

Supplementary Materials

Targeted Characterization of the Chemical Composition of JUUL Systems Aerosol and Comparison with 3R4F Reference Cigarettes and IQOS Heat Sticks

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Table S1. Supplementary Methods.

Compounds Classification	Compounds	Method of Capture	Analysis Method	Instrument	Testing Lab	Method Reference Code	ISO17025 Status
Nicotine, Water, Composition, Menthol	diethylene glycol, ethylene glycol, glycerol, menthol, NFDPM, nicotine, propylene glycol, Water, ACM, DML, Carbon monoxide	Pad/impinger	Pads were extracted with IPA	GC-TCD/FID, NDIR	Labstat	TMS- ⁰⁰ 115a Appendix E	Accredited
Benzoic acid	Benzoic acid	Pad	Pads were extracted with H ₃ PO ₄	HPLC-UV	Labstat	TMS- ⁰⁰ 115a Appendix F	Accredited
Volatile Compounds	Benzene, Toluene, Acrylonitrile, Propylene Oxide	Pad	Sample were puffed through pad into a cryogenic trap containing methanol.	GC-MS (SIM)	Labstat	TMS- ⁰⁰ 124 Appendix G	Accredited
	1,3-Butadiene, Isoprene	Pad/Impinger	Pads were extracted with IPA	GC-MS	Enthalpy	ENT208 Rev. 7.0	Accredited
Tobacco Specific Nitrosamines	N-nitrosornicotine, 4-(N-nitrosomethylamino)-1-(3-pyridyl)-1-butanone	Pad	Pads were spiked with internal standard solution containing 4 TSNA analogues and TSN analogues were extraction	LC-MS/MS (ESI)	Labstat	TMS- ⁰⁰ 135 Appendix I	Accredited

			into ammonium acetate solution.				
Nicotine Degradation Products	Nicotine-N-Oxide, Cotinine, B-nicotyrine	Pad	Pads were extracted with ammonium acetate solution	LC-MS/MS	Labstat	TMS ⁰⁰¹⁵³	Accredited
	Anatabine, Anabasine, Myosmine, Nornicotine	Pad	Pads are extracted with methanol/water	LC-MS/MS (ESI)	Enthalpy	AM ⁻²³⁸ v3.1	Accredited
Carbonyls	Formaldehyde, Acetaldehyde, Acrolein, Isobutyraldehyde, Butyraldehyde, Crotonaldehyde, Diacetyl, Acetyl Propionyl, Ethyl Acetoacetate	Pad/Impinger	Sample were puffed through pad into a cryogenic trap containing acetonitrile, extracted with the impinger solution, and derivatized with PFBHA, followed by extraction in toluene.	GC-MS (SIM)	Labstat	TMS ⁰⁰¹⁵⁵ and TMS-00155 Appendix G	Accredited
Heavy Metal	Cadmium, Lead, Chromium, Nickel, Copper, Gold	Pad	Quartz Pad was extracted with 10% (v/v) ultra-high purity nitric acid.	ICP-MS	Labstat	TMS ⁰⁰¹⁶⁰	Accredited
Aromatic Flavourants	Methyl Acetate, Ethyl Acetate, 1-Butanol, Isobutyl Acetate, Furfural, Isoamyl Acetate, Benzyl Acetate	Pad/Impinger	Pads were extracted with the impinger solution containing acetonitrile	GC-MS	Labstat	TMS ⁰⁰¹⁷⁵	Accredited
Aromatic Amines	1-aminonaphthalene, 2-aminonaphthalene, 4-aminobiphenyl	Pad	Pad was extracted with dichloromethane	GC-MS (NCI)	Enthalpy	SOP AM ⁻²²¹ v4.0	Accredited
Propionic Acid	Propionic Acid	Pad/Impinger	Sample were puffed through pad into a cryogenic trap containing acetonitrile	GC-MS (SIM)	Labstat	TMS ⁰⁰¹⁷⁷	Accredited
Glycidol	Glycidol	Impinger	Aerosol was collected in impingers containing	GC-MS	Enthalpy	ENT203 Rev. 1.0	Accredited

			trapping solution of internal standard, hydrochloric acid, and p-toluenesulfonyl chloride, followed by hexane addition.				
Water	Water	Pad	Pad was analyzed for water by gas chromatography with thermal conductivity detection (GC-TCD) using a porous polymer packed column.	GC-TCD	Labstat	TMS-00115a Appendix E	Accredited
Ammonia	Ammonia	Pad/impinger	Vapor was passed through a filter pad and impinger containing 40 mN H2SO4	Ion exchange chromatography	Enthalpy	ENT307 Rev 2.0	Accredited
Benzo(a)pyrene	Benzo(a)pyrene	Pad	Pad were extracted for benzo[a]pyrene	GC-MS	Enthalpy	ENT217 Rev 1.0	Accredited

Table S2. Method LOD and LOQ for Me3 analysis.

Parameter/Constituent	Units	LOD	LOQ
1,3-Butadiene	µg	0.03	0.32
1-Butanol	µg	0.06	0.20
2-Aminonaphthalene	ng	6.75×10 ⁻⁰⁴	2.02×10 ⁻⁰³
4-Aminobiphenyl	ng	3.32×10 ⁻⁰⁴	9.97×10 ⁻⁰⁴
β-Nicotyrine	µg	3.81×10 ⁻⁰³	0.01
Acetaldehyde	µg	0.01	0.03
Acetyl Propionyl	µg	3.51×10 ⁻⁰³	0.01
Acrolein	µg	0.01	0.03
Acrylonitrile	µg	0.01	0.02
Ammonia	µg	0.01	0.12
Anabasine	µg	1.29×10 ⁻⁰³	0.01
Anatabine	µg	6.02×10 ⁻⁰⁴	5.99×10 ⁻⁰³
Benzene	µg	3.41×10 ⁻⁰³	0.01
Benzo(a)pyrene	ng	1.86×10 ⁻⁰³	0.01
Benzoic Acid	mg	9.59×10 ⁻⁰⁵	3.20×10 ⁻⁰⁴
Benzyl Acetate	µg	0.06	0.20
Cadmium	ng	0.01	0.04
Carbon Monoxide	mg	NA	NA
Chromium	ng	0.11	0.35
Copper	ng	0.13	0.44
Cotinine	µg	1.87×10 ⁻⁰³	0.01
Crotonaldehyde	µg	0.01	0.02

Diacetyl	µg	1.74×10 ⁻⁰³	0.01
Diethylene Glycol	mg	2.40×10 ⁻⁰⁴	8.00×10 ⁻⁰⁴
Ethyl Acetate	µg	0.06	0.20
Ethyl Acetoacetate	µg	4.80×10 ⁻⁰³	0.02
Ethylene Glycol	mg	5.05×10 ⁻⁰⁵	1.68×10 ⁻⁰⁴
Formaldehyde	µg	0.01	0.02
Furfural	µg	0.08	0.28
Glycerol	mg	1.44×10 ⁻⁰³	4.80×10 ⁻⁰³
Glycidol	µg	NA	NA
Gold	ng	NA	NA
Isoamyl Acetate	µg	0.10	0.32
Isobutyl Acetate	µg	0.06	0.20
Isobutyraldehyde	µg	1.65×10 ⁻⁰³	0.01
Isoprene	µg	0.32	3.21
Lead	ng	0.02	0.07
Menthol	mg	2.44×10 ⁻⁰⁴	8.14×10 ⁻⁰⁴
Methyl Acetate	µg	0.07	0.24
Myosmine	µg	5.95×10 ⁻⁰⁴	0.01
n-Butyraldehyde	µg	3.51×10 ⁻⁰³	0.01
Nickel	ng	0.21	0.70
Nicotine	mg	1.35×10 ⁻⁰⁴	4.49×10 ⁻⁰⁴
Nicotine-N-Oxide	µg	0.02	0.06
NNK	ng	0.02	0.05
NNN	ng	0.01	0.03
Nornicotine	µg	9.45×10 ⁻⁰⁴	5.88×10 ⁻⁰³
pH	Unitless	NA	NA
Propionic Acid	µg	0.04	0.12
Propylene Glycol	mg	2.40×10 ⁻⁰⁴	8.01×10 ⁻⁰⁴
Propylene Oxide	ng	3.12	10.40
Toluene	µg	0.01	0.04
Water	mg	3.83×10 ⁻⁰³	0.01

Table S3. Method LOD and LOQ for VT5, VT3 and Me5 analysis.

Parameter/Constituent	Units	LOD	LOQ
1-Aminonaphthalene	ng	1.64×10 ⁻⁰³	0.01
1,3-Butadiene	µg	5.70×10 ⁻⁰³	1.90×10 ⁻⁰²
1-Butanol	µg	0.06	0.20
2-Aminonaphthalene	ng	7.12×10 ⁻⁰⁴	2.37×10 ⁻⁰³
4-Aminobiphenyl	ng	2.86×10 ⁻⁰⁴	9.53×10 ⁻⁰⁴
β-Nicotyrine	µg	3.81×10 ⁻⁰³	0.01
Acetaldehyde	µg	0.01	0.03
Acetyl Propionyl	µg	3.51×10 ⁻⁰³	0.01
Acrolein	µg	0.01	0.03
Acrylonitrile	µg	0.01	0.02
Ammonia	µg	0.02	0.06
Anabasine	µg	0.01	0.02
Anatabine	µg	4.76×10 ⁻⁰³	0.02
Benzene	µg	3.41×10 ⁻⁰³	0.01
Benzo(a)pyrene	ng	1.06×10 ⁻⁰²	0.04
Benzoic Acid	mg	9.59×10 ⁻⁰⁵	3.20×10 ⁻⁰⁴
Benzyl Acetate	µg	0.06	0.20
Cadmium	ng	0.01	0.04
Carbon Monoxide	mg	0.01	0.03
Chromium	ng	0.11	0.35

Copper	ng	0.13	0.44
Cotinine	µg	1.87×10 ⁻⁰³	0.01
Crotonaldehyde	µg	0.01	0.02
Diacetyl	µg	1.74×10 ⁻⁰³	0.01
Diethylene Glycol	mg	2.40×10 ⁻⁰⁴	8.00×10 ⁻⁰⁴
Ethyl Acetate	µg	0.06	0.20
Ethyl Acetoacetate	µg	4.80×10 ⁻⁰³	0.02
Ethylene Glycol	mg	5.05×10 ⁻⁰⁵	1.68×10 ⁻⁰⁴
Formaldehyde	µg	0.01	0.02
Furfural	µg	0.08	0.28
Glycerol	mg	1.44×10 ⁻⁰³	4.80×10 ⁻⁰³
Glycidol	µg	NA	NA
Gold	ng	0.01	0.04
Isoamyl Acetate	µg	0.10	0.32
Isobutyl Acetate	µg	0.06	0.20
Isobutyraldehyde	µg	1.65×10 ⁻⁰³	0.01
Isoprene	µg	8.12×10 ⁻⁰³	0.03
Lead	ng	0.02	0.07
Menthol	mg	2.44×10 ⁻⁰⁴	8.14×10 ⁻⁰⁴
Methyl Acetate	µg	0.07	0.24
Myosmine	µg	0.01	0.03
n-Butyraldehyde	µg	3.51×10 ⁻⁰³	0.01
Nickel	ng	0.21	0.70
Nicotine	mg	1.35×10 ⁻⁰⁴	4.49×10 ⁻⁰⁴
Nicotine-N-Oxide	µg	0.02	0.06
NNK	ng	0.02	0.05
NNN	ng	0.01	0.03
Nornicotine	µg	4.76×10 ⁻⁰³	0.02
pH	Unitless	NA	NA
Propionic Acid	µg	0.04	0.12
Propylene Glycol	mg	2.40×10 ⁻⁰⁴	8.01×10 ⁻⁰⁴
Propylene Oxide	ng	3.12	10.40
Toluene	µg	0.01	0.04
Water	mg	3.83×10 ⁻⁰³	0.01

Table S4. Comparison of HPHC and Chemical Intense Aerosol Levels in Virginia Tobacco 5.0% and Smoke Levels in 3R4F Reference Cigarette.

HPHC Chemical	JUUL Virginia Tobacco 5.0% (mg/puff)		3R4F (mg/cig)		Source Journal	Chemical and HPHC Normalized by Nicotine (mg/mg)		% Difference vs_3R4F
	HPHC or Chemical	Nicotine	HPHC or Chemical	Nicotine		JUUL Virginia Tobacco 5.0%	3R4F	
1-Aminonaphthalene	≤8.19×10 ⁻¹⁰	0.04	2.91×10 ⁻⁰⁵	1.99	a	≤1.96×10 ⁻⁰⁸	1.46×10 ⁻⁰⁵	↓ ≥99.87
1-Butanol	≤3.00×10 ⁻⁰⁵	0.10	N/A	N/A	N/A	≤3.00×10 ⁻⁰⁴	N/A	N/A
1,3-Butadiene	≤2.85×10 ⁻⁰⁶	0.04	1.00×10 ⁻⁰¹	1.99	a	≤6.83×10 ⁻⁰⁵	5.03×10 ⁻⁰²	↓ ≥99.86
2-Aminonaphthalene	≤3.56×10 ⁻¹⁰	0.04	1.81×10 ⁻⁰⁵	1.99	a	≤8.53×10 ⁻⁰⁹	9.10×10 ⁻⁰⁶	↓ ≥99.91
4-Aminobiphenyl	≤6.20×10 ⁻¹⁰	0.04	3.91×10 ⁻⁰⁶	1.99	a	≤1.48×10 ⁻⁰⁸	1.96×10 ⁻⁰⁶	↓ ≥99.24

Acetaldehyde	$\leq 2.16 \times 10^{-05}$	0.10	$1.84 \times 10^{+00}$	1.99	a	$\leq 2.16 \times 10^{-04}$	9.24×10^{-01}	↓ ≥ 99.98
Acetyl Propionyl	$\leq 1.76 \times 10^{-06}$	0.10	9.19×10^{-02}	1.99	b	$\leq 1.76 \times 10^{-05}$	4.62×10^{-02}	↓ ≥ 99.96
Acrolein	$\leq 2.01 \times 10^{-05}$	0.17	1.80×10^{-01}	1.99	a	$\leq 1.17 \times 10^{-04}$	9.05×10^{-02}	↓ ≥ 99.87
Acrylonitrile	$\leq 3.20 \times 10^{-06}$	0.10	2.05×10^{-02}	1.99	a	$\leq 3.20 \times 10^{-05}$	1.03×10^{-02}	↓ ≥ 99.69
Ammonia	NDFB	0.04	3.40×10^{-02}	1.99	a	NDFB	1.71×10^{-02}	NC
Anabasine	$\leq 1.24 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 2.98 \times 10^{-04}$	N/A	N/A
Anatabine	$\leq 2.38 \times 10^{-06}$	0.04	N/A	N/A	N/A	$\leq 5.70 \times 10^{-05}$	N/A	N/A
Benzene	$\leq 1.71 \times 10^{-06}$	0.10	8.88×10^{-02}	1.99	a	$\leq 1.71 \times 10^{-05}$	4.46×10^{-02}	↓ ≥ 99.96
Benzo(a)pyrene	$\leq 5.31 \times 10^{-09}$	0.04	1.51×10^{-05}	1.99	a	$\leq 1.27 \times 10^{-07}$	7.59×10^{-06}	↓ ≥ 98.32
Benzoic Acid	1.37×10^{-01}	0.17	N/A	N/A	N/A	7.94×10^{-01}	N/A	N/A
Benzyl Acetate	$\leq 3.00 \times 10^{-05}$	0.10	N/A	N/A	N/A	$\leq 3.00 \times 10^{-04}$	N/A	N/A
β-Nicotyrine	$\leq 8.25 \times 10^{-06}$	0.17	N/A	N/A	N/A	$\leq 4.79 \times 10^{-05}$	N/A	N/A
Cadmium	$\leq 5.25 \times 10^{-09}$	0.10	9.32×10^{-05}	1.99	a	$\leq 5.26 \times 10^{-08}$	4.68×10^{-05}	↓ ≥ 99.89
Carbon Monoxide	$\leq 5.25 \times 10^{-03}$	0.04	$3.05 \times 10^{+01}$	1.99	a	$\leq 1.26 \times 10^{-01}$	$1.53 \times 10^{+01}$	↓ ≥ 99.18
Chromium	NDFB	0.10	$\leq 1.19 \times 10^{-05}$	1.74	c	NDFB	$\leq 6.84 \times 10^{-06}$	NC
Copper	$\leq 6.56 \times 10^{-08}$	0.10	N/A	N/A	N/A	$\leq 6.57 \times 10^{-07}$	N/A	N/A
Cotinine	6.57×10^{-06}	0.17	N/A	N/A	N/A	3.81×10^{-05}	N/A	N/A
Crotonaldehyde	$\leq 3.11 \times 10^{-06}$	0.10	5.95×10^{-02}	1.99	a	$\leq 3.12 \times 10^{-05}$	2.99×10^{-02}	↓ ≥ 99.90
Diacetyl	$\leq 8.70 \times 10^{-07}$	0.10	3.37×10^{-01}	1.99	a	$\leq 8.71 \times 10^{-06}$	1.69×10^{-01}	↓ ≥ 99.99
Diethylene Glycol	$\leq 1.20 \times 10^{-04}$	0.10	N/A	N/A	N/A	$\leq 1.20 \times 10^{-03}$	N/A	N/A
Ethyl Acetate	$\leq 1.30 \times 10^{-04}$	0.04	N/A	N/A	N/A	$\leq 3.45 \times 10^{-03}$	N/A	N/A
Ethyl Acetoacetate	$\leq 2.40 \times 10^{-06}$	0.10	N/A	N/A	N/A	$\leq 2.40 \times 10^{-05}$	N/A	N/A
Ethylene Glycol	$\leq 1.09 \times 10^{-04}$	0.10	N/A	N/A	N/A	$\leq 1.09 \times 10^{-03}$	N/A	N/A
Formaldehyde	6.03×10^{-05}	0.17	8.71×10^{-02}	1.99	a	3.50×10^{-04}	4.38×10^{-02}	↓ 99.2
Furfural	$\leq 4.20 \times 10^{-05}$	0.10	2.59×10^{-02}	1.74	c	$\leq 4.20 \times 10^{-04}$	1.49×10^{-02}	↓ ≥ 97.18
Glycerol	$2.12 \times 10^{+00}$	0.17	$2.70 \times 10^{+00}$	1.99	a	$1.23 \times 10^{+01}$	$1.36 \times 10^{+00}$	808.58
Glycidol	NR	0.10	1.76×10^{-03}	1.99	a	NR	8.84×10^{-04}	N/A
Gold	$\leq 6.33 \times 10^{-09}$	0.04	N/A	N/A	N/A	$\leq 1.52 \times 10^{-07}$	N/A	N/A
Isoamyl Acetate	$\leq 4.80 \times 10^{-05}$	0.10	N/A	N/A	N/A	$\leq 4.80 \times 10^{-04}$	N/A	N/A
Isobutyl Acetate	$\leq 3.00 \times 10^{-05}$	0.10	N/A	N/A	N/A	$\leq 3.00 \times 10^{-04}$	N/A	N/A
Isobutyraldehyde	$\leq 8.26 \times 10^{-07}$	0.10	N/A	N/A	N/A	$\leq 8.27 \times 10^{-06}$	N/A	N/A
Isoprene	$\leq 4.06 \times 10^{-06}$	0.04	7.99×10^{-01}	1.99	a	$\leq 9.72 \times 10^{-05}$	4.02×10^{-01}	↓ ≥ 99.98
Lead	$\leq 4.55 \times 10^{-08}$	0.10	3.12×10^{-05}	1.74	c	$\leq 4.55 \times 10^{-07}$	1.79×10^{-05}	↓ ≥ 97.46
Menthol	$\leq 1.22 \times 10^{-04}$	0.10	$\leq 1.00 \times 10^{-05}$	2.10	d	$\leq 1.22 \times 10^{-03}$	$\leq 4.76 \times 10^{-06}$	NC
Methyl Acetate	$\leq 3.60 \times 10^{-05}$	0.10	N/A	N/A	N/A	$\leq 3.60 \times 10^{-04}$	N/A	N/A
Myosmine	$\leq 1.93 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 4.62 \times 10^{-04}$	N/A	N/A
n-Butyraldehyde	$\leq 1.76 \times 10^{-06}$	0.10	9.30×10^{-02}	1.99	a	$\leq 1.76 \times 10^{-05}$	4.67×10^{-02}	↓ ≥ 99.96
Nickel	$\leq 1.05 \times 10^{-07}$	0.10	$\leq 1.29 \times 10^{-05}$	1.74	c	$\leq 1.05 \times 10^{-06}$	$\leq 7.41 \times 10^{-06}$	NC
Nicotine	1.72×10^{-01}	0.17	$1.99 \times 10^{+00}$	1.99	a	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	N/A

Nicotine-N-Oxide	$\leq 8.72 \times 10^{-06}$	0.10	N/A	N/A	N/A	$\leq 8.73 \times 10^{-05}$	N/A	N/A
NNK	$\leq 7.53 \times 10^{-09}$	0.10	2.95×10^{-04}	1.99	a	$\leq 7.54 \times 10^{-08}$	1.48×10^{-04}	$\downarrow \geq 99.95$
NNN	$\leq 4.92 \times 10^{-09}$	0.10	3.37×10^{-04}	1.99	a	$\leq 4.93 \times 10^{-08}$	1.69×10^{-04}	$\downarrow \geq 99.97$
Normicotine	2.42×10^{-05}	0.04	N/A	N/A	N/A	5.78×10^{-04}	N/A	N/A
Propionic Acid	$\leq 1.80 \times 10^{-05}$	0.10	N/A	N/A	N/A	$\leq 1.80 \times 10^{-04}$	N/A	N/A
Propylene Glycol	8.30×10^{-01}	0.17	2.37×10^{-02}	1.74	c	$4.82 \times 10^{+00}$	1.36×10^{-02}	35265.37
Propylene Oxide	$\leq 1.56 \times 10^{-06}$	0.10	$1.00 \times 10^{+00}$	1.99	a	$\leq 1.56 \times 10^{-05}$	5.03×10^{-01}	$\downarrow \geq 100.00$
Toluene	$\leq 6.12 \times 10^{-06}$	0.10	1.53×10^{-01}	1.99	a	$\leq 6.12 \times 10^{-05}$	7.69×10^{-02}	$\downarrow \geq 99.92$
Water	4.31×10^{-01}	0.17	$1.58 \times 10^{+01}$	1.89	e	$2.50 \times 10^{+00}$	$8.36 \times 10^{+00}$	$\downarrow 70.11$

Average % Difference, Excluding Glycerol, PG and Water. a: Jaccard et al. 2019 b: Moldoveanu et al. 2017 c: Helen et al. 2018 d: Uchiyama et al. 2018 e: Schaller et al. 2016 f: Pappas et al. 2014 g: Roemer et al. 2012 h: IQOS PMTA, 2019.

