

# Source To Outcome Pathway (STOP) – Next Generation Risk Assessment (NGRA) put into practice

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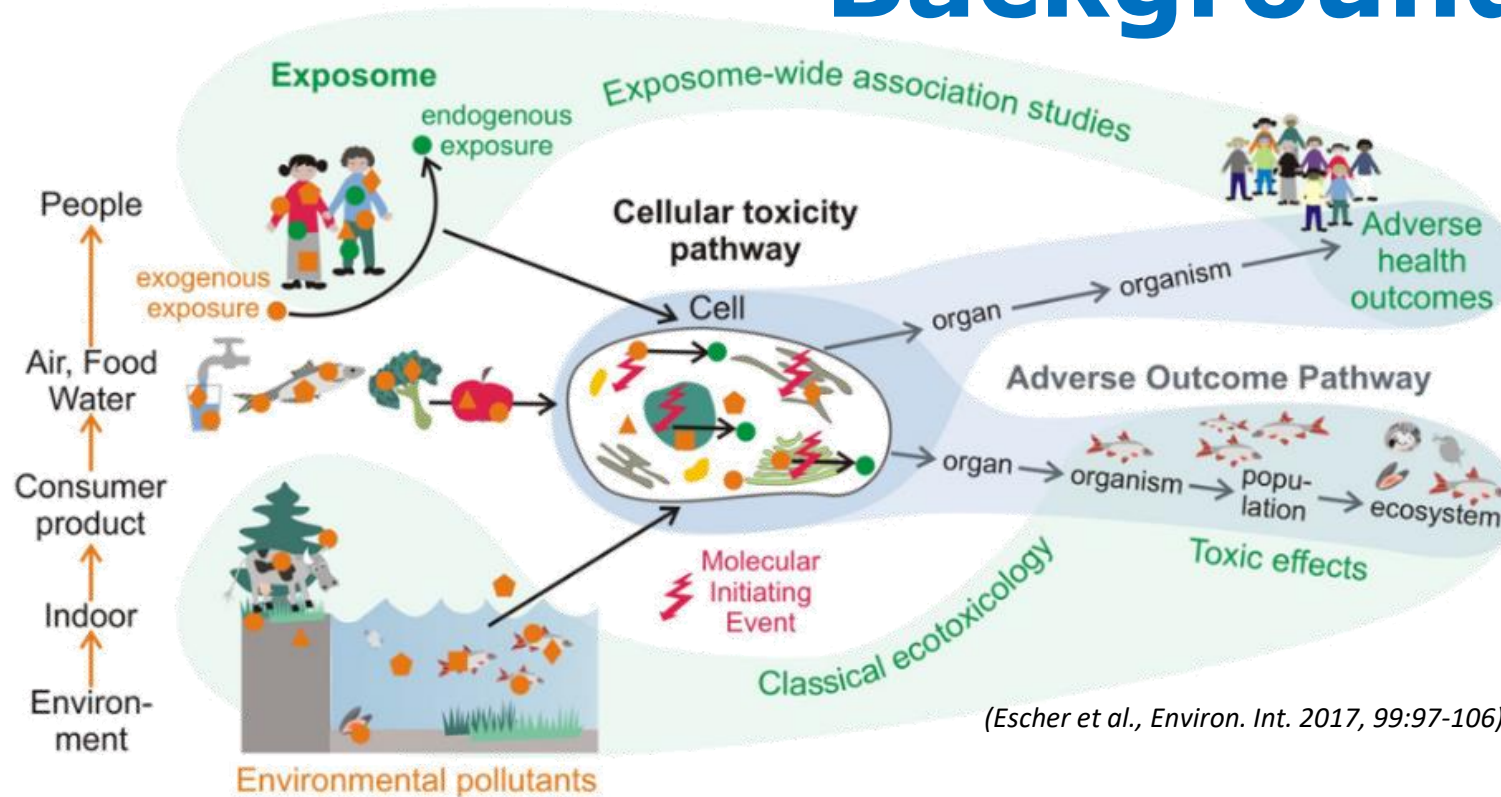
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10<sup>th</sup> Norwegian Environmental Toxicology  
Symposium (NETS)  
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# Background



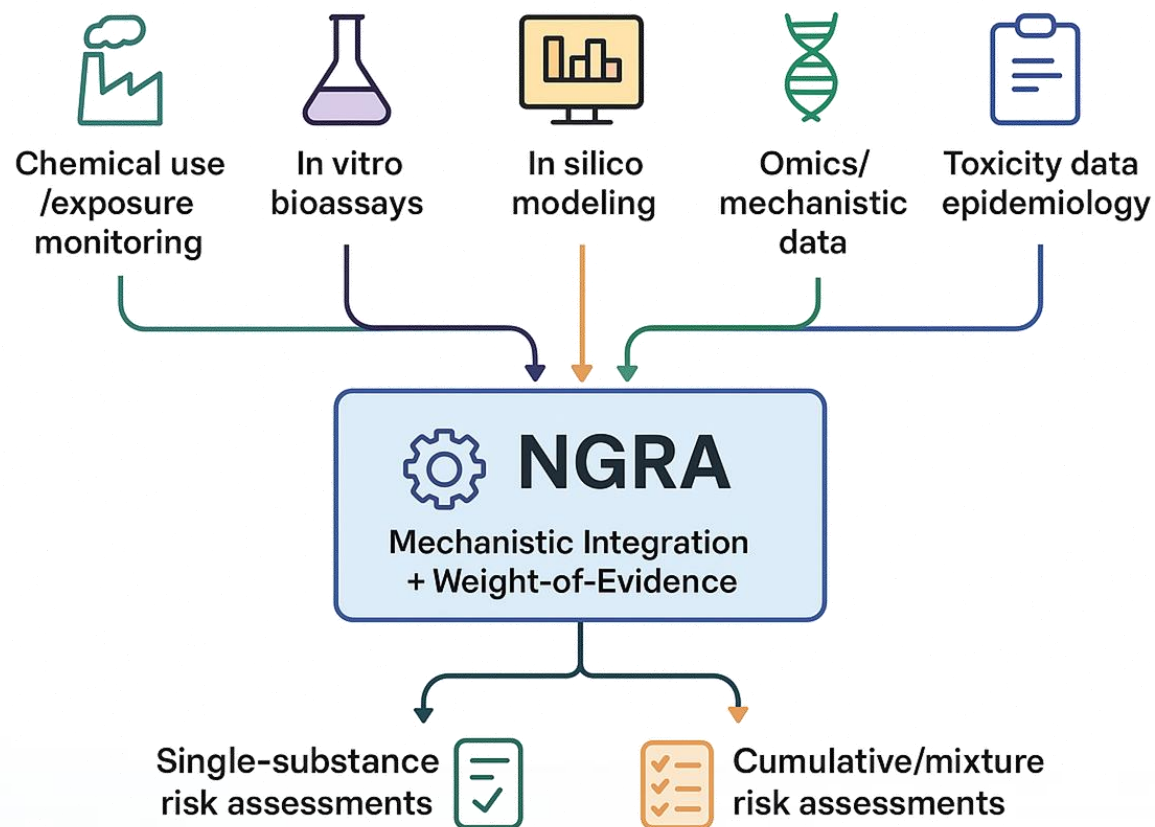
- **High # chemicals**
- **Multiple sources**
- **Multiple exposure pathways**
- **Multiple exposure routes**
- **High # target species**
- **Multiple Modes of Action**
- **Multiple stressors (mixtures)**

