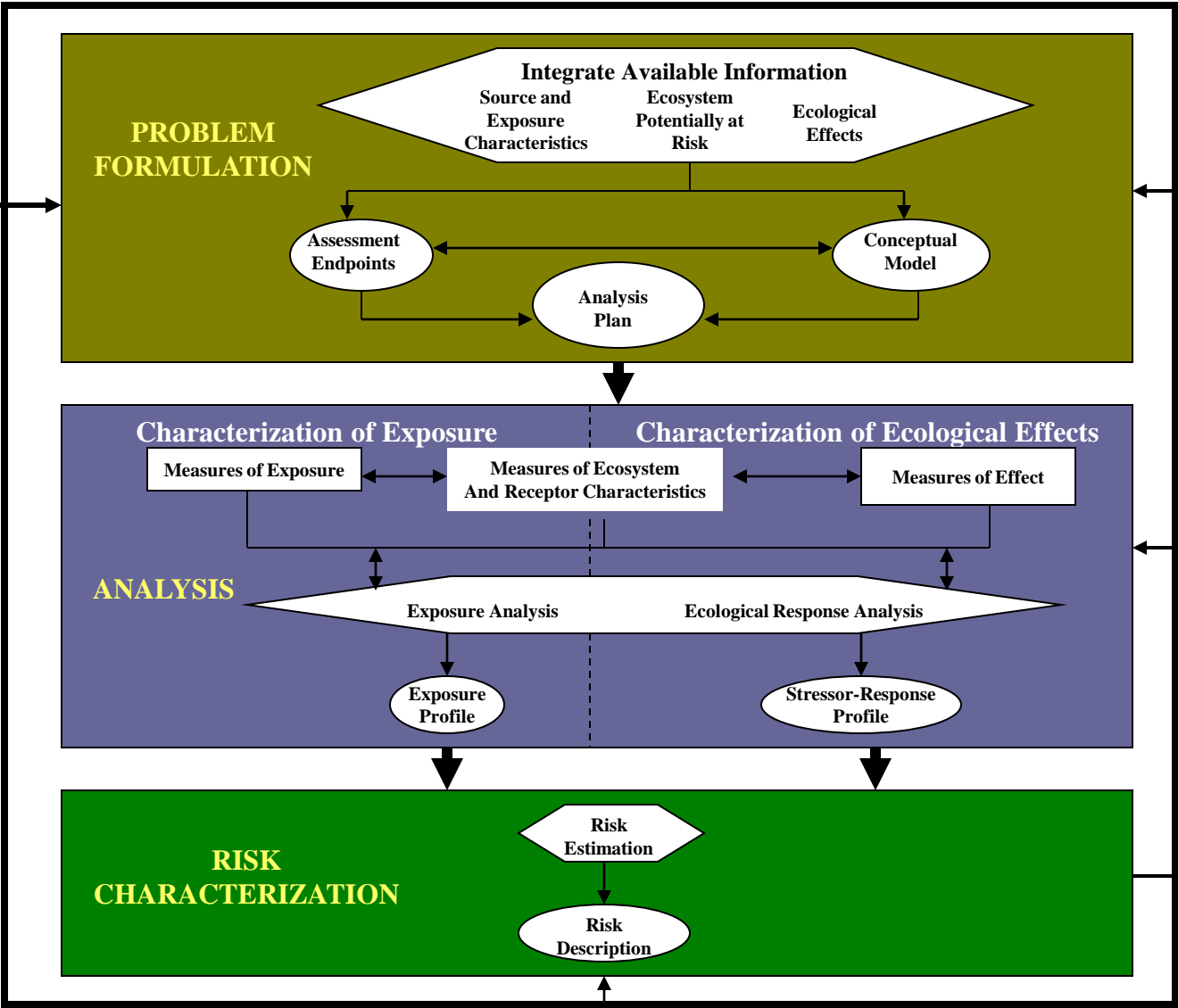
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- Planning dialogue with risk managers on goals & needs
- Evaluate the nature of the problem, including the nature of the stressor(s) and exposure characterization
 - ▣ Assess the available information regarding the pesticide, effects, & exposure characteristics
 - ▣ Identify data and information gaps
- Develop a plan for analyzing data and characterizing risk

FRAMEWORK FOR ECOLOGICAL RISK ASSESSMENT

**Planning
(Risk Assessor/
Risk Manager
Dialogue)**

- 1. Management Goals
- 2. Management Options
- 3. Scope, Complexity, and Focus
- 4. Resources
- 5. Scheduling

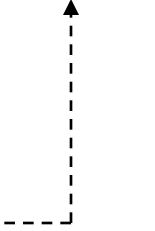


As Necessary

Acquire Data,
Iterate Process,
Monitor Results

Communicating Results to the Risk Manager

Risk Management





Types of Risk Mitigation Measures

- ❑ Cancel or delete uses
- ❑ Limit amount, timing, frequency of use
- ❑ Buffer zones
- ❑ Ecological safeguards
- ❑ Ground and surface water safeguards
- ❑ Specific to workers:
 - ▣ Restrict use to certified applicators
 - ▣ Personal protective equipment, restricted entry intervals, post harvest intervals
 - ▣ Special packaging, engineering controls

