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Industry Perspectives on Environmental Epidemiology

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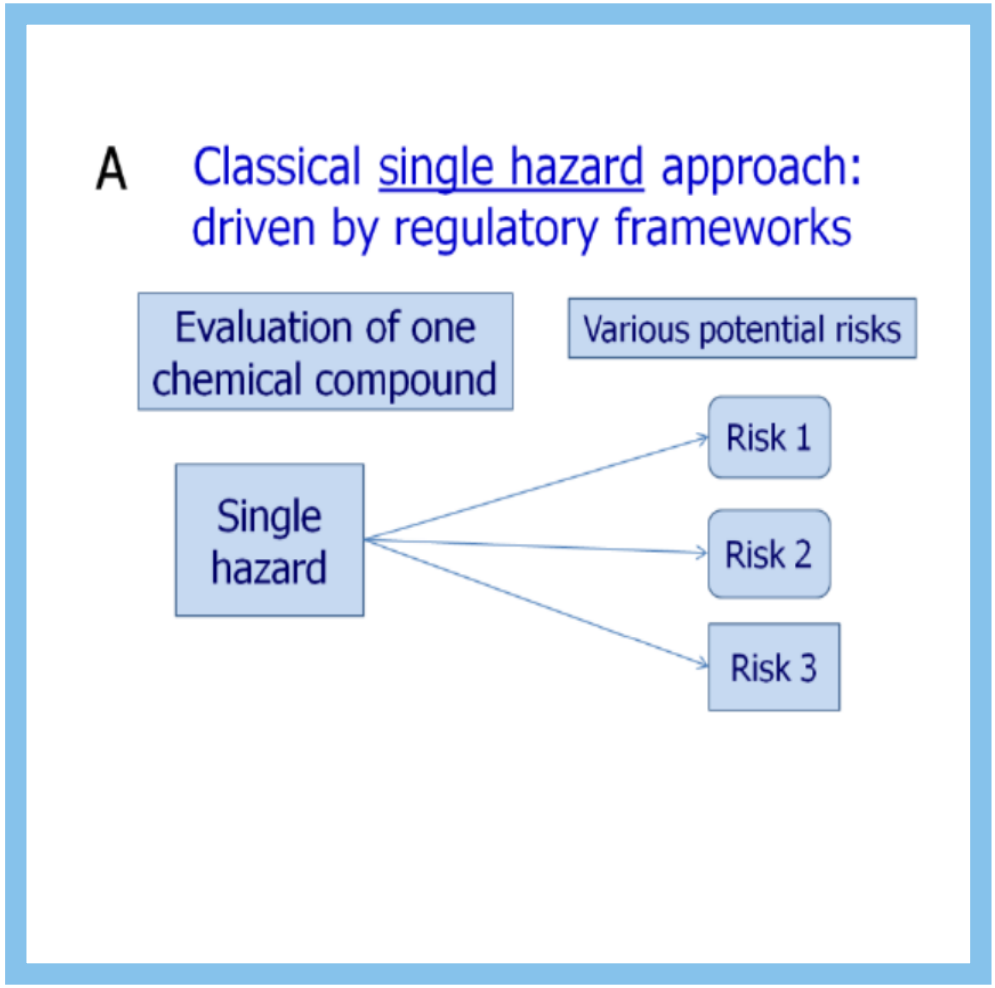
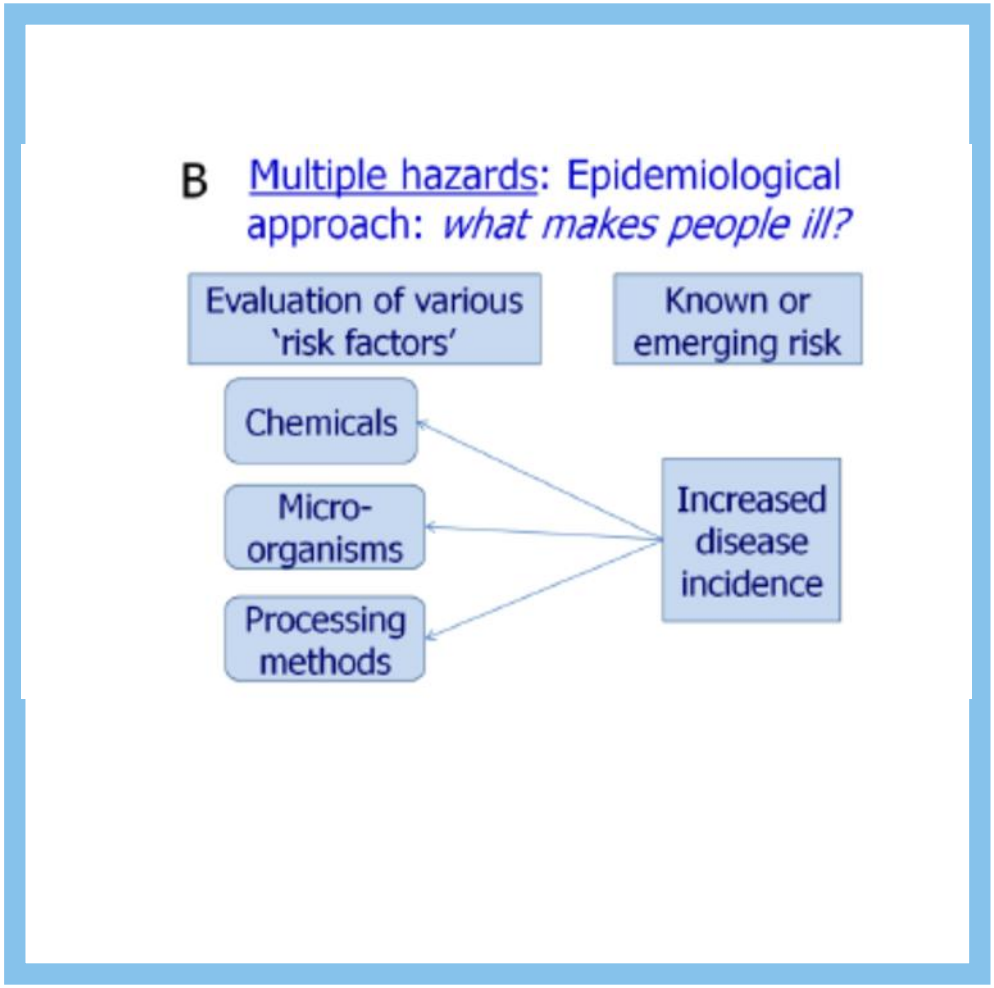