(Escher et al., Environ. Int. 2017, 99:97-106)

## Traditional Risk Assessment

- One chemical – lack of real-life complexity
- No or little mechanistic insight – not exploiting available data
- Limit applicability to other areas of relevance

# Next Generation Risk Assessment (NGRA)

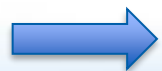


**OECD:** structured, hypothesis-driven, and iterative approach to chemical safety evaluation that **integrates New Approach Methodologies** (NAMs), such as **in vitro assays**, **high-throughput screening**, and **computational modeling**, to assess potential risks without reliance on animal testing.

**ECHA: Exposure-led, integrative** framework that moves beyond traditional hazard-based assessments to incorporate **mechanistic data**, **probabilistic modeling**, and real-world exposure considerations.

**WHO:** An adaptive and evolving framework that incorporates novel scientific methods to better understand chemical risks in complex environmental and biological systems. It emphasizes the use of **alternative test methods**, **exposure science**, and **data integration** to inform public health decision-making.

**US EPA: data-driven** framework that leverages **computational toxicology**, **machine learning**, and **mechanistic biological knowledge** to predict chemical hazards and exposure scenarios.

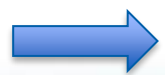
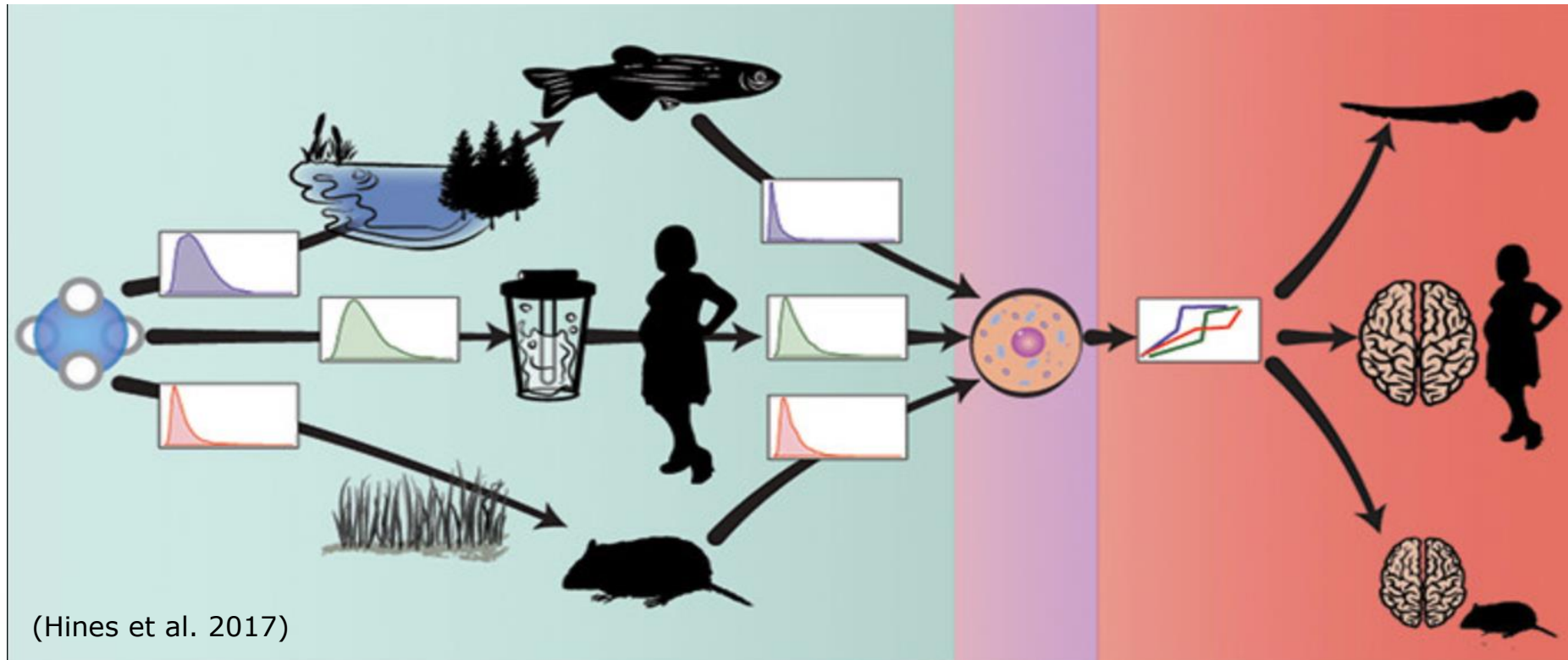


**shift towards a more predictive, mechanistic, and high-throughput risk assessment for (eco)relevant exposure scenarios**

# Source To Outcome Pathway (STOP)

Aggregate Exposure Pathway (AEP)