Table S5. Comparison of HPHC and Chemical Non-Intense Aerosol Levels in Virginia Tobacco 5.0% and Smoke Levels in 3R4F Reference Cigarette.

HPHC Chemical	JUUL Virginia Tobacco 5.0% (mg/puff)		3R4F (mg/cig)		Source Journal	Chemical and HPHC Normalized by Nicotine (mg/mg)		% Difference vs_3R4F
	HPHC or Chemical	Nicotine	HPHC or Chemical	Nicotine		JUUL Virginia Tobacco 5.0%	3R4F	
1-Aminonaphthalene	$\leq 8.19 \times 10^{-10}$	0.04	1.42×10^{-05}	0.70	a	$\leq 1.96 \times 10^{-08}$	2.02×10^{-05}	$\downarrow \geq 99.90$
1-Butanol	$\leq 3.00 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 5.52 \times 10^{-04}$	N/A	N/A
1,3-Butadiene	$\leq 2.85 \times 10^{-06}$	0.04	3.79×10^{-02}	0.70	a	$\leq 6.83 \times 10^{-05}$	5.40×10^{-02}	$\downarrow \geq 99.87$
2-Aminonaphthalene	$\leq 3.56 \times 10^{-10}$	0.04	8.77×10^{-06}	0.70	a	$\leq 8.53 \times 10^{-09}$	1.25×10^{-05}	$\downarrow \geq 99.93$
4-Aminobiphenyl	$\leq 6.20 \times 10^{-10}$	0.04	1.54×10^{-06}	0.70	a	$\leq 1.48 \times 10^{-08}$	2.19×10^{-06}	$\downarrow \geq 99.32$
Acetaldehyde	$\leq 2.16 \times 10^{-05}$	0.05	5.97×10^{-01}	0.70	a	$\leq 3.97 \times 10^{-04}$	8.50×10^{-01}	$\downarrow \geq 99.95$
Acetyl Propionyl	$\leq 1.76 \times 10^{-06}$	0.05	2.95×10^{-02}	0.70	b	$\leq 3.23 \times 10^{-05}$	4.21×10^{-02}	$\downarrow \geq 99.92$
Acrolein	$\leq 2.01 \times 10^{-05}$	0.10	5.32×10^{-02}	0.70	a	$\leq 1.92 \times 10^{-04}$	7.58×10^{-02}	$\downarrow \geq 99.75$
Acrylonitrile	$\leq 3.20 \times 10^{-06}$	0.05	5.23×10^{-03}	0.70	a	$\leq 5.89 \times 10^{-05}$	7.45×10^{-03}	$\downarrow \geq 99.21$
Ammonia	NDFB	0.04	9.64×10^{-03}	0.70	a	NDFB	1.37×10^{-02}	NC
Anabasine	$\leq 1.24 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 2.98 \times 10^{-04}$	N/A	N/A
Anatabine	$\leq 2.38 \times 10^{-06}$	0.04	N/A	N/A	N/A	$\leq 5.70 \times 10^{-05}$	N/A	N/A
Benzene	$\leq 1.71 \times 10^{-06}$	0.05	3.36×10^{-02}	0.70	a	$\leq 3.14 \times 10^{-05}$	4.79×10^{-02}	$\downarrow \geq 99.93$
Benzo(a)pyrene	$\leq 5.31 \times 10^{-09}$	0.04	6.30×10^{-06}	0.70	a	$\leq 1.27 \times 10^{-07}$	8.97×10^{-06}	$\downarrow \geq 98.58$
Benzoic Acid	7.81×10^{-02}	0.10	N/A	N/A	N/A	7.45×10^{-01}	N/A	N/A
Benzyl Acetate	$\leq 3.00 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 5.52 \times 10^{-04}$	N/A	N/A
β -Nicotyrine	$\leq 8.25 \times 10^{-06}$	0.08	N/A	N/A	N/A	$\leq 9.72 \times 10^{-05}$	N/A	N/A
Cadmium	$\leq 5.25 \times 10^{-09}$	0.05	2.45×10^{-05}	0.70	a	$\leq 9.66 \times 10^{-08}$	3.49×10^{-05}	$\downarrow \geq 99.72$
Carbon Monoxide	$\leq 5.25 \times 10^{-03}$	0.04	$1.00 \times 10^{+01}$	0.70	a	$\leq 1.26 \times 10^{-01}$	$1.42 \times 10^{+01}$	$\downarrow \geq 99.12$
Chromium	NDFB	0.05	$\leq 8.80 \times 10^{-07}$	0.70	f	NDFB	$\leq 1.25 \times 10^{-06}$	NC

Copper	$\leq 2.84 \times 10^{-07}$	0.10	N/A	N/A	N/A	$\leq 2.71 \times 10^{-06}$	N/A	N/A
Cotinine	$\leq 4.06 \times 10^{-06}$	0.05	N/A	N/A	N/A	$\leq 7.48 \times 10^{-05}$	N/A	N/A
Crotonaldehyde	$\leq 3.11 \times 10^{-06}$	0.05	9.89×10^{-03}	0.70	a	$\leq 5.73 \times 10^{-05}$	1.41×10^{-02}	↓ ≥ 99.59
Diacetyl	$\leq 8.70 \times 10^{-07}$	0.05	1.15×10^{-01}	0.70	b	$\leq 1.60 \times 10^{-05}$	1.64×10^{-01}	↓ ≥ 99.99
Diethylene Glycol	$\leq 1.20 \times 10^{-04}$	0.05	N/A	N/A	N/A	$\leq 2.21 \times 10^{-03}$	N/A	N/A
Ethyl Acetate	$\leq 3.00 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 5.52 \times 10^{-04}$	N/A	N/A
Ethyl Acetoacetate	$\leq 2.40 \times 10^{-06}$	0.05	N/A	N/A	N/A	$\leq 4.42 \times 10^{-05}$	N/A	N/A
Ethylene Glycol	$\leq 1.09 \times 10^{-04}$	0.05	N/A	N/A	N/A	$\leq 2.01 \times 10^{-03}$	N/A	N/A
Formaldehyde	8.33×10^{-05}	0.08	2.47×10^{-02}	0.70	a	9.82×10^{-04}	3.52×10^{-02}	↓ 97.21
Furfural	$\leq 4.20 \times 10^{-05}$	0.05	1.40×10^{-02}	0.76	d	$\leq 7.73 \times 10^{-04}$	1.84×10^{-02}	↓ ≥ 95.80
Glycerol	$1.24 \times 10^{+00}$	0.10	$2.70 \times 10^{+00}$	0.70	a	$1.19 \times 10^{+01}$	$3.85 \times 10^{+00}$	208.86
Glycidol	NR	0.05	N/A	N/A	N/A	NR	N/A	N/A
Gold	$\leq 6.33 \times 10^{-09}$	0.04	N/A	N/A	N/A	$\leq 1.52 \times 10^{-07}$	N/A	N/A
Isoamyl Acetate	$\leq 4.80 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 8.83 \times 10^{-04}$	N/A	N/A
Isobutyl Acetate	$\leq 3.00 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 5.52 \times 10^{-04}$	N/A	N/A
Isobutyraldehyde	$\leq 8.26 \times 10^{-07}$	0.05	N/A	N/A	N/A	$\leq 1.52 \times 10^{-05}$	N/A	N/A
Isoprene	$\leq 4.06 \times 10^{-06}$	0.04	2.88×10^{-01}	0.70	a	$\leq 9.72 \times 10^{-05}$	4.10×10^{-01}	↓ ≥ 99.98
Lead	$\leq 4.55 \times 10^{-08}$	0.10	9.20×10^{-06}	0.70	f	$\leq 4.34 \times 10^{-07}$	1.31×10^{-05}	↓ ≥ 96.69
Menthol	$\leq 1.22 \times 10^{-04}$	0.05	$\leq 1.00 \times 10^{-05}$	0.76	a	$\leq 2.25 \times 10^{-03}$	$\leq 1.32 \times 10^{-05}$	NC
Methyl Acetate	$\leq 3.60 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 6.62 \times 10^{-04}$	N/A	N/A
Myosmine	$\leq 1.93 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 4.62 \times 10^{-04}$	N/A	N/A
n-Butyraldehyde	$\leq 1.76 \times 10^{-06}$	0.05	2.84×10^{-02}	0.70	a	$\leq 3.23 \times 10^{-05}$	4.05×10^{-02}	↓ ≥ 99.92
Nickel	$\leq 4.55 \times 10^{-07}$	0.05	$\leq 3.80 \times 10^{-07}$	0.70	f	$\leq 8.37 \times 10^{-06}$	$\leq 5.41 \times 10^{-07}$	NC
Nicotine	1.05×10^{-01}	0.10	7.02×10^{-01}	0.70	a	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	N/A
Nicotine-N-Oxide	$\leq 8.72 \times 10^{-06}$	0.05	N/A	N/A	N/A	$\leq 1.60 \times 10^{-04}$	N/A	N/A
NNK	$\leq 7.53 \times 10^{-09}$	0.05	1.13×10^{-04}	0.70	a	$\leq 1.39 \times 10^{-07}$	1.61×10^{-04}	↓ ≥ 99.91
NNN	$\leq 4.92 \times 10^{-09}$	0.05	1.31×10^{-04}	0.70	a	$\leq 9.06 \times 10^{-08}$	1.87×10^{-04}	↓ ≥ 99.95
Normicotine	2.42×10^{-05}	0.04	N/A	N/A	N/A	5.78×10^{-04}	N/A	N/A
Propionic Acid	$\leq 1.80 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 3.31 \times 10^{-04}$	N/A	N/A
Propylene Glycol	5.32×10^{-01}	0.10	3.20×10^{-03}	0.76	d	$5.07 \times 10^{+00}$	4.21×10^{-03}	120417.77
Propylene Oxide	$\leq 1.56 \times 10^{-06}$	0.05	2.97×10^{-01}	0.70	a	$\leq 2.87 \times 10^{-05}$	4.23×10^{-01}	↓ ≥ 99.99
Toluene	$\leq 6.12 \times 10^{-06}$	0.05	5.14×10^{-02}	0.70	a	$\leq 1.13 \times 10^{-04}$	7.32×10^{-02}	↓ ≥ 99.85
Water	2.82×10^{-01}	0.10	$3.20 \times 10^{+00}$	0.76	d	$2.69 \times 10^{+00}$	$4.21 \times 10^{+00}$	↓ 36.14

Average % Difference, Excluding Glycerol, PG and Water. a: Jaccard et al. 2019 b: Moldoveanu et al. 2017 c: Helen et al. 2018 d: Uchiyama et al. 2018 e: Schaller et al. 2016 f: Pappas et al. 2014 g: Roemer et al. 2012 h: IQOS PMTA, 2019.

Table S6. Comparison of HPHC and Chemical Non-Intense Aerosol Levels in Virginia Tobacco 5.0% and Smoke Levels in IQOS regular.

HPHC Chemical	JUUL Virginia Tobacco 5.0% (mg/puff)		IQOS (mg/cig)			Chemical and HPHC Normalized by Nicotine (mg/mg)		% Difference vs_IQOS
	HPHC or Chemical	Nicotine	HPHC or Chemical	Nicotine	Source Journal	JUUL Virginia Tobacco 5.0%	IQOS	
1-Aminonaphthalene	$\leq 8.19 \times 10^{-10}$	0.04	7.70×10^{-08}	1.32	e	$\leq 1.96 \times 10^{-08}$	5.83×10^{-08}	↓ ≥66.39
1-Butanol	$\leq 3.00 \times 10^{-05}$	0.10	N/A	N/A	N/A	$\leq 3.00 \times 10^{-04}$	N/A	N/A
1,3-Butadiene	$\leq 2.85 \times 10^{-06}$	0.04	2.94×10^{-04}	1.32	e	$\leq 6.83 \times 10^{-05}$	2.23×10^{-04}	↓ ≥69.34
2-Aminonaphthalene	$\leq 3.56 \times 10^{-10}$	0.04	4.60×10^{-08}	1.32	e	$\leq 8.53 \times 10^{-09}$	3.48×10^{-08}	↓ ≥75.53
4-Aminobiphenyl	$\leq 6.20 \times 10^{-10}$	0.04	9.00×10^{-09}	1.29	c	$\leq 1.48 \times 10^{-08}$	6.98×10^{-09}	NC
Acetaldehyde	$\leq 2.16 \times 10^{-05}$	0.10	2.19×10^{-01}	1.32	e	$\leq 2.16 \times 10^{-04}$	1.66×10^{-01}	↓ ≥99.87
Acetyl Propionyl	$\leq 1.76 \times 10^{-06}$	0.10	N/A	N/A	N/A	$\leq 1.76 \times 10^{-05}$	N/A	N/A
Acrolein	$\leq 2.01 \times 10^{-05}$	0.17	1.13×10^{-02}	1.32	e	$\leq 1.17 \times 10^{-04}$	8.56×10^{-03}	↓ ≥98.64
Acrylonitrile	$\leq 3.20 \times 10^{-06}$	0.10	2.58×10^{-04}	1.32	e	$\leq 3.20 \times 10^{-05}$	1.95×10^{-04}	↓ ≥83.61
Ammonia	NDFB	0.04	1.42×10^{-02}	1.32	e	NDFB	1.08×10^{-02}	NC
Anabasine	$\leq 1.24 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 2.98 \times 10^{-04}$	N/A	N/A
Anatabine	$\leq 2.38 \times 10^{-06}$	0.04	N/A	N/A	N/A	$\leq 5.70 \times 10^{-05}$	N/A	N/A
Benzene	$\leq 1.71 \times 10^{-06}$	0.10	6.49×10^{-04}	1.32	e	$\leq 1.71 \times 10^{-05}$	4.92×10^{-04}	↓ ≥96.53
Benzo(a)pyrene	$\leq 5.31 \times 10^{-09}$	0.04	7.36×10^{-07}	1.29	c	$\leq 1.27 \times 10^{-07}$	5.71×10^{-07}	↓ ≥77.70
Benzoic Acid	1.37×10^{-01}	0.17	N/A	N/A	N/A	7.94×10^{-01}	N/A	N/A
Benzyl Acetate	$\leq 3.00 \times 10^{-05}$	0.10	N/A	N/A	N/A	$\leq 3.00 \times 10^{-04}$	N/A	N/A
β-Nicotyrine	$\leq 8.25 \times 10^{-06}$	0.17	N/A	N/A	N/A	$\leq 4.79 \times 10^{-05}$	N/A	N/A
Cadmium	$\leq 5.25 \times 10^{-09}$	0.10	$\leq 3.50 \times 10^{-07}$	1.32	e	$\leq 5.26 \times 10^{-08}$	$\leq 2.65 \times 10^{-07}$	NC
Carbon Monoxide	$\leq 5.25 \times 10^{-03}$	0.04	5.31×10^{-01}	1.32	e	$\leq 1.26 \times 10^{-01}$	4.02×10^{-01}	↓ ≥68.75
Chromium	NDBF	0.10	$\leq 5.50 \times 10^{-07}$	1.32	e	NDFB	$\leq 4.17 \times 10^{-07}$	NC
Copper	$\leq 6.56 \times 10^{-08}$	0.10	N/A	N/A	N/A	$\leq 6.57 \times 10^{-07}$	N/A	N/A
Cotinine	6.57×10^{-06}	0.17	N/A	N/A	N/A	3.81×10^{-05}	N/A	N/A
Crotonaldehyde	$\leq 3.11 \times 10^{-06}$	0.10	4.14×10^{-03}	1.32	e	$\leq 3.12 \times 10^{-05}$	3.14×10^{-03}	↓ ≥99.01
Diacetyl	$\leq 8.70 \times 10^{-07}$	0.10	4.30×10^{-02}	1.2	d	$\leq 8.71 \times 10^{-06}$	3.58×10^{-02}	↓ ≥99.98
Diethylene Glycol	$\leq 1.20 \times 10^{-04}$	0.10	N/A	N/A	N/A	$\leq 1.20 \times 10^{-03}$	N/A	N/A
Ethyl Acetate	$\leq 1.30 \times 10^{-04}$	0.04	N/A	N/A	N/A	$\leq 3.45 \times 10^{-03}$	N/A	N/A
Ethyl Acetoacetate	$\leq 2.40 \times 10^{-06}$	0.10	N/A	N/A	N/A	$\leq 2.40 \times 10^{-05}$	N/A	N/A
Ethylene Glycol	$\leq 1.09 \times 10^{-04}$	0.10	N/A	N/A	N/A	$\leq 1.09 \times 10^{-03}$	N/A	N/A
Formaldehyde	6.03×10^{-05}	0.17	5.53×10^{-03}	1.32	e	3.50×10^{-04}	4.19×10^{-03}	↓ 91.64
Furfural	$\leq 4.20 \times 10^{-05}$	0.10	3.11×10^{-02}	1.29	c	$\leq 4.20 \times 10^{-04}$	2.41×10^{-02}	↓ ≥98.26
Glycerol	$2.12 \times 10^{+00}$	0.17	$4.63 \times 10^{+00}$	1.32	e	$1.23 \times 10^{+01}$	$3.51 \times 10^{+00}$	251.45

Glycidol	NR	0.10	5.71×10 ⁻⁰³	1.29	c	NR	4.43×10 ⁻⁰³	N/A
Gold	≤6.33×10 ⁻⁰⁹	0.04	N/A	N/A	N/A	≤1.52×10 ⁻⁰⁷	N/A	N/A
Isoamyl Acetate	≤4.80×10 ⁻⁰⁵	0.10	N/A	N/A	N/A	≤4.80×10 ⁻⁰⁴	N/A	N/A
Isobutyl Acetate	≤3.00×10 ⁻⁰⁵	0.10	N/A	N/A	N/A	≤3.00×10 ⁻⁰⁴	N/A	N/A
Isobutyraldehyde	≤8.26×10 ⁻⁰⁷	0.10	N/A	N/A	N/A	≤8.27×10 ⁻⁰⁶	N/A	N/A
Isoprene	≤4.06×10 ⁻⁰⁶	0.04	2.35×10 ⁻⁰³	1.32	e	≤9.72×10 ⁻⁰⁵	1.78×10 ⁻⁰³	↓ ≥94.54
Lead	≤4.55×10 ⁻⁰⁸	0.10	2.23×10 ⁻⁰⁶	1.29	c	≤4.55×10 ⁻⁰⁷	1.73×10 ⁻⁰⁶	↓ ≥73.65
Menthol	≤1.22×10 ⁻⁰⁴	0.10	4.10×10 ⁻⁰⁴	1.20	d	≤1.22×10 ⁻⁰³	3.42×10 ⁻⁰⁴	NC
Methyl Acetate	≤3.60×10 ⁻⁰⁵	0.10	N/A	N/A	N/A	≤3.60×10 ⁻⁰⁴	N/A	N/A
Myosmine	≤1.93×10 ⁻⁰⁵	0.04	N/A	N/A	N/A	≤4.62×10 ⁻⁰⁴	N/A	N/A
n-Butyraldehyde	≤1.76×10 ⁻⁰⁶	0.10	2.61×10 ⁻⁰²	1.32	e	≤1.76×10 ⁻⁰⁵	1.98×10 ⁻⁰²	↓ ≥99.91
Nickel	≤1.05×10 ⁻⁰⁷	0.10	≤5.50×10 ⁻⁰⁷	1.32	e	≤1.05×10 ⁻⁰⁶	≤4.17×10 ⁻⁰⁷	NC
Nicotine	1.72×10 ⁻⁰¹	0.17	1.32×10 ⁺⁰⁰	1.32	e	1.00×10 ⁺⁰⁰	1.00×10 ⁺⁰⁰	N/A
Nicotine-N-Oxide	≤8.72×10 ⁻⁰⁶	0.10	N/A	N/A	N/A	≤8.73×10 ⁻⁰⁵	N/A	N/A
NNK	≤7.53×10 ⁻⁰⁹	0.10	6.70×10 ⁻⁰⁶	1.32	e	≤7.54×10 ⁻⁰⁸	5.08×10 ⁻⁰⁶	↓ ≥98.52
NNN	≤4.92×10 ⁻⁰⁹	0.10	1.72×10 ⁻⁰⁵	1.32	e	≤4.93×10 ⁻⁰⁸	1.30×10 ⁻⁰⁵	↓ ≥99.62
Nornicotine	2.42×10 ⁻⁰⁵	0.04	N/A	N/A	N/A	5.78×10 ⁻⁰⁴	N/A	N/A
Propionic Acid	≤1.80×10 ⁻⁰⁵	0.10	N/A	N/A	N/A	≤1.80×10 ⁻⁰⁴	N/A	N/A
Propylene Glycol	8.30×10 ⁻⁰¹	0.17	1.75×10 ⁻⁰¹	1.29	c	4.82×10 ⁺⁰⁰	1.36×10 ⁻⁰¹	3450.82
Propylene Oxide	≤1.56×10 ⁻⁰⁶	0.10	1.48×10 ⁻⁰⁴	1.32	e	≤1.56×10 ⁻⁰⁵	1.12×10 ⁻⁰⁴	↓ ≥86.07
Toluene	≤6.12×10 ⁻⁰⁶	0.10	2.59×10 ⁻⁰³	1.32	e	≤6.12×10 ⁻⁰⁵	1.96×10 ⁻⁰³	↓ ≥96.88
Water	4.31×10 ⁻⁰¹	0.17	3.65×10 ⁺⁰¹	1.32	e	2.50×10 ⁺⁰⁰	2.77×10 ⁺⁰¹	↓ 90.96

Average % Difference, Excluding Glycerol, PG and Water. a: Jaccard et al. 2019 b: Moldoveanu et al. 2017 c: Helen et al. 2018 d: Uchiyama et al. 2018 e: Schaller et al. 2016 f: Pappas et al. 2014 g: Roemer et al. 2012 h: IQOS PMTA, 2019.

