The Triangulum: The Future is Now!

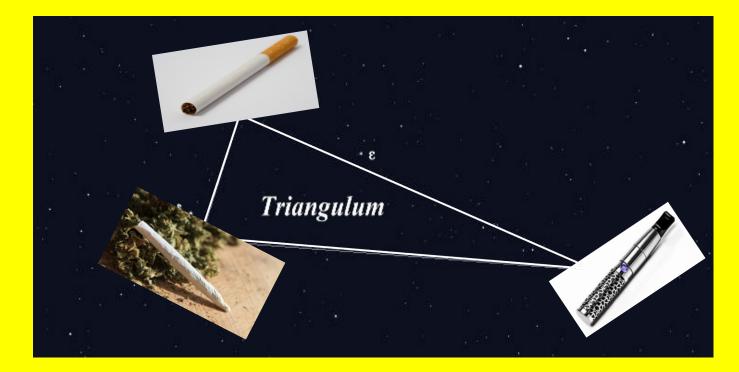
Phillip S. Gardiner, Dr. P. H.

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Washington State Prevention Conference

November 2,2021

The Triangulum: Tobacco, Marijuana and E-Cigarettes



The Future is Now!

The New Frontier

- 21st Century presents us with widely diverse array of new forms of "smoking" and "smoking" devices.
- Radically altered landscape, especially for youths and young adults.

The Evolving "Smoking" Landscape

- Hookah pens aerosolizing flavored liquids, with and without nicotine
- Heat-not-burn products that produce an aerosol, but no fire or smoke
- Colorfully packaged, flavored little cigars and cigarillos, both regular and electronic
- Butane derived marijuana that you can dab
- Liquid THC, which you can aerosolize.

Co-Mingling; Dual and Poly Use

• Blunts

Hollowed out Cigars filled with marijuana

• Caviar

• Adding Crack cocaine or crystal meth to Blunts

Roll Your Own

• Spliffs

Mix Your Own

• Cocktails (assorted e-liquids, favors and nicotine)

Blunts: Hollowed-out Cigars Filled with Marijuana







Reduced Exposure Products

Camel Dissolvables deliver between 0.0 to 3.1 milligrams of nicotine, while cigarette smokers typically inhale about 1mg per cigarette.

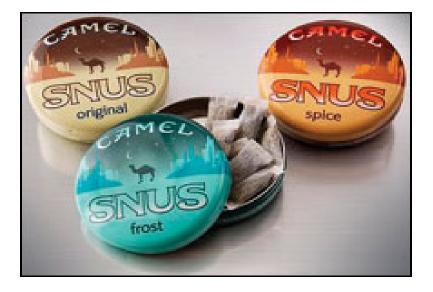
Emerging Products by R.J. Reynolds

Camel Dissolvable Sticks: Camel Orbs: Strips:



Camel Snus

- Spit-less pouch
- The juice can be swallowed

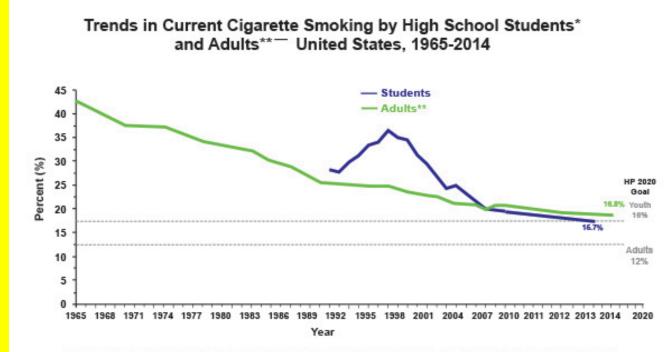




The New Pouch on the Block



Cigarette Use Approaching Historic Lows (CDC, 2017)



*Percentage of high school students who smoked cigarettes on 1 or more of the 30 days preceding the survey (Youth Risk Behavior Survey, 1991-2013). **Percentage of adults who are current cigarette smokers (National Health Interview Survey, 1965-2014).

MJ; Up, Up and Away

- North American *marijuana* sales grew by an unprecedented 30% in 2016 to \$6.7 billion as the legal *market* expands in the U.S. and Canada (Forbes, 2017)
- Marijuana industry could be worth \$50 billion annually by 2026 (MarketWatch, 2017)

Electronic Cigarettes

21st Century Nicotine Addiction

Diversity of E-Cigarette Products



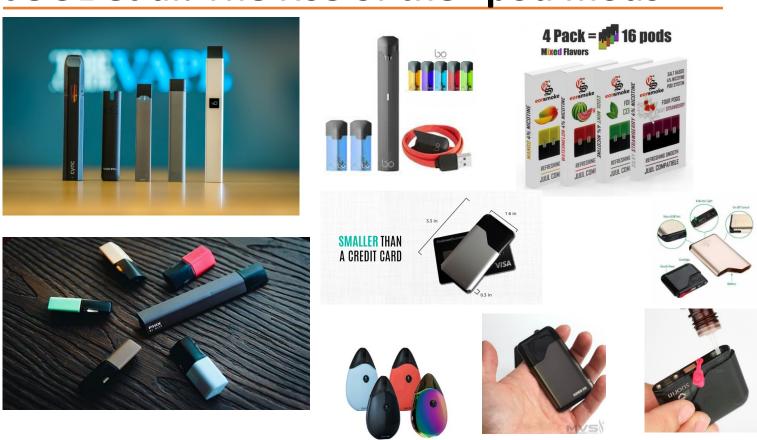
E-Cigars

• Swisher Sweets E-cigars (Swisher International)



1st, 2nd and 3rd Generations





JUUL et al: The rise of the "pod mods"

SUORIN AIR ULTRA PORTABLE SYSTEM

New Kids on the Block





• E-Cigarette Liquid contains:

- Nicotine, extracted from tobacco leaves
 - Large variation in content between and within brands (Cheah et al 2012; Trtchounian et al 2011; Goniewicz et al 2013)
 - Lethal if ingested; 60 mg Adult; 6 mg Children
 - Detrimental to fetuses (Martz, 2009)
 - Tobacco specific nitrosamines (TSNAs) (Laugesen, 2008; Westenberger, 2009; Goniewicz et al 2013)
 - 1.2mg of nicotine in each cigarette, or 24mg of nicotine per pack (1.2mg x 20 cigarettes)= ~ 1 e-cigarette

Nicotine Is Not Benign

- Nicotine is acutely Toxic; Poisonous and Addictive
- Nicotine activates multiple biological pathways through which smoking increases risk for cardiovascular disease
 - Raise blood pressure
 - Build-up of plaque
 - Constrict blood vessels
 - Inflammatory Response
 - Damage to vascular tissue
 - Elevate glucose levels
 - Exacerbate existing heart disease

- E-Cigarette Liquid contains:
 - Propylene Glycol the vapor; the fog
 - FDA approved food additive (humectant, solvent for colors and flavors), cosmetics, and medicines.
 - Short term exposure causes eye, throat, and airway irritation (Wieslander et al 2001; Vardavas et al 2012,)
 - Long term exposure can result in children developing asthma. (Choi et al 2010)
 - Chemical composition changes when heated (Henderson et al, 1981)

• E-Cigarette Liquid contains:

- **Glycerin:** A humectant used instead of or in combination with propylene glycol in EC fluids for aerosol production.
- FDA Approved for ingestion.
- Slightly hazardous in case of skin and eye contact, ingestion, and inhalation; prolonged exposure may cause organ damage.

