Update from EPA's Office of Pollution Prevention and Toxics (OPPT)

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BOSC Review Draft

The New Chemicals Collaborative Research Program: Modernizing the Process and Bringing Innovative Science to Evaluate New Chemicals Under TSCA

A Summary Report to the Board of Scientific Counselors (BOSC) on an integrative research plan within the 2023-2026 Chemical Safety for Sustainability Strategic Research Action Plan

October 2022


BOSC

BOARD OF SCIENTIFIC COUNSELORS

REPORT OF THE U.S. ENVIRONMENTAL PROTECTION AGENCY BOARD OF SCIENTIFIC COUNSELORS NEW CHEMICALS COLLABORATIVE RESEARCH PROGRAM (NCCRP) PANEL

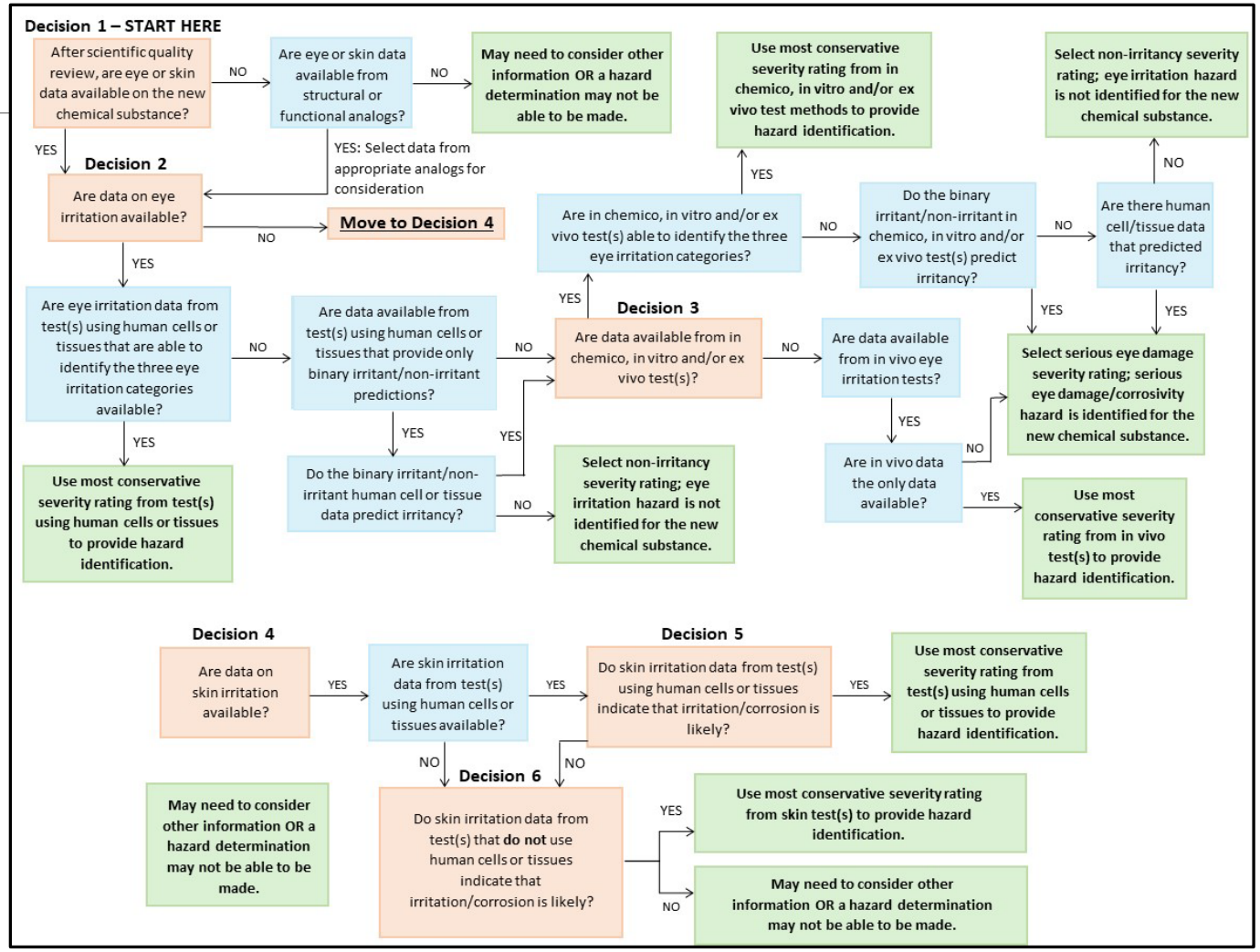
RESPONSES TO CHARGE QUESTIONS

New Chemicals Collaborative Research Program

- In February 2022, EPA launched a new effort under the Toxic Substances Control Act (TSCA) to modernize the process and bring innovative science to the review of new chemicals before they can enter the marketplace.