Table S7. Comparison of HPHC and Chemical Intense Aerosol Levels in Virginia Tobacco 3.0% and Smoke Levels in 3R4F Reference Cigarette.

HPHC or Chemical	JUUL Virginia Tobacco 3.0% 3R4F (mg/cig)					Chemical and HPHC Normalized by Nicotine (mg/mg)		% Difference vs_3R4F
	HPHC or Chemical	Nicotine	HPHC or Chemical	Nicotine	Source Journal	JUUL Virginia Tobacco 3.0%	3R4F	
1-Aminonaphthalene	≤8.19×10 ⁻¹⁰	0.07	2.91×10 ⁻⁰⁵	1.99	a	≤1.22×10 ⁻⁰⁸	1.46×10 ⁻⁰⁵	↓ ≥99.92
1-Butanol	≤3.00×10 ⁻⁰⁵	0.05	N/A	N/A	N/A	≤5.68×10 ⁻⁰⁴	N/A	N/A
1,3-Butadiene	≤2.85×10 ⁻⁰⁶	0.07	1.00×10 ⁻⁰¹	1.99	a	≤4.23×10 ⁻⁰⁵	5.03×10 ⁻⁰²	↓ ≥99.92
2-Aminonaphthalene	≤3.56×10 ⁻¹⁰	0.07	1.81×10 ⁻⁰⁵	1.99	a	≤5.29×10 ⁻⁰⁹	9.10×10 ⁻⁰⁶	↓ ≥99.94
4-Aminobiphenyl	≤1.43×10 ⁻¹⁰	0.07	3.91×10 ⁻⁰⁶	1.99	a	≤2.12×10 ⁻⁰⁹	1.96×10 ⁻⁰⁶	↓ ≥99.89

Acetaldehyde	4.35×10^{-05}	0.11	$1.84 \times 10^{+00}$	1.99	a	4.13×10^{-04}	9.24×10^{-01}	↓ 99.96
Acetyl Propionyl	$\leq 1.76 \times 10^{-06}$	0.05	9.19×10^{-02}	1.99	b	$\leq 3.33 \times 10^{-05}$	4.62×10^{-02}	↓ ≥99.93
Acrolein	$\leq 2.01 \times 10^{-05}$	0.11	1.80×10^{-01}	1.99	a	$\leq 1.91 \times 10^{-04}$	9.05×10^{-02}	↓ ≥99.79
Acrylonitrile	$\leq 3.20 \times 10^{-06}$	0.05	2.05×10^{-02}	1.99	a	$\leq 6.06 \times 10^{-05}$	1.03×10^{-02}	↓ ≥99.41
Ammonia	$\leq 3.99 \times 10^{-05}$	0.07	3.40×10^{-02}	1.99	a	$\leq 5.92 \times 10^{-04}$	1.71×10^{-02}	↓ ≥96.53
Anabasine	$\leq 2.87 \times 10^{-06}$	0.07	N/A	N/A	N/A	$\leq 4.27 \times 10^{-05}$	N/A	N/A
Anatabine	$\leq 2.38 \times 10^{-06}$	0.07	N/A	N/A	N/A	$\leq 3.53 \times 10^{-05}$	N/A	N/A
Benzene	$\leq 1.71 \times 10^{-06}$	0.05	8.88×10^{-02}	1.99	a	$\leq 3.23 \times 10^{-05}$	4.46×10^{-02}	↓ ≥99.93
Benzo(a)pyrene	$\leq 5.31 \times 10^{-09}$	0.07	1.51×10^{-05}	1.99	a	$\leq 7.89 \times 10^{-08}$	7.59×10^{-06}	↓ ≥98.96
Benzoic Acid	8.41×10^{-02}	0.11	N/A	N/A	N/A	7.97×10^{-01}	N/A	N/A
Benzyl Acetate	$\leq 3.00 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 5.68 \times 10^{-04}$	N/A	N/A
β-Nicotyrine	$\leq 8.25 \times 10^{-06}$	0.11	N/A	N/A	N/A	$\leq 7.82 \times 10^{-05}$	N/A	N/A
Cadmium	$\leq 5.25 \times 10^{-09}$	0.05	9.32×10^{-05}	1.99	a	$\leq 9.94 \times 10^{-08}$	4.68×10^{-05}	↓ ≥99.79
Carbon Monoxide	$\leq 5.25 \times 10^{-03}$	0.07	$3.05 \times 10^{+01}$	1.99	a	$\leq 7.80 \times 10^{-02}$	$1.53 \times 10^{+01}$	↓ ≥99.49
Chromium	NDFB	0.05	$\leq 1.19 \times 10^{-05}$	1.74	c	NDFB	$\leq 6.84 \times 10^{-06}$	NC
Copper	$\leq 2.84 \times 10^{-07}$	0.05	N/A	N/A	N/A	$\leq 5.39 \times 10^{-06}$	N/A	N/A
Cotinine	$\leq 9.37 \times 10^{-07}$	0.05	N/A	N/A	N/A	$\leq 1.78 \times 10^{-05}$	N/A	N/A
Crotonaldehyde	$\leq 3.11 \times 10^{-06}$	0.05	5.95×10^{-02}	1.99	a	$\leq 5.90 \times 10^{-05}$	2.99×10^{-02}	↓ ≥99.80
Diacetyl	$\leq 8.70 \times 10^{-07}$	0.05	3.37×10^{-01}	1.99	a	$\leq 1.65 \times 10^{-05}$	1.69×10^{-01}	↓ ≥99.99
Diethylene Glycol	$\leq 1.20 \times 10^{-04}$	0.05	N/A	N/A	N/A	$\leq 2.27 \times 10^{-03}$	N/A	N/A
Ethyl Acetate	$\leq 1.30 \times 10^{-04}$	0.11	N/A	N/A	N/A	$\leq 1.23 \times 10^{-03}$	N/A	N/A
Ethyl Acetoacetate	$\leq 2.40 \times 10^{-06}$	0.05	N/A	N/A	N/A	$\leq 4.54 \times 10^{-05}$	N/A	N/A
Ethylene Glycol	$\leq 1.09 \times 10^{-04}$	0.05	N/A	N/A	N/A	$\leq 2.07 \times 10^{-03}$	N/A	N/A
Formaldehyde	8.72×10^{-05}	0.11	8.71×10^{-02}	1.99	a	8.27×10^{-04}	4.38×10^{-02}	↓ 98.11
Furfural	$\leq 4.20 \times 10^{-05}$	0.05	2.59×10^{-02}	1.74	c	$\leq 7.95 \times 10^{-04}$	1.49×10^{-02}	↓ ≥94.66
Glycerol	$2.40 \times 10^{+00}$	0.11	$2.70 \times 10^{+00}$	1.99	a	$2.27 \times 10^{+01}$	$1.36 \times 10^{+00}$	1574
Glycidol	NR	0.05	1.76×10^{-03}	1.99	a	NR	8.84×10^{-04}	N/A
Gold	$\leq 6.33 \times 10^{-09}$	0.07	N/A	N/A	N/A	$\leq 9.40 \times 10^{-08}$	N/A	N/A
Isoamyl Acetate	$\leq 4.80 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 9.09 \times 10^{-04}$	N/A	N/A
Isobutyl Acetate	$\leq 3.00 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 5.68 \times 10^{-04}$	N/A	N/A
Isobutyraldehyde	$\leq 8.26 \times 10^{-07}$	0.05	N/A	N/A	N/A	$\leq 1.57 \times 10^{-05}$	N/A	N/A
Isoprene	$\leq 4.06 \times 10^{-06}$	0.07	7.99×10^{-01}	1.99	a	$\leq 6.03 \times 10^{-05}$	4.02×10^{-01}	↓ ≥99.98
Lead	NDFB	0.05	3.12×10^{-05}	1.74	c	NDFB	1.79×10^{-05}	NC
Menthol	$\leq 1.22 \times 10^{-04}$	0.05	$\leq 1.00 \times 10^{-05}$	2.10	d	$\leq 2.31 \times 10^{-03}$	$\leq 4.76 \times 10^{-06}$	NC
Methyl Acetate	$\leq 3.60 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 6.82 \times 10^{-04}$	N/A	N/A
Myosmine	$\leq 1.93 \times 10^{-05}$	0.07	N/A	N/A	N/A	$\leq 2.86 \times 10^{-04}$	N/A	N/A
n- Butyraldehyde	$\leq 1.76 \times 10^{-06}$	0.05	9.30×10^{-02}	1.99	a	$\leq 3.33 \times 10^{-05}$	4.67×10^{-02}	↓ ≥99.93
Nickel	$\leq 4.55 \times 10^{-07}$	0.05	$\leq 1.29 \times 10^{-05}$	1.74	c	$\leq 8.62 \times 10^{-06}$	$\leq 7.41 \times 10^{-06}$	NC
Nicotine	1.05×10^{-01}	0.11	$1.99 \times 10^{+00}$	1.99	a	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	N/A

Nicotine-N-Oxide	$\leq 8.72 \times 10^{-06}$	0.05	N/A	N/A	N/A	$\leq 1.65 \times 10^{-04}$	N/A	N/A
NNK	$\leq 7.53 \times 10^{-09}$	0.05	2.95×10^{-04}	1.99	a	$\leq 1.43 \times 10^{-07}$	1.48×10^{-04}	↓ ≥ 99.90
NNN	$\leq 4.92 \times 10^{-09}$	0.05	3.37×10^{-04}	1.99	a	$\leq 9.32 \times 10^{-08}$	1.69×10^{-04}	↓ ≥ 99.94
Normicotine	1.66×10^{-05}	0.07	N/A	N/A	N/A	2.47×10^{-04}	N/A	N/A
Propionic Acid	$\leq 7.80 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 1.79 \times 10^{-03}$	N/A	N/A
Propylene Glycol	9.19×10^{-01}	0.11	2.37×10^{-02}	1.74	c	$8.71 \times 10^{+00}$	1.36×10^{-02}	63861.53
Propylene Oxide	$\leq 1.56 \times 10^{-06}$	0.05	$1.00 \times 10^{+00}$	1.99	a	$\leq 2.96 \times 10^{-05}$	5.03×10^{-01}	↓ ≥ 99.99
Toluene	$\leq 6.12 \times 10^{-06}$	0.05	1.53×10^{-01}	1.99	a	$\leq 1.16 \times 10^{-04}$	7.69×10^{-02}	↓ ≥ 99.85
Water	4.57×10^{-01}	0.11	$1.58 \times 10^{+01}$	1.89	e	$4.33 \times 10^{+00}$	$8.36 \times 10^{+00}$	↓ 48.2

Average % Difference, Excluding Glycerol, PG and Water. a: Jaccard et al. 2019 b: Moldoveanu et al. 2017 c: Helen et al. 2018 d: Uchiyama et al. 2018 e: Schaller et al. 2016 f: Pappas et al. 2014 g: Roemer et al. 2012 h: IQOS PMTA, 2019.

Table S8. Comparison of HPHC and Chemical Non-Intense Aerosol Levels in Virginia Tobacco 3.0% and Smoke Levels in 3R4F Reference Cigarette.

HPHC Chemical	JUUL Virginia Tobacco 3.0% (mg/puff)		3R4F (mg/cig)			Chemical and HPHC Normalized by Nicotine (mg/mg)		% Difference vs_3R4F
	HPHC Chemical	or Nicotine	HPHC Chemical	or Nicotine	Source Journal	JUUL Virginia Tobacco 3.0%	3R4F	
1-Aminonaphthalene	$\leq 8.19 \times 10^{-10}$	0.07	1.42×10^{-05}	0.70	a	$\leq 1.22 \times 10^{-08}$	2.02×10^{-05}	↓ ≥ 99.94
1-Butanol	$\leq 3.00 \times 10^{-05}$	0.03	N/A	N/A	N/A	$\leq 1.02 \times 10^{-03}$	N/A	N/A
1,3-Butadiene	$\leq 2.85 \times 10^{-06}$	0.07	3.79×10^{-02}	0.70	a	$\leq 4.24 \times 10^{-05}$	5.40×10^{-02}	↓ ≥ 99.92
2-Aminonaphthalene	$\leq 3.56 \times 10^{-10}$	0.07	8.77×10^{-06}	0.70	a	$\leq 5.29 \times 10^{-09}$	1.25×10^{-05}	↓ ≥ 99.96
4-Aminobiphenyl	$\leq 1.43 \times 10^{-10}$	0.07	1.54×10^{-06}	0.70	a	$\leq 2.13 \times 10^{-09}$	2.19×10^{-06}	↓ ≥ 99.90
Acetaldehyde	3.47×10^{-05}	0.05	5.97×10^{-01}	0.70	a	6.49×10^{-04}	8.50×10^{-01}	↓ 99.92
Acetyl Propionyl	$\leq 1.76 \times 10^{-06}$	0.03	2.95×10^{-02}	0.70	b	$\leq 5.99 \times 10^{-05}$	4.21×10^{-02}	↓ ≥ 99.86
Acrolein	$\leq 2.01 \times 10^{-05}$	0.06	5.32×10^{-02}	0.70	a	$\leq 3.55 \times 10^{-04}$	7.58×10^{-02}	↓ ≥ 99.53
Acrylonitrile	$\leq 3.20 \times 10^{-06}$	0.03	5.23×10^{-03}	0.70	a	$\leq 1.09 \times 10^{-04}$	7.45×10^{-03}	↓ ≥ 98.53
Ammonia	$\leq 3.99 \times 10^{-05}$	0.07	9.64×10^{-03}	0.70	a	$\leq 5.92 \times 10^{-04}$	1.37×10^{-02}	↓ ≥ 95.69
Anabasine	$\leq 2.87 \times 10^{-06}$	0.07	N/A	N/A	N/A	$\leq 4.27 \times 10^{-05}$	N/A	N/A
Anatabine	$\leq 2.38 \times 10^{-06}$	0.07	N/A	N/A	N/A	$\leq 3.53 \times 10^{-05}$	N/A	N/A
Benzene	$\leq 1.71 \times 10^{-06}$	0.03	3.36×10^{-02}	0.70	a	$\leq 5.82 \times 10^{-05}$	4.79×10^{-02}	↓ ≥ 99.88
Benzo(a)pyrene	$\leq 5.31 \times 10^{-09}$	0.07	6.30×10^{-06}	0.70	a	$\leq 7.89 \times 10^{-08}$	8.97×10^{-06}	↓ ≥ 99.12
Benzoic Acid	4.79×10^{-02}	0.06	N/A	N/A	N/A	8.46×10^{-01}	N/A	N/A
Benzyl Acetate	$\leq 3.00 \times 10^{-05}$	0.03	N/A	N/A	N/A	$\leq 1.02 \times 10^{-03}$	N/A	N/A
β-Nicotyrine	$\leq 8.25 \times 10^{-06}$	0.06	N/A	N/A	N/A	$\leq 1.46 \times 10^{-04}$	N/A	N/A
Cadmium	$\leq 5.25 \times 10^{-09}$	0.03	2.45×10^{-05}	0.70	a	$\leq 1.79 \times 10^{-07}$	3.49×10^{-05}	↓ ≥ 99.49
Carbon Monoxide	$\leq 5.25 \times 10^{-03}$	0.07	$1.00 \times 10^{+01}$	0.70	a	$\leq 7.80 \times 10^{-02}$	$1.42 \times 10^{+01}$	↓ ≥ 99.45
Chromium	NDFB	0.03	$\leq 8.80 \times 10^{-07}$	0.70	f	NDFB	$\leq 1.25 \times 10^{-06}$	NC

Copper	$\leq 2.84 \times 10^{-07}$	0.03	N/A	N/A	N/A	$\leq 9.70 \times 10^{-06}$	N/A	N/A
Cotinine	$\leq 4.06 \times 10^{-06}$	0.03	N/A	N/A	N/A	$\leq 1.39 \times 10^{-04}$	N/A	N/A
Crotonaldehyde	$\leq 3.11 \times 10^{-06}$	0.03	9.89×10^{-03}	0.70	a	$\leq 1.06 \times 10^{-04}$	1.41×10^{-02}	↓ ≥ 99.25
Diacetyl	$\leq 8.70 \times 10^{-07}$	0.03	1.15×10^{-01}	0.70	b	$\leq 2.97 \times 10^{-05}$	1.64×10^{-01}	↓ ≥ 99.98
Diethylene Glycol	$\leq 1.20 \times 10^{-04}$	0.03	N/A	N/A	N/A	$\leq 4.09 \times 10^{-03}$	N/A	N/A
Ethyl Acetate	$\leq 1.30 \times 10^{-04}$	0.03	N/A	N/A	N/A	$\leq 4.43 \times 10^{-03}$	N/A	N/A
Ethyl Acetoacetate	$\leq 2.40 \times 10^{-06}$	0.03	N/A	N/A	N/A	$\leq 8.19 \times 10^{-05}$	N/A	N/A
Ethylene Glycol	$\leq 1.09 \times 10^{-04}$	0.03	N/A	N/A	N/A	$\leq 3.73 \times 10^{-03}$	N/A	N/A
Formaldehyde	7.24×10^{-05}	0.05	2.47×10^{-02}	0.70	a	1.35×10^{-03}	3.52×10^{-02}	↓ 96.16
Furfural	$\leq 4.20 \times 10^{-05}$	0.03	1.40×10^{-02}	0.76	d	$\leq 1.43 \times 10^{-03}$	1.84×10^{-02}	↓ ≥ 92.22
Glycerol	$1.23 \times 10^{+00}$	0.05	$2.70 \times 10^{+00}$	0.70	a	$2.31 \times 10^{+01}$	$3.85 \times 10^{+00}$	499.45
Glycidol	NR	0.03	N/A	N/A	N/A	NR	N/A	N/A
Gold	$\leq 6.33 \times 10^{-09}$	0.07	N/A	N/A	N/A	$\leq 9.41 \times 10^{-08}$	N/A	N/A
Isoamyl Acetate	$\leq 4.80 \times 10^{-05}$	0.03	N/A	N/A	N/A	$\leq 1.64 \times 10^{-03}$	N/A	N/A
Isobutyl Acetate	$\leq 3.00 \times 10^{-05}$	0.03	N/A	N/A	N/A	$\leq 1.02 \times 10^{-03}$	N/A	N/A
Isobutyraldehyde	$\leq 8.26 \times 10^{-07}$	0.03	N/A	N/A	N/A	$\leq 2.82 \times 10^{-05}$	N/A	N/A
Isoprene	$\leq 4.06 \times 10^{-06}$	0.07	2.88×10^{-01}	0.70	a	$\leq 6.03 \times 10^{-05}$	4.10×10^{-01}	↓ ≥ 99.99
Lead	$\leq 4.55 \times 10^{-08}$	0.03	9.20×10^{-06}	0.70	f	$\leq 1.55 \times 10^{-06}$	1.31×10^{-05}	↓ ≥ 88.16
Menthol	$\leq 1.22 \times 10^{-04}$	0.03	$\leq 1.00 \times 10^{-05}$	0.76	a	$\leq 4.17 \times 10^{-03}$	$\leq 1.32 \times 10^{-05}$	NC
Methyl Acetate	$\leq 3.60 \times 10^{-05}$	0.03	N/A	N/A	N/A	$\leq 1.23 \times 10^{-03}$	N/A	N/A
Myosmine	$\leq 1.93 \times 10^{-05}$	0.07	N/A	N/A	N/A	$\leq 2.86 \times 10^{-04}$	N/A	N/A
n-Butyraldehyde	$\leq 1.76 \times 10^{-06}$	0.03	2.84×10^{-02}	0.70	a	$\leq 5.99 \times 10^{-05}$	4.05×10^{-02}	↓ ≥ 99.85
Nickel	$\leq 4.55 \times 10^{-07}$	0.06	$\leq 3.80 \times 10^{-07}$	0.70	f	$\leq 8.03 \times 10^{-06}$	$\leq 5.41 \times 10^{-07}$	NC
Nicotine	5.67×10^{-02}	0.06	7.02×10^{-01}	0.70	a	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	N/A
Nicotine-N-Oxide	$\leq 8.72 \times 10^{-06}$	0.03	N/A	N/A	N/A	$\leq 2.97 \times 10^{-04}$	N/A	N/A
NNK	$\leq 7.53 \times 10^{-09}$	0.03	1.13×10^{-04}	0.70	a	$\leq 2.57 \times 10^{-07}$	1.61×10^{-04}	↓ ≥ 99.84
NNN	$\leq 4.92 \times 10^{-09}$	0.03	1.31×10^{-04}	0.70	a	$\leq 1.68 \times 10^{-07}$	1.87×10^{-04}	↓ ≥ 99.91
Nornicotine	1.66×10^{-05}	0.07	N/A	N/A	N/A	2.47×10^{-04}	N/A	N/A
Propionic Acid	$\leq 7.80 \times 10^{-05}$	0.03	N/A	N/A	N/A	$\leq 2.66 \times 10^{-03}$	N/A	N/A
Propylene Glycol	5.01×10^{-01}	0.06	3.20×10^{-03}	0.76	d	$8.85 \times 10^{+00}$	4.21×10^{-03}	210011.2
Propylene Oxide	$\leq 1.56 \times 10^{-06}$	0.03	2.97×10^{-01}	0.70	a	$\leq 5.32 \times 10^{-05}$	4.23×10^{-01}	↓ ≥ 99.99
Toluene	$\leq 6.12 \times 10^{-06}$	0.03	5.14×10^{-02}	0.70	a	$\leq 2.09 \times 10^{-04}$	7.32×10^{-02}	↓ ≥ 99.72
Water	2.75×10^{-01}	0.05	$3.20 \times 10^{+00}$	0.76	d	$5.13 \times 10^{+00}$	$4.21 \times 10^{+00}$	21.78

Average % Difference, Excluding Glycerol, PG and Water. a: Jaccard et al. 2019 b: Moldoveanu et al. 2017 c: Helen et al. 2018 d: Uchiyama et al. 2018 e: Schaller et al. 2016 f: Pappas et al. 2014 g: Roemer et al. 2012 h: IQOS PMTA, 2019.

