BLUE FROG SCIENTIFIC

SETAC EU 2026 - Presentation ID: 1.03.P-Tu022

Bioaccumulation Assessment Using New Approach Methodologies for Difficult Substances

Authors: Pauline Remuzat[1], Kai Paul[2], Marianne Matzke[2], Virginie Burosse[1], Jamie Marshall[2]
Affiliation: [1]Blue Frog Scientific SAS, Lyon, France; [2]Blue Frog Scientific Limited, Edinburgh, United Kingdom
Contact Us: www.bluefrogscientific.com / pauline.remuzat@bluefrogscientific.com

Screening for bioaccumulation traditionally relies on surrogate metrics such as octanol-water partition coefficient (log K_{ow}), which has been widely used and accepted for decades and underpins many quantitative structure-activity relationships ((Q)SARs) models.

However, the log Kow cut-off values as a screening tool for bioaccumulation potential in aquatic organisms are not always relevant (Gimeno et al., 2024).

In addition, the accuracy of the log K_{ow} for the bioaccumulation assessment is limited to certain substance classes and primarily reflect one accumulation mechanism – partitioning into storage lipids.

For substances such as surfactants, ionisable compounds, or per- and polyfluoroalkyl substances (PFAS), bioaccumulation may involve alternative mechanisms, including specific biological binding interactions and depuration processes.

How to address these limitations and improve bioaccumulation assessment for a broader range of substances (including difficult test substances)?

A non-animal bioaccumulation testing strategy was developed and presented below, combining up to five *in chemico / in vitro* assays, followed by *in silico* predictions.

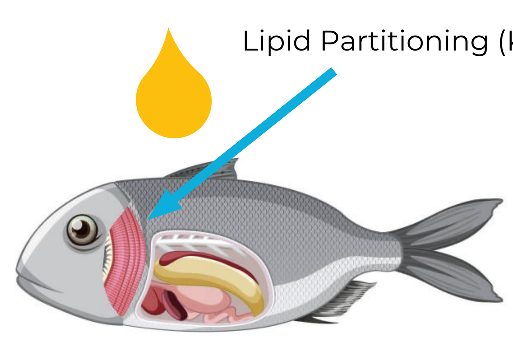
Traditional Screening Approach

Chemical Classes: Neutral, hydrophobic organic chemicals

Chemical Property: Log K_{ow}

Assumed Mechanism:
- Passive partitioning into storage lipids (hydrophobicity)

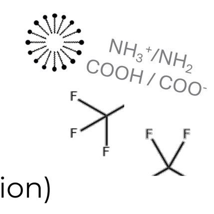
Predicted Outcome: Bioaccumulation potential



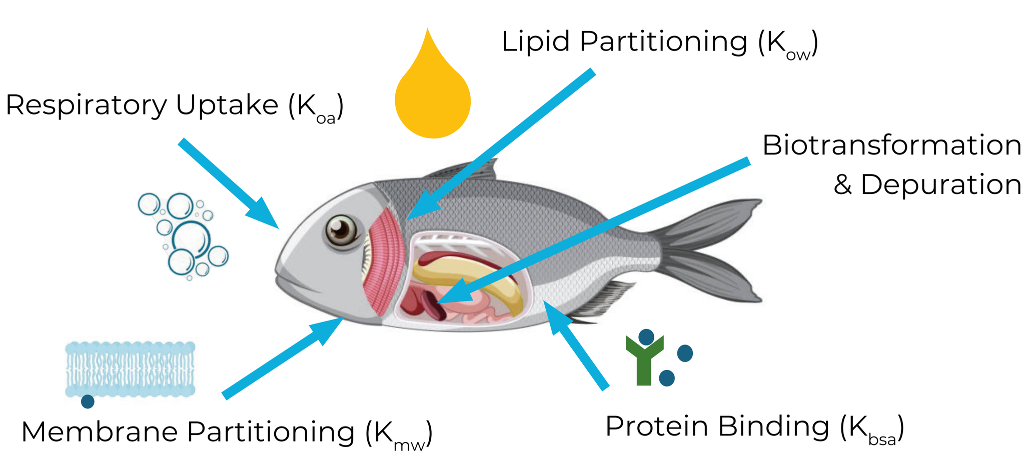
Broader Reality for Many Substances

Chemical Classes: Surfactant, ionisable compounds, PFAS

Multiple Mechanisms:
- Passive partitioning into storage lipids (hydrophobicity)
- Binding to proteins (e.g. serum albumin)
- Electrostatic interactions with cells membranes
- Depuration mechanisms (biotransformation, detoxification)



