

# Fighting unknown chemicals: analytical strategies for risk prioritization

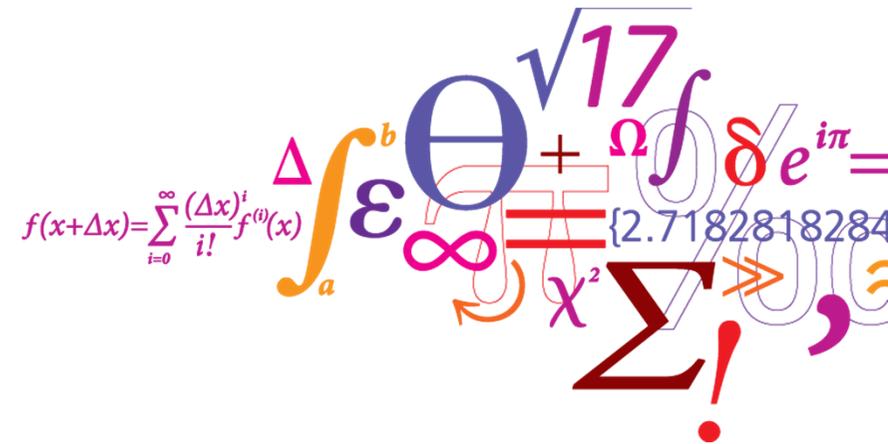
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Berlin, Germany  
30 November 2017

DTU Food  
National Food Institute

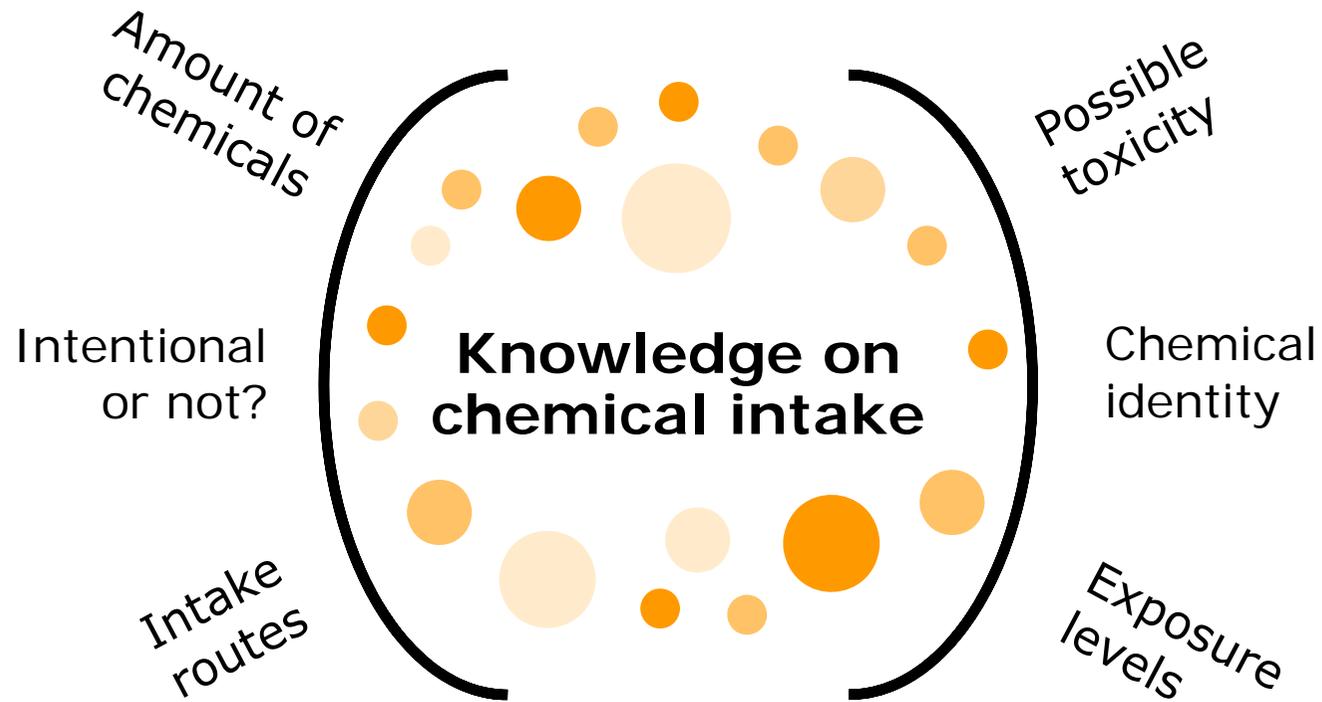
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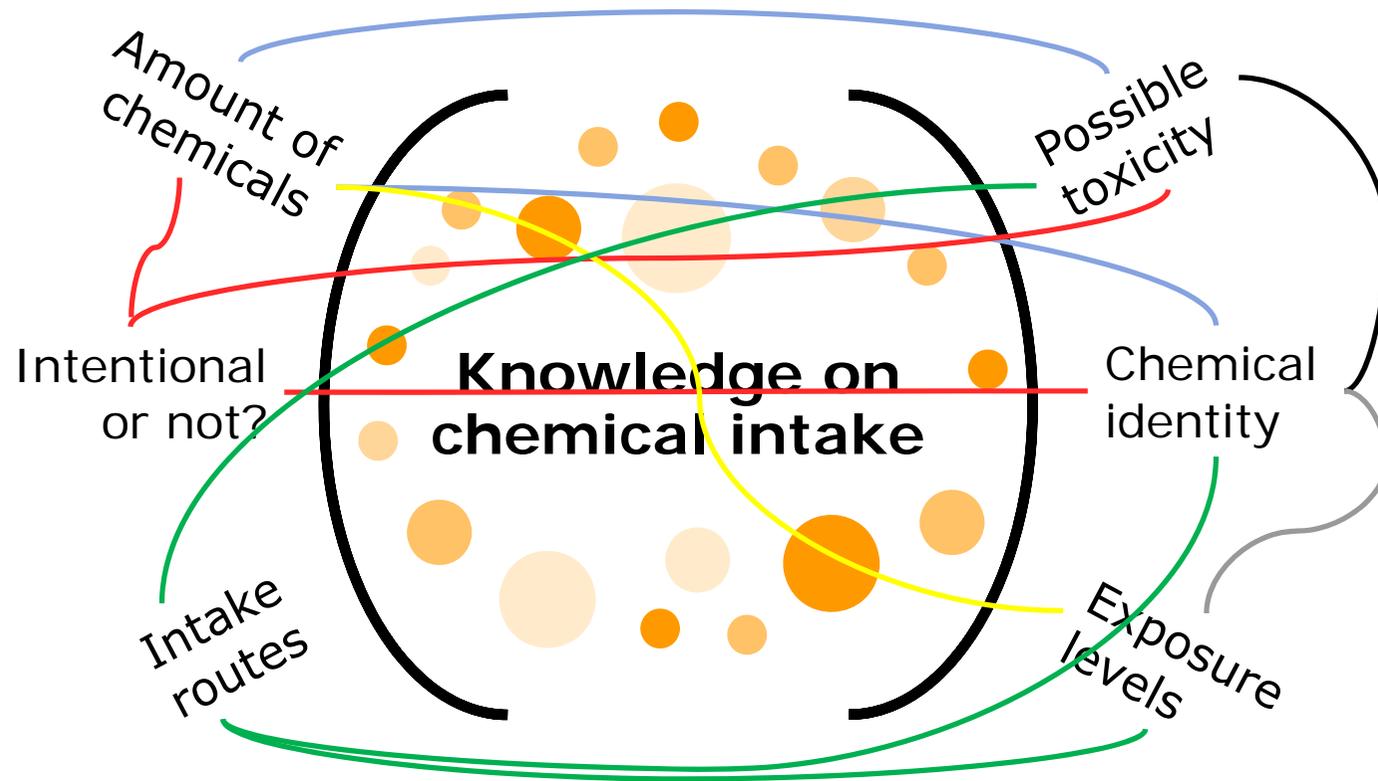
# In this talk:

- Introduction to **IAS & NIAS**: the chemical headache in food
  - Knowledge gaps
  - The analytical “Pillars of Knowledge”
  - Difference between IAS and NIAS
  - Risk-assessing IAS and NIAS
  
- Proposed methods for closing the knowledge gap (not detailed)
  - Quantification (*how much?*)
  - Identification (*what?*)
  - Hazard character (*how bad?*)
  - Preliminary risk (*priority?*)