- Multi-year collaborative research program in partnership with the Agency's Office of Research and Development (ORD) and other federal entities to focus on approaches for performing risk assessments on new chemical substances under TSCA.
- In October, 2022, the Board of Scientific Counselors (BOSC) reviewed program.
  - White paper & BOSC review: https://www.epa.gov/bosc/bosc-review-panel-meeting-october-2022

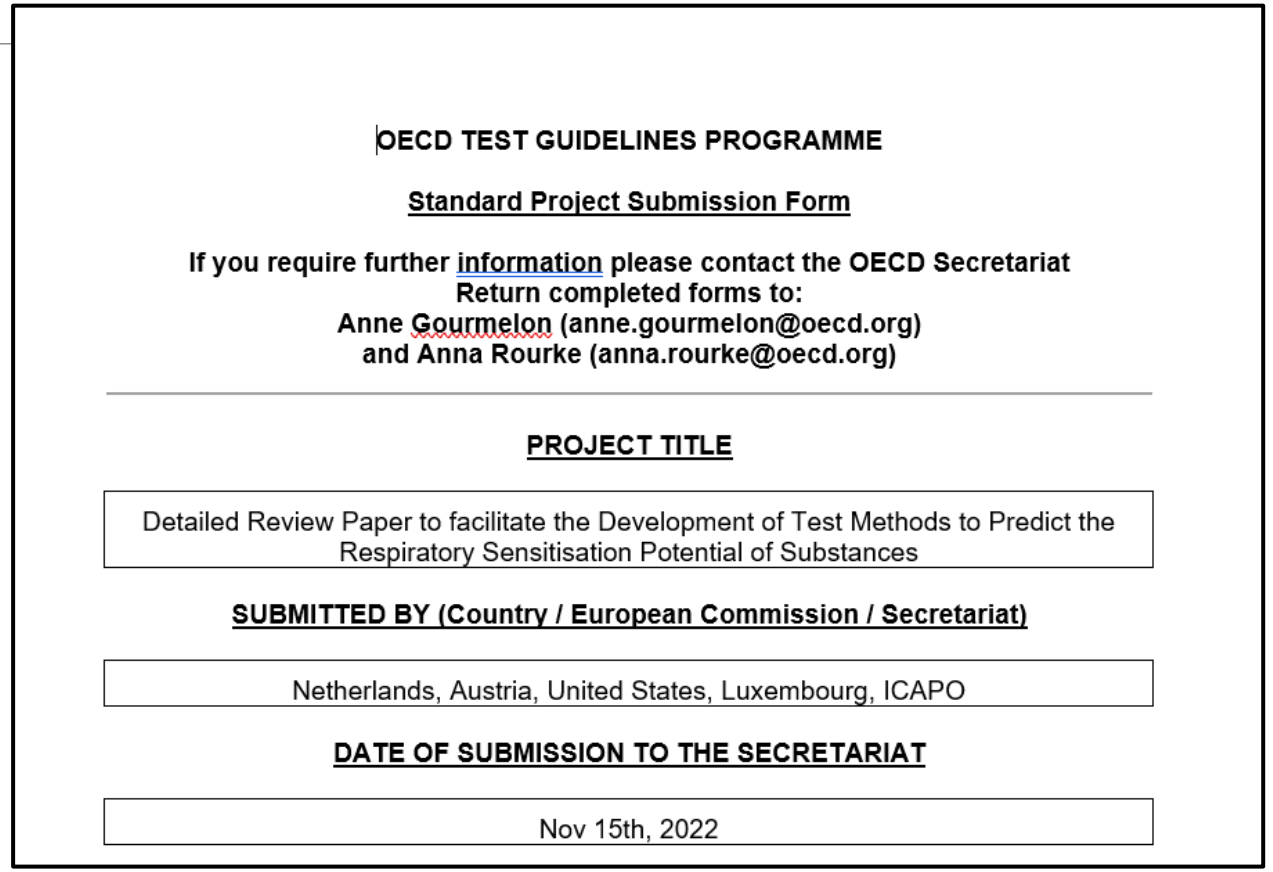
New Chemicals Program Decision Framework for Hazard Identification of Eye Irritation

- OPPT NCD is collaborating with colleagues from the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), Institute for In Vitro Sciences, Inc. and PETA Science Consortium International e.V. to develop a decision framework to evaluate eye irritation hazards for new chemicals under TSCA.
- This framework prioritizes use of data from NAMs over in vivo studies in animal models for the prediction of eye irritation in humans.



