Propyl 4-Hydroxybenzoate (Propyl Paraben) (CAS no. 94-13-3)

Tier 1 *in vivo* Test

(1) Results

Fish were exposed to concentrations of 0.311, 0.926 and 2.94mg/L (measured). No significant differences were observed in male and female mortality, total length, body weight, gonadosomatic index, hepatosomatic index and secondary sex characteristics.

At 0.311mg/L and higher, a significant increase was observed in male hepatic vitellogenin level.

At 0.926mg/L and higher, a significant decrease was observed in number of fertile eggs.

A significant decrease was observed in number of eggs and fertility rate while a significant increase in female hepatic vitellogenin level was observed at 2.94mg/L.

(2) Summary

Estrogenic activity of propyl 4-hydroxybenzoate (propyl paraben) has been indicated from literature.

In this study, an increase in male hepatic vitellogenin level was observed at sublethal concentrations indicating its estrogenic effect. It was concluded that propyl 4-hydroxybenzoate (propyl paraben) is an estrogenic compound.

A significant decrease in number of fertile eggs at 0.926mg/L and higher, and a significant decrease in number of eggs and fertility rate at 2.94mg/L, were considered adverse reproductive effects on Medaka.

The adverse exposure level of 0.926mg/L was ca. 58,000 times as high as the highest environmental water concentration of 0.016μg/L that was measured in MOE's Environmental Survey and Monitoring of Chemicals in FY2012.

The non-adverse exposure level of 0.311mg/L was ca. 19,000 times as high as the highest environmental water concentration of 0.016μg/L that was measured in MOE's Environmental Survey and Monitoring of Chemicals in FY2012.

Table 1-A Results

Measured concentration (mg/L)	Number of fish		Mortality (%)		Total length (mm)		Body weight (mg)	
	male	female	male	female	male	female	male	female
Control	12	12	0	8.3	36.8±0.6	36.1±0.7	536±33	520±19
0.311	12	12	0	0	36.4±1.3	36.1±0.2	525±13	525±27
0.926	12	12	0	0	37.1±1.7	36.8±0.8	515±49	539±21
2.94	12	12	0	0	36.5±0.9	36.5±1.5	490±26	549±83

Table 1-B Results (continued)

Measured concentration (mg/L)	Number of eggs (eggs/female/day)	Number of fertile eggs (eggs/female/day)	Fertility rate (%)	Gonadosomatic Index (%)	
				male	female
Control	26.1±1.0	25.1±0.7	96.0±1.0	0.79±0.076	9.7±1.2
0.311	28.3±1.6	26.3±0.8	93.0±3.1	0.74±0.14	10±0.16
0.926	23.4±2.0	21.8±1.6 *	93.5±3.7	0.78±0.053	9.9±1.1
2.94	10.3±4.7 *	4.9±4.1 *	40.8±22.7 *	0.81±0.21	10±1.1

Table 1-C Results (continued)

Measured concentration (mg/L)	Hepatosomatic Index (%)		Vitellogenin (ng/mg liver)		Secondary sex characteristics	
	male	female	male	female	male	female
Control	2.1±0.26	5.0±0.43	ND	1,170±71.6	125±7.8	0±0
0.311	2.7±0.98	5.4±0.75	23.7±9.0 *	1,190±238	125±3.8	0±0
0.926	2.7±0.23	5.1±0.20	42.2±36.8 *	1,590±271	127±15	0±0
2.94	2.3±0.14	4.3±0.77	4,170±513 *	3,540±1,080 *	125±8.0	0±0

Table 1-D Results (continued)

Measured concentration (mg/L)	Other observations
Control	Not found
0.311	Not found
0.926	Not found
2.94	Day 1 of exposure: Excitement and loss of equilibrium (1-2 fish per vessel) After Day 2 of exposure: Long-term dwelling at bottom of vessel, long-term floating near the water surface and light discoloration (1-2 fish in total of all four vessels)

Data show mean ± SD (standard deviation)
Statistically significant differences from control group (**p<0.01, *p<0.05)
nd: not detected (below detection limit of vitellogenin: 1ng/mg liver)
(-): not measured
Secondary sex characteristics: number of joint plates with papillary processes