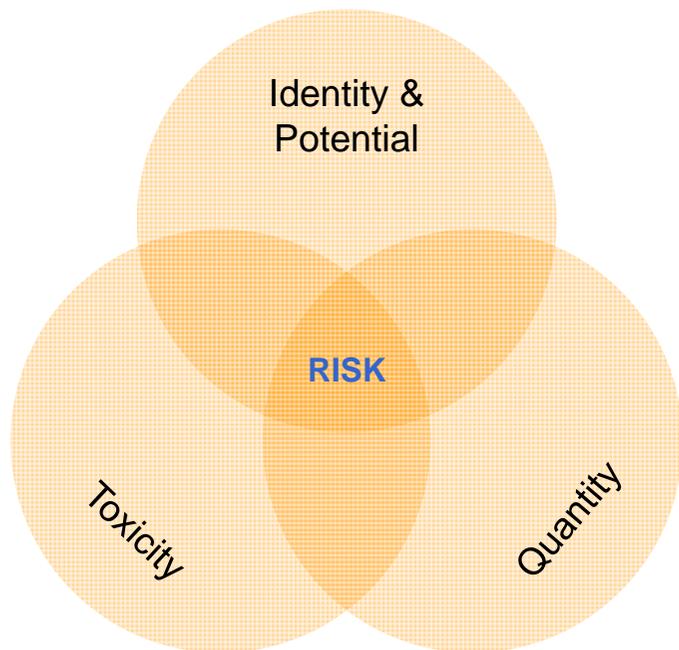
# Knowledge gaps in Risk Assessment



# Knowledge gaps in Risk Assessment



# Introducing the Pillars



[Identity & Potential] + [Quantity] = Exposure

[Toxicity] + [Identity & Potential] = Hazard

[Toxicity] + [Quantity] = Effect level

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**Risk** = Exposure + Hazard + Effect level

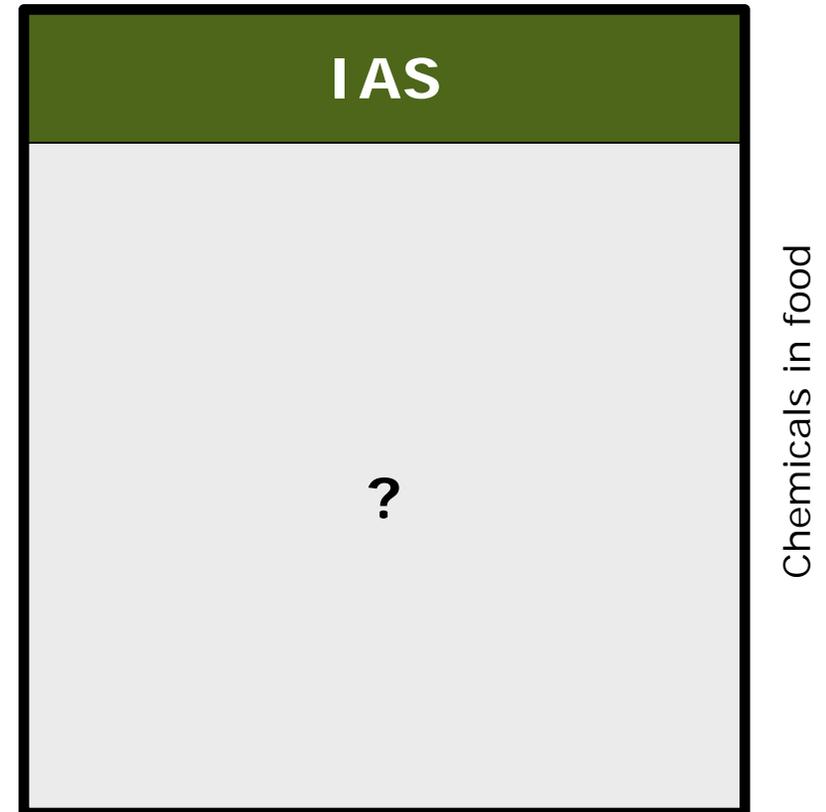
# A story of IAS and NIAS

- Intentionally Added Substances (**IAS**):

- Limited number
- Pillars OK (well-defined data)
- Validated methods
- Substances are regulated

- ❖ Existing tools & knowledge

- ❖ Rarely problematic



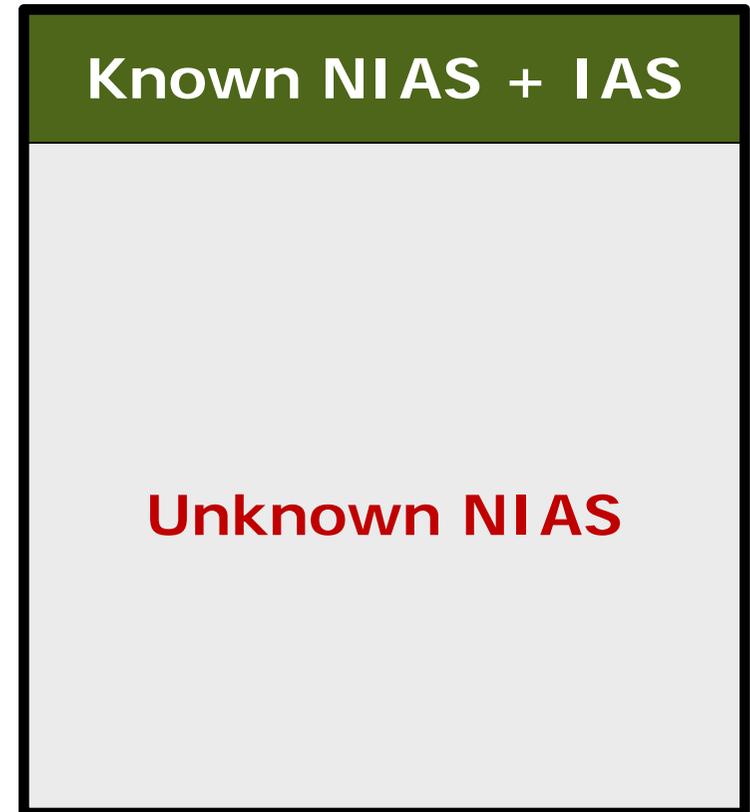
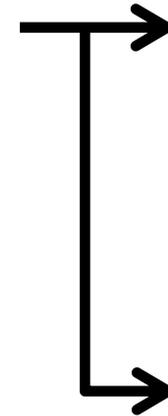
# A story of IAS and NIAS

- Non-Intentionally Added Substances (**NIAS**):

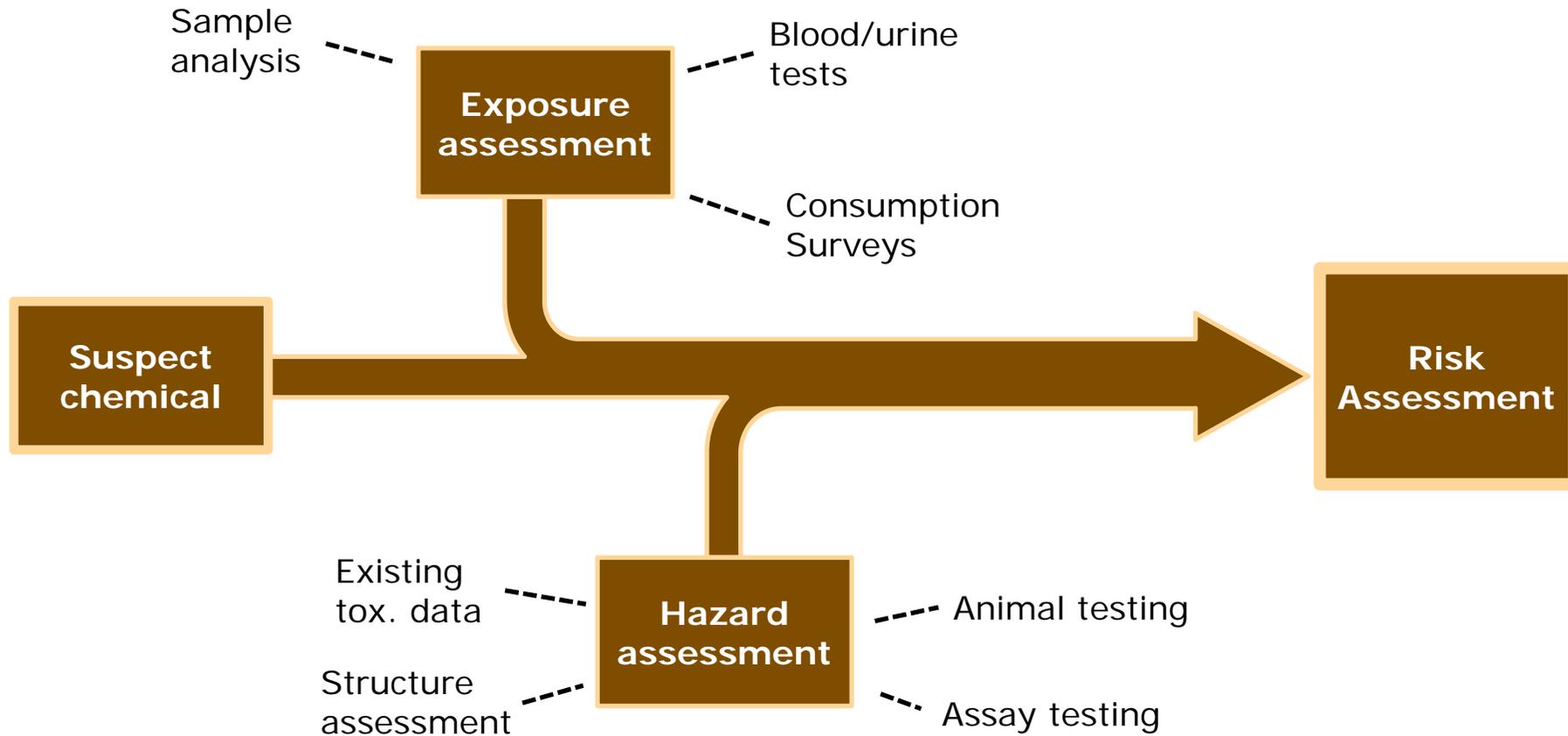
- Virtually unlimited number
- Pillars **NOT OK** (missing data)
- No formalized methodology
- No effective regulation

