Food contact paper & board chemicals: establishing priorities by “Exploration” strategies

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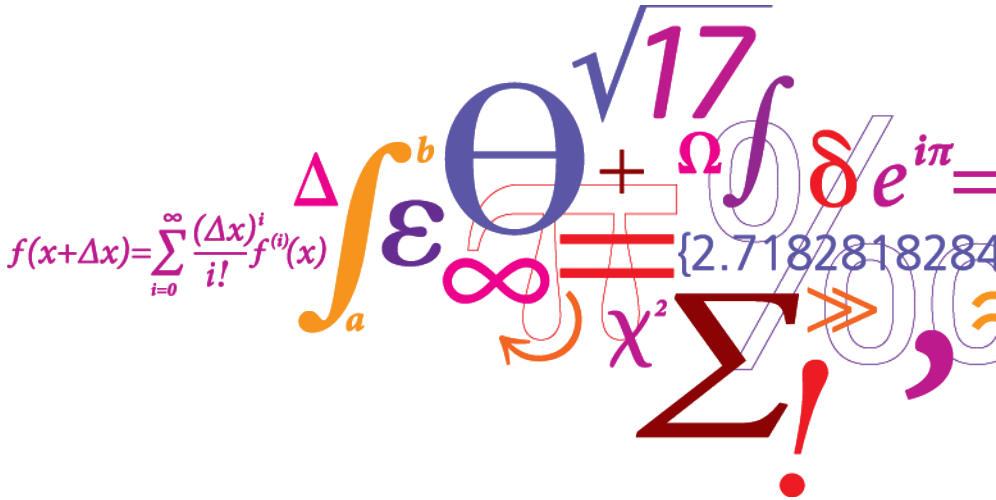


