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Cumulative Risk Assessment at the EPA – Steps Towards Guidance

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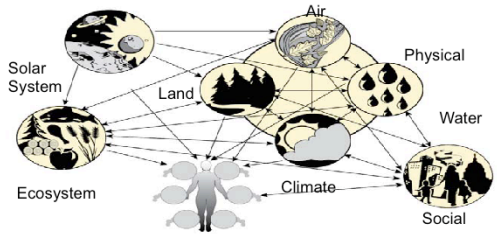
Risk Assessment Forum



May 5, 2009

1

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Overview of Presentation

- Steps toward cumulative risk assessment:
  - A brief history
- EPA Risk Assessment Forum efforts:
  - Framework for Cumulative Risk Assessment
  - Integrating current knowledge:
    - Issue Papers
    - Case study examples
    - Research Needs [pending]
- Integrating CRA approaches

2

Acknowledgments and Disclaimer

Risk Assessment Forum Technical Panel for Cumulative Risk Assessment:

- Edward Bender, OSA (retired)
- George Bollweg, Region 5 (co-chair)
- Mike Callahan, Region 6 (retired)
- Elaine Cohen Hubal, NCCT
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- Anna Lowit, OPPTS/OPP
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- Winona Victery, Region 9

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What is Cumulative Risk Assessment?

- **Aggregate exposure assessment:** An estimate of the exposure to a given chemical by ingestion, inhalation and dermal absorption for a defined population, from all relevant media.
- **Cumulative Risk:** The combined risks from aggregate exposures to multiple agents or stressors.
- **Cumulative risk assessment:** An analysis, characterization, and possible quantification of the combined risks to health or the environment from multiple agents or stressors.
- **Not to be confused** with risk ranking and weighting approaches:
  - Comparative risk
  - Relative risk

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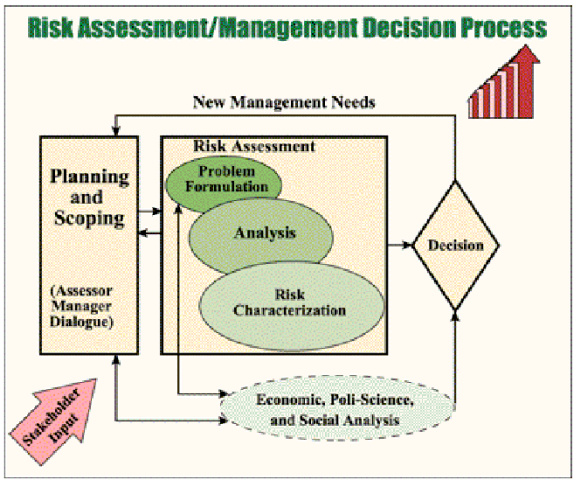

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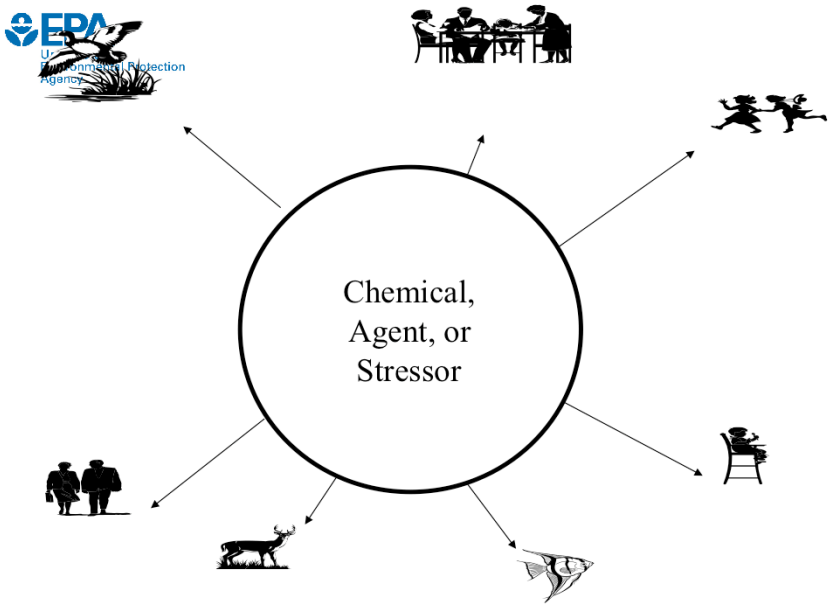
Stages in the integrated Risk Assessment Process



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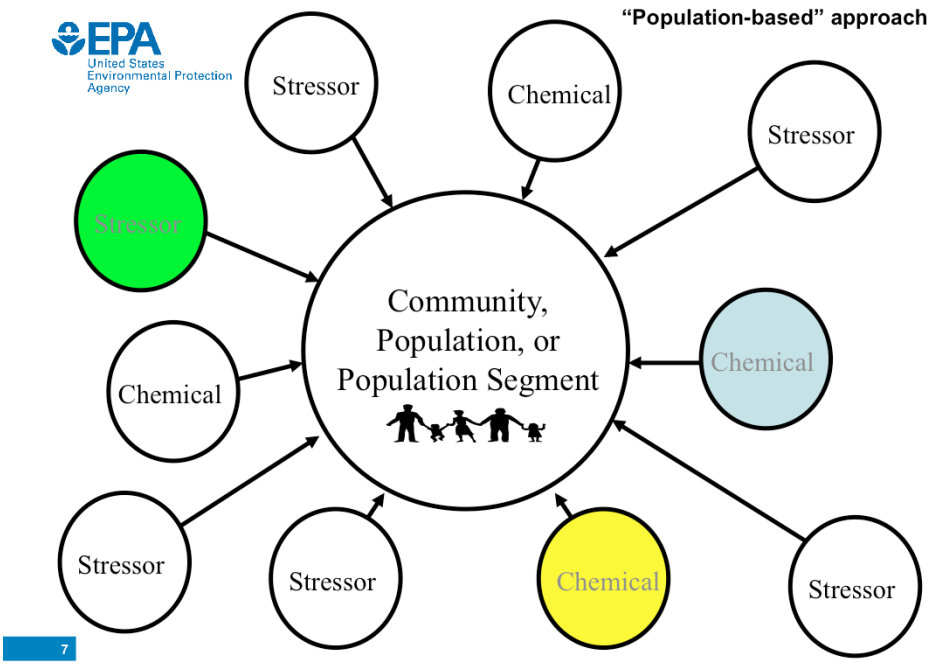
"Traditional" approach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"Population-based" approach
Stressor
Chemical
Stressor
Stressor
Community,
Population, or
Population Segment
Chemical
Chemical
Stressor
Stressor
Chemical
Stressor
7

