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Collaborative on Health and the Environment

Partnership Call - Advancing Risk Assessment: Progress and Ongoing Obstacles

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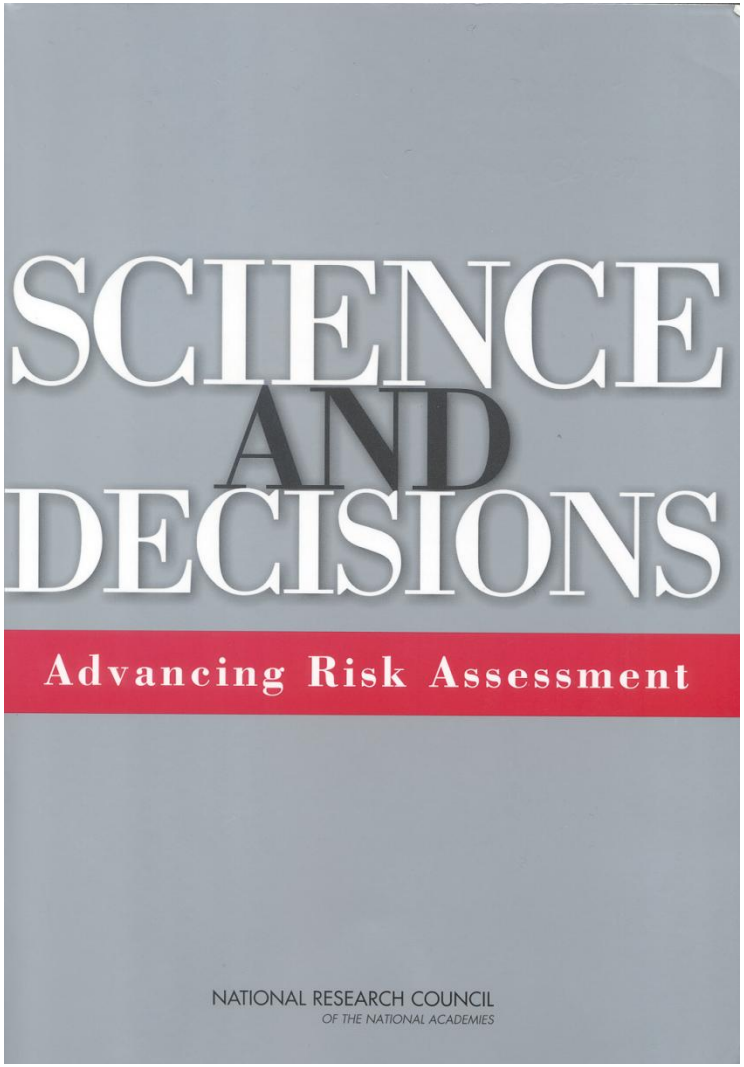
Disclaimer: These comments do not necessarily represent the views of the Office of Environmental Health Hazard Assessment, the California Environmental Protection Agency or the State of California

Focus of Recommended Improvements



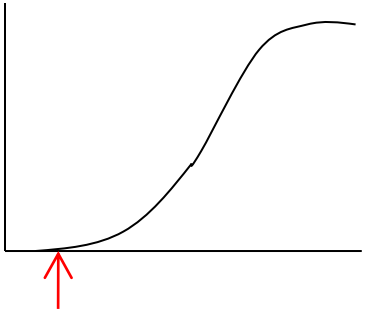
1. Technical analysis
   Improve science of risk characterizations
   - Design of risk assessment
   - Default inferences
   - Uncertainty and variability
   - Dose response
   - Cumulative risk assessment

