

The IQOS Heating System

**Tobacco Products Scientific
Advisory Committee**

January 24, 2018





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CC-1



