Novel effect-based tools

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Cité Universitaire - Paris

Alice meets the Caterpillar
John Tenniel

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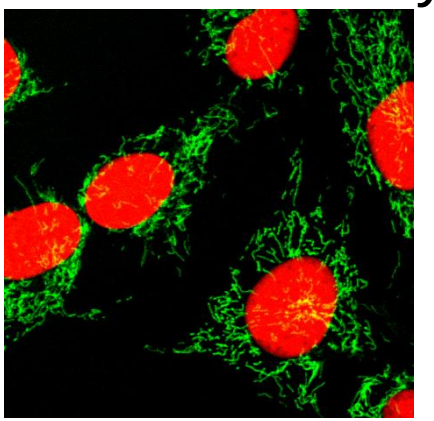
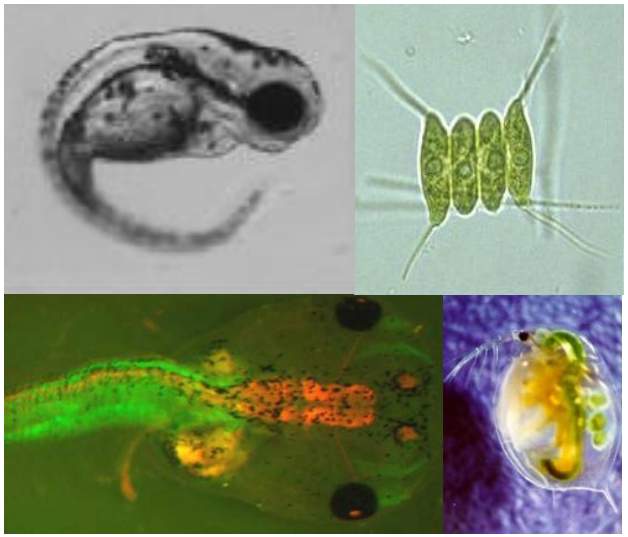
What are effect-based tools ?

In vitro

Receptor- and cell-based assays





Organism-based biotests

In vivo

In situ monitoring

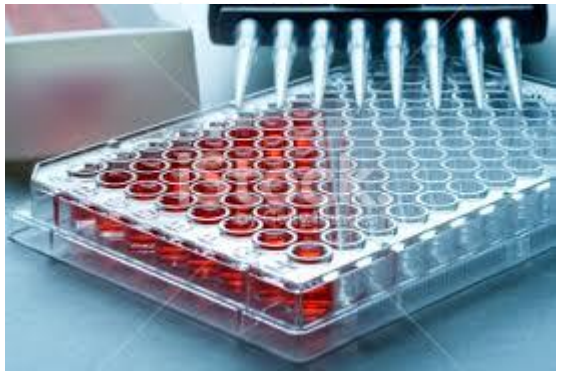
Individuals,
Populations,
Communities

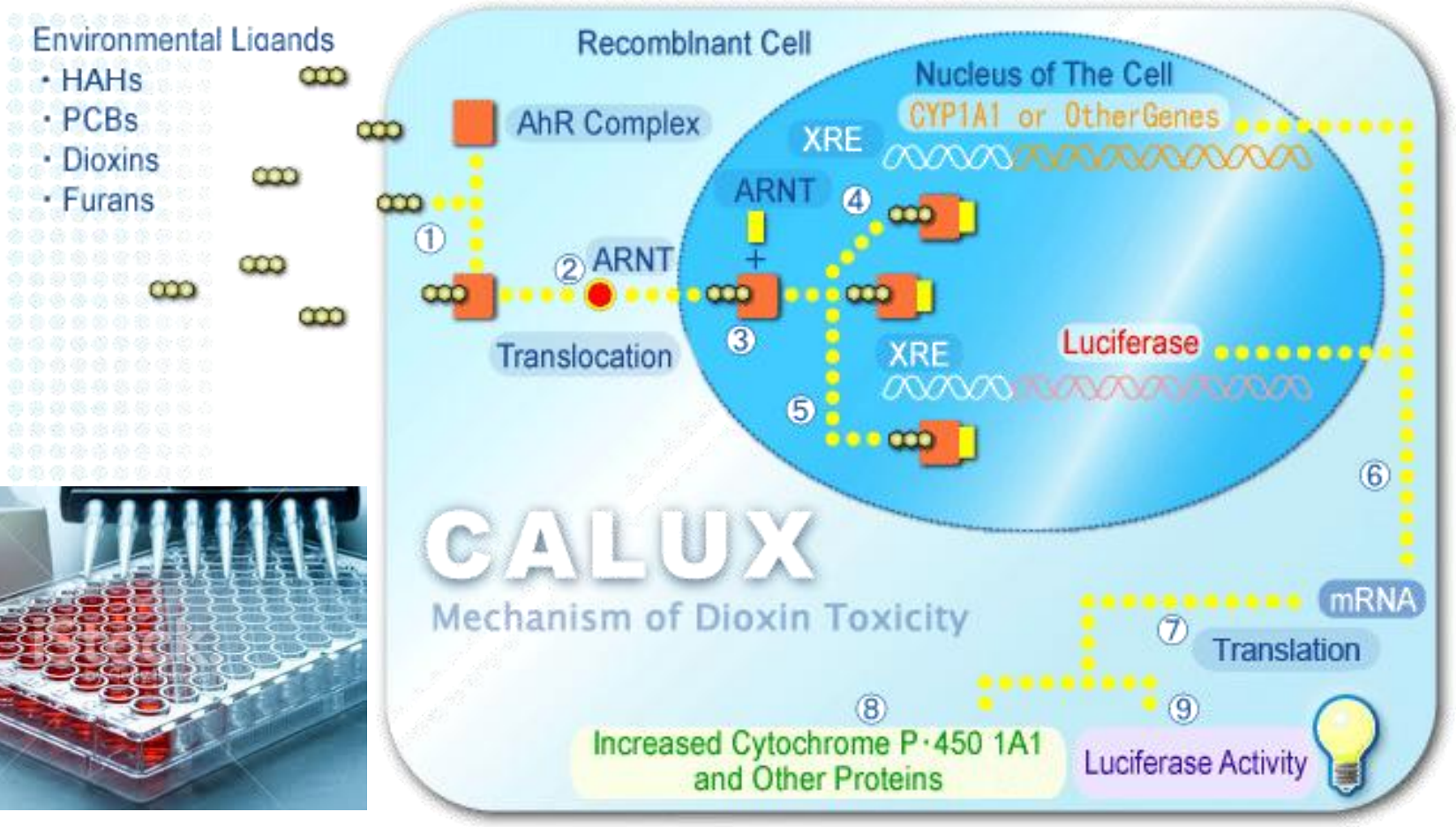
- Biomarkers;
- Pathology;
- Traits;
- Community functioning.