Metals

• Tin particles found in E-liquid (Williams et al., 2013)

• E-Cigarette Liquid contains:

• Flavorants. Key one Menthol; Candy flavoring

- Anesthetic effects,; promotes deeper inhalation; greater cell permeability
- Allows the poison to go down easier!
- Not GRAS! Ingestion vs. Inhalation
- 15,000+ flavors; appeals to kids (bubblegum, strawberry, gummy bears, etc.)
- Exotic for adults (Sex on the Beach, Aces and 8's)
- Mix your Own (ala roll your own)

The Aerosol: Its Not Just Water Vapor

• E-Cigarette Aerosol Contains:

- Propylene glycol, glycerol, flavorings, and nicotine, which are found in the e-liquid, are also found in the e-Aerosol
- Propylene oxide
- Volatile Organic Compounds: Benzene and Toluene
- Menthol

The Aerosol: Its Not Just Water Vapor

• E-Cigarette Aerosol Contains:

- Carbonyl Compounds: Formaldehyde, acetaldehyde, and acrolein
- Metals: tin, silver, iron, nickel aluminum, sodium, chromium, copper, magnesium, manganese, lead, potassium and silicate nanoparticles
- Tobacco Specific Nitrosamines (TSNAs) carcinogenic compounds found in tobacco and tobacco smoke.
 - (Schripp et al, 2012: Westenberger 2009; Goniewicz et al, 2013; Williams et al, 2013; Henderson, 1981)

E-Cigarette Emit Metals used in Their Manufacturing

 "Considering the potential adverse health effects associated with the inhalation of these metals (particularly Ni and Zn, and the emission observed both in our analysis as well as the study by Williams et al.13), attention should be directed toward eliminating the use of these metals in the cartridges during the manufacturing process of e-cigarettes."

• (Saffari et al., 2014)

Flavors R Us!

All 15,000 of them and Counting*

Flavorings GRAS? Not For Inhalation

- Aldehydes toxicologically are primary irritants of the mucosa of the respiratory tract
- The lungs have a different spectrum of toxicity than the intestinal tract, substances known to be safe when swallowed can still be dangerous when inhaled
 - (Williams, James, and Robert, 2015)

The Ultimate Candy Flavoring; Menthol Helps The Poison Go Down Easier

- Chief Constituent of Peppermint Oil; Minty-Candy Taste; Masks the Harshness of Smoking
- Cooling Sensation; activates taste buds; cold receptors; increases throat grab
- Anesthetic effects; Mimics Bronchial Dilatation; easier to inhale; deeper inhalation; more nicotine taken in.
- Mentholated cigarette smoking inhibits nicotine metabolism

The Ultimate Candy Flavoring; Menthol Helps The Poison Go Down Easier

Independent Sensory Activation Neurotransmitters (Brody, 2013)

• Greater Cell Permeability (Ferris, 2004; Benowitz, 2004)

Flavors = Aldehydes

- Cause Respiratory Inflammation
- Impairs Immune Cell Functions
- Dysregulates antioxidant Responses
- Increases Susceptibility to Infection
- Contribute to emphysema and COPD

Cinnamaldehyde in Flavored E-Cigarette Liquids

- Suppresses bronchial epithelial cell ciliary motility
- Dysregulation of mitochondrial function
- With essential respiratory defenses down, inhalation of cinnamaldehyde may increase the risk of respiratory infections in ecigarette users.
 - (Clapp et al., 2019)

Cariogenic Potential of Sweet Flavors in Electronic-Cigarette Liquids

- "Aerosols have similar physio-chemical properties as high-sucrose, gelatinous candies and acidic drinks
- The combination of the viscosity of e-liquids and some classes of chemicals in sweet flavors may increase the risk of cariogenic potential."
 - (Kim et al., 2018) <u>https://journals.plos.org/plosone/article?id=10.1371/journal.pone</u> <u>.0203717</u>

Evaluation of Electronic Cigarette Liquids and Aerosol for the Presence of Selected Inhalation Toxins

- Diacetyl (DA) and acetyl propionyl (AP) are chemicals approved for food use but are associated with respiratory disease when inhaled.
- 159 distinct liquids and aerosols were analyzed
 - DA and AP were found in 74.2% of the samples (Farsalinios, et al 2014

Diacetyl: Popcorn Lung

- "Popcorn lung" comes from inhaling diacetyl, a chemical widely used in the flavor industry to simulate dairy (e.g. butter, cheese, yogurt), fruit flavors (e.g. strawberry, bananas), and so-called brown flavors (e.g. coffee, butterscotch)
- In flavoring-induced lung disease, the tiny bronchiole passages located near the air exchanging alveoli become gradually scarred shut. One can become progressively shorter of breath due to poor oxygen absorption
- Diacetyl has been found in many e-cigarette vapors, especially sweet flavors.
 - (Tierney et al., 2015; Farsalinos, 2014)

Flavoring Chemicals in E-Cigarettes: Diacetyl, 2,3-Pentanedione, and Acetoin in a Sample of 51 Products, Including Fruit-, Candy-, and Cocktail-Flavored E-Cigarettes

 51 types of flavored e-cigarettes sold by leading e-cigarette brands and flavors we deemed were appealing to youth.

• Diacetyl was detected above the laboratory limit of detection in 39 of the 51 flavors tested

• (Allen et al., 2016; <u>https://ehp.niehs.nih.gov/15-10185/</u>

<u>Cardiorespiratory and Immunologic</u> <u>Effects of Electronic Cigarettes.</u>

• The use of e-cigarettes in humans is associated with significant adverse cardiorespiratory and immunological changes. Data from animal models and in vitro studies support the notion that long-term use of e-cigarettes may pose significant health risks.

• Bhatnagar, 2021

Study Finds Aldehyde Levels Not Safe

- Within the tested e-cigarette brands, thermal decomposition of flavoring compounds dominates formation of aldehydes during vaping, producing levels that exceed occupational safety standards
 - Flavoring Compounds Dominate Toxic Aldehyde Production during E-Cigarette Vaping; Environmental Science & Technology, November, 2016; Andrey Khlystov and Vera Samburova

Flavors and the Heart

 The vape flavorings so popular with kids and young adults are cardiotoxic and disrupt the heart's normal electrical activity

- Disrupts Rhythm
- Increased toxicity in Cardio cells

 "In Vitro and In Vivo Cardiac Toxicity of Flavored Electronic Nicotine Delivery Systems" by Obada Abou-Assali, Mengmeng Chang, Bojjibabu Chidipi, Jose L. Martinez-de-Juan, Michelle Reiser, Manasa Kanithi, Ravi Soni, Thomas Vincent McDonald, Bengt Herweg, Javier Saiz, Laurent Calcul and Sami F. Noujaim, 20 November 2020, *American Journal of Physiology-Heart and Circulatory Physiology*. DOI: 10.1152/ajpheart.00283.2020

E-Cigs and Mental Health

- Vaping, smoking and dual use were associated with self-reported serious difficulty concentrating, remembering, or making decisions
 - 18535; nationally representative sample of all US students from grade 6 to 12
 - Highest among Dual-Users
 - Highest among NH- AI/AN
 - Highest among Males

Association of electronic cigarette use with self-reported difficulty concentrating, remembering, or making decisions in US youth

Tob. Induc. Dis. 2020;18(December):106

Catherine Xie, Zidian Xie, Dongmei Li

E-Cigs and Popular Culture

 "Among music videos with e-cigarette product placement and imagery, the most prevalent theme was *Image/Lifestyle/Sociability* (e.g., ostentatious lifestyle, partying) and the most prevalent genre was Hip Hop."

