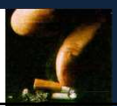
Heated tobacco products
Recent data on IQOS

Aigner Kurt & Manfred Neuberger

ENSP Capacity Building Workshop
12th – 14th November 2018
Vienna

ENSP
European Network for Smoking and Tobacco Prevention

INITIATIVE ÄRZTE GEGEN RAUCHERSCHÄDEN
AUSTRIAN COUNCIL ON SMOKING AND HEALTH



www.ensp.org
www.aerzteinitiative.at

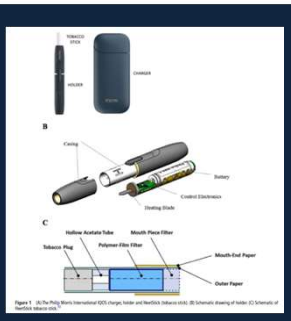
No Conflicts of Interest

IQOS

I Quit Ordinary Smoking

Heated tobacco products: the example of IQOS

Stanton A Glantz



Glantz SA. Tob Control 2018; 27: s1-s6

Table 1 Availability of HTP by major cigarette company and country of availability (January 2018)

Company	Product	Year launched	Countries/Comments
British American Tobacco[30]	iFuse* glo	2015 2016	Romania, Japan, Switzerland, Canada, South Korea, Russia
China National Tobacco Corporation / SMTA[32]	Not reported	Not launched	A few of the companies claim to have over 30 patents of HTP and continue to be engaged in research and development of these products. But none yet are in the market.
Imperial Brands[33]	Not reported	Not launched	Focusing on e-cigarettes at the moment, claims to have options to launch when it deems that time is right
Japan Tobacco International[31]	Ploom TECH†	2016	Japan, Switzerland
KT&G Corp.[34]	lil	2017	South Korea
Philip Morris International‡ [4]	IQOS TEEPS§	2014 Not yet launched	Canada, Guatemala, Colombia, Czech Republic, Denmark, France, Germany, Greece, Israel, Italy, Kazakhstan, Lithuania, Monaco, Netherlands, Poland, Portugal, Romania, Russia, Serbia, Slovak Republic, Slovenia, Spain, Switzerland, Ukraine, UK, South Africa, South Korea, Japan, New Zealand

*It is unclear that iFuse will remain in the market in Romania, where Glo was introduced in 2018.
†Ploom TECH is described as a hybrid between a HTP and a vaporiser. It is to be used with Mevius capsules. Mevius is one of JTI's best-selling cigarette brands. The capsules contain tobacco which are then heated by vapour.
‡PMI website states that it is developing a new heated nicotine delivery product that has no tobacco, STEEM, among other 'reduced risk' products.
§ We do not know what TEEPS stands for, it is not included in the product's description (https://www.pmi.com/smoke-free-products/teeps-carbon-heated-tobacco-product).
HTP, heated tobacco product.

Glantz SA. Tob Control 2018;27 : s1-s6

https://www.pmi.com/smoke-free-products/iqos-our-tobacco-heating-system 30. 10. 2018

HTP in US

	2016	2017
• Adult awareness	9,3 %	12,4%
• Ever use	1,4%	2,2%
• Current use	0,5%	1,1%

- Non-white adults, cigarette smokers, both current and former users of e-cigarettes were more likely to use HTP

As of July 2018, the FDA has not authorised HTP for sale in the USA

Nyman AL et al. Tob Control 2018;27:s55-s61

PMI's own in vivo clinical data on biomarkers of potential harm in Americans show that IQOS is not detectably different from conventional cigarettes

Stanton A Glantz[1,2]

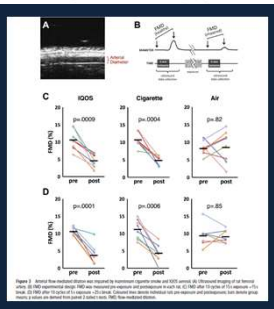
Results:

Among American adults, there is no statistical dedectable difference between IQOS and conventional cigarettes for 23 of the 24 biomarkers of harm in PMI's studies.

Glantz SA. Tob Control 2018;27:s9-s12

Vascular endothelial function is impaired by aerosol from a single IQOS HeatStick to the same extent as by cigarette smoke

Pooneh Nabavizadeh,[1] Jiangtao Liu,[1] Christopher M Havel,[2] Sharina Ibrahim,[3] Ronak Derakhshandeh,[1] Peyton Jacob III,[2,4] Matthew L Springer[1,3,4]



Nabavizadeh P, Liu J, Havel CM et al. Tob Control 2018;27:s13-s19

Assessment of industry data on pulmonary and immunosuppressive effects of IQOS

Farzad Moazed,[1] Lauren Chun,[2] Michael A Matthay,[3] Carolyn S Calfee,[3] Jeffrey Gotts[1]

Table 1 Summary of preclinical pulmonary findings for I-Quit-Ordinary-Smoking (IQOS) compared with sham and 3R4F research cigarette groups