Table S9. Comparison of HPHC and Chemical Intense Aerosol Levels in Virginia Tobacco 3.0% and Aerosol Levels in IQOS Regular.

HPHC Chemical	JUUL Virginia Tobacco 3.0% (mg/puff)		IQOS (mg/cig)		Source Journal	Chemical and HPHC Normalized by Nicotine (mg/mg)		% Difference vs_3R4F
	HPHC Chemical	or Nicotine	HPHC Chemical	or Nicotine		JUUL Virginia Tobacco 3.0%	3R4F	
1-Aminonaphthalene	$\leq 8.19 \times 10^{-10}$	0.07	7.70×10^{-08}	1.32	e	$\leq 1.22 \times 10^{-08}$	5.83×10^{-08}	↓ ≥ 79.16
1-Butanol	$\leq 3.00 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 5.68 \times 10^{-04}$	N/A	N/A
1,3-Butadiene	$\leq 2.85 \times 10^{-06}$	0.07	2.94×10^{-04}	1.32	e	$\leq 4.23 \times 10^{-05}$	2.23×10^{-04}	↓ ≥ 80.99
2-Aminonaphthalene	$\leq 3.56 \times 10^{-10}$	0.07	4.60×10^{-08}	1.32	e	$\leq 5.29 \times 10^{-09}$	3.48×10^{-08}	↓ ≥ 84.82
4-Aminobiphenyl	$\leq 1.43 \times 10^{-10}$	0.07	9.00×10^{-09}	1.29	c	$\leq 2.12 \times 10^{-09}$	6.98×10^{-09}	↓ ≥ 69.55
Acetaldehyde	4.35×10^{-05}	0.11	2.19×10^{-01}	1.32	e	4.13×10^{-04}	1.66×10^{-01}	-99.75
Acetyl Propionyl	$\leq 1.76 \times 10^{-06}$	0.05	N/A	N/A	N/A	$\leq 3.33 \times 10^{-05}$	N/A	N/A
Acrolein	$\leq 2.01 \times 10^{-05}$	0.11	1.13×10^{-02}	1.32	e	$\leq 1.91 \times 10^{-04}$	8.56×10^{-03}	↓ ≥ 97.77
Acrylonitrile	$\leq 3.20 \times 10^{-06}$	0.05	2.58×10^{-04}	1.32	e	$\leq 6.06 \times 10^{-05}$	1.95×10^{-04}	↓ ≥ 68.99
Ammonia	$\leq 3.99 \times 10^{-05}$	0.07	1.42×10^{-02}	1.32	e	$\leq 5.92 \times 10^{-04}$	1.08×10^{-02}	↓ ≥ 94.50
Anabasine	$\leq 2.87 \times 10^{-06}$	0.07	N/A	N/A	N/A	$\leq 4.27 \times 10^{-05}$	N/A	N/A
Anatabine	$\leq 2.38 \times 10^{-06}$	0.07	N/A	N/A	N/A	$\leq 3.53 \times 10^{-05}$	N/A	N/A
Benzene	$\leq 1.71 \times 10^{-06}$	0.05	6.49×10^{-04}	1.32	e	$\leq 3.23 \times 10^{-05}$	4.92×10^{-04}	↓ ≥ 93.43
Benzo(a)pyrene	$\leq 5.31 \times 10^{-09}$	0.07	7.36×10^{-07}	1.29	c	$\leq 7.89 \times 10^{-08}$	5.71×10^{-07}	↓ ≥ 86.17
Benzoic Acid	8.41×10^{-02}	0.11	N/A	N/A	N/A	7.97×10^{-01}	N/A	N/A
Benzyl Acetate	$\leq 3.00 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 5.68 \times 10^{-04}$	N/A	N/A
β-Nicotyrine	$\leq 8.25 \times 10^{-06}$	0.11	N/A	N/A	N/A	$\leq 7.82 \times 10^{-05}$	N/A	N/A
Cadmium	$\leq 5.25 \times 10^{-09}$	0.05	$\leq 3.50 \times 10^{-07}$	1.32	e	$\leq 9.94 \times 10^{-08}$	$\leq 2.65 \times 10^{-07}$	NC
Carbon Monoxide	$\leq 5.25 \times 10^{-03}$	0.07	5.31×10^{-01}	1.32	e	$\leq 7.80 \times 10^{-02}$	4.02×10^{-01}	↓ ≥ 80.62
Chromium	NDFB	0.05	$\leq 5.50 \times 10^{-07}$	1.32	e	NDFB	$\leq 4.17 \times 10^{-07}$	NC
Copper	$\leq 2.84 \times 10^{-07}$	0.05	N/A	N/A	N/A	$\leq 5.39 \times 10^{-06}$	N/A	N/A
Cotinine	$\leq 9.37 \times 10^{-07}$	0.05	N/A	N/A	N/A	$\leq 1.78 \times 10^{-05}$	N/A	N/A
Crotonaldehyde	$\leq 3.11 \times 10^{-06}$	0.05	4.14×10^{-03}	1.32	e	$\leq 5.90 \times 10^{-05}$	3.14×10^{-03}	↓ ≥ 98.12
Diacetyl	$\leq 8.70 \times 10^{-07}$	0.05	4.30×10^{-02}	1.20	d	$\leq 1.65 \times 10^{-05}$	3.58×10^{-02}	↓ ≥ 99.95
Diethylene Glycol	$\leq 1.20 \times 10^{-04}$	0.05	N/A	N/A	N/A	$\leq 2.27 \times 10^{-03}$	N/A	N/A
Ethyl Acetate	$\leq 1.30 \times 10^{-04}$	0.11	N/A	N/A	N/A	$\leq 1.23 \times 10^{-03}$	N/A	N/A
Ethyl Acetoacetate	$\leq 2.40 \times 10^{-06}$	0.05	N/A	N/A	N/A	$\leq 4.54 \times 10^{-05}$	N/A	N/A
Ethylene Glycol	$\leq 1.09 \times 10^{-04}$	0.05	N/A	N/A	N/A	$\leq 2.07 \times 10^{-03}$	N/A	N/A
Formaldehyde	8.72×10^{-05}	0.11	5.53×10^{-03}	1.32	e	8.27×10^{-04}	4.19×10^{-03}	↓ 80.27
Furfural	$\leq 4.20 \times 10^{-05}$	0.05	3.11×10^{-02}	1.29	c	$\leq 7.95 \times 10^{-04}$	2.41×10^{-02}	↓ ≥ 96.70
Glycerol	$2.40 \times 10^{+00}$	0.11	$4.63 \times 10^{+00}$	1.32	e	$2.27 \times 10^{+01}$	$3.51 \times 10^{+00}$	547.53

Glycidol	NR	0.05	5.71×10 ⁻⁰³	1.29	c	NR	4.43×10 ⁻⁰³	N/A
Gold	≤6.33×10 ⁻⁰⁹	0.07	N/A	N/A	N/A	≤9.40×10 ⁻⁰⁸	N/A	N/A
Isoamyl Acetate	≤4.80×10 ⁻⁰⁵	0.05	N/A	N/A	N/A	≤9.09×10 ⁻⁰⁴	N/A	N/A
Isobutyl Acetate	≤3.00×10 ⁻⁰⁵	0.05	N/A	N/A	N/A	≤5.68×10 ⁻⁰⁴	N/A	N/A
Isobutyraldehyde	≤8.26×10 ⁻⁰⁷	0.05	N/A	N/A	N/A	≤1.57×10 ⁻⁰⁵	N/A	N/A
Isoprene	≤4.06×10 ⁻⁰⁶	0.07	2.35×10 ⁻⁰³	1.32	e	≤6.03×10 ⁻⁰⁵	1.78×10 ⁻⁰³	↓ ≥96.61
Lead	NDFB	0.05	2.23×10 ⁻⁰⁶	1.29	c	NDFB	1.73×10 ⁻⁰⁶	NC
Menthol	≤1.22×10 ⁻⁰⁴	0.05	4.10×10 ⁻⁰⁴	1.20	d	≤2.31×10 ⁻⁰³	3.42×10 ⁻⁰⁴	NC
Methyl Acetate	≤3.60×10 ⁻⁰⁵	0.05	N/A	N/A	N/A	≤6.82×10 ⁻⁰⁴	N/A	N/A
Myosmine	≤1.93×10 ⁻⁰⁵	0.07	N/A	N/A	N/A	≤2.86×10 ⁻⁰⁴	N/A	N/A
n-Butyraldehyde	≤1.76×10 ⁻⁰⁶	0.05	2.61×10 ⁻⁰²	1.32	e	≤3.33×10 ⁻⁰⁵	1.98×10 ⁻⁰²	↓ ≥99.83
Nickel	≤4.55×10 ⁻⁰⁷	0.05	≤5.50×10 ⁻⁰⁷	1.32	e	≤8.62×10 ⁻⁰⁶	≤4.17×10 ⁻⁰⁷	NC
Nicotine	1.05×10 ⁻⁰¹	0.11	1.32×10 ⁺⁰⁰	1.32	e	1.00×10 ⁺⁰⁰	1.00×10 ⁺⁰⁰	N/A
Nicotine-N-Oxide	≤8.72×10 ⁻⁰⁶	0.05	N/A	N/A	N/A	≤1.65×10 ⁻⁰⁴	N/A	N/A
NNK	≤7.53×10 ⁻⁰⁹	0.05	6.70×10 ⁻⁰⁶	1.32	e	≤1.43×10 ⁻⁰⁷	5.08×10 ⁻⁰⁶	↓ ≥97.19
NNN	≤4.92×10 ⁻⁰⁹	0.05	1.72×10 ⁻⁰⁵	1.32	e	≤9.32×10 ⁻⁰⁸	1.30×10 ⁻⁰⁵	↓ ≥99.28
Nornicotine	1.66×10 ⁻⁰⁵	0.07	N/A	N/A	N/A	2.47×10 ⁻⁰⁴	N/A	N/A
Propionic Acid	≤7.80×10 ⁻⁰⁵	0.04	N/A	N/A	N/A	≤1.79×10 ⁻⁰³	N/A	N/A
Propylene Glycol	9.19×10 ⁻⁰¹	0.11	1.75×10 ⁻⁰¹	1.29	c	8.71×10 ⁺⁰⁰	1.36×10 ⁻⁰¹	6321.99
Propylene Oxide	≤1.56×10 ⁻⁰⁶	0.05	1.48×10 ⁻⁰⁴	1.32	e	≤2.96×10 ⁻⁰⁵	1.12×10 ⁻⁰⁴	↓ ≥73.64
Toluene	≤6.12×10 ⁻⁰⁶	0.05	2.59×10 ⁻⁰³	1.32	e	≤1.16×10 ⁻⁰⁴	1.96×10 ⁻⁰³	↓ ≥94.10
Water	4.57×10 ⁻⁰¹	0.11	3.65×10 ⁺⁰¹	1.32	e	4.33×10 ⁺⁰⁰	2.77×10 ⁺⁰¹	↓ 84.34

Average % Difference, Excluding Glycerol, PG and Water. a: Jaccard et al. 2019 b: Moldoveanu et al. 2017 c: Helen et al. 2018 d: Uchiyama et al. 2018 e: Schaller et al. 2016 f: Pappas et al. 2014 g: Roemer et al. 2012 h: IQOS PMTA, 2019.

Table S10. Comparison of HPHC and Chemical Intense Aerosol Levels in 10enthol 5.0% and Smoke Levels 3R4F Reference Cigarette.

HPHC Chemical	JUUL Menthol 5.0% (mg/puff)		3R4F (mg/cig)			Chemical and HPHC Normalized by Nicotine (mg/mg)		% Difference vs_3R4F
	HPHC Chemical	or Nicotine	HPHC Chemical	or Nicotine	Source Journal	JUUL Virginia Tobacco 3.0%	3R4F	
1-Aminonaphthalene	≤8.19×10 ⁻¹⁰	0.04	2.91×10 ⁻⁰⁵	1.99	a	≤2.25×10 ⁻⁰⁸	1.46×10 ⁻⁰⁵	↓ ≥99.85
1-Butanol	≤3.00×10 ⁻⁰⁵	0.07	N/A	N/A	N/A	≤4.33×10 ⁻⁰⁴	N/A	N/A
1,3-Butadiene	≤2.85×10 ⁻⁰⁶	0.04	1.00×10 ⁻⁰¹	1.99	a	≤7.85×10 ⁻⁰⁵	5.03×10 ⁻⁰²	↓ ≥99.84
2-Aminonaphthalene	≤3.56×10 ⁻¹⁰	0.04	1.81×10 ⁻⁰⁵	1.99	a	≤9.80×10 ⁻⁰⁹	9.10×10 ⁻⁰⁶	↓ ≥99.89
4-Aminobiphenyl	≤1.43×10 ⁻¹⁰	0.04	3.91×10 ⁻⁰⁶	1.99	a	≤3.94×10 ⁻⁰⁹	1.96×10 ⁻⁰⁶	↓ ≥99.80

Acetaldehyde	3.57×10^{-05}	0.16	$1.84 \times 10^{+00}$	1.99	a	2.30×10^{-04}	9.24×10^{-01}	↓ 99.98
Acetyl Propionyl	$\leq 1.76 \times 10^{-06}$	0.07	9.19×10^{-02}	1.99	b	$\leq 2.54 \times 10^{-05}$	4.62×10^{-02}	↓ ≥99.95
Acrolein	$\leq 2.01 \times 10^{-05}$	0.16	1.80×10^{-01}	1.99	a	$\leq 1.29 \times 10^{-04}$	9.05×10^{-02}	↓ ≥99.86
Acrylonitrile	$\leq 3.20 \times 10^{-06}$	0.07	2.05×10^{-02}	1.99	a	$\leq 4.63 \times 10^{-05}$	1.03×10^{-02}	↓ ≥99.55
Ammonia	NDFB	0.04	3.40×10^{-02}	1.99	a	NDFB	1.71×10^{-02}	NC
Anabasine	$\leq 1.24 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 3.43 \times 10^{-04}$	N/A	N/A
Anatabine	$\leq 1.03 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 2.84 \times 10^{-04}$	N/A	N/A
Benzene	$\leq 1.71 \times 10^{-06}$	0.07	8.88×10^{-02}	1.99	a	$\leq 2.46 \times 10^{-05}$	4.46×10^{-02}	↓ ≥99.94
Benzo(a)pyrene	$\leq 5.31 \times 10^{-09}$	0.04	1.51×10^{-05}	1.99	a	$\leq 1.46 \times 10^{-07}$	7.59×10^{-06}	↓ ≥98.07
Benzoic Acid	1.17×10^{-01}	0.16	N/A	N/A	N/A	7.48×10^{-01}	N/A	N/A
Benzyl Acetate	$\leq 3.00 \times 10^{-05}$	0.07	N/A	N/A	N/A	$\leq 4.33 \times 10^{-04}$	N/A	N/A
β-Nicotyrine	1.33×10^{-05}	0.16	N/A	N/A	N/A	8.49×10^{-05}	N/A	N/A
Cadmium	$\leq 5.25 \times 10^{-09}$	0.07	9.32×10^{-05}	1.99	a	$\leq 7.59 \times 10^{-08}$	4.68×10^{-05}	↓ ≥99.84
Carbon Monoxide	$\leq 5.25 \times 10^{-03}$	0.04	$3.05 \times 10^{+01}$	1.99	a	$\leq 1.44 \times 10^{-01}$	$1.53 \times 10^{+01}$	↓ ≥99.06
Chromium	NDFB	0.07	$\leq 1.19 \times 10^{-05}$	1.74	c	NDFB	$\leq 6.84 \times 10^{-06}$	NC
Copper	$\leq 6.56 \times 10^{-08}$	0.07	N/A	N/A	N/A	$\leq 9.48 \times 10^{-07}$	N/A	N/A
Cotinine	$\leq 4.06 \times 10^{-06}$	0.07	N/A	N/A	N/A	$\leq 5.87 \times 10^{-05}$	N/A	N/A
Crotonaldehyde	$\leq 3.11 \times 10^{-06}$	0.07	5.95×10^{-02}	1.99	a	$\leq 4.50 \times 10^{-05}$	2.99×10^{-02}	↓ ≥99.85
Diacetyl	$\leq 8.70 \times 10^{-07}$	0.07	3.37×10^{-01}	1.99	a	$\leq 1.26 \times 10^{-05}$	1.69×10^{-01}	↓ ≥99.99
Diethylene Glycol	$\leq 1.20 \times 10^{-04}$	0.07	N/A	N/A	N/A	$\leq 1.73 \times 10^{-03}$	N/A	N/A
Ethyl Acetate	$\leq 1.30 \times 10^{-04}$	0.16	N/A	N/A	N/A	$\leq 8.32 \times 10^{-04}$	N/A	N/A
Ethyl Acetoacetate	$\leq 2.40 \times 10^{-06}$	0.07	N/A	N/A	N/A	$\leq 3.47 \times 10^{-05}$	N/A	N/A
Ethylene Glycol	$\leq 1.09 \times 10^{-04}$	0.16	N/A	N/A	N/A	$\leq 7.05 \times 10^{-04}$	N/A	N/A
Formaldehyde	7.56×10^{-05}	0.16	8.71×10^{-02}	1.99	a	4.88×10^{-04}	4.38×10^{-02}	↓ 98.89
Furfural	$\leq 4.20 \times 10^{-05}$	0.07	2.59×10^{-02}	1.74	c	$\leq 6.07 \times 10^{-04}$	1.49×10^{-02}	↓ ≥95.92
Glycerol	$1.99 \times 10^{+00}$	0.16	$2.70 \times 10^{+00}$	1.99	a	$1.29 \times 10^{+01}$	$1.36 \times 10^{+00}$	847.29
Glycidol	NR	0.07	1.76×10^{-03}	1.99	a	NR	8.84×10^{-04}	N/A
Gold	$\leq 6.33 \times 10^{-09}$	0.04	N/A	N/A	N/A	$\leq 1.74 \times 10^{-07}$	N/A	N/A
Isoamyl Acetate	$\leq 4.80 \times 10^{-05}$	0.07	N/A	N/A	N/A	$\leq 6.94 \times 10^{-04}$	N/A	N/A
Isobutyl Acetate	$\leq 3.00 \times 10^{-05}$	0.07	N/A	N/A	N/A	$\leq 4.33 \times 10^{-04}$	N/A	N/A
Isobutyraldehyde	$\leq 3.58 \times 10^{-06}$	0.07	N/A	N/A	N/A	$\leq 5.17 \times 10^{-05}$	N/A	N/A
Isoprene	$\leq 4.06 \times 10^{-06}$	0.04	7.99×10^{-01}	1.99	a	$\leq 1.12 \times 10^{-04}$	4.02×10^{-01}	↓ ≥99.97
Lead	$\leq 4.55 \times 10^{-08}$	0.07	3.12×10^{-05}	1.74	c	$\leq 6.57 \times 10^{-07}$	1.79×10^{-05}	↓ ≥96.33
Menthol	2.90×10^{-02}	0.16	$\leq 1.00 \times 10^{-05}$	2.10	d	1.87×10^{-01}	$\leq 4.76 \times 10^{-06}$	NC
Methyl Acetate	$\leq 3.60 \times 10^{-05}$	0.07	N/A	N/A	N/A	$\leq 5.20 \times 10^{-04}$	N/A	N/A
Myosmine	$\leq 1.93 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 5.30 \times 10^{-04}$	N/A	N/A
n-Butyraldehyde	$\leq 1.76 \times 10^{-06}$	0.07	9.30×10^{-02}	1.99	a	$\leq 2.54 \times 10^{-05}$	4.67×10^{-02}	↓ ≥99.95
Nickel	$\leq 4.55 \times 10^{-07}$	0.07	$\leq 1.29 \times 10^{-05}$	1.74	c	$\leq 6.57 \times 10^{-06}$	$\leq 7.41 \times 10^{-06}$	NC
Nicotine	1.56×10^{-01}	0.16	$1.99 \times 10^{+00}$	1.99	a	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	N/A

