

# Chemical Mixtures Calculator

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# What is the Chemical mixtures calculator?

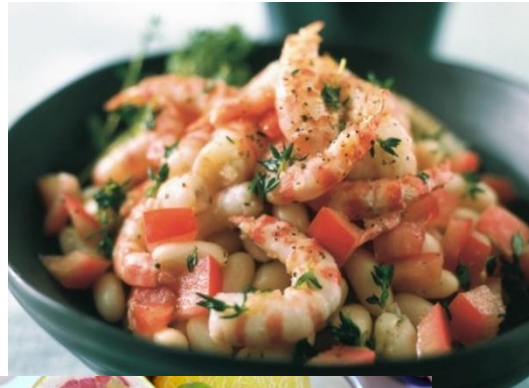
A tool/database for **pragmatic mixture risk assessment**

- Chemical exposures from food and environment
- Toxicity data collected to set human "safe dose" for various endpoints
- Grouping based on similar effects and/or mode of action



# Using the Chemical mixtures calculator

- performing cumulative risk assessment
- determining critical food groups or chemicals
- determining the impact of altering food habits and intake patterns



## Being on the safe side...

$$\text{Hazard Quotient} = \frac{\text{Exposure}}{\text{"safe dose"}}$$

- If Hazard Quotient >1, a potential risk is identified

Hazard Index: sum of Hazard Quotients



# What does this tool do?

1. Filtering for toxic endpoint, chemical group and more
2. Calculation of Hazard Index for dietary and environmental exposure

**HI = Exposure<sub>1</sub>/"safe dose"<sub>1</sub> + Exposure<sub>2</sub>/"safe dose"<sub>2</sub> + ... (low concern if HI<1)**

**Different levels of refinement: Grouping based on specific toxic endpoint**

We make toxicity grouping possible

We use exposure data from food and environment

## Filtering Criteria

▶ Clear filter

### Consumer group

Adults ▼

### Chemical class

- ☐ Acrylamide
- ☐ Bisphenols
- ☐ Brominated flame retardants
- ☐ Dioxin and PCBs
- ☐ Mycotoxins
- ☐ Perfluorinated compounds
- ☐ Pesticides
- ☐ Phthalates
- ☐ Polycyclic aromatic hydrocarbons

### CAG1 - Organ System

- ☐ Developmental and reproductive
- ☐ Kidney
- ☐ Liver
- ☐ Nervous system

## Hazard Index Value [Adults]: 1,08

All values are in µg/kg bw/day

▶ Id	▶ Chemical Name	▶ Dose	▶ Mean <u>U</u>	▶ High <u>U</u>	▶ Mean <u>U</u>	▶ High <u>U</u>	▶ Mean <u>U</u>	▶ High <u>U</u>
1	▶ 2,4-D (sum)	50	0,0023	0	0	0	0	0,000046
2	▶ Acephate	30	0,0012	0	0	0	0	0,000024
3	▶ Acetamiprid	70	0,011	0	0	0	0	0,00022
4	▶ Aclonifen	70	0,00003	0	0	0	0	0,000006
5	▶ Acrylamide	1,8	0,19	0,33	0	0	0	0,00036
6	▶ Aldicarb (sum)	3	0,0013	0	0	0	0	0,000026
7	▶ Aldrin and Dieldrin	0,1	0,00023	0	0	0	0	0,000005
12	▶ Atrazine	20	0,000041	0	0	0	0	0,000008
13	▶ Azinphos-methyl	5	0,022	0	0	0	0	0,00044
14	▶ Azoxystrobin	200	0,021	0	0	0	0	0,00042
15	▶ BBP	500	0	0,04	0	0,0154	0,248	0,000308
16	▶ BDE-153	0,83	0,00003	0,00007	0	0	0	0,0000361
17	▶ BDE-209	17	0,00035	0,0007	0	0	0	0,0000206
18	▶ BDE-47	3,09	0,00029	0,0011	0	0	0	0,0000939
19	▶ BDE-209	0,13	0,00001	0,00002	0	0	0	0,0000017



# Data collection

## Exposure

- Danish data on chemical content in food and dietary intake
- Published reports from e.g. EFSA and ECHA
  - Dietary and non-dietary exposures
- Mean and "high" exposure values

