

Workshop 5: Combined Exposures & Synergistic Effects



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Second International Conference on Risk Assessment

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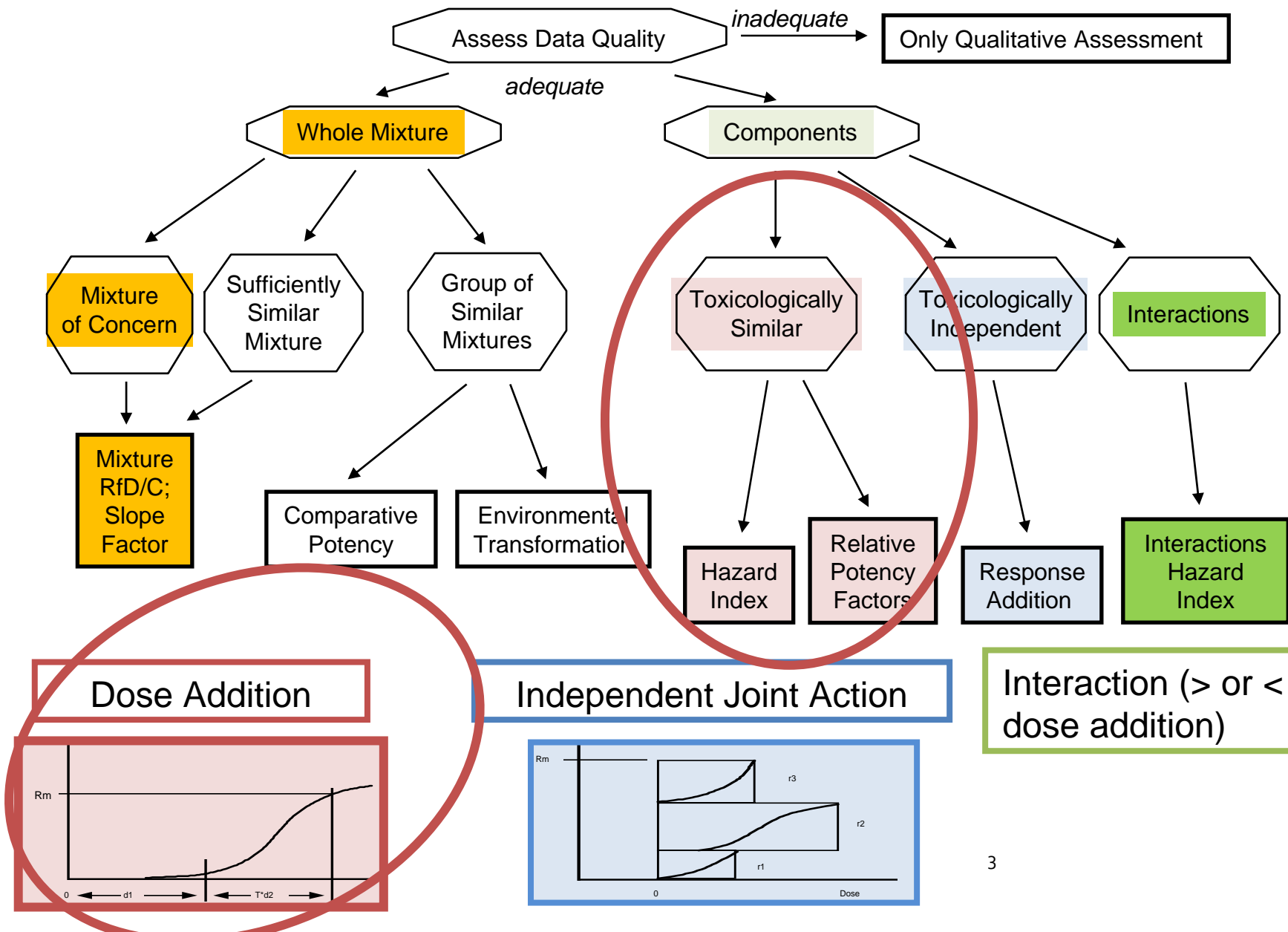


Outline

- State of the Art – Assessment of Mixtures (aka “Combined Exposures to Multiple Chemicals”)
- Recent International Developments
 - WHO IPCS Framework/Case Studies
- Needs/Issues
- Path Forward

Assessment for Combined Exposures

State of the Art





Questions for Consideration

- Need for assessments of combined exposures
- Barriers/challenges to assessments of combined exposures?
- Appropriate criteria for consideration of combined exposures? (toxicological similarity)
- Suggestions for further elaboration of approaches for combined exposures assessment?



Need for Combined Exposures Assessments

- Increasing legal imperative
 - Addressed informally to some degree in other programs
- Increasingly exposed to combinations
- Public demand/expectation
- Protection of public health

But:

- Extent of risk is currently unknown/needs addressing
 - Synergy rare
- Need for careful and effective communication moving forward



Some Barriers

- Lack of legal mandate
- Diverging views on grouping criteria
- Limitations of available approaches/tools/data
 - Chemical specific vs. disease outcomes
 - Potential contribution of epidemiology
 - Better integration of toxicological/epidemiological approaches
 - Exposure assessment
 - Dichotomous approach to cancer/non-cancer effects



Grouping Criteria

- Context dependent
- Co-exposure a prerequisite

Increasing need to consider:

- Common effect/endpoint/disease
- Common early key events/pathways
- Common metabolite,

Rather than (e.g.) chemical similarity

Path Forward

- Move forward collectively, considering case studies within a common framework
- Identifying the most common/relevant scenarios, mixtures of concern
 - Expanding to include non chemical stressor
 - Pharmaceuticals
 - Indoor air
- Evolving approaches
 - Common early key events/pathways
 - Common effect/endpoint/disease
 - Common metabolite
 - Potential to identify critical “drivers”?