Nicotine-N-Oxide	$\leq 8.72 \times 10^{-6}$	0.07	N/A	N/A	N/A	$\leq 1.26 \times 10^{-4}$	N/A	N/A
NNK	$\leq 7.53 \times 10^{-9}$	0.07	2.95×10^{-4}	1.99	a	$\leq 1.09 \times 10^{-7}$	1.48×10^{-4}	↓ ≥ 99.93
NNN	$\leq 4.92 \times 10^{-9}$	0.07	3.37×10^{-4}	1.99	a	$\leq 7.11 \times 10^{-8}$	1.69×10^{-4}	↓ ≥ 99.96
Normicotine	1.99×10^{-5}	0.04	N/A	N/A	N/A	5.48×10^{-4}	N/A	N/A
Propionic Acid	$\leq 7.80 \times 10^{-5}$	0.07	N/A	N/A	N/A	$\leq 1.13 \times 10^{-3}$	N/A	N/A
Propylene Glycol	7.83×10^{-1}	0.16	2.37×10^{-2}	1.74	c	$5.05 \times 10^{+0}$	1.36×10^{-2}	37003.23
Propylene Oxide	$\leq 1.56 \times 10^{-6}$	0.07	$1.00 \times 10^{+0}$	1.99	a	$\leq 2.26 \times 10^{-5}$	5.03×10^{-1}	↓ ≥ 99.996
Toluene	$\leq 6.12 \times 10^{-6}$	0.07	1.53×10^{-1}	1.99	a	$\leq 8.84 \times 10^{-5}$	7.69×10^{-2}	↓ ≥ 99.89
Water	3.84×10^{-1}	0.16	$1.58 \times 10^{+1}$	1.89	e	$2.47 \times 10^{+0}$	$8.36 \times 10^{+0}$	↓ 70.40

Average % Difference, Excluding Glycerol, PG and Water. a: Jaccard et al. 2019 b: Moldoveanu et al. 2017 c: Helen et al. 2018 d: Uchiyama et al. 2018 e: Schaller et al. 2016 f: Pappas et al. 2014 g: Roemer et al. 2012 h: IQOS PMTA, 2019.

Table S11. Comparison of HPHC and Chemical Non-Intense Aerosol Levels in Menthol 5.0% and Smoke Levels in 3R4F Reference Cigarette.

HPHC Chemical	JUUL Menthol 5.0% (mg/puff)		3R4F (mg/cig)			Chemical and HPHC Normalized by Nicotine (mg/mg)		% Difference vs_3R4F
	HPHC Chemical	or Nicotine	HPHC Chemical	or Nicotine	Source Journal	JUUL Virginia Tobacco 3.0%	3R4F	
1-Aminonaphthalene	$\leq 8.19 \times 10^{-10}$	0.04	1.42×10^{-5}	0.70	a	$\leq 2.25 \times 10^{-8}$	2.02×10^{-5}	↓ ≥ 99.89
1-Butanol	$\leq 3.00 \times 10^{-5}$	0.04	N/A	N/A	N/A	$\leq 7.45 \times 10^{-4}$	N/A	N/A
1,3-Butadiene	$\leq 2.85 \times 10^{-6}$	0.04	3.79×10^{-2}	0.70	a	$\leq 7.85 \times 10^{-5}$	5.40×10^{-2}	↓ ≥ 99.85
2-Aminonaphthalene	$\leq 3.56 \times 10^{-10}$	0.04	8.77×10^{-6}	0.70	a	$\leq 9.80 \times 10^{-9}$	1.25×10^{-5}	↓ ≥ 99.92
4-Aminobiphenyl	$\leq 1.43 \times 10^{-10}$	0.04	1.54×10^{-6}	0.70	a	$\leq 3.94 \times 10^{-9}$	2.19×10^{-6}	↓ ≥ 99.82
Acetaldehyde	$\leq 2.16 \times 10^{-5}$	0.04	5.97×10^{-1}	0.70	a	$\leq 5.35 \times 10^{-4}$	8.50×10^{-1}	↓ ≥ 99.94
Acetyl Propionyl	$\leq 1.76 \times 10^{-6}$	0.04	2.95×10^{-2}	0.70	b	$\leq 4.36 \times 10^{-5}$	4.21×10^{-2}	↓ ≥ 99.90
Acrolein	$\leq 2.01 \times 10^{-5}$	0.08	5.32×10^{-2}	0.70	a	$\leq 2.44 \times 10^{-4}$	7.58×10^{-2}	↓ ≥ 99.68
Acrylonitrile	$\leq 3.20 \times 10^{-6}$	0.04	5.23×10^{-3}	0.70	a	$\leq 7.95 \times 10^{-5}$	7.45×10^{-3}	↓ ≥ 98.93
Ammonia	NDFB	0.04	9.64×10^{-3}	0.70	a	NDFB	1.37×10^{-2}	NC
Anabasine	$\leq 1.24 \times 10^{-5}$	0.04	N/A	N/A	N/A	$\leq 3.43 \times 10^{-4}$	N/A	N/A
Anatabine	$\leq 1.03 \times 10^{-5}$	0.04	N/A	N/A	N/A	$\leq 2.84 \times 10^{-4}$	N/A	N/A
Benzene	$\leq 1.71 \times 10^{-6}$	0.04	3.36×10^{-2}	0.70	a	$\leq 4.24 \times 10^{-5}$	4.79×10^{-2}	↓ ≥ 99.91
Benzo(a)pyrene	$\leq 5.31 \times 10^{-9}$	0.04	6.30×10^{-6}	0.70	a	$\leq 1.46 \times 10^{-7}$	8.97×10^{-6}	↓ ≥ 98.37
Benzoic Acid	7.30×10^{-2}	0.09	N/A	N/A	N/A	8.17×10^{-1}	N/A	N/A
Benzyl Acetate	$\leq 3.00 \times 10^{-5}$	0.04	N/A	N/A	N/A	$\leq 7.45 \times 10^{-4}$	N/A	N/A
β-Nicotyrine	$\leq 8.25 \times 10^{-6}$	0.09	N/A	N/A	N/A	$\leq 9.24 \times 10^{-5}$	N/A	N/A
Cadmium	$\leq 5.25 \times 10^{-9}$	0.04	2.45×10^{-5}	0.70	a	$\leq 1.30 \times 10^{-7}$	3.49×10^{-5}	↓ ≥ 99.63
Carbon Monoxide	$\leq 5.25 \times 10^{-3}$	0.04	$1.00 \times 10^{+1}$	0.70	a	$\leq 1.44 \times 10^{-1}$	$1.42 \times 10^{+1}$	↓ ≥ 98.99
Chromium	NDFB	0.04	$\leq 8.80 \times 10^{-7}$	0.70	f	NDFB	$\leq 1.25 \times 10^{-6}$	NC

Copper	$\leq 6.56 \times 10^{-08}$	0.04	N/A	N/A	N/A	$\leq 1.63 \times 10^{-06}$	N/A	N/A
Cotinine	$\leq 4.06 \times 10^{-06}$	0.04	N/A	N/A	N/A	$\leq 1.01 \times 10^{-04}$	N/A	N/A
Crotonaldehyde	$\leq 3.11 \times 10^{-06}$	0.04	9.89×10^{-03}	0.70	a	$\leq 7.73 \times 10^{-05}$	1.41×10^{-02}	↓ ≥99.45
Diacetyl	$\leq 8.70 \times 10^{-07}$	0.04	1.15×10^{-01}	0.70	b	$\leq 2.16 \times 10^{-05}$	1.64×10^{-01}	↓ ≥99.99
Diethylene Glycol	$\leq 1.20 \times 10^{-04}$	0.04	N/A	N/A	N/A	$\leq 2.98 \times 10^{-03}$	N/A	N/A
Ethyl Acetate	$\leq 3.00 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 7.45 \times 10^{-04}$	N/A	N/A
Ethyl Acetoacetate	$\leq 2.40 \times 10^{-06}$	0.04	N/A	N/A	N/A	$\leq 5.96 \times 10^{-05}$	N/A	N/A
Ethylene Glycol	$\leq 1.09 \times 10^{-04}$	0.04	N/A	N/A	N/A	$\leq 2.71 \times 10^{-03}$	N/A	N/A
Formaldehyde	3.94×10^{-05}	0.09	2.47×10^{-02}	0.70	a	4.41×10^{-04}	3.52×10^{-02}	↓ 98.75
Furfural	$\leq 4.20 \times 10^{-05}$	0.04	1.40×10^{-02}	0.76	d	$\leq 1.04 \times 10^{-03}$	1.84×10^{-02}	↓ ≥94.34
Glycerol	$1.23 \times 10^{+00}$	0.09	$2.70 \times 10^{+00}$	0.70	a	$1.38 \times 10^{+01}$	$3.85 \times 10^{+00}$	258.69
Glycidol	NR	0.04	N/A	N/A	N/A	NR	N/A	N/A
Gold	$\leq 6.33 \times 10^{-09}$	0.04	N/A	N/A	N/A	$\leq 1.74 \times 10^{-07}$	N/A	N/A
Isoamyl Acetate	$\leq 4.80 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 1.19 \times 10^{-03}$	N/A	N/A
Isobutyl Acetate	$\leq 3.00 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 7.45 \times 10^{-04}$	N/A	N/A
Isobutyraldehyde	$\leq 8.26 \times 10^{-07}$	0.04	N/A	N/A	N/A	$\leq 2.05 \times 10^{-05}$	N/A	N/A
Isoprene	$\leq 4.06 \times 10^{-06}$	0.04	2.88×10^{-01}	0.70	a	$\leq 1.12 \times 10^{-04}$	4.10×10^{-01}	↓ ≥99.97
Lead	$\leq 4.55 \times 10^{-08}$	0.08	9.20×10^{-06}	0.70	f	$\leq 5.52 \times 10^{-07}$	1.31×10^{-05}	↓ ≥95.79
Menthol	1.81×10^{-02}	0.09	$\leq 1.00 \times 10^{-05}$	0.76	a	2.02×10^{-01}	$\leq 1.32 \times 10^{-05}$	NC
Methyl Acetate	$\leq 3.60 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 8.94 \times 10^{-04}$	N/A	N/A
Myosmine	$\leq 1.93 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 5.30 \times 10^{-04}$	N/A	N/A
n-Butyraldehyde	$\leq 1.76 \times 10^{-06}$	0.04	2.84×10^{-02}	0.70	a	$\leq 4.36 \times 10^{-05}$	4.05×10^{-02}	↓ ≥99.89
Nickel	$\leq 4.55 \times 10^{-07}$	0.04	$\leq 3.80 \times 10^{-07}$	0.70	f	$\leq 1.13 \times 10^{-05}$	$\leq 5.41 \times 10^{-07}$	NC
Nicotine	8.93×10^{-02}	0.09	7.02×10^{-01}	0.70	a	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	N/A
Nicotine-N-Oxide	$\leq 8.72 \times 10^{-06}$	0.04	N/A	N/A	N/A	$\leq 2.16 \times 10^{-04}$	N/A	N/A
NNK	$\leq 7.53 \times 10^{-09}$	0.04	1.13×10^{-04}	0.70	a	$\leq 1.87 \times 10^{-07}$	1.61×10^{-04}	↓ ≥99.88
NNN	$\leq 4.92 \times 10^{-09}$	0.04	1.31×10^{-04}	0.70	a	$\leq 1.22 \times 10^{-07}$	1.87×10^{-04}	↓ ≥99.93
Normicotine	1.99×10^{-05}	0.04	N/A	N/A	N/A	5.48×10^{-04}	N/A	N/A
Propionic Acid	$\leq 7.80 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 1.94 \times 10^{-03}$	N/A	N/A
Propylene Glycol	4.24×10^{-01}	0.08	3.20×10^{-03}	0.76	d	$5.14 \times 10^{+00}$	4.21×10^{-03}	122083.26
Propylene Oxide	$\leq 1.56 \times 10^{-06}$	0.04	2.97×10^{-01}	0.70	a	$\leq 3.87 \times 10^{-05}$	4.23×10^{-01}	↓ ≥99.99
Toluene	$\leq 6.12 \times 10^{-06}$	0.04	5.14×10^{-02}	0.70	a	$\leq 1.52 \times 10^{-04}$	7.32×10^{-02}	↓ ≥99.79
Water	2.52×10^{-01}	0.09	$3.20 \times 10^{+00}$	0.76	d	$2.82 \times 10^{+00}$	$4.21 \times 10^{+00}$	↓ 33.00

Average % Difference, Excluding Glycerol, PG and Water. a: Jaccard et al. 2019 b: Moldoveanu et al. 2017 c: Helen et al. 2018 d: Uchiyama et al. 2018 e: Schaller et al. 2016 f: Pappas et al. 2014 g: Roemer et al. 2012 h: IQOS PMTA, 2019.

Table S12. Comparison of HPHC and Chemical Intense Aerosol Levels in Menthol 5.0% and Aerosol in IQOS Menthol.

HPHC Chemical	JUUL Menthol 5.0% (mg/puff)		IQOS Menthol (mg/cig)			Chemical and HPHC Normalized by Nicotine (mg/mg)		% Difference vs_3R4F
	HPHC Chemical	or Nicotine	HPHC Chemical	or Nicotine	Source Journal	JUUL Virginia Tobacco 3.0%	3R4F	
1-Aminonaphthalene	$\leq 8.19 \times 10^{-10}$	0.04	8.60×10^{-08}	1.21	e	$\leq 2.25 \times 10^{-08}$	7.11×10^{-08}	↓ ≥68.30
1-Butanol	$\leq 3.00 \times 10^{-05}$	0.07	N/A	N/A	N/A	$\leq 4.33 \times 10^{-04}$	N/A	N/A
1,3-Butadiene	$\leq 2.85 \times 10^{-06}$	0.04	2.65×10^{-04}	1.21	e	$\leq 7.85 \times 10^{-05}$	2.19×10^{-04}	↓ ≥64.17
2-Aminonaphthalene	$\leq 3.56 \times 10^{-10}$	0.04	$\leq 3.50 \times 10^{-08}$	1.21	e	$\leq 9.80 \times 10^{-09}$	$\leq 2.89 \times 10^{-08}$	NC
4-Aminobiphenyl	$\leq 1.43 \times 10^{-10}$	0.04	$\leq 5.10 \times 10^{-08}$	1.21	e	$\leq 3.94 \times 10^{-09}$	$\leq 4.21 \times 10^{-08}$	NC
Acetaldehyde	3.57×10^{-05}	0.16	2.05×10^{-01}	1.21	e	2.30×10^{-04}	1.69×10^{-01}	↓ 99.86
Acetyl Propionyl	$\leq 1.76 \times 10^{-06}$	0.07	N/A	N/A	N/A	$\leq 2.54 \times 10^{-05}$	N/A	N/A
Acrolein	$\leq 2.01 \times 10^{-05}$	0.16	9.15×10^{-03}	1.21	e	$\leq 1.29 \times 10^{-04}$	7.56×10^{-03}	↓ ≥98.30
Acrylonitrile	$\leq 3.20 \times 10^{-06}$	0.07	2.20×10^{-04}	1.21	e	$\leq 4.63 \times 10^{-05}$	1.82×10^{-04}	↓ ≥74.56
Ammonia	NDFB	0.04	1.38×10^{-02}	1.21	e	NDFB	1.14×10^{-02}	NC
Anabasine	$\leq 1.24 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 3.43 \times 10^{-04}$	N/A	N/A
Anatabine	$\leq 1.03 \times 10^{-05}$	0.04	N/A	N/A	N/A	$\leq 2.84 \times 10^{-04}$	N/A	N/A
Benzene	$\leq 1.71 \times 10^{-06}$	0.07	6.40×10^{-04}	1.21	e	$\leq 2.46 \times 10^{-05}$	5.29×10^{-04}	↓ ≥95.34
Benzo(a)pyrene	$\leq 5.31 \times 10^{-09}$	0.04	1.29×10^{-06}	1.21	e	$\leq 1.46 \times 10^{-07}$	1.07×10^{-06}	↓ ≥86.29
Benzoic Acid	1.17×10^{-01}	0.16	N/A	N/A	N/A	7.48×10^{-01}	N/A	N/A
Benzyl Acetate	$\leq 3.00 \times 10^{-05}$	0.07	N/A	N/A	N/A	$\leq 4.33 \times 10^{-04}$	N/A	N/A
β-Nicotyrine	1.33×10^{-05}	0.16	N/A	N/A	N/A	8.49×10^{-05}	N/A	N/A
Cadmium	$\leq 5.25 \times 10^{-09}$	0.07	$\leq 3.50 \times 10^{-07}$	1.21	e	$\leq 7.59 \times 10^{-08}$	$\leq 2.89 \times 10^{-07}$	NC
Carbon Monoxide	$\leq 5.25 \times 10^{-03}$	0.04	5.94×10^{-01}	1.21	e	$\leq 1.44 \times 10^{-01}$	4.91×10^{-01}	↓ ≥70.57
Chromium	NDFB	0.07	$\leq 5.50 \times 10^{-07}$	1.21	e	NDFB	$\leq 4.55 \times 10^{-07}$	NC
Copper	$\leq 6.56 \times 10^{-08}$	0.07	N/A	N/A	N/A	$\leq 9.48 \times 10^{-07}$	N/A	N/A
Cotinine	$\leq 4.06 \times 10^{-06}$	0.07	N/A	N/A	N/A	$\leq 5.87 \times 10^{-05}$	N/A	N/A
Crotonaldehyde	$\leq 3.11 \times 10^{-06}$	0.07	3.24×10^{-03}	1.21	e	$\leq 4.50 \times 10^{-05}$	2.68×10^{-03}	↓ ≥98.32
Diacetyl	$\leq 8.70 \times 10^{-07}$	0.07	6.50×10^{-02}	1.20	d	$\leq 1.26 \times 10^{-05}$	5.42×10^{-02}	↓ ≥99.98
Diethylene Glycol	$\leq 1.20 \times 10^{-04}$	0.07	N/A	N/A	N/A	$\leq 1.73 \times 10^{-03}$	N/A	N/A
Ethyl Acetate	$\leq 1.30 \times 10^{-04}$	0.16	N/A	N/A	N/A	$\leq 8.32 \times 10^{-04}$	N/A	N/A
Ethyl Acetoacetate	$\leq 2.40 \times 10^{-06}$	0.07	N/A	N/A	N/A	$\leq 3.47 \times 10^{-05}$	N/A	N/A
Ethylene Glycol	$\leq 1.09 \times 10^{-04}$	0.16	N/A	N/A	N/A	$\leq 7.05 \times 10^{-04}$	N/A	N/A
Formaldehyde	7.56×10^{-05}	0.16	4.55×10^{-03}	1.21	e	4.88×10^{-04}	3.76×10^{-03}	↓ 87.03
Furfural	$\leq 4.20 \times 10^{-05}$	0.07	N/A	N/A	N/A	$\leq 6.07 \times 10^{-04}$	N/A	N/A
Glycerol	$1.99 \times 10^{+00}$	0.16	$3.94 \times 10^{+00}$	N/A	N/A	$1.29 \times 10^{+01}$	$3.26 \times 10^{+00}$	294.71