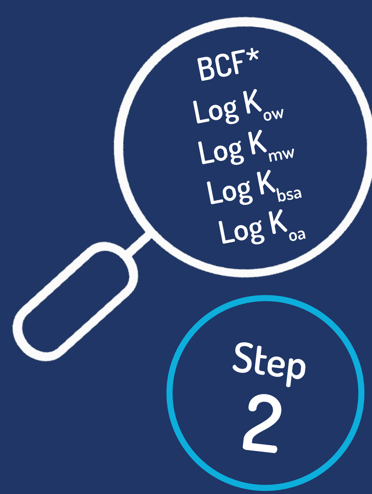
Observed Outcome: Bioaccumulation behavior



Materials & Methods

In silico analysis on bioaccumulation

During this investigation, various *in silico* models (**VEGA, BAT, BIONIC**) are tested for acquiring an estimate of **BCF** and to discover additional input parameters that may be useful for determining BCF within the models and increase their accuracy (i.e. K_{ow}, K_{oa}, K_{mw}, K_{bsa}, **biotransformation**).



Interpretation of in silico results and selection of the most impactful factor(s)

Based on the *in silico* results, the input parameter(s) that are the most impactful factor(s) regarding the bioaccumulation mechanisms are determined and subject to experimental testing.

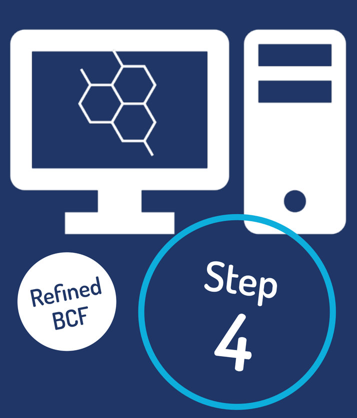
** with or without biotransformation.*

Experimental studies on one or several parameters with validated analytical methods

Standard Test Methods:
- K_{ow} : OECD TG 123 or OECD TG 107
- **Biotransformation**: OECD TG 319A

No internationally recognised test methods. Protocols developed based on literature data
- K_{oa} : Headspace method
- K_{mw} : Solid-supported lipid membrane (SSLM)
- K_{bsa} : Rapid Equilibrium Dialysis (RED)

Results & Discussion



Update of BAT model

Once the experimental studies completed, the *in silico* BAT model is updated, incorporating the new values, to **better estimate BCF for both fish and invertebrates by removing uncertainties** in the algorithm predicting such values from the log K_{ow} alone.

Redaction of a Weight of Evidence (WoE) report

Compiling the **Lines of Evidence** from steps above, the WoE report concludes on the **bioaccumulation assessment of the substance of concern**.

Conclusion

Bioaccumulation Assessment

Each test aids in the removal of specific uncertainties related to substances that may accumulate via other processes than that indicated by K_{ow} alone. These data can inform WoE approaches and serve as input for the BAT "Bioaccumulation Assessment Tool" QSAR model, improving accuracy of BCF predictions.

Incorporating these parameters into modelling software increases the Precision, Accuracy and Predictability in an *in vitro - in vivo* extrapolation (IVIVE) approach.

The testing strategy proposed permits a robust conclusion on bioaccumulation under Persistent, Bioaccumulative, and Toxic (PBT) assessment regulatory frameworks, avoiding unnecessary animal testing.

#SETAC2026 #Bioaccumulation #NAMs

www.bluefrogscientific.com

*References :
- K_{ow} - Octanol/water partition coefficient
- K_{oa} - Octanol/air partition coefficient
- K_{mw} - Membrane lipid/water partition coefficient
- K_{bsa} - Bovine serum albumin (BSA) solution/water partition coefficient