



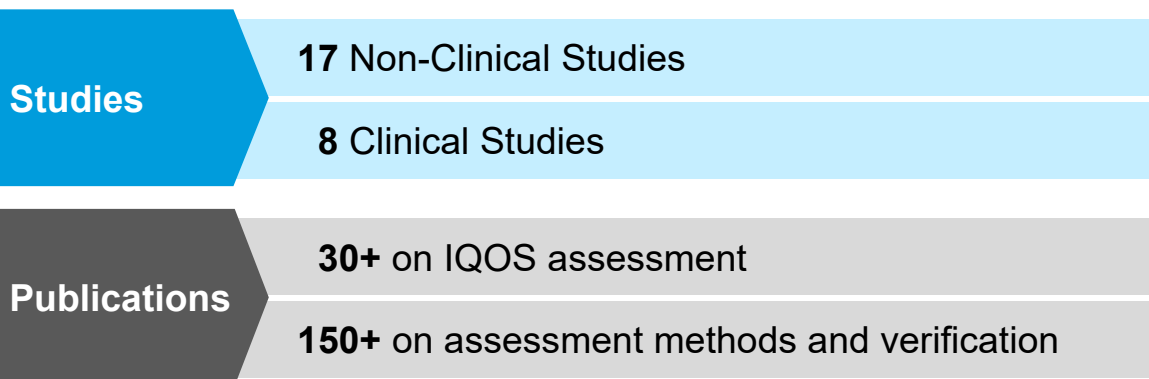
The IQOS Heating System

Tobacco Products Scientific Advisory Committee

January 25, 2018

CC-117

Scientific Assessment



Hoeng *et al.* A Network-Based Approach to Quantify the Impact of Biologically Active Substances. *Drug Discov. Today* 2012; 17:413-418.
Sturla *et al.* Systems Toxicology: from basic research to risk assessment. *Chem. Res. Toxicol.* 2014; 27:314-329.

CC-118

IQOS Usage Patterns

Actual Use Study

IQOS and Cigarettes Use: Observational Period Actual Use Study






	Week 1 n=1,106	Week 2 n=1,061	Week 3 n=1,038	Week 4 n=1,009	Week 5 n=977	Week 6 n=968
100% IQOS	5%	6%	7%	7%	6%	6%
Exclusive Use: [95-100%] IQOS	7%	8%	9%	8%	7%	8%

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CC-119

IQOS In Market Usage Patterns

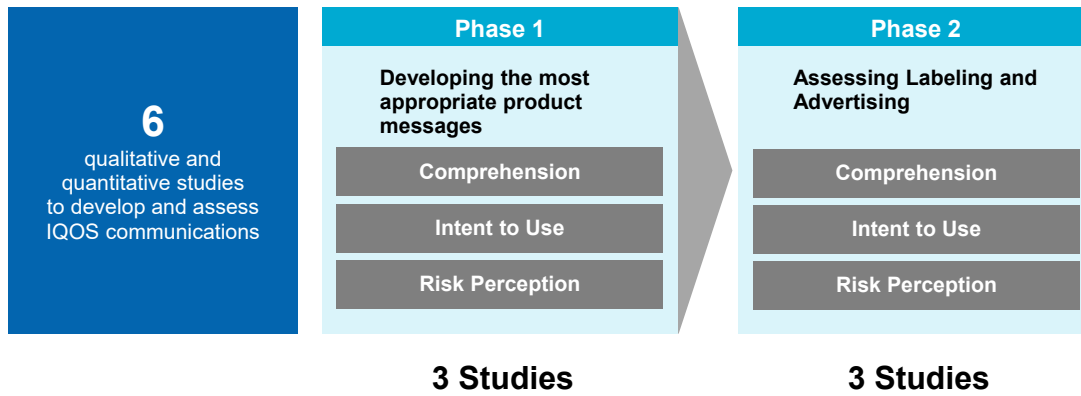
Post-Market Consumer Panel Surveys

	 South Korea n=631	 Japan n=6925	 Italy n=4197	 Germany n=2249	 Switzerland n=2101
100% IQOS	63%	68%	57%	50%	47%
Exclusive Use: [95-100%] IQOS	73%	72%	61%	55%	51%