Technical report on aquatic effect-based monitoring tools EU, 2014

What are effect-based tools ?

e.g. AhR/XRE Nuclear receptor reporter assay





What are effect-based tools ?

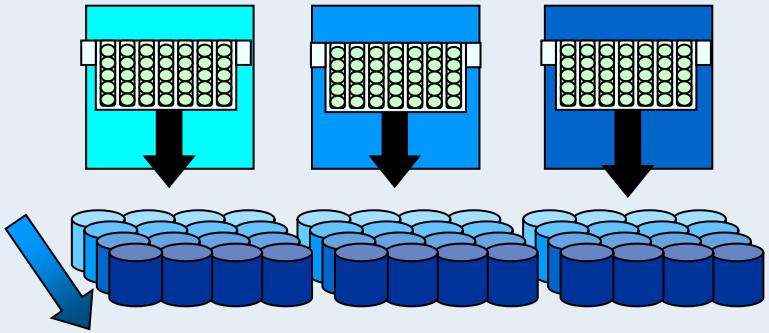
e.g. Community tolerance assay

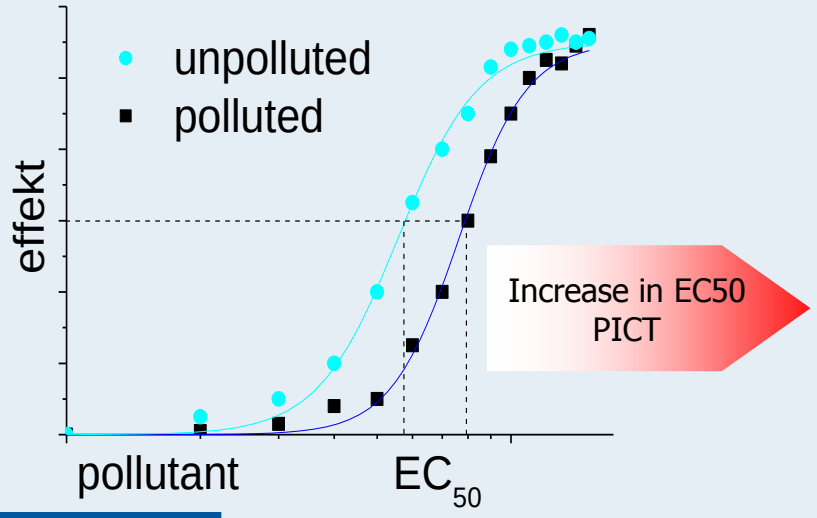
(1) Long-term exposure (weeks) to concentration series of a toxicant or at a polluted site

(2) Short-term testing (1h) to the addressed stressor

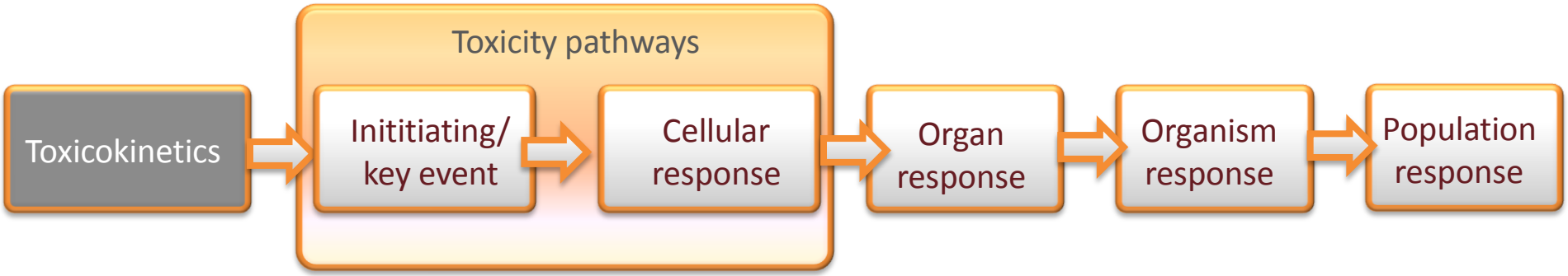
(3) Concentration-response-curve

(4) Comparison of effect parameter



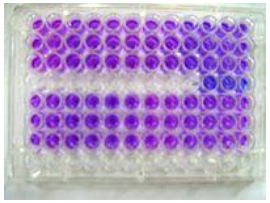
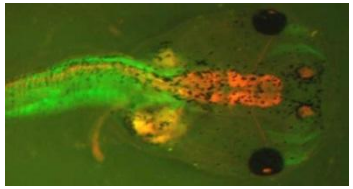
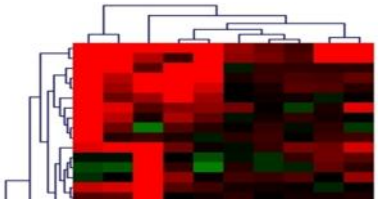
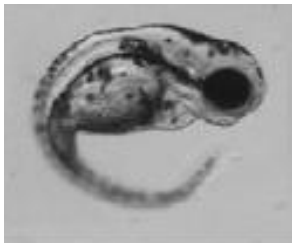


