Health effects of mixtures

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Research Question

Is mixture risk assessment feasible with exposure and effect data from the literature?
Approach

Case studies, focusing on human health endpoints of concern

- Endocrine disruption with a focus on disruptions of male reproductive health
- Developmental neurotoxicity
- Cancers, including e.g. lung cancer in occupational settings
- Nephrotoxicity
Focus: Male reproductive health

Declines in semen quality
Approach

Sums of risk quotients

\[ HI = \sum_{i=1}^{n} \frac{Exposure\ level}{Reference\ dose} \]

Concern if sum > 1

Specific reference doses for deteriorations in semen quality
Multiple chemicals monitored in the same sample

- **Phthalates**: DiBP, DnBP, DEHP, DiNP, BBzP
- **Bisphenols**: BPA, BPS, BPF
- **Painkillers**: Paracetamol

Changes in urinary excretion of phthalates, phthalate substitutes, bisphenols, and other polychlorinated and phenolic substances in young Danish men, 2009–2017

Hanne Frederiksen, Ole Nielsen, Helge M. Koch, Niels E. Skakkebaek, Anders Juul, Niels Jørgensen, Anna-Maria Andersson

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International Center for Aerosol and Health, Department of Reproduction and Child Health, Rigshospitalet, University of Copenhagen, Denmark.
Phthalates

Combined risk vs Complexity

- Complexity scale:
  - 0.0010
  - 0.0100
  - 0.1000
  - 1.0000
  - 10.0000
  - 100.0000
  - 1000.0000

- Combined risk scale:
  - 1.5
  - 2
  - 2.5
  - 3
  - 3.5
  - 4
  - 5

The graph shows a scatter plot with points representing the combined risk and complexity of phthalates. The x-axis represents complexity, while the y-axis represents combined risk. The scattered data points are distributed across the plot, indicating the relationship between these two factors.
Phthalates, bisphenol F, S

Combined risk vs. Complexity

Combined risk scale:
- 0.0010
- 0.0100
- 0.1000
- 1.0000
- 10.0000
- 100.0000
- 1000.0000

Complexity scale:
- 1
- 1.5
- 2
- 2.5
- 3
- 3.5
- 4
- 4.0
- 7

Legend:
- 7
Phthalates, bisphenols and paracetamol
Phthalates, bisphenols, paracetamol + 20 background chemicals
What this means

Everyone is “over the line”

Safety margins are exhausted

Some approach doses associated with effects in lab animals
Drivers of mixture risks

- Bisphenol A
- Paracetamol
- PCDD/F
- Bisphenol S
- Bisphenol F
- DEHP
Policy implications

There is **no protection** against mixture risks

Single-chemical risk assessments **underestimate** risks

Even consideration of groups of chemicals (e.g. phthalates) is **not enough**

Limits for single chemicals are **too high**
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