An Open-Label Clinical Study to Evaluate Selected Constituents in Exhaled Breath and Room Air after the Use of Vapor Products and Conventional Cigarettes under Conditions of Residential, Office and Hospitality Environments

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Objective

This study evaluated the contents and quantity of the exhaled breath and secondhand emissions profiles of two vapor products (JUUL Nicotine Salt Pod System, "NSPS", Virginia Tobacco flavor, 5%; VUSE SOLO Original Flavor, 4.8%), and the subjects' usual combusted cigarette.

The purpose was to assess comparative environmental effects of the different products. NSPS is temperature-regulated and does not have a burning tip continuously emitting smoke; we hypothesized that NSPS would emit lower levels of toxicants vs. cigarettes.

Methods

Thirty adult smokers (≥10 cigarettes per day) were equally allocated into three groups, based on the sequential order of recruitment.

Three environments were constructed that provided representative air exchange rates for residential, office, and hospitality settings. Each group of 10 subjects used one product in each of the 3 different settings over a 3-week period (Figure 1).

Analytes contained in the room atmosphere and exhaled breath were characterized and quantified through dedicated collection systems. Products were evaluated under *ad libitum* (all products) and stereotyped puffing use (vapor products) conditions for 4 hours in each environment and room air samples were compared to baseline (sham) conditions. Select analytes were also measured in exhaled breath samples taken during a 10-puff stereotyped inhalation session; content was compared to that of samples from sham product inhalation sessions.

Figure 1: Testing Sequence Per Arm

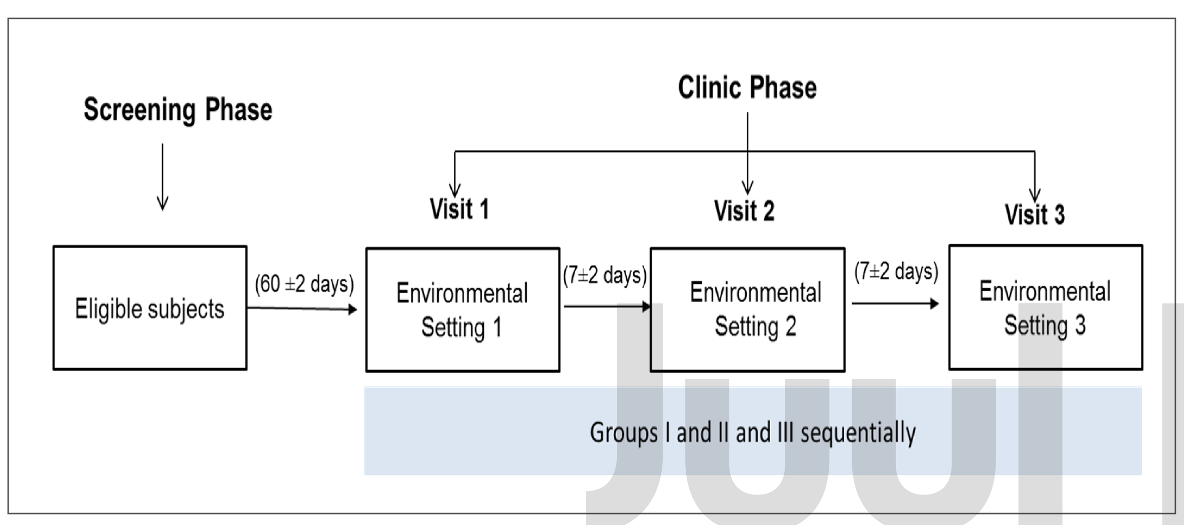

Table 1: Change in Respirable Particles in Room Air

Particle Diameter (uM)	Setting	Group I Stereotyped	Group I Ad Lib	Group II Stereotyped	Group II Ad Lib	Group III Ad Lib
>0.3-1.0	Residential	60,190	86,038	(NA*)	(NA)	815,578
	Office	28,117	16,798	115,856	67,704	760,487
	Hospitality	31,976	45,439	87,726	23,872	656,673
>1.0-2.5	Residential	1,832	1,720	(NA)	(NA)	5,700
	Office	550	171	13,069	2,727	2,296
	Hospitality	654	443	4,716	744	2,286
>2.5-3.0	Residential	82	73	(NA)	(NA)	176
	Office	20	6	760	186	43
	Hospitality	28	18	233	44	53
>3.0-5.0	Residential	91	80	(NA)	(NA)	163
	Office	22	5	878	246	29
	Hospitality	24	20	254	58	42
>5.0-10.0	Residential	16	12	(NA)	(NA)	20
	Office	5	(1)	118	40	1
	Hospitality	3	4	33	10	5