2. Assessment utility
   Improve relevance and use for decisions
   - "Risk-based Decision-making Framework"

Default Inferences

Example Default Inferences

Effects in animal studies indicate human effects



Non-cancer effects have threshold-like dose response relationships

A factor of 1, 3, or 10 accounts for human differences in non-cancer effects

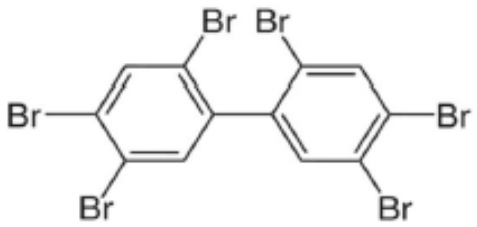
Recommendation

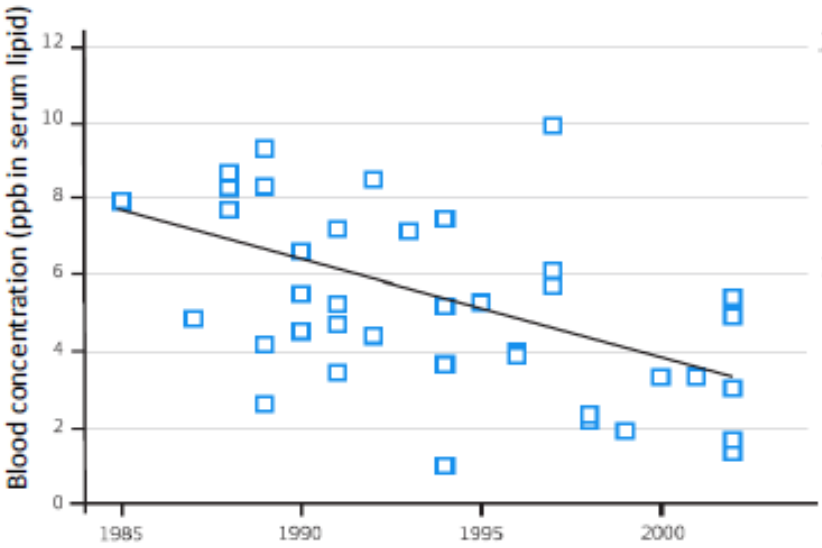
- Defaults need to be maintained
- Develop clear, general evidence standards for departure from default “the alternative is ‘clearly superior’”
- Address missing defaults

Missing Default Examples

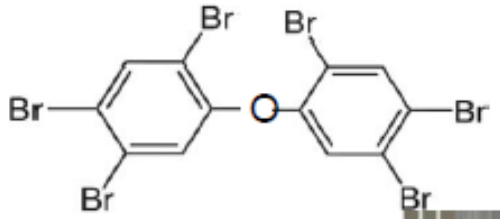
- Chemicals without data pose no risk worthy of regulatory attention
- All people are equally susceptible to mutagenic carcinogens
- Chemicals have no in utero carcinogenic activity
- Threshold-like agents act independently of “background” or “host susceptibility”

- **PBBs: Phase out - 1974**





- **PBDEs: A substitute**



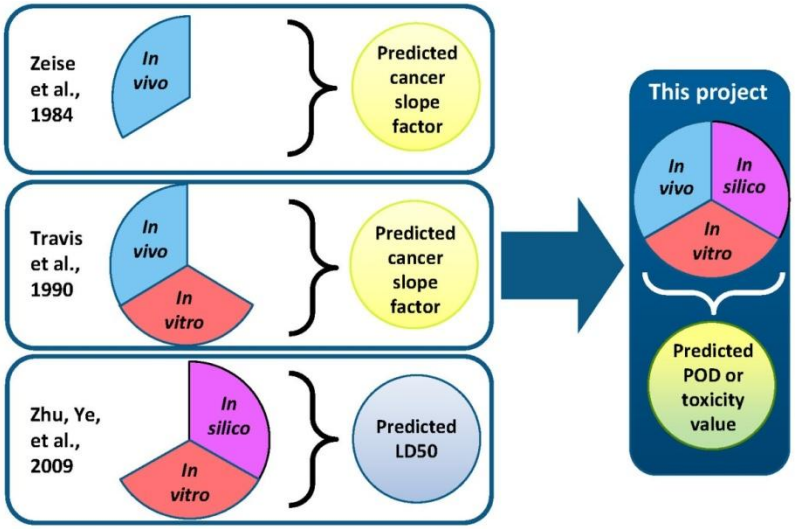
Developing data gap filling defaults

- Integrating data streams
  - ➢ Wignall, Rusyn, Woodruff, Guyton, Chiu, Zeise, SOT 2012