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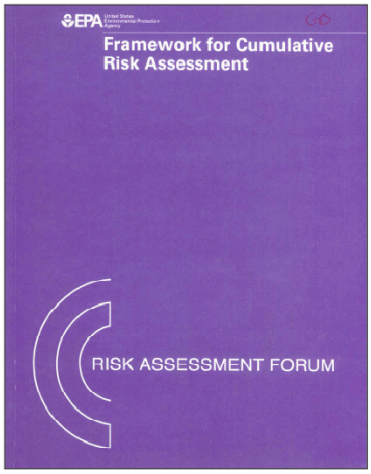
Long-term Effort to Develop Guidance

- **1997:** EPA Science Policy Council issued guidance on planning and scoping for cumulative risk assessments
- **2003:** Published the *"Framework for Cumulative Risk Assessment"* (Phase 1)
- **Today:** Producing a report, "*Issues, Case Studies, and Research Needs in Cumulative Risk Assessment"* (Phase 2)
- **Future:** Agency guidelines for cumulative risk assessment (Phase 3)

8



Framework identified the basic elements of the cumulative risk assessment process and identified questions which ought to be answered prior to, or during the development of specific guidance

Technical panel was constituted

•to address the specific **issues** raised in the *Framework*;

-to identify or develop **case studies** exemplifying elements of cumulative risk assessment

-to identify remaining **research needs** for the Agency, in support of guidance development.

**These topics will be discussed in the following slides.

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(1997) CRA Guidance:
Planning/Scoping, Problem Formulation

- Overall purpose and general scope of the risk assessment;
- Products needed by management for risk decision-making;
- Approaches, including technical elements that may be evaluated in the assessment ;
- Relationships among potential assessment end points and risk management options and;
- Analysis plan and a conceptual model;
- Resources (for example, data or models) required or available;
- Identify necessary participants and stakeholders
- Schedule

Risk Assessment Planning and Scoping: Team Participants

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10

Thanks to: Dr. Marian Olsen, R-2

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(2003) CRA Guidance: Framework for Cumulative Risk Assessment

1. Planning, Scoping, and Problem Formulation Phase
2. Analysis Phase
3. Risk Characterization Phase
4. Risk Management Phase
5. Iterative process!

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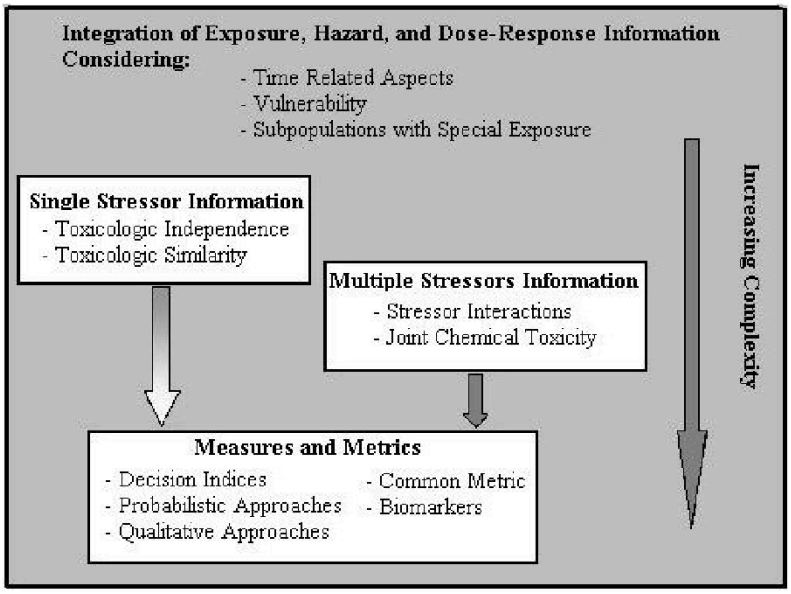

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Current CRA Efforts: Issues, Case Studies, and Research Needs in Cumulative Risk Assessment

- Purpose: to assist risk assessors in planning and conducting cumulative risk assessments
  - –Provides illustrative examples, methods, tools
- Attempts to equally address ecological and human health approaches
- Format follows the *Framework*
  - –Planning and Scoping/Problem Formulation
  - –Analysis
  - –Risk Characterization

13

Planning and Scoping/Problem Formulation

-Stakeholder involvement

-Tiered Approaches to setting scope

-Approaches for selecting stressors and assessment endpoints

-Conceptual model and analysis plan development

Analysis

•Approaches for evaluating the combined effects of chemical and non-chemical stressors

•Vulnerability of innately sensitive or susceptible populations

•Approaches for reporting combined probability of harm

•Probabilistic and statistical approaches

•Tools to managing cumulative risk by assessing stressor sources

Risk Characterization

•Risk estimation

•Risk description

•Uncertainty analysis

•Risk management

Integration of Human and Ecological Risk: Advantages

- Presents coherent and consistent assessment for decision-making
- Incorporates *all* of the science
- Incorporates community values for environment
- Non-human organisms may be more sensitive, therefore protective of human health
- Conservation of scientific resources
- Consideration of non-chemical stressors
- Values ecosystem services
- Encourages stakeholder + manager involvement
- Common endpoints at population-level or cellular-level

Source: Glenn Suter, EPA

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Current CRA Efforts: "Issues Papers" on Cumulative Risk Assessment

- Published in *Environmental Health Perspectives* (2007)
- Topics:
  - Overview / rationale for cumulative risk assessment
  - Integrating / disaggregating health effects data
  - Combining multiple chemical and non-chemical stressors
  - Vulnerability due to environmental effects, lack of resilience or resources

15

-5 papers (12 authors)

If Cumulative Risk Assessment Is the Answer, What Is the Question? (Callahan and Sexton)

A Phased Approach for Assessing Combined Effects from Multiple Stressors (Menzie *et al*.)

