

Abstract

Bioaccumulation potential of chemicals is typically assessed from bioconcentration, conventionally measured according to Test Guideline (TG) [OECD 305](#). This study type is a regulatory requirement for a chemical with properties that suggest that it has the potential to bioaccumulate, i.e., $K_{ow} \geq 3.0$ and when its use may result in the exposure of aquatic organisms to the test chemical in aquatic environments. Historically, the test is performed by exposing a group of fish to the test substance at two concentrations in a flow-through test system. The new revised TG (October 2012), consistent with the three R's, has proposed the use of a single exposure concentration in order to use fewer fish primarily for animal welfare reasons. However, the revised design is more cost-effective as well. This presentation is a comparative analysis of data to demonstrate that for many classes of compounds, the bioconcentration factor (BCF) is independent of exposure concentration and confirm that one exposure concentration is a scientifically-sound method to determine a fish BCF.

Introduction

- BCF study results are typically used in the assessment of the PBT criteria for pesticides, biocides, human and veterinary products
- The OECD, the US EPA/ OCSPP, and JMAFF provide test guidelines for fish BCF assessment.
- Testing involves two phases: an exposure or uptake phase where fish are exposed to the chemical in water and a depuration phase when the fish are transferred to clean water, free of the chemical in a flow-through test system.
- Study is typically performed with ^{14}C -labeled test compound and the resulting BCF is calculated based on total radioactive residue (TRR).
- BCF can also be calculated based on test compound concentration in water and fish.
- Most Test Guidelines require two exposure concentrations, resulting in the use of large numbers of fish.
- The new revised TG (October 2012) OECD 305 has proposed the use of a single exposure concentration in order to use fewer fish.
- Creton et al. (2012) provided an analysis for supporting the use of single exposure concentration for plant protection product (PPP) active substances.
- This poster provides additional supporting evidence by looking at thirty-three active pharmaceutical ingredients (APIs) and PPPs.
- By using a single exposure concentration, the number of fish will be reduced by over 30 percent.

Materials and Methods

- Data for studies performed at Smithers Viscient since 2007 were collected from archived final reports.
- BCF values (whole body, TRR and lipid-normalized) were retrieved from reports and tabulated for analysis.
- Data were available from a total of 33 studies of which 4 did not have a calculated BCF value due to rapid degradation of test substance and 2 used only one test concentration and these were therefore excluded.
- The remaining 29 datasets were comprised of 23 pharmaceutical ingredients (API) and 4 pesticides (PPP).
- All pesticides and 20 pharmaceutical studies were conducted using bluegill sunfish while 3 pharmaceutical experiments used rainbow trout.
- Statistical analyses were performed using Minitab™ software package, version 16.2.3.

Results and Discussion

- Figure 1 shows the linear relationship between low and high concentration BCF values based on whole body (A) total radioactive residue (TRR), (B) parent concentration and (C) lipid-normalized.
- In all cases the high exposure concentration BCF is a strong predictor of the low concentration BCF (p -value<0.001).
- The largest difference was observed for TRR of API 20, with a 1.4-fold difference in BCF between the low and high concentration.
- The calculated TRR-based BCF for API 7 was similar for both low and high concentration; but the BCF calculated from parent radioactivity had a 1.4-fold difference, indicating a higher uptake of parent material at high concentration.



Example of a flow-through diluter system

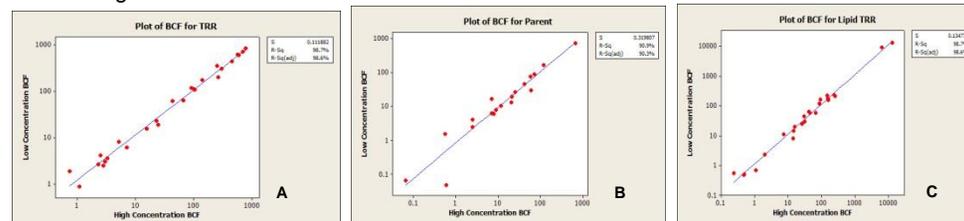


Figure 1: Relationship between BCF values from low and high exposure concentrations for whole body (A) TRR, (B) parent concentration and (C) lipid-normalized

Conclusions

- The dataset for this analysis included pharmaceutical and pesticide active ingredients differing in physico-chemical properties and tested using bluegill sunfish and rainbow trout species likely of different size and lipid content.
- There was no indication of a concentration dependency of BCF values for API or PPP active ingredients.
- Therefore, one exposure concentration is scientifically sufficient to assess bioconcentration in fish for API or PPP active ingredients, supporting the recent revision of OECD test guideline 305.