  Predicting degree of toxicity from available data

- Using high throughput data
  - ➢ EPA CompTox

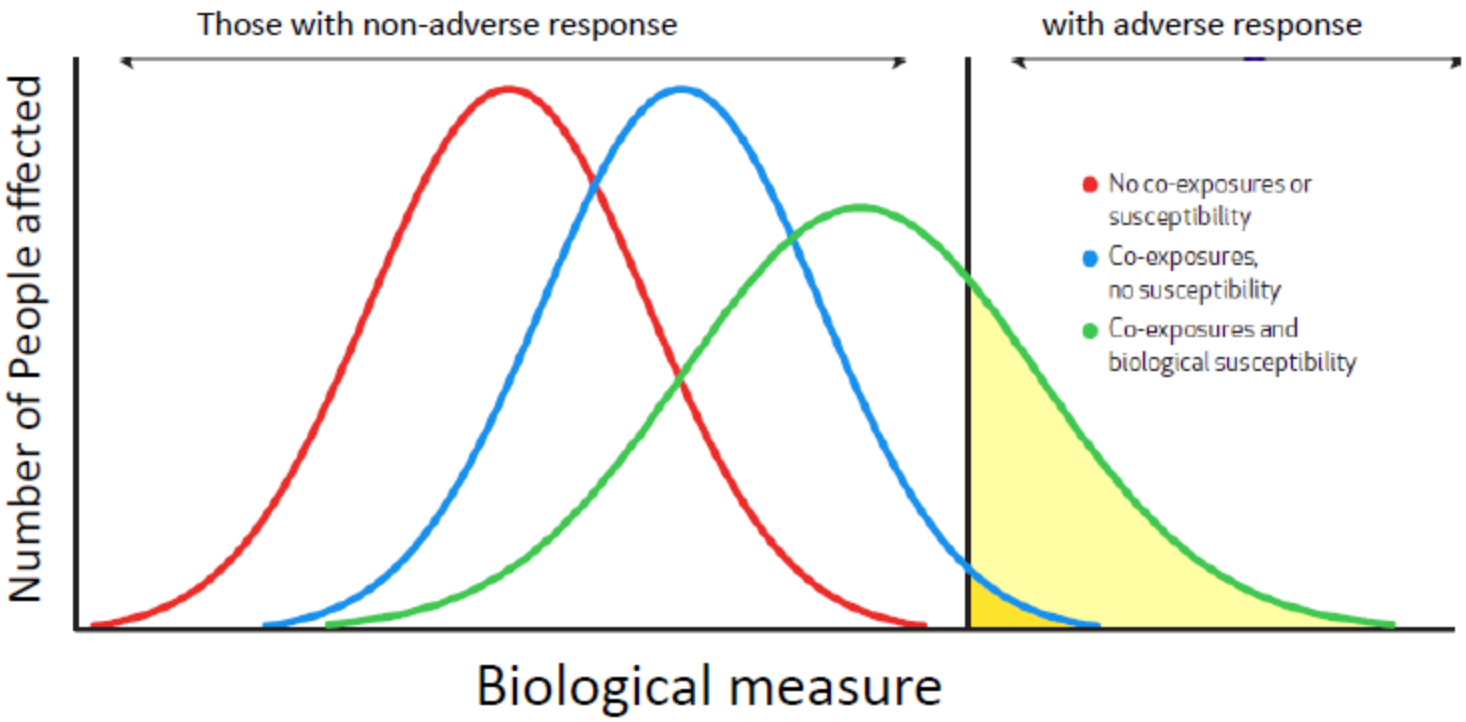
  Predicting degree of toxicity from ‘omics data