NOTES: Particle counts are expressed as 1000's per m^3.
*Group II data for residential setting was not available

Results – Exhaled Breath

Nicotine and propylene glycol were elevated in exhaled breath for each product (Figure 2). After cigarette use, formaldehyde and carbon monoxide were consistently elevated ($p<0.05$). Comparatively, mean changes in formaldehyde and carbon monoxide in exhaled breath were reduced by 99% or more with vapor products vs. cigarettes (Figure 3).

Results – Room Air

Concentrations of respirable particles (≤2.5um) were elevated in every environment and product combination (Table 1). The mean elevation in concentration of respirable particles was lower with NSPS vs. cigarettes (89% lower in residential, 98%, lower in office, and 93% lower in hospitality environments) In addition, NSPS emissions cleared more quickly than comparator vapor product and cigarettes.

Elevations in secondhand room air nicotine were 91%-95% lower following ad libitum NSPS use vs. cigarettes. Concentrations of trace metals in room air were below the level of quantification for all products. Formaldehyde and acetaldehyde were consistently elevated in all settings following cigarette use; these values were reduced with NSPS on average 99% in residential, 98% in office, and 100% in hospitality settings. Six VOC's (1.3-butadiene, benzene, toluene, isoprene, furan and ethylbenzene) were consistently elevated in all settings with cigarettes (Table 2). These values were reduced with NSPS (Figure 4) by 96% in residential, 91% in office, and 87% in hospitality settings, following ad libitum use.

Conclusion

Across a range of simulated environments, use of NSPS resulted in lower concentrations of respirable particles vs. cigarettes in room air samples. Use of either vapor product resulted in lower emissions of key toxicants compared to combustible cigarette use, as measured in both exhaled breath and room air samples.

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Figure 2: Change in Content of Exhaled Breath Samples After *Ad Libitum* Product Use

