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1	Smoke by any other name: heat-not-burn tobacco cigarettes								
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15	Introduction: The tobacco industry's most recent response to the documented harms of								
16	cigarette smoking was to launch new, "heat-not-burn" (HNB) tobacco cigarettes. <sup>1</sup> Philip Morris								
17	International (PMI) created IQOS $^{ extsf{B}}$ (I-Quit-Ordinary-Smoking): disposable tobacco sticks soaked								

in propylene glycol, which are inserted in a holder in the HNB cigarette. The tobacco is heated

19 with an electric blade at 350°C (662°F). PMI markets them as a "revolutionary technology that

20 heats tobacco without burning it, giving you the true taste of tobacco, with no smoke, no ash

21 and less smell." <sup>2</sup> In many countries, laws that protect people from passive smoke only apply to

 $^{22}$  'smoked' to bacco products. PMI claims that  $\mathsf{IQOS}^{\$}$  releases no 'smoke' because the to bacco

23 does not 'combust' and that the tobacco leaves are only heated, not burned. But there can be

smoke without fire. The harmful components of tobacco cigarette smoke are products of

25 incomplete combustion (pyrolysis), and the degradation of tobacco cigarettes through heat

26 (thermogenic degradation). Complete combustion occurs at high temperature [>1300°C;

27 2372°F], higher than the heat generated by smoking a tobacco cigarette [<800°C; <1472°F].

28 Typical markers of pyrolysis and thermogenic degradation of tobacco cigarette are

29 acetaldehyde, an irritant carcinogenic volatile organic compound, benzo[a]pyrene, a

30 carcinogenic polycyclic aromatic hydrocarbon, and carbon monoxide.

Pilot programs for IQOS<sup>®</sup> began in 2014 in Japan, and in 2015 in Switzerland and Italy. An 31 internet survey in Japan published in 2015 suggested younger people (15 to 39 years old) were 32 more likely to use IQOS<sup>®</sup>, as were former smoker and current smokers.<sup>3</sup> Since 2016, 19 33 countries have allowed the sale of IQOS<sup>®</sup> cigarettes. In June 2016, data from PMI showed 34 IQOS<sup>®</sup> had captured 2.2% of the cigarette market in Japan.<sup>4</sup> IQOS<sup>®</sup> are not yet sold in the US, 35 but, in December 2016, PMI submitted a Modified Risk Tobacco Product application to the Food 36 and Drug Administration (FDA). If successful, PMI will be less restricted in its marketing for the 37 IQOS<sup>®</sup> than for conventional tobacco cigarettes. Smokers and non-smokers need accurate 38 information about toxic compounds released in IQOS<sup>®</sup> smoke. This information should come 39 from sources independent of the tobacco industry, but the only analyses we found were from 40 PMI and PMI competitors.<sup>1,5</sup> 41

**Methods**: We compared the contents of IQOS<sup>®</sup> smoke with those of conventional cigarettes. 42 We used a smoking device designed and tested in our facility to capture the mainstream 43 aerosol, and developed to meet standards for common cigarettes and e-cigarettes.<sup>6</sup> We 44 45 followed the ISO standards for puff volume (35 mL) at 2 puffs per minute, based on observation of IQOS<sup>®</sup> smokers, who took an average of 14 puffs over 5-6 minutes. We analyzed volatile 46 organic compounds and nicotine by gas chromatography coupled to a flame ionization detector, 47 and polycyclic aromatic hydrocarbons using high-performance liquid chromatography coupled to 48 a fluorescence detector, as previously described.<sup>6</sup> We did not analyze polycyclic aromatic 49 hydrocarbons generated by conventional cigarettes and present average values in 35 best-50 selling cigarettes brands in the US, as reported by Vu, et al.<sup>7</sup> We monitored the temperature 51 near the heater blade inside the IQOS<sup>®</sup> holder and the core of the conventional cigarette, at a 52 sampling rate of 3Hz. 53

Results: Volatile organic compounds, polycyclic aromatic hydrocarbons, and carbon monoxide
were present in IQOS<sup>®</sup> smoke (Table). The temperature of the IQOS<sup>®</sup> was lower (330°C; 626°F)
than the conventional cigarette (684°C, 1263°F).<sup>7</sup> IQOS<sup>®</sup> smoke had 84% of the nicotine found
in conventional cigarettes smoke.