Vulnerability as a Function of Individual and Group Resources in Cumulative Risk Assessment (deFur *et al*.)

Assessing Cumulative Health Risks from Exposure to Environmental Mixtures—Three Fundamental Questions (Sexton and Hattis)

Using Biomarkers to Inform Cumulative Risk Assessment (Ryan et al.)

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Acknowledgements: Issues Papers Authors

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Issues Papers: Addressing Challenging Technical Issues in Cumulative Risk Assessment

- Combined effects from multiple stressors
- Disaggregating health effects
- Vulnerability due to exposure to environmental stressors
- Vulnerability due to decreased resilience or resources

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Issues Papers: Approaches for Assessing Combined Effects from Multiple Stressors

- Conceptual overview on how to assess combined effects from multiple stressors:
  - Types of stressors and effects that may be combined:
    - physical, biological, and chemical
- Compiled and defined:
  - Types and nature of the interactions among stressors
  - Both adverse and beneficial outcomes

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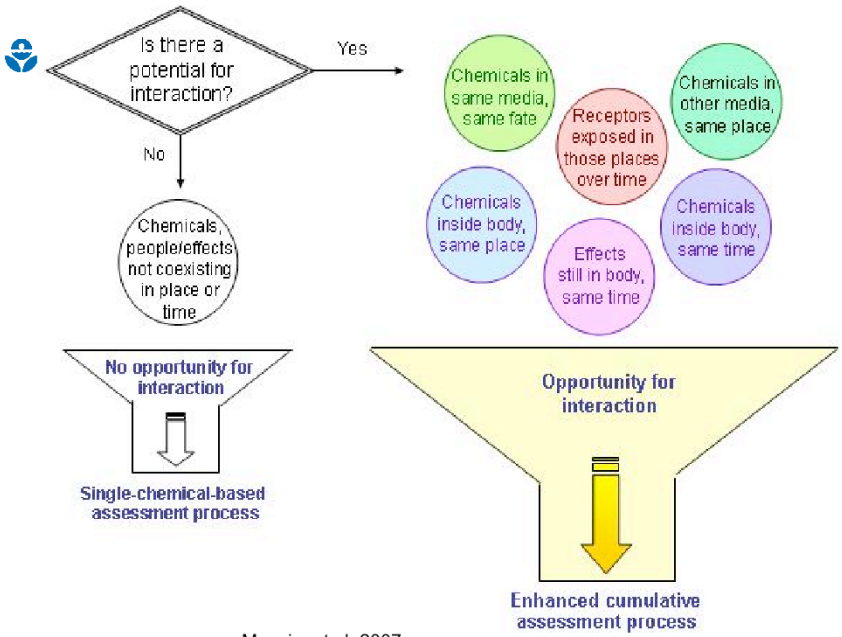
Issues Papers: Approaches for Assessing Combined Effects from Multiple Stressors - 2

- Approaches for combining effects included
  - Interactive conceptual models
  - Screening methods
  - Analytic methods, combining multiple methods, e.g.,
    - advanced statistical techniques and process models.
- Discusses the significance of the exposure groups –
  - Integrating for both human health and ecological risk assessments,
  - And/or ecological systems for ecological risk assessments

19



Menzie, et al. 2007

20

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Issues Papers: Using Biomarkers to Inform Cumulative Risk Assessment

- Biomarkers can reflect cumulated influences or exposures and can add significantly to environmental health studies.
- Ideal biomarker:
  - Persistent
  - Easily collected
  - Reliable
  - Linked to a disease
- Array of biomarkers is more useful in disaggregating sources and pathways of exposure, and may have applications in tracking disease burden.

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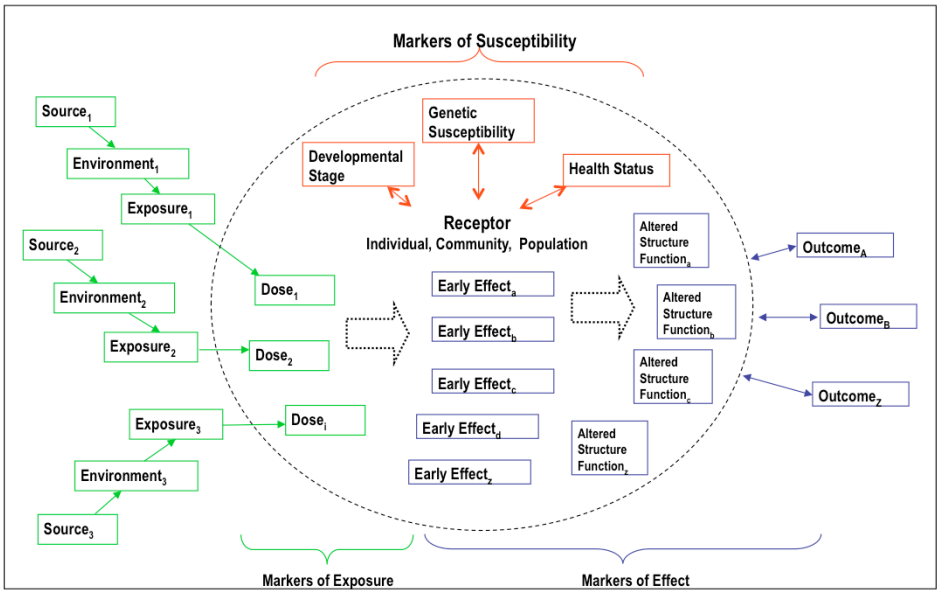
Issues Papers: Using Biomarkers to Inform Cumulative Risk Assessment - 2