Glycidol	NR	0.07	1.10×10 ⁻⁰³	1.19	h	NR	9.24×10 ⁻⁰⁴	N/A
Gold	≤6.33×10 ⁻⁰⁹	0.04	N/A	N/A	N/A	≤1.74×10 ⁻⁰⁷	N/A	N/A
Isoamyl Acetate	≤4.80×10 ⁻⁰⁵	0.07	N/A	N/A	N/A	≤6.94×10 ⁻⁰⁴	N/A	N/A
Isobutyl Acetate	≤3.00×10 ⁻⁰⁵	0.07	N/A	N/A	N/A	≤4.33×10 ⁻⁰⁴	N/A	N/A
Isobutyraldehyde	≤3.58×10 ⁻⁰⁶	0.07	N/A	N/A	N/A	≤5.17×10 ⁻⁰⁵	N/A	N/A
Isoprene	≤4.06×10 ⁻⁰⁶	0.04	2.11×10 ⁻⁰³	1.21	e	≤1.12×10 ⁻⁰⁴	1.74×10 ⁻⁰³	↓ ≥93.59
Lead	≤4.55×10 ⁻⁰⁸	0.07	≤3.35×10 ⁻⁰⁶	1.21	e	≤6.57×10 ⁻⁰⁷	≤2.77×10 ⁻⁰⁶	NC
Menthol	2.90×10 ⁻⁰²	0.16	2.62×10 ⁺⁰⁰	1.21	e	1.87×10 ⁻⁰¹	2.17×10 ⁺⁰⁰	↓ 91.37
Methyl Acetate	≤3.60×10 ⁻⁰⁵	0.07	N/A	N/A	N/A	≤5.20×10 ⁻⁰⁴	N/A	N/A
Myosmine	≤1.93×10 ⁻⁰⁵	0.04	N/A	N/A	N/A	≤5.30×10 ⁻⁰⁴	N/A	N/A
n-Butyraldehyde	≤1.76×10 ⁻⁰⁶	0.07	2.67×10 ⁻⁰²	1.21	e	≤2.54×10 ⁻⁰⁵	2.21×10 ⁻⁰²	↓ ≥99.89
Nickel	≤4.55×10 ⁻⁰⁷	0.07	≤5.50×10 ⁻⁰⁷	1.21	e	≤6.57×10 ⁻⁰⁶	≤4.55×10 ⁻⁰⁷	NC
Nicotine	1.56×10 ⁻⁰¹	0.16	1.21×10 ⁺⁰⁰	1.21	e	1.00×10 ⁺⁰⁰	1.00×10 ⁺⁰⁰	N/A
Nicotine-N-Oxide	≤8.72×10 ⁻⁰⁶	0.07	N/A	N/A	N/A	≤1.26×10 ⁻⁰⁴	N/A	N/A
NNK	≤7.53×10 ⁻⁰⁹	0.07	5.90×10 ⁻⁰⁶	N/A	N/A	≤1.09×10 ⁻⁰⁷	4.88×10 ⁻⁰⁶	↓ ≥97.77
NNN	≤4.92×10 ⁻⁰⁹	0.07	1.37×10 ⁻⁰⁵	1.21	e	≤7.11×10 ⁻⁰⁸	1.13×10 ⁻⁰⁵	↓ ≥99.37
Nornicotine	1.99×10 ⁻⁰⁵	0.04	N/A	N/A	N/A	5.48×10 ⁻⁰⁴	N/A	N/A
Propionic Acid	≤7.80×10 ⁻⁰⁵	0.07	N/A	N/A	N/A	≤1.13×10 ⁻⁰³	N/A	N/A
Propylene Glycol	7.83×10 ⁻⁰¹	0.16	3.90×10 ⁻⁰¹	1.20	d	5.05×10 ⁺⁰⁰	3.25×10 ⁻⁰¹	1454.99
Propylene Oxide	≤1.56×10 ⁻⁰⁶	0.07	1.49×10 ⁻⁰⁴	1.21	e	≤2.26×10 ⁻⁰⁵	1.23×10 ⁻⁰⁴	↓ ≥81.69
Toluene	≤6.12×10 ⁻⁰⁶	0.07	2.39×10 ⁻⁰³	1.21	e	≤8.84×10 ⁻⁰⁵	1.98×10 ⁻⁰³	↓ ≥95.53
Water	3.84×10 ⁻⁰¹	0.16	2.97×10 ⁺⁰¹	1.21	e	2.47×10 ⁺⁰⁰	2.45×10 ⁺⁰¹	↓ 89.92

Average % Difference, Excluding Glycerol, PG and Water. a: Jaccard et al. 2019 b: Moldoveanu et al. 2017 c: Helen et al. 2018 d: Uchiyama et al. 2018 e: Schaller et al. 2016 f: Pappas et al. 2014 g: Roemer et al. 2012 h: IQOS PMTA, 2019.

Table S13. Comparison of HPHC and Chemical Intense Aerosol Levels in Menthol 13.0% and Smoke Levels 3R4F Reference Cigarette.

HPHC Chemical	JUUL Menthol 3.0% (mg/puff)		3R4F (mg/cig)			Chemical and HPHC Normalized by Nicotine (mg/mg)		% Difference vs_3R4F
	HPHC Chemical	or Nicotine	HPHC Chemical	or Nicotine	Source Journal	JUUL Virginia Tobacco 3.0%	3R4F	
1-Aminonaphthalene	≤3.31×10 ⁻¹⁰	0.03	2.91×10 ⁻⁰⁵	1.99	a	≤9.66×10 ⁻⁰⁹	1.46×10 ⁻⁰⁵	↓ ≥99.93
1-Butanol	≤3.00×10 ⁻⁰⁵	0.05	N/A	N/A	N/A	≤6.58×10 ⁻⁰⁴	N/A	N/A
1,3-Butadiene	≤1.61×10 ⁻⁰⁵	0.03	1.00×10 ⁻⁰¹	1.99	a	≤4.69×10 ⁻⁰⁴	5.03×10 ⁻⁰²	↓ ≥99.07
2-Aminonaphthalene	≤3.37×10 ⁻¹⁰	0.03	1.81×10 ⁻⁰⁵	1.99	a	≤9.84×10 ⁻⁰⁹	9.10×10 ⁻⁰⁶	↓ ≥99.89
4-Aminobiphenyl	≤1.66×10 ⁻¹⁰	0.03	3.91×10 ⁻⁰⁶	1.99	a	≤4.85×10 ⁻⁰⁹	1.96×10 ⁻⁰⁶	↓ ≥99.75

Acetaldehyde	3.56×10^{-05}	0.11	$1.84 \times 10^{+00}$	1.99	a	3.31×10^{-04}	9.24×10^{-01}	↓ 99.96
Acetyl Propionyl	$\leq 1.76 \times 10^{-06}$	0.05	9.19×10^{-02}	1.99	b	$\leq 3.85 \times 10^{-05}$	4.62×10^{-02}	↓ ≥99.92
Acrolein	$\leq 2.01 \times 10^{-05}$	0.09	1.80×10^{-01}	1.99	a	$\leq 2.14 \times 10^{-04}$	9.05×10^{-02}	↓ ≥99.76
Acrylonitrile	$\leq 3.20 \times 10^{-06}$	0.05	2.05×10^{-02}	1.99	a	$\leq 7.02 \times 10^{-05}$	1.03×10^{-02}	↓ ≥99.32
Ammonia	$\leq 6.64 \times 10^{-05}$	0.03	3.40×10^{-02}	1.99	a	$\leq 1.94 \times 10^{-03}$	1.71×10^{-02}	↓ ≥88.65
Anabasine	$\leq 3.64 \times 10^{-06}$	0.03	N/A	N/A	N/A	$\leq 1.06 \times 10^{-04}$	N/A	N/A
Anatabine	$\leq 3.30 \times 10^{-06}$	0.03	N/A	N/A	N/A	$\leq 9.62 \times 10^{-05}$	N/A	N/A
Benzene	$\leq 1.71 \times 10^{-06}$	0.05	8.88×10^{-02}	1.99	a	$\leq 3.74 \times 10^{-05}$	4.46×10^{-02}	↓ ≥99.92
Benzo(a)pyrene	$\leq 9.31 \times 10^{-10}$	0.03	1.51×10^{-05}	1.99	a	$\leq 2.72 \times 10^{-08}$	7.59×10^{-06}	↓ ≥99.64
Benzoic Acid	8.57×10^{-02}	0.11	N/A	N/A	N/A	7.97×10^{-01}	N/A	N/A
Benzyl Acetate	$\leq 3.00 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 6.58 \times 10^{-04}$	N/A	N/A
β-Nicotyrine	$\leq 8.25 \times 10^{-06}$	0.09	N/A	N/A	N/A	$\leq 8.79 \times 10^{-05}$	N/A	N/A
Cadmium	$\leq 5.25 \times 10^{-09}$	0.05	9.32×10^{-05}	1.99	a	$\leq 1.15 \times 10^{-07}$	4.68×10^{-05}	↓ ≥99.75
Carbon Monoxide	NT	0.03	$3.05 \times 10^{+01}$	1.99	a	NT	$1.53 \times 10^{+01}$	N/A
Chromium	NDFB	0.05	$\leq 1.19 \times 10^{-05}$	1.74	c	NDFB	$\leq 6.84 \times 10^{-06}$	NC
Copper	$\leq 2.84 \times 10^{-07}$	0.09	N/A	N/A	N/A	$\leq 3.03 \times 10^{-06}$	N/A	N/A
Cotinine	$\leq 4.06 \times 10^{-06}$	0.05	N/A	N/A	N/A	$\leq 8.92 \times 10^{-05}$	N/A	N/A
Crotonaldehyde	$\leq 3.11 \times 10^{-06}$	0.05	5.95×10^{-02}	1.99	a	$\leq 6.83 \times 10^{-05}$	2.99×10^{-02}	↓ ≥99.77
Diacetyl	$\leq 8.70 \times 10^{-07}$	0.05	3.37×10^{-01}	1.99	a	$\leq 1.91 \times 10^{-05}$	1.69×10^{-01}	↓ ≥99.99
Diethylene Glycol	$\leq 1.20 \times 10^{-04}$	0.05	N/A	N/A	N/A	$\leq 2.63 \times 10^{-03}$	N/A	N/A
Ethyl Acetate	$\leq 1.30 \times 10^{-04}$	0.05	N/A	N/A	N/A	$\leq 2.85 \times 10^{-03}$	N/A	N/A
Ethyl Acetoacetate	$\leq 2.40 \times 10^{-06}$	0.05	N/A	N/A	N/A	$\leq 5.27 \times 10^{-05}$	N/A	N/A
Ethylene Glycol	$\leq 2.52 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 5.54 \times 10^{-04}$	N/A	N/A
Formaldehyde	4.47×10^{-05}	0.11	8.71×10^{-02}	1.99	a	4.16×10^{-04}	4.38×10^{-02}	↓ 99.05
Furfural	$\leq 4.20 \times 10^{-05}$	0.05	2.59×10^{-02}	1.74	c	$\leq 9.22 \times 10^{-04}$	1.49×10^{-02}	↓ ≥93.81
Glycerol	$2.46 \times 10^{+00}$	0.11	$2.70 \times 10^{+00}$	1.99	a	$2.29 \times 10^{+01}$	$1.36 \times 10^{+00}$	1584.45
Glycidol	NR	0.05	1.76×10^{-03}	1.99	a	NR	8.84×10^{-04}	N/A
Gold	NT	0.03	N/A	N/A	N/A	NT	N/A	N/A
Isoamyl Acetate	$\leq 4.80 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 1.05 \times 10^{-03}$	N/A	N/A
Isobutyl Acetate	$\leq 3.00 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 6.58 \times 10^{-04}$	N/A	N/A
Isobutyraldehyde	$\leq 8.26 \times 10^{-07}$	0.05	N/A	N/A	N/A	$\leq 1.81 \times 10^{-05}$	N/A	N/A
Isoprene	$\leq 1.61 \times 10^{-04}$	0.03	7.99×10^{-01}	1.99	a	$\leq 4.69 \times 10^{-03}$	4.02×10^{-01}	↓ ≥98.83
Lead	$\leq 4.55 \times 10^{-08}$	0.05	3.12×10^{-05}	1.74	c	$\leq 9.99 \times 10^{-07}$	1.79×10^{-05}	↓ ≥94.43
Menthol	3.44×10^{-02}	0.11	$\leq 1.00 \times 10^{-05}$	2.10	d	3.20×10^{-01}	$\leq 4.76 \times 10^{-06}$	NC
Methyl Acetate	$\leq 3.60 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 7.90 \times 10^{-04}$	N/A	N/A
Myosmine	$\leq 3.28 \times 10^{-06}$	0.03	N/A	N/A	N/A	$\leq 9.56 \times 10^{-05}$	N/A	N/A
n-Butyraldehyde	$\leq 1.76 \times 10^{-06}$	0.05	9.30×10^{-02}	1.99	a	$\leq 3.85 \times 10^{-05}$	4.67×10^{-02}	↓ ≥99.92
Nickel	$\leq 4.55 \times 10^{-07}$	0.11	$\leq 1.29 \times 10^{-05}$	1.74	c	$\leq 4.23 \times 10^{-06}$	$\leq 7.41 \times 10^{-06}$	NC
Nicotine	1.07×10^{-01}	0.11	$1.99 \times 10^{+00}$	1.99	a	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	N/A

Nicotine-N-Oxide	$\leq 8.72 \times 10^{-6}$	0.05	N/A	N/A	N/A	$\leq 1.91 \times 10^{-4}$	N/A	N/A
NNK	$\leq 7.53 \times 10^{-9}$	0.05	2.95×10^{-4}	1.99	a	$\leq 1.65 \times 10^{-7}$	1.48×10^{-4}	↓ ≥ 99.89
NNN	$\leq 4.92 \times 10^{-9}$	0.05	3.37×10^{-4}	1.99	a	$\leq 1.08 \times 10^{-7}$	1.69×10^{-4}	↓ ≥ 99.94
Nornicotine	$\leq 3.41 \times 10^{-6}$	0.03	N/A	N/A	N/A	$\leq 9.96 \times 10^{-5}$	N/A	N/A
Propionic Acid	$\leq 1.80 \times 10^{-5}$	0.05	N/A	N/A	N/A	$\leq 3.95 \times 10^{-4}$	N/A	N/A
Propylene Glycol	9.92×10^{-1}	0.11	2.37×10^{-2}	1.74	c	$9.23 \times 10^{+0}$	1.36×10^{-2}	67634.83
Propylene Oxide	$\leq 1.56 \times 10^{-6}$	0.05	$1.00 \times 10^{+0}$	1.99	a	$\leq 3.43 \times 10^{-5}$	5.03×10^{-1}	↓ ≥ 99.99
Toluene	$\leq 6.12 \times 10^{-6}$	0.05	1.53×10^{-1}	1.99	a	$\leq 1.34 \times 10^{-4}$	7.69×10^{-2}	↓ ≥ 99.83
Water	4.95×10^{-1}	0.11	$1.58 \times 10^{+1}$	1.89	e	$4.61 \times 10^{+0}$	$8.36 \times 10^{+0}$	↓ 44.87

Average % Difference, Excluding Glycerol, PG and Water. a: Jaccard et al. 2019 b: Moldoveanu et al. 2017 c: Helen et al. 2018 d: Uchiyama et al. 2018 e: Schaller et al. 2016 f: Pappas et al. 2014 g: Roemer et al. 2012 h: IQOS PMTA, 2019.

Table S14. Comparison of HPHC and Chemical Non-Intense Aerosol Levels in Menthol 3.0% and Smoke Levels in 3R4F Reference Cigarette.

HPHC Chemical	JUUL Menthol 3.0% (mg/puff)		3R4F (mg/cig)			Chemical and HPHC Normalized by Nicotine (mg/mg)		% Difference vs_3R4F
	HPHC Chemical	or Nicotine	HPHC Chemical	or Nicotine	Source Journal	JUUL Virginia Tobacco 3.0%	3R4F	
1-Aminonaphthalene	$\leq 3.31 \times 10^{-10}$	0.03	1.42×10^{-5}	0.70	a	$\leq 9.66 \times 10^{-9}$	2.02×10^{-5}	↓ ≥ 99.95
1-Butanol	$\leq 3.00 \times 10^{-5}$	0.03	N/A	N/A	N/A	$\leq 1.18 \times 10^{-3}$	N/A	N/A
1,3-Butadiene	$\leq 1.61 \times 10^{-5}$	0.03	3.79×10^{-2}	0.70	a	$\leq 4.69 \times 10^{-4}$	5.40×10^{-2}	↓ ≥ 99.13
2-Aminonaphthalene	$\leq 3.37 \times 10^{-10}$	0.03	8.77×10^{-6}	0.70	a	$\leq 9.84 \times 10^{-9}$	1.25×10^{-5}	↓ ≥ 99.92
4-Aminobiphenyl	$\leq 1.66 \times 10^{-10}$	0.03	1.54×10^{-6}	0.70	a	$\leq 4.85 \times 10^{-9}$	2.19×10^{-6}	↓ ≥ 99.78
Acetaldehyde	$\leq 2.16 \times 10^{-5}$	0.03	5.97×10^{-1}	0.70	a	$\leq 8.45 \times 10^{-4}$	8.50×10^{-1}	↓ ≥ 99.90
Acetyl Propionyl	$\leq 1.76 \times 10^{-6}$	0.03	2.95×10^{-2}	0.70	b	$\leq 6.88 \times 10^{-5}$	4.21×10^{-2}	↓ ≥ 99.84
Acrolein	$\leq 2.01 \times 10^{-5}$	0.05	5.32×10^{-2}	0.70	a	$\leq 4.03 \times 10^{-4}$	7.58×10^{-2}	↓ ≥ 99.47
Acrylonitrile	$\leq 3.20 \times 10^{-6}$	0.03	5.23×10^{-3}	0.70	a	$\leq 1.25 \times 10^{-4}$	7.45×10^{-3}	↓ ≥ 98.32
Ammonia	$\leq 6.64 \times 10^{-5}$	0.03	9.64×10^{-3}	0.70	a	$\leq 1.94 \times 10^{-3}$	1.37×10^{-2}	↓ ≥ 85.88
Anabasine	$\leq 3.64 \times 10^{-6}$	0.03	N/A	N/A	N/A	$\leq 1.06 \times 10^{-4}$	N/A	N/A
Anatabine	$\leq 3.30 \times 10^{-6}$	0.03	N/A	N/A	N/A	$\leq 9.62 \times 10^{-5}$	N/A	N/A
Benzene	$\leq 1.71 \times 10^{-6}$	0.03	3.36×10^{-2}	0.70	a	$\leq 6.68 \times 10^{-5}$	4.79×10^{-2}	↓ ≥ 99.86
Benzo(a)pyrene	$\leq 9.31 \times 10^{-10}$	0.03	6.30×10^{-6}	0.70	a	$\leq 2.72 \times 10^{-8}$	8.97×10^{-6}	↓ ≥ 99.70
Benzoic Acid	4.10×10^{-2}	0.05	N/A	N/A	N/A	8.24×10^{-1}	N/A	N/A
Benzyl Acetate	$\leq 3.00 \times 10^{-5}$	0.03	N/A	N/A	N/A	$\leq 1.18 \times 10^{-3}$	N/A	N/A
β-Nicotyrine	$\leq 8.25 \times 10^{-6}$	0.05	N/A	N/A	N/A	$\leq 1.66 \times 10^{-4}$	N/A	N/A
Cadmium	$\leq 5.25 \times 10^{-9}$	0.03	2.45×10^{-5}	0.70	a	$\leq 2.06 \times 10^{-7}$	3.49×10^{-5}	↓ ≥ 99.41
Carbon Monoxide	NT	0.03	$1.00 \times 10^{+1}$	0.70	a	NT	$1.42 \times 10^{+1}$	N/A
Chromium	NDFB	0.03	$\leq 8.80 \times 10^{-7}$	0.70	f	NDFB	$\leq 1.25 \times 10^{-6}$	NC