Respiratory Sensitization

- Occupational exposures to compounds that result in respiratory sensitization can be a serious health issue.
- There are currently no validated methods that are specific to the detection of respiratory sensitizers.
- Skin sensitization methods are not accurate for the detection of respiratory sensitizers.
- On-going efforts to develop a NAMs approach for respiratory sensitization
  - Detailed Review Paper proposal to the OECD was approved in April 2023
  - NTP testing of GARD Air
    - Chemical recommendations from multiple ICCVAM agencies
    - Approximately 100 chemicals to be tested



OECD TEST GUIDELINES PROGRAMME

Standard Project Submission Form

If you require further information please contact the OECD Secretariat
Return completed forms to:
Anne Gourmelon (anne.gourmelon@oecd.org)
and Anna Rourke (anna.rourke@oecd.org)

PROJECT TITLE

Detailed Review Paper to facilitate the Development of Test Methods to Predict the Respiratory Sensitisation Potential of Substances

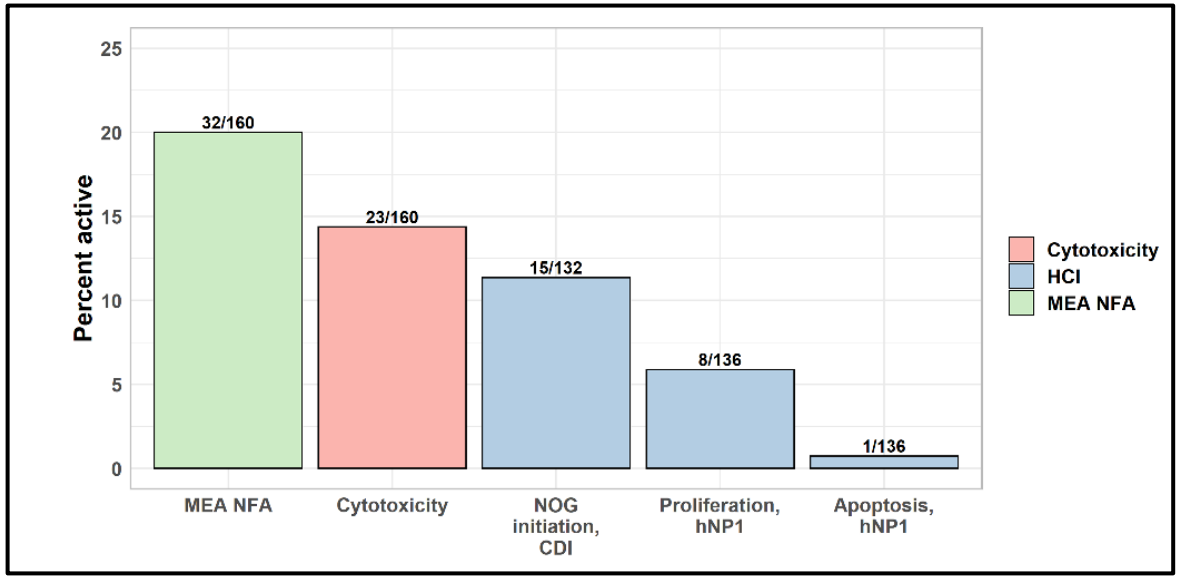
SUBMITTED BY (Country / European Commission / Secretariat)