- Only 7 of 180 (3.7%) had e-cig imagery
- Yet, they were seen over a Billion times!!
- Disproportionate impact in Communities of Color

E-cigarette product placement and imagery in popular music videos Nicotine & Tobacco Research, ntaa273. Published: 26 December 2020 Patricia Escobedo, Erica L Rosenthal, Camille J Saucier, Jennifer B Unger, Tess B Cruz, Matt Kirkpatrick, Jon-Patrick Allem

https://academic.oup.com/ntr/advance-article-abstract/doi/10.1093/ntr/ntaa273/6053005

E-Cigarettes: The Second Generation

• 1st Generation:

- Cig-a-likes; Most Toxins Emitted in the Aerosol Lower than Regular Cigarettes (Goniewicz et al., 2013)
- Aerosolizing Temperature 100 250c

• 2nd Generation

- Tank Systems; refillables
- Some Toxins Emitted Approaching Levels found in Regular Cigarettes
- Aerosolizing Temperatures >250*

Platelet Activation: Same as Regular Cigarettes

- Hemostatic System most sensitive to fine particulate matter
- The fine particulate matter found in electronic cigarette aerosol is in the same range as mainstream and side-stream tobacco smoke.
 - (Hom et al., 2016)



As Battery Voltage Increase, Toxins Increase

- On Average, Toxins were 13 807-Fold Lower than Tobacco Cigarettes
- However, when voltage was increased from 3.2 to 4.8V:
 - 4 to over 200 times increase in formaldehyde, acetaldehyde, and acetone levels
 - The levels of formaldehyde were in the range of levels reported in tobacco smoke

(Kosmider et al., 2014)

The I Phone of E-Cigarettes



JUUL and Pods: What's in Them?

- The nicotine salts content is 0.7mL (or 59 mg/mL) per pod, which is approximately equivalent to one pack of cigarettes, or 200 puffs.
- E-Liquid contains glycerol and propylene glycol, nicotine, benzoic acid, and flavorants. (Nicotine Salts and Benzoic acid, this is the catch)
- Virginia tobacco, cool mint, fruit medley, creme brulee, and mango, ad nauseum.
- Lithium-ion polymer battery.

"Dripping"



"Dripping"



"Dripping"

• **Dripping**: Dripping *e-liquids* directly onto heated atomizers (metal coil filament)

 Among 1080 ever e-cigarette users, 26.1% of students reported ever using e-cigarettes for dripping.

- produced thicker clouds of vapor (63.5%)
- made flavors taste better (38.7%)
- produced a stronger throat hit (27.7%)
 - (Krishnan-Sarin, et al., 2017)

Dripping and Formaldehyde Formation

- "Volatile aldehyde emissions, including formaldehyde, greatly exceeded values previously reported for conventional ECIGs and combustible cigarettes . . ."
 - Increasing the inter-drip interval resulted in greater VA emissions
 - the higher temperatures attained while Dripping are inherently likely to produce high toxicant emissions
 - (Talih et al., 2016)

Dual and Poly Use on the Rise

Sherine El-Toukhy & Kelvin Choi, N=3,202; 9-17year; 2012 NYTS

 Cigarette Only Users Non-cigarette Combustibles • cigars, cigarillos, bidis, roll-your own, hookah, clove cigs Non-Combustibles • Chewing tobacco, snus, snuff, dip, dissolvables and ecigarettes Dual Use

Poly-tobacco Use

Youth Smoking Prevalence's

Dual Use	30.5%
 Non-cigarette Combustibles 	26.7%
 Poly-tobacco Use 	17.5%
 Cigarettes Only 	14.9%
 Non-Combustibles Only 	10.4%

Racial & Ethnic Difference

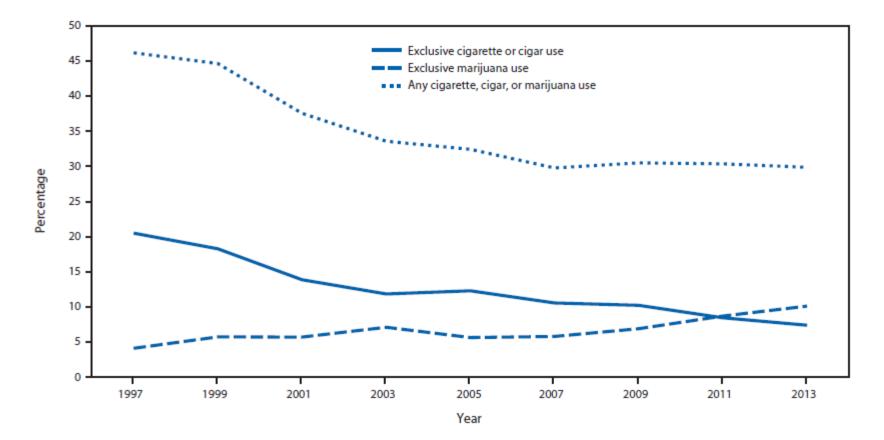
(http://ntr.oxfordjournals.org/content/early/2016/01/12/ntr.ntw008.full.pdf+html)

Tobacco-use pattern	Ciga	rettes only		oustible only er than cig)	Non-o	combustible	Dual only		Dual only Poly-tobacco only		tobacco only
	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% Cl)	
Total	466	14.9 <i>(13.3-16.7)</i>	849	26.7 (24.2-29.3)	329	10.4 (8.4-12.9)	992	30.5 (28.1-32.9)	566	17.5 (15.3-19.9)	
Race/Ethnicity											
Non-Hispanic White	265	15.8 <i>(13.6-18.3)</i>	332	19.7 (16.9-22.7)	227	13.2 (10.3-16.7)	556	32.3 (29.5-35.3)	328	19.0 <i>(16.2-22.3)</i>	
Non-Hispanic Black	48	11.1 (7.2-16.7)	216	50.9 (44.1-57.6)	25	6.4 (3.4-11.6)	110	26.9 (22.4-31.9)	24	4.8 (2.7-8.2)	
Hispanic	119	15.2 (11.9-19.3)	241	28.6 (25.2-32.4)	56	6.6 <i>(4.8-8.9)</i>	248	28.1 (24.2-32.4)	168	21.4 (18.7-24.5)	
Non-Hispanic Asian	8	12.1 (4.4-29.3)	24	38.9 (22.5-58.3)	5	8.5 (3.0-21.7)	18	26.4 (13.6-44.8)	7	14.1 (7.2-25.6)	
American Native	10	9.9 (4.7-19.4)	16	19.4 <i>(11.3-31.3)</i>	8	8.5 (4.1-16.8)	34	37.3 (27.1-48.7)	23	25.0 (15.2-38.2)	

Marijuana

Widely Used; Recreationally legal in 18 States

Prevalence of exclusive cigarette or cigar use, exclusive marijuana use, and any cigarette, cigar, or marijuana use (MMWR, 2015) (High School)



High School Students' Use of Electronic Cigarettes to Vaporize Cannabis

- Nearly 4000 High School Students in Connecticut completed an anonymous survey
 - 27% who have used both marijuana and e-cigarettes reported using e-cigarette aerosolizers to vaporize cannabis including hash oil, and wax THC. (Morean et al., 2015)

Table 9. PAHs and Aza-arenes Determined in Mainstream Smoke from Tobacco and Marijuana under Two Smoking

Table 4. Various Analytes Including Tobacco-Specific Compounds and Heavy Metals Determined in Sidestream Smoke from Tobacco and Marijuana under Two Smoking