Food Packaging Forum

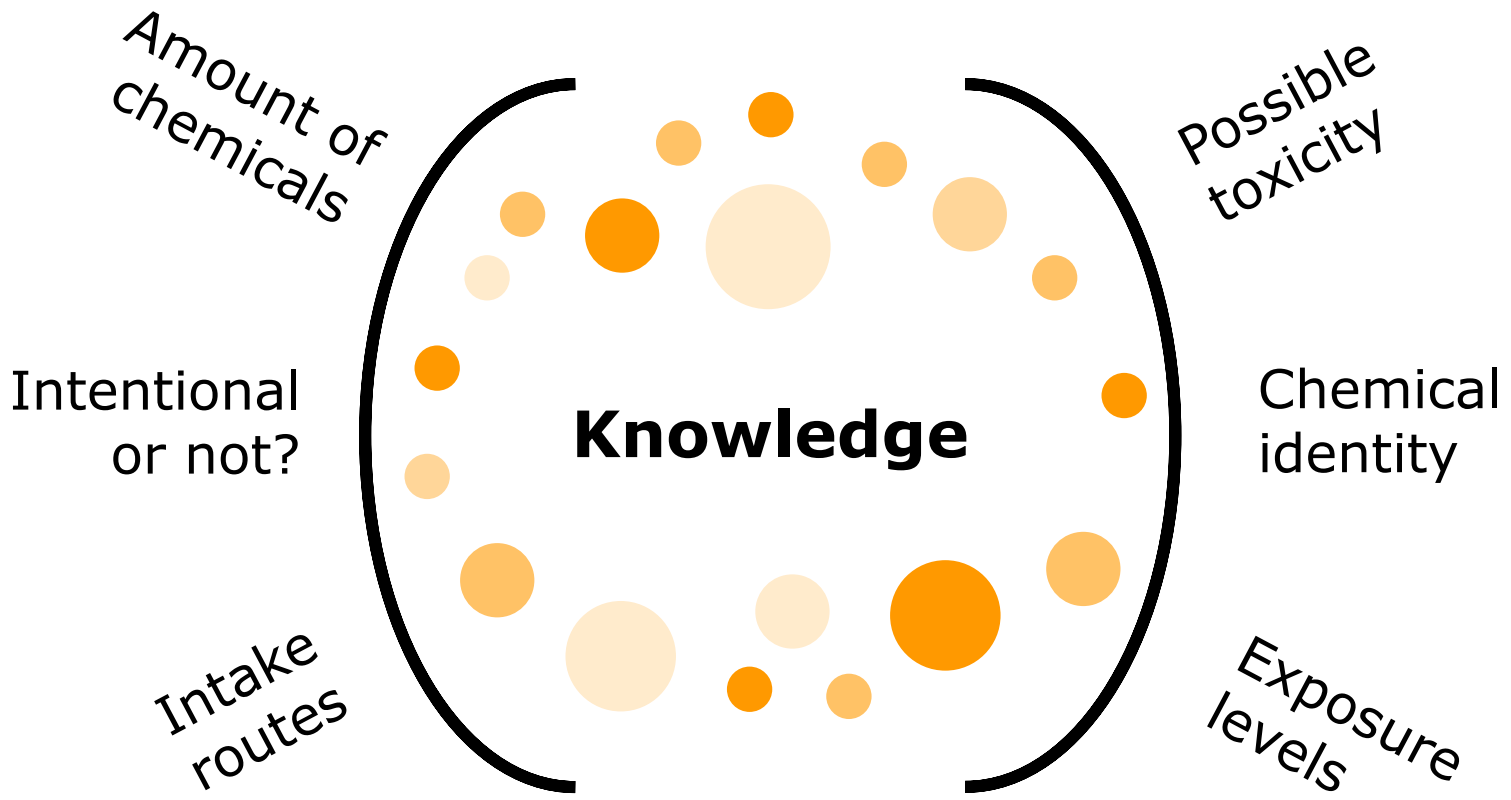
Webinar
08 February 2018

DTU Food
National Food Institute

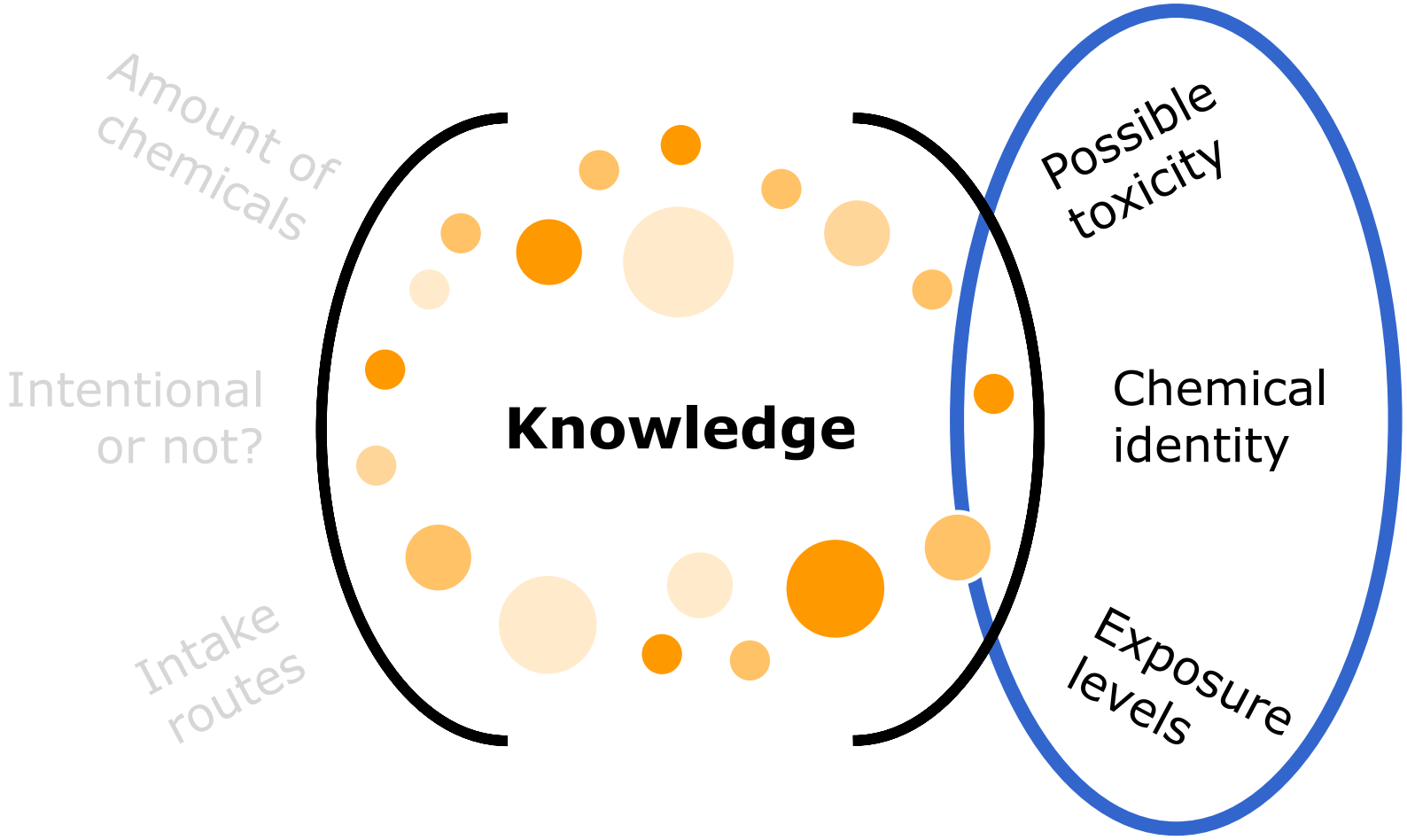
Agenda

- Why are NIAS (potentially) a problem?
- What is “Exploration”?
- Determining how much is present: semi-quantification
- Investigating what is present: tentative identification
- Risk prioritization

Assessment of chemicals is knowledge-based



Assessment of chemicals is knowledge-based



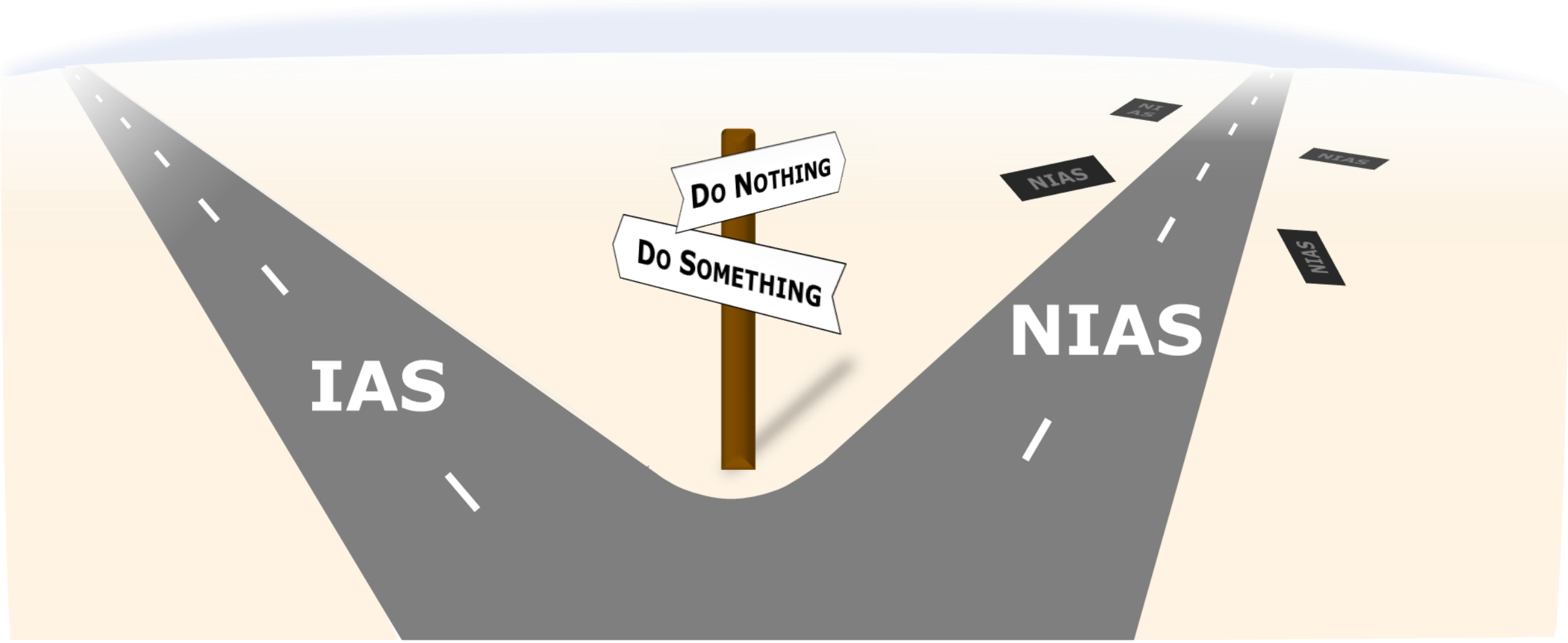
For NIAS:

Most of these factors are unknown

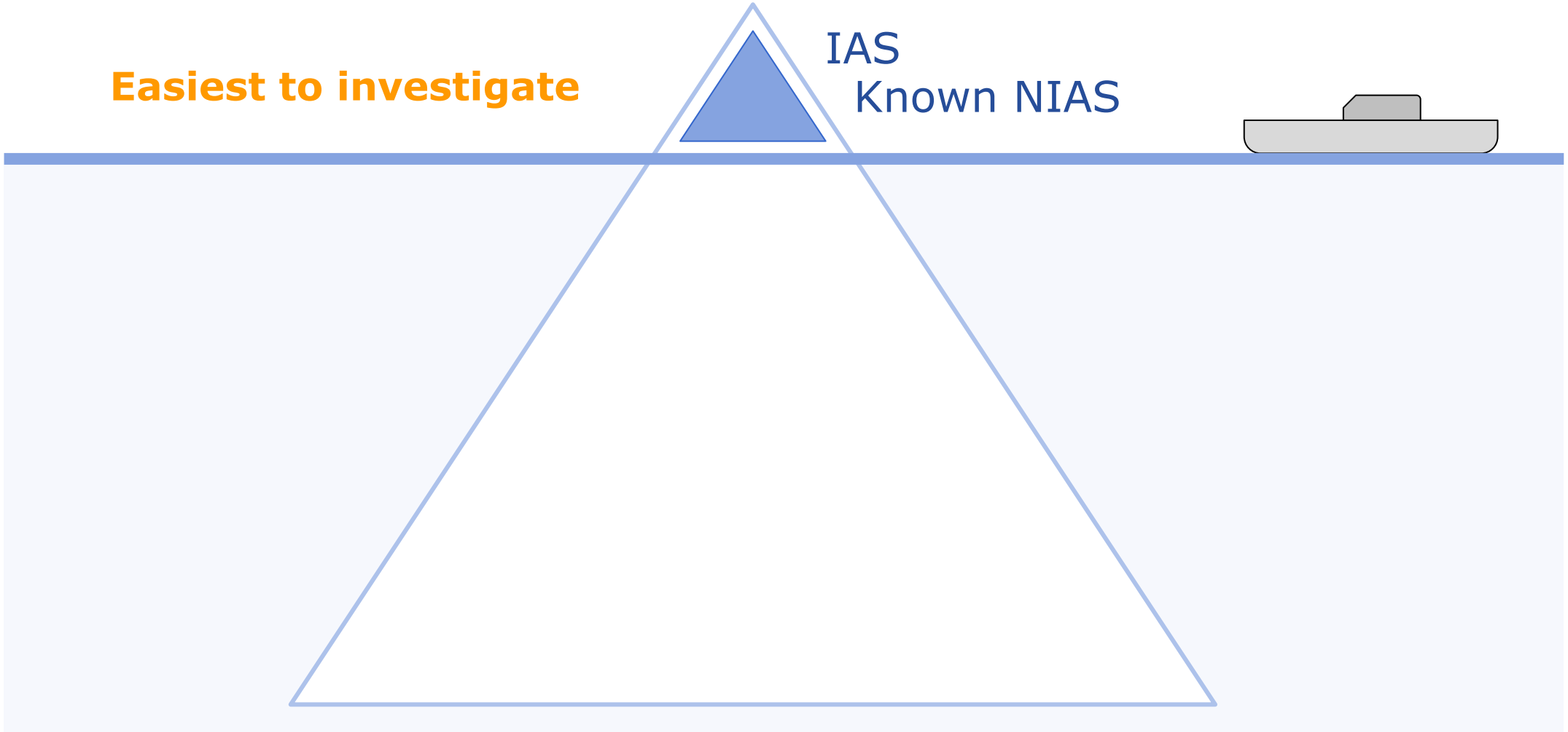
Why NIAS are (potentially) a problem

A. Ensuring safety is knowledge-based
B. We have **very little knowledge** of NIAS
C. We **do not have tools** to improve knowledge