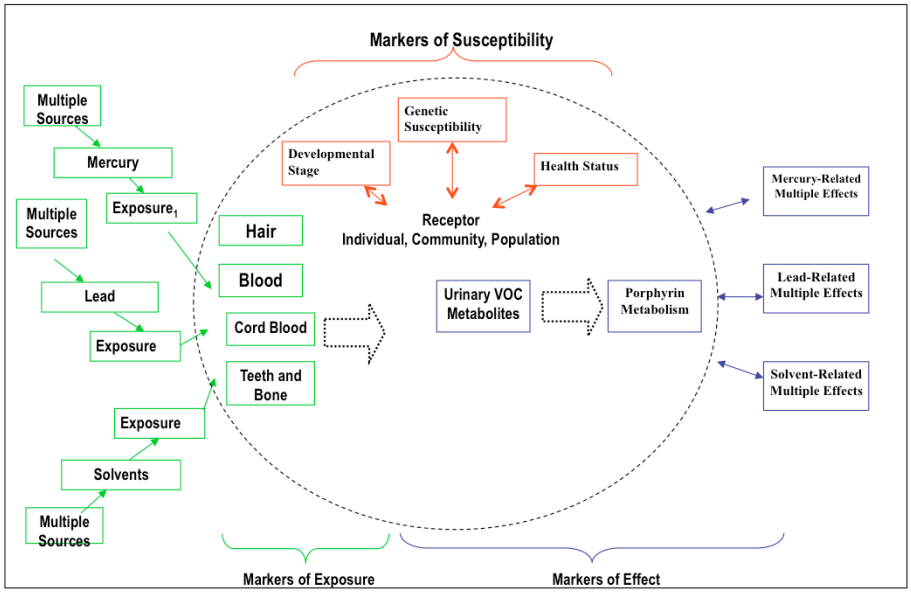
- A cumulative framework was developed and applied to case examples:
  - Asthma (e.g., associated with VOCs, ETS, PM)
  - Neurobehavioral endpoints (e.g. associated with mercury, lead, and organic solvents exposure)
  - Multifactorial effects (e.g., developmental and reproductive disorders)
  - Endocrine disrupting effects upon ecological communities.



Framework for Biomonitoring.

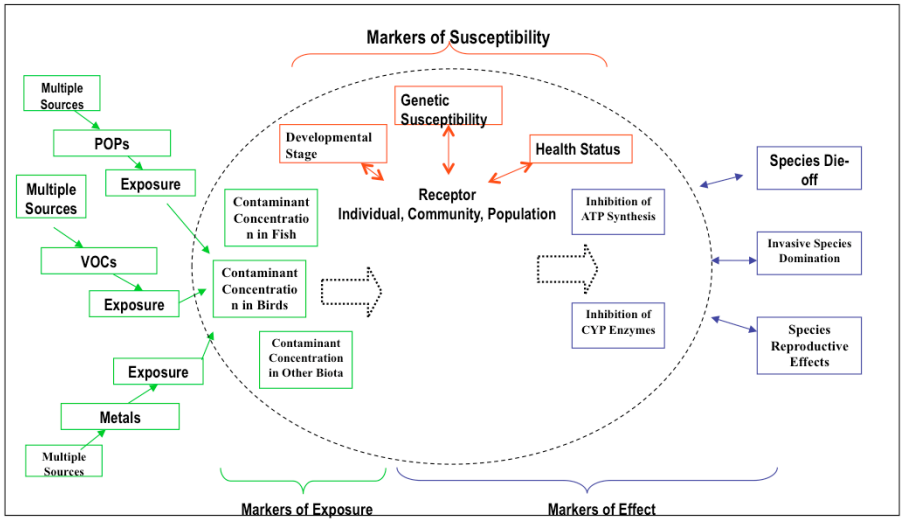
Ryan, et al. 2007

23



Framework Applied to Neurobehavioral Endpoints Case Study

Ryan et al. 2007



Framework Applied to Endocrine Disruption Endpoints Case Study. The primary impact here is upon ecological communities

Ryan, et al. 2006

25

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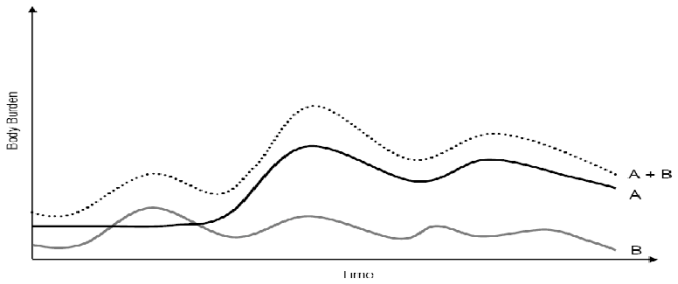
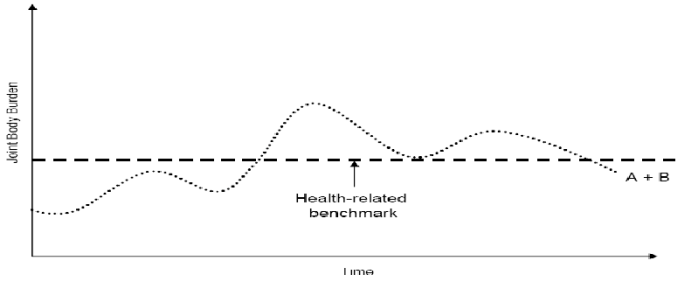
Issues Papers: The Challenge of Assessing Cumulative Exposure and Related Combined Effects

How can differential exposure to mixtures of environmental agents - biological, chemical, physical, and psychosocial stressors - contribute to increased vulnerability of human populations and ecological systems?