❖ **Lack of tools & knowledge**

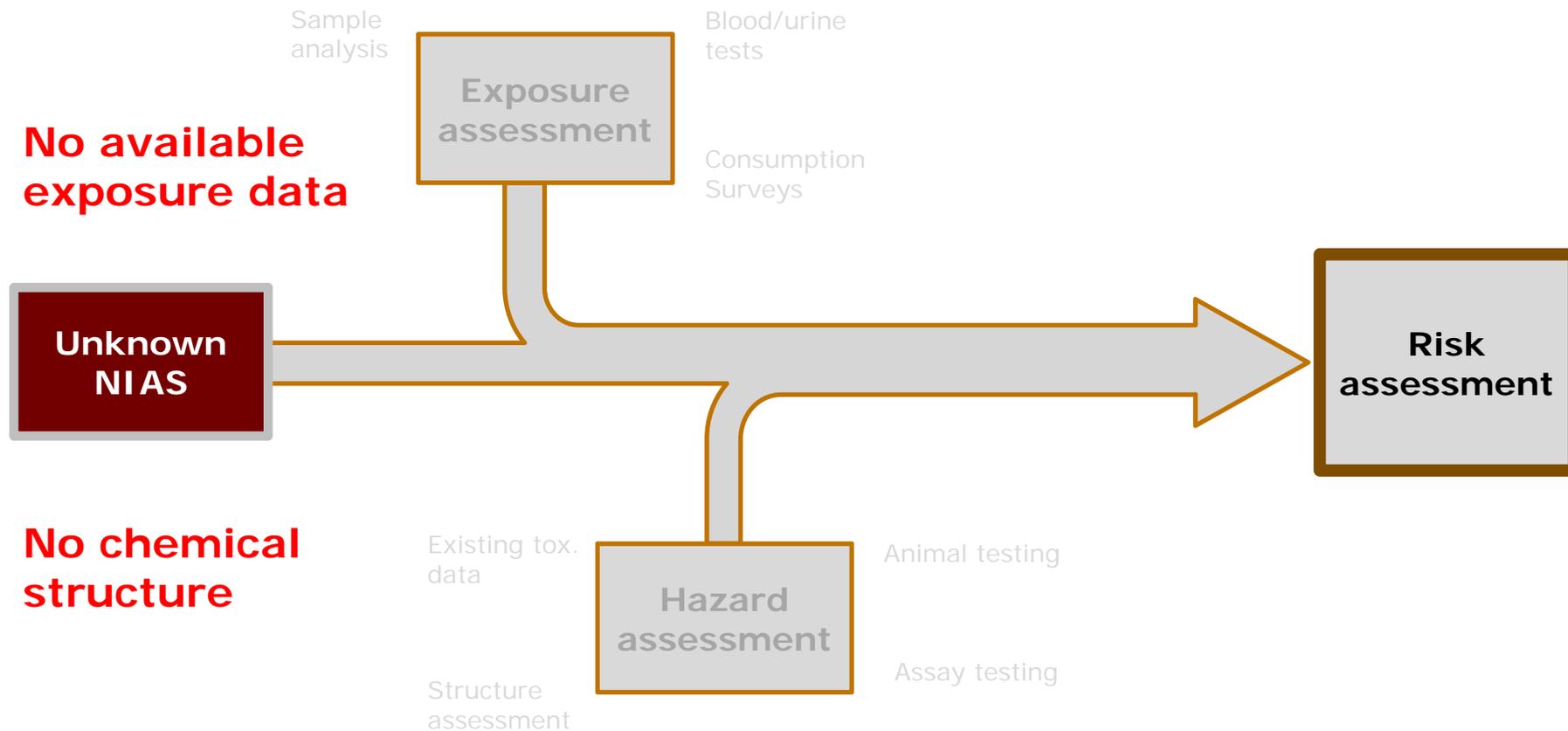
❖ **Unknown & undefined risk!**



# Risk Assessment

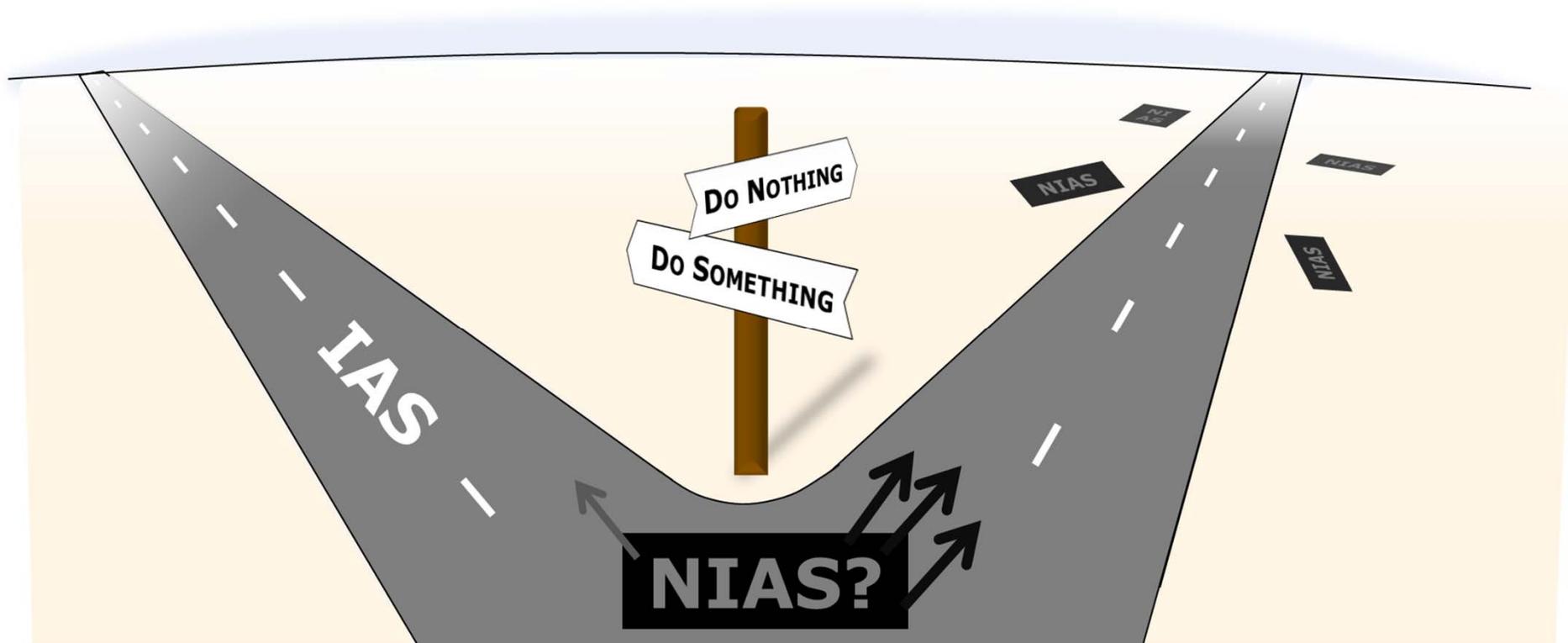


# Risk Assessment for unknown NIAS



# Making informed decisions without tools?

Because of inadequate tools, there is **no choice**

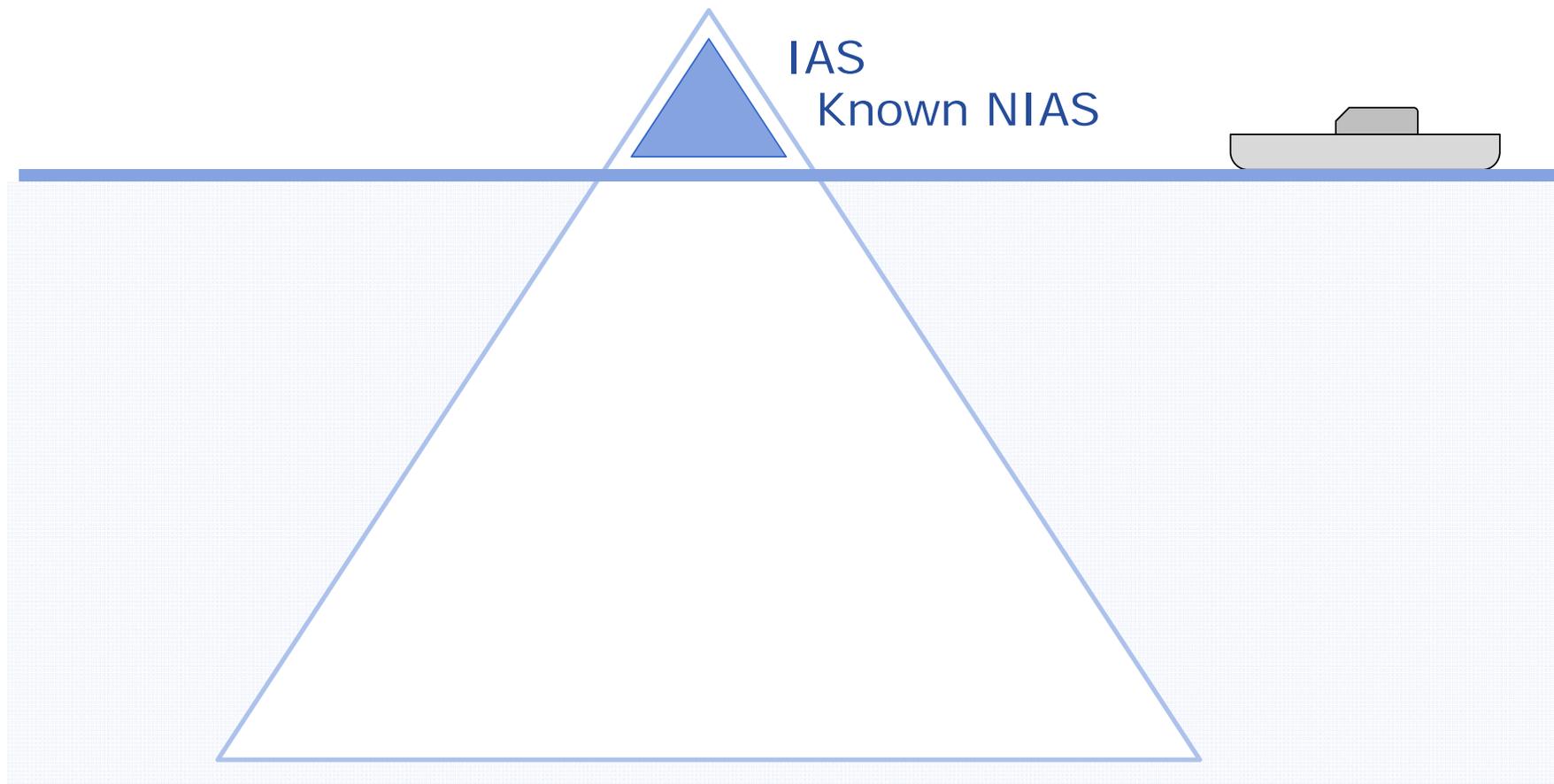


