

Supplementary Table 4. Analysis of Biomarkers of Exposure – THS and Dual Use vs. Cigarette Smoking.

Biomarker of Exposure	Time Point	LS Means (95% CI)			LS Means Ratio / Difference** (95% CI)	
		THS	Dual Use	Cigarette Smoking	THS vs. Cigarettes	Dual Use vs. Cigarettes
MHBMA (pg/mg creat.)	Baseline*	1887 (1615 ; 2206)	1805 (1482 ; 2199)	2043 (1831 ; 2281)	----	----
	Month 3	1054 (916 ; 1214)	1654 (1397 ; 1957)	1981 (1757 ; 2234)	53.2 (46.4 ; 61.0)	83.5 (70.7 ; 98.6)
	Month 6	1125 (965 ; 1311)	1714 (1423 ; 2063)	1970 (1735 ; 2237)	57.1 (48.9 ; 66.7)	87.0 (72.0 ; 105)
3-HPMA (ng/mg creat.)	Baseline*	1254 (1146 ; 1372)	1358 (1209 ; 1525)	1314 (1231 ; 1404)	----	----
	Month 3	878 (814 ; 948)	1201 (1090 ; 1324)	1300 (1277 ; 1379)	67.5 (61.7 ; 74.0)	92.4 (82.8 ; 103)
	Month 6	951 (874 ; 1035)	1175 (1054 ; 1310)	1268 (1190 ; 1352)	75.0 (67.7 ; 83.0)	92.6 (82.0 ; 105)
Total NNN (pg/mg creat.)	Baseline*	8.73 (7.50 ; 10.2)	11.8 (9.43 ; 14.7)	10.5 (9.34 ; 11.9)	----	----
	Month 3	5.43 (4.53 ; 6.50)	7.42 (5.97 ; 9.21)	8.14 (7.00 ; 9.48)	66.7 (55.5 ; 80.0)	91.1 (73.0 ; 114)
	Month 6	5.11 (4.25 ; 6.14)	7.66 (6.14 ; 9.56)	8.63 (7.41 ; 10.1)	59.2 (49.1 ; 71.4)	88.8 (70.8 ; 111)
CEMA (ng/mg creat.)	Baseline*	160 (143 ; 178)	179 (159 ; 202)	168 (155 ; 182)	----	----
	Month 3	81.4 (72.9 ; 90.8)	149 (130 ; 172)	170 (156 ; 184)	48.0 (42.1 ; 54.7)	88.2 (75.4 ; 103)
	Month 6	81.5 (71.4 ; 93.0)	143 (121 ; 170)	158 (143 ; 175)	51.4 (43.8 ; 60.3)	90.2 (74.5 ; 109)
3-OH-B[a]P (fg/mg creat.)	Baseline*	161 (147 ; 176)	165 (147 ; 186)	159 (149 ; 170)	----	----
	Month 3	113 (101 ; 127)	159 (139 ; 181)	160 (144 ; 177)	70.7 (63.9 ; 78.1)	99.1 (87.7 ; 112)
	Month 6	116 (103 ; 131)	150 (130 ; 173)	160 (144 ; 178)	72.7 (65.2 ; 81.1)	94.0 (82.3 ; 107)
3-HMPMA (ng/mg creat.)	Baseline*	303 (279 ; 330)	320 (285 ; 358)	317 (297 ; 339)	----	----
	Month 3	198 (180 ; 217)	299 (268 ; 334)	310 (288 ; 335)	63.8 (57.8 ; 70.4)	96.4 (85.6 ; 109)
	Month 6	218 (199 ; 240)	290 (258 ; 325)	305 (283 ; 329)	71.6 (64.6 ; 79.3)	94.9 (83.8 ; 107)
Total 1-OHP (pg/mg creat.)	Baseline*	291 (268 ; 315)	301 (270 ; 336)	279 (261 ; 298)	----	----
	Month 3	226 (205 ; 248)	279 (248 ; 313)	286 (264 ; 310)	78.9 (71.4 ; 87.2)	97.4 (86.2 ; 110)
	Month 6	229 (207 ; 254)	266 (235 ; 301)	273 (252 ; 297)	83.8 (75.1 ; 93.4)	97.4 (85.4 ; 111)
Neq (mg/g creat.)	Baseline*	9.20 (8.36 ; 10.1)	10.3 (9.22 ; 11.4)	10.1 (9.41 ; 10.7)	----	----
	Month 3	9.11 (8.51 ; 9.75)	9.15 (8.38 ; 9.98)	9.46 (8.98 ; 9.97)	96.2 (88.8 ; 104)	96.6 (87.7 ; 107)
	Month 6	8.92 (8.22 ; 9.67)	8.34 (7.51 ; 9.26)	8.86 (8.34 ; 9.42)	101 (91.2 ; 111)	94.1 (83.6 ; 106)
CO exhaled (ppm)	Baseline*	21.9 (20.4 ; 23.5)	24.4 (21.8 ; 27.1)	23.6 (22.3 ; 25.0)	----	----
	Month 3	15.0 (12.9 ; 17.1)	19.9 (17.5 ; 22.3)	20.5 (18.7 ; 22.4)	-5.50 (-7.24 ; -3.77)	-0.642 (-2.76 ; 1.47)
	Month 6	16.7 (12.4 ; 21.1)	19.7 (14.0 ; 25.3)	24.1 (20.7 ; 27.5)	-7.37 (-12.5 ; -2.22)	-4.46 (-10.7 ; 1.81)

* Geometric Means in case of Baseline of MHBMA, 3-HPMA, Total NNN, CEMA, 3-OH-B[a]P, HMPMA, Total 1-OHP, Neq, ordinary means in case of CO exhaled.

** LS Mean Ratios in case of MHBMA, 3-HPMA, Total NNN, CEMA, 3-OH-B[a]P, 3-HMPMA, Total 1-OHP, Neq.

LS Mean Differences in case of CO exhaled.

MHBMA = monohydroxybutenylmercapturic acid; 3-HPMA = 3-hydroxypropylmercapturic acid, Total NNN = total N-nitrososnormicotine, CEMA = 2-cyanoethylmercapturic acid, 3-OH-B[a]P = 3-hydroxybenzo(a)pyrene, 3-HMPMA = 3-hydroxy-1-methylpropylmercapturic acid, Total 1-OHP = total 1-hydroxypyrene, Neq = nicotine equivalents, CO exhaled = carbon monoxide exhaled.

THS refers to predominant THS use of 70% or more; Dual Use refers to THS use of less than 70% and at least 1%; Cigarette Smoking refers to THS use of less than 1%.

Visit 7 and Visit 10 data represent Months 3 and 6, respectively.