Compounds and Heavy Metals Determined in Smoke from Tobacco and Marijuana under T	1 Sidestream Sidestream S Iwo Smoking	smoke from Tobacco and Marijuana under Two	ant cmaka	Con	ISO		
ISO e		Dried pla	ant smoke	tobacco			
tobacco marijuana tobacco	marijuana	ioourro marganna ioourro Imarganna			$2070 \pm 290^{\circ}$ $2057 \pm 302^{\circ}$		1459 ± 646 1409 ± 604
r (mg/cig) 24.3 ± 1.8 $49.7 \pm 2.5^{*}$ 172 ± 1.4 O (μ g/cig) 1101 ± 47 $2087 \pm 152^{*}$ $1452 \pm 1452^{*}$	milar c	hemicals	in varied p	ron	ortior	3600 ± 374 2 51 4 51 2	$2917 \pm 477^{\circ}$ $459 \pm 60^{\circ}$ $213 \pm 48^{\circ}$
$\begin{array}{c} \text{Dx} (\mu g/\text{cig}) & 1172 \pm 44 & 2284 \pm 229^* & 1.528 \\ \text{D} (\text{mg/cig}) & 61.7 \pm 2.0 & 54.0 \pm 3.7^* & 61.6 \pm 2.9 \\ \text{mg/cig} & 4.77 \pm 0.26 & 0.065 \pm 0.018^* & 2.11 \pm 0.22 \\ \text{mg/cig} & 4.77 \pm 0.26 & 0.065 \pm 0.018^* & 2.11 \pm 0.22 \\ \text{mg/cig} & 4.77 \pm 0.26 & 0.065 \pm 0.018^* & 2.11 \pm 0.22 \\ \text{mg/cig} & 4.77 \pm 0.26 & 0.065 \pm 0.018^* & 2.11 \pm 0.22 \\ \text{mg/cig} & 4.77 \pm 0.26 & 0.065 \pm 0.018^* & 2.11 \pm 0.22 \\ \text{mg/cig} & 4.77 \pm 0.26 & 0.065 \pm 0.018^* & 2.11 \pm 0.22 \\ \text{mg/cig} & 4.77 \pm 0.26 & 0.065 \pm 0.018^* & 2.11 \pm 0.22 \\ \text{mg/cig} & 4.77 \pm 0.26 & 0.065 \pm 0.018^* & 2.11 \pm 0.22 \\ \text{mg/cig} & 4.77 \pm 0.26 & 0.065 \pm 0.018^* & 2.11 \pm 0.22 \\ \text{mg/cig} & 0.065 \pm 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.065 \pm 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.065 \pm 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.065 \pm 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.065 \pm 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.065 \pm 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^* & 0.018^* & 0.018^* & 0.018^* & 0.018^* \\ \text{mg/cig} & 0.018^*$	$50.6 \pm 3.9^{\circ}$ 4-aminobipheny	$A = 1.56 \pm 0.13 \ 6.17 \pm 0.44^{*} \ 2.54 \pm 0.17 \ 13.5 \pm 1.5$	⁶ ⁶ ¹ luorene ⁷ ⁷	769 ± 42 293 ± 14	366 ± 37* 273 + 23	1369 ± 100 6 515 ± 32 4	$559 \pm 64^{\circ}$ 576 ± 45
$\begin{array}{rcl} \text{form} & 4.77 \pm 0.20 & 0.005 \pm 0.018^{\circ} & 5.11 \pm 0.25 \\ \text{mg/cig} & & & \\ \text{mg/nig} & & & \\ & & & \\ \text{5568} \pm 322 & 14270 \pm 472^{\circ} & 3010 \pm 327 \\ \end{array}$		sidestream tlene 195 ± 16 $305 \pm 21^{\circ}$ 144 ± 8 $266 \pm 23^{\circ}$	8 anthracene 9 fluoranthene	91.8 ± 5.4 96.8 ± 3.7			
$\frac{1}{\mu g/cig} = \frac{1}{2} \sum_{i=1}^{n} \frac{1}{i} \sum_{j=1}^{n} \frac{1}{i} \sum_{i=1}^{n} \frac{1}{i} \sum_{j=1}^{n} \frac{1}{i} $	2-aminonaphtha 3-aminobipher	dene 136 ± 7 $177 \pm 19^{\circ}$ 79.4 ± 7.4 $139 \pm 12^{\circ}$ 33 ± 2.1 $50.4 \pm 3.7^{\circ}$ 19.7 ± 1.6 40.6 ± 2.4		88.8 ± 4.3 30.5 ± 2.5	$45.6 \pm 4.4*$		32.3 ± 11.2 $13.1 \pm 7.9^{\circ}$
Sample con	iparisons of	components of t	obacco and marij	uanas	seconunai	IQ SINOKE	3 ± 7.9 $6.2 \pm 3.6^{\circ}$
AB 2.71 ± 0.52 $<0.793^{*}$ $0.79-2.5$ NK 92 ± 11.7 $<4.65^{\circ}$ 61 ± 5.1	<0.793 cigarette. * <i>P</i> <	0.05 vs tobacco.	14 benzo(k)fluoranthene 15 benzo(c)pyrene 16 benzo(a)pyrene	3.42 ± 0.32 11 ± 0.6 14.3 ± 1.2	1.52 ± 0.26* 6.15 ± 0.37*	7.45 ± 1.47 4	$.54 \pm 0.96$ $\frac{2.6 \pm 2.7}{5 \pm 2.9}$
ercury $8.32 \pm 0.57 < 4.40^{\circ}$ 6.31 ± 0.61 dmium 478 ± 19 $4.0-13.4^{\circ}$ 360 ± 20	<4.40 tobacco rable 7. 5 4.0-13.4* Mainstree	Select Marijuana unds Determined in m and Sidestream Smoke from Tobacco and	17 perylene 18 indeno(1.2.3cd)nyrene	3.9 ± 0.46 4.58 ± 0.89	tobacco	marijuana	10 ± 0.82 105 ± 3.11
tar (mg/cig) 103 531.0	$^{31.0-}_{33.5}$ 24.3 ± 1.8	49.7 ± 2.5*	naphthalene (ng/cig)	1.15 ± 0.21 3.77 ± 0.66	6861 ± 419	16748 ± 2	396*
NO (µg/cig)	<11.3 1101 ± 47	2087 ± 152*tobacco marijuana	formaldehyde (µg/cig)	< 0.035 11.5 ± 1.4	888 ± 47	383 ± 27*	*0.071 7.6 ± 1.4
CO (mg/cig) deviations. For the	61.7 ± 2.0 chydd	54.0 ± 3.7* 543 ± 91 66.5 ± 11.8	acetaldehyde (μ g/cig)	5.81 ± 0.44 < 0.314 < 0.260	1587 ± 45	1170 ± 69	2.2 ± 2.1 0.628 < 0.519
nicotine (mg/cig)	4.77 ± 0.26	0.065 ± 0.018*	acrolein (µg/cig)		437 ± 10	304 ± 20*	<0.278 <0.634
ammonia (µg/cig)	5568 ± 322	14270 ± 472*	methyl ethyl ketone (µc	/cig)	222 ± 9	160 ± 11*	
d HCNm (µg/cig) obacco and Mai	83.8 ± 7.8	tone 135 ± 16 $624 \pm 55^{*}$ 265 ± 27 $140 \pm 7^{*}$ 685 $\pm 429^{3.8}$ 77.1 ± 10.0 $110 \pm 8^{*}$	phenol (µg/cig)	0.177-0.589 Units are ng/cigard	264 ± 13	260 ± 11	=0.354 elow the l
pyridine (µg/cig)	extreme 265 ± 101maldehyde	307:7±31427* 662±29 202±34*	m + p-cresols (µg/cig)		64.6 ± 2.5	104 ± 6*	
benzene (µg/cig)	290 ± 1 1 1 1 1 1	$341^{22} \pm 512^{40}$ 720 ± 22 405 ± 54^{60} 1383 ± 37 896 ± 112	pyrene P(ng/cig)arenes Determin	ned in Sidestrea		. 1.609 ± 60*	Smokin
toluene (µg/cig)	516 ± 20	$704 \pm 29^{*}$	benzo(e)pyrene (ng/cig	Con	94.9 ± 6.9	87.9 ± 7.5)
styrene (µg/cig)	138 132 105 ± 10 ^{raldehyde}	tone 162 ± 10^{118} 202 ± 17 $116 \pm 13^{\circ}$ 60.2 ± 1.7 $139 \pm 13^{\circ}$	anthracene (ng/cig)	tobacco	755 ± 38	1135 ± 75	
ylonitrite 13 ± 1.2 36.6 ± 4.5 24 ± 0.9 izene 62.2 ± 3.5 58.3 ± 5.9 94.6 ± 2.6	$\begin{array}{c} 66.9 \pm 9.5^{*} \\ 84.4 \pm 8.9^{*} \end{array} \qquad \ \ ^{a} \text{ Values are} \end{array}$	provided \pm standard deviations; $n = 7$. Units are μg	1 naphthalene 2 1-methylnaphthalene	6861 ± 419 6265 ± 365	$16748 \pm 2396^{\circ}$ $14812 \pm 1511^{\circ}$	$\begin{array}{ccc} 10111 \pm 758 & 143 \\ 7115 \pm 787 & 110 \end{array}$	

