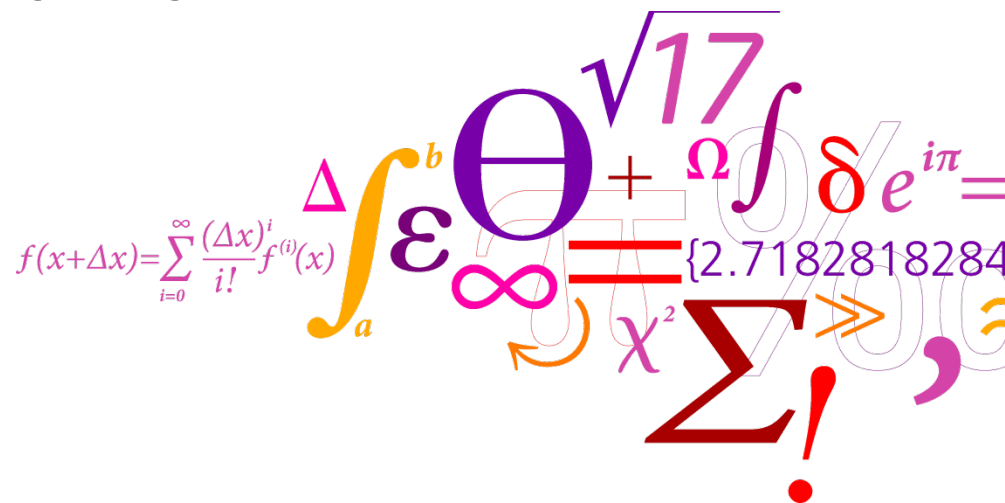




# Toxicological evaluations and risk of human exposure to mixtures of chemicals

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# Exposure to FCM chemicals contribute to human health effects

## Bisphenol A



## Phthalates



## Fluor chemicals

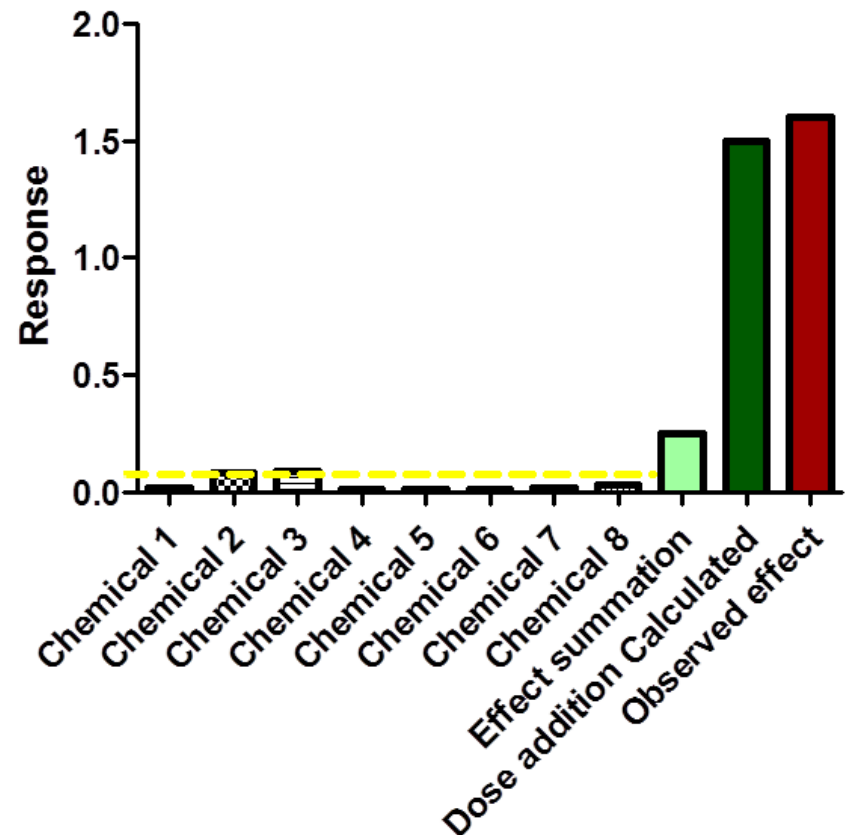


# Risk assessment should take into account mixture effects

Mixture effects have been documented in experimental studies for decades

⇒ Chemicals can 'join forces' to cause an effect even at low doses

Ref: Svingen & Vinggaard, The risk of chemical cocktail effects and how to deal with the issue. Editorial, JECH, Nov 2015





# The current paradigm for evaluation of safety of FCMS is insufficient

It doesn't take into account

- 1) mixture effects of chemicals
- 2) adverse effects like endocrine disruption, neurotoxicity etc.
- 3) FCMS of paper & board

**Underestimation of human risk to FCMS**

# How do we address the challenge of risk assessing FCMs in the future?

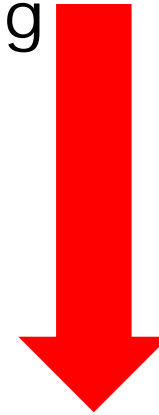
Toxicological profiling  
in silico, in vitro & in  
vivo