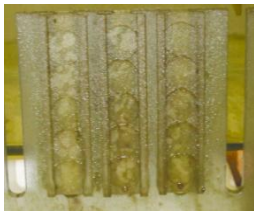
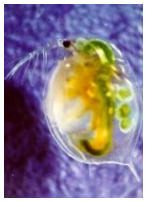
How could they help in chemical prioritisation ?

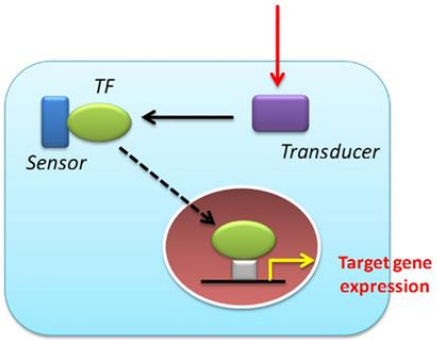


Adverse outcome pathways

How could they help in chemical prioritisation ?

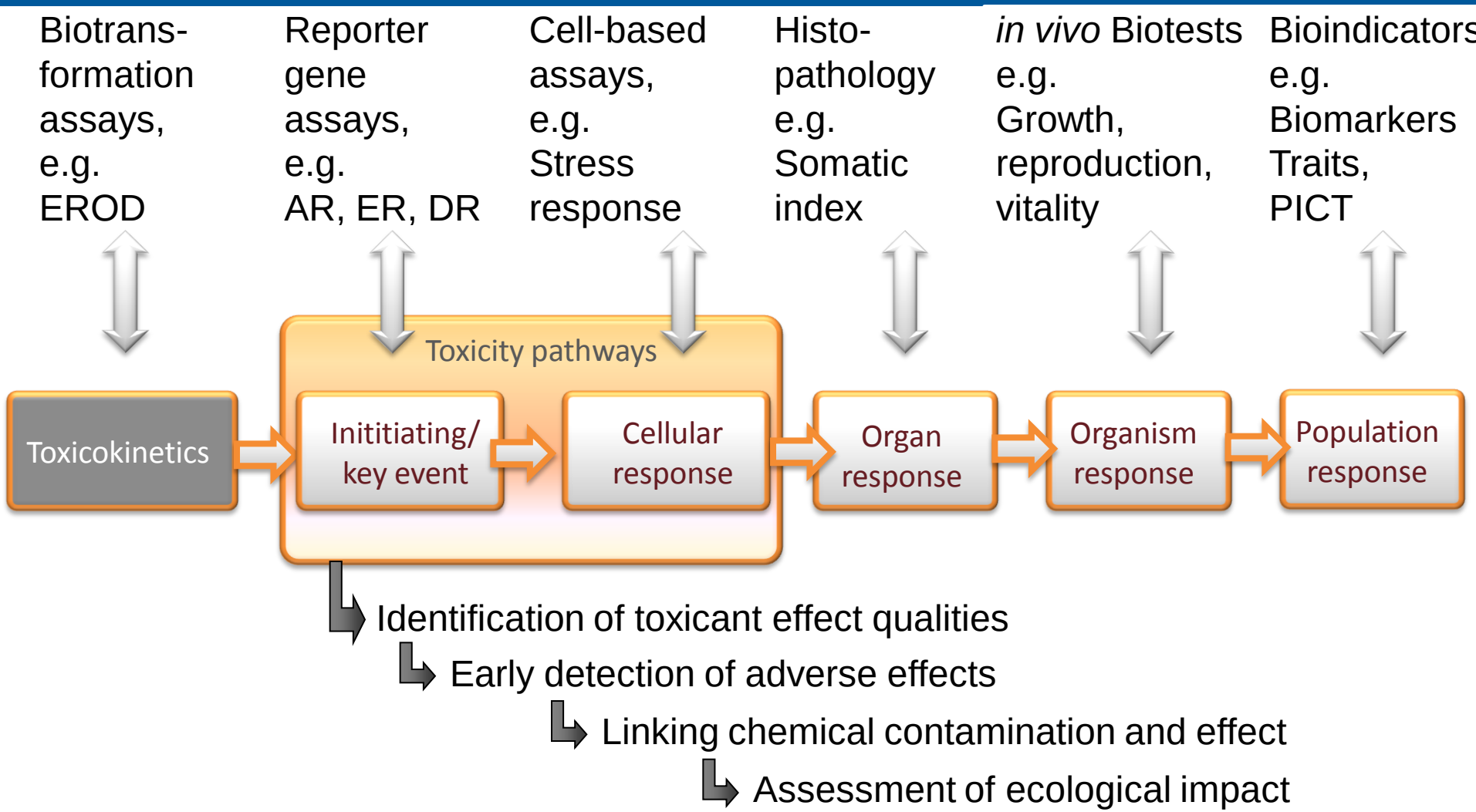