The Label is The Law



Mode of Action Framework

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Modified Bradford Hill Criteria

- Postulated mode of action
 - ▣ Identify sequence of key events on the path to health outcome
- Experimental support
 - ▣ Concordance of dose-response for key events
 - ▣ Temporal relationships for key events
- Biological plausibility & coherence
- Strength, consistency & specificity
- Other modes of action
- Identify uncertainties
- Conclusion

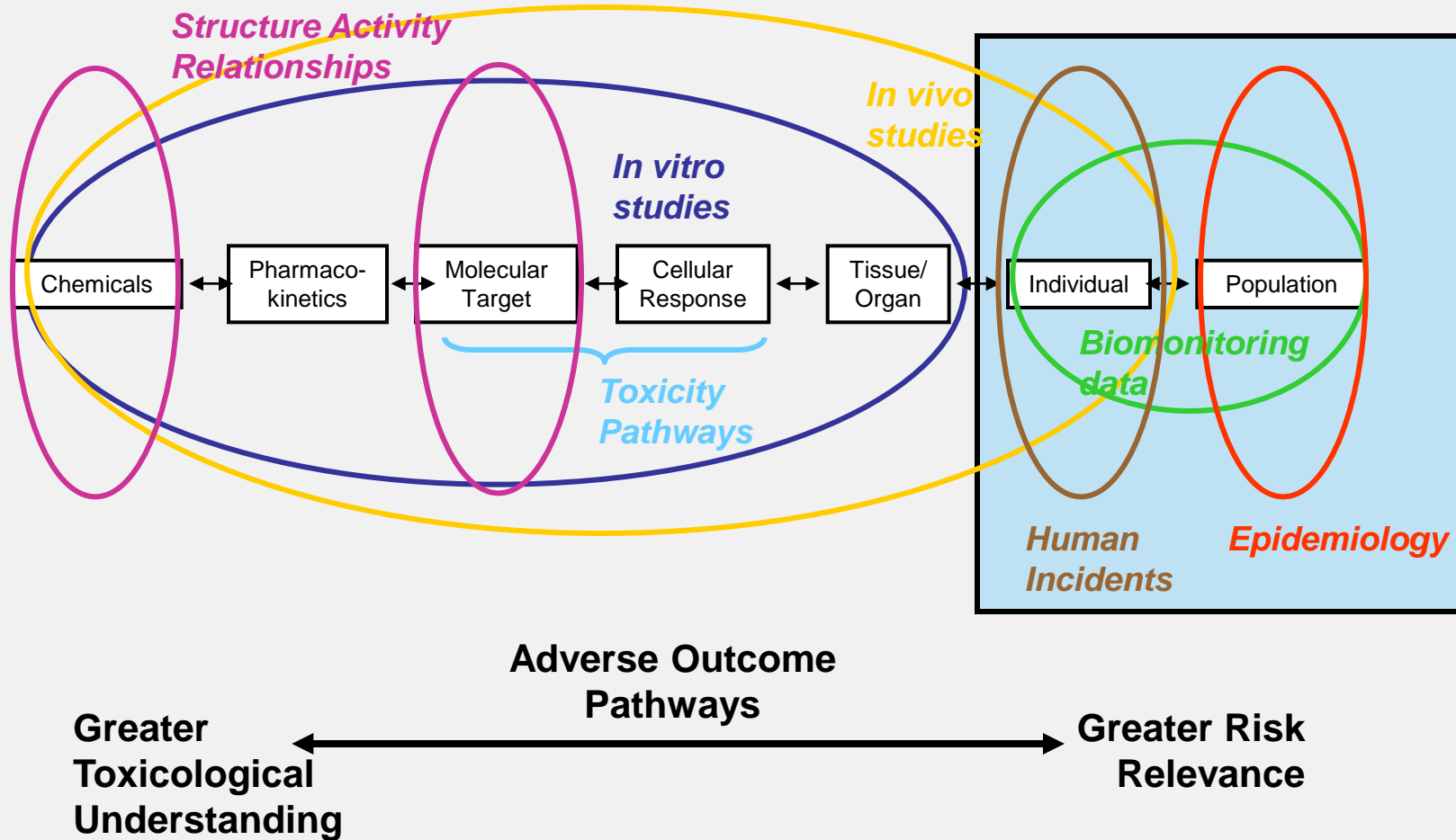


Mode of Action Framework

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- Promote maximal use of relevant information
- Focus species & dose-response extrapolations in mode of action context
- Basis for explicit consideration of confidence & certainty
 - ▣ Improves transparency
- Harmonize across endpoints
- Tool for integrating data across many sources
 - ▣ Including those from new technologies