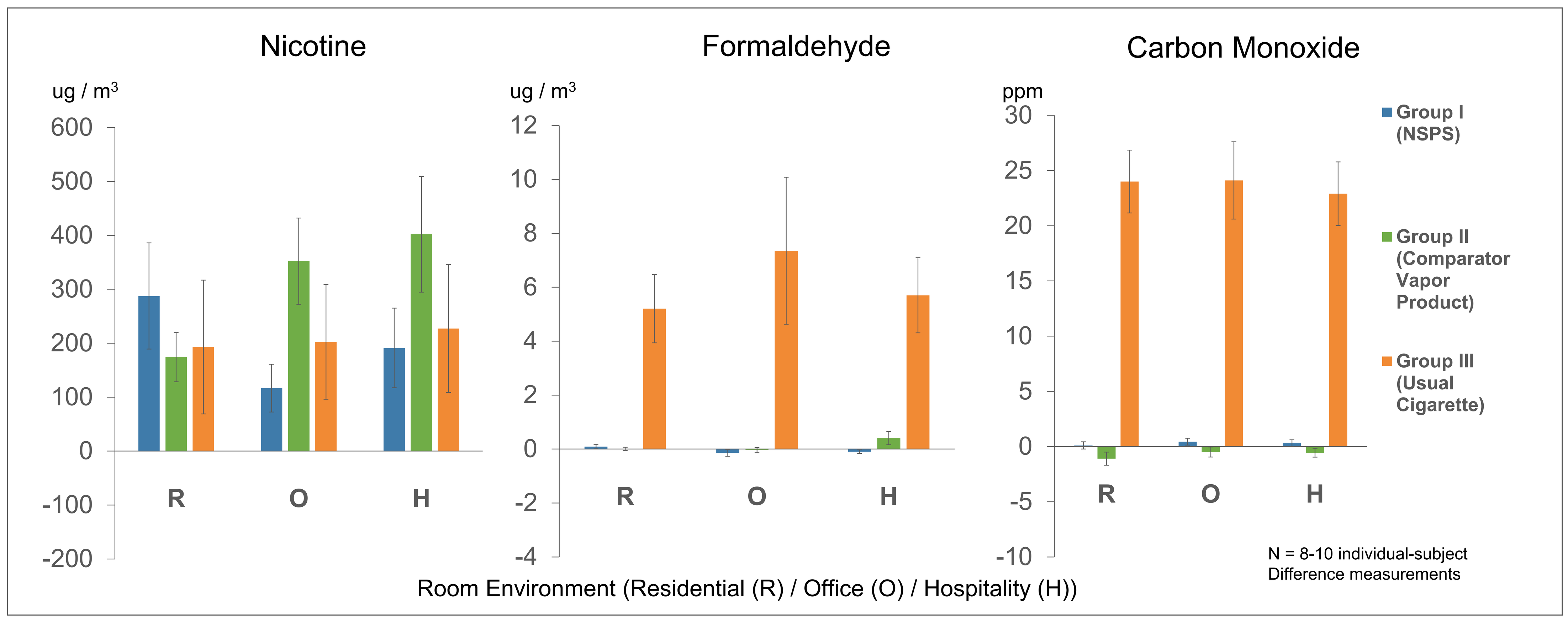


Figure 3: Change in Content of Room Air Samples After Product Use - VOCs

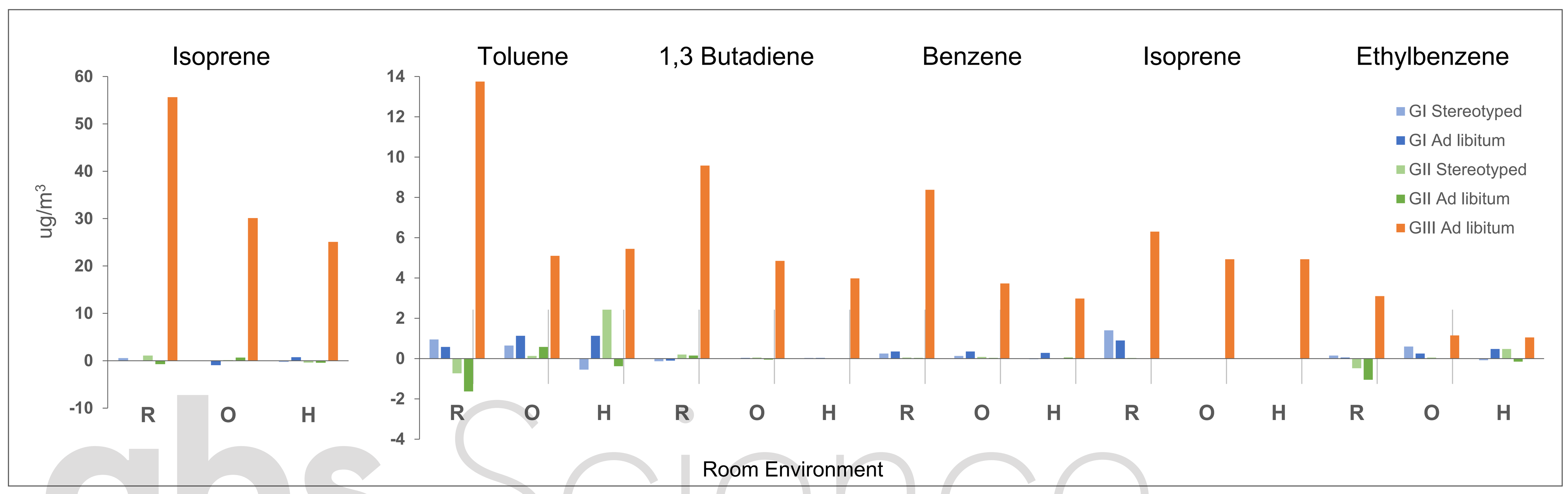
