Proposal for an Integrated Assessment Strategy for Aquatic and Terrestrial Bioaccumulation

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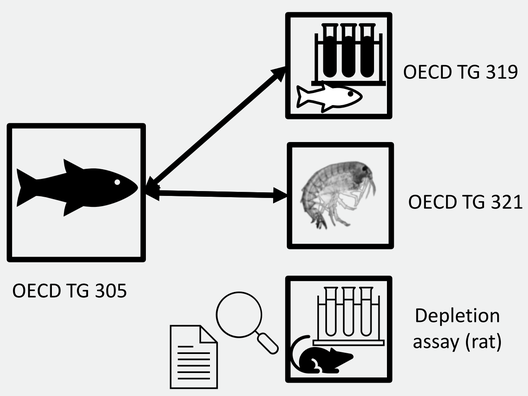
Background

Across the regulatory frameworks (REACH, Biocidal Products Regulation (BPR), Plant Protection Products Regulation (PPPR), and regulations concerning human and veterinary medicinal products), the regulatory landscape shows consistent reliance on fish bioaccumulation testing despite the availability of validated non-vertebrate and in vitro approaches. This reveals lack of certainty among the regulatory community and industry about applicability domains, advantages and disadvantages of the available New Approach Methodologies (NAMs). Also, there are vast differences among the EU chemical regulations in data requirements and the possibility to use other/additional data for hazard or risk assessment in a Weight of Evidence approach (WoE).

Thus, the German Environment Agency had initiated a project to develop an *Integrated Assessment Strategy for Aquatic and Terrestrial Bioaccumulation* (Figure 1) and to evaluate whether the NAMs for aquatic bioaccumulation assessment are fit for use in regulatory decision making.

Test systems



Test data for 26 substances were collected and compared: Fish in vivo, fish in vitro and *Hyalella azteca* in vivo BCFs. Existing test data as well as tests performed within the project were used (Table 1).

The usability of the rat depletion assay to evaluate the bioaccumulation potential in air breathers for some substances was evaluated.

Lessons learned

NAMs are well suited for reliably assessing bioaccumulation potential within their domain of applicability, thus reducing need for vertebrate testing. Nonetheless, the data also show the importance of critical evaluation of all test results, expert judgement, and the need to consider all available data in a WoE evaluation.

Variability: Physico-chemical data (e.g. log K_{OW}), which decide whether a substance needs a B-assessment, can vary *substantially* (*cf*. poster 3.01.P-Mo143).

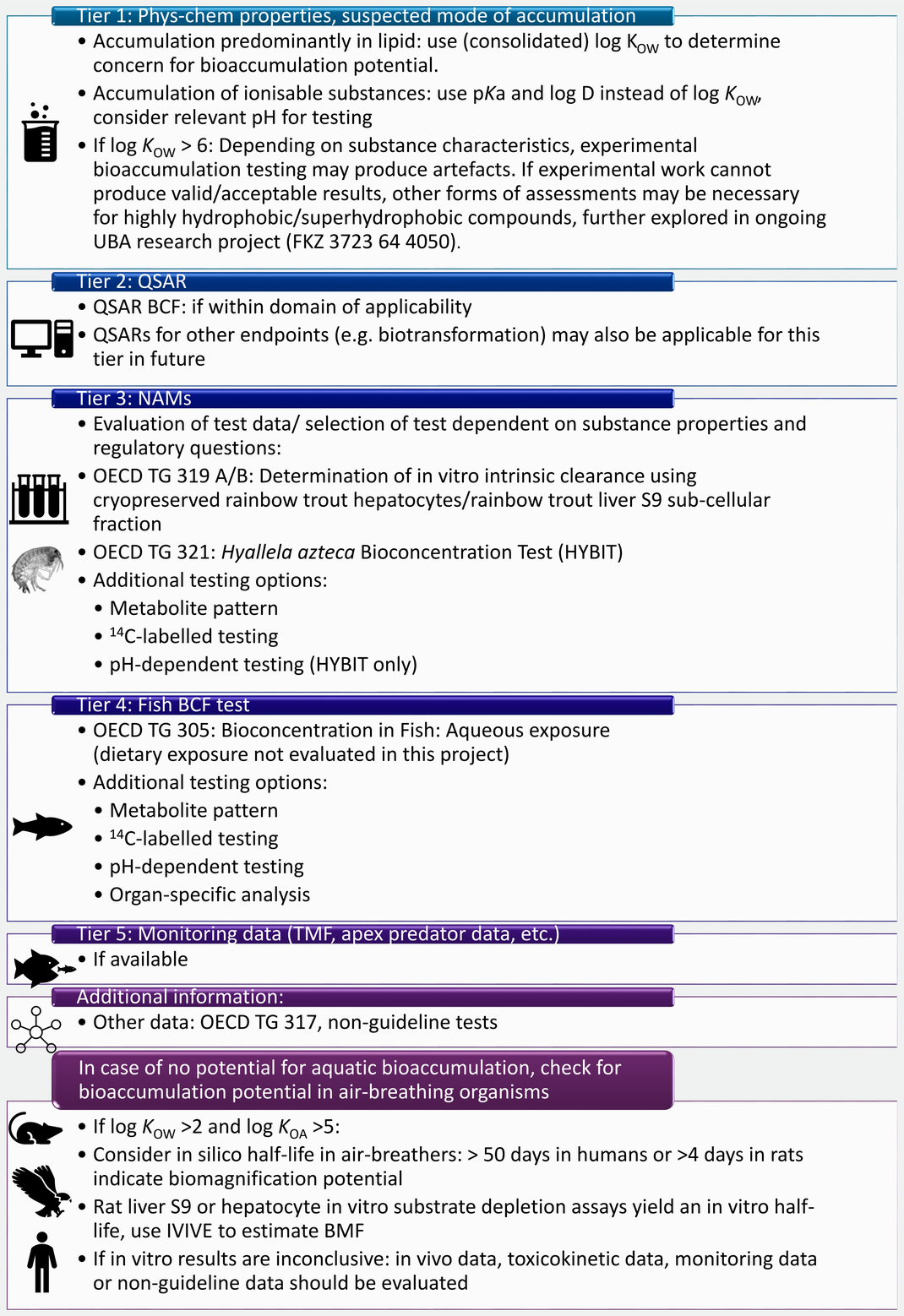
Fish in vitro (OECD TG 319 A/B): If no biotransformation can be determined in a substrate depletion assay, it may be unclear if the substance does not biotransform or if the assay conditions were not suitable for the test substance. Also, the IVIVE BCF is solely based on the IVIVE model, its parameterisation and the substance-specific input data (e.g. log K_{OW}).

