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What's the Functional Solubility?

The landscape, challenges and current limitations faced when working with 'difficult-to-test' substances in aquatic matrices.

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Regulatory Requirements

Aquatic Ecotoxicology Testing

- Multiple treatment levels required by OECD/OCSPP guidelines
- Analytical recovery requirements 80-120% of nominal or ±20% of mean measured concentrations.
- OECD, 2000 and USEPA, 1996 define “poorly soluble” as solubility limit <100 mg/L

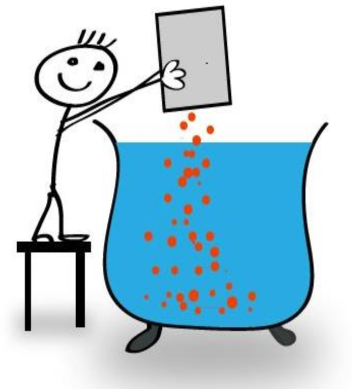
Physico-Chemical Properties

Impacting Test Substance Behavior In Water:

- Solubility
- Kow
- Kd
- Hydrolysis
- Photolysis
- Oxidation
- Biodegradation
- Volatility

Additional Contributors

- Matrix-Related Factors
  - pH
  - Total Organic Carbon
  - Water Hardness
  - Salinity



- Water can vary between labs – all freshwater is not the same

- It's important to note that **functional solubility <u>within an exposure system</u>** is often quite different than reported solubility (e.g., shake-flask)

Examples of 'Difficult-to-Test' Substances




- Pesticide AI's and formulations
- Pharmaceuticals
- Personal Care Products
- Petroleum distillates
- Complex mixtures
- UVCBs

Delivery Methodologies

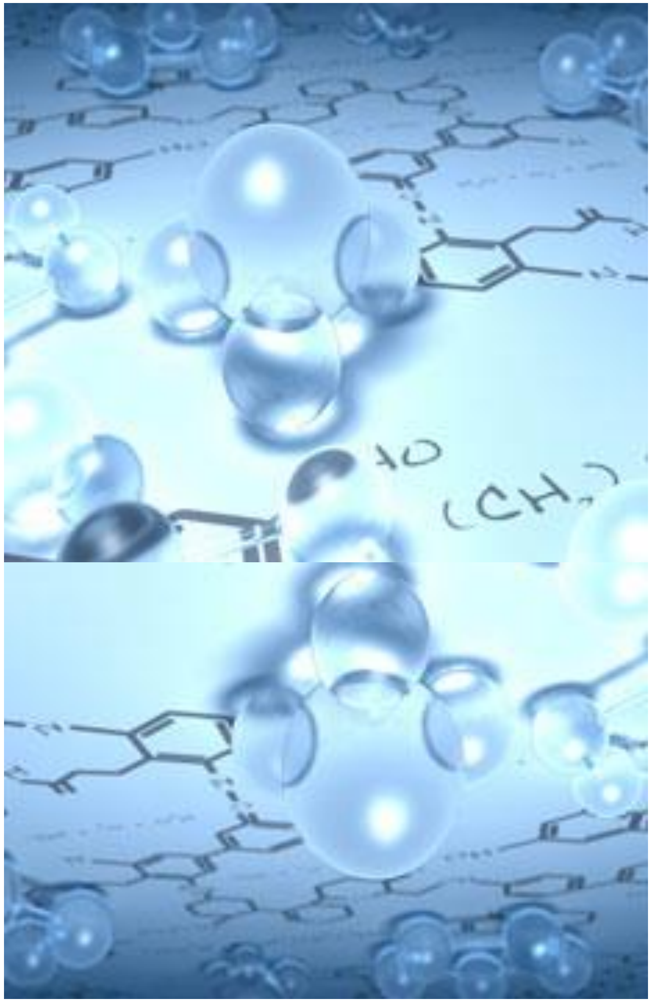
- The use of carrier solvents, up to 100 µL/L, is acceptable under the guidelines, but there are potential confounding issues resulting from their use, especially during chronic exposures.
  - Biofilms
  - Statistical comparisons

Non-solvent options for delivery:

- Direct addition
- Water Accommodated Fraction (WAF)
- Saturator systems:
  - Glass wool saturator columns
  - Solid-liquid saturator (slow-stir)
  - Liquid-liquid saturator (slow-stir)
  - Passive dosing methods
- Each of these methods has limitations and can require resources to explore options


CASE STUDY

Model Compound – broad-spectrum fungicide



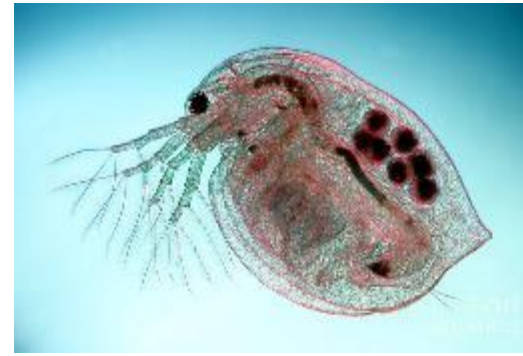
Test Substance Characteristics	
Physical State:	Solid Powder
Water Solubility:	1.8 mg/L (low solubility)
Solvent Solubility:	190 g/L in acetone
Log Pow:	4.14
:	pKa1 = < 0 (acidic) pKa2 = 14 (basic)
Aqueous Hydrolysis:	Stable at pH 5, 7 and 9
Aqueous Photolysis:	DT_{50} = 10 days at pH 7
Vapor Pressure:	3.9 x10^{-7} Pa at 25°C (non-volatile)