Netherlands, Austria, United States, Luxembourg, ICAPO

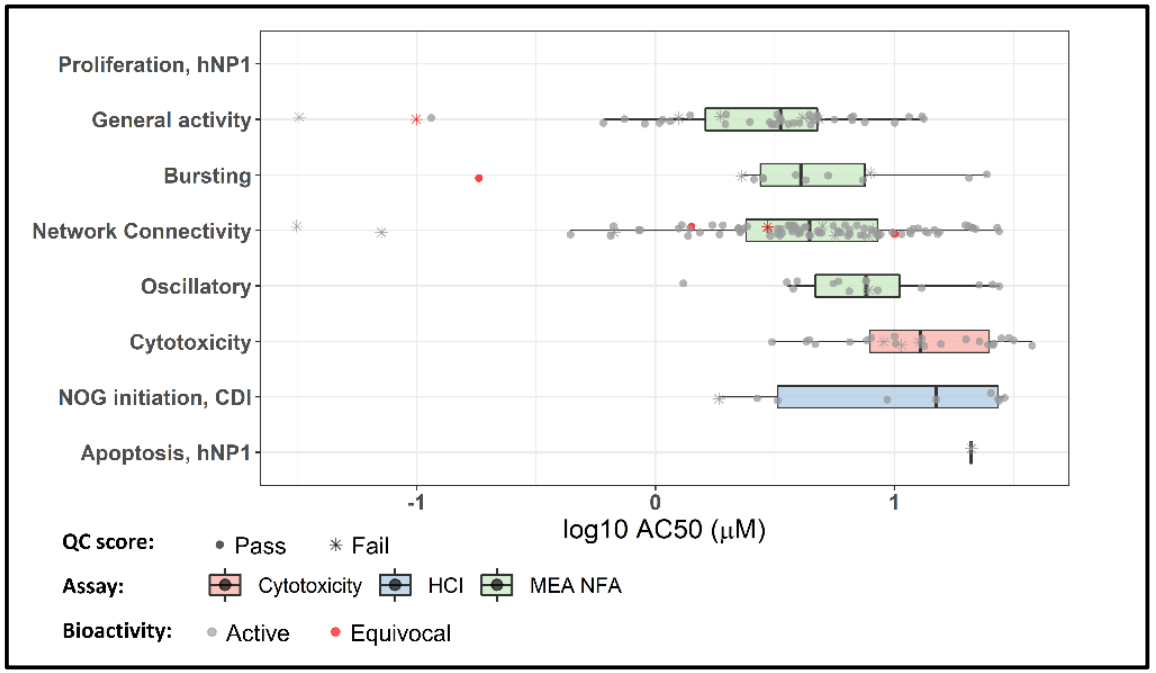
DATE OF SUBMISSION TO THE SECRETARIAT

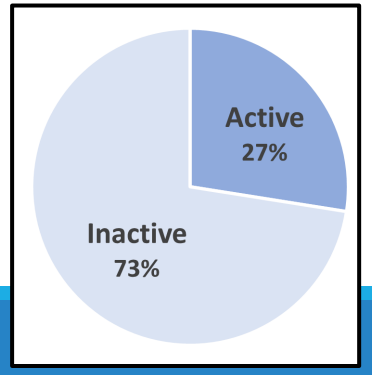
Nov 15th, 2022

Screening Level Information for 160 PFAS Compounds



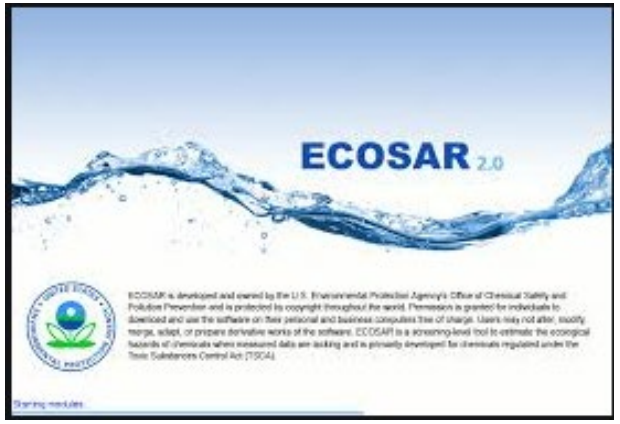
Extracted from Carstens et al, 2023, Figure 1





- Out of a set of 160 PFAS, 118 were inactive, leaving 42 active PFAS that decreased measures of neural network formation, neurite outgrowth, proliferation, or apoptosis
- 24 PFAS demonstrate moderate or low selective activity

Utilizing Structure Activity Relationships (SARs)



Chemical class-based SAR to predict aquatic toxicity
Classification scheme identifies excess toxicity
Estimates **acute** and **chronic toxicity** based on accumulated data and past decisional precedents