CONSUMER PANEL SURVEYS, August 2017

CC-120

PBA Studies to Develop and Assess IQOS Messages



CC-121

The IQOS Opportunity

- **Millions fewer smokers**
- **Reduced harm and tobacco-related disease**
- **An important step forward**

CC-122

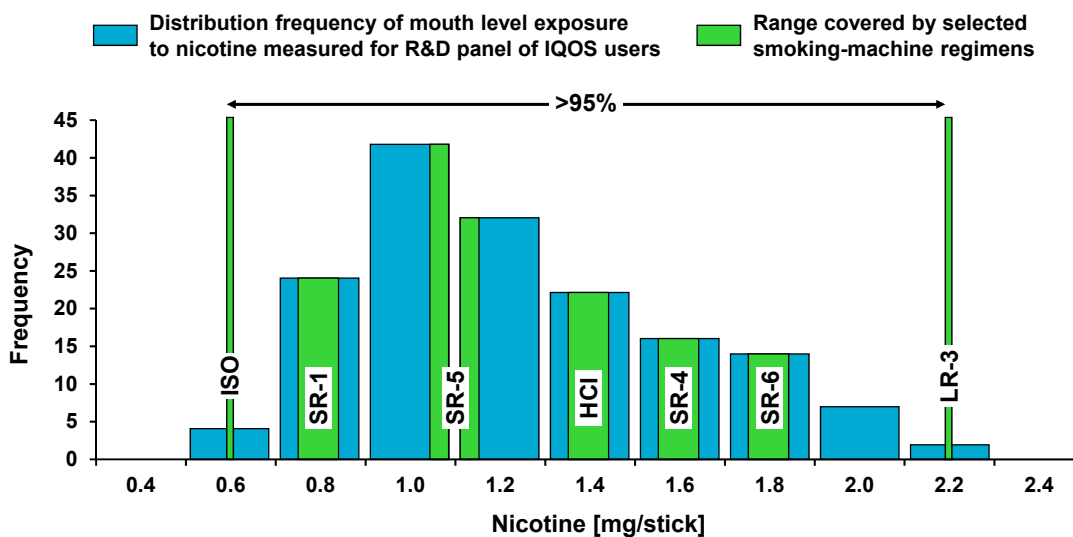


Tobacco Products Scientific Advisory Committee

Sponsor backup slides shown

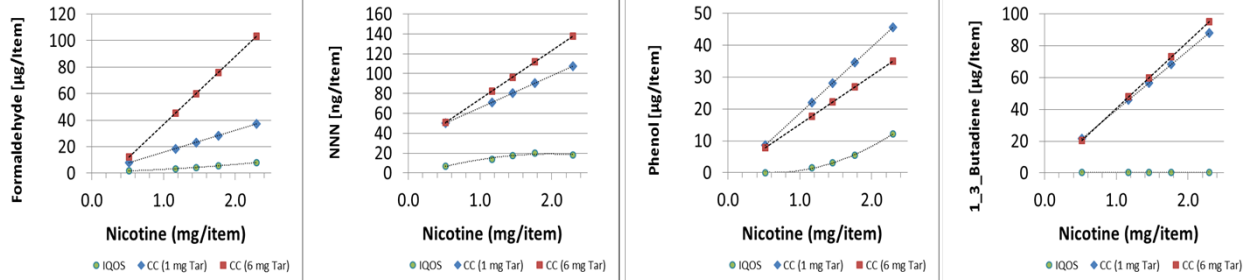
January 25, 2018

Human vs Machine-smoking Range



AC-47

HPHCs Response to Puffing Regime Reduction vs. cigarette is maintained



Linear

Ammonia, acrylamide, ethylene oxide, acrylonitrile, crotonaldehyde, acrolein, acetamide, o-toluidine and NAB

“Plateau”

NAT, NNK, isoprene, styrene, toluene, benzene, pyridine, acetone, MEK, acetaldehyde, butyraldehyde, hydroquinone, resorcinol, and nitrogen oxides