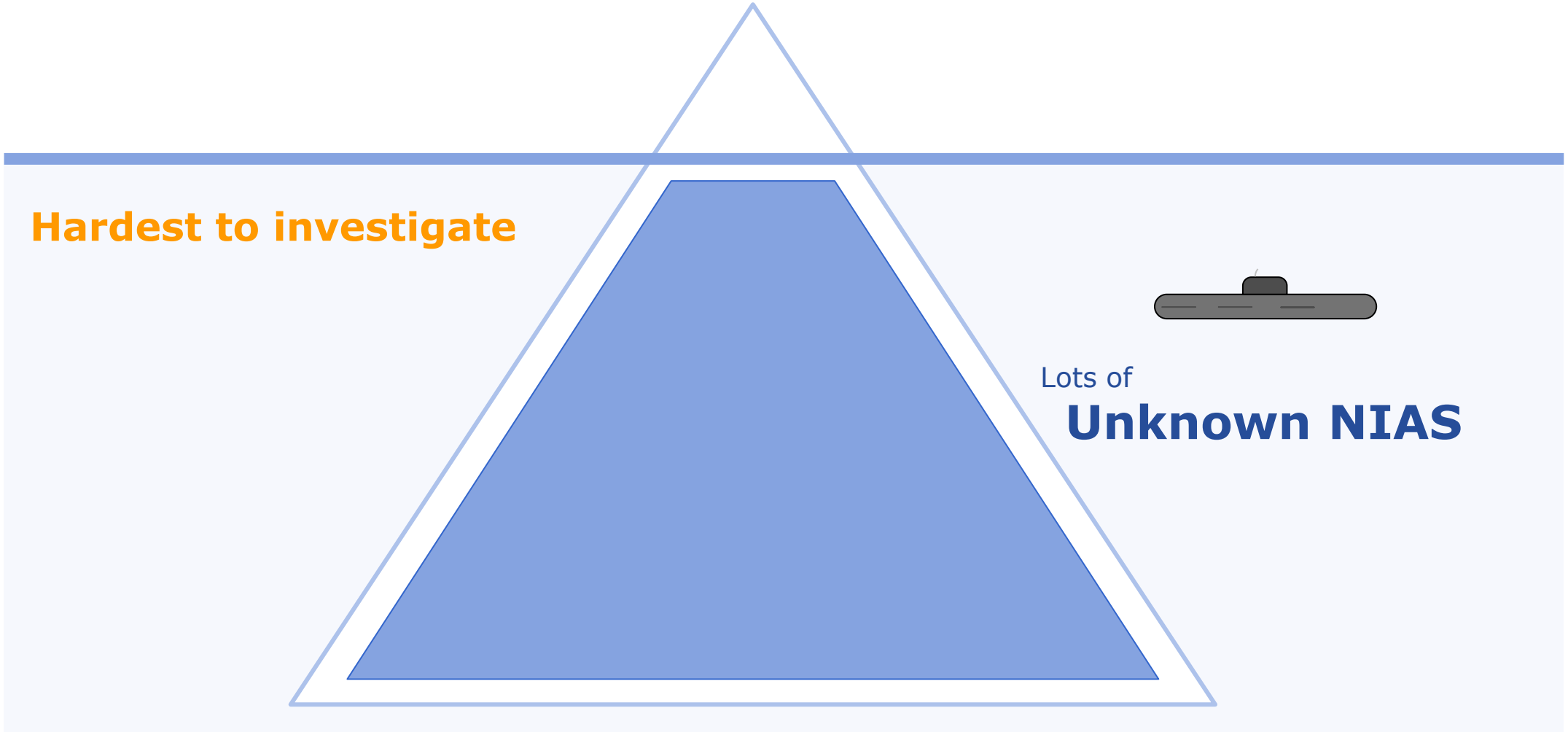
How the knowledge gap affects NIAS



The tip of the iceberg

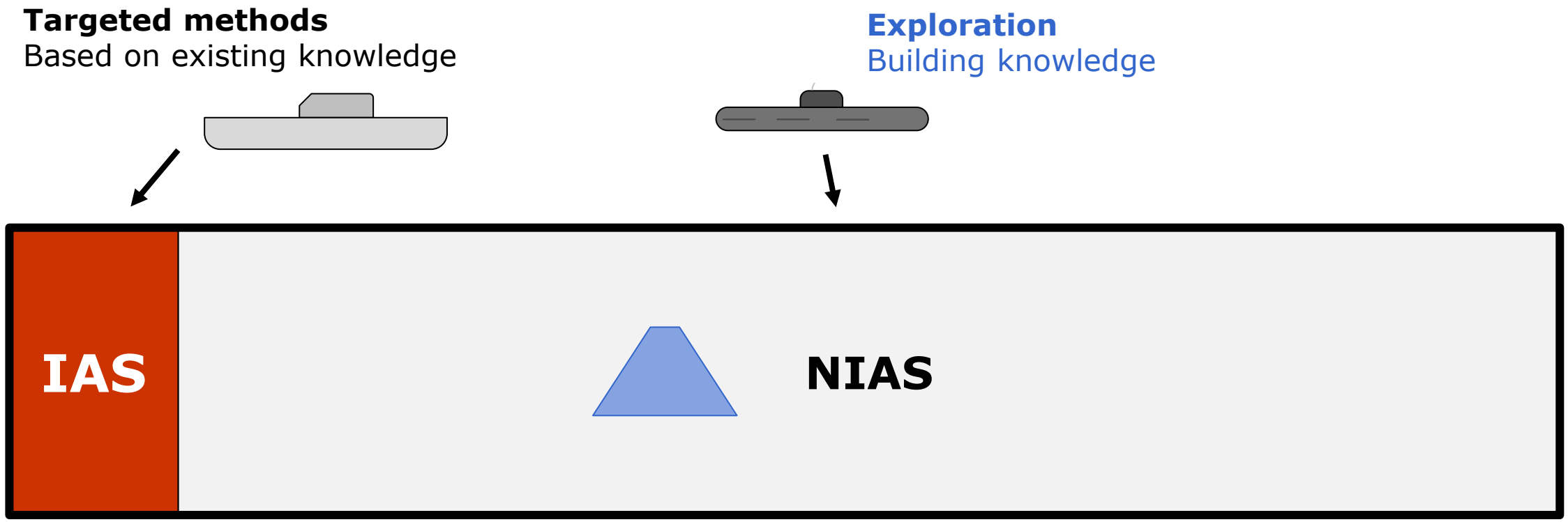


The bottom of the iceberg



What is chemical exploration?