Existing Data (1991 – 2011)

Study Type	Year	Solvent Type	Solvent Load (µL/L)	High Dose (µg/L)	Percent Recovery	Perceived Solvent Effects?	Repeat Required?
Daphnia Acute	1993	Acetone	1000	5000	38	No	No
Daphnia Life Cycle	1991	Acetone	17	320	59	Yes	Yes
FHM Early Life-Stage	1992	Acetone	18	300	90	Yes	Yes
FHM Early Life-Stage	1994	Acetone	280	150	96	Yes	Yes
SHM Early Life-Stage	2011	DMF	100	625	92	Yes	Yes

Evaluating Test Design & Generating New Data

Daphnia Magna Life-Cycle



- Data considered:
- Hydrolytically stable = semi-static design
- Toxicity and solubility data derived from previous studies

- Benchtop solubility in DI water
  - 1000 µg/L nominal yielded 600 µg/L

- Highest recovery in test water = 35 µg/L
  - Test water = hard water

- Concentrations considerably less than water solubility (1800 µg/L)

Mysid & Fish Studies (2014)

Updated Delivery Method:

- Data considered:
  - Saturator column suitable for log Kow >2.75
  - Column trial:
    - Measured **1800 µg/L** (freshwater)
      1300 µg/L (saltwater)
    - Column life: **≥ 30 days**

Study Type	High Dose (µg/L)	Mean Measured Dose (µg/L)	Percent Recovery
Mysid Life Cycle	80	96	120
SHM Early Life Stage	300	330	110
FHM Life Cycle	90	86	96

- ***Avoided solvent-related effects***

Lessons Learned

Using solvent may save time and money upfront, however...

- Solvent effects (*or the perception of effects*) can be difficult to avoid

- Costs are increased with repeating studies
  - Cost for repeating *Daphnia* and chronic fish studies for this DCI: **~$120,000**

  - Cost for developing saturator column data: **~$7,000**

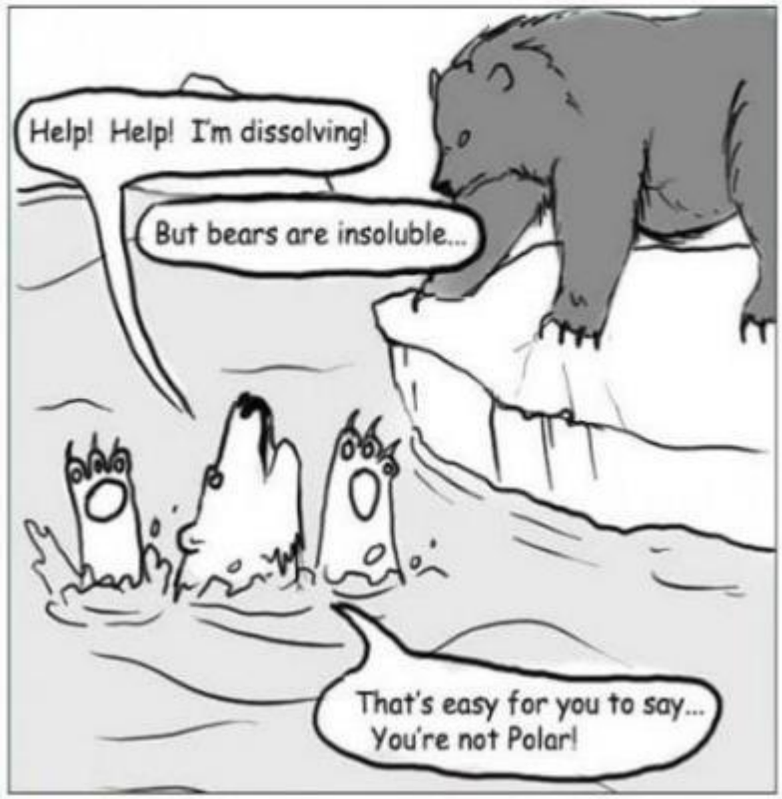
Additional Considerations

- Limitations of non-solvent delivery
  - Some methods not practical for every compound

- Importance of benchtop lab trials
  - Can result in additional costs, but the trade-off is worthwhile

- When would a saturator column not be appropriate?
  - Some compounds can be challenging due to highly variable column output
  - Liquids, especially hydrocarbons are not good candidates, but other methodologies are available

- Sometimes solvent use is unavoidable, but use must be considered carefully



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Thank You…

Questions?

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