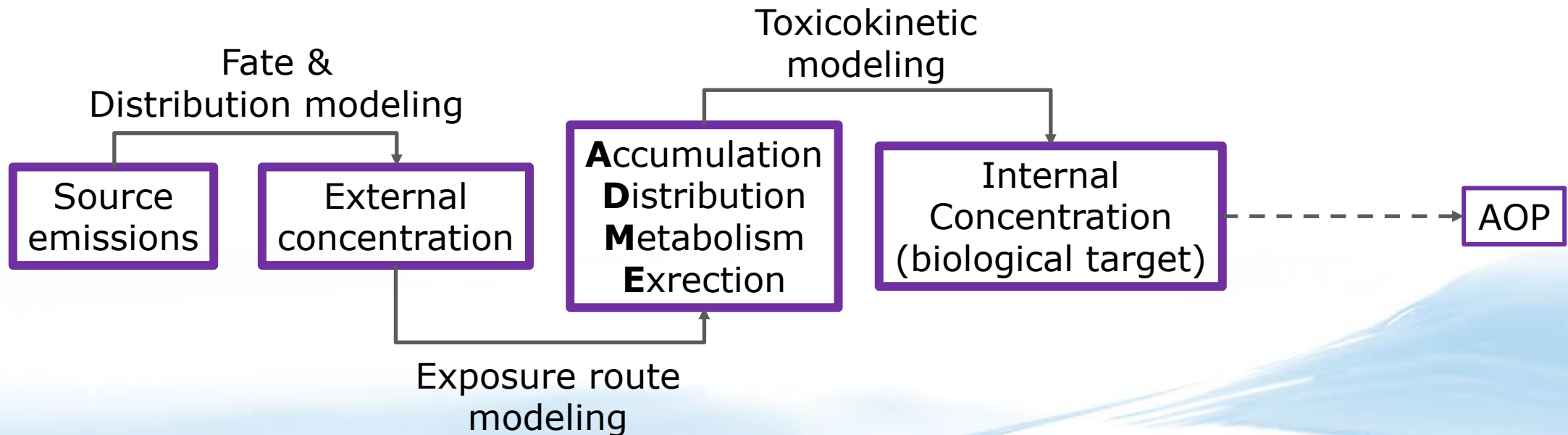
Adverse Outcome Pathway (AOP)



STOP combines **exposure-driven** (AEP) and **effect-driven** (AOP) frameworks into one integrated approach for mechanistic, holistic risk assessment.

# Aggregate Exposure Pathway (AEP)

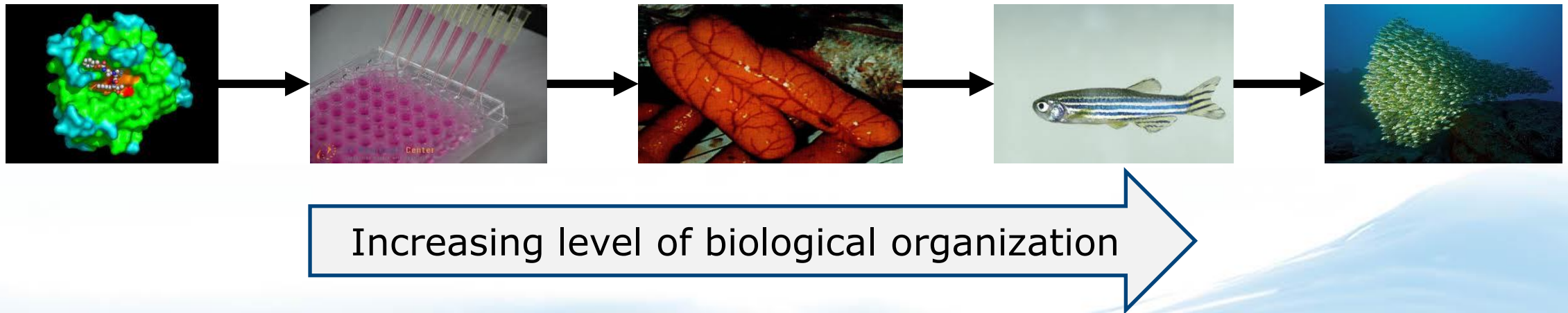
An **Aggregate Exposure Pathway (AEP)** is a conceptual framework that organizes and describes **the sequence of key exposure states and processes linking** an **external exposure** source to an **internal dose** at a biological target site relevant for risk assessment and regulatory decision-making.





# Adverse Outcome Pathway (AOP)

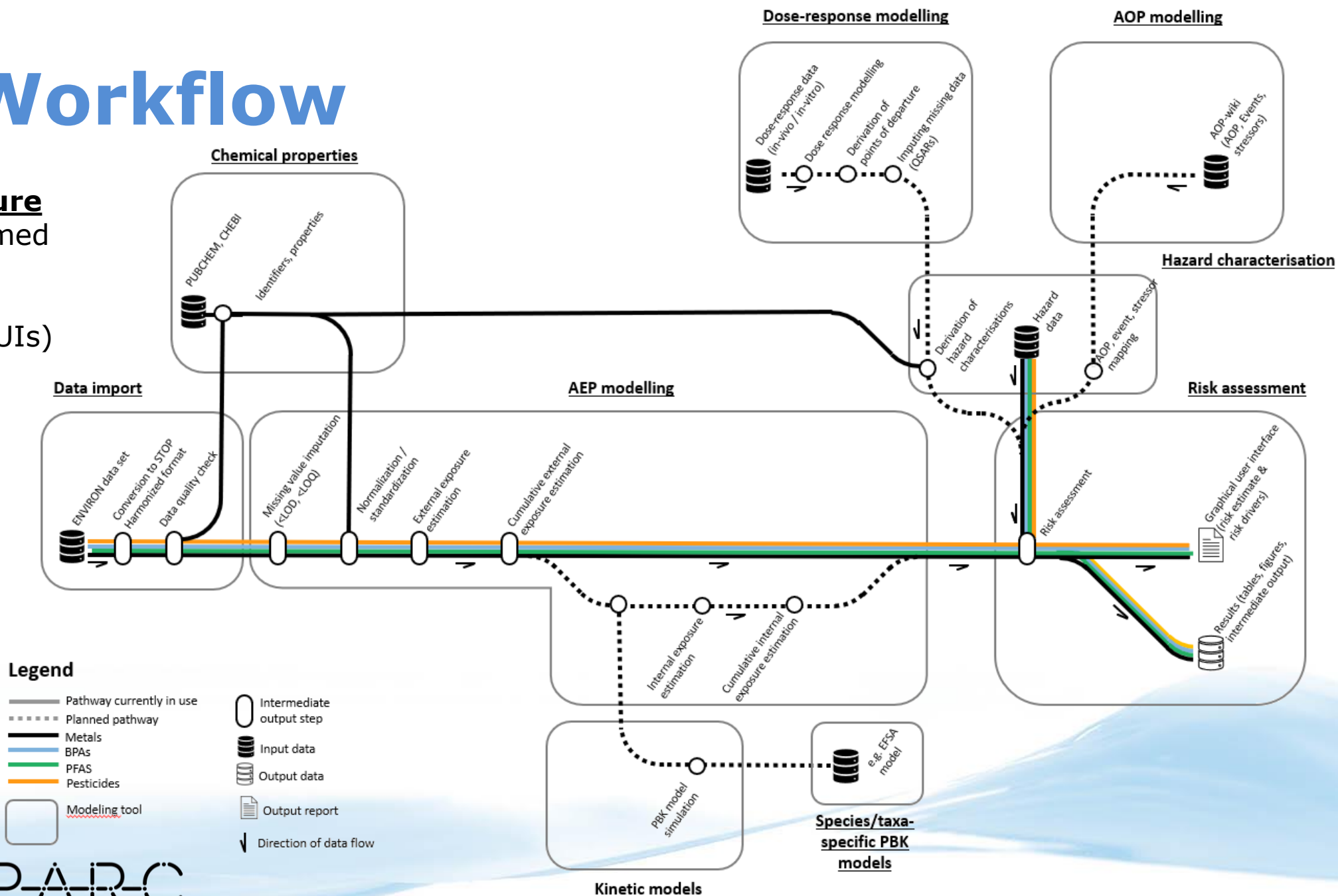
An Adverse Outcome Pathway (AOP) is a conceptual framework that **portrays existing knowledge** concerning the **linkage** between a direct **molecular initiating event** and an **adverse outcome**, at a level of biological organization relevant to **risk assessment**.