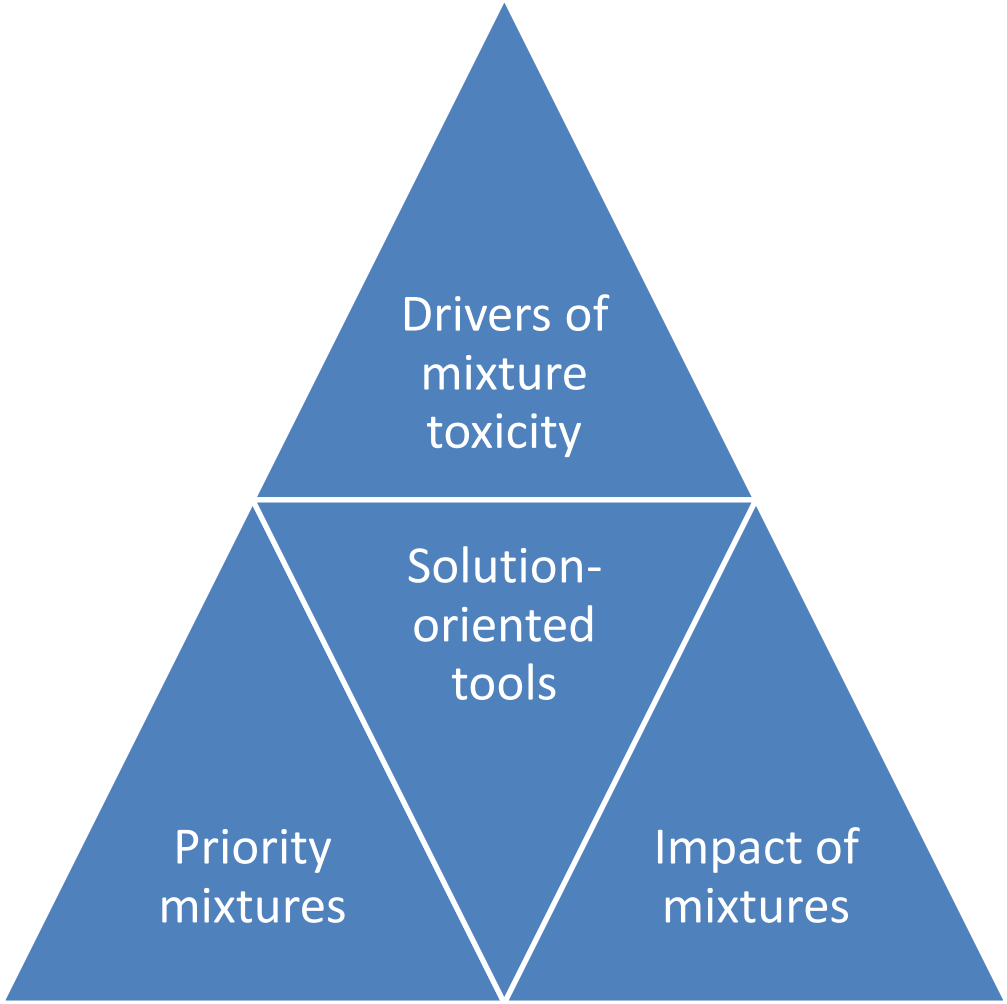
Toxicity pathways

Toxicokinetics → Inititiating/ key event → Cellular response → Organ response → Organism response → Population response

How could they help in chemical prioritisation ?

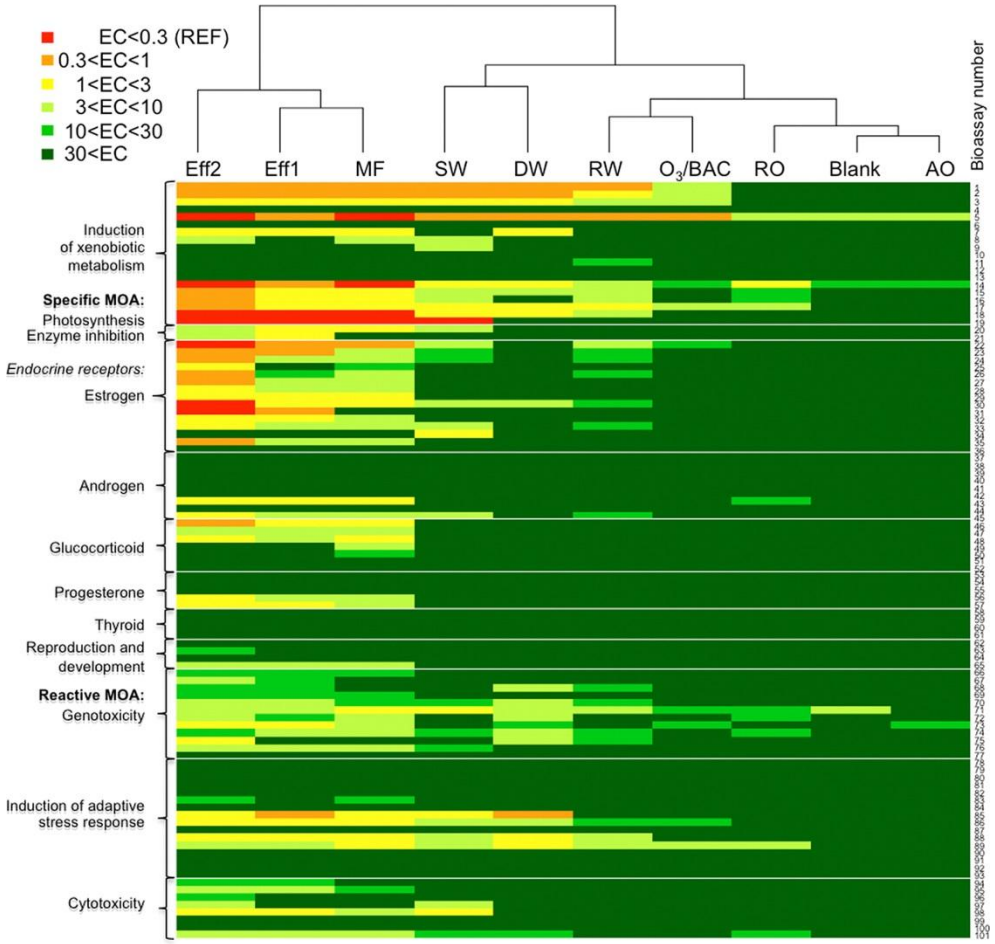


How could they help in mixture prioritisation ?