Quadratic

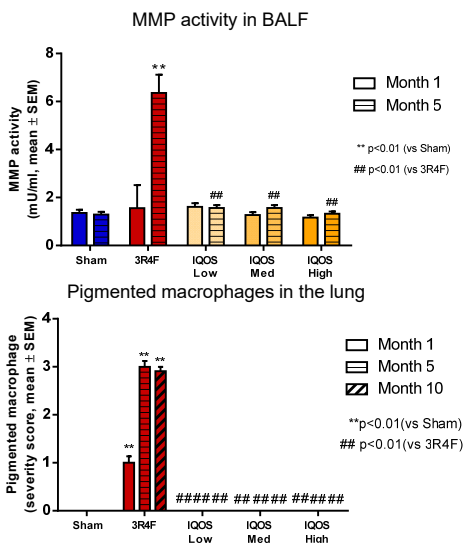
m-cresol, o-cresol, p-cresol and quinoline

Flat

Pyrene, benzo[a]pyrene, dibenzo[a,h]anthracene, 1-aminonaphtalene, 2-aminonaphtalene, 3-aminobiphenyl, 4-aminobiphenyl and vinyl chloride

AC-48

Systemic Toxicity – Lung inflammation Combined Chronic Toxicity and Carcinogenicity Study – A/J mice



	Month 1				Month 5			
vWF	4.75	0.83	0.79	0.60	5.33	1.20	1.23	1.02
VEGF-A	9.93	1.05	0.97	1.19	4.00	1.12	1.04	0.99
VCAM-1	11.1	1.31	1.45	1.02	13.4	1.15	1.15	1.17
TNF-alpha	7.97	1.38	1.00	1.00	7.97	1.14	1.32	1.00
TIMP-1 Mouse	10.7	1.12	1.14	1.09	6.74	1.13	1.22	1.05
Thrombopoietin	5.01	1.00	1.00	1.00	5.70	1.23	1.42	1.41
SCF	7.42	1.09	0.85	0.90	6.83	1.02	0.91	0.74
SAP	1.35	1.00	1.00	1.00	1.93	1.00	1.18	1.00
Resistin	1.30	0.94	0.97	1.17	1.04	0.85	0.89	0.83
PAI-1	5.00	1.03	0.99	1.01	4.37	1.01	1.05	1.07
Oncostatin-M	5.38	1.00	1.00	1.00	5.25	1.00	1.00	1.00
Myoglobin	0.84	1.61	1.12	1.38	4.32	2.40	2.79	7.64
MCP-5	70.8	1.00	1.00	1.00	29.2	1.00	1.00	1.00
MCP-3	350	1.00	1.51	1.00	200	1.07	1.19	0.79
MCP-1	1498	1.00	1.78	1.00	417	1.12	0.88	0.76
MMP-9	181	0.51	0.89	0.47	51.8	1.22	0.70	0.62
MIP-3	4.72	0.91	0.88	0.87	4.62	1.24	1.10	1.13
MIP-2	6.43	0.94	1.03	1.13	3.55	1.12	1.04	0.94
MIP-1 gamma	17.5	1.05	1.07	0.93	32.4	0.83	0.97	1.03
MIP-1 beta	84.4	1.04	0.98	1.07	101	0.80	1.13	0.75
MIP-1 alpha	7.82	1.00	1.00	1.00	14.5	1.00	1.00	1.00
MDC	20.1	1.01	1.02	0.92	9.54	0.93	0.96	0.92
M-CSF-1	7.27	1.08	1.07	1.11	5.20	1.10	0.97	1.01
LIF	5.97	1.02	0.87	0.86	4.08	0.98	0.86	0.96
Leptin	0.92	0.76	0.87	0.89	0.70	0.63	0.89	0.73
IL-10	7.47	1.00	1.00	1.00	3.59	0.99	1.20	1.02
IL-11	2.32	1.00	1.00	1.00	2.24	1.00	1.00	1.00
IL-7	2.96	1.10	1.00	1.00	3.08	1.00	1.00	1.00
IL-6	8.61	1.27	1.22	1.00	5.83	1.00	1.14	1.00
IL-4	1.87	1.21	1.11	1.10	1.12	1.00	1.11	1.00
IL-1 beta	3.01	1.00	1.00	1.00	2.85	1.00	1.00	1.00
IL-1 alpha	13.7	1.00	1.00	1.00	16.6	1.00	1.00	1.00
IP-10	30.4	1.00	1.00	1.11	6.00	1.00	1.00	1.11
Insulin	1.08	1.27	0.78	1.17	0.68	0.71	0.96	0.87
IgA	6.88	0.81	5.35	0.66	6.66	1.01	1.08	0.93
Haptoglobin	1.00	0.97	0.97	0.96	1.02	1.00	1.00	1.00
KC/GRO	68.3	1.19	1.00	1.00	20.2	1.13	1.00	1.00
GM-CSF	6.28	1.00	1.00	1.00	2.59	1.00	1.00	1.00
cCR-2 Mouse	2.44	0.78	0.69	0.76	2.86	1.17	0.82	0.82
FGF-basic	1.40	1.00	1.00	1.00	1.87	0.90	1.44	1.00
Fibrinogen	5.28	0.86	0.90	0.85	4.32	1.11	2.02	1.31
ECF Mouse	4.40	1.00	1.00	1.00	5.52	0.63	0.89	0.85
Eotaxin	5.14	0.88	0.93	0.75	4.78	0.93	1.05	0.89
CRP Mouse	1.95	1.00	1.00	1.00	1.64	1.00	1.17	1.00
App A1	1.66	0.91	0.51	0.59				