# STOP Workflow

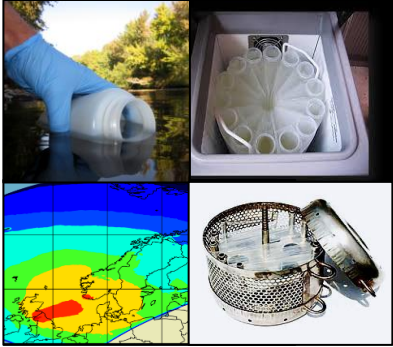
## Model infrastructure

- AEP & AOP-informed
- Module-based
- Databases
- User interfaces (UIs)
- Models

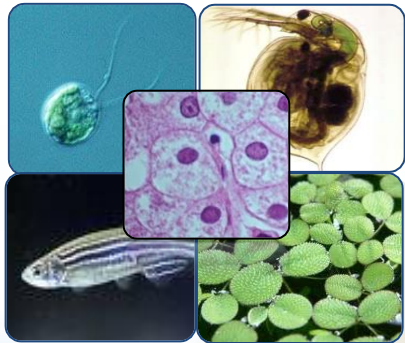


# Case study – Risk prediction

## Exposure



## Hazard



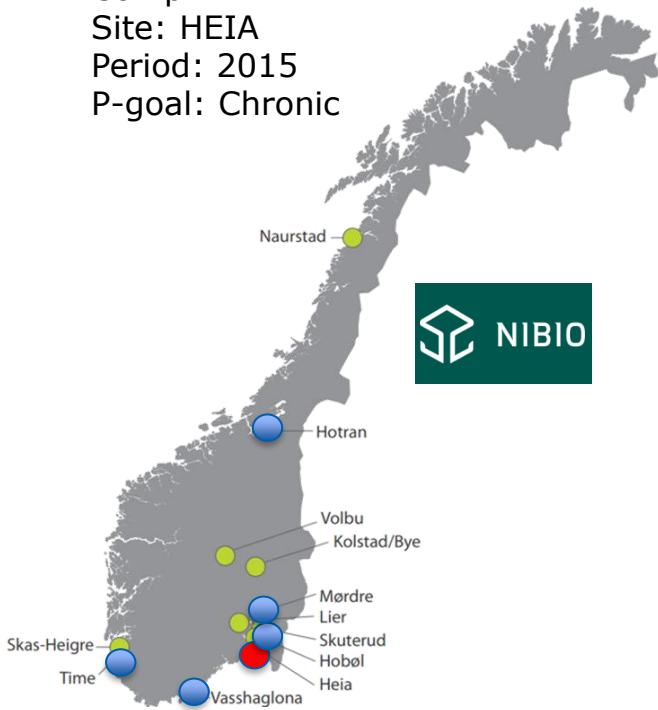
$$\text{Risk Quotient (RQ)} = \sum_{n=1}^n C_{\text{exposure}} / C_{\text{hazard}} \quad (\text{CA assumption})$$

Is there a risk to non-target organisms?

RQ > 1 (Risk)  
RQ < 1 (No risk)



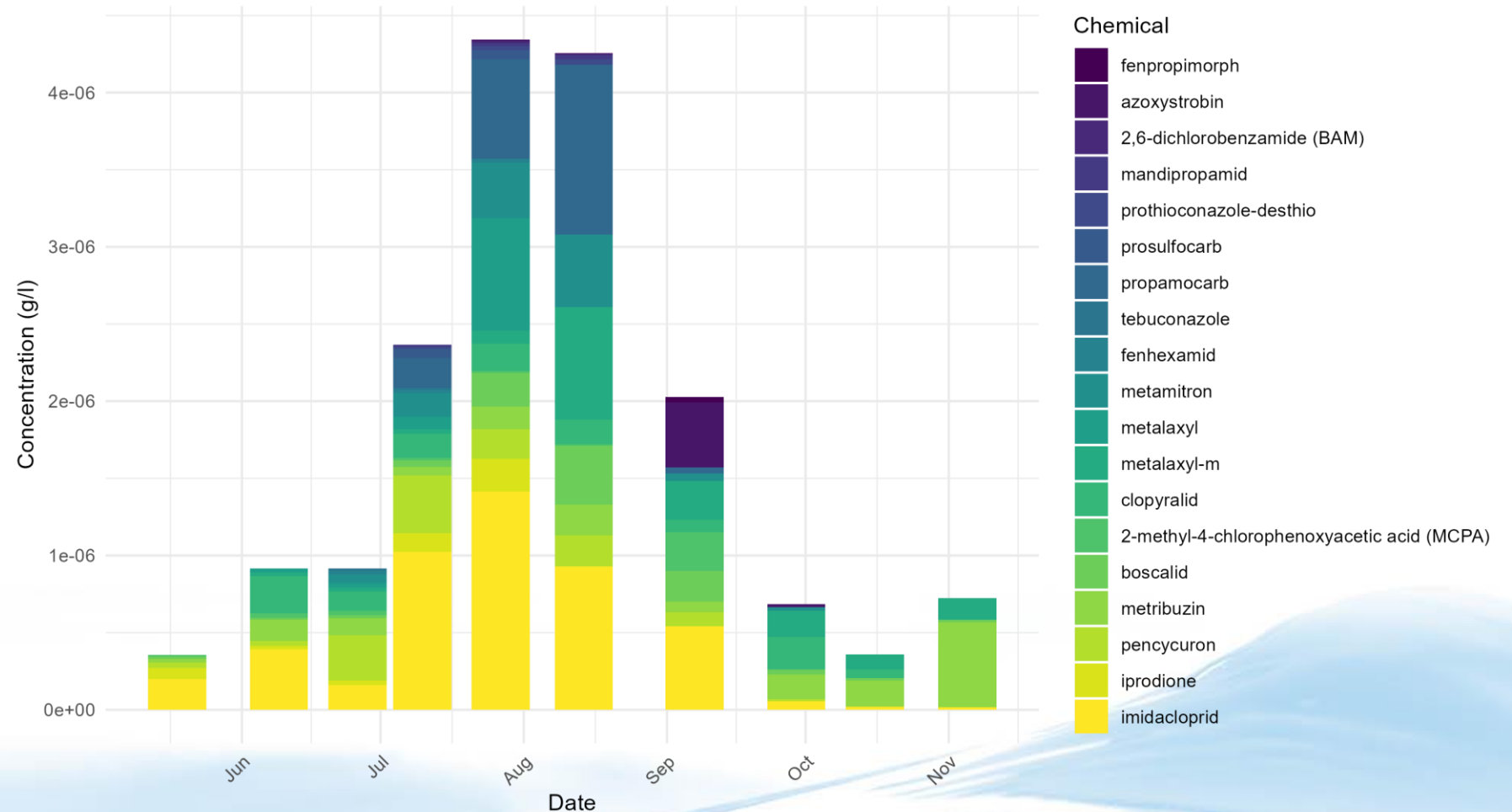
Comp: FW  
Site: HEIA  
Period: 2015  
P-goal: Chronic