Contents of the WHO/IPCS Framework

- Provides overview harmonizing construct
 - Builds upon other related initiatives and methodologies
- When to conduct a combined assessment
- Generic description of the framework approach
 - Hierarchical structure with iterative consideration of exposure and hazard
- Three case studies (examples, only)
 - Priority setting for drinking water contaminants
 - Screening assessment on PBDEs
 - Full assessment on conazoles

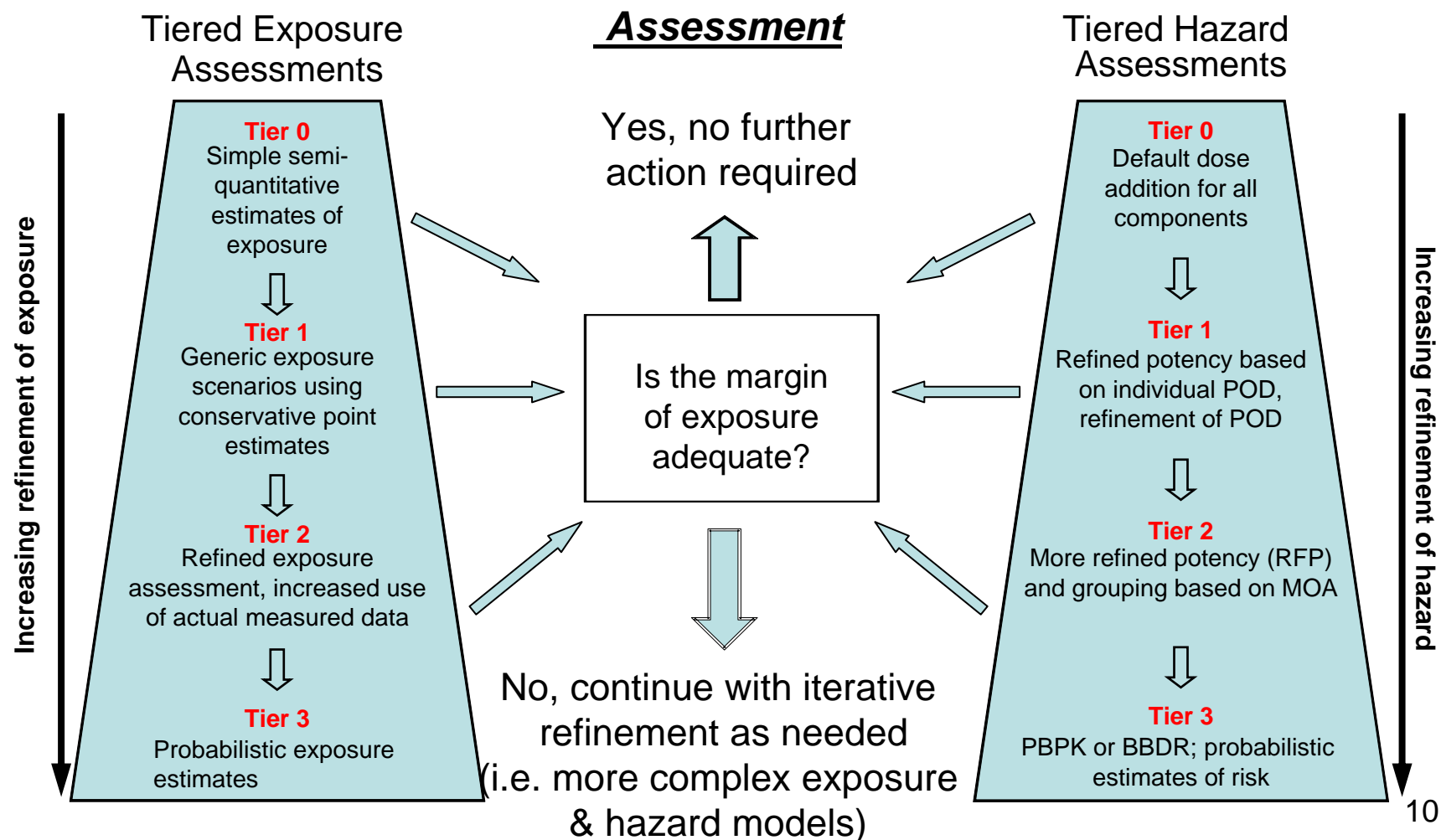
Problem Formulation

Nature of exposure?

Is exposure likely?

Co-exposure within a relevant timeframe?

Rationale for considering compounds in an assessment group?





Development – WHO IPCS Combined Exposures

- Overview workshop to review terminology & methodology in March/07
 - 27 invited senior experts from relevant agencies worldwide; 5 reps from partnering organizations
 - Recommendations to harmonize terminology
- Post workshop development of framework/case studies
 - WHO IPCS
 - International Life Sciences Institute (ILSI)
 - European Centre for Ecotoxicology & Toxicology of Chemicals (ECETOC)
- Framework & case studies posted for public comment
 - Comment period closed October 31/09
- Framework revised based on public comment
 - Feb/2010 meeting – London
- In publication
- Joint OECD/WHO/ILSI workshop
 - February/11

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