Test material	Fish Species	Low Concentration	High Concentration	Low Concentration BCF			High Concentration BCF			Log BCF	
		(µg/L)	(µg/L)	TRR	Parent	Lipid BCF	TRR	Parent	Lipid BCF		
API 1	Bluegill Sunfish	25.0	250.0	7.98	0.0473	10.9	0.90	5.11	0.594	7.42	0.71
API 2	Bluegill Sunfish	0.8	8.0	15.5	10.5	14.2	1.19	15.5	11.5	14.6	1.19
API 3	Bluegill Sunfish	6.0	60.0	22.8	11	43.8	1.36	23.1	14.8/19.0	30.8	1.36
API 4	Bluegill Sunfish	20.0	200.0	1.88	1.51	0.55	0.27	0.74	0.55	0.24	-0.13
API 5	Bluegill Sunfish	15.0	150.0	4.08	4.08	62.3	0.61	2.5	2.5	42.4	0.40
API 6	Bluegill Sunfish	0.01	0.03	200	0.0665	214	2.30	265	0.0651	253	2.42
API 7	Rainbow Trout	2.0	20.0	6336	3534	145444	3.80	6336	4931	181871	3.80
API 8	Rainbow Trout	0.13	1.3	625	30	181	2.80	576	60	153	2.76
API 9	Bluegill Sunfish	8.0	80	61	8	20	1.79	43	9	16	1.63
API 10	Rainbow Trout	0.20	2.0	308	76	9053	2.49	302	58	6522	2.48
API 11	Bluegill Sunfish	5.0	50.0	6.16	6.14	153	0.79	7.05	6.97	161	0.85
API 12	Bluegill Sunfish	0.85	8.5	439	ND	12900	2.64	454	ND	13300	2.66
API 13	Rainbow Trout	1.0	10	110	88	57	2.04	103	71	67	2.01
API 14	Bluegill Sunfish	1.3	13.0	119	19.4	117	2.08	91.4	21.4	87.2	1.96
API 15	Bluegill Sunfish	0.8	8.0	858	719	169	2.93	776	672	163	2.89
API 16	Bluegill Sunfish	10.0	100.0	2.47	2.47	0.486	0.39	2.79	2.5	0.478	0.45
API 17	Bluegill Sunfish	0.2	1.8	3.54	ND	2.34	0.55	3.25	ND	2.05	0.51
API 18	Bluegill Sunfish	30.0	300.0	0.862	ND	NA	-0.06	1.07	ND	ND	0.03
API 19	Bluegill Sunfish	3.0	30.0	2.6	ND	0.5	0.41	2.3	ND	0.5	0.36
API 20	Bluegill Sunfish	0.5	5.0	357.9	164.7	162	2.55	253.4	119.9	92.3	2.40
API 21	Bluegill Sunfish	0.4	4.0	19.1	12.9	8.2	1.28	24.3	20.5	14.4	1.39
API 22	Bluegill Sunfish	0.01	0.04	107.1	16.7	25.1	2.03	104.9	7.1	26.6	2.02
API 23	Bluegill Sunfish	0.5	5.0	3.0	ND	0.7	0.48	3.0	ND	1.1	0.48
PPP 1	Bluegill Sunfish	1.0	10.0	174	26	57	2.24	140	25	45	2.15
PPP 2	Bluegill Sunfish	0.1	0.3	612	NA	232	2.79	600	NA	235	2.78
PPP 3	Bluegill Sunfish	1	10	63	6.0	30	1.80	66	8.0	32	1.82
PPP 4	Bluegill Sunfish	0.1	0.3	712	45	226	2.85	694	42	151	2.84

Table 1: Fish bioconcentration studies conducted at two exposure concentrations retrieved from Smithers Viscient archived final reports

ND - not determined