# Pesticides - JOVA

## Exposure data

- Water concentrations
- >115 active substances
- Multiple sites
- >20 yrs of data



# Hazard data

## No-effect thresholds

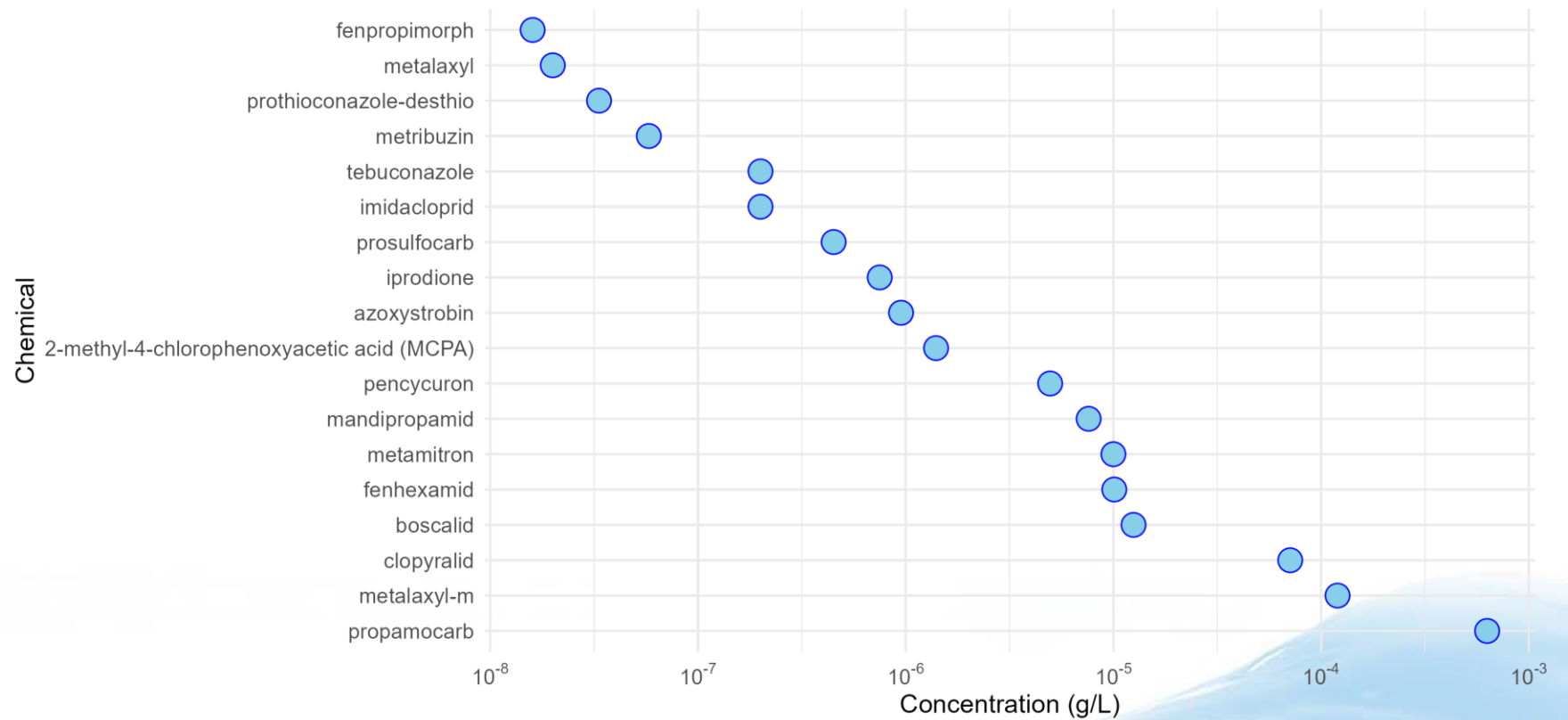
Acute (AMF) & Chronic (MF)