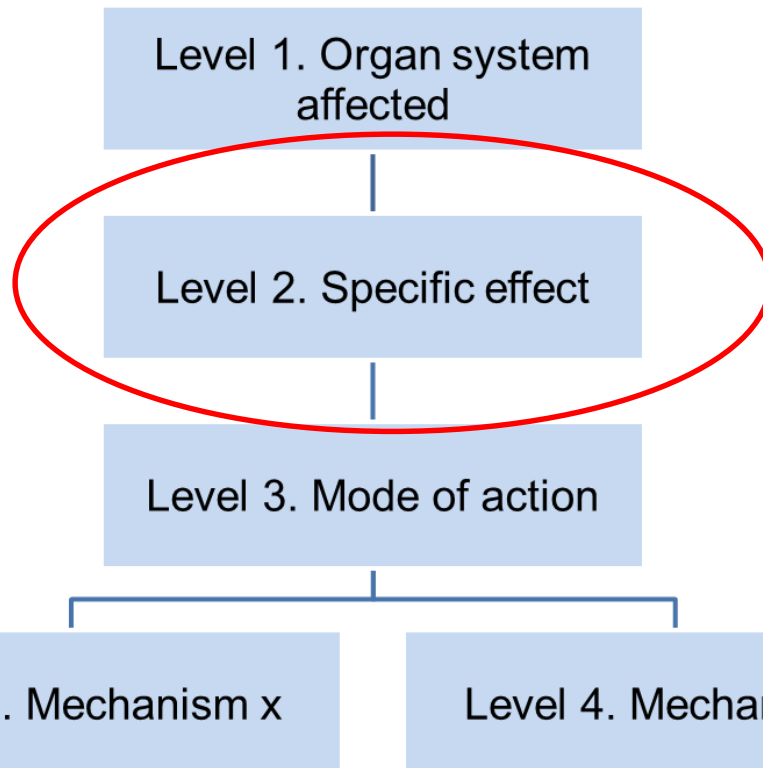
## Toxicity

- Reports from EFSA and ECHA
- (TDI / ADI)
- Target organ specific doses



# Grouping:

## CAGs - Cumulative assessment groups



Less adequate for grouping  
- conservative

Possibly adequate for grouping  
- Preferred here

Adequate for grouping  
- But few available data

Adequate for grouping  
- But few available data

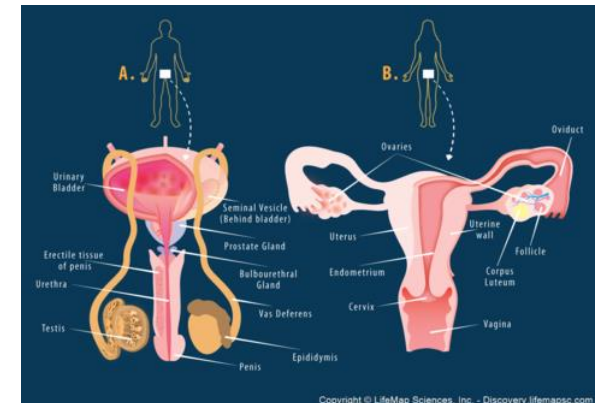
# **Selected organ systems in Chemical mixtures calculator**

- Nervous system
- Reproductive and developmental toxicity
- Thyroid gland
- Haematological system
- Kidney
- Liver



# Examples of **Subgrouping** in the Chemical mixtures calculator

- CAG 1: Nervous system
  - CAG 2: Functional changes related to motor division
    - CAG 3: Modulation of the cholinergic transmission
      - CAG 4: Acetylcholinesterase inhibition
  
- CAG 1: Reproductive and developmental toxicity
  - CAG 2: Delayed development and decreased body weight
  - CAG 2: Malformations and variations
  - CAG 2: Prenatal death
  - CAG 2: Postnatal death
  - CAG 2: Changes in reproductive organs of male/female offspring
    - CAG 3: Anti-androgenic mode of action
      - CAG 4: Androgen Receptor antagonism



# Examples of using the Chemical mixtures calculator

- Mixture risk assessment for chemical groups
- Mixture risk assessment for population groups