3R4F IQOS (L) IQOS (M) IQOS (H) 3R4F IQOS (L) IQOS (M) IQOS (H)

Significance and fold-change vs. respective Sham

▼ p<0.001 ▲ p<0.001 ▼ p<0.01 ▲ p<0.01 ▼ p<0.05 ▲ p<0.05






h.s.

Study number 15020

SD-1071

IQOS In Market Usage Patterns

Post-Market Consumer Panel Surveys

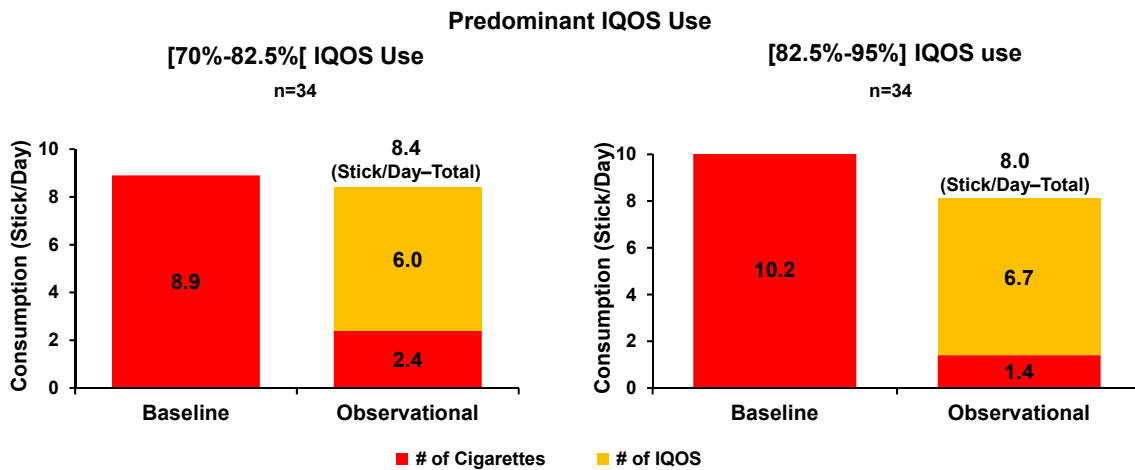
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XX-5

No Increase in IQOS and Cigarettes Consumption Between Baseline and Observational Period

Actual Use Study: IQOS + Cigarette Consumption



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XX-7