- Algae
- Crustaceans
- Plants
- Fish

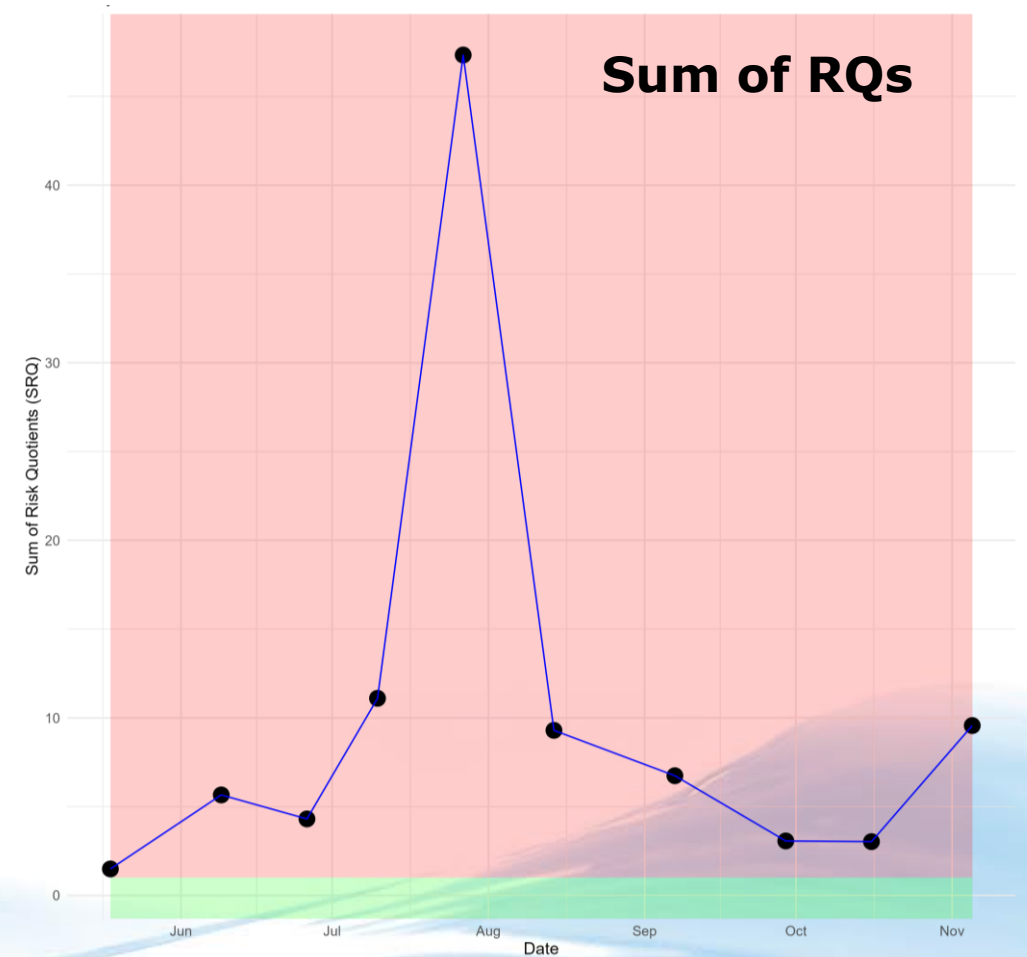
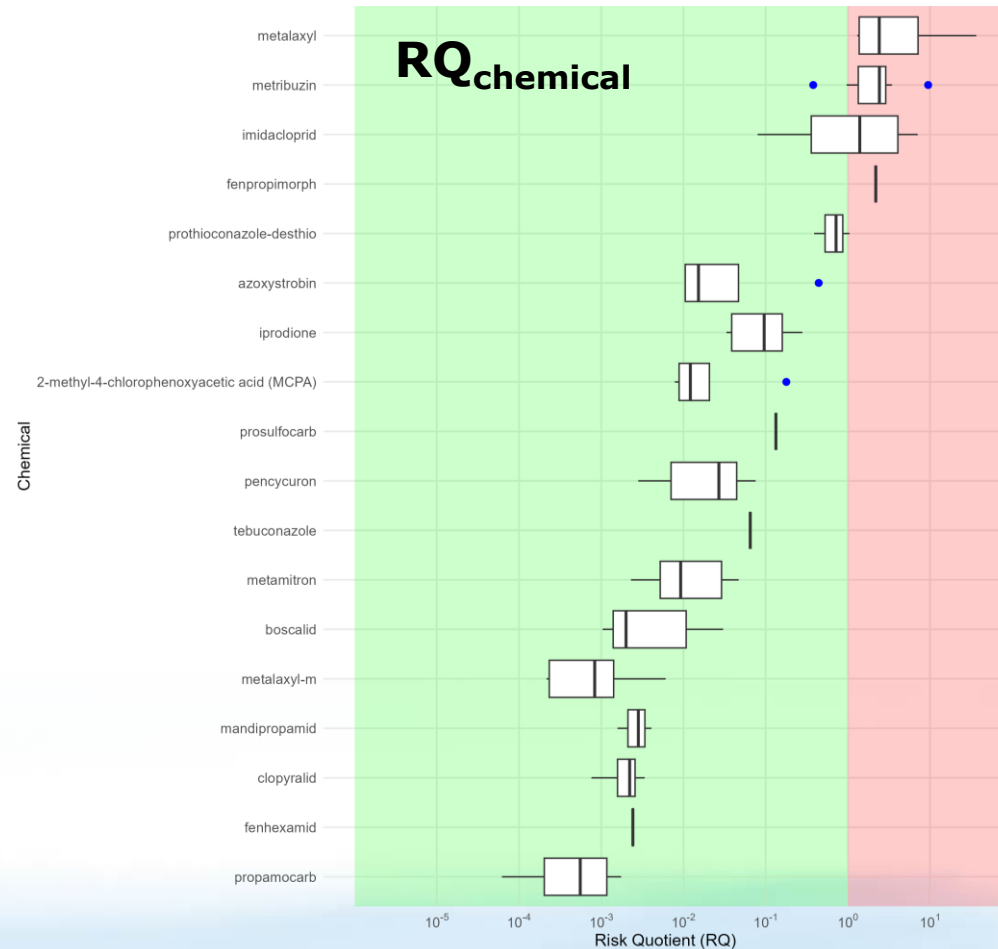


[Plantevernmidler - Nibio](#)