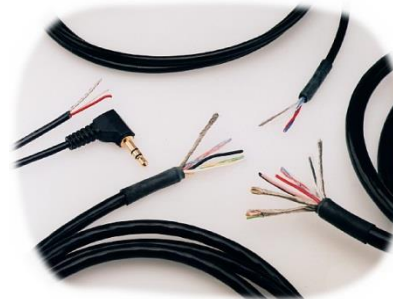


# Example 1: Phthalates

- Previously: ECHA mixture risk assessment on 4 phthalates based on male reproductive effects
  - Concern for toddlers exposed via food and environment

## Chemical Mixtures Calculator

- Exposure data: food and environment
- Toxicity groups: Reproduction/development, kidney, thyroid, liver
  - Same overall conclusions as ECHA, but for several toxicity targets
  - Grouping with numerous other chemical groups/sources possible
  - Level of refinement matters



## Example 2: Comparing population groups

Chemical exposure in two populations with different degree of fulfilling dietary guidelines

Chemical mixture calculator

- Exposure data: fit-for-purpose
- Toxicity groups: MRA at several levels of refinement possible

Conclusion

- Mixture risk assessment directs the focus to most influential chemicals

Petersen et al. *Under revision*

Boberg et al. *In prep*



# Take home messages

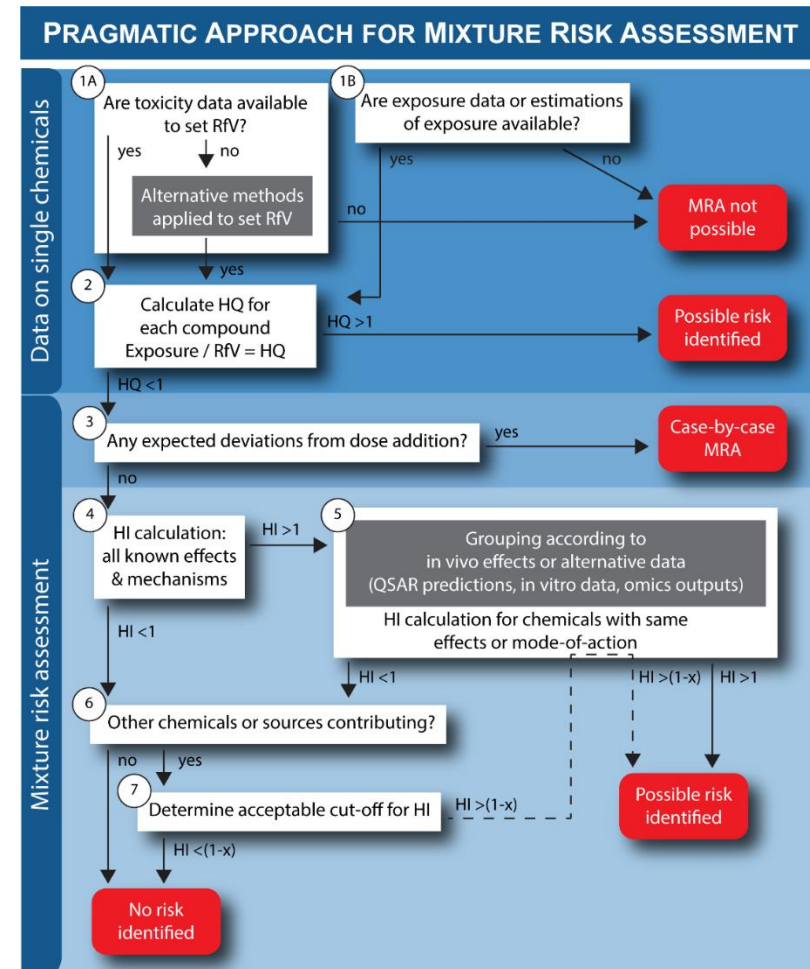
- Chemical mixtures calculator can be used as a pragmatic tool for mixture risk assessment
  - Identification of the chemicals and food groups that are main contributors to the overall risk
  - Grouping across chemical classes and sources
  - Level of refinement makes a large difference in results

# Expanding the Chemical mixtures calculator

- Lack of information limits the number of chemicals in database
  - Toxicity and exposure data
- Perspective: including risk assessment based on “alternative” data
  - In vitro/human biomonitoring
  - In vitro-in vivo extrapolations
  - Relative potency factors

Boberg et al. A pragmatic approach for human risk assessment of chemical mixtures.

Current Opinion in Toxicology 2019, 15:1–7.





# THANK YOU 😊

- Tool expected online early 2020