Acute Effects:
Fish 96-hr LC_{50}
Daphnid 48-hr EC_{50}
Algae 72/96-hr EC_{50}

Chronic Effects:
Fish ChV
Daphnid ChV
Algae ChV

- **OPPT Uses**
  - New Chemicals – used extensively to predict aquatic toxicity
  - Existing Chemicals – used as part of a Weight of Evidence and for analogue selection (looking at concordance between predicted values of the assessment chemical and analogue as well as empirical data for analogue)
- **Recent / Current Activities**
  - Version 2.2 released in 2022
    - User can input *measured* water solubility values
  - Validation efforts
    - Primary sources for every data point in the QSAR training sets
    - Chemical classes
  - **Data updates**! - *no data updates since 2017*
    - Updating classes with data submitted under TSCA
    - Identifying data-poor QSARs
  - Automatic incorporation on new chemical data submissions in future
  - Public release of QSARs online with live updates

Utilizing Structure Activity Relationships (SARs)

OPPT Uses

- New chemicals – assessors use OECD QSAR Toolbox on any incoming new chemical (within the chemical domain of applicability) to make predictions and gather available data on the parent chemical and its metabolites
  - Metabolism profiler
  - Oncologic– predicts carcinogenicity (provides a classification)
  - Skin Sensitization profiler –predicts protein binding
  - Respiratory Sensitization
  - Data Gathering – identifies studies on human health, ADME, Bioaccumulation, ToxCast, Toxicokinetics
- Existing chemicals – A framework for analogue identification and selection is under development utilizing the OECD QSAR Toolbox's analogue prediction and data gathering features

WebICE: Interspecies Correlation Estimation (ICE) Models

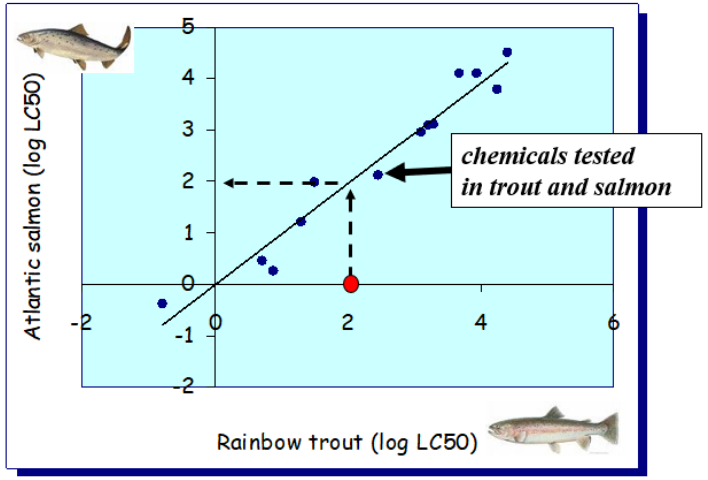
- Log-linear relationships of inherent sensitivity derived from the acute toxicity of chemicals tested in two species.
- Predict toxicity for untested species; provides additional data for Species Sensitivity Distribution Curves (SSDs)
- Probabilistic (SSD) approach to determining a toxicity value is preferred over traditional deterministic (applying an assessment factor) approach

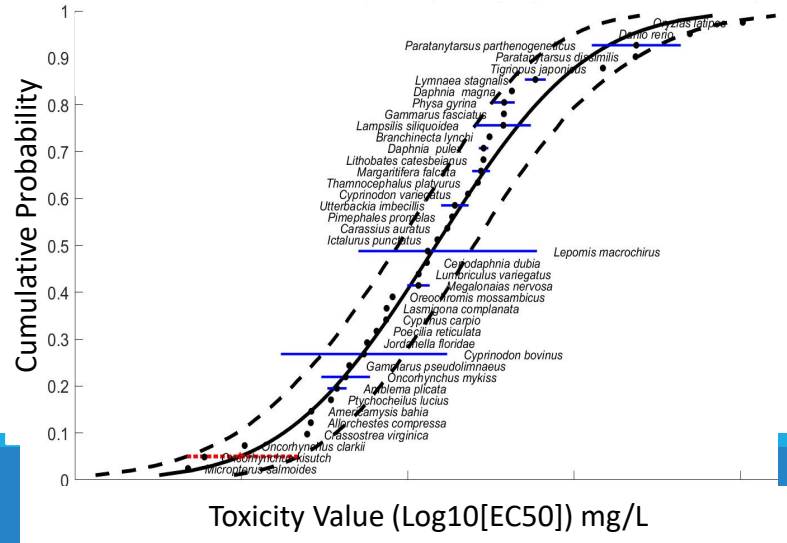
1. Use existing data on many chemicals to relate inherent sensitivity of two species

2. Predict additional acute toxicity values for your chemical of interest to untested species

3.Populate SSD: empirical and predicted values

4. Determine Concentration of Concern (COC) HC_{05} or lower confidence interval of HC_{05}





Thank You