## Chronic No-effect threshold (MF)



# Risk prediction (Chronic)



# Species at risk

## No-effect thresholds

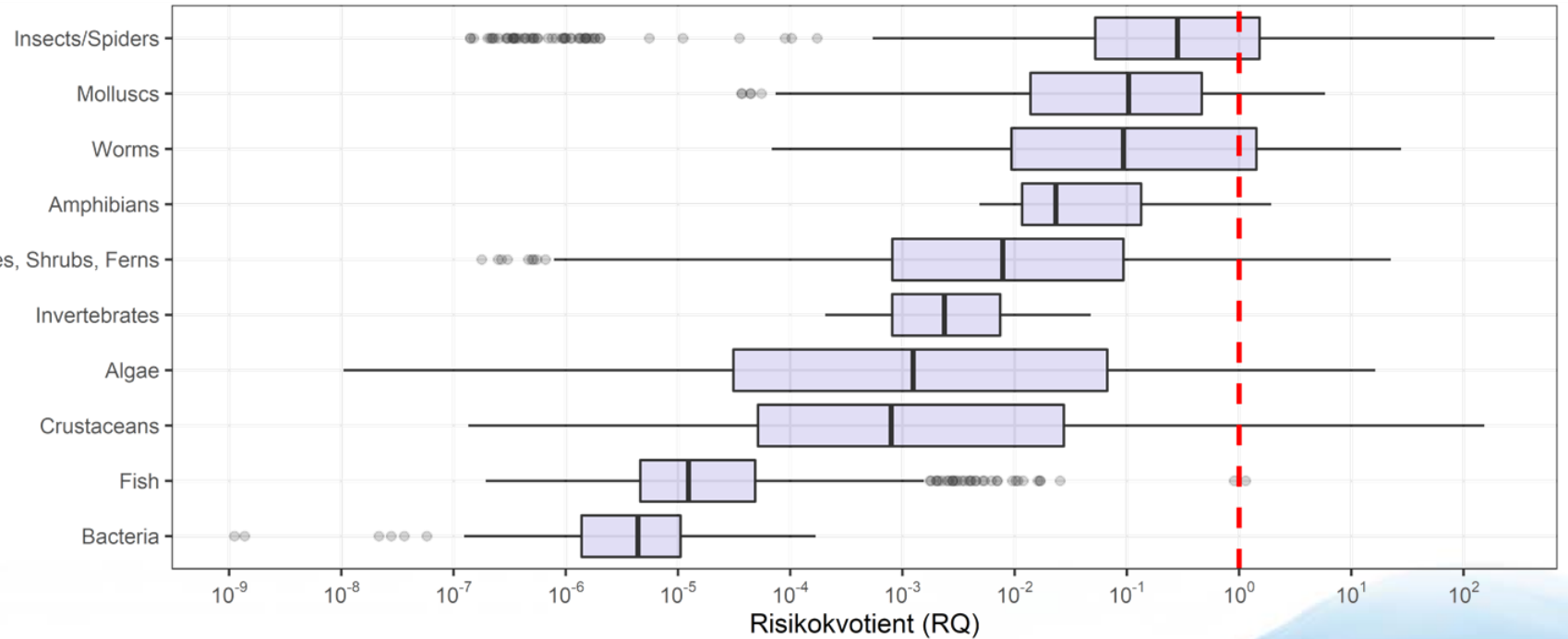
- ECOTOX (Chronic, NOEC)
- Multiple species groups



## **Most susceptible species**

Insects/spiders/crustaceans

Molluscs, worms



# Toxicity targets (arthropods)

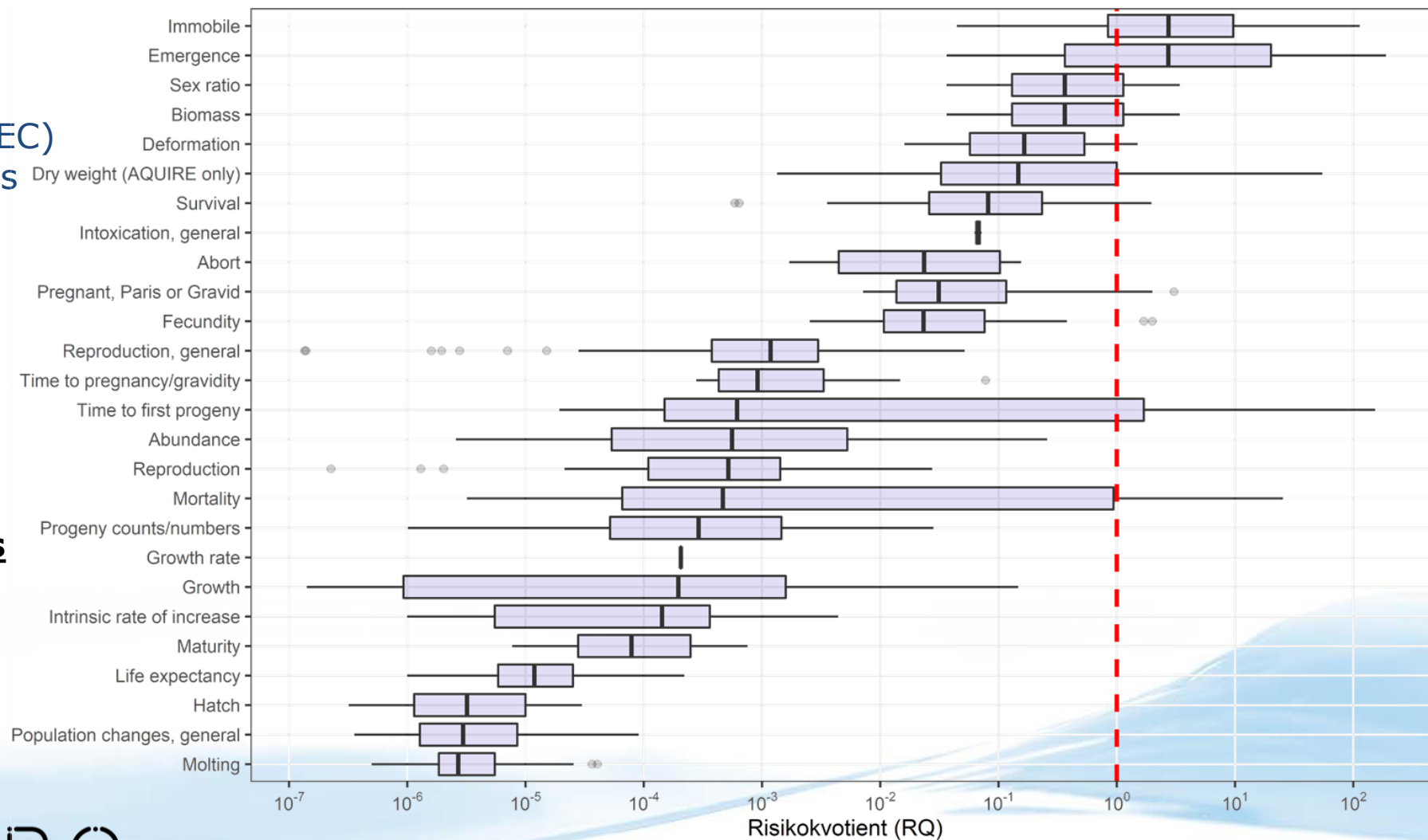
## No-effect thresholds

- ECOTOX (Chronic, NOEC)
- Multiple species groups



## **Most relevant targets**

Mortality/survival  
Development  
Growth





**Developing an Aggregate Exposure Pathway for Arctic Copper Pollution: Protocol and First Steps**

Sam A. Welsh<sup>1</sup>, Pierre Blavien<sup>2</sup>, Richard Handy<sup>3</sup> & Knut Erik Tollefsen<sup>1\*</sup>