# What is needed?

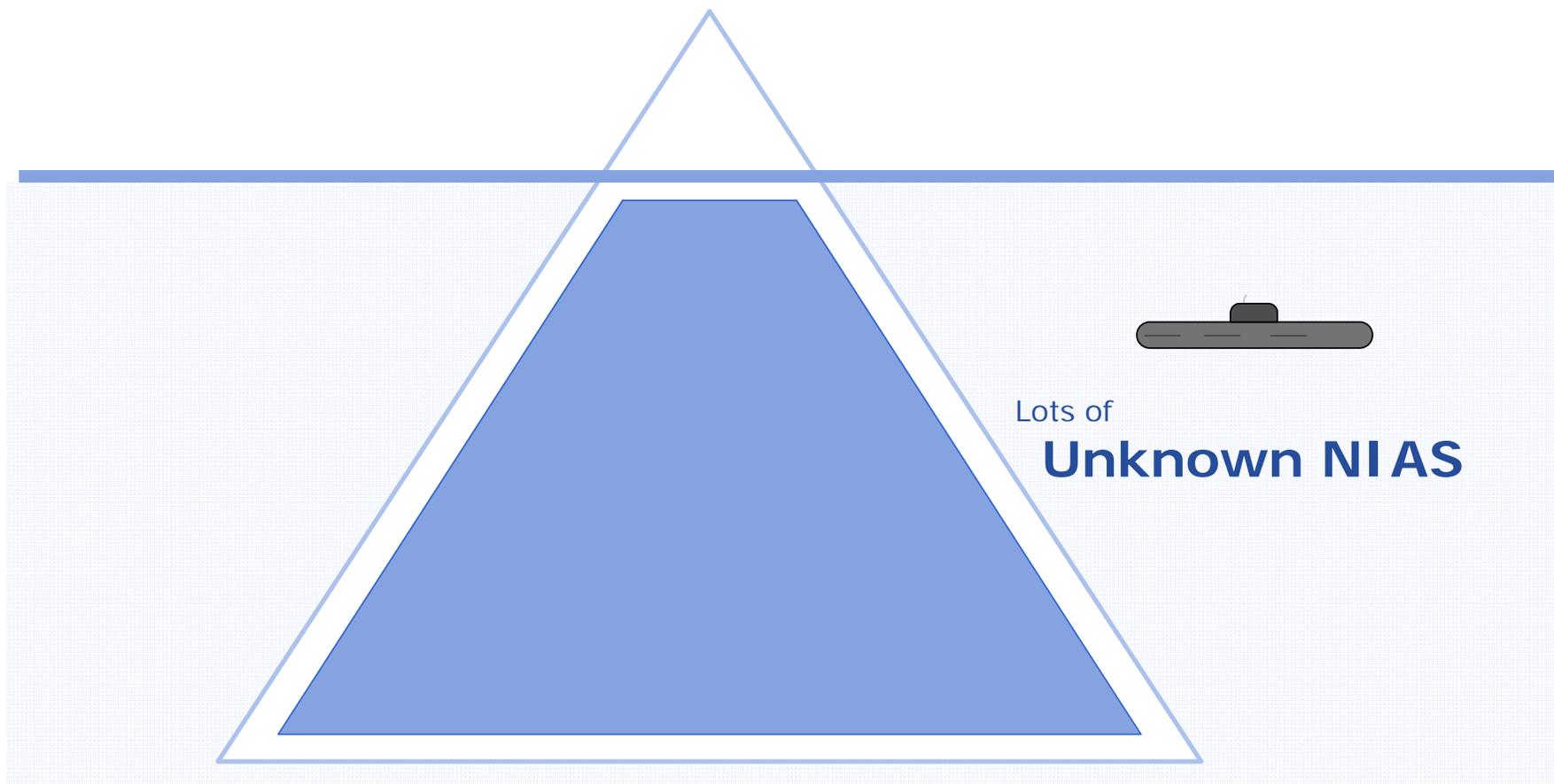
- Methods to **explore** what is present & any effect on human health
- Decisions on unknowns should be **information-based**
- Data must be available **fast & nonexhaustive**:
  - » time is precious;
  - » information is expensive.

(standard matching, animal tests, identification studies, ...)