EC COM 252. 2012 The combination effects of chemicals – Chemical mixtures.

Priority mixtures -> prioritising samples



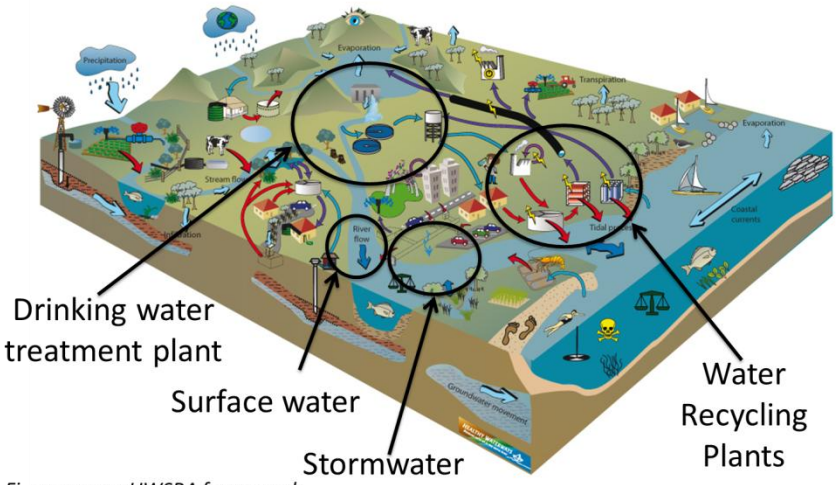


Figure source UWSRA framework
http://www.urbanwateralliance.org.au/

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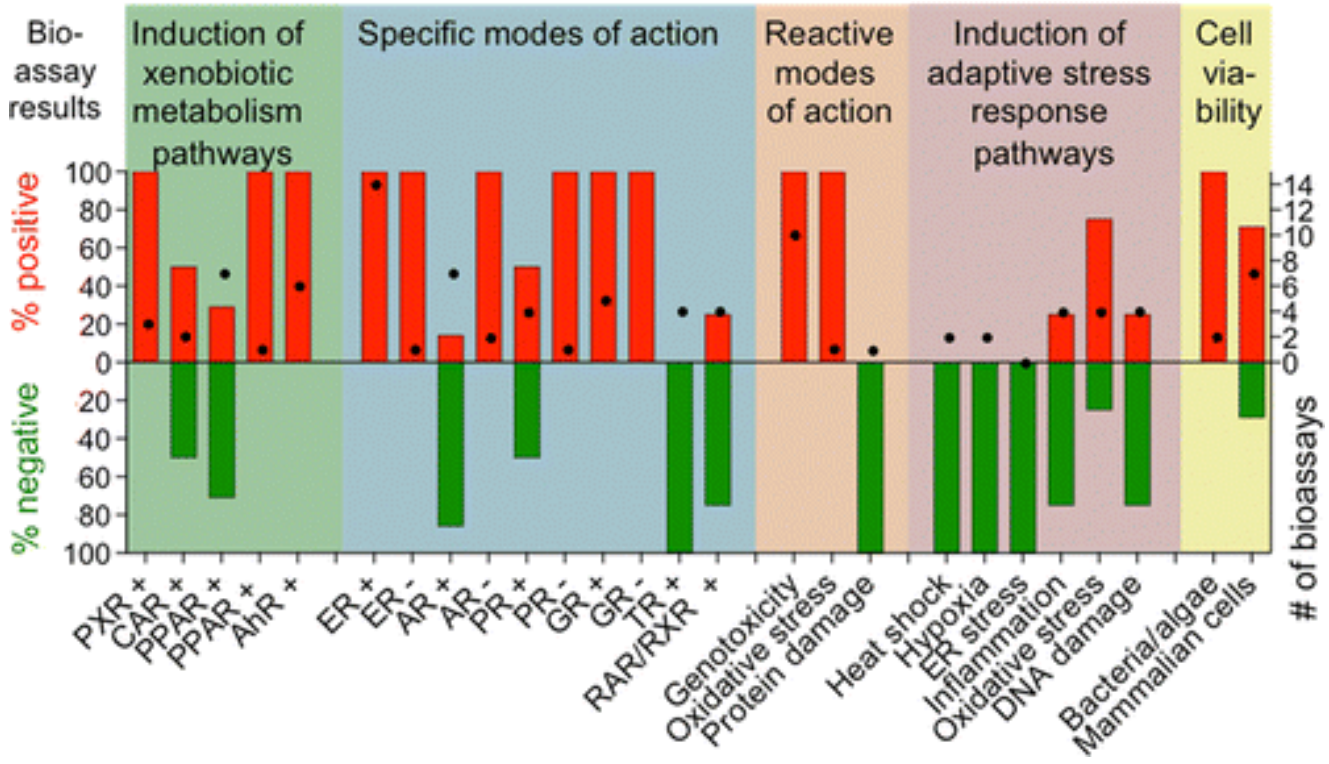
Escher et al. 2014
ES&T 48:1940-56