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**P-09**

**eData: A format and toolset for FAIR monitoring data**

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**PH-04**

**PARC** **CLEMSON** **NIVA**

**Physiologically Based Pharmacokinetic (PBPK) model for Atlantic halibut (*Hippoglossus hippoglossus*)**

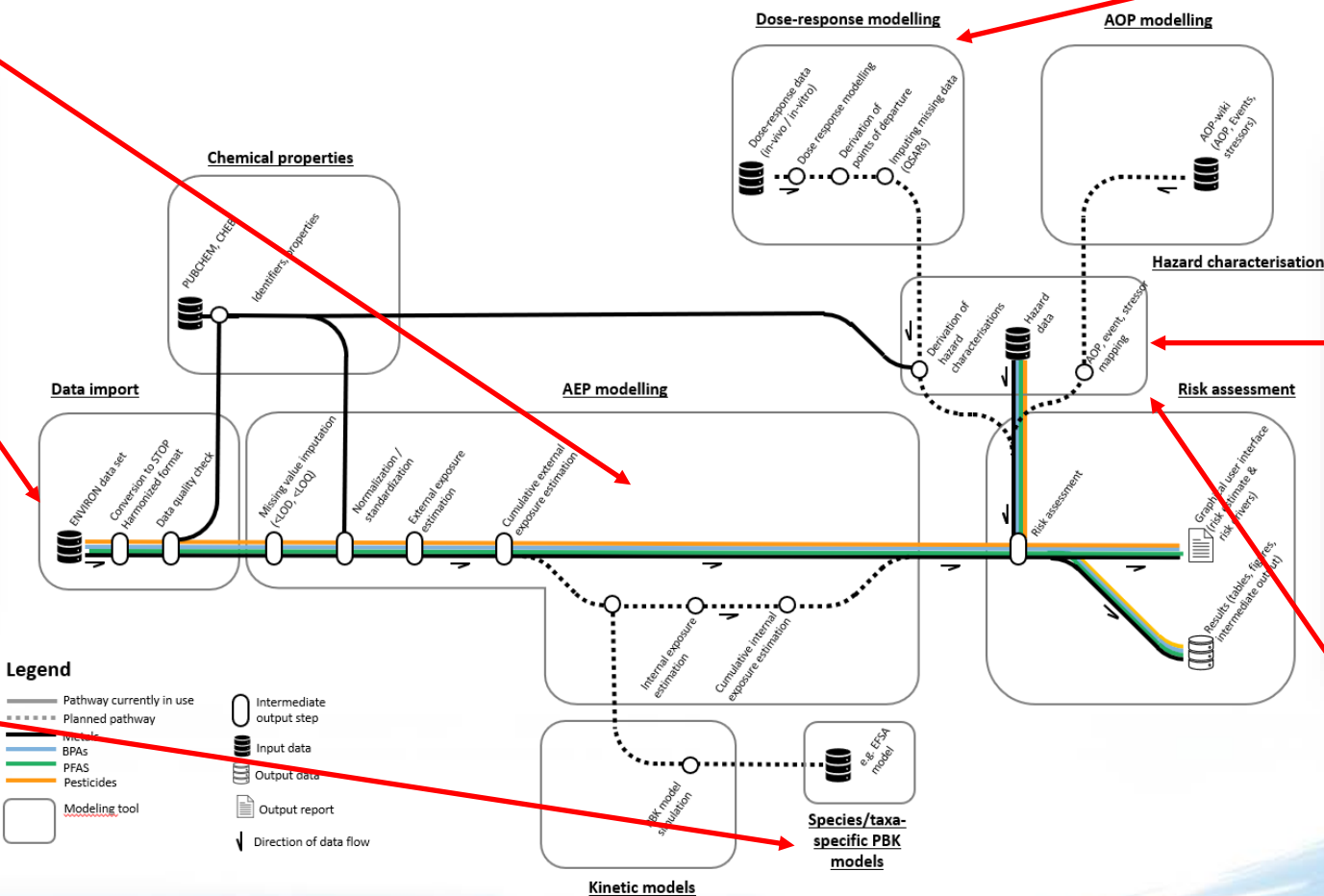
Hanne Gladhaug Wæien Mo<sup>1</sup>, Gregory Langlois<sup>1</sup>, Ian Edlund<sup>2</sup>, Peter van den Hurk<sup>3</sup>, Knut Erik Tollefsen<sup>1\*</sup>

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# New developments



**PARC** **NIVA**

**qData – a web-based FAIRification workflow for (eco)toxicological dose(concentration)-response data**

Knut Erik Tollefsen<sup>1</sup>, Li Xia<sup>2</sup>, Kim Leivins<sup>3</sup>, Sam A. Welsh<sup>4</sup>, Walter Zöfel<sup>5</sup> and Viviane Girardin<sup>1</sup>

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**PH-05**

**PARC** **NIVA**

**Integrating Point of Departure and Structural Equation Modelling to AOP**

**Development: A Case Study of Diuron Toxicity in Microalgae**

Li Xia<sup>1</sup>, Mei He<sup>2</sup>, Walter Zöfel<sup>3</sup>, You Song<sup>4</sup>, Lei Tian<sup>5</sup>, Knut Erik Tollefsen<sup>1\*</sup>

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**PH-06**

**PARC** **SINTEF** **NIVA**

**Molting inhibition in *Calanus finmarchicus* after exposure to the chitin synthesis inhibitor teflubenzuron**

Caline Vilga<sup>1</sup>, Bjørn Henrik Hansen<sup>1</sup>, Li Xia<sup>2</sup>, Dag Altin<sup>3</sup>, Knut Erik Tollefsen<sup>1\*</sup>

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# Summary

- **Conceptual STOP model using in-house data, databases, and models proposed**
- **Selected modules of a STOP modeling framework developed and tested**
- **Data reporting formats, User Interfaces (UI) and analysis prototyped**
- **Effects modeling (e.g. using AOPs, DR-modeling & tox thresholds) mature**
- **Exposure modeling (e.g. using AEP & monitoring data) still in the scoping**
- **Integration of the full model infrastructure pending**

# Acknowledgements



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Marit Hauken  
Roger Holten  
Sven Roar Odenmarck

## More information ?



**NCTP**



**EXPECT**



**STOP**



**PARC**

## The EXPECT team



## Funding



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