Copper	$\leq 6.56 \times 10^{-08}$	0.03	N/A	N/A	N/A	$\leq 2.57 \times 10^{-06}$	N/A	N/A
Cotinine	$\leq 4.06 \times 10^{-06}$	0.05	N/A	N/A	N/A	$\leq 8.16 \times 10^{-05}$	N/A	N/A
Crotonaldehyde	$\leq 3.11 \times 10^{-06}$	0.03	9.89×10^{-03}	0.70	a	$\leq 1.22 \times 10^{-04}$	1.41×10^{-02}	↓ ≥ 99.13
Diacetyl	$\leq 8.70 \times 10^{-07}$	0.03	1.15×10^{-01}	0.70	b	$\leq 3.41 \times 10^{-05}$	1.64×10^{-01}	↓ ≥ 99.98
Diethylene Glycol	$\leq 1.20 \times 10^{-04}$	0.03	N/A	N/A	N/A	$\leq 4.70 \times 10^{-03}$	N/A	N/A
Ethyl Acetate	$\leq 1.30 \times 10^{-04}$	0.03	N/A	N/A	N/A	$\leq 5.09 \times 10^{-03}$	N/A	N/A
Ethyl Acetoacetate	$\leq 2.40 \times 10^{-06}$	0.03	N/A	N/A	N/A	$\leq 9.40 \times 10^{-05}$	N/A	N/A
Ethylene Glycol	$\leq 1.09 \times 10^{-04}$	0.03	N/A	N/A	N/A	$\leq 4.28 \times 10^{-03}$	N/A	N/A
Formaldehyde	2.19×10^{-05}	0.05	2.47×10^{-02}	0.70	a	4.35×10^{-04}	3.52×10^{-02}	↓ 98.76
Furfural	$\leq 4.20 \times 10^{-05}$	0.03	1.40×10^{-02}	0.76	d	$\leq 1.65 \times 10^{-03}$	1.84×10^{-02}	↓ ≥ 91.07
Glycerol	$1.22 \times 10^{+00}$	0.05	$2.70 \times 10^{+00}$	0.70	a	$2.45 \times 10^{+01}$	$3.85 \times 10^{+00}$	536.05
Glycidol	NR	0.03	N/A	N/A	N/A	NR	N/A	N/A
Gold	NT	0.03	N/A	N/A	N/A	NT	N/A	N/A
Isoamyl Acetate	$\leq 4.80 \times 10^{-05}$	0.03	N/A	N/A	N/A	$\leq 1.88 \times 10^{-03}$	N/A	N/A
Isobutyl Acetate	$\leq 3.00 \times 10^{-05}$	0.03	N/A	N/A	N/A	$\leq 1.18 \times 10^{-03}$	N/A	N/A
Isobutyraldehyde	$\leq 8.26 \times 10^{-07}$	0.03	N/A	N/A	N/A	$\leq 3.24 \times 10^{-05}$	N/A	N/A
Isoprene	$\leq 1.61 \times 10^{-04}$	0.03	2.88×10^{-01}	0.70	a	$\leq 4.69 \times 10^{-03}$	4.10×10^{-01}	↓ ≥ 98.86
Lead	$\leq 4.55 \times 10^{-08}$	0.03	9.20×10^{-06}	0.70	f	$\leq 1.78 \times 10^{-06}$	1.31×10^{-05}	↓ ≥ 86.39
Menthol	1.79×10^{-02}	0.05	$\leq 1.00 \times 10^{-05}$	0.76	a	3.55×10^{-01}	$\leq 1.32 \times 10^{-05}$	NC
Methyl Acetate	$\leq 3.60 \times 10^{-05}$	0.03	N/A	N/A	N/A	$\leq 1.41 \times 10^{-03}$	N/A	N/A
Myosmine	$\leq 3.28 \times 10^{-06}$	0.03	N/A	N/A	N/A	$\leq 9.56 \times 10^{-05}$	N/A	N/A
n-Butyraldehyde	$\leq 1.76 \times 10^{-06}$	0.03	2.84×10^{-02}	0.70	a	$\leq 6.88 \times 10^{-05}$	4.05×10^{-02}	↓ ≥ 99.83
Nickel	$\leq 1.05 \times 10^{-07}$	0.03	$\leq 3.80 \times 10^{-07}$	0.70	f	$\leq 4.11 \times 10^{-06}$	$\leq 5.41 \times 10^{-07}$	NC
Nicotine	5.04×10^{-02}	0.05	7.02×10^{-01}	0.70	a	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	N/A
Nicotine-N-Oxide	$\leq 8.72 \times 10^{-06}$	0.03	N/A	N/A	N/A	$\leq 3.42 \times 10^{-04}$	N/A	N/A
NNK	$\leq 7.53 \times 10^{-09}$	0.03	1.13×10^{-04}	0.70	a	$\leq 2.95 \times 10^{-07}$	1.61×10^{-04}	↓ ≥ 99.82
NNN	$\leq 4.92 \times 10^{-09}$	0.03	1.31×10^{-04}	0.70	a	$\leq 1.93 \times 10^{-07}$	1.87×10^{-04}	↓ ≥ 99.90
Normicotine	$\leq 3.41 \times 10^{-06}$	0.03	N/A	N/A	N/A	$\leq 9.96 \times 10^{-05}$	N/A	N/A
Propionic Acid	$\leq 7.80 \times 10^{-05}$	0.03	N/A	N/A	N/A	$\leq 3.06 \times 10^{-03}$	N/A	N/A
Propylene Glycol	4.55×10^{-01}	0.05	3.20×10^{-03}	0.76	d	$9.02 \times 10^{+00}$	4.21×10^{-03}	214132.49
Propylene Oxide	$\leq 1.56 \times 10^{-06}$	0.03	2.97×10^{-01}	0.70	a	$\leq 6.12 \times 10^{-05}$	4.23×10^{-01}	↓ ≥ 99.99
Toluene	$\leq 6.12 \times 10^{-06}$	0.03	5.14×10^{-02}	0.70	a	$\leq 2.40 \times 10^{-04}$	7.32×10^{-02}	↓ ≥ 99.67
Water	2.51×10^{-01}	0.05	$3.20 \times 10^{+00}$	0.76	d	$5.04 \times 10^{+00}$	$4.21 \times 10^{+00}$	19.67

Average % Difference, Excluding Glycerol, PG and Water. a: Jaccard et al. 2019 b: Moldoveanu et al. 2017 c: Helen et al. 2018 d: Uchiyama et al. 2018 e: Schaller et al. 2016 f: Pappas et al. 2014 g: Roemer et al. 2012 h: IQOS PMTA, 2019.

Table S15. Comparison of HPHC and Chemical Intense Aerosol Levels in Menthol 3.0% and Aerosol Levels in IQOS Menthol.

HPHC Chemical	JUUL Menthol 3.0% (mg/puff)		IQOS Menthol (mg/cig)			Chemical and HPHC Normalized by Nicotine (mg/mg)		% Difference vs_3R4F
	HPHC Chemical	or Nicotine	HPHC Chemical	or Nicotine	Source Journal	JUUL Virginia Tobacco 3.0%	3R4F	
1-Aminonaphthalene	$\leq 3.31 \times 10^{-10}$	0.03	8.60×10^{-08}	1.21	e	$\leq 9.66 \times 10^{-09}$	7.11×10^{-08}	↓ ≥86.41
1-Butanol	$\leq 3.00 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 6.58 \times 10^{-04}$	N/A	N/A
1,3-Butadiene	$\leq 1.61 \times 10^{-05}$	0.03	2.65×10^{-04}	1.21	e	$\leq 4.69 \times 10^{-04}$	2.19×10^{-04}	NC
2-Aminonaphthalene	$\leq 3.37 \times 10^{-10}$	0.03	$\leq 3.50 \times 10^{-08}$	1.21	e	$\leq 9.84 \times 10^{-09}$	$\leq 2.89 \times 10^{-08}$	NC
4-Aminobiphenyl	$\leq 1.66 \times 10^{-10}$	0.03	$\leq 5.10 \times 10^{-08}$	1.21	e	$\leq 4.85 \times 10^{-09}$	$\leq 4.21 \times 10^{-08}$	NC
Acetaldehyde	3.56×10^{-05}	0.11	2.05×10^{-01}	1.21	e	3.31×10^{-04}	1.69×10^{-01}	↓ 99.80
Acetyl Propionyl	$\leq 1.76 \times 10^{-06}$	0.05	N/A	N/A	N/A	$\leq 3.85 \times 10^{-05}$	N/A	N/A
Acrolein	$\leq 2.01 \times 10^{-05}$	0.09	9.15×10^{-03}	1.21	e	$\leq 2.14 \times 10^{-04}$	7.56×10^{-03}	↓ ≥97.17
Acrylonitrile	$\leq 3.20 \times 10^{-06}$	0.05	2.20×10^{-04}	1.21	e	$\leq 7.02 \times 10^{-05}$	1.82×10^{-04}	↓ ≥61.36
Ammonia	$\leq 6.64 \times 10^{-05}$	0.03	1.38×10^{-02}	1.21	e	$\leq 1.94 \times 10^{-03}$	1.14×10^{-02}	↓ ≥83.00
Anabasine	$\leq 3.64 \times 10^{-06}$	0.03	N/A	N/A	N/A	$\leq 1.06 \times 10^{-04}$	N/A	N/A
Anatabine	$\leq 3.30 \times 10^{-06}$	0.03	N/A	N/A	N/A	$\leq 9.62 \times 10^{-05}$	N/A	N/A
Benzene	$\leq 1.71 \times 10^{-06}$	0.05	6.40×10^{-04}	1.21	e	$\leq 3.74 \times 10^{-05}$	5.29×10^{-04}	↓ ≥92.92
Benzo(a)pyrene	$\leq 9.31 \times 10^{-10}$	0.03	1.29×10^{-06}	1.21	e	$\leq 2.72 \times 10^{-08}$	1.07×10^{-06}	↓ ≥97.45
Benzoic Acid	8.57×10^{-02}	0.11	N/A	N/A	N/A	7.97×10^{-01}	N/A	N/A
Benzyl Acetate	$\leq 3.00 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 6.58 \times 10^{-04}$	N/A	N/A
β-Nicotyrine	$\leq 8.25 \times 10^{-06}$	0.09	N/A	N/A	N/A	$\leq 8.79 \times 10^{-05}$	N/A	N/A
Cadmium	$\leq 5.25 \times 10^{-09}$	0.05	$\leq 3.50 \times 10^{-07}$	1.21	e	$\leq 1.15 \times 10^{-07}$	$\leq 2.89 \times 10^{-07}$	NC
Carbon Monoxide	NT	0.03	5.94×10^{-01}	1.21	e	NT	4.91×10^{-01}	N/A
Chromium	NDFB	0.05	$\leq 5.50 \times 10^{-07}$	1.21	e	NDFB	$\leq 4.55 \times 10^{-07}$	NC
Copper	$\leq 2.84 \times 10^{-07}$	0.09	N/A	N/A	N/A	$\leq 3.03 \times 10^{-06}$	N/A	N/A
Cotinine	$\leq 4.06 \times 10^{-06}$	0.05	N/A	N/A	N/A	$\leq 8.92 \times 10^{-05}$	N/A	N/A
Crotonaldehyde	$\leq 3.11 \times 10^{-06}$	0.05	3.24×10^{-03}	1.21	e	$\leq 6.83 \times 10^{-05}$	2.68×10^{-03}	↓ ≥97.45
Diacetyl	$\leq 8.70 \times 10^{-07}$	0.05	6.50×10^{-02}	1.20	d	$\leq 1.91 \times 10^{-05}$	5.42×10^{-02}	↓ ≥99.96
Diethylene Glycol	$\leq 1.20 \times 10^{-04}$	0.05	N/A	N/A	N/A	$\leq 2.63 \times 10^{-03}$	N/A	N/A
Ethyl Acetate	$\leq 1.30 \times 10^{-04}$	0.05	N/A	N/A	N/A	$\leq 2.85 \times 10^{-03}$	N/A	N/A
Ethyl Acetoacetate	$\leq 2.40 \times 10^{-06}$	0.05	N/A	N/A	N/A	$\leq 5.27 \times 10^{-05}$	N/A	N/A
Ethylene Glycol	$\leq 2.52 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 5.54 \times 10^{-04}$	N/A	N/A
Formaldehyde	4.47×10^{-05}	0.11	4.55×10^{-03}	1.21	e	4.16×10^{-04}	3.76×10^{-03}	↓ 88.94
Furfural	$\leq 4.20 \times 10^{-05}$	0.05	N/A	N/A	N/A	$\leq 9.22 \times 10^{-04}$	N/A	N/A
Glycerol	$2.46 \times 10^{+00}$	0.11	$3.94 \times 10^{+00}$	1.21	N/A	$2.29 \times 10^{+01}$	$3.26 \times 10^{+00}$	601.87

Glycidol	NR	0.05	1.10×10 ⁻⁰³	1.19	h	NR	9.24×10 ⁻⁰⁴	N/A
Gold	NT	0.03	N/A	N/A	N/A	NT	N/A	N/A
Isoamyl Acetate	≤4.80×10 ⁻⁰⁵	0.05	N/A	N/A	N/A	≤1.05×10 ⁻⁰³	N/A	N/A
Isobutyl Acetate	≤3.00×10 ⁻⁰⁵	0.05	N/A	N/A	N/A	≤6.58×10 ⁻⁰⁴	N/A	N/A
Isobutyraldehyde	≤8.26×10 ⁻⁰⁷	0.05	N/A	N/A	N/A	≤1.81×10 ⁻⁰⁵	N/A	N/A
Isoprene	≤1.61×10 ⁻⁰⁴	0.03	2.11×10 ⁻⁰³	1.21	e	≤4.69×10 ⁻⁰³	1.74×10 ⁻⁰³	NC
Lead	≤4.55×10 ⁻⁰⁸	0.05	≤3.35×10 ⁻⁰⁶	1.21	e	≤9.99×10 ⁻⁰⁷	≤2.77×10 ⁻⁰⁶	NC
Menthol	3.44×10 ⁻⁰²	0.11	2.62×10 ⁺⁰⁰	1.21	e	3.20×10 ⁻⁰¹	2.17×10 ⁺⁰⁰	↓ 85.22
Methyl Acetate	≤3.60×10 ⁻⁰⁵	0.05	N/A	N/A	N/A	≤7.90×10 ⁻⁰⁴	N/A	N/A
Myosmine	≤3.28×10 ⁻⁰⁶	0.03	N/A	N/A	N/A	≤9.56×10 ⁻⁰⁵	N/A	N/A
n-Butyraldehyde	≤1.76×10 ⁻⁰⁶	0.05	2.67×10 ⁻⁰²	1.21	e	≤3.85×10 ⁻⁰⁵	2.21×10 ⁻⁰²	↓ ≥99.83
Nickel	≤4.55×10 ⁻⁰⁷	0.11	≤5.50×10 ⁻⁰⁷	1.21	e	≤4.23×10 ⁻⁰⁶	≤4.55×10 ⁻⁰⁷	NC
Nicotine	1.07×10 ⁻⁰¹	0.11	1.21×10 ⁺⁰⁰	1.21	e	1.00×10 ⁺⁰⁰	1.00×10 ⁺⁰⁰	N/A
Nicotine-N-Oxide	≤8.72×10 ⁻⁰⁶	0.05	N/A	N/A	N/A	≤1.91×10 ⁻⁰⁴	N/A	N/A
NNK	≤7.53×10 ⁻⁰⁹	0.05	5.90×10 ⁻⁰⁶	1.21	N/A	≤1.65×10 ⁻⁰⁷	4.88×10 ⁻⁰⁶	↓ ≥96.61
NNN	≤4.92×10 ⁻⁰⁹	0.05	1.37×10 ⁻⁰⁵	1.21	e	≤1.08×10 ⁻⁰⁷	1.13×10 ⁻⁰⁵	↓ ≥99.05
Nornicotine	≤3.41×10 ⁻⁰⁶	0.03	N/A	N/A	N/A	≤9.96×10 ⁻⁰⁵	N/A	N/A
Propionic Acid	≤1.80×10 ⁻⁰⁵	0.05	N/A	N/A	N/A	≤3.95×10 ⁻⁰⁴	N/A	N/A
Propylene Glycol	9.92×10 ⁻⁰¹	0.11	3.90×10 ⁻⁰¹	1.20	d	9.23×10 ⁺⁰⁰	3.25×10 ⁻⁰¹	2738.75
Propylene Oxide	≤1.56×10 ⁻⁰⁶	0.05	1.49×10 ⁻⁰⁴	1.21	e	≤3.43×10 ⁻⁰⁵	1.23×10 ⁻⁰⁴	↓ ≥72.19
Toluene	≤6.12×10 ⁻⁰⁶	0.05	2.39×10 ⁻⁰³	1.21	e	≤1.34×10 ⁻⁰⁴	1.98×10 ⁻⁰³	↓ ≥93.20
Water	4.95×10 ⁻⁰¹	0.11	2.97×10 ⁺⁰¹	1.21	e	4.61×10 ⁺⁰⁰	2.45×10 ⁺⁰¹	↓ 81.22

Average % Difference, Excluding Glycerol, PG and Water. a: Jaccard et al. 2019 b: Moldoveanu et al. 2017 c: Helen et al. 2018 d: Uchiyama et al. 2018 e: Schaller et al. 2016 f: Pappas et al. 2014 g: Roemer et al. 2012 h: IQOS PMTA, 2019.

Table S16. Comparison of HPHCs in VT3 aerosol vs. comparator products.

Chemical and HPHC	HPHC or Chemical Normalized by Nicotine (mg/mg)					% Difference		
	VT3		3R4F		IQOS	vs 3R4F		vs IQOS
	NI	Intense	NI	Intense	Intense	NI	Intense	Intense
1-Aminonaphthalene	≤1.22×10 ^{-08a}	≤1.22×10 ^{-08a}	2.02×10 ⁻⁰⁵	1.46×10 ⁻⁰⁵	5.83×10 ⁻⁰⁸	↓ ≥99.94	↓ ≥99.92	↓ ≥79.16
1-Butanol	≤1.02×10 ^{-03a}	≤5.68×10 ^{-04a}	N/A	N/A	N/A	N/A	N/A	N/A
1,3-Butadiene	≤4.24×10 ^{-05a}	≤4.23×10 ^{-05a}	5.40×10 ⁻⁰²	5.03×10 ⁻⁰²	2.23×10 ⁻⁰⁴	↓ ≥99.92	↓ ≥99.92	↓ ≥80.99
2-Aminonaphthalene	≤5.29×10 ^{-09a}	≤5.29×10 ^{-09a}	1.25×10 ⁻⁰⁵	9.10×10 ⁻⁰⁶	3.48×10 ⁻⁰⁸	↓ ≥99.96	↓ ≥99.94	↓ ≥84.82
4-Aminobiphenyl	≤2.13×10 ^{-09a}	≤2.12×10 ^{-09a}	2.19×10 ⁻⁰⁶	1.96×10 ⁻⁰⁶	6.98×10 ⁻⁰⁹	↓ ≥99.90	↓ ≥99.89	↓ ≥69.55
Acetaldehyde	6.49×10⁻⁰⁴	4.13×10⁻⁰⁴	8.50×10 ⁻⁰¹	9.24×10 ⁻⁰¹	1.66×10 ⁻⁰¹	↓ 99.92	↓ 99.96	↓ 99.75
Acetyl Propionyl	≤5.99×10 ^{-05a}	≤3.33×10 ^{-05a}	4.21×10 ⁻⁰²	4.62×10 ⁻⁰²	N/A	↓ ≥99.86	↓ ≥99.93	N/A
Acrolein	≤3.55×10 ^{-04a,b}	≤1.91×10 ^{-04a,b}	7.58×10 ⁻⁰²	9.05×10 ⁻⁰²	8.56×10 ⁻⁰³	↓ ≥99.53	↓ ≥99.79	↓ ≥97.77