From Moir et al., 2008. Subset of 65 components analyzed under standard tobacco smoking conditions

	$307 \pm 14^{*}$		$278 \pm 22^{*}$
9.94 ± 0.92		8.53 ± 0.54	
	$412 \pm 27^{*}$		$420 \pm 22^{*}$
1459 ± 82	$656 \pm 40^{*}$	1153 ± 51	$614 \pm 31^{*}$
102 ± 4		73.8 ± 4.7	
290 ± 11			$328 \pm 18^{*}$
516 ± 20	$704 \pm 29^{*}$		
		85.2 ± 10.6	

Inhaling a whole

found at levels about 20-fold those in tobacco in mainstream smoke (Table 3) and about 3-fold there in sidestream smoke (Table 4), although the absolut **Carp Enduct State** in sidestream smoke. The amount of minate fertilizer applied during growth (*30*). The simplest explanation for the very high levels of ammonia found in marijuana smoke may be that the marijuana used for this study contained more nitrate than the tobacco sample. The marijuana plants were grown on soil-less growth medium. All fertilizers were commercially available and consisted of water-soluble hydroponic vegetable fertilizers used for horticulture and contained nitrogen

it is not now to what extent the differences in the growi conditions between the marijuana and the tobacco, includi the types of fertilizers used, influenced the levels of nitra in the plants. The temperature of combustion can also influer the production of ammonia. Burning tobacco results in reduction of nitrate to ammonia, which is released to a grea extent during sidestream smoke formation (31), suggesting the lower combustion temperatures favor the production of a monit way hold the contributed to the differences

ammonia yield, but this was not verified.

y to bacco-specific introstantings were not round in the main y and the back of backs and 4). This result was expected, giv y and the back of backs are derived from nicotine. Arsenic and which is consistent with the certificate of analysis provided wi the plant material (data not shown). Again, this could be function of the relatively controlled growth conditions.

NO and NO_x were significantly elevated in the marijuan smoke under both smoking regimes and in mainstream (Tabi 3) and sidestream smoke (Table 4). A logical explanation woul be that these are arising from the nitrate present in the fertilize and would be consistent with the very high ammonia yield





with "<" were below the limit of

Marijuana and SHS (Springer, 2014)

Marijuana SHS for one minute substantially impairs blood vessel function in rats.

Neither THC nor paper smoke are required for marijuana SHS to impair blood vessel function.

...nicotine is not required for impairment of blood vessel function by smoke.

One minute of marijuana SHS exposure impairs blood vessel function for at least 90 minutes.

Comparing MJ users and non-users: Alcohol and other drug use (N=1987)

- Compared to those who only smoked cigarettes, those who also used MJ were more likely to have past month:
 - Alcohol use (87.4 vs. 68.3)
 - Other drug use (31.5 vs. 4.0)
- And among those who drank, MJ users had more:
 - Total drinks per month (44.5 vs. 31.9)
 - Drinking days per month (8.5 vs. 6.9)
 - Drinks per drinking day (5.0 vs. 4.5)
 - Heavy drinking days (4.12 vs. 3.0)

Dabbing



Dabbing

- Dabbing: Inhaling the vapors from a concentrated form of marijuana made by an extracting THC using butane gas.
- Dabs, also known as butane hash oil BHO) "bladder," "honeycomb" or "earwax"

THC Concentrate (BHO)



3 in 1: Herb, Liquid or Wax



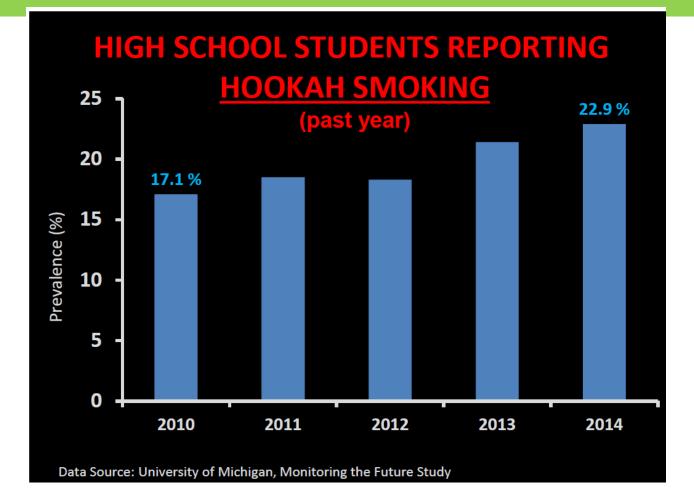
Pod Switching!

 Pod switching; People using multiple substances (*Can you say Triangulum*); <u>https://www.youtube.com/watch?v=S7o-Sm5zuTc</u>

Hookah

Its More Than Flavored Tobacco in Water

Hookah Use on the Rise Among Youth



Hookahs

- From 2011 to 2016, current use of hookahs increased among High School and College students went up.
 - Nearly 5 of every 100 high school students (4.8%) reported in 2016 that they had used hookah in the past 30 days—an increase from 4.1% in 2011.
 - The Fall 2018 National College Health Assessment found that 14.7% of college students had ever used hookah and 3.1% had used it in the past month.
 - (CDC, 2017); (NCHA, 2018)

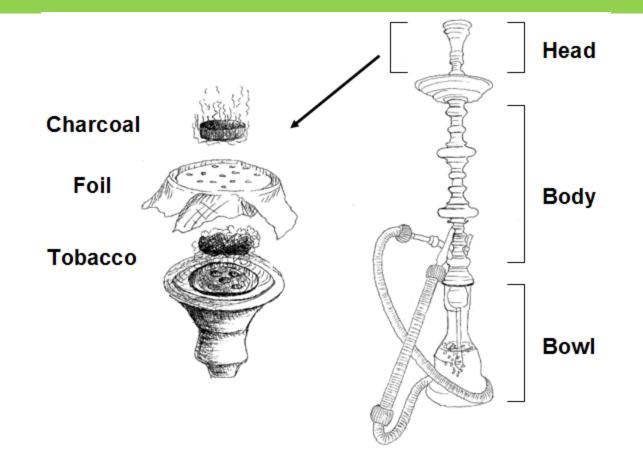
E-Pens; E-Hookah Pens

- Cherry, Chocolate,
- Vanilla, Bubblegum





Schematic Showing The Major Components of a Hookah



In Comparison

- A single hookah tobacco smoking session (40 to 45 minutes) exposes its users to:
 - 25 times the tar
 - 125 times the smoke
 - 2.5 times the nicotine
 - 10 times the carbon monoxide
- As Compared to a single cigarette!