- Which mixtures are most important from a public health perspective?
- What are the nature and magnitude of relevant cumulative exposures?
- What are the nature and magnitude of the mixture's interactive effects on exposed populations?
- Need
  - Improved assessment methods for cumulative exposure
  - Better understanding of biological mechanisms that determine toxicological interactions among mixture constituents



A. Joint Burden Derived by Additivity



B. Joint Burden vs. Benchmark

Sexton, et al. 2006

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Issues Papers: Vulnerability as a Function of Individual and Group Resources in a Cumulative Risk Assessment

- How individuals or groups of individuals or organisms react to and recover from stressors
- Focus
  - Non-chemical stressors, e.g., psychosocial stress
  - Community structure and function
  - Population assessment and response

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Issues Papers: Vulnerability as a Function of Individual and Group Resources in a Cumulative Risk Assessment - 2

- What factors affect how a person, animal, an ecological population or community might be more or less vulnerable?
  - Capacities and resources
  - Coping mechanisms, supports
  - Size and complexity of the group
- Metrics to qualitatively or quantitatively assess individual, community or ecosystem vulnerability

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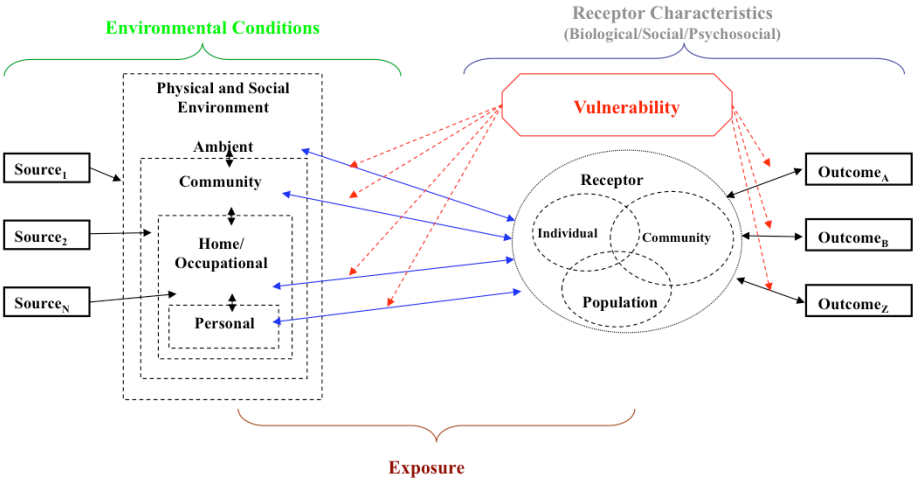
Vulnerability as a Function of Individual and Group Resources in a Cumulative Risk Assessment



deFur, et al, 2007

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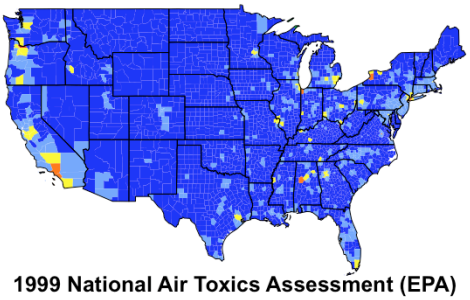
Current CRA Efforts: Illustrative Case Studies

- Large-scale assessments
  - –Ecological: watershed, landscape level approaches
  - –Human health: community, population-centered assessments
- "Integrated" human health and ecological risk assessments



1999 National Air Toxics Assessment (EPA)
National Scale Assessment Predicted County Level Cancer Risk– County Medians

31

12 case studies

Figure is for illustrative purposes of large-scale assessment

RED means the Mean risk level is >100 in a million

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Current CRA Efforts: Example Case Studies

- National Air Toxics Assessment
- Cumulative Organophosphate Risk Assessment
- Disinfection By-Products
- Baltimore Community Risk Assessment
- Mid-Atlantic Ecological Risk Assessment
- Regional Air Impact Modeling Initiative (RAIMI)

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Application of Case Studies

Cumulative risk or community risk assessment: Not one size fits all

- All begin with population-centered planning, scoping
- Tiered approach, priority-setting
- Short-term and long-term goals
- Regulation-driven examples
- Hazard-only assessments
- Human-health, ecological or integrated assessments
- Small (local) scale or area / landscape level

33

Idea that CRA is not one-size fits all

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Integrating CRA Approaches

- Cumulative risk assessment is a tool
- It is not appropriate for every task
- Cumulative risk assessments will be most useful in situations where questions need to be addressed concerning the impacts of multiple stressors acting together
- Currently, there are methods limitations

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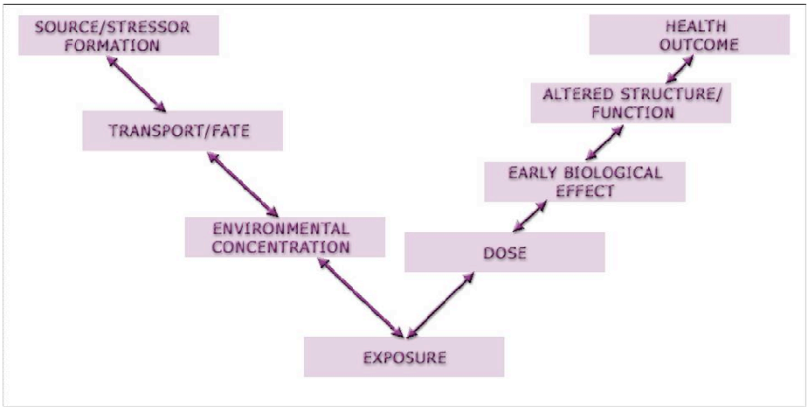
Source – to – Effect Continuum