**Known** chemicals in  
food packaging with  
**unknown** effects



**Unknowns** in food  
packaging



Effect-directed analysis  
& analytical chemistry

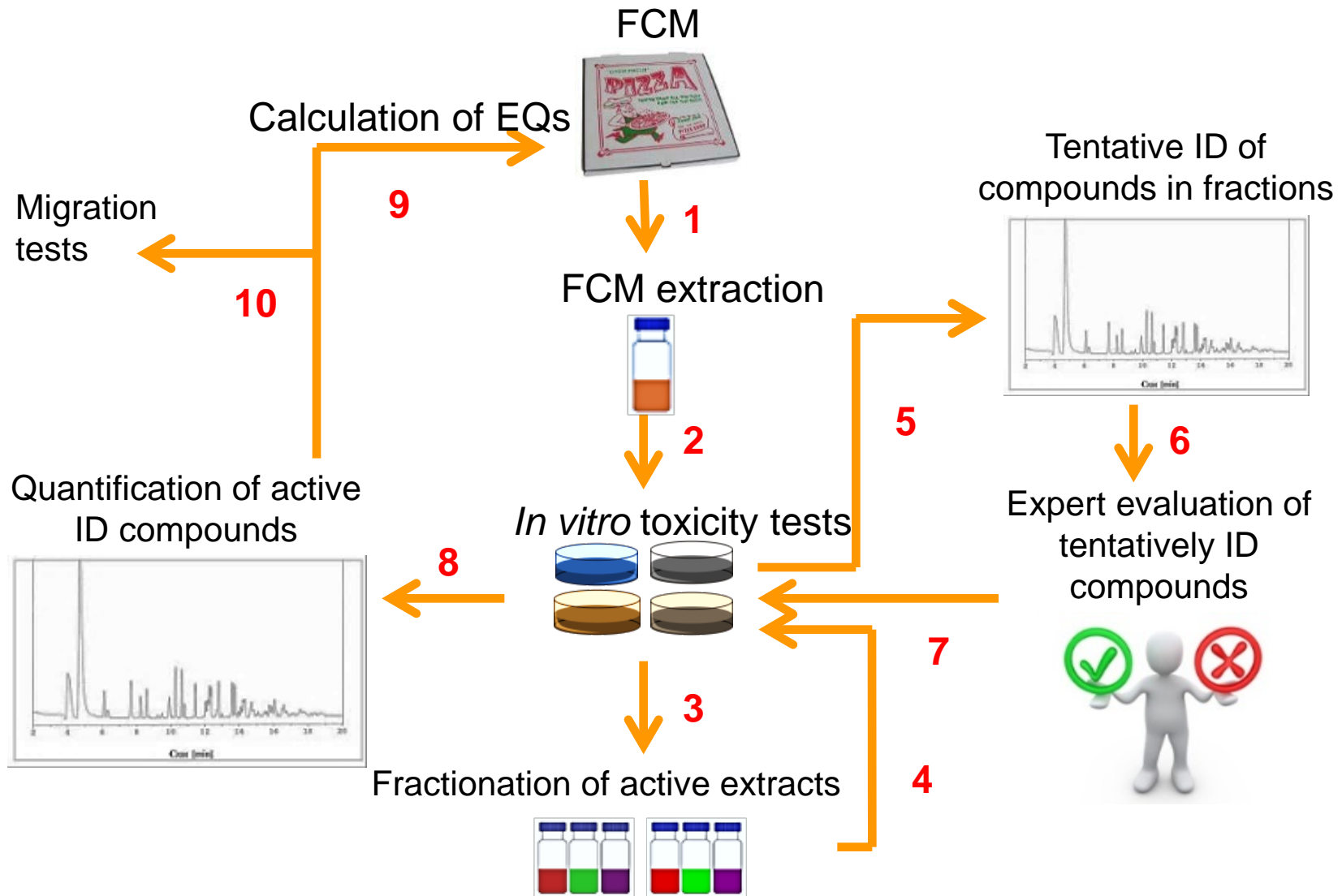


# In vitro tests for assessing integrated mixture effects in FCM

| Potential endocrine disruption  | Cytotoxicity  | Genotoxicity<br>Potential carcinogenicity  |
|---|---|--|
| Estrogen receptor<br>Androgen receptor<br>PPARs<br>GR, PR, TR<br>etc<br><br>Steroidogenesis | Cell organelle health<br>Cell proliferation & death | Indicator assays for genotoxicity<br><br>Mutagenicity tests<br><br>Potential carcinogenicity |

Ref.: ILSI report Europe, 2015 (modification of figure)

# Effect-directed analysis





AR ↑

AR ↓

ER

AhR

PPAR $\gamma$

RAR

Nrf2

p53

Ames

Sandwich wrapper

Muffin forms

Baking paper

Flour bag

Pizza box

White pizza box

Microwave pizza box

Popcorn bag 1

Popcorn bag 2

Sausage tray

Fish tray

Tomato tray

Cereal box

Nordic paper

Basis paper

Chinese paper 1

Chinese paper 2

Board w UV print

Board w watersol print

Board w offset print

Unpublished data



# Take home messages

- More focus on FCM is needed as it can be a significant source of human exposure to chemicals
- Mixture effects of chemicals have to be taken into account (also) when risk assessing FCMs
- Our effect-directed analysis covering endocrine disruption, cyto- and genotoxicity is quantitative and valuable for identification of emerging chemicals (reduces uncertainty)

# Thanks!



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