# Development of Acute-to-Chronic Ratios (ACRs) to Support Ecotoxicity Prediction for Surfactants

Unilever

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## Introduction and Aims

### Context

Chemical safety testing is increasingly shifting away from the use of vertebrates; however, many substances still lack chronic (long-term) aquatic ecotoxicity data.

### Problem

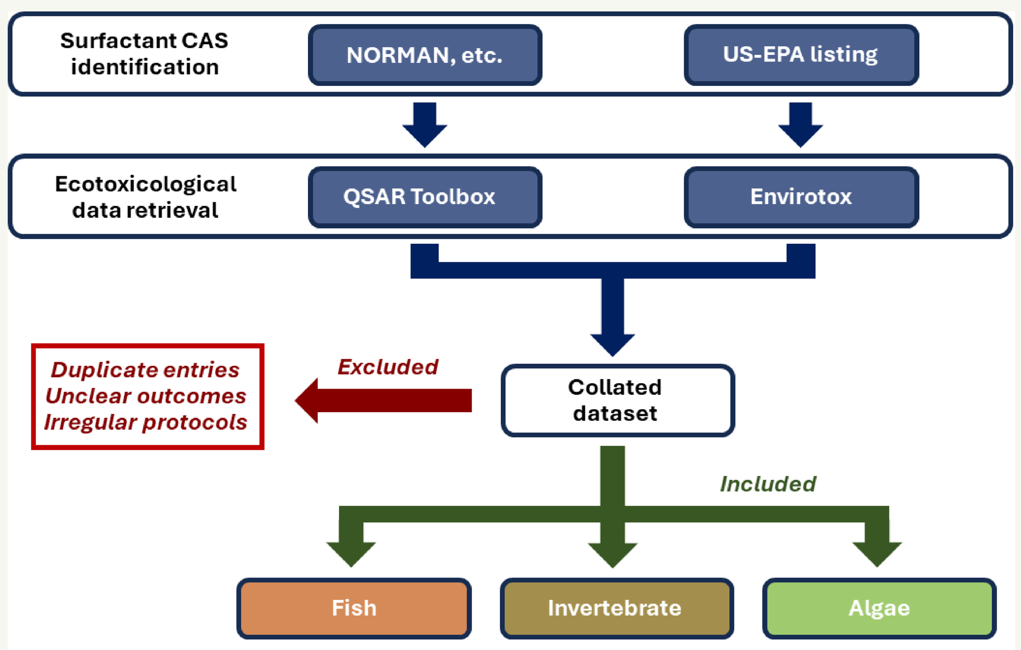
Surfactants are produced and used at high volumes and require safety assessment. While historical ecotoxicity datasets exist, chronic endpoints are missing for some surfactants.

### Aim

To develop robust and transparent, surfactant-tailored acute-to-chronic ratios (ACRs) for three regulatory trophic levels (algae, daphnids, fish) and to evaluate their performance using an independent external test set.

## Methodology

### 1. Data Curation Workflow




| | | Fish | Invertebrate | Algae |
|---|---|---|---|---|
| Test species | | All teleost (e.g., *P. promelas*) | *Daphnia magna*, *Ceriodaphnia dubia* | Common test species (e.g., *D. subspicatus*) |
| Acute | Duration | 96 hour | 48 hour | 72 or 96 hour |
| Acute | Effect | Lethality | Lethality, immobility, intoxication | Growth rate (preferred), biomass, cell count |
| Acute | Endpoint | LC50, EC50 | LC50, EC50 | EC50 |
| Chronic | Duration | ≥ 21 day | *D. magna*: ≥ 21 day<br>*C. dubia*: 7 day | 72 or 96 hour |
| Chronic | Effect | Growth, lethality, others with health relevance | Reproduction (preferred), lethality, intoxication | Growth rate (preferred), biomass, cell count |
| Chronic | Endpoint | EC10 > EC20 > NOEC (order of preference) | EC10 > EC20 > NOEC (order of preference) | EC10 > EC20 > NOEC (order of preference) |

### 2. Acute and Chronic Data Pairing

- For each trophic level and CAS number, acute and chronic toxicity values were first aggregated within species using **geometric means** across studies, then combined across species using an equal-weight geometric mean to derive single acute and chronic values.
- This two-stage approach **minimises bias** from uneven data availability and prevents species with abundant data from disproportionately influencing the final estimate.