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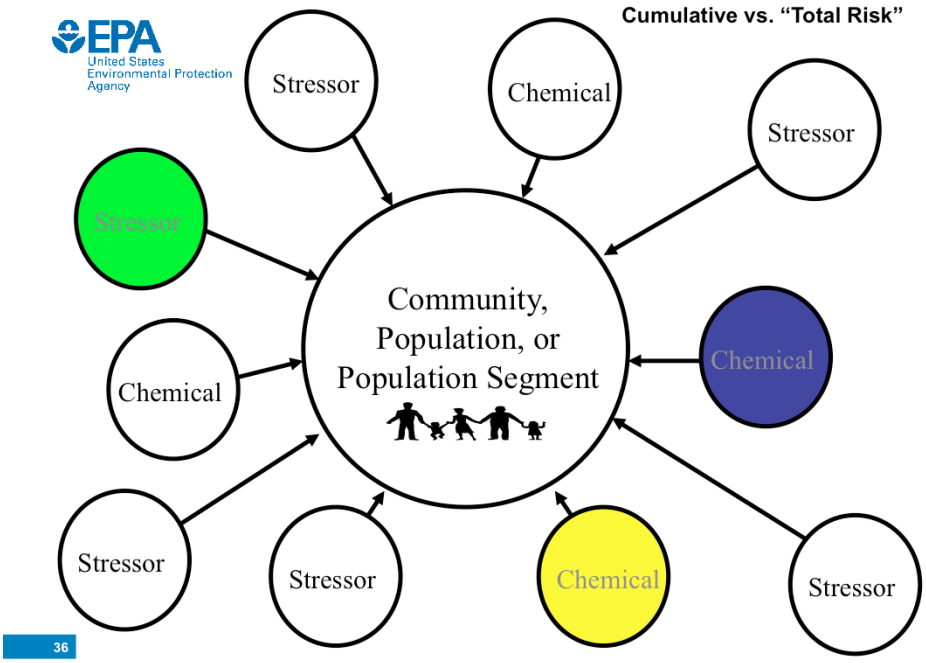
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Cumulative vs. "Total Risk"
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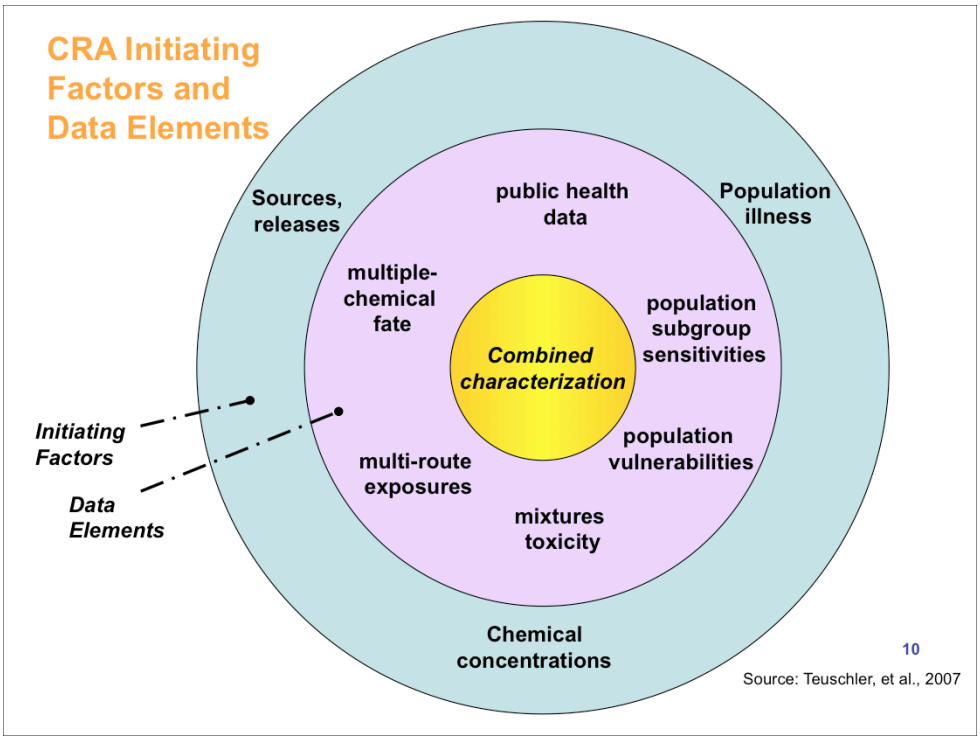

Figure 1-5. Common Initiating Factors and Elements of Cumulative Assessments

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General Approach to Screening Multiple Stressors

1. Develop a conceptual model sufficient to bound the problem;
2. Screen stressors to arrive at an appropriate and manageable number for the problem,
3. Evaluate the individual effects of individual stressors as there may be a predominant stressor that is contributing or could contribute to an effect;
4. Evaluate the combined effects of stressors without considering the potential for interactions (i.e., a stressor has a synergistic or antagonistic effect; and
5. Evaluate the combined effects of stressors taking into account potential interactions among the stressors.