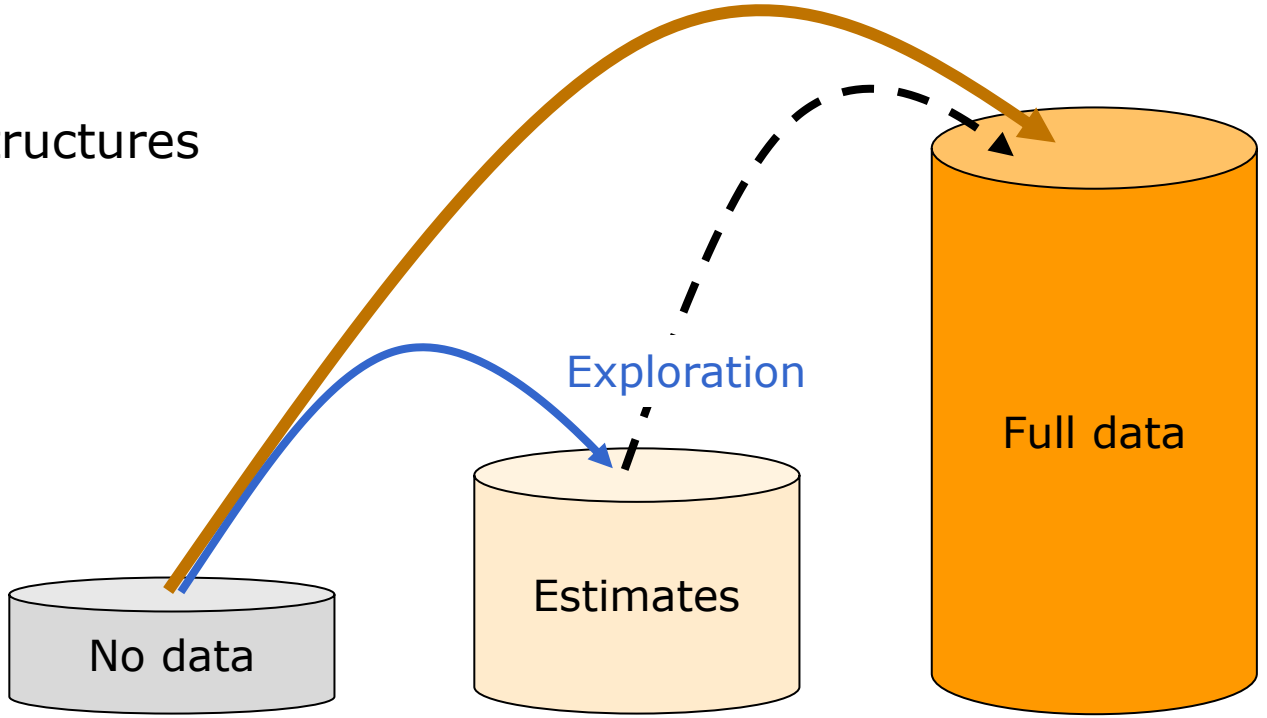
- Exploration is a type of untargeted discovery in complex samples



Where does chemical exploration work?

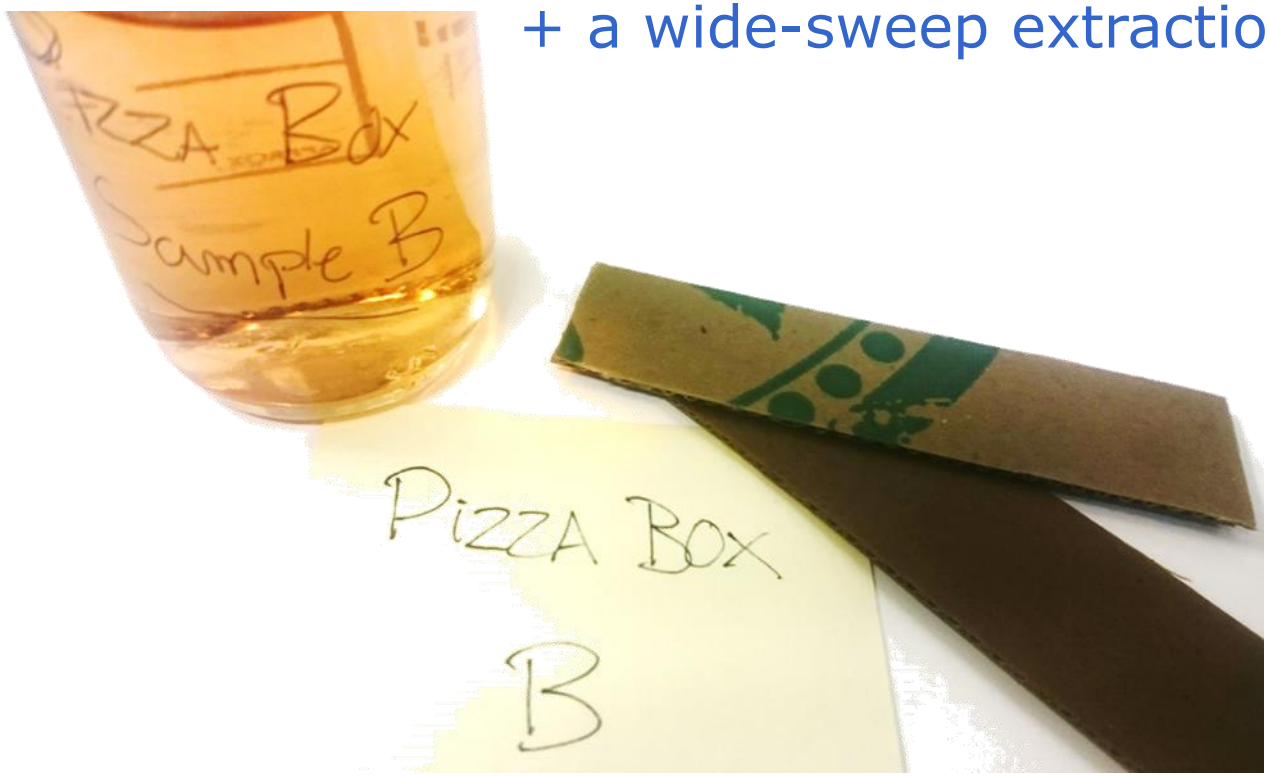
- Exploration is the first step in **filling information gaps** in early-stage assessments

- It seeks to provide:
  - A rough concentration estimate
  - Suggestions for possible chemical structures
  - *Assist in risk prioritization*



Performing exploration

Exploration is a unbiased analysis
+ a wide-sweep extraction



LC-QTOF-MS

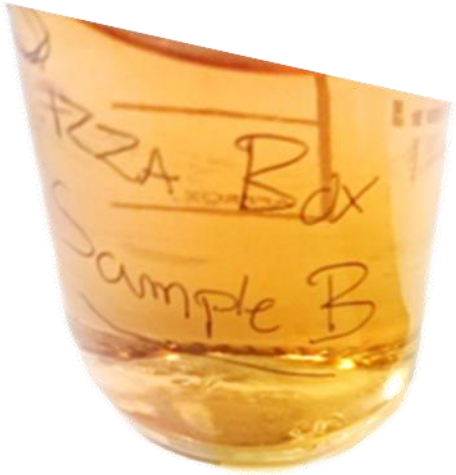
LC *Liquid Chromatography*
QTOF *Quadrupole x Time of Flight*
MS *Mass Spectrometry*

