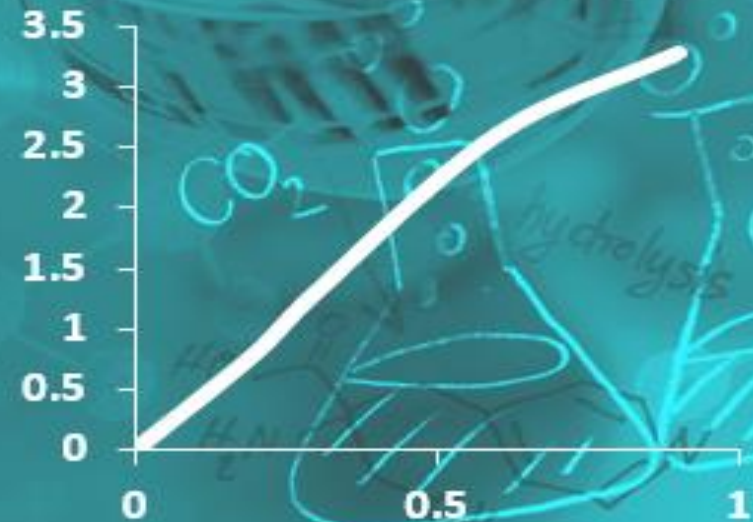
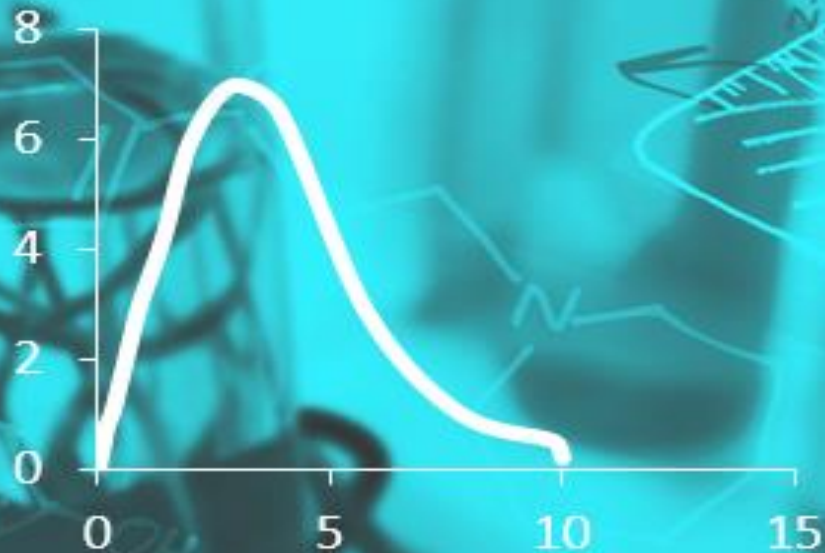


# WORKSHOP on Quantitative Response – Response Relationships (qAOPs)

## BREAK-OUT GROUP 3

19<sup>th</sup> October 2022



# General thoughts

- **Context dependency is key to all questions set!**
    - Context: quantitative risk assessment...
  - **Hence problem formulation should be the starting point**
    - But if end-users (regulators\*) do not know why they need qAOPs then how do to do that?
  - ...
  - ...
- \* Note: risk assessors in industry are also end-users!

## Q3

How do we ensure the quality assurance and accessibility of qAOP models and their predictions?

What would be the quality assurance criteria for the underlying data?

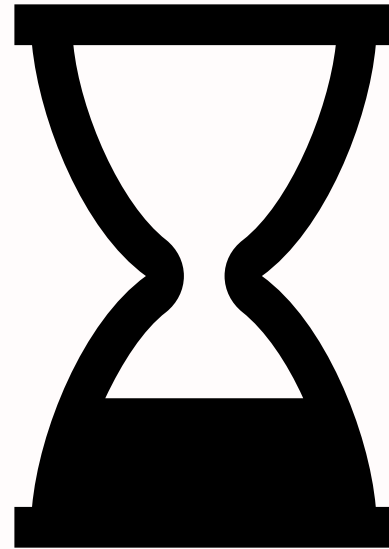
- **Context dependent, problem definition first!**
- Define QA criteria first (minimal criteria)
  - Model overview, problem definition, application area, parameters, documentation
  - Separate: model – parameters – data
  - and check match to problem definition, incl. **causality linking!**
  - Model AOP or one or more KERs?
  - How much lower level detail is needed? → Context/question dependent.
  - Calibration, validation
- **Existing QSAR, PBPK & EFSA ecological modelling guidance as starting points**

## Q3

How do we ensure the quality assurance and accessibility of qAOP models and their predictions?

Which open standards support qAOP development? Are there any gaps?

- ...

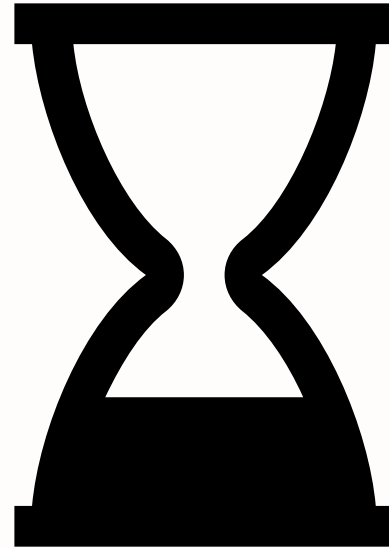


## Q3

How do we ensure the quality assurance and accessibility of qAOP models and their predictions?