Source: Menzie et al. 2007

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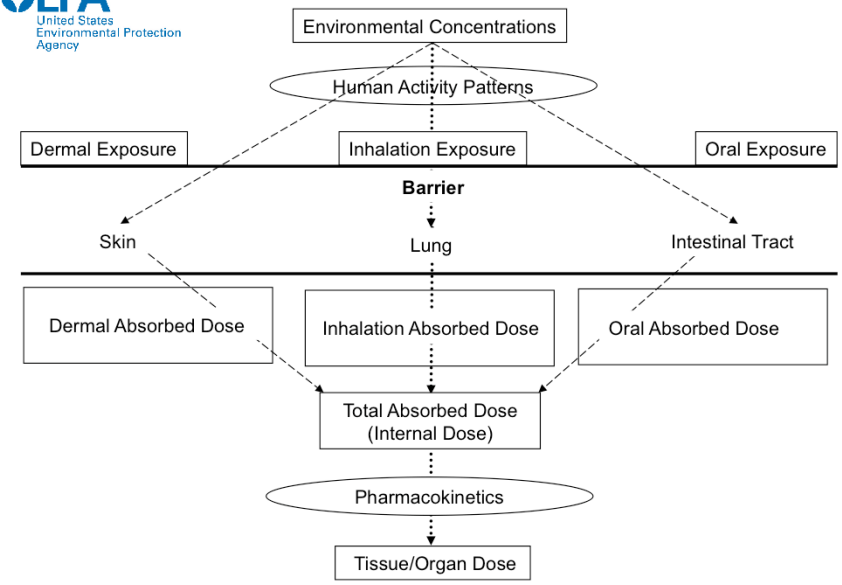
Combining Different Stressors

- Can different types of stressors, or effects, be combined?
- Additivity vs. independence
- Interactions, synergism
- Approaches:
  - Common metric
  - Index approach
  - Relative potency

Dose-Response Considerations

- Identify toxic components of the mixture
- Assess existing dose-response information
  - Multiple exposure routes
  - Various durations *(acute, subchronic, chronic)*
- Determine assessment basis for dose-response
  - Surrogate chemical to represent the mixture
  - Multiple components
  - Measure of the whole mixture
- Dose-Response Data: Potential Dose or Internal Dose
  - *Single*
  - *Multiple chemicals*

Dose Measures for Environmental Contaminants



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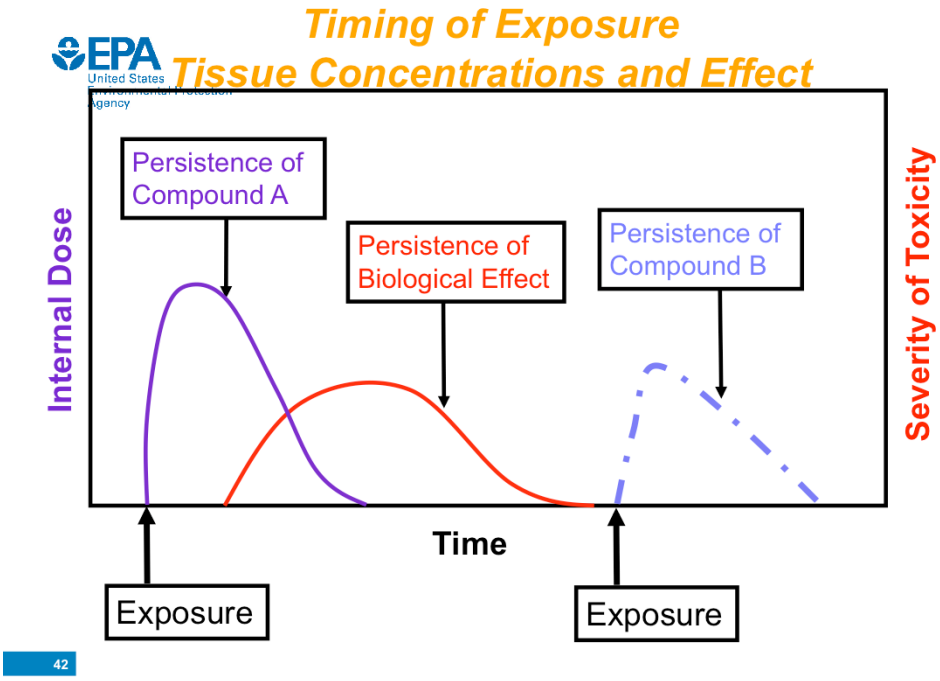
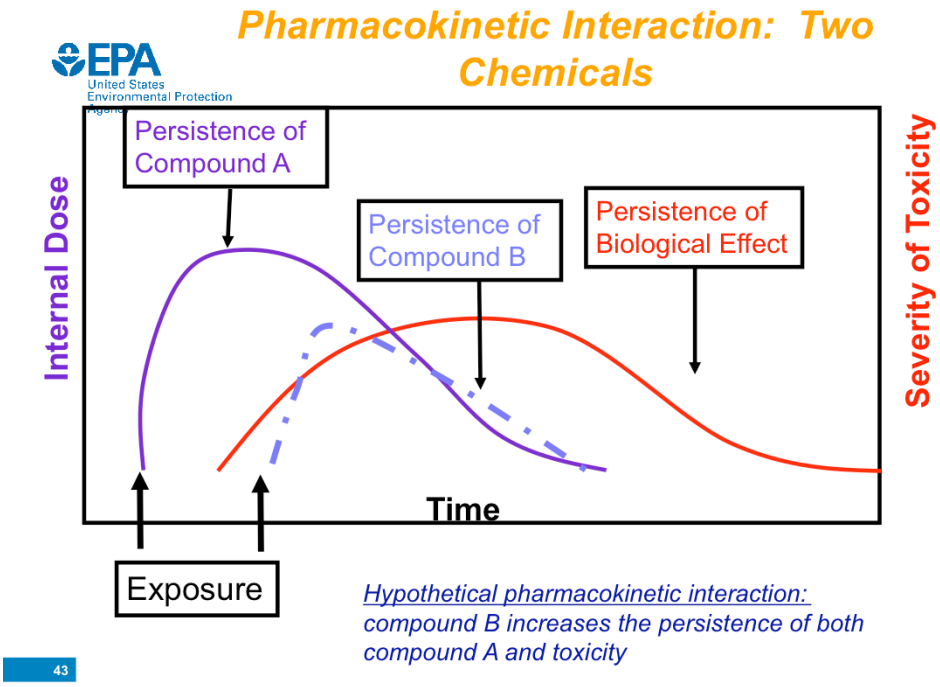