(Primack et al., 2016)

E-Cigarettes are Sooo Last Year!

Enter: Heat not Burn

An Emerging Tobacco Industry Philosophy

- E-cigs a niche product
- Need a product that
 - Tastes like tobacco
 - "Smokes" like tobacco
 - Has the throat grab (feels like tobacco)
- But it has to be safer that conventional cigarettes

But is It?

Reduced Risk Products: Harm Reduction and Regulation

- RRPs are a fundamental complement to regulatory efforts to reduce smoking prevalence
- Our ambition is to convince all adult smokers that intend to continue smoking to switch to RRPs as soon as possible
- The principle of harm reduction through RRPs needs to be embraced and appropriate regulatory frameworks implemented (Catantzopoulos, 2016)

The IQOS Heating System



Marlboro Heetsticks Heat not Burn





Digital Addiction

- <u>https://www.pmi.com/glossary-section/glossary/electronic-heating-blade</u>
- <u>https://www.pmi.com/smoke-free-products/iqos-our-tobacco-heating-system</u>

IQOS Facts

- Lithium Ion Battery
- Re-constituted into tobacco sheets, called cast-leaf.
- 156 distinct flavors added to the tobacco cast-leaf
 - Menthol, cocoa, vanilla, sugar, lemon, lime; on infinitum
- Propylene Glycol; Glycerol (the same humectants used in e-cigarettes
- Tobacco heated to 300-350 Celsius by a Gold Platinum and Ceramic Blade
 - <u>https://www.pmi.com/our-business/about-us/products/making-heated-tobacco-products</u>

List of ingredients: (United Kingdom)

https://www.pmi.com/our-business/about-us/products/making-heated-tobacco-products

	Amount %	mg/cig		
tobacco	24.7	201.5		
glycerol	6.4	52.3		
water	4.4	36.1		
guar gum	1	7.8		
cellulose	0.6	5.2		
propylene glycol	0.3	2.6		
natural & artificial flavourings	0.017	0.141		
filtration material	44.3	361		
HeatStick paper and wrappers	14.3	116.7		
tipping paper and tipping paper inks	2.5	20		
adhesives	1.3	10.8		

IQOS and Your Health

- IQOS exposure is as detrimental as cigarette smoking and vaping to human lung cells.
- Persistent allergic, smoke or environmental-triggered inflammation leads to airway remodelling/scarring
- Disturbs the way that cells convert oxygen into energy for the cells to use (mitochondrial dysfunction)
- Mitochondrial dysfunction is the primary cause of airflow limitation in people with Asthma and COPD
 - (Sohal et al., 2018; https://openres.ersjournals.com/content/5/1/00159-2018