How do we ensure the FAIRification of qAOP models and underlying data?

- ...



## Q1

How would you choose the most appropriate level of biological detail to include in your qAOP?

What data should we get and how to organise it? **Data requirements?**

- Relevance
- Quantitative
- Cover key events
- Structural identifiability analysis
- Reproducibility
  
- Reporting requirements, standard protocols, ... reliability scoring (Klimisch criteria?)
  
- Comparability? How much of the AOP in one experiment? Adjacent KERs?

..

# Q1

How would you choose the most appropriate level of biological detail to include in your qAOP?

## What data should we get and how to organise it? **Data organisation?**

- Follow data reporting guidelines, standardised
  - Bottom up may not work, patterns more important, we are looking for particular types of information (not just everything)
- Role of canonical information?
- **Organising data around certain organs or pathways?**
- **Quantitative threshold effects + need to collect below that level?**
- Is not all this data available?

..

## Q1

How would you choose the most appropriate level of biological detail to include in your qAOP?

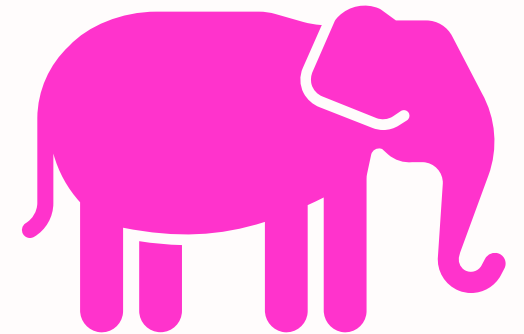
How do you judge **how complete** (in term of the number of key events required to describe the toxicological response) a qAOP needs to be?

Or

What is most appropriate **level of detail** for qAOP?

- Depends on current understanding & data
- Depends on question / problem definition
- Need **temporal** data
- Cell, organ, organism specific, is level of KE important?
- **Equivalency** between cell types and species? If yes, **modular** modelling approach!

- *Parsimony principle, start simple*





## Q1

How would you choose the most appropriate level of biological detail to include in your qAOP?

How do you judge the level of complexity (in terms of detailed biochemical/physiological/biological mechanisms and feedbacks) that is required?

- [See previous slide...](#)

## Q2

How and why would you choose the most appropriate modelling approach?

What are the pros and cons of different modelling approaches?

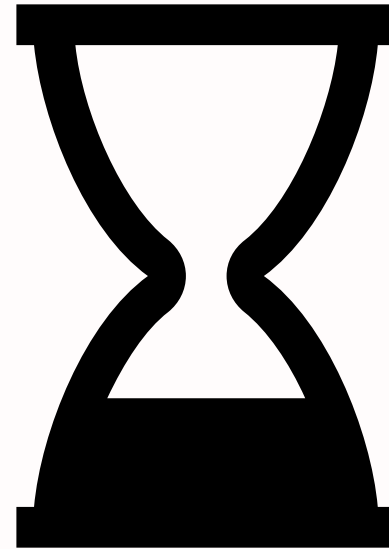
- **Not just one approach, use complementary approaches**
- **More important to characterise the KER**, e.g. Linear, non-linear, feedbacks yes/no, thresholds, temporal scale, ...
- Model education may be important
- (Some) qsar modellers use a battery of models
- **Modelling approach is not so important, building trust and confidence is more important** → How do you know the model is good enough?
- 3 groups: modellers, regulators, risk assessors
- Training in model approaches & uses is critical
- Role of (research) funders, incl. regulators?

## Q2

How and why would you choose the most appropriate modelling approach?

What are the methods for extrapolating from short-term to longer term exposures?

- ...

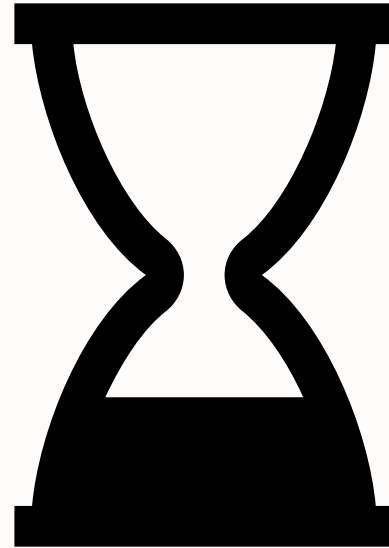


## Q2

How and why would you choose the most appropriate modelling approach?

How faithful should the model structure be to the qualitative AOP?

- ...



# Q3

- How do we ensure the quality assurance and accessibility of qAOP models and their predictions?
- What would be the quality assurance criteria for the underlying data?
- Which open standards support qAOP development? Are there any gaps?
- How do we ensure the FAIRification of qAOP models and underlying data?