Figure 3-14. Conceptual Illustration Showing the Persistence of a Biological Effect Exceeds the Duration of the Exposure



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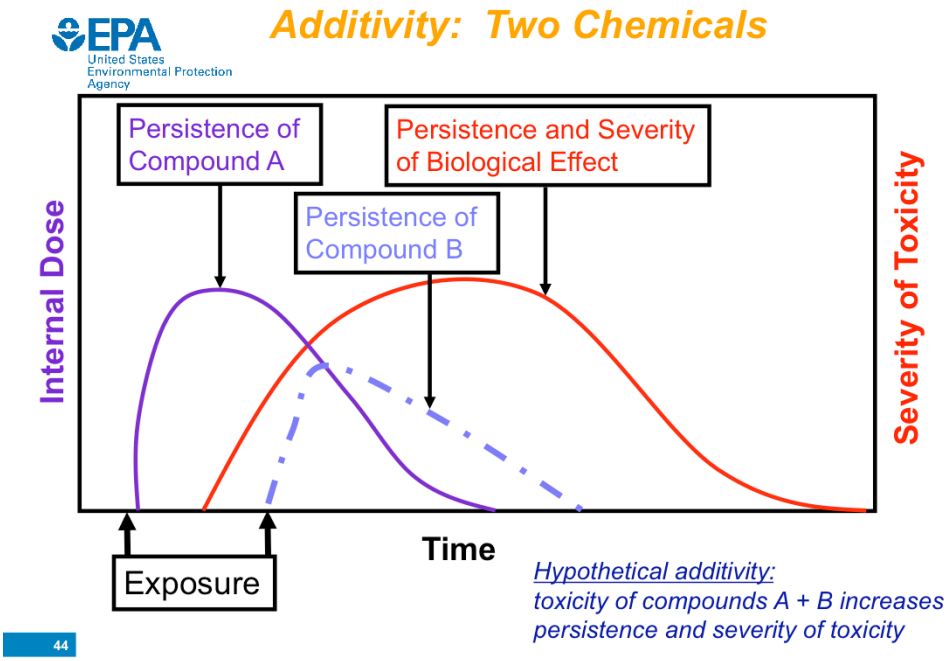

Figure 3-14. Conceptual Illustration Showing the Persistence of a Biological Effect Exceeds the Duration of the Exposure

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Qualitative Analysis

Primary Methods of Qualitative Analysis:

- **Questionnaires, interviews, and panels**
- **Checklists**
- **Risk Matrices**
- **Control Banding**
- **Networks and system diagrams**
- **Modeling**
- **Trends analysis**
- **Overlay mapping and GIS**

White House Council of Environmental Quality, "Considering Cumulative Effects Under the National Environmental Policy Act"

Can biomonitoring data be used to characterize cumulative risk?

- Given multiple exposures, multiple outcomes, across time, how do we understand the relationships in this multidimensional space?
- Biomonitoring and other health data are used to characterize:
  - receptor (individual, community or population)
  - potential exposures
  - health outcomes.
- Consider an array of metrics across the exposure-outcome continuum to address the multi-factorial nature of environmental disease and cumulative risk

Source: (Ryan, Burke, McKone, Cohen Hubal, et al.)

Exposure Assessment and Probabilistic Techniques: Example from Pesticides

- Probabilistic exposure techniques are routinely applied by OPP for virtually all its pesticide risk assessments
  - More accurate estimate of the entire range of exposures and their associated probabilities
- OPP's Cumulative Risk Assessments rely on probabilistic (Monte-Carlo) techniques to evaluate exposure
  - Food, drinking water, residential uses, multi-pathway

47

probabilistic techniques permit the the entire distribution of pesticide concentration levels in food/water to be combined with the distribution of food or water consumption

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Modeling Aggregate and Cumlative Exposures and Risk

- Computational toxicology models
- Biological systems modeling: “virtual organism”
- OPP has used several software models to perform its risk assessments

Dietary **E**xposure **E**valuation **M**odel /**C**alendex

STOCHASTIC **H**UMAN **E**XPOSURE & **D**OSE **S**IMULATION MODEL

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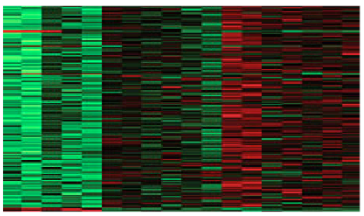
Vulnerability

Use of Genomics Data:

- Variability of response
- Susceptibility/Sensitivity
- Differential exposure
- Differential preparedness
- Differential ability to recover



Some Overarching Research Needs

- GIS-based technologies for accessing, retrieving, processing data
- Methods to couple environmental and public health data with epidemiologic information
- Computational methods to connect multiple data layers and capture uncertainties
- Improved decision frameworks and criteria to integrate cumulative effects to guide decisions and policies
  - Qualitative and quantitative approaches for various metrics
- Advanced methods: biologically-based modeling, toxicogenomics, nanoscale monitoring, etc.
- Input from Chicago 2009 Workshop

50

More specifics:

- Screening methods to prioritize and group stressors, receptors, effects

-Improved knowledge about chemical stressor interactions for exposure characterization

-Combined and cascading effects

- Non-chemical stressors and vulnerability

- Assessment endpoints and metrics

- Interpreting biomarkers and effects

- Selecting indicators and endpoints

-Integrating ecological and human health

-Eco-social approach

-Importance of resilience

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Final Thoughts: Looking Forward

- Need for integrated environmental-health (human + ecological) assessments and decisions
- Cumulative risk assessment is one tool
- Alternatives decision-making: multiple parties mean more potential solutions
- Balancing precaution and uncertainty (a bias for action?)
- Consideration of all the evidence:
  - Benefits, costs
  - Reasonable, feasible

Thank You

After viewing the links to additional resources, please complete our online feedback form.