# Chemicals in the tip of the iceberg



# Chemicals in the bottom of the iceberg



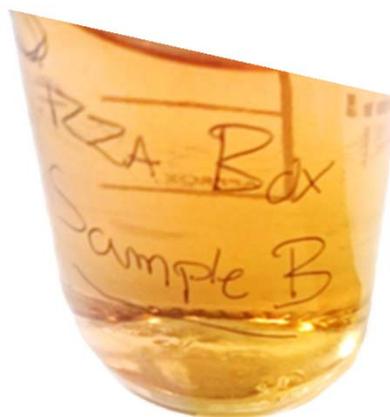
# New tools to explore unknown chemicals

## LC-QTOF-MS

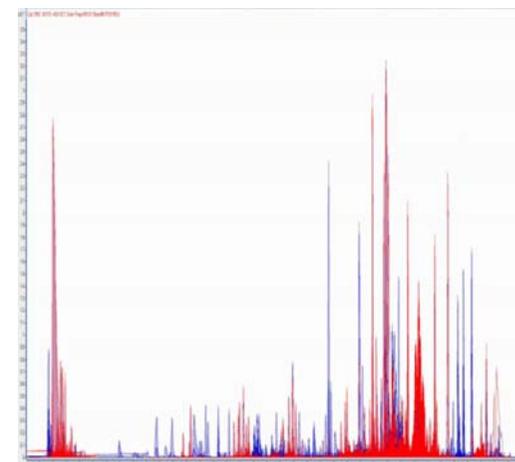
LC *Liquid Chromatography*  
QTOF *Quadrupole x Time of Flight*  
MS *Mass Spectrometry*

## TCM

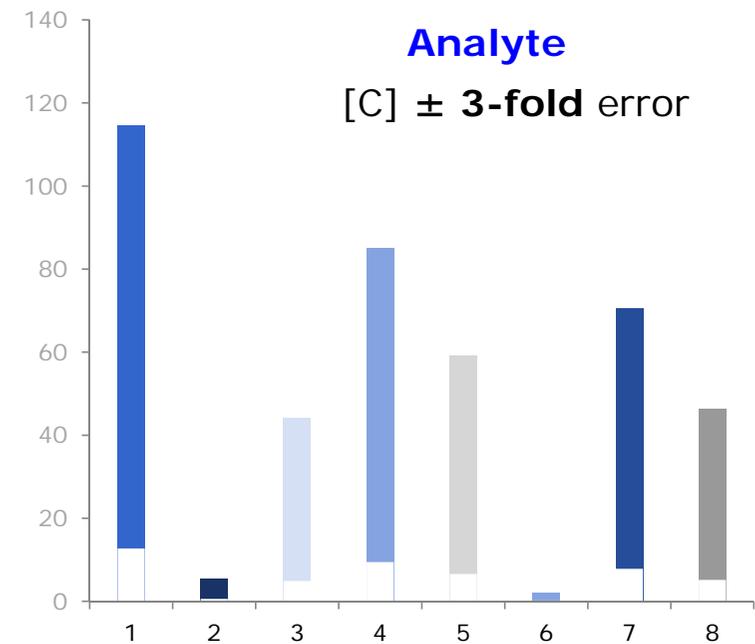
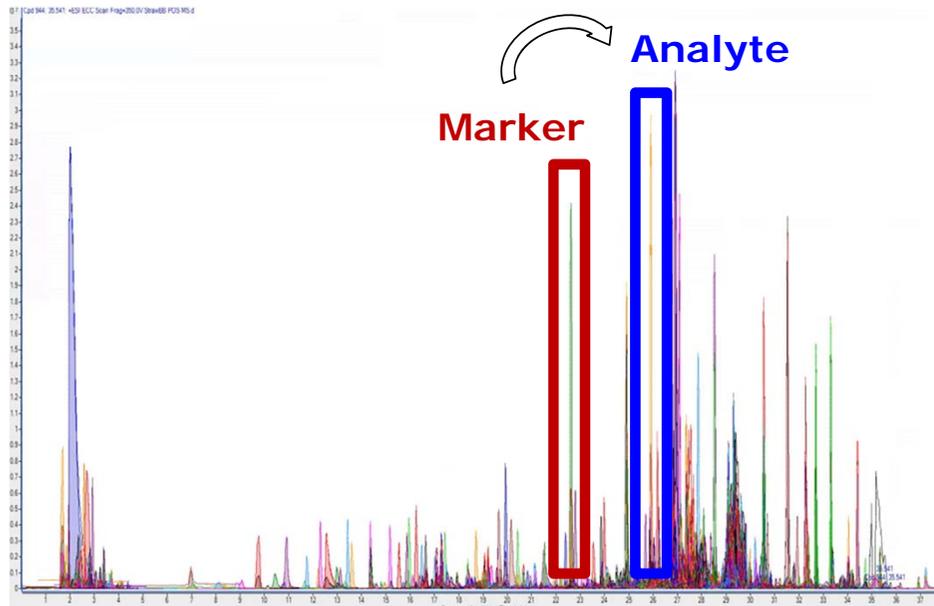
*Total Migratable Content: The chemical portion of a sample that has potential to migrate to food.*



## Quantitative data



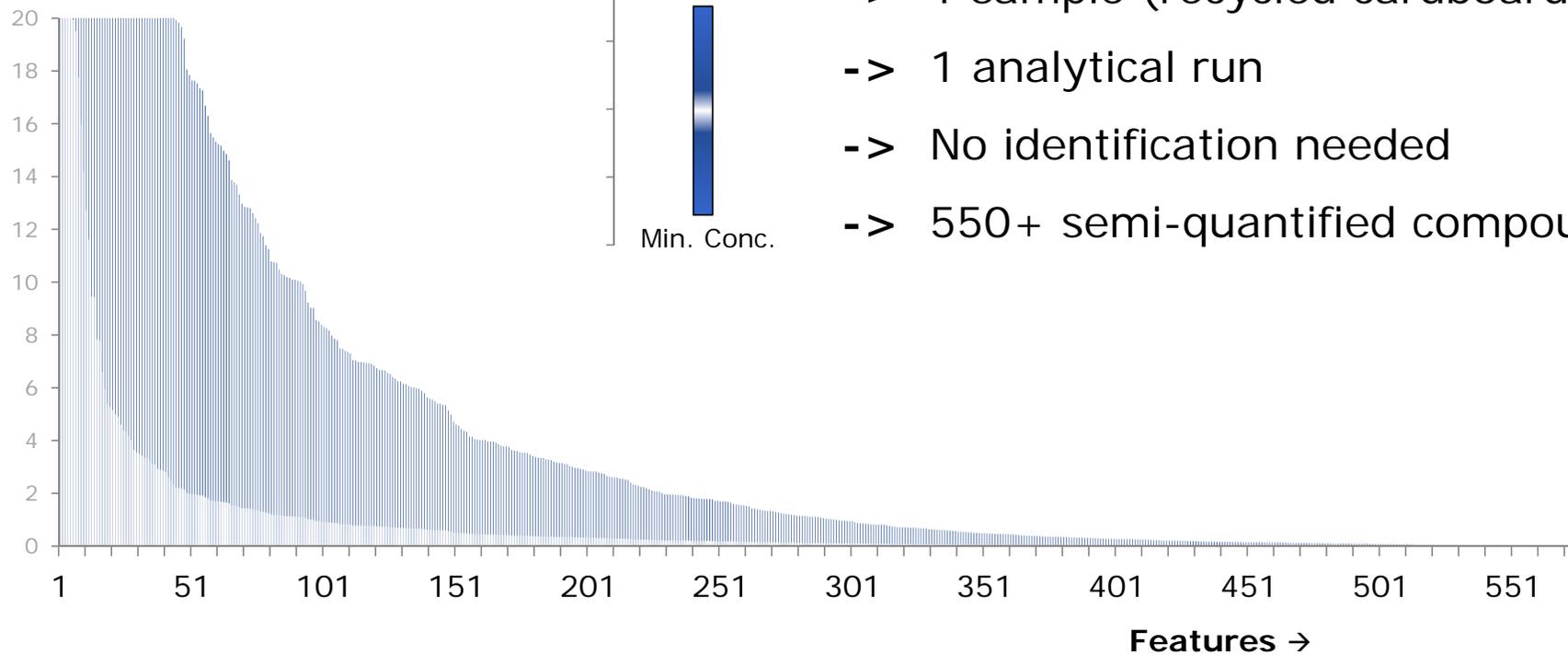
# Semi-quantitative tools



Pieke et al., *Anal Chim Acta*. 2017 vol. 975, pp. 30-41.  
DOI: [10.1016/j.aca.2017.03.054](https://doi.org/10.1016/j.aca.2017.03.054).