Table 1: Data set of the 26 chemicals

		Water breathing organisms						Air breathing organisms
		Tier 1		Tier 2	Tier 3		Tier 4	
Substance name	CAS	Consolidated log K_{OW}	Consolidated log K_{OA}	Mean fish QSAR BCF	IVIVE BCF	HYBIT BCF	Experimental fish BCF range	IVIVE BMF (rat)
Simazine	122-34-9	2.12	8.94	10	7	9	1 - 214	
Azoxystrobin	131860-33-8	3.00	13.9	58	34	5	N/A	
Terbutryn	886-50-0	3.41	9.83	33	50	46	9 - 44	
17a-Ethinylestradiol	57-63-6	3.84	13.6	249	324	47	269 - 331	
β-Hexachlorocyclohexane	319-85-7	3.87	7.59	814	367	887	293 - 1460	24
Prochloraz	67747-09-5	3.91	12.2	696	399	185	197 – 393	
Fluorene	86-73-7	4.06	6.69	781	374 (HEP) 433 (S9)	285	58 - 1288	
Anthracene	120-12-7	4.41	7.44	1252	647 (HEP) 698 (S9)	1800	191 - 6000	
Phenanthrene	85-01-8	4.43	7.45	1436	662 (S9) 799 (HEP)	465	708 - 6118	
Chlorpyrifos	2921-88-2	4.89	9.47	934	509	1163	40 - 3162	0.08
Pyrene	129-00-0	4.91	8.75	1618	144	3050	50 - 1351	0.773
Triclosan	3380-34-5	4.91	11.08	1553	146	N/A	1 - 1995	
Octamethylcyclo-tetrasiloxane (D4)	556-67-2	4.98	4.13	1679	1935	test failed	5012 - 14900	test failed
Trifloxystrobin	141517-21-7	5.08	11.2	579	672	568	372 - 537	
Pentachlorobenzene	608-93-5	5.11	6.53	6603	5499	1913	3981 - 22909	
Methoxychlor	72-43-5	5.25	10.6	2623	1928 (S9) 3404 – 3765 (HEP)	9396	621 - 8300	1.5
o-terphenyl	84-15-1	5.58	8.80	3555	test failed	6086	501 - 12882	
Benzo[a]pyrene	50-32-8	6.07	11.0	3669	787	3911	3 - 631	
PCB 153	35065-27-1	7.08	10.0	195265	13596	155373	8913 - 740000	
UV-234	70321-86-7	7.68	15.32	5761	7464	1670	1286	4 - 33
Ionisable substances								
Fluoxetine	54910-89-3	4.33	10.0	323	0 - 1040	19 - 348	13 - 330	
Diclofenac	15307-86-5	4.35	12.9	376	0 - 944	3 - 73	5 - 9	0 – 0.12
Pentachlorophenol	87-86-5	4.81	9.31	835	14 - 2976	132	195 - 479	
Substances not applicable to schemes 1 & 2								
GenX	62037-80-3	3.26	5.09	5.4	91	7	1 - 8	
PFOS	1763-23-1	4.42	5.81	91.3	N/A	302	255 - 5400	
Lauric acid	143-07-7	4.84	8.51	238	N/A	6	255	

BCF Classification
BCF <100
BCF 100-500
BCF 500-1000
BCF 1000-2000
BCF 2000 - 5000
BCF >5000

Figure 1: Proposal for an *Integrated Assessment Strategy for Aquatic and Terrestrial Bioaccumulation*



HYBIT (OECD TG 321): Available HYBIT data reflect the results of data used for regulatory decisions. Metabolic differences of *H. azteca* to fish are visible for PAHs.

Depletion assay (rat): It was demonstrated that for air-breathing organisms, in vitro biotransformation data from rat hepatocytes or S9 fractions can be generated in analogy to OECD TG 319 A/B. Refinement and validation of the rat assays are necessary.

Current limitations:

Difficult substances like superhydrophobic chemicals, ionisables and surfactants require extra care in evaluation to avoid misinterpretation of test data → Applicability domain!

Way forward:

For the rat in vitro tests, the estimation of a BMF through IVIVE models needs further development. Also, an agreed OECD test guideline for air-breathing organisms (rodents and possibly bird and human cell lines) would be helpful for regulatory application.

NAMs for regulatory bioaccumulation assessment are ready be integrated into the different substance regulations, also beyond REACH, to reduce reliance on animal testing while maintaining the same level of protection as current EU regulatory approaches.

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