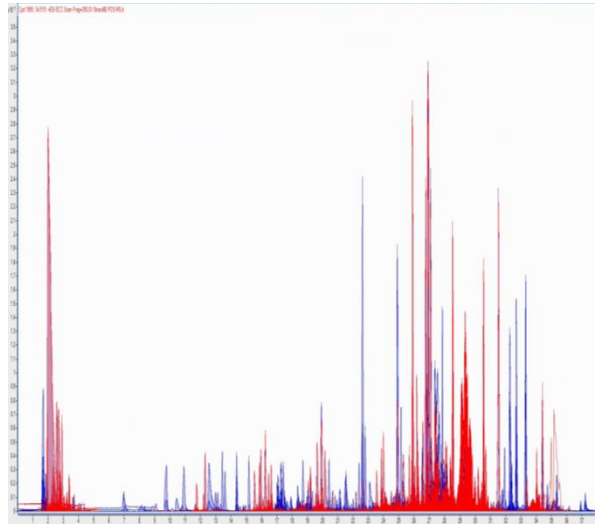
TCM

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

Exploring the world of chemicals

Quantitative data

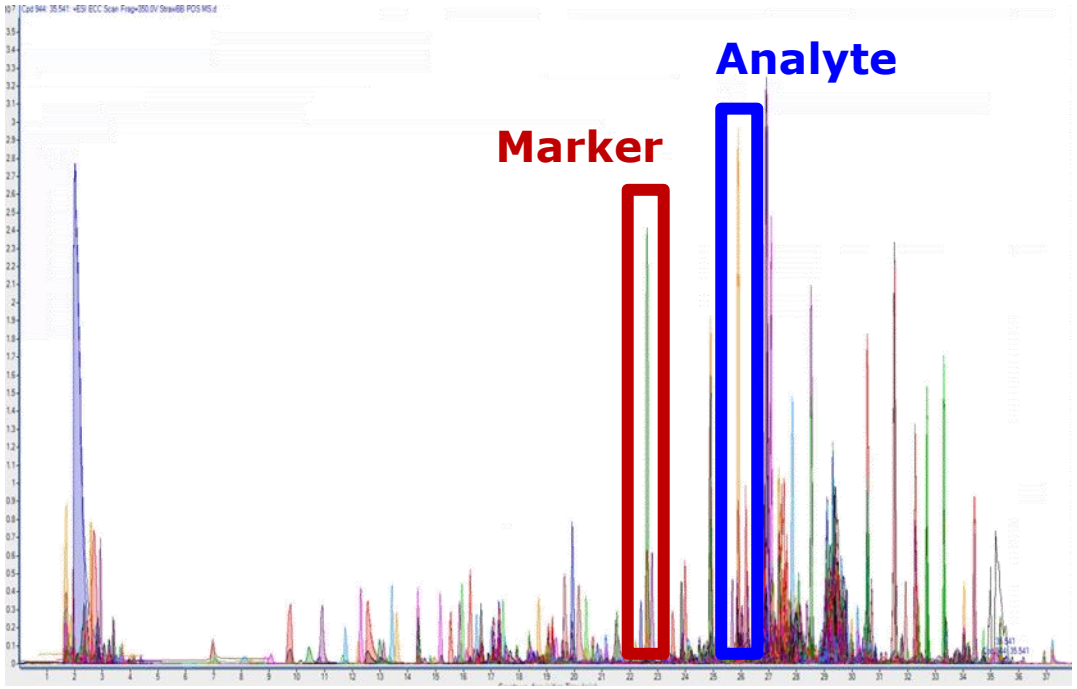




How **much** is there?

Obtaining non-target semi-quantitative data

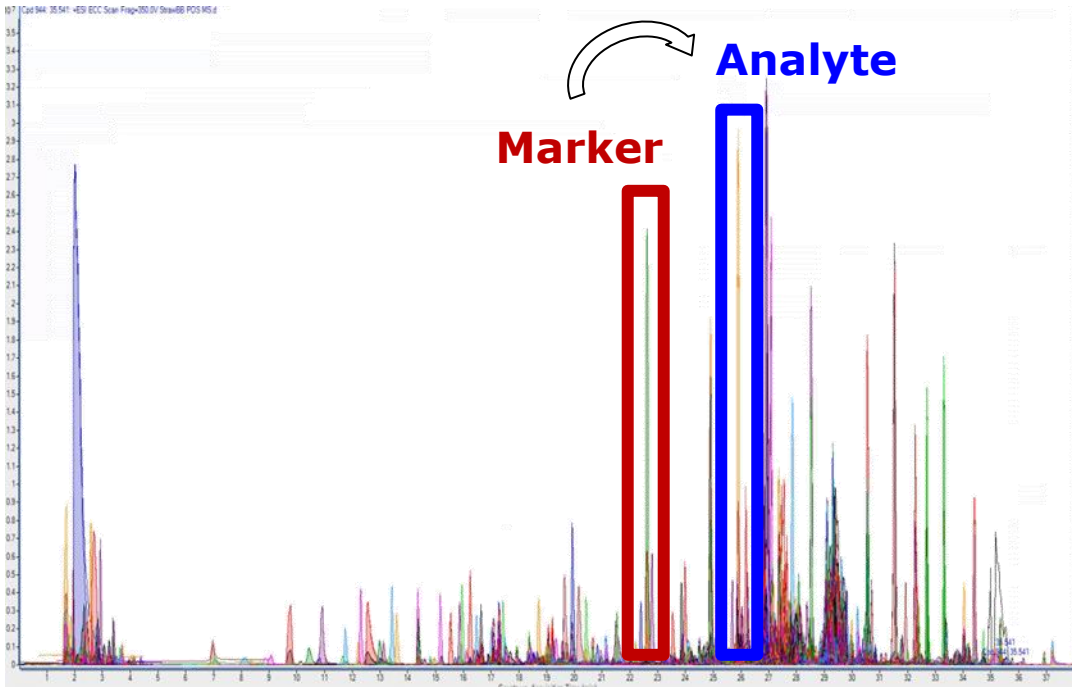
Untargeted quantification



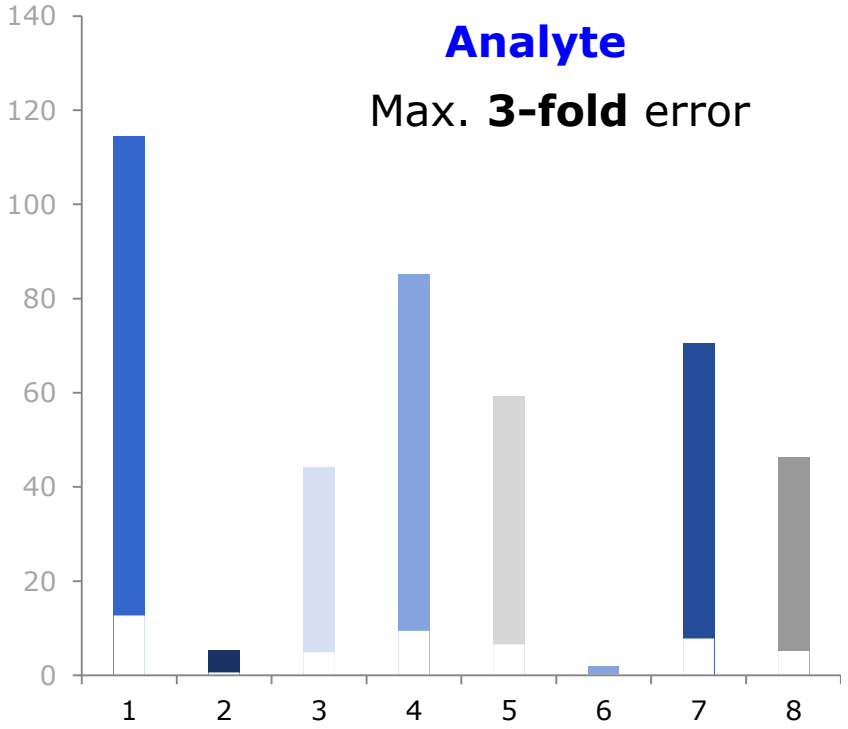
Pieke, E.N. et al., 2017. Analytica Chimica Acta, 975, pp.30–41. http://dx.doi.org/10.1016/j.aca.2017.03.054

Obtaining non-target semi-quantitative data

Untargeted quantification



Semi-quantify



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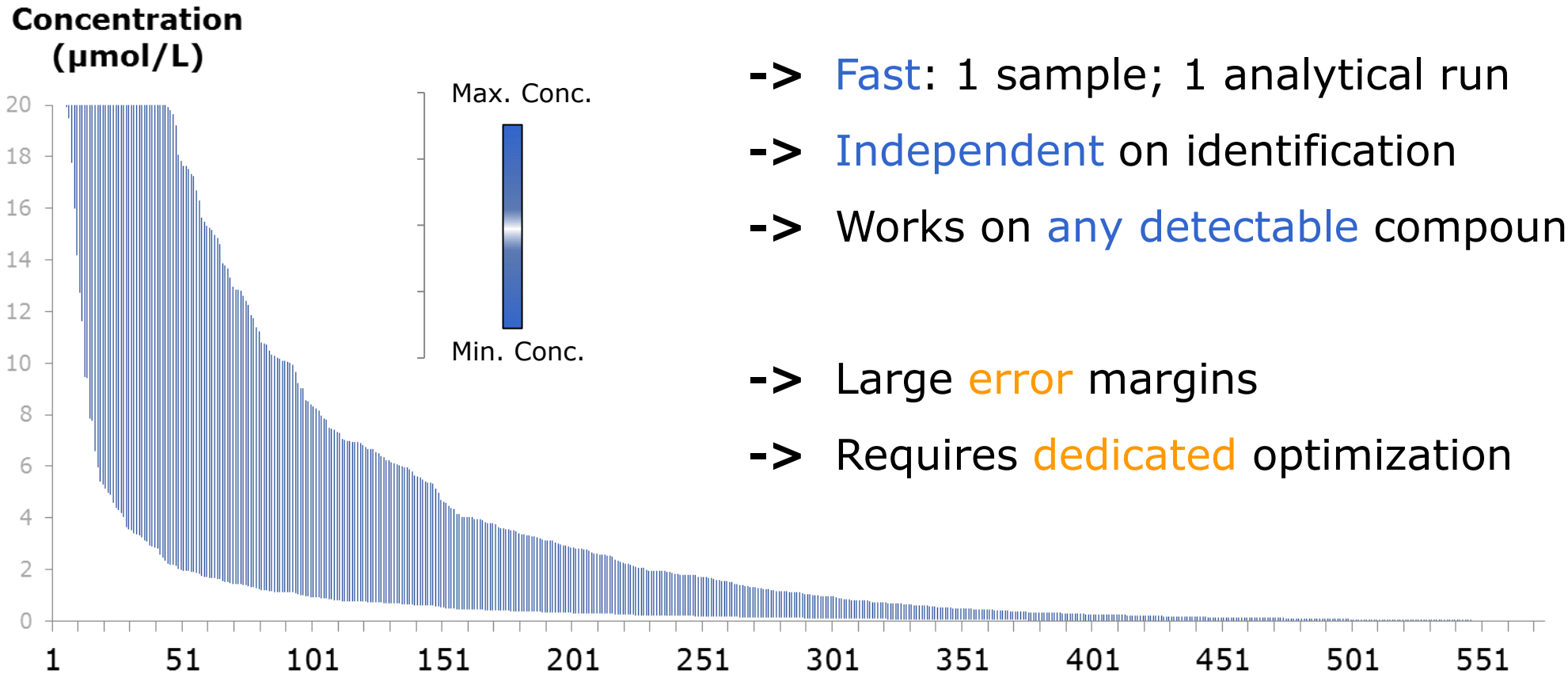
Obtaining non-target semi-quantitative data