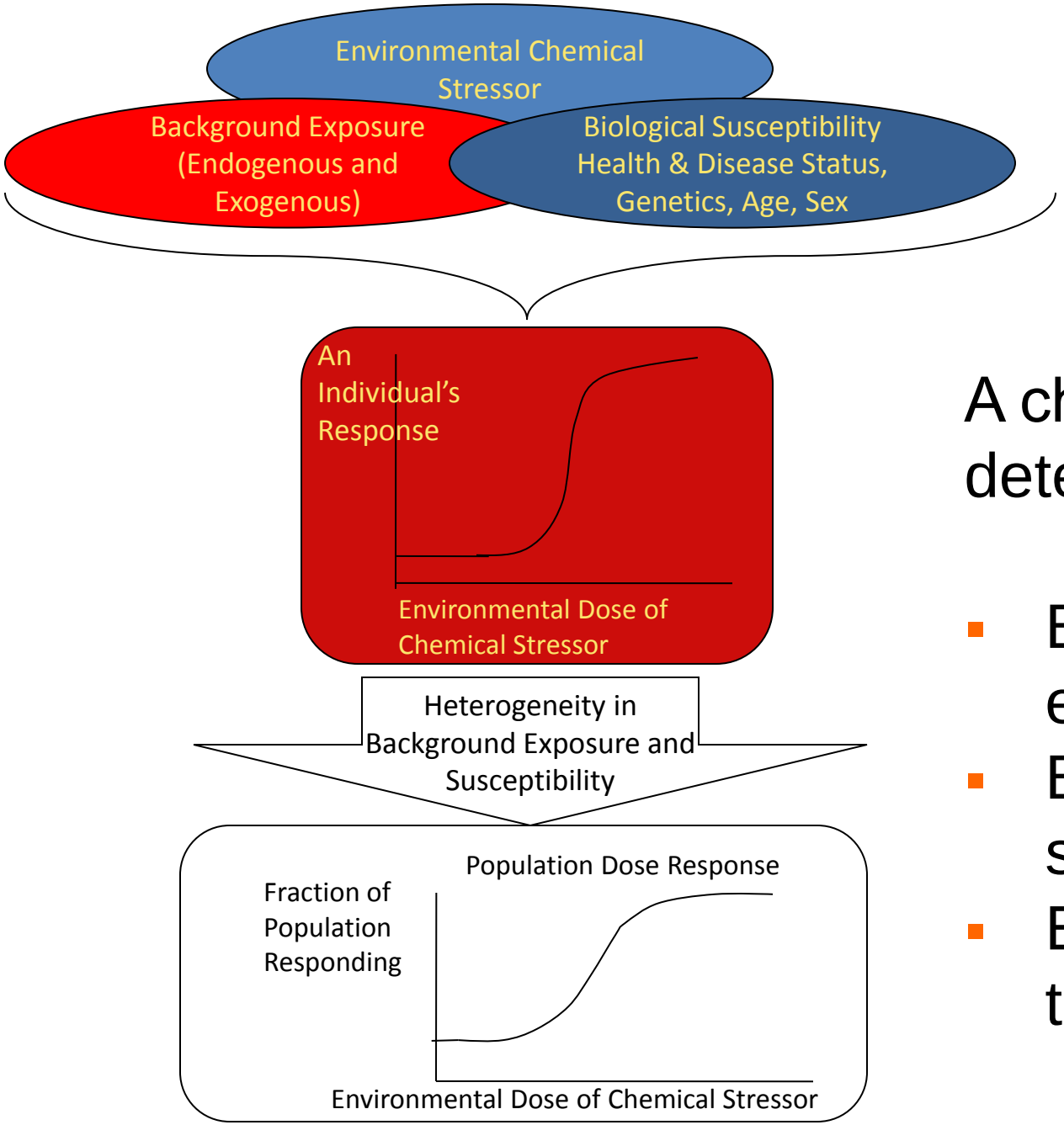
Science and Decisions: *“[A] key priorit[y] should be development of default approaches to support risk estimation for chemicals lacking chemical-specific information … to develop a dose-response relationship.”*

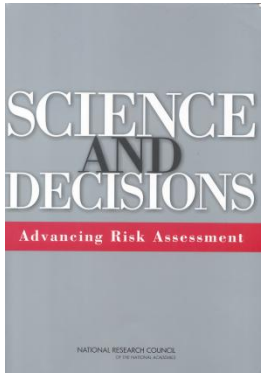
Variability

Biological Susceptibility and Chemical Co-exposures
Effect on Adverse Health Effects