Parameter	Sham (n=10)	IQOS (n=8–10)	3R4F (n=9)
Lung weight (normalised to body weight)	35.8 (1.4)	40.3 (1.0)*	50.6 (1.4)*†
BAL cell count‡ (×10⁷/lung)	22.9 (3.4)	42.5 (7.1)*	116.4 (13.4)*†
BAL inflammatory markers MIP-1β, MCP-3, MPO, PAI-1		†*	†*†
Respiratory epithelial hyperplasia and metaplasia		†*	†*†

Unless otherwise specified, results signify those from male rats at the highest nicotine exposure levels for each group.
*Significantly increased compared with sham.
†Significantly increased compared with IQOS.
‡Female rats at targeted nicotine 23 µg/L.
BAL, bronchoalveolar lavage; MCP, monocyte chemoattractant protein; MIP, macrophage inflammatory protein; MPO, myeloperoxidase; PAI, plasminogen activator inhibitor.

Moazed F, Chun L, Matthay MA, et al. Tob Control 2018;27:s20-s25

Assessment of industry data on pulmonary and immunosuppressive effects of IQOS

Farzad Moazed,[1] Lauren Chun,[2] Michael A Matthay,[3] Carolyn S Calfee,[3] Jeffrey Gotts[1]

Table 2 Summary of preclinical systemic immune effects of I-Quit-Ordinary-Smoking (IQOS) compared with sham and 3R4F research cigarettes

Parameter	Sham (n=8–10)	IQOS (n=7–9)	3R4F (n=9–10)
Blood neutrophil count (10⁹/L)	1.3 (0.3)	4.8 (2.1)*	2.7 (0.4)*
Thymus weight	4.0 (0.4)	2.6 (0.6)*	2.5 (0.3)*
Histological thymic atrophy score	0.1 (0.1)	1.8 (0.4)*	1.1 (0.4)*

Unless otherwise specified, results signify those from male rats at the highest nicotine exposure levels for each group.
*Significantly different compared with sham; statistical comparisons between IQOS and 3R4F were not reported for blood neutrophil count or thymic atrophy score.

Moazed F, Chun L, Matthay MA, et al. Tob Control 2018;27:s20-s25

Assessment of industry data on pulmonary and immunosuppressive effects of IQOS

Farzad Moazed,[1] Lauren Chun,[2] Michael A Matthay,[3] Carolyn S Calfee,[3] Jeffrey Gotts[1]

What this paper adds

- Heated tobacco products are being touted as reduced harm tobacco products by tobacco companies across the world despite limited scientific evidence supporting this claim.
- Philip Morris's modified risk tobacco product (MRTP) application for I-Quit-Ordinary-Smoking (IQOS) shows that IQOS generates significant pulmonary and immunomodulatory harm, most notably in human studies.
- With regards to pulmonary and immunomodulatory harm, based on the limited available data to date, IQOS use does not appear to significantly differ from conventional cigarettes.

➢ **No studies on dual use !**

Moazed F, Chun L, Matthay MA, et al. Tob Control 2018;27:s20-s25

IQOS: examination of Philip Morris International's claim of reduced exposure

Gideon St.Helen,[1,2] Peyton Jacob III,[1,2] Natalie Nardone,[1] Neal L Benowitz[1,2,3]

Methods We examined PMI's MRTP application, specifically sections on aerosol chemistry and human exposure assessment, to assess the validity of PMI's claims of reduced exposure and risk.
Findings PMI reported levels for only 40 of 93 harmful and potentially harmful constituents (HPHCs) on FDA's HPHC list in IQOS mainstream aerosol. All substances in PMI's list of 58 constituents (PMI-58) were lower in IQOS emissions compared with mainstream smoke of 3R4F reference cigarettes. However, levels of 56 other constituents, which are not included in the PMI-58 list or FDA's list of HPHCs, were higher in IQOS emissions; 22 were >200% higher and seven were >1000% higher than in 3R4F reference cigarette smoke. PMI's studies also show significantly lower systemic exposure to some HPHCs from use of IQOS compared with smoking combustible cigarettes.

St.Helen G, Jacob III P, Nardone N, et al. Tob Control 2018; 27: s30-s36

Cytotoxic effects of heated tobacco products (HTP) on human bronchial epithelial cells

Noel J Leigh, Phillip L Tran, Richard J O'Connor, Maciej Lukasz Goniewicz

Methods Inhalation toxicity of HTP (IQOS; tobacco flavour), e-cigarette (MarkTen; tobacco flavour) and tobacco cigarette (Marlboro Red) was examined in vitro using an air–liquid interface with human bronchial epithelial cells (H292). Cells were exposed directly to 55 puffs from the e-cigarette, 12 puffs from the HTP and 8 puffs from the tobacco cigarette to equilibrate nicotine delivery to the cells across products. Cytotoxicity was measured using neutral red uptake and trypan blue assays. Cytotoxic effects of each tested product (HTP, e-cigarette and tobacco cigarette) were compared with an air control. Release of inflammatory markers (cytokines) was measured using ELISA.