# Semi-quantitative tools

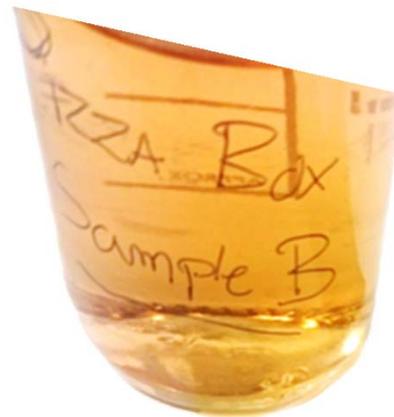
Concentration  
( $\mu\text{mol/L}$ )



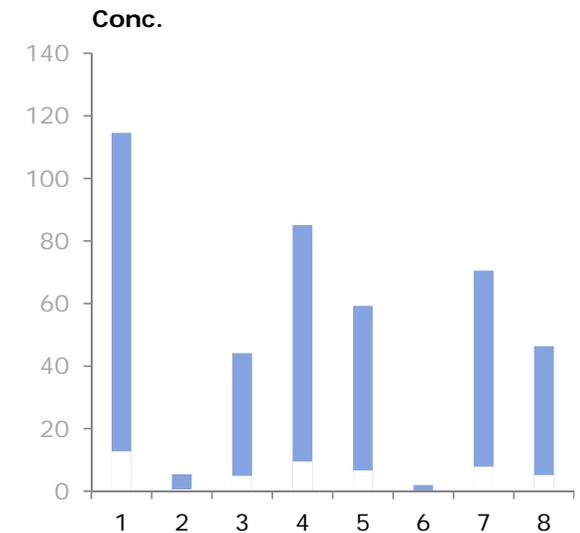
- > 1 sample (recycled cardboard)
- > 1 analytical run
- > No identification needed
- > 550+ semi-quantified compounds

*Pieke et al., Anal Chim Acta. 2017 vol. 975, pp. 30-41.  
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# Exploring the world of unknown chemicals

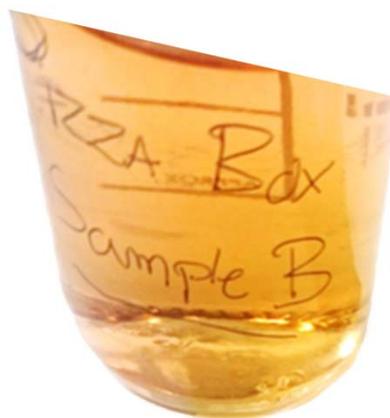
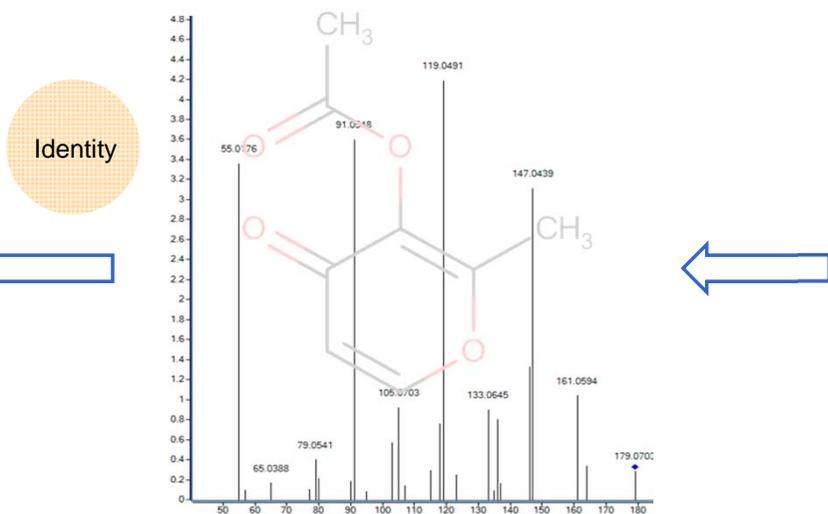


## Semi-quantitative data

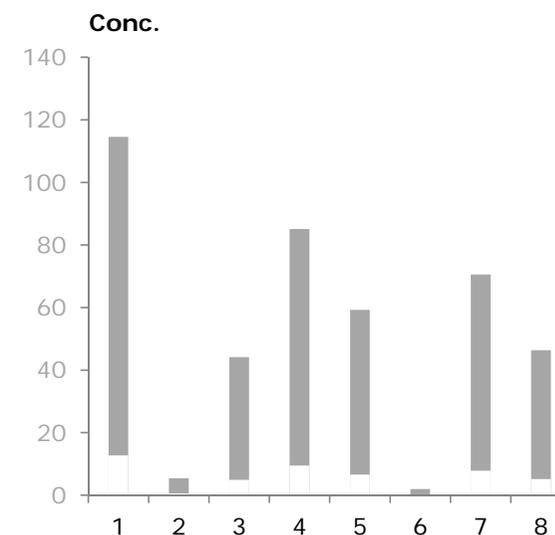


# Exploring the world of unknown chemicals

## Chemical structure data

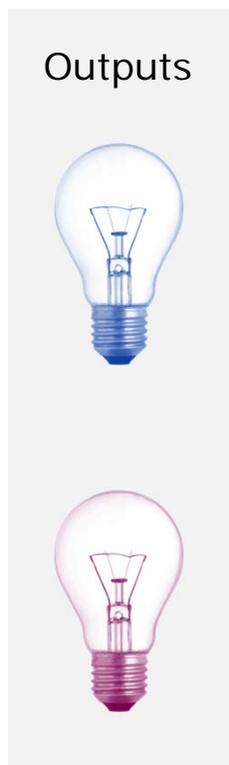


## Semi-quantitative data



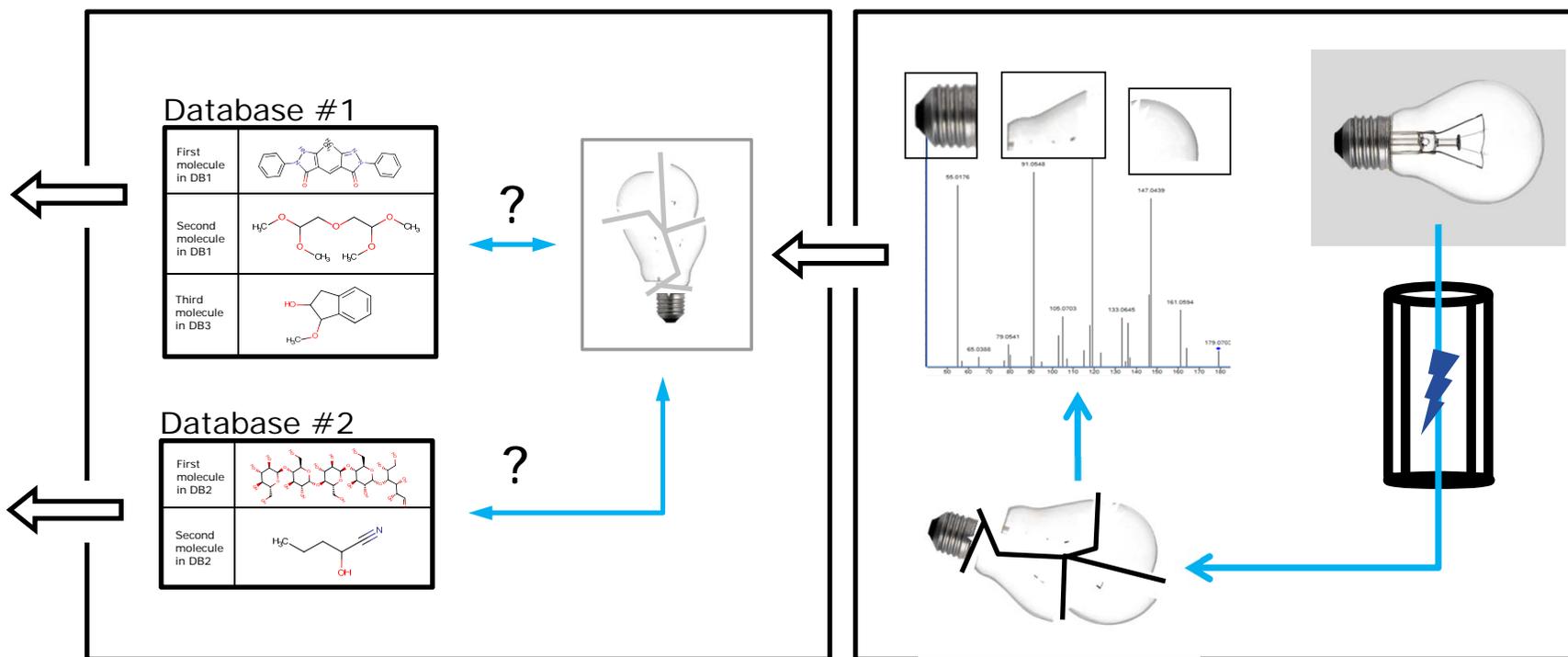


# Ambiguous structure assessment



## Similarity Correlations

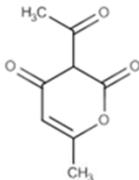
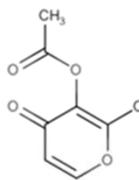
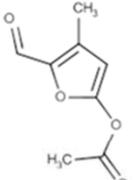
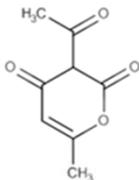
## Controlled Fragmentation



Piekie et al. (in press), J. Mass Spectrom.