Country Launch Cities Commercial Price.pk - RSP/20s Pack (in USS) 1. Japan National Nov-14 \$98.76 \$4.14 Mariboro \$42.33 2. taly Bologna, Mian, Modena, Rome and Turin (focus are Nov-14 \$98.76 \$4.14 Mariboro \$42.33 3. Switzerland Basel, Bern, Geneva, Lausanne, Neuchätel and Zur Aug 15 \$101.66 \$8.22 Mariboro \$4.73 5. Portugal Lisbon (focus area) Nov-14 \$79.96 \$5.37 Mariboro \$4.12 6. Romania Top-16 cities Nov-15 \$79.96 \$5.37 Mariboro \$4.12 7. Russia Moscow and St. Petersburg (focus area) Nov-15 \$89.98 \$4.25 Mariboro \$4.12 8. Uraine Kiev and select cities Feb-16 \$114.42 \$1.34 Pariiament \$2.76 8. Uraine Kiew and select PoS in other cities Mar-16 \$79.96 \$8.00 Mariboro \$8.00 10. Denmark Copenhagen and select PoS in other cities Sep-16 \$11.422 \$4.57 Mariboro \$5.7				QOS Geographic Markets	- As of C	October	1,201/	/	
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14.SpainMadrid and select citiesOct-16\$79.96\$5.54Marlboro\$5.6515.CanadaCalgary, Toronto and VancouverDec-16\$109.31\$8.64Belmont\$9.2616.IsraelSelect citiesDec-16\$98.09\$9.53Marlboro\$9.5317.KazakhstanAlmatyDec-16\$113.73\$1.23Marlboro\$1.1718.New ZealandAucklandDec-16\$107.57\$13.63Marlboro\$18.8619.South AfricaCape Tow n and JohannesburgDec-16\$113.42\$2.99Marlboro\$2.9920.United KingdomLondonDec-16\$115.45\$10.38Marlboro\$1.4321.LithuaniaVilnius and select citiesFeb-17\$33.08\$1.09Marlboro\$1.1722.ColombiaBogotaMar-17\$105.21\$1.70Marlboro\$1.7023.PolandWarsaw and select citiesApr-17\$107.71\$4.31Marlboro\$4.3124.SerbiaBelgradeApr-17\$107.71\$4.31Marlboro\$2.9325.FranceNice & ParisJun-17\$106.04\$3.80Marlboro\$3.9827.Czech RepublicPrague and select citiesJul-17\$117.04\$4.35Marlboro\$3.9827.Czech RepublicPrague and select citiesJul-17\$117.04\$4.35Marlboro\$3.9829.Slovak RepublicBratislava & select c		12.	Greece	Attica Region	Sep-16	\$114.22	\$4.57	Marlboro	\$5.14
15. Canada Calgary, Toronto and Vancouver Dec-16 \$109.31 \$8.64 Belmont \$9.26 16. Israel Select cities Dec-16 \$98.09 \$9.53 Marlboro \$9.53 17. Kazakhstan Almaty Dec-16 \$113.73 \$1.23 Marlboro \$1.17 18. New Zealand Auckland Dec-16 \$107.57 \$13.63 Marlboro \$1.86 19. South Africa Cape Tow n and Johannesburg Dec-16 \$113.42 \$2.99 Marlboro \$13.43 21. Lithuania Vinius and select cities Feb-17 \$33.08 \$1.09 Marlboro \$1.17 22. Colombia Bogota Mar-17 \$105.21 \$1.70 Marlboro \$1.17 23. Poland Warsaw and select cities Apr-17 \$107.71 \$4.31 Marlboro \$2.93 24. Serbia Belgrade Apr-17 \$107.71 \$4.31 Marlboro \$2.93 25. France Nice & Paris Jun-17 \$106.04 \$3.80 Marlboro \$3.98 <tr< td=""><td></td><td>13.</td><td>Netherlands</td><td>Amsterdam and select PoS in other cities</td><td>Sep-16</td><td>\$79.96</td><td>\$6.85</td><td>Marlboro</td><td>\$7.65</td></tr<>		13.	Netherlands	Amsterdam and select PoS in other cities	Sep-16	\$79.96	\$6.85	Marlboro	\$7.65
16. Israel Select cities Dec-16 \$98.09 \$9.53 Marlboro \$9.53 17. Kazakhstan Almaty Dec-16 \$113.73 \$1.23 Marlboro \$1.17 18. New Zealand Auckland Dec-16 \$107.57 \$13.63 Marlboro \$1.86 19. South Africa Cape Tow n and Johannesburg Dec-16 \$113.42 \$2.99 Marlboro \$13.43 21. Lithuania Vilnius and select cities Feb-17 \$33.08 \$1.09 Marlboro \$13.43 21. Lithuania Vilnius and select cities Feb-17 \$33.08 \$1.09 Marlboro \$11.70 22. Colombia Bogota Mar-17 \$105.21 \$1.70 Marlboro \$4.31 24. Serbia Belgrade Apr-17 \$107.71 \$4.31 Marlboro \$2.93 25. France Nice & Paris May-17 \$79.96 \$8.00 Marlboro \$3.98 27. Czech Republic	-E	14.	Spain	Madrid and select cities	Oct-16	\$79.96	\$5.54	Marlboro	\$5.65
17. Kazakhstan Almaty Dec-16 \$113.73 \$1.23 Marlboro \$1.17 18. New Zealand Auckland Dec-16 \$107.57 \$13.63 Marlboro \$18.86 19. South Africa Cape Tow n and Johannesburg Dec-16 \$113.42 \$2.99 Marlboro \$13.43 20. United Kingdom London Dec-16 \$115.45 \$10.38 Marlboro \$13.43 21. Lithuania Vilnius and select cities Feb-17 \$33.08 \$1.09 Marlboro \$11.70 22. Colombia Bogota Mar-17 \$105.21 \$1.70 Marlboro \$1.70 23. Poland Warsaw and select cities Apr-17 \$107.71 \$4.31 Marlboro \$2.93 25. France Nice & Paris May-17 \$79.96 \$8.00 Marlboro \$3.98 26. South Korea Seoul Jun-17 \$106.04 \$3.80 Marlboro \$3.98 27. Czech Republic Prague and select cities Jul-17 \$117.04 \$4.35 Marlboro \$3.98 <t< td=""><td></td><td>15.</td><td>Canada</td><td>Calgary, Toronto and Vancouver</td><td>Dec-16</td><td>\$109.31</td><td>\$8.64</td><td>Belmont</td><td>\$9.26</td></t<>		15.	Canada	Calgary, Toronto and Vancouver	Dec-16	\$109.31	\$8.64	Belmont	\$9.26
18.New ZealandAucklandDec-16\$107.57\$13.63Marlboro\$18.8619.South AfricaCape Tow n and JohannesburgDec-16\$113.42\$2.99Marlboro\$2.9920.United KingdomLondonDec-16\$115.45\$10.38Marlboro\$13.4321.LithuaniaVilnius and select citiesFeb-17\$33.08\$1.09Marlboro\$1.1722.ColombiaBogotaMar-17\$105.21\$1.70Marlboro\$1.7023.PolandWarsaw and select citiesApr-17\$107.71\$4.31Marlboro\$4.3124.SerbiaBelgradeApr-17\$121.82\$2.36Marlboro\$2.9325.FranceNice & ParisMay-17\$79.96\$8.00Marlboro\$3.9827.Czech RepublicPrague and select citiesJul-17\$117.04\$4.35Marlboro\$3.9827.Czech RepublicPrague and select citiesJul-17\$117.04\$4.35Marlboro\$3.9829.Slovak RepublicBratislava & select citiesAug-17\$113.08\$4.00Marlboro\$3.1429.Slovak RepublicBratislava & select citiesAug-17\$113.08\$4.00Marlboro\$3.1430.PalestineSelect citiesOct-17\$98.09\$7.01Marlboro\$7.01	-E	16.	Israel	Select cities	Dec-16	\$98.09	\$9.53	Marlboro	\$9.53
19.South AfricaCape Tow n and JohannesburgDec-16\$113.42\$2.99Marlboro\$2.9920.United KingdomLondonDec-16\$115.45\$10.38Marlboro\$13.4321.LithuaniaVilnius and select citiesFeb-17\$33.08\$1.09Marlboro\$1.1722.ColombiaBogotaMar-17\$105.21\$1.70Marlboro\$1.7023.PolandWarsaw and select citiesApr-17\$107.71\$4.31Marlboro\$4.3124.SerbiaBelgradeApr-17\$121.82\$2.36Marlboro\$2.9325.FranceNice & ParisMay-17\$79.96\$8.00Marlboro\$8.0026.South KoreaSeoulJun-17\$106.04\$3.80Marlboro\$3.9827.Czech RepublicPrague and select citiesJul-17\$117.04\$4.35Marlboro\$3.1428.GuatemalaGuatemala cityAug-17\$116.13\$3.28Marlboro\$3.1429.Slovak RepublicBratislava & select citiesAug-17\$113.08\$4.00Marlboro\$4.3430.PalestineSelect citiesOct-17\$98.09\$7.01Marlboro\$7.01		17.	Kazakhstan	Almaty	Dec-16	\$113.73	\$1.23	Marlboro	\$1.17
20. United Kingdom London Dec-16 \$115.45 \$10.38 Marlboro \$13.43 21. Lithuania Vilnius and select cities Feb-17 \$33.08 \$1.09 Marlboro \$1.17 22. Colombia Bogota Mar-17 \$105.21 \$1.70 Marlboro \$1.17 23. Poland Warsaw and select cities Apr-17 \$107.71 \$4.31 Marlboro \$4.31 24. Serbia Belgrade Apr-17 \$121.82 \$2.36 Marlboro \$2.93 25. France Nice & Paris May-17 \$79.96 \$8.00 Marlboro \$8.00 26. South Korea Seoul Jun-17 \$106.04 \$3.80 Marlboro \$3.98 27. Czech Republic Prague and select cities Jul-17 \$117.04 \$4.35 Marlboro \$3.14 28. Guatemala Guatemala city Aug-17 \$113.08 \$4.00 Marlboro \$3.14 29. Slovak Republic Bratis	-E	18.	New Zealand	Auckland	Dec-16	\$107.57	\$13.63	Marlboro	\$18.86
21.LithuaniaVilnius and select citiesFeb-17\$33.08\$1.09Marlboro\$1.1722.ColombiaBogotaMar-17\$105.21\$1.70Marlboro\$1.7023.PolandWarsaw and select citiesApr-17\$107.71\$4.31Marlboro\$4.3124.SerbiaBelgradeApr-17\$121.82\$2.36Marlboro\$2.9325.FranceNice & ParisMay-17\$79.96\$8.00Marlboro\$8.0026.South KoreaSeoulJun-17\$106.04\$3.80Marlboro\$3.9827.Czech RepublicPrague and select citiesJul-17\$117.04\$4.35Marlboro\$3.1428.GuatemalaGuatemala cityAug-17\$116.13\$3.28Marlboro\$3.1429.Slovak RepublicBratislava & select citiesAug-17\$113.08\$4.00Marlboro\$4.3430.PalestineSelect citiesOct-17\$98.09\$7.01Marlboro\$7.01		19.	South Africa	Cape Tow n and Johannesburg	Dec-16	\$113.42	\$2.99	Marlboro	\$2.99
22. ColombiaBogotaMar-17\$105.21\$1.70Mar/boro\$1.7023. PolandWarsaw and select citiesApr-17\$107.71\$4.31Mar/boro\$4.3124. SerbiaBelgradeApr-17\$121.82\$2.36Mar/boro\$2.9325. FranceNice & ParisMay-17\$79.96\$8.00Mar/boro\$8.0026. South KoreaSeoulJun-17\$106.04\$3.80Mar/boro\$3.9827. Czech RepublicPrague and select citiesJul-17\$117.04\$4.35Mar/boro\$3.9828. GuatemalaGuatemala cityAug-17\$116.13\$3.28Mar/boro\$3.1429. Slovak RepublicBratislava & select citiesAug-17\$113.08\$4.00Mar/boro\$4.3430. PalestineSelect citiesOct-17\$98.09\$7.01Mar/boro\$7.01	-E	20.	United Kingdom	London	Dec-16	\$115.45	\$10.38	Marlboro	\$13.43
23. Poland Warsaw and select cities Apr-17 \$107.71 \$4.31 Marlboro \$4.31 24. Serbia Belgrade Apr-17 \$121.82 \$2.36 Marlboro \$2.93 25. France Nice & Paris May-17 \$79.96 \$8.00 Marlboro \$8.00 26. South Korea Seoul Jun-17 \$106.04 \$3.80 Marlboro \$3.98 27. Czech Republic Prague and select cities Jul-17 \$117.04 \$4.35 Marlboro \$4.44 28. Guatemala Guatemala city Aug-17 \$116.13 \$3.28 Marlboro \$3.14 29. Slovak Republic Bratislava & select cities Aug-17 \$113.08 \$4.00 Marlboro \$4.34 30. Palestine Select cities Oct-17 \$98.09 \$7.01 Marlboro \$7.01		21.	Lithuania	Vilnius and select cities	Feb-17	\$33.08	\$1.09	Marlboro	\$1.17
24. Serbia Belgrade Apr-17 \$121.82 \$2.36 Marlboro \$2.93 25. France Nice & Paris May-17 \$79.96 \$8.00 Marlboro \$8.00 26. South Korea Seoul Jun-17 \$106.04 \$3.80 Marlboro \$3.98 27. Czech Republic Prague and select cities Jul-17 \$117.04 \$4.35 Marlboro \$4.44 28. Guatemala Guatemala city Aug-17 \$116.13 \$3.28 Marlboro \$3.14 29. Slovak Republic Bratislava & select cities Aug-17 \$113.08 \$4.00 Marlboro \$4.34 30. Palestine Select cities Oct-17 \$98.09 \$7.01 Marlboro \$7.01		22.	Colombia	Bogota	Mar-17	\$105.21	\$1.70	Marlboro	\$1.70
25. France Nice & Paris May-17 \$79.96 \$8.00 Marlboro \$8.00 26. South Korea Seoul Jun-17 \$106.04 \$3.80 Marlboro \$3.98 27. Czech Republic Prague and select cities Jul-17 \$117.04 \$4.35 Marlboro \$4.44 28. Guatemala Guatemala city Aug-17 \$116.13 \$3.28 Marlboro \$3.14 29. Slovak Republic Bratislava & select cities Aug-17 \$113.08 \$4.00 Marlboro \$4.34 30. Palestine Select cities Oct-17 \$98.09 \$7.01 Marlboro \$7.01		23.	Poland	Warsaw and select cities	Apr-17	\$107.71	\$4.31	Marlboro	\$4.31
26. South Korea Seoul Jun-17 \$106.04 \$3.80 Marlboro \$3.98 27. Czech Republic Prague and select cities Jul-17 \$117.04 \$4.35 Marlboro \$4.44 28. Guatemala Guatemala city Aug-17 \$116.13 \$3.28 Marlboro \$3.14 29. Slovak Republic Bratislava & select cities Aug-17 \$113.08 \$4.00 Marlboro \$4.34 30. Palestine Select cities Oct-17 \$98.09 \$7.01 Marlboro \$7.01	-E	24.	Serbia	Belgrade	Apr-17	\$121.82	\$2.36	Marlboro	\$2.93
27. Czech Republic Prague and select cities Jul-17 \$117.04 \$4.35 Marlboro \$4.44 28. Guatemala Guatemala city Aug-17 \$116.13 \$3.28 Marlboro \$3.14 29. Slovak Republic Bratislava & select cities Aug-17 \$113.08 \$4.00 Marlboro \$4.34 30. Palestine Select cities Oct-17 \$98.09 \$7.01 Marlboro \$7.01		25.	France	Nice & Paris	May-17	\$79.96	\$8.00	Marlboro	\$8.00
28. Guatemala Guatemala city Aug-17 \$116.13 \$3.28 Marlboro \$3.14 29. Slovak Republic Bratislava & select cities Aug-17 \$113.08 \$4.00 Marlboro \$4.34 30. Palestine Select cities Oct-17 \$98.09 \$7.01 Marlboro \$7.01	- Ľ	26.	South Korea	Seoul	Jun-17	\$106.04	\$3.80	Marlboro	\$3.98
29. Slovak Republic Bratislava & select cities Aug-17 \$113.08 \$4.00 Marlboro \$4.34 30. Palestine Select cities Oct-17 \$98.09 \$7.01 Marlboro \$7.01		27.	Czech Republic	Prague and select cities	Jul-17	\$117.04	\$4.35	Marlboro	\$4.44
30. Palestine Select cities Oct-17 \$98.09 \$7.01 Marlboro \$7.01		28.	Guatemala	Guatemala city	Aug-17	\$116.13	\$3.28	Marlboro	\$3.14
30. Palestine Select cities Oct-17 \$98.09 \$7.01 Marlboro \$7.01		29.	Slovak Republic	Bratislava & select cities	Aug-17	\$113.08	\$4.00	Marlboro	\$4.34
31. Slovenia Ljubljana & select cities Oct-17 \$113.08 \$4.57 Marlboro \$4.68		30.	-		Oct-17	\$98.09	\$7.01	Marlboro	\$7.01
		31.	Slovenia	Ljubljana & select cities	Oct-17	\$113.08	\$4.57	Marlboro	\$4.68