### 3. ACR Derivation Equation

$$ACR = e^{\sqrt[n]{\prod_{i=1}^{n}(ln(Acute_i)-ln(Chronic_i))}} = \frac{Geomean(Acute)}{Geomean(Chronic)}$$

- Based on the distribution of ACR values for individual CAS within a certain trophic level, the corresponding median, 90th and 95th percentile ACRs were determined.

### 4. ACR Performance Evaluation using HERA Data

- Validation was performed against **an external test set**, consisting of surfactant data sourced from the Human and Environmental Risk Assessment (HERA) initiative (www.heraproject.com). Chronic toxicity estimates, acquired through ACR extrapolation of acute output, were compared relative to their recorded experimental counterparts.

**Measured chronic** toxicity (mg/L)

**Predicted chronic** toxicity (mg/L) **= Measured acute** toxicity**/ACR**

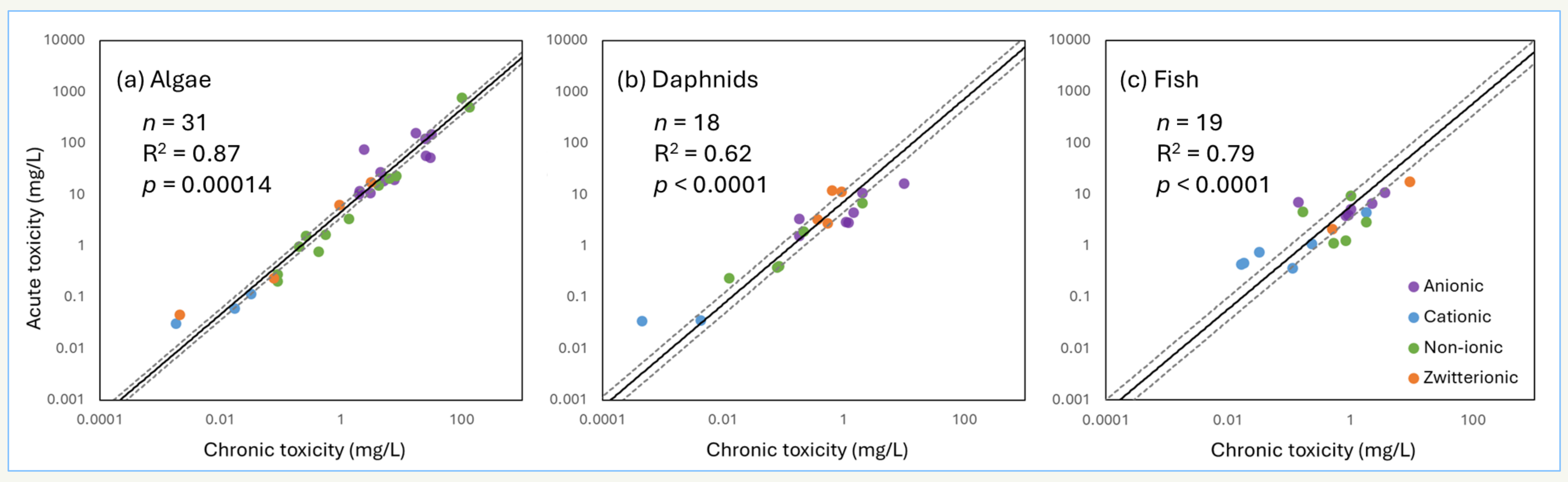
## Overview of Collated Data for ACR Derivation

| | | Fish | Invert. | Algae | Total |
|---|---|---|---|---|---|
| **n. Data entries** | Total | 501 | 257 | 125 | **883** |
| | Acute | 446 | 224 | 64 | 734 |
| | Chronic | 55 | 33 | 61 | 149 |
| **n. Surfactants with Acute-chronic data pairings** | Total | **19** | **18** | **31** | **51 *** |
| | Cationic | 6 | 2 | 3 | |
| | Anionic | 6 | 7 | 13 | |
| | Non-ionic | 5 | 5 | 11 | |
| | Zwitterionic | 2 | 4 | 4 | |

* 51 unique surfactants had matched acute + chronic data in at least one trophic level