# Ambiguous structure assessment

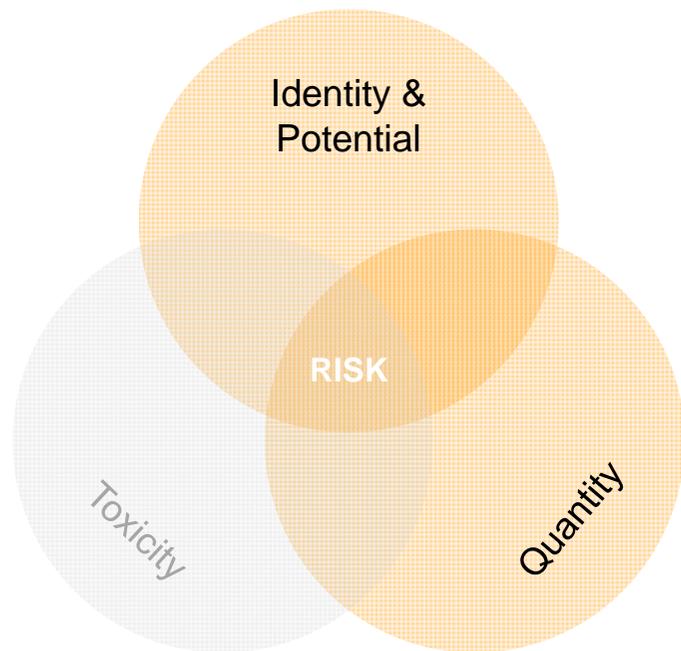
- **Result:** best-matching similar compound from available databases:

DB#1			DB#2			DB#3			DB#4		
Formula	Structure	Score	Formula	Structure	Score	Formula	Structure	Score	Formula	Structure	Score
$C_8H_8O_4$		75.5	$C_8H_8O_4$		76.1	$C_8H_8O_4$		78.6	$C_8H_8O_4$		75.5



*Piekie et al. (in press), J. Mass Spectrom.*

# The Three Pillars: incomplete



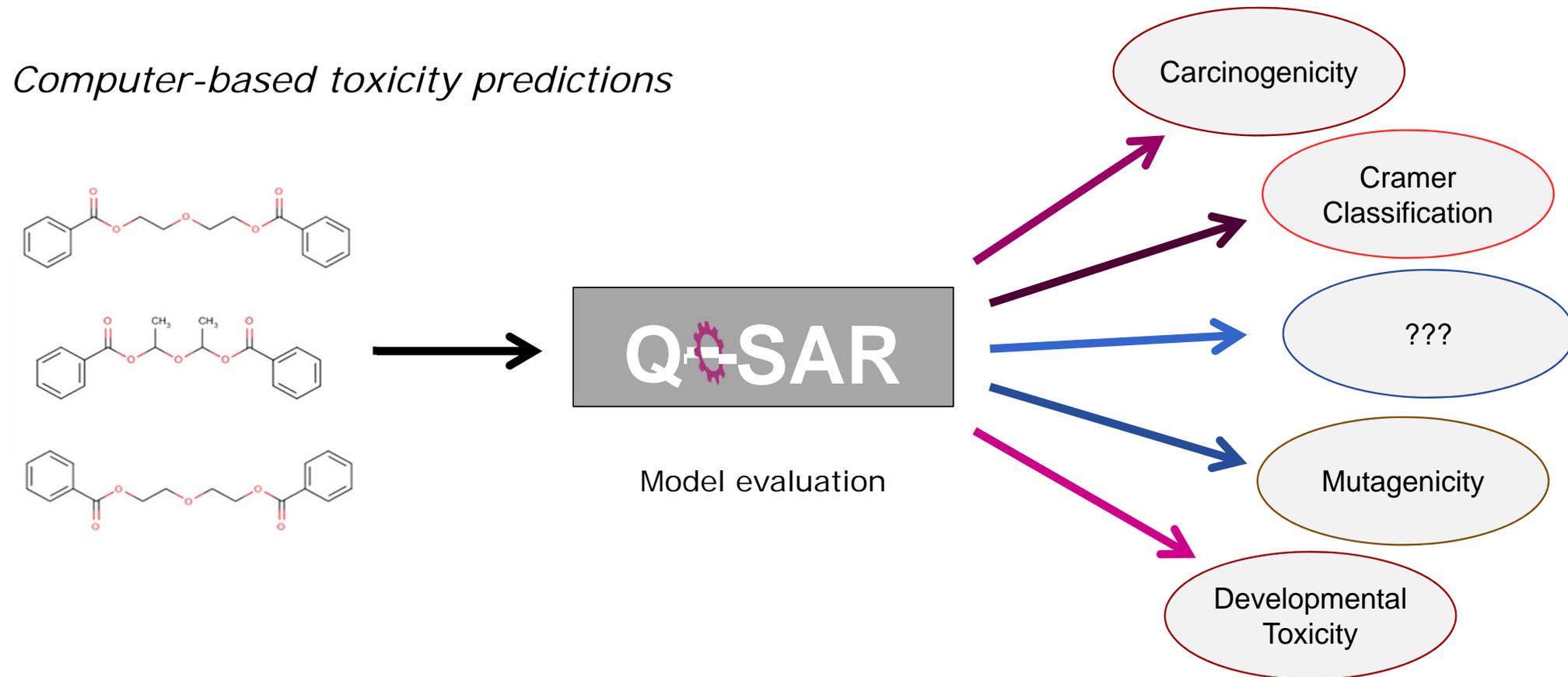
[Quantity] ← Semi-quantification

[Identity] ← Structure **prediction**

[Toxicity] ← ???

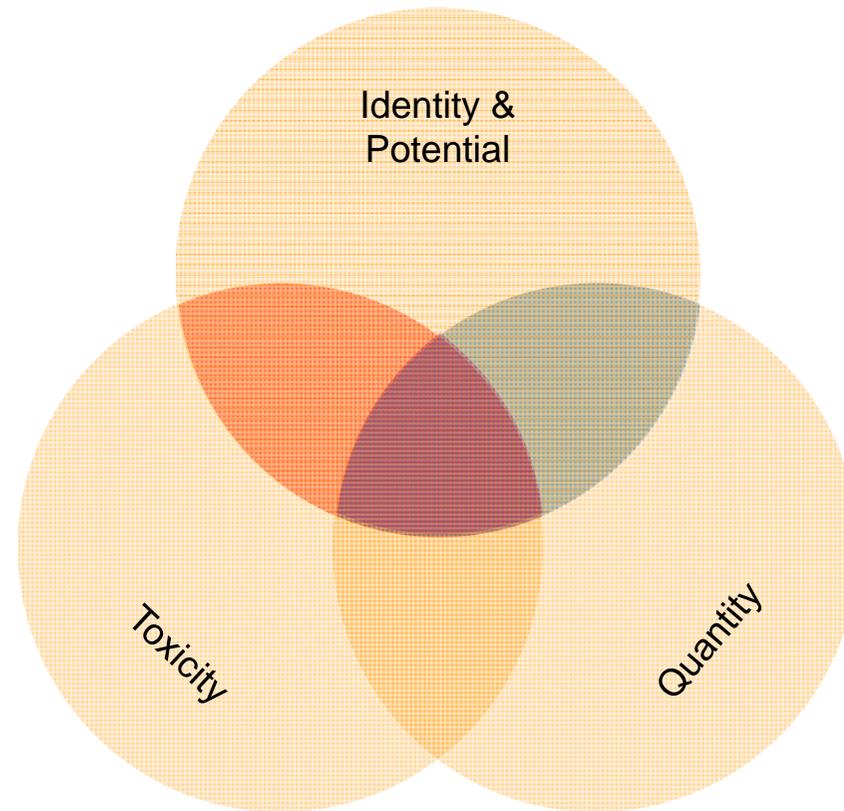
# The toxicity of tentative chemicals?

*Computer-based toxicity predictions*



# The Three Pillars: nonexact data

$$\text{Risk} = \text{Hazard} * \text{Exposure}$$



Placeholders...