iQOS Geographic Markets - As of October 1, 2017

Japan Lounge



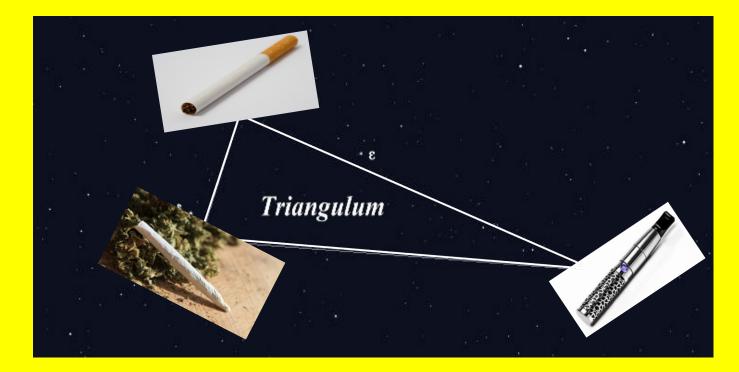
Switzerland Lounge



Atlanta Lounges



The Triangulum: Tobacco, Marijuana and E-Cigarettes



The Future is Now!

The 21st Century "Smoking" Landscape

- Combustible Tobacco Products
- Aerosolized Nicotine (E-Cigs)
 - Heat Not Burn, IQOS
 - Dabbing; Dripping; Blunts
 - Hookah
- Gums, Chews, Orbs, Patches, et al.
 - Did I mention Marijuana?

We are only 20 years into the Century!

Thank You!

Phillip Gardiner, Dr. P.H.

gmoney.gardiner@gmail.com

AATCLC

Saving Black Lives

www.savingblacklives