Dose Response

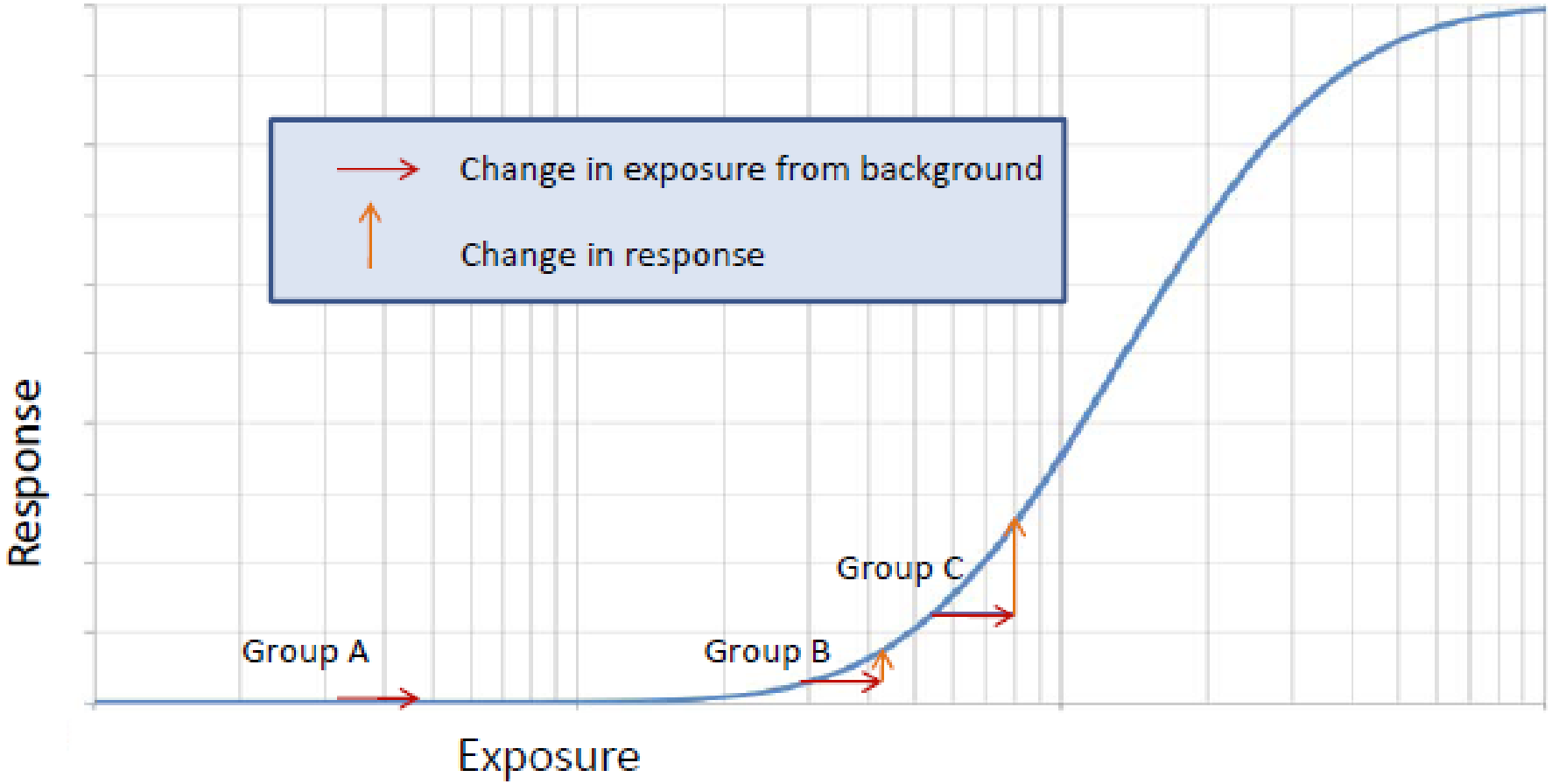




A chemical's risk is determined by:

- Background exposures
- Biological susceptibility
- Exposure level to the chemical

The “background” issue



Cumulative Risk Assessment