Acrylonitrile	$\leq 1.09 \times 10^{-04a}$	$\leq 6.06 \times 10^{-05a}$	7.45×10^{-03}	1.03×10^{-02}	1.95×10^{-04}	$\downarrow \geq 98.53$	$\downarrow \geq 99.41$	$\downarrow \geq 68.99$
Ammonia	$\leq 5.92 \times 10^{-04a}$	$\leq 5.92 \times 10^{-04a}$	1.37×10^{-02}	1.71×10^{-02}	1.08×10^{-02}	$\downarrow \geq 95.69$	$\downarrow \geq 96.53$	$\downarrow \geq 94.50$
Anabasine	$\leq 4.27 \times 10^{-05a}$	$\leq 4.27 \times 10^{-05a}$	N/A	N/A	N/A	N/A	N/A	N/A
Anatabine	$\leq 3.53 \times 10^{-05a}$	$\leq 3.53 \times 10^{-05a}$	N/A	N/A	N/A	N/A	N/A	N/A
Benzene	$\leq 5.82 \times 10^{-05a}$	$\leq 3.23 \times 10^{-05a}$	4.79×10^{-02}	4.46×10^{-02}	4.92×10^{-04}	$\downarrow \geq 99.88$	$\downarrow \geq 99.93$	$\downarrow \geq 93.43$
Benzo(a)pyrene	$\leq 7.89 \times 10^{-08a}$	$\leq 7.89 \times 10^{-08a}$	8.97×10^{-06}	7.59×10^{-06}	5.71×10^{-07}	$\downarrow \geq 99.12$	$\downarrow \geq 98.96$	$\downarrow \geq 86.17$
Benzoic Acid	8.46×10^{-01}	7.97×10^{-01}	N/A	N/A	N/A	N/A	N/A	N/A
Benzyl Acetate	$\leq 1.02 \times 10^{-03a}$	$\leq 5.68 \times 10^{-04a}$	N/A	N/A	N/A	N/A	N/A	N/A
β-Nicotyrine	$\leq 1.46 \times 10^{-04a,b}$	$\leq 7.82 \times 10^{-05a,b}$	N/A	N/A	N/A	N/A	N/A	N/A
Cadmium	$\leq 1.79 \times 10^{-07a}$	$\leq 9.94 \times 10^{-08a}$	3.49×10^{-05}	4.68×10^{-05}	$\leq 2.65 \times 10^{-07}$	$\downarrow \geq 99.49$	$\downarrow \geq 99.79$	NC
Carbon Monoxide	$\leq 7.80 \times 10^{-02a}$	$\leq 7.80 \times 10^{-02a}$	$1.42 \times 10^{+01}$	$1.53 \times 10^{+01}$	4.02×10^{-01}	$\downarrow \geq 99.45$	$\downarrow \geq 99.49$	$\downarrow \geq 80.62$
Chromium	NDFB	NDFB	$\leq 1.25 \times 10^{-06}$	$\leq 6.84 \times 10^{-06}$	$\leq 4.17 \times 10^{-07}$	NC	NC	NC
Copper	$\leq 9.70 \times 10^{-06a,b}$	$\leq 5.39 \times 10^{-06a,b}$	N/A	N/A	N/A	N/A	N/A	N/A
Cotinine	$\leq 1.39 \times 10^{-04b}$	$\leq 1.78 \times 10^{-05a}$	N/A	N/A	N/A	N/A	N/A	N/A
Crotonaldehyde	$\leq 1.06 \times 10^{-04a}$	$\leq 5.90 \times 10^{-05a}$	1.41×10^{-02}	2.99×10^{-02}	3.14×10^{-03}	$\downarrow \geq 99.25$	$\downarrow \geq 99.80$	$\downarrow \geq 98.12$
Diacetyl	$\leq 2.97 \times 10^{-05a}$	$\leq 1.65 \times 10^{-05a}$	1.64×10^{-01}	1.69×10^{-01}	3.58×10^{-02}	$\downarrow \geq 99.98$	$\downarrow \geq 99.99$	$\downarrow \geq 99.95$
Diethylene Glycol	$\leq 4.09 \times 10^{-03a}$	$\leq 2.27 \times 10^{-03a}$	N/A	N/A	N/A	N/A	N/A	N/A
Ethyl Acetate	$\leq 4.43 \times 10^{-03a,b}$	$\leq 1.23 \times 10^{-03a,b}$	N/A	N/A	N/A	N/A	N/A	N/A
Ethyl Acetoacetate	$\leq 8.19 \times 10^{-05a}$	$\leq 4.54 \times 10^{-05a}$	N/A	N/A	N/A	N/A	N/A	N/A
Ethylene Glycol	$\leq 3.73 \times 10^{-03b}$	$\leq 2.07 \times 10^{-03b}$	N/A	N/A	N/A	N/A	N/A	N/A
Formaldehyde	1.35×10^{-03}	8.27×10^{-04}	3.52×10^{-02}	4.38×10^{-02}	4.19×10^{-03}	$\downarrow \geq 96.16$	$\downarrow \geq 98.11$	$\downarrow \geq 80.27$
Furfural	$\leq 1.43 \times 10^{-03a}$	$\leq 7.95 \times 10^{-04a}$	1.84×10^{-02}	1.49×10^{-02}	2.41×10^{-02}	$\downarrow \geq 92.22$	$\downarrow \geq 94.66$	$\downarrow \geq 96.70$
Glycerol	$2.31 \times 10^{+01}$	$2.27 \times 10^{+01}$	$3.85 \times 10^{+00}$	$1.36 \times 10^{+00}$	$3.51 \times 10^{+00}$	$4.99 \times 10^{+02}$	$1.57 \times 10^{+03}$	$5.47 \times 10^{+02}$
Glycidol	NR	NR	N/A	8.84×10^{-04}	4.43×10^{-03}	NC	NC	NC
Gold	$\leq 9.41 \times 10^{-08a}$	$\leq 9.40 \times 10^{-08a}$	N/A	N/A	N/A	N/A	N/A	N/A
Isoamyl Acetate	$\leq 1.64 \times 10^{-03a}$	$\leq 9.09 \times 10^{-04a}$	N/A	N/A	N/A	N/A	N/A	N/A
Isobutyl Acetate	$\leq 1.02 \times 10^{-03a}$	$\leq 5.68 \times 10^{-04a}$	N/A	N/A	N/A	N/A	N/A	N/A
Isobutyraldehyde	$\leq 2.82 \times 10^{-05a}$	$\leq 1.57 \times 10^{-05a}$	N/A	N/A	N/A	N/A	N/A	N/A
Isoprene	$\leq 6.03 \times 10^{-05a}$	$\leq 6.03 \times 10^{-05a}$	4.10×10^{-01}	4.02×10^{-01}	1.78×10^{-03}	$\downarrow \geq 99.99$	$\downarrow \geq 99.98$	$\downarrow \geq 96.61$
Lead	$\leq 1.55 \times 10^{-06b}$	NDFB	1.31×10^{-05}	1.79×10^{-05}	1.73×10^{-06}	$\downarrow \geq 88.16$	NC	NC
Menthol	$\leq 4.17 \times 10^{-03a}$	$\leq 2.31 \times 10^{-03a}$	$\leq 1.32 \times 10^{-05}$	$\leq 4.76 \times 10^{-06}$	3.42×10^{-04}	NC	NC	NC
Methyl Acetate	$\leq 1.23 \times 10^{-03a}$	$\leq 6.82 \times 10^{-04a}$	N/A	N/A	N/A	N/A	N/A	N/A
Myosmine	$\leq 2.86 \times 10^{-04a}$	$\leq 2.86 \times 10^{-04a}$	N/A	N/A	N/A	N/A	N/A	N/A
n-Butyraldehyde	$\leq 5.99 \times 10^{-05a}$	$\leq 3.33 \times 10^{-05a}$	4.05×10^{-02}	4.67×10^{-02}	1.98×10^{-02}	$\downarrow \geq 99.85$	$\downarrow \geq 99.93$	$\downarrow \geq 99.83$
Nickel	$\leq 8.03 \times 10^{-06b}$	$\leq 8.62 \times 10^{-06b}$	$\leq 5.41 \times 10^{-07}$	$\leq 7.41 \times 10^{-06}$	$\leq 4.17 \times 10^{-07}$	NC	NC	NC
Nicotine	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	N/A	N/A	N/A
Nicotine-N-Oxide	$\leq 2.97 \times 10^{-04a}$	$\leq 1.65 \times 10^{-04a}$	N/A	N/A	N/A	N/A	N/A	N/A

NNK	$\leq 2.57 \times 10^{-07a}$	$\leq 1.43 \times 10^{-07a}$	1.61×10^{-04}	1.48×10^{-04}	5.08×10^{-06}	$\downarrow \geq 99.84$	$\downarrow \geq 99.90$	$\downarrow \geq 97.19$
NNN	$\leq 1.68 \times 10^{-07a}$	$\leq 9.32 \times 10^{-08a}$	1.87×10^{-04}	1.69×10^{-04}	1.30×10^{-05}	$\downarrow \geq 99.91$	$\downarrow \geq 99.94$	$\downarrow \geq 99.28$
<i>Nornicotine</i>	2.47×10^{-04d}	2.47×10^{-04d}	N/A	N/A	N/A	N/A	N/A	N/A
Propionic Acid	$\leq 2.66 \times 10^{-03b}$	$\leq 1.79 \times 10^{-03a,b}$	N/A	N/A	N/A	N/A	N/A	N/A
Propylene Glycol	$8.85 \times 10^{+00}$	$8.71 \times 10^{+00}$	4.21×10^{-03}	1.36×10^{-02}	1.36×10^{-01}	$2.10 \times 10^{+05}$	$6.39 \times 10^{+04}$	$6.32 \times 10^{+03}$
Propylene Oxide	$\leq 5.32 \times 10^{-05a}$	$\leq 2.96 \times 10^{-05a}$	4.23×10^{-01}	5.03×10^{-01}	1.12×10^{-04}	$\downarrow \geq 99.99$	$\downarrow \geq 99.99$	$\downarrow \geq 73.64$
Toluene	$\leq 2.09 \times 10^{-04a}$	$\leq 1.16 \times 10^{-04a}$	7.32×10^{-02}	7.69×10^{-02}	1.96×10^{-03}	$\downarrow \geq 99.72$	$\downarrow \geq 99.85$	$\downarrow \geq 94.10$
Water	$5.13 \times 10^{+00}$	$4.33 \times 10^{+00}$	$4.21 \times 10^{+00}$	$8.36 \times 10^{+00}$	$2.77 \times 10^{+01}$	21.78	\downarrow 48.20	\downarrow 84.34
						Average ^c	Average ^c	Average ^c
						\downarrow 98.59	\downarrow 99.37	\downarrow 89.12

BLOD = Below limit of quantitation; BLOQ=Below limit of quantitation; NDFB=Not different from background, \downarrow = less than, Bolded reductions were based on quantifiable values. Analytes in italics were tested under a single modified puffing regimen: 70mL puff, 3 second duration, 30 second interval^a analyte was BLOD for all three 50 puff blocks ^b analyte was BLOQ for all three 50 puff blocks ^{a,b} analyte was either BLOD or BLOQ for all three 50 puff blocks ^c excluding PG,VG and water.

Table S17. Comparison of HPHCs in Me3 aerosol vs. comparator products.

Chemical and HPHC	HPHC or Chemical Normalized by Nicotine (mg/mg)					% Difference		
	VT3		3R4F		IQOS	vs IQOS		
	NI	Intense	NI	Intense	Intense	NI	Intense	Intense
1-								
<i>Aminonaphthalene</i>	$\leq 9.66 \times 10^{-09a}$	$\leq 9.66 \times 10^{-09a}$	2.02×10^{-05}	1.46×10^{-05}	7.11×10^{-08}	$\downarrow \geq 99.95$	$\downarrow \geq 99.93$	$\downarrow \geq 86.41$
1-Butanol	$\leq 1.18 \times 10^{-03}$	$\leq 6.58 \times 10^{-04}$	N/A	N/A	N/A	N/A	N/A	N/A
1,3-Butadiene	$\leq 4.69 \times 10^{-04a}$	$\leq 4.69 \times 10^{-04a}$	5.40×10^{-02}	5.03×10^{-02}	2.19×10^{-04}	$\downarrow \geq 99.13$	$\downarrow \geq 99.07$	NC
2-								
<i>Aminonaphthalene</i>	$\leq 9.84 \times 10^{-09a}$	$\leq 9.84 \times 10^{-09a}$	1.25×10^{-05}	9.10×10^{-06}	$\leq 2.89 \times 10^{-08}$	$\downarrow \geq 99.92$	$\downarrow \geq 99.89$	NC
4-								
<i>Aminobiphenyl</i>	$\leq 4.85 \times 10^{-09a}$	$\leq 4.85 \times 10^{-09a}$	2.19×10^{-06}	1.96×10^{-06}	$\leq 4.21 \times 10^{-08}$	$\downarrow \geq 99.78$	$\downarrow \geq 99.75$	NC
Acetaldehyde	$\leq 8.45 \times 10^{-04b}$	3.31×10^{-04}	8.50×10^{-01}	9.24×10^{-01}	1.69×10^{-01}	$\downarrow \geq 99.90$	\downarrow 99.96	\downarrow 99.80
Acetyl Propionyl	$\leq 6.88 \times 10^{-05a}$	$\leq 3.85 \times 10^{-05a}$	4.21×10^{-02}	4.62×10^{-02}	N/A	$\downarrow \geq 99.84$	$\downarrow \geq 99.92$	N/A
Acrolein	$\leq 4.03 \times 10^{-04a,b}$	$\leq 2.14 \times 10^{-04a,b}$	7.58×10^{-02}	9.05×10^{-02}	7.56×10^{-03}	$\downarrow \geq 99.47$	$\downarrow \geq 99.76$	$\downarrow \geq 97.17$
Acrylonitrile	$\leq 1.25 \times 10^{-04a}$	$\leq 7.02 \times 10^{-05a}$	7.45×10^{-03}	1.03×10^{-02}	1.82×10^{-04}	$\downarrow \geq 98.32$	$\downarrow \geq 99.32$	$\downarrow \geq 61.36$
Ammonia	$\leq 1.94 \times 10^{-03a}$	$\leq 1.94 \times 10^{-03a}$	1.37×10^{-02}	1.71×10^{-02}	1.14×10^{-02}	$\downarrow \geq 85.88$	$\downarrow \geq 88.65$	$\downarrow \geq 83.00$
Anabasine	$\leq 1.06 \times 10^{-04d}$	$\leq 1.06 \times 10^{-04d}$	N/A	N/A	N/A	N/A	N/A	N/A
Anatabine	$\leq 9.62 \times 10^{-05d}$	$\leq 9.62 \times 10^{-05d}$	N/A	N/A	N/A	N/A	N/A	N/A
Benzene	$\leq 6.68 \times 10^{-05a}$	$\leq 3.74 \times 10^{-05a}$	4.79×10^{-02}	4.46×10^{-02}	5.29×10^{-04}	$\downarrow \geq 99.86$	$\downarrow \geq 99.92$	$\downarrow \geq 92.92$
Benzo(a)pyrene	$\leq 2.72 \times 10^{-08d}$	$\leq 2.72 \times 10^{-08d}$	8.97×10^{-06}	7.59×10^{-06}	1.07×10^{-06}	$\downarrow \geq 99.70$	$\downarrow \geq 99.64$	$\downarrow \geq 97.45$
Benzoic Acid	8.24×10^{-01}	7.97×10^{-01}	N/A	N/A	N/A	N/A	N/A	N/A
Benzyl Acetate	$\leq 1.18 \times 10^{-03a}$	$\leq 6.58 \times 10^{-04a}$	N/A	N/A	N/A	N/A	N/A	N/A
β -Nicotyrine	$\leq 1.66 \times 10^{-04a,b}$	$\leq 8.79 \times 10^{-05a,b}$	N/A	N/A	N/A	N/A	N/A	N/A
Cadmium	$\leq 2.06 \times 10^{-07a}$	$\leq 1.15 \times 10^{-07a}$	3.49×10^{-05}	4.68×10^{-05}	$\leq 2.89 \times 10^{-07}$	$\downarrow \geq 99.41$	$\downarrow \geq 99.75$	NC
Carbon Monoxide	NT	NT	$1.42 \times 10^{+01}$	$1.53 \times 10^{+01}$	$4.91 \times 10^{+01}$	N/A	N/A	N/A
Chromium	NDFB	NDFB	$\leq 1.25 \times 10^{-06}$	$\leq 6.84 \times 10^{-06}$	$\leq 4.55 \times 10^{-07}$	NC	NC	NC

Copper	$\leq 2.57 \times 10^{-6a}$	$\leq 3.03 \times 10^{-6a,b}$	N/A	N/A	N/A	N/A	N/A	N/A
Cotinine	$\leq 8.16 \times 10^{-5a,b}$	$\leq 8.92 \times 10^{-5b}$	N/A	N/A	N/A	N/A	N/A	N/A
Crotonaldehyde	$\leq 1.22 \times 10^{-4a}$	$\leq 6.83 \times 10^{-5a}$	1.41×10^{-2}	2.99×10^{-2}	2.68×10^{-3}	$\downarrow \geq 99.13$	$\downarrow \geq 99.77$	$\downarrow \geq 97.45$
Diacetyl	$\leq 3.41 \times 10^{-5a}$	$\leq 1.91 \times 10^{-5a}$	1.64×10^{-1}	1.69×10^{-1}	5.42×10^{-2}	$\downarrow \geq 99.98$	$\downarrow \geq 99.99$	$\downarrow \geq 99.96$
Diethylene Glycol	$\leq 4.70 \times 10^{-3a}$	$\leq 2.63 \times 10^{-3a}$	N/A	N/A	N/A	N/A	N/A	N/A
Ethyl Acetate	$\leq 5.09 \times 10^{-3b}$	$\leq 2.85 \times 10^{-3a,b}$	N/A	N/A	N/A	N/A	N/A	N/A
Ethyl Acetoacetate	$\leq 9.40 \times 10^{-5a}$	$\leq 5.27 \times 10^{-5a}$	N/A	N/A	N/A	N/A	N/A	N/A
Ethylene Glycol	$\leq 4.28 \times 10^{-3b}$	$\leq 5.54 \times 10^{-4b}$	N/A	N/A	N/A	N/A	N/A	N/A
Formaldehyde	4.35×10^{-4}	4.16×10^{-4}	3.52×10^{-2}	4.38×10^{-2}	3.76×10^{-3}	\downarrow 98.76	\downarrow 99.05	\downarrow 88.94
Furfural	$\leq 1.65 \times 10^{-3a}$	$\leq 9.22 \times 10^{-4a}$	1.84×10^{-2}	1.49×10^{-2}	N/A	$\downarrow \geq 91.07$	$\downarrow \geq 93.81$	N/A
Glycerol	$2.45 \times 10^{+01}$	$2.29 \times 10^{+01}$	$3.85 \times 10^{+00}$	$1.36 \times 10^{+00}$	$3.26 \times 10^{+00}$	$5.36 \times 10^{+02}$	$1.58 \times 10^{+03}$	$6.01 \times 10^{+02}$
Glycidol	NR	NR	N/A	8.84×10^{-4}	9.24×10^{-4}	NC	NC	NC
Gold	NT	NT	N/A	N/A	N/A	N/A	N/A	N/A
Isoamyl Acetate	$\leq 1.88 \times 10^{-3a}$	$\leq 1.05 \times 10^{-3a}$	N/A	N/A	N/A	N/A	N/A	N/A
Isobutyl Acetate	$\leq 1.18 \times 10^{-3a}$	$\leq 6.58 \times 10^{-4a}$	N/A	N/A	N/A	N/A	N/A	N/A
Isobutyraldehyde	$\leq 3.24 \times 10^{-5a}$	$\leq 1.81 \times 10^{-5a}$	N/A	N/A	N/A	N/A	N/A	N/A
<i>Isoprene</i>	$\leq 4.69 \times 10^{-3a}$	$\leq 4.69 \times 10^{-3a}$	4.10×10^{-1}	4.02×10^{-1}	1.74×10^{-3}	$\downarrow \geq 98.86$	$\downarrow \geq 98.83$	NC
Lead	$\leq 1.78 \times 10^{-6b}$	$\leq 9.99 \times 10^{-7a,b}$	1.31×10^{-5}	1.79×10^{-5}	$\leq 2.77 \times 10^{-6}$	$\downarrow \geq 86.39$	$\downarrow \geq 94.43$	NC
Menthol	3.55×10^{-1}	3.20×10^{-1}	$\leq 1.32 \times 10^{-5}$	$\leq 4.76 \times 10^{-6}$	$2.17 \times 10^{+00}$	NC	NC	\downarrow 85.22
Methyl Acetate	$\leq 1.41 \times 10^{-3a}$	$\leq 7.90 \times 10^{-4a}$	N/A	N/A	N/A	N/A	N/A	N/A
<i>Myosmine</i>	$\leq 9.56 \times 10^{-5a}$	$\leq 9.56 \times 10^{-5a}$	N/A	N/A	N/A	N/A	N/A	N/A
n-Butyraldehyde	$\leq 6.88 \times 10^{-5a}$	$\leq 3.85 \times 10^{-5a}$	4.05×10^{-2}	4.67×10^{-2}	2.21×10^{-2}	$\downarrow \geq 99.83$	$\downarrow \geq 99.92$	$\downarrow \geq 99.83$
Nickel	$\leq 4.11 \times 10^{-6a}$	$\leq 4.23 \times 10^{-6a,b}$	$\leq 5.41 \times 10^{-7}$	$\leq 7.41 \times 10^{-6}$	$\leq 4.55 \times 10^{-7}$	NC	NC	NC
Nicotine	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	$1.00 \times 10^{+00}$	N/A	N/A	N/A
Nicotine-N-Oxide	$\leq 3.42 \times 10^{-4a}$	$\leq 1.91 \times 10^{-4a}$	N/A	N/A	N/A	N/A	N/A	N/A
NNK	$\leq 2.95 \times 10^{-7a}$	$\leq 1.65 \times 10^{-7a}$	1.61×10^{-4}	1.48×10^{-4}	4.88×10^{-6}	$\downarrow \geq 99.82$	$\downarrow \geq 99.89$	$\downarrow \geq 96.61$
NNN	$\leq 1.93 \times 10^{-7a}$	$\leq 1.08 \times 10^{-7a}$	1.87×10^{-4}	1.69×10^{-4}	1.13×10^{-5}	$\downarrow \geq 99.90$	$\downarrow \geq 99.94$	$\downarrow \geq 99.05$
<i>Nornicotine</i>	$\leq 9.96 \times 10^{-5a}$	$\leq 9.96 \times 10^{-5a}$	N/A	N/A	N/A	N/A	N/A	N/A
Propionic Acid	$\leq 3.06 \times 10^{-3b}$	$\leq 3.95 \times 10^{-4a}$	N/A	N/A	N/A	N/A	N/A	N/A
Propylene Glycol	$9.02 \times 10^{+00}$	$9.23 \times 10^{+00}$	4.21×10^{-3}	1.36×10^{-2}	3.25×10^{-1}	$2.14 \times 10^{+05}$	$6.76 \times 10^{+04}$	$2.73 \times 10^{+03}$
Propylene Oxide	$\leq 6.12 \times 10^{-5a}$	$\leq 3.43 \times 10^{-5a}$	4.23×10^{-1}	5.03×10^{-1}	1.23×10^{-4}	$\downarrow \geq 99.99$	$\downarrow \geq 99.99$	$\downarrow \geq 72.19$
Toluene	$\leq 2.40 \times 10^{-4a}$	$\leq 1.34 \times 10^{-4a}$	7.32×10^{-2}	7.69×10^{-2}	1.98×10^{-3}	$\downarrow \geq 99.67$	$\downarrow \geq 99.83$	$\downarrow \geq 93.20$
Water	$5.04 \times 10^{+00}$	$4.61 \times 10^{+00}$	$4.21 \times 10^{+00}$	$8.36 \times 10^{+00}$	$2.45 \times 10^{+01}$	19.67	-44.87	-81.22
						Average^c	Average^c	Average^c
						\downarrow 98.02	\downarrow 98.74	\downarrow 90.66

BLOD=Below limit of quantitation; BLOQ=Below limit of quantitation; NDFB=Not different from background, \downarrow = less than, Bolded reductions were based on quantifiable values. Analytes in italics were tested under a single modified puffing

regimen: 70mL puff, 3 second duration, 30 second interval ^a analyte was BLOD for all three 50 puff blocks ^b analyte was BLOQ for all three 50 puff blocks ^{a,b} analyte was either BLOD or BLOQ for all three 50 puff blocks ^c excluding PG, VG and water.