-> Fast: 1 sample; 1 analytical run

-> Independent on identification

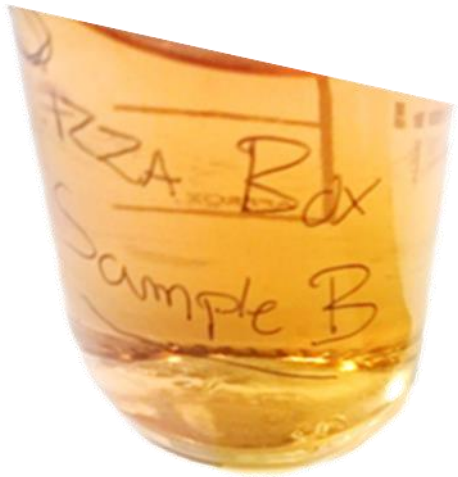
-> Works on any detectable compound

-> Large error margins

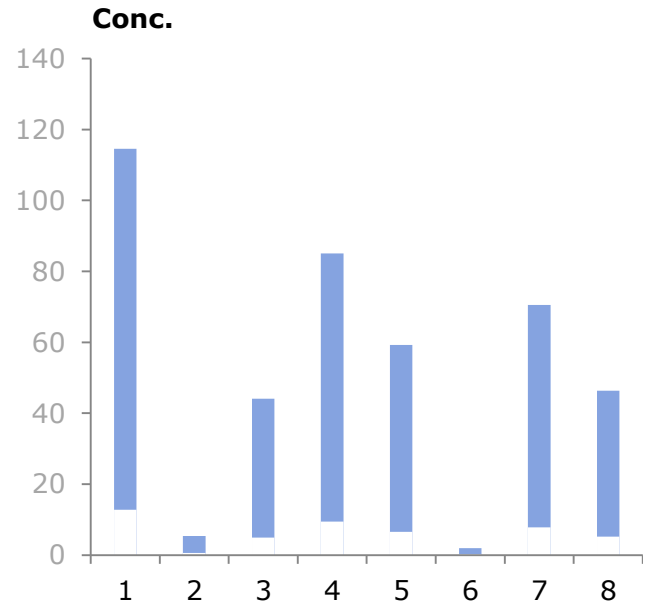
-> Requires dedicated optimization

Pieke, E.N. et al., 2017. Analytica Chimica Acta, 975, pp.30–41. http://dx.doi.org/10.1016/j.aca.2017.03.054

Exploring the world of chemicals



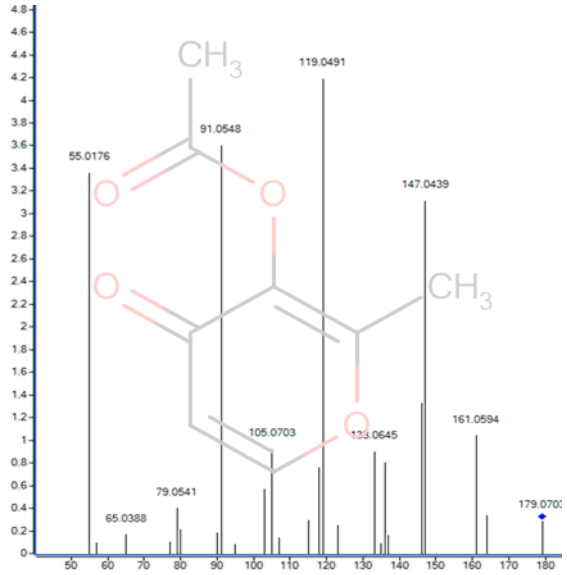
Semi-quantitative data

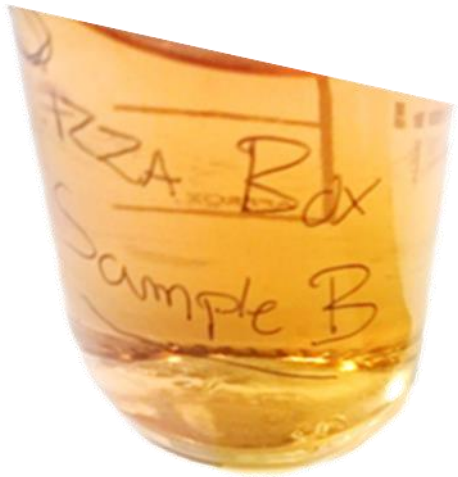


How **much** is there?

Exploring the world of chemicals

Chemical structure data





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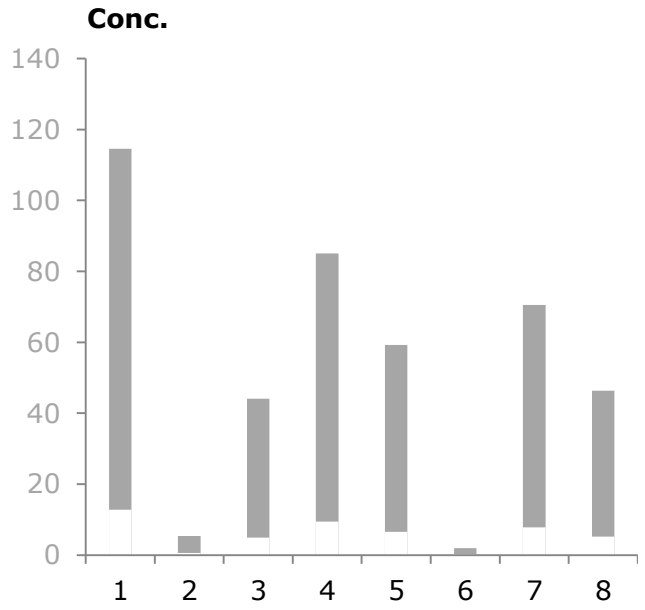
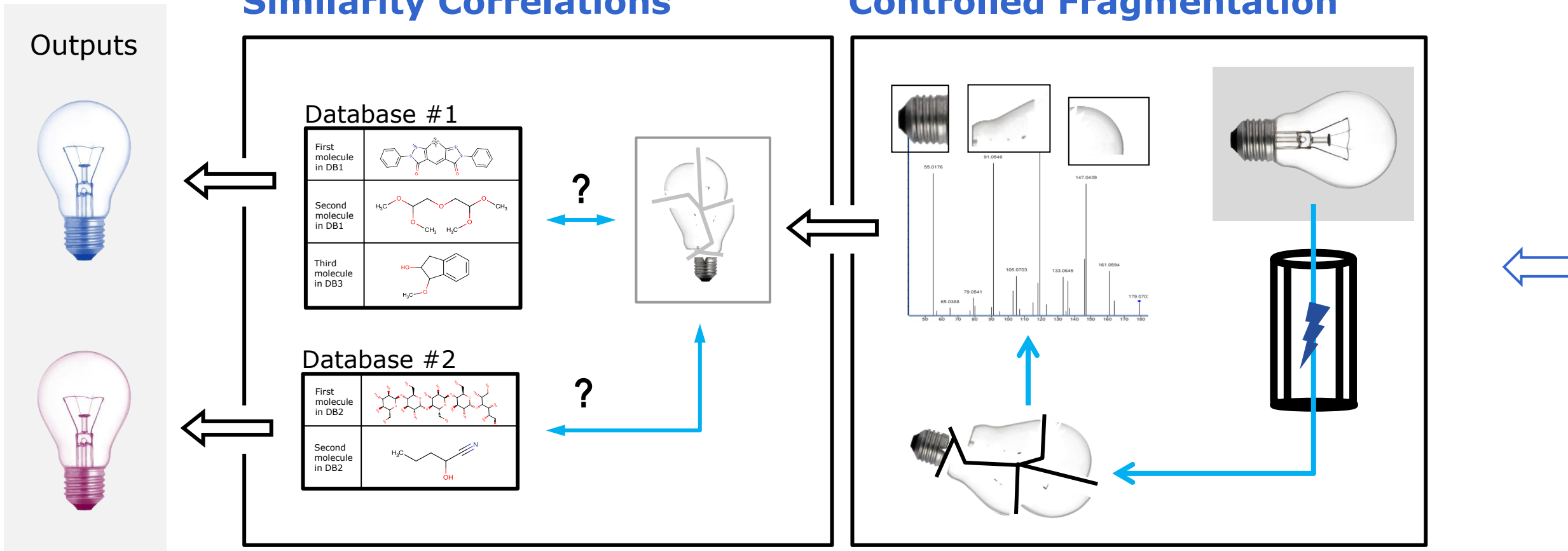