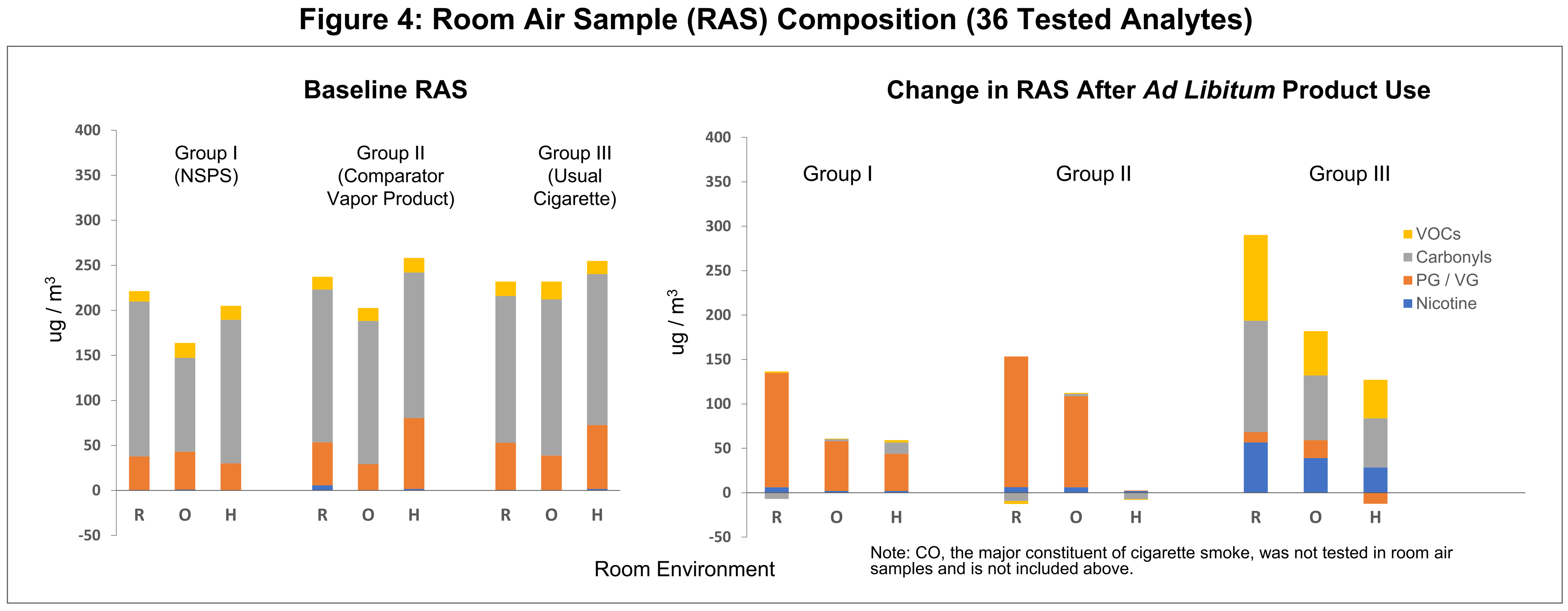


Table 2: Change in Room Air Samples After *Ad Libitum* Product Use - Carbonyls and VOCs