**Discussion**: The smoke IQOS<sup>®</sup> releases contains elements from pyrolysis and thermogenic 58 degradation. These are the same harmful constituents of conventional tobacco cigarette smoke. 59 PMI invited international experts to describe the IQOS<sup>®</sup> aerosol; one claims that "less than 2% of 60 the weight of the aerosol components derive from the pyrolysis of tobacco product, which would 61 not be sufficient to characterize the aerosol as 'smoke'".<sup>8</sup> In contrast, our analyses show that 62 advertising slogans like "heat-not-burn" are no substitute for science. Dancing around the 63 definition of smoke to avoid indoor-smoking bans is unethical. Principle 1 for implementing 64 Article 8 of the WHO convention on tobacco control highlights that we should reject ideas that 65 there is a threshold value for toxicity from second-hand smoke.<sup>9</sup> Independent studies should 66 further evaluate the health effects of the IQOS<sup>®</sup>. In the meantime, "heated" tobacco products 67 like IQOS<sup>®</sup> should fall under the same indoor-smoking bans as for conventional tobacco 68 cigarettes. 69

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**Table**: Concentrations of 8 volatile organic compounds, 16 polycyclic aromatic hydrocarbons, 3 inorganic compounds and nicotine in mainstream aerosol and temperature of the heat-not-burn (HNB) IQOS<sup>®</sup> cigarette<sup>a</sup> and conventional cigarettes (CC)<sup>b</sup>

	HNB cigarette		Conventional cigarette (CC)		Proportion of the		
					chemical in		
Analysed compounds	Amount (SD)	n°	Amount (SD)	n°	HNB/CC (%)		
Volatile organic compounds (μg/cig) <sup>d</sup>							
Acetaldehyde	133 (35)	5	610	1	22		
Acetone	12.0 (12.9)	5	95.5 (13.5)	2	13		
Acroleine	0.9 (0.6)	2	1.1	1	82		
Benzaldehyde	1.2 (1.4)	5	2.4 (2.6)	2	50		
Crotonaldehyde	0.7 (0.9)	5	17.4	1	4		
Formaldehyde	3.2 (2.7)	5	4.3 (0.4)	2	74		
Isovaleraldehyde	3.5 (3.1)	5	8.5 (10.8)	2	41		
Propionaldehyde	7.8 (4.3)	5	29.6 (36.6)	2	26		
Polycyclic Aromatic Hydrocarbons (ng/cig) <sup>e,f</sup>							
Naphtahlene	1.6 (0.5)	4	1105 (269)	7	0.1		
Acenaphthylene	1.9 (0.6)	4	235 (39)	7	0.8		
Acenaphthene	145 (54)	4	49 (9)	7	295		
Fluorene	1.5 (0.6)	4	371 (56)	7	0.4		
Anthracene	0.3 (0.1)	4	130 (18)	7	0.2		
Phenanthrene	2.0 (0.2)	4	292 (44)	7	0.7		
Fluoranthene	7.3 (1.1)	4	123 (18)	7	6		
Pyrene	6.4 (1.1)	4	89 (15)	7	7		
Benz[a]anthracene	1.8 (0.4)	4	33 (4.2)	7	6		
Chrysene	1.5 (0.3)	4	48 (6.2)	7	3		
Benzo[b]fluoranthene	0.5 (0.2)	4	24 (2.9)	7	2		
Benzo[k]fluoranthene	0.4 (0.2)	4	4.3 (2.8)	7	9		
Benzo[a]pyrene	0.8 (0.1)	4	20 (2.9)	7	4		
Indeno[1,2,3-cd]pyrene	n.d.	4	n.a.		-		
Benzo[ghi]perylene	n.d.	4	n.a.		-		
Dibenzo[a,h]anthracene	n.d.	4	n.a.		-		
<i>Inorganics (ppm in the</i> mainstream <i>smoke)<sup>g</sup></i>							
CO <sub>2</sub>	3057 (532)	5	>9000	3	-		
CO	328 (76)	5	>2000	3	-		
NO	5.5 (1.5)	5	89.4 (71.6)	3	6		
Other measures							
Nicotine (µg/cig) <sup>ª</sup>	301 (213)	4	361	1	84		