What is there?

How **much** is there?

Ambiguous structural identifications

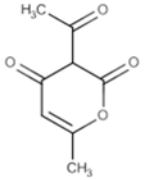
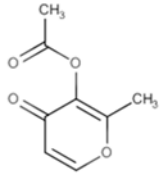
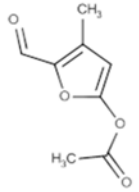
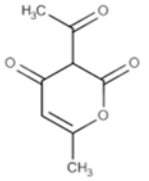


Pieke, E.N., Smedsgaard, J. & Granby, K., 2017. Journal of Mass Spectrometry. http://dx.doi.org/10.1002/jms.4052

Using multiple database correlations

- Reports the best-matching structure from a database
- Database are easy to generate
- Independent from reference standards

- Predictions are limited to database scope
- Predictions are *in silico*, hence error prone

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

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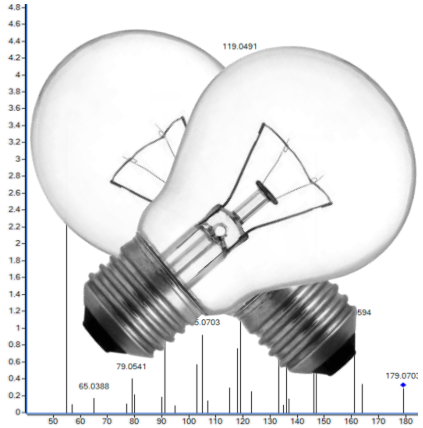
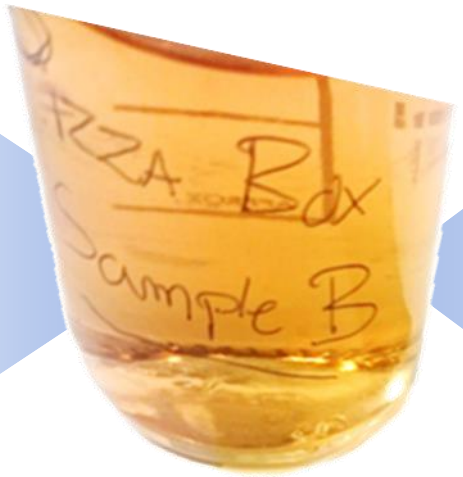
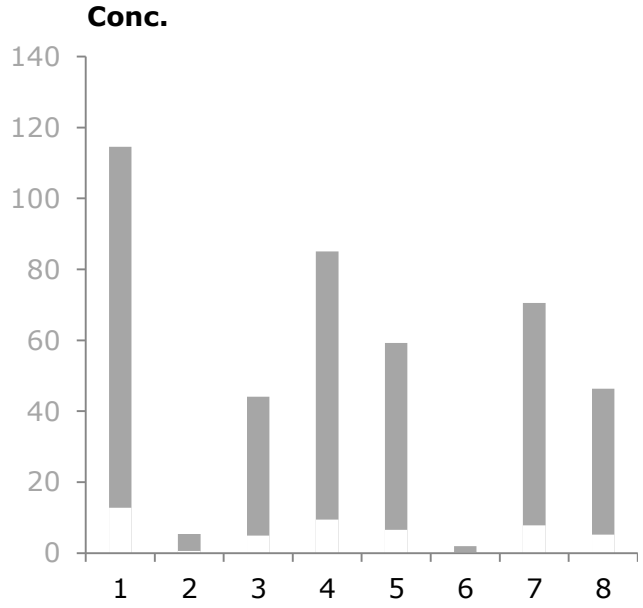
Exploration as an investigative tool

Suggested structures





Semi-quantitative data



What is there?

How **much** is there?

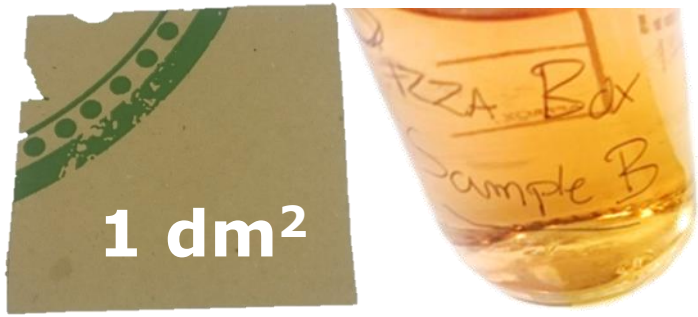
Converting semi-quantification to exposure

Worst case

(used by the European Food Safety Authority)

Example case

(used in our research studies)



Estimating the intake

Assume:

=

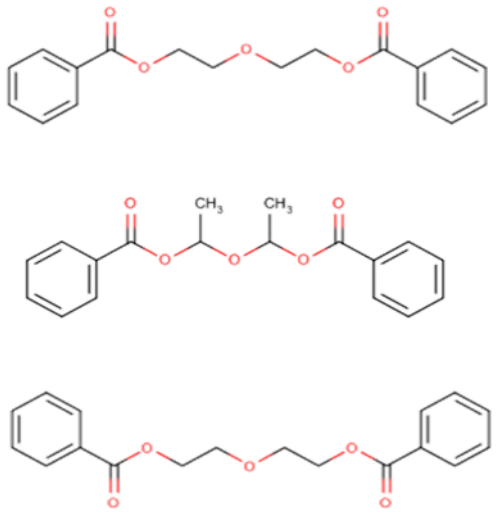
Total migratable content
for 1 dm^2 of contact

$$[C]_{total} = \sum_{i=1}^{n} [C]_i$$

$$\textbf{intake} = f([C]_{total})$$

- Gives an **estimated daily intake** per person per day (µg/person/day)

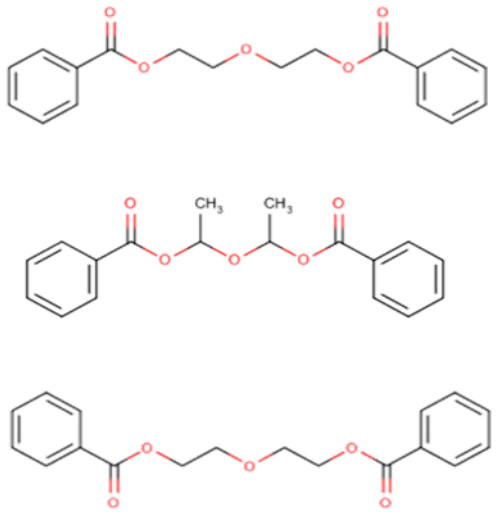
Converting structure to hazard



1. Tentative identification gives multiple structure suggestions per discovered chemical
2. Significant probability that toxicological information does not exist for most tentative identifications

