

Supplementary file 4: Threshold of Toxicological Concern (TTC)

Table S4: TTC approach for the 13 flavorings with insufficient toxicological data to apply an MoE approach

Substance name	TTC		Substance concentration in e-liquids according to EU-CEG (mg/mL)		Daily dose scenario 4 (µg/kg bw/dag)		Daily dose scenario 3 (µg/kg bw/dag)		Daily dose scenario 2 (µg/kg bw/dag)		Daily dose scenario 1 (µg/kg bw/dag)	
	(µg/person/day)	TTC ¹ (µg/kg bw/day)	Median	Maximum	Median	Maximum	Median	Maximum	Median	Maximum	Median	Maximum
Damascenone	1800	25.71	0.03	36.99	2.60	3698.63	0.72	1023.29	0.31	447.69	0.16	223.85
beta-Damascone	1800	25.71	0.54	10.94	54.00	1094.40	14.94	302.79	6.54	132.47	3.27	66.23
(E)-beta-Damascone	1800	25.71	0.14	8.40	14.09	839.50	3.90	232.26	1.71	101.62	0.85	50.81
(Z)-beta-Damascone	1800	25.71	0.10	0.92	10.40	92.16	2.88	25.50	1.26	11.16	0.63	5.58
Keto-isophorone	540	7.71	0.03	0.72	3.00	71.73	0.83	19.84	0.36	8.68	0.18	4.34
(E)-beta-Damascenone	1800	25.71	0.12	4.22	11.55	422.00	3.20	116.75	1.40	51.08	0.70	25.54
Isovaleric acid	1800	25.71	0.00	1.58	0.18	158.20	0.05	43.77	0.02	19.15	0.01	9.57
2-Hydroxy-3,5,5-trimethyl-2-cyclohexenone	540	7.71	0.52	4.10	51.98	410.09	14.38	113.46	6.29	49.64	3.15	24.82
3-Acetylpyridine	540	7.71	0.08	0.36	8.31	36.38	2.30	10.07	1.01	4.40	0.50	2.20
2,6-Dimethoxyphenol	1800	25.71	0.02	0.46	1.78	46.10	0.49	12.75	0.22	5.58	0.11	2.79
Ambroxide	90.00	1.29	0.00	0.32	0.26	31.99	0.07	8.85	0.03	3.87	0.02	1.94
3-Ethylpyridine	540	7.71	0.00	0.20	0.05	20.00	0.01	5.53	0.01	2.42	0.00	1.21
(3aR)-(+)-Sclareolide	90.00	1.29	0.00	0.25	0.10	25.00	0.03	6.92	0.01	3.03	0.01	1.51

¹ The daily dose is used to calculate a dose relative to body weight (bw) by using an average body weight of 70 kg.

Numbers in bold indicate for which scenario, substance and concentration in the e-liquid there may be a health risk concern.