Toxicology approach

Glass is half empty

Page 54, Figure 4. EFSA 2017 Scientific Opinion

Epidemiology approach



Glass is half full

Page 54, Figure 4, 2017 EFSA Scientific Opinion

How do we fill the glass?

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Industry is involved

- **ECPA Funding exposure validation study (IOM)**
  - Builds from US Farm Family Exposure Study
- **CLI workshop (2016)**
  - Better studies yield better decisions
- **ILSI HESI (Government, Industry, Academia)**
  - Evaluating uncertainty in epidemiology
    - Workshop and publication 2012
  - Improving application of epidemiology
    - In progress, multiple focus groups for 2018

Outline*

- Glow – areas of agreement
- Grow – areas for discussion
- The weeds – points to ponder

*** 2017: Scientific Opinion of the PPR Panel on the follow-up of the findings of the External Scientific Report "Literature review of epidemiological studies linking exposure to pesticides and health effects"**

"GLOW"

Areas of agreement

- **Quality is important**
- **Statistical significance is subjective**
  - More than yes/no
  - Effect size magnification occurs
- **Direction of misclassification bias is unpredictable**
- **Evidence integration should rely on best data**

“GLOW”

Certain epidemiology parameters should be considered for quality and relevance

- Exposure – adequate assessment, preferably to allow for dose-response
- Outcome – well defined clinical entities (or validated surrogates
- Analysis – adequate accounting for confounding
- Analysis – subgroups by gender, age, ethnicity