Leigh NJ, Tran PL, O'Connor RJ, et al. Tob Control 2018; 27: s26-s29

Cytotoxic effects of heated tobacco products (HTP) on human bronchial epithelial cells

Noel J Leigh, Phillip L Tran, Richard J O'Connor, Maciej Lukasz Goniewicz

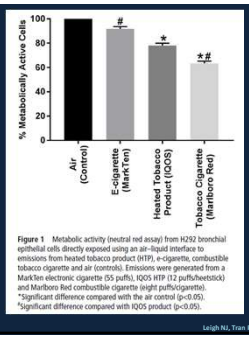


Figure 1 Metabolic activity (neutral red assay) from H292 bronchial epithelial cells directly exposed using an air–liquid interface to emissions from heated tobacco product (HTP), e-cigarette, combustible tobacco cigarette and air (controls). Emissions were generated from a MarkTen electronic cigarette (55 puffs), IQOS HTP (12 puffs/heatstick) and Marlboro Red combustible cigarette (eight puffs/cigarette). *Significant difference compared with the air control ($p<0.05$). #Significant difference compared with IQOS product ($p<0.05$).

Leigh NJ, Tran PL, O'Connor RJ, et al. Tob Control 2018; 27: s26-s29

Tobacco-specific nitrosamines (TSNA) in heated tobacco product IQOS

Noel J Leigh, Mary N Palumbo, Anthony M Marino, Richard J O'Connor, Maciej Lukasz Goniewicz
Department of Health Behavior, Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA

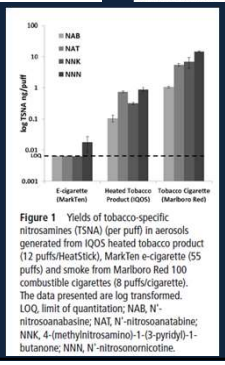


Figure 1 Yields of tobacco-specific nitrosamines (TSNA) (per puff) in aerosols generated from IQOS heated tobacco product (12 puffs/HeatStick), MarkTen e-cigarette (55 puffs) and smoke from Marlboro Red 100 combustible cigarettes (8 puffs/cigarette). The data presented are log transformed. LOQ, limit of quantitation; NAB, N'-nitrosoanabasine; NAT, N'-nitrosoanatabine; NNK, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNN, N'-nitrosonornicotine.

Leigh NJ, Palumbo NN, Marino AM, et al. Tob Control 2018; 27: s37-38

Possible hepatotoxicity of IQOS

Lauren Chun,[1] Farzad Moazed,[1] Michael Matthay,[1,2,3] Carolyn Calfee,[1,2,3] Jeffrey Gotts[1]

Table 1 Liver parameters in Sprague Dawley rats after 90 days of exposure

	Female			Male		
	Sham	IQOS	3R4F	Sham	IQOS	3R4F
ALT levels (IU/L)	51.0±4.4	73.0±3.2**,****	54.0±2.6	57.0±6.5	75.0±6.7*	68.0±5.8
Liver weight†	339.6±6.6	442.6±10.2***,****	386.7±15.1*	329.3±5.1	381.7±13.2**	373.0±7.9***
Hepatocellular vacuolisation	0.7±0.4	1.5±0.2*	1.2±0.3	1.4±0.3	0.8±0.4	1.8±0.8

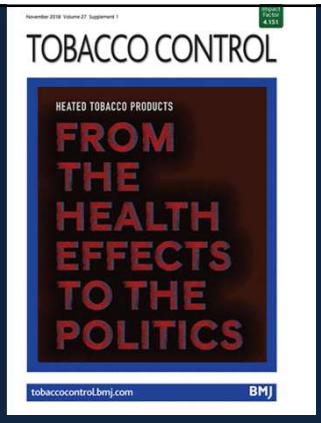
Data are from Wong *et al*[1] and are presented as mean±SEM.
*P<0.05 relative to sham; **P<0.01 relative to sham; ***P<0.001 relative to sham; ****P<0.01 relative to 3R4F.
†Normalised to body weight and reported as $\times 10^{-4}$.
ALT, alanine aminotransferase.

Chun L, Moazed F, Matthay M, et al. Tob Control 2018; 27: s39-s40

Secondhand IQOS exposure

- **Sore throat** **20.6%**
- **Eye pain** **22.3 %**
- **Feeling ill** **25.1 %**
- **Other injury or symptom** **13.4%**
- **Any symptom** **37.0%**

Tabuchi T, et al. Tob Control 2018; 27: e25-e33



https://tobaccocontrol.bmj.com/content/27/Suppl_1

…there is no safe level of smoking…

Maki Inoue-Choi, Ph.D., NCI, Division of Cancer Epidemiology and Genetics
JAMA Internal Medicine, 5. 12. 2016, DOI: 10.1001/jamainternmed.2016.7511

…there is also no safe level of IQOS aerosols…