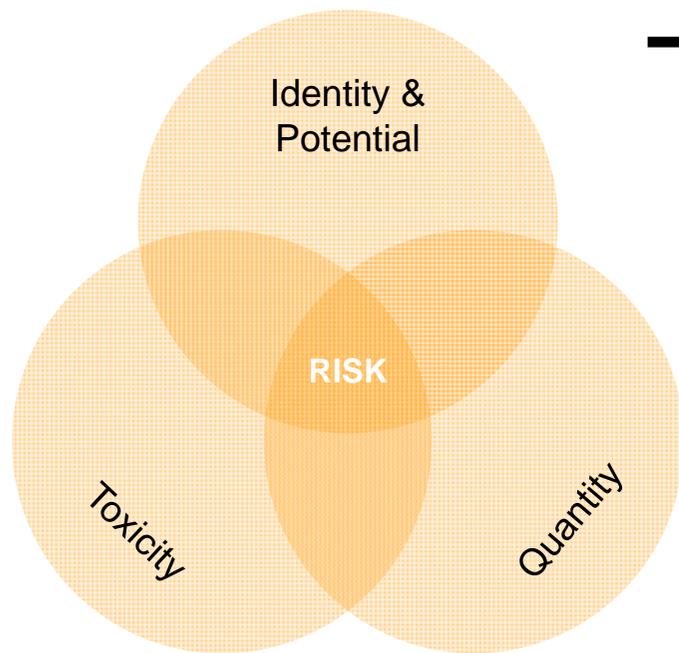
# Risk: starting from tentative data

- We may not be able to calculate the true **risk** from approximated data, but ...
- We can still get a nonconclusive **perception of risk**: *preliminary risk assessment*

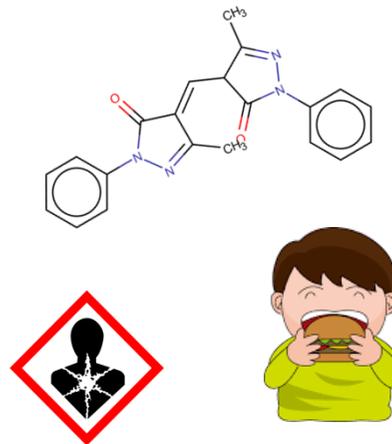




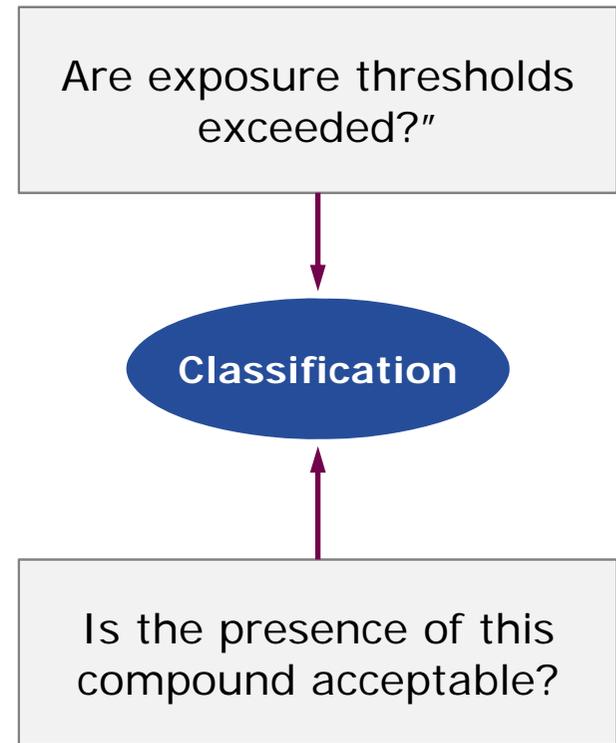
# Risk: a classification method



*Rule-based decisions*



*Expertise decisions*

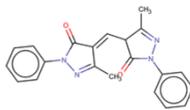




# Risk: the first things first

## FACTORS

Identification



QSAR alerts



Exposure



## CLASSIFICATION

**A:** Substances of direct concern

**B:** Substances of lesser concern

**C:** Insufficient or incomplete data

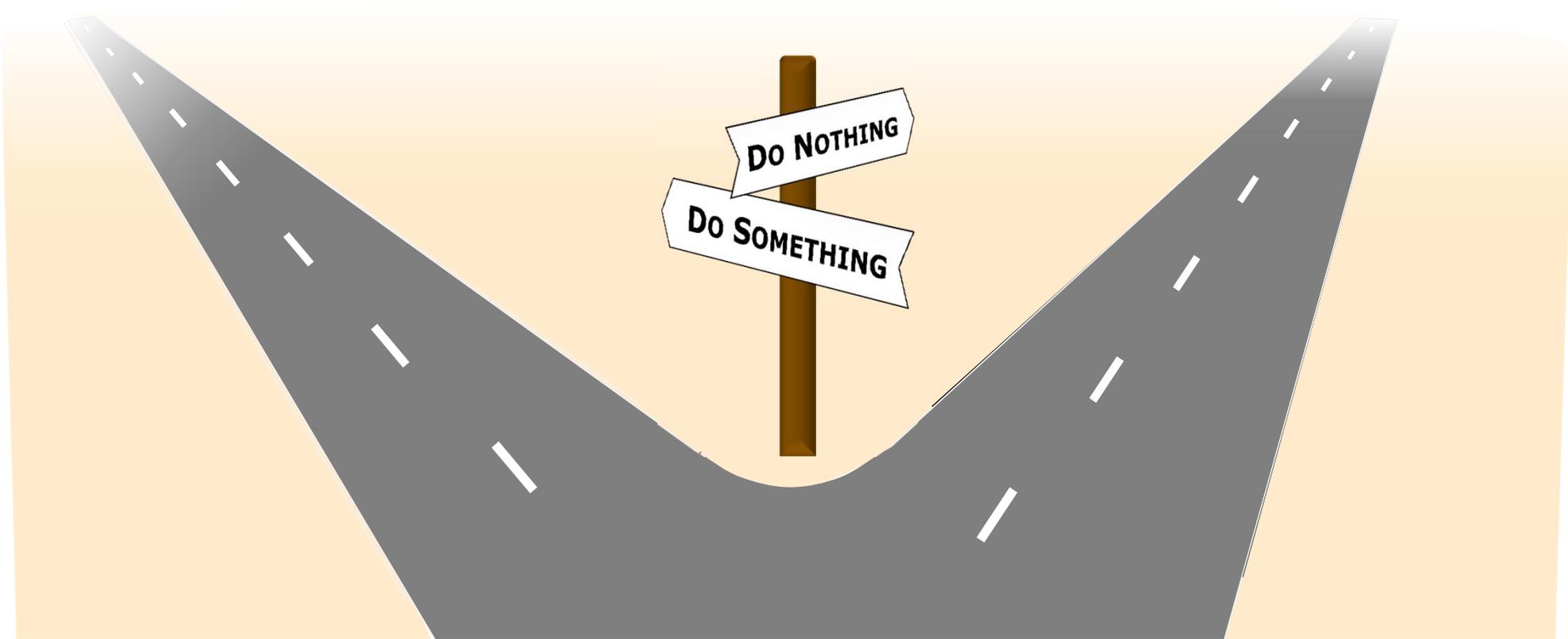
# The purpose of tentative data

We need  
**tentative data**

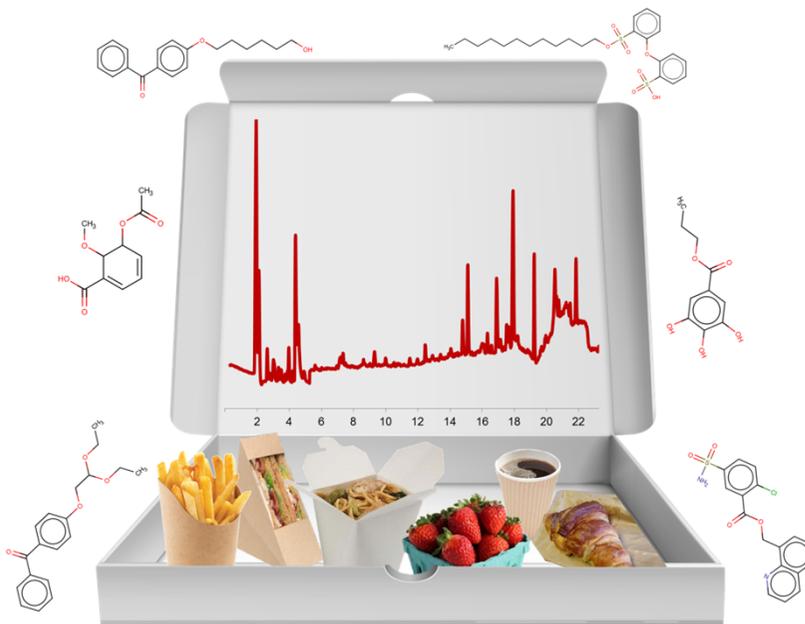
... because the alternative is  
**no data!**

# The purpose of tentative data

The choice to do nothing should be deliberate



# Thank you for your attention



**Eelco Nicolaas Pieke**

✉ [enpi\(at\)food.dtu.dk](mailto:enpi(at)food.dtu.dk)

Thanks to:

**DTU Food**  
National Food Institute

- Kit Granby
- Jørn Smedsgaard



- Gilles Riviere
- Bruno Teste

**GDSI**  
Global Decision Support Initiative

- Elena Boriani

# Wish-list for NIAS screening

- **Better identification methods and tools** – more knowledge on HRMS needed
- **Greatly improved databases for possible IAS & NIAS** – ideally from the source
- **More comprehensive tools for hazard** – QSAR is not mature and subject to discussion
- **More work on sampling & semi-quantification** – reduce the uncertainty in the assessment