"GROW"

Areas for discussion

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- **Gold standard rarely possible**
- **No minimum requirements for study quality**
  - Can more detail be provided?
  - What if only low-quality studies are available?
- **No explicit guidance for systematic review/meta-analyses**
  - Only as good as the contributing studies and selected findings
- **No recommendations for evidence integration**
  - With toxicity, mechanistic and epidemiology data

“GROW”

Specific Issues to develop

- **Distinguish hypothesis-generating *vs.* hypothesis-testing studies**
  - Is study done for regulatory purpose?
- **Define biologically relevant effects**
  - Clinical diagnosis vs. mean difference?
  - Is statistical significance adequate?
- **Discuss dose-response more fully**
  - How would you use an Odds Ratio?
  - Is there concordance of exposure-outcome findings

Example
Adverse Outcomes

- **What does quality assessment look like?**
  - A case study of pyrethroid epidemiology studies (Burns and Pastoor, Crit Rev Tox, in review)

Quality Outcome Evaluation

	OUTCOME - EFSA/OPP	OUTCOME Example
TIER 1	Valid and reliable outcome assessment	**Medical Record** or diagnosis confirmed
TIER 2	Standardized outcome, not validated in population, or screening tool; or, medical record non-confirmed.	**Self -reported** disease, symptoms, test scores, screening tool. Multiple biological samples
TIER 3	Non-standardized and non-validated health outcome.	**Single sample** of a short-lived chemical or hormone

Approach of Biomonitoring, Environmental Epidemiology, and Short-lived Chemicals (LaKind et al., 2014)

Outcome quality varies by effect
(examples from pyrethroid epidemiology)

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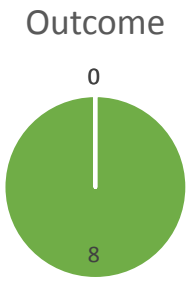
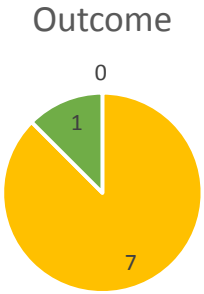
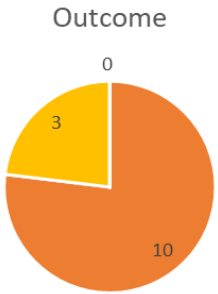
Birth weight



Developmental delay



Sperm quality



Example: Adverse outcome (8.1c)

Can we have more detail?

- **"Outcomes under study should be well-defined"**
  - What is adverse? An IQ point? Mean difference?
  - What is biologically relevant? (EFSA 2017a)
  - Are there differences in screening vs. diagnostic?
- **"Use should be made of biological markers…"**
  - How can they be validated?
  - Should multiple collections be taken?

Concluding…

Risk Assessment Process

- **Hazard identification**
  - Relies upon transparency and complete reporting
- **Exposure assessment**
  - Impacted by quality, validity, and reliability
- **Dose-response assessment**
  - Requires more than low vs. high
- **Risk characterization**
  - Is epidemiology for reassurance or “what if”?

The weeds (1 of 3)

Synchronization of results

- How can EFSA connect the TIMING between review process and the output of epidemiological studies?
- Can data analyses of pesticide X in the AHS occur before (re)-registration of pesticide X?

Page 9, 2017 EFSA Scientific Opinion

The weeds

Transparency of results

- **How can null data be viewed as important?**
- **Can dose-response be used to identify a no-effect level?**
  - When does a null study confirm a NOEL (or BMD)?
- **Can we use existing models from other disciplines?**
  - Can results (or data) be shared online before peer review?

The weeds

Can EFSA influence change?

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- "propose potential refinements for future epidemiological studies to increase the quality, relevance and reliability of the findings and how they may impact pesticide risk assessment"
- **Are there incentives for investigators?**
  - "Discovery" vs. "regulatory" science
  - "Our" problems are not "their" problems
- **Can barriers be reduced?**
  - Quality can be expensive, time consuming

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Questions

Mouse + Man: Fill the glass with best data