Priority mixtures -> prioritising effects



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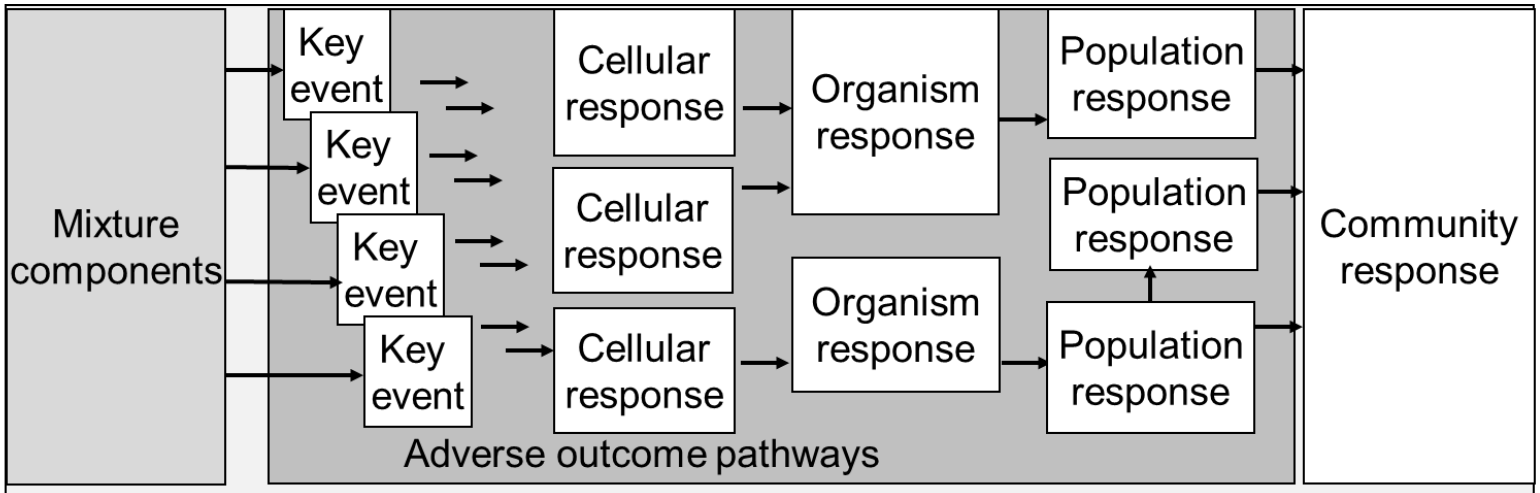
Impact of mixtures