## ACR Summary and Comparisons

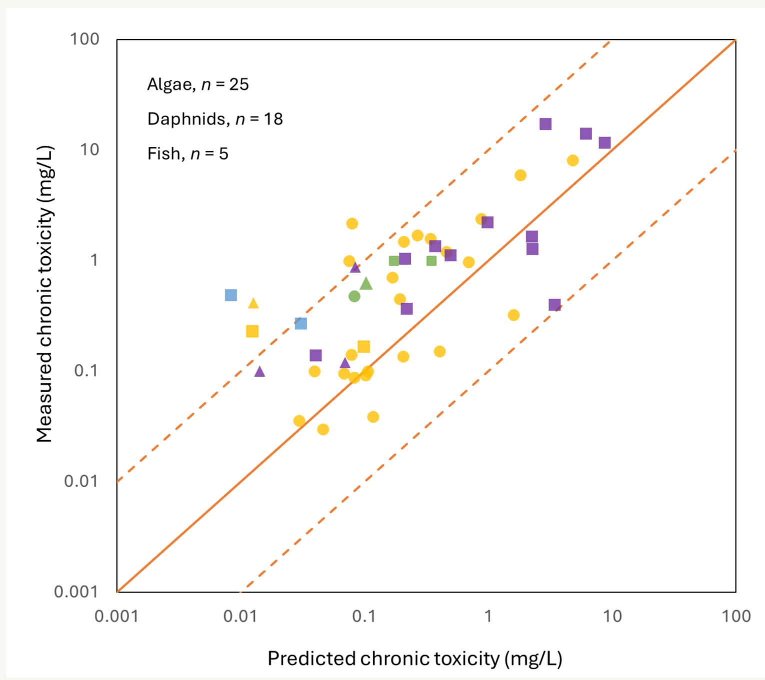
- **Strong linear relationships between acute and chronic toxicity across trophic levels.** The best fit was reported for algae, as their acute and chronic outcomes often arise as different statistical endpoints from the same test.




| Trophic level | ACR values | | | | |
|---|---|---|---|---|---|
| | Minimum | **Median** | **90th pctl.** | 95th pctl. | Maximum |
| **Algae** | 1.8 | **3.8** | **9.4** | 19.9 | 32.4 |
| **Daphnids** | 1.7 | **7.1** | **19.4** | 28.5 | 78.7 |
| **Fish** | 1.5 | **4.5** | **27.4** | 30.6 | 50.7 |

- **The 90th percentile ACR was preferred for further use**, as it offers a balance between conservatism and statistical robustness.
- **ACR values for individual surfactant classes were not obtainable**, owing to sample size limitations.
- **The median ACRs derived are similar to the surfactant values reported by the US EPA**, and consistent with literature values for chemicals sharing narcotic modes of action.

## ACR Performance in Chronic Toxicity Estimation




- Using **median ACRs**, **46 out of 48 predicted chronic values were comparable to measured chronic values,** i.e., no more than one order of magnitude higher.
- Using **90th percentile ACRs**, **all** predicted chronic toxicity values were comparable to experimental values regardless of surfactant class (see left plot).

## Applications and Limitations

### Surfactant-tailored ACR Application

- The **surfactant-specific 90th percentile ACRs** performed well in predicting chronic toxicity from the measured acute toxicity values.
- These ACRs provide a transparent and robust tool to fill chronic aquatic toxicity data gaps from acute data, supporting the **derivation of predicted no-effect concentrations (PNECs)** and weight-of-evidence justifications for **waiving additional chronic testing** under regulatory frameworks.

### Limitations and Considerations

- **Not all data** complied with the relevant **OECD test guidelines**, for various reasons.
- Detail-scarcity and heterogeneity in **experimental protocols** and **exposure conditions** (e.g., actual exposure concentrations), as well as in **species and life-stages**, can introduce **variability and uncertainty** into ACR derivation.
- These **uncertainties should be taken into account** when applying the ACRs in regulatory or predictive contexts.

## Take-home Messages

- This study establishes **scientifically robust and transparent surfactant-specific** ACRs.
- The **90th percentile ACRs** (9.4 for algae, 19.4 for daphnids, and 27.4 for fish) yield **comparable estimates of chronic toxicity** and are therefore recommended as **a line of evidence in regulatory safety assessment**.

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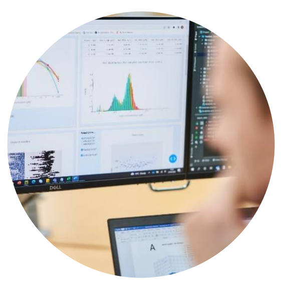

**Note**

The ACR data presented in this poster are subject to minor revision during manuscript finalisation. Please refer to the final published article for definitive values.

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