	HNB cigarette		Conventional cigarette (CC)		Proportion of the chemical in
Analysed compounds	Amount (SD)	n°	Amount (SD)	n°	HNB/CC (%)
Temperature (°C) <sup>h</sup>	330 (10)	2	684 (197)	1	-
Puff total count <sup>a</sup>	12.6 (2.4)	32	13.3 (3.1)	6	-

cig. = cigarette; n.a. = not analyzed; n.d. = not detected; ppm = parts per million; SD = standard deviation.

<sup>a</sup> We bought the IQOS<sup>®</sup> Holder, IQOS<sup>®</sup> Pocket Charger, Marlboro HeatSticks (regular) and Heets in Lausanne, Switzerland (Philipp Morris S.A., Neuchâtel, Switzerland).

<sup>b</sup> Lucky Strike Blue Lights were our conventional cigarette.

<sup>c</sup> Number of replications for each assay.

<sup>d</sup> We applied the methods described previously in Varlet et al. 2016 to analyse volatile organic compounds and nicotine.

<sup>e</sup> We sorted polycyclic aromatic hydrocarbons by molecular weight, and then by boiling point. Polycyclic aromatic hydrocarbons from the smoke generated by the IQOS<sup>®</sup> cigarette were trapped in one glass filter (Whatman 37 mm Ø GF/B) mounted in line with an XAD2 cartridge. For each sampling, 10 IQOS<sup>®</sup> cigarettes were smoked. Each sampling support was desorbed in 10 mL of acetonitrile and sonicated for 1h. The eluate was evaporated in a vacuum concentrator (Speed Vac SC-200, Thermo, set with 30 mbar and 1000 rpm) until the residue was almost dry, to prevent evaporation of the most volatile polycyclic aromatic hydrocarbons. The residue was filtered with polytetrafluoroethylene (PTFE) membrane (Acrodisc CR 13 mm, 0.45μm) before it was analyzed with a high-performance liquid chromatography (HPLC) device (Ultimate 3000, Thermo) equipped with a fluorescence detector (FLD-3000RS), ultraviolet detector (VWD-3000), and a separation column Nucleodur EC 150×3 mm C18 3μm (Macherey-Nagel, Germany) under isocratic conditions (1.2 mL.min<sup>-1</sup>). We injected 2 μl in the HPLC chain; (Methanol/Water-70/30)/Acetonitrile was the eluent solvent at an initial ratio of 100%/0% (4 min) and a linear gradient up to 100% acetonitrile (12 min).

<sup>f</sup> We present values reported from Vu, et al. 2015 for the ISO smoking regimen, and for an average of 35 top-selling U.S. cigarette brands.

<sup>g</sup> CO<sub>2</sub> was measured with a TESTO 535 (Testo, Mönchaltorf, Switzerland) and CO and NO were measured with a Pac<sup>®</sup> 7000 that detected CO (Draeger, Liebefeld/Bern, Switzerland). The apparatus measured the smoke when it was released from the syringe-pump.

<sup>h</sup> The temperature of the heater blade inside the IQOS<sup>®</sup> holder and the inside core of the conventional cigarette were monitored at a sampling rate of 3Hz with a type k thermocouple.