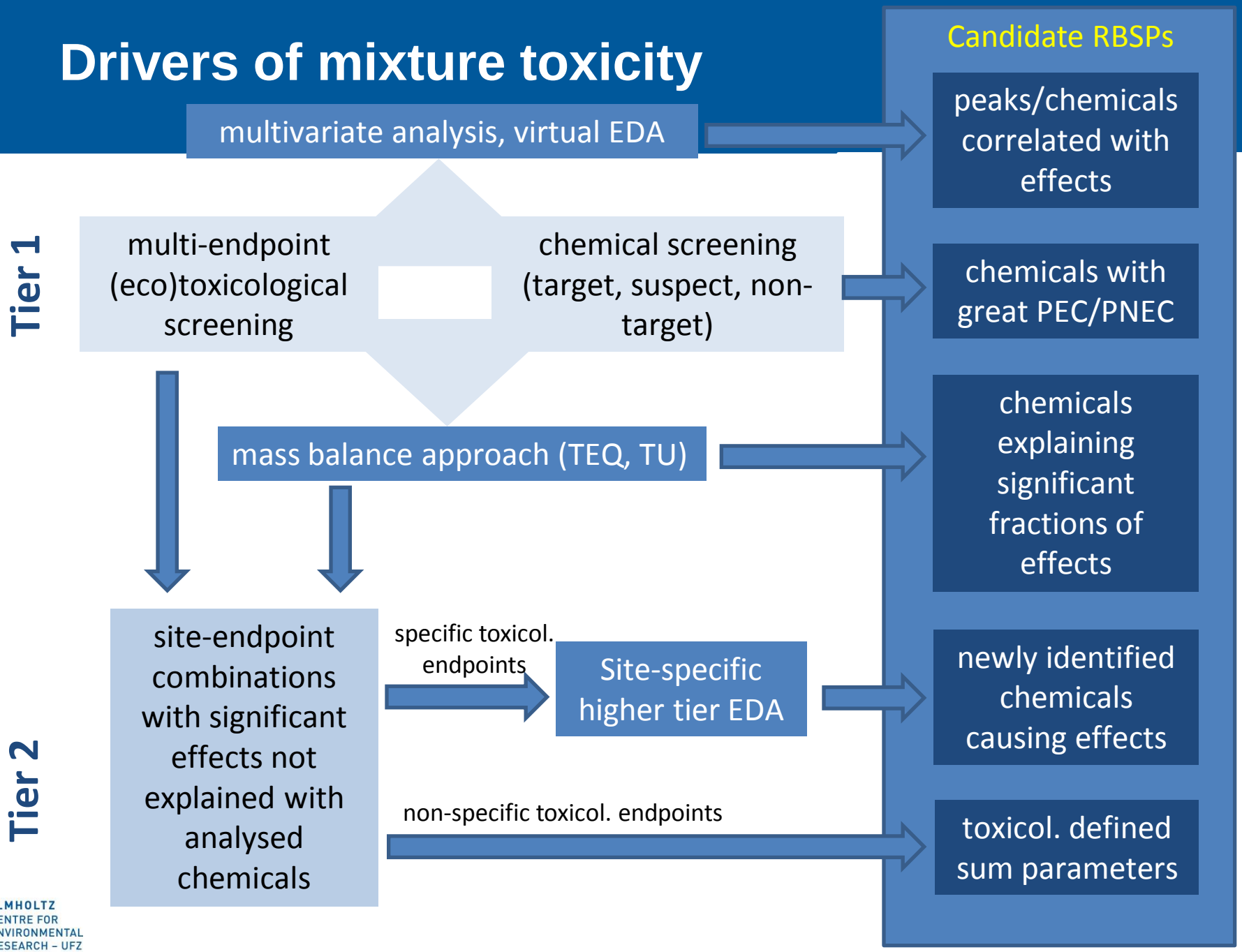


Key event detectors:
arylhydrocarbon receptor,
anti-estrogen,
anti-androgen,
anti-glucocorticoid,
anti-thyroid,
acetylcholinesterase,
mutagenicity,
stress-response nuclear receptors,
functional adaptive stress responses

Organism bioassays:
Algae,
Daphnids;
Fish;
Frog

Biological quality element observations:
Fish - biomarkers
Invertebrates – traits
Algae – community tolerance

Drivers of mixture toxicity



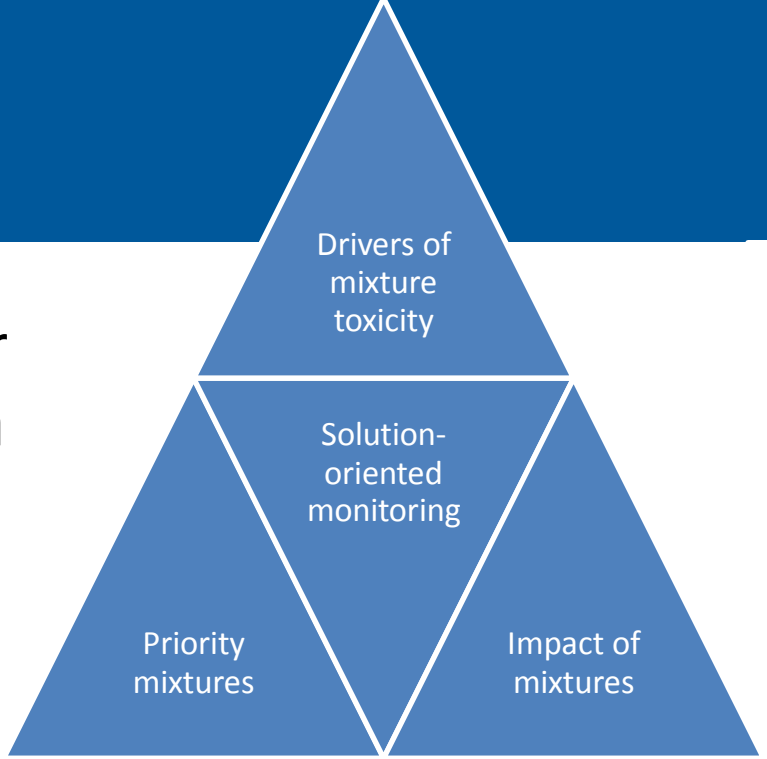
Science Fiction

We target

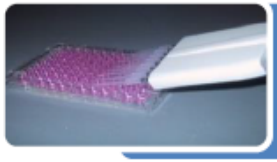
- Characterisation of priority mixtures;
- Assessment of mixture impact;
- Identification of drivers of mixture toxicity;
- Solution-oriented monitoring using effect-based tools.

Stairway to heaven
Bath cathedral

Thank you for your attention

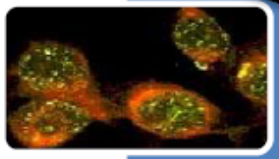


Comments ?