Constituents (Change from Baseline) (ug/m³)									
	Group I (N=4 sensors per reading*)			Group II (N=4)			Group III (N=4)		
Environmental Settings	R	O	H	R	0	H	R	O	H
Intended Ingredients									
Propylene Glycol	51.17 ± 10.03	7.45 ± 23.66	9.51 ± 11.94	37.12 ± 5.40	32.95 ± 6.12	-3.53 ± 25.96	-8.75 ± 11.09	3.43 ± 9.62	2.63 ± 8.62
Vegetable Glycerol	77.50 ± 24.25	48.60 ± 17.82	32.30 ± 5.41	110.55 ± 18.82	69.63 ± 17.33	4.18 ± 62.97	20.38 ± 4.05	16.60 ± 4.22	-15.08 ± 31.74
Nicotine	6.14 ± 1.31	1.95 ± 0.46	1.91 ± 0.42	6.23 ± 4.31	6.11 ± 1.12	1.87 ± 2.56	56.68 ± 8.28	39.02 ± 1.59	28.49± 1.76
Carbonyl Compounds									
Formaldehyde	0.03 ± 1.45	1.13 ± 1.18	-0.36 ± 1.75	-0.29 ± 0.74	0.13 ± 1.88	-1.24 ± 1.53	41.53 ± 4.61	24.48 ± 1.39	20.16 ± 1.27
Acetaldehyde	0.52 ± 2.97	-0.11 ± 1.12	-0.55 ± 0.74	0.40 ± 1.10	-0.03 ± 2.37	0.01 ± 0.25	58.45 ± 8.87	37.28 ± 2.26	28.98 ± 1.70
Acetone	-11.58 ± 4.58	5.10 ± 6.53	6.55 ± 5.31	-9.70 ± 9.44	3.28 ± 12.49	-5.08 ± 3.53	21.43 ± 4.97	6.83 ± 11.12	5.13 ± 7.35
Propionaldehyde	5.11 ± 1.65	-0.49 ± 0.81	0.82 ± 0.84	-0.08 ± 0.13	0.39 ± 0.72	-1.02 ± 1.83	1.25 ± 0.55	0.84 ± 2.41	-2.22 ± 1.84
Methyl Ethyl Ketone	0.93 ± 2.30	-0.28 ± 0.21	-0.17 ± 1.35	0.41 ± 0.95	0.33 ± 0.80	-0.16 ± 0.37	2.79 ± 1.84	3.72 ± 0.66	3.36 ± 2.33
VOCs									
1,3-Butadiene	-0.10 ± 0.08	0.03 ± 0.05	0.03 ± 0.05	0.15 ± 0.06	-0.05 ± 0.06	0.00 ± 0.00	9.58 ± 0.78	4.85 ± 0.33	3.98 ± 1.01
Benzene	0.35 ± 0.06	0.35 ± 0.06	0.28 ± 0.15	0.03 ± 0.05	0.03 ± 0.05	0.05 ± 0.17	8.38 ± 0.67	3.73 ± 0.39	2.95 ± 0.17
Isoprene	-0.03 ± 1.41	-0.93 ± 0.45	0.73 ± 0.51	-0.73 ± 1.33	0.65 ± 0.59	-0.43 ± 0.73	55.63 ± 5.27	30.13 ± 4.04	25.08 ± 4.86
Toluene	0.58 ± 0.05	1.13 ± 0.05	1.13 ± 0.05	-1.63 ± 0.32	0.58 ± 0.10	-0.38 ± 0.10	13.75 ± 1.35	5.10 ± 0.27	5.45 ± 0.48
Furan	0.90 ± 0.56	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	6.30 ± 1.87	4.93 ± 0.28	3.50 ± 0.54
Ethylbenzene	0.05 ± 0.06	0.25 ± 0.06	0.48 ± 0.05	-1.05 ± 0.17	0.00 ± 0.00	-0.15 ± 0.10	3.10 ± 0.29	1.15 ± 0.06	1.05 ± 0.06

*Results from 4 room air samples, single 4 hour session with 10 participants in room, baseline subtracted).
Carbonyls were also background adjusted to help cancel out background environmental sources not associated with product use.

Figure 4: Room Air Sample (RAS) Composition (36 Tested Analytes)



Analytes Tested in Room Aerosol Samples

36 analytes were tested for presence in room aerosol (Table 2): intended ingredients (N=3), trace metals (N=4), carbonyls (N=15), VOCs (N=12). No significant changes were observed under any experimental conditions for the following carbonyls and VOCs: crotonaldehyde, o-tohualdehyde, butyraldehyde, m&p-tolualdehyde, isovaleraldehyde, hexanaldehyde, valeraldehyde, 1,3-butadiene, 2,5-dimethylbenzaldehyde, ethylene oxide, vinyl chloride, propylene oxide, nitromethane, 2-nitropropane, and vinyl acetate. Trace metals (arsenic, cadmium, chromium and nickel) were below limit of quantification in this experimental setting.

Study Limitations

This study compared emissions from tobacco-flavored ENDS and combustible cigarettes for a delimited panel of analytes. Intra-day and inter-day variability in background levels of environmental sources, and small sample sizes, contributed to limitations in the sensitivity of measures of room air samples. In particular, additional studies may be warranted to quantify differences in room air levels of key toxicants for non-use and product use cases.

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