Using QSAR for predicting effects

Computer-based toxicity predictions



Model evaluation

- Carcinogenicity
- Cramer Classification
- ???
- Mutagenicity
- Developmental Toxicity

Evaluating risk based on approximated data

- We may not be able to calculate the true **risk** from approximated data, but …
- We can still get a nonconclusive **perception of risk** useful for risk priority

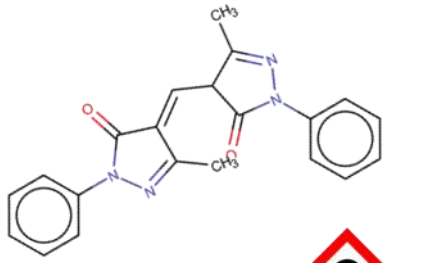
The classification of chemical substances

Chemical structures

Predicted hazards

Estimated exposure

Rule-based decisions



Human expertise decisions

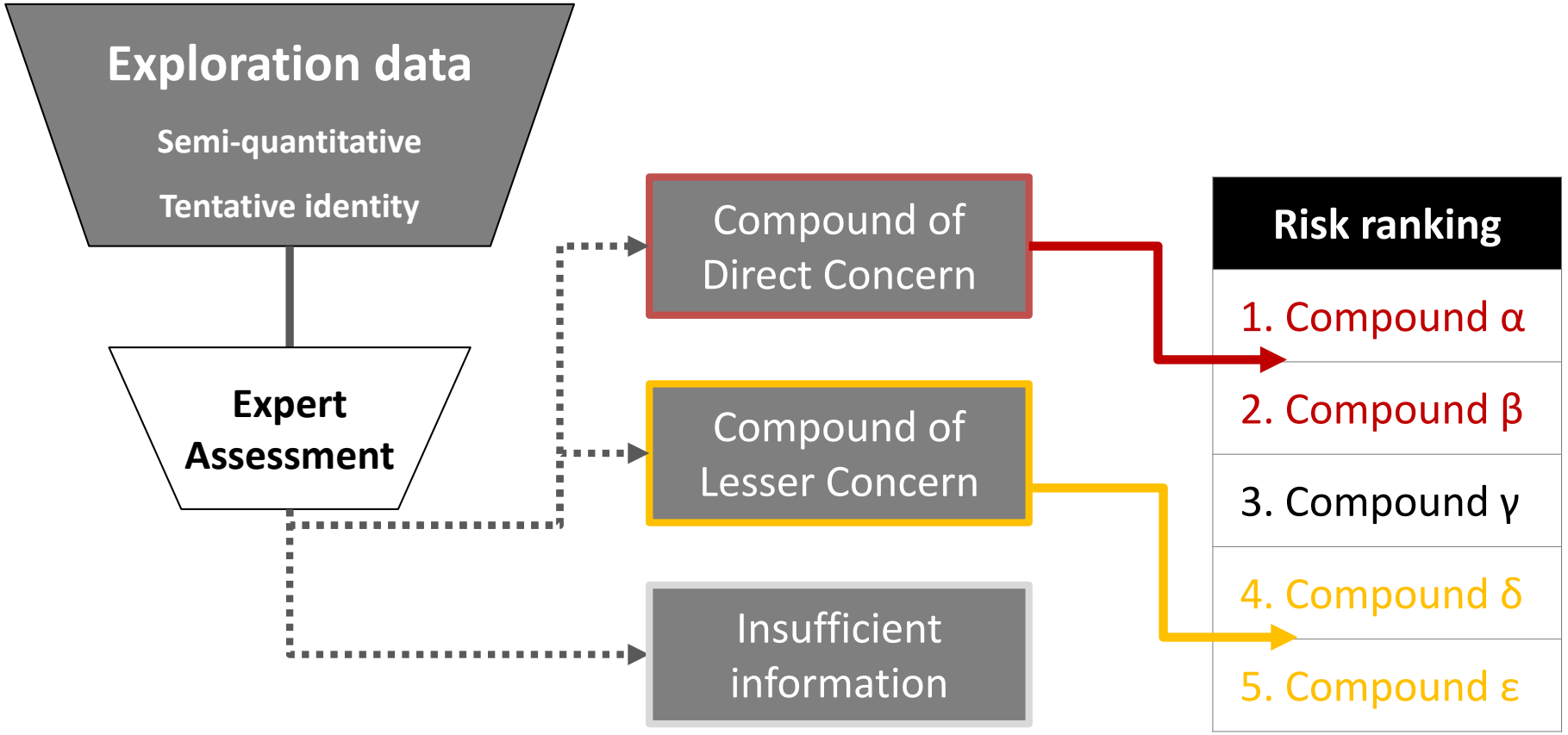
"Are exposure thresholds exceeded?"

Classification

"Is the presence of this compound acceptable?"

Pieke, E.N., Granby, K., Teste, B., Smedsgaard, J. & Rivière, G., 2018. Article in preparation.

The big picture of risk prioritization



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What Exploration & Prioritization IS NOT

- It **is not** a replacement for or a way to avoid Risk Assessment
- It **is not** a complete representative image of chemicals in food
- It **is not** intended to replace hazard / exposure assessment or migration testing

- **It is not a definitive answer to an increasingly difficult question**

  … but is a step in the direction of comprehending this problem

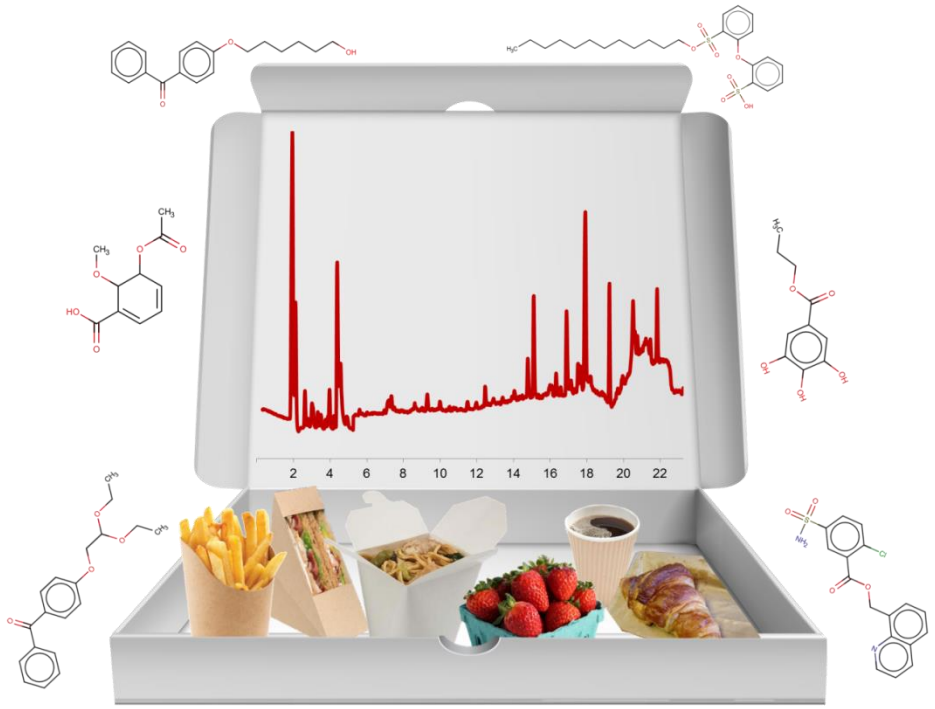
What Exploration & Prioritization IS

- It **is** a way to provide early-stage knowledge on undiscovered chemicals
- It **is** capable to obtain preliminary assessments for possible hazards and exposures
- It **is** a way to identify possible risk from poorly-studied or unexpected chemicals

- **It is a strategy to assist in knowledge-building and aiding Risk Assessment by providing a way to prioritize chemical compounds**

Back at the intersection of choice

Thank you for your attention



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Thanks to:

DTU Food
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- Kit Granby
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anses
French agency for food, environmental and occupational health safety

- Gilles Riviere
- Bruno Teste

GDSI
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- Elena Boriani