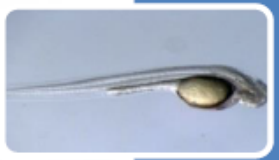
Cell-free bioassays

- Acetylcholinesterase (AChE) inhibition



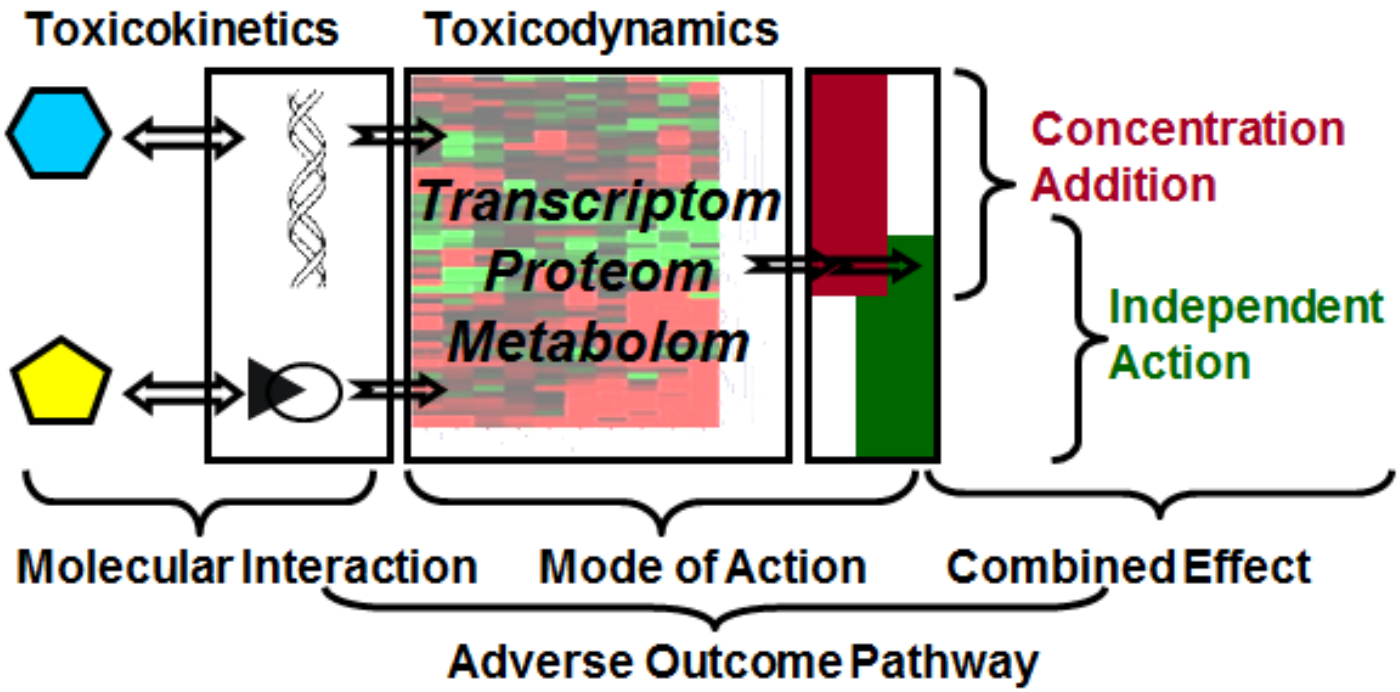
Cellular bioassays

- Ecoli stress Res assay
- Yeast mutant screen
- Ames/Ames fluctuation assay
- Mutatox
- GR CALUX, AhR CALUX (CAFLUX)
- CellSensor p53RE-bla HCT-116
- AREc32 gene reporter assay
- CellSensor nfkappaB-bla THP1
- GH3-TRE (T-Screen)
- ER/AR MELN cell line
- ZFL-zfERα/β2 cell line
- MDA-kB2 (AR) cell line
- AR/ERα/GR/PR/TRβ cell lines
- PPARα/PR/RARα/RXRα cell lines
- ARE/HRE/NFκB/p53RE cell lines

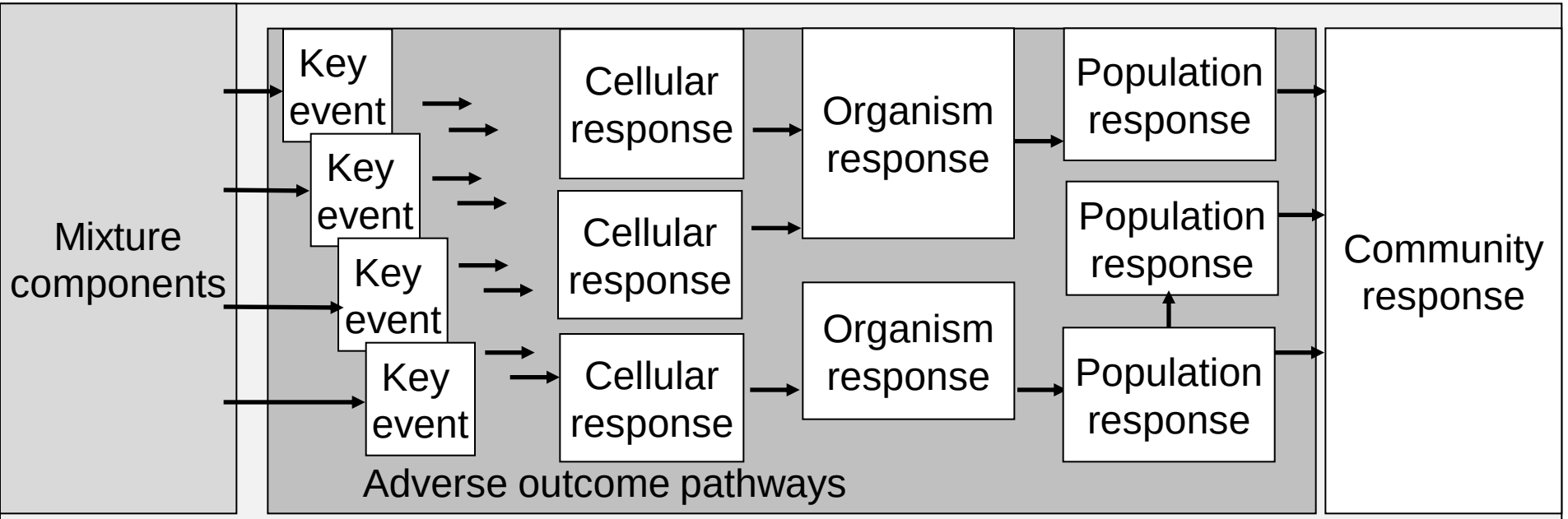


Whole organism bioassays

- *Chlamydomonas reinhardtii*
- *Daphnia magna*
- Zebrafish embryos
- cyp19a1b-GFP transgenic zebrafish embryo assay
- THbZIP-GFP amphibian thyroid assay


Toxicokinetics
Toxicodynamics
Transcriptom
Proteom
Metabolom
Concentration Addition
Independent Action
Molecular Interaction
Mode of Action
Combined Effect
Adverse Outcome Pathway

Impact of mixtures



Bioanalytical tools in mixture impact assessment

Effect-based tools

- *Similar action*
  - *Interaction indicators*
    - *Dissimilar action*

Ecological tools

- *Traits for correlated reponses*
  - *Functional tolerance indications*