Source to Effects Pathway, Adapted from NRC, 2007



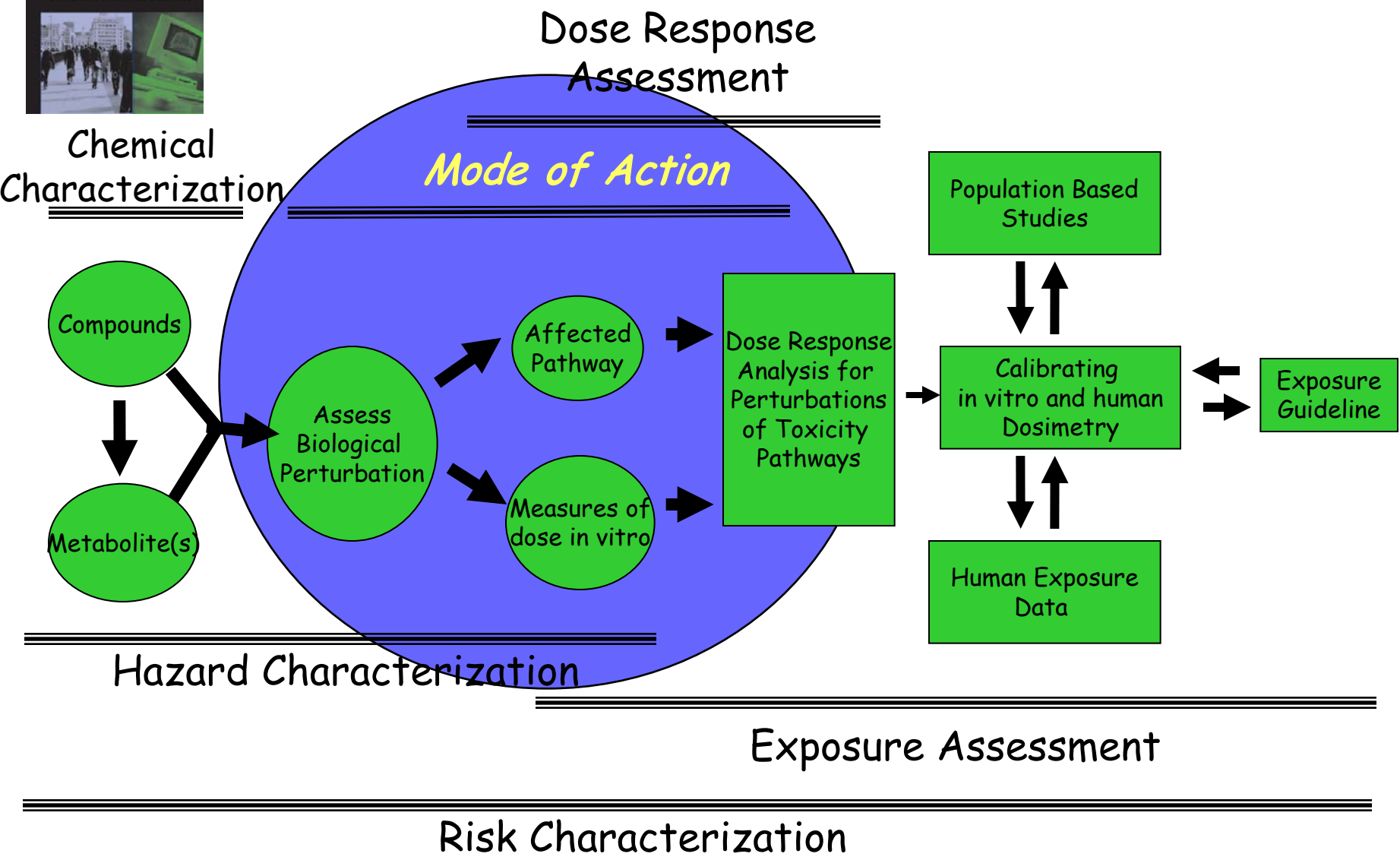
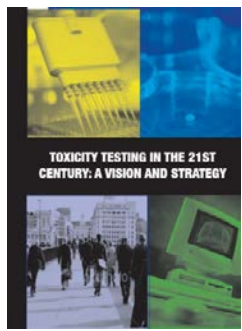


Fig 3-7 Risk Assessment Components



Human Health Risk Assessment

- Risk assessments are developed with a transparent public process
- Numerous scientific peer reviews on approaches, guidance documents, & models
- Advisory boards:
 - FIFRA Scientific Advisory Panel (SAP)
 - EPA's Science Advisory Board (SAB)
 - Pesticide Program Dialogue Committee (PPDC)
- Public participation
 - Opportunities for public to provide comments on assessments
 - http://www.epa.gov/oppsrrd1/registration_review/public_involvement.htm
 - <http://www.epa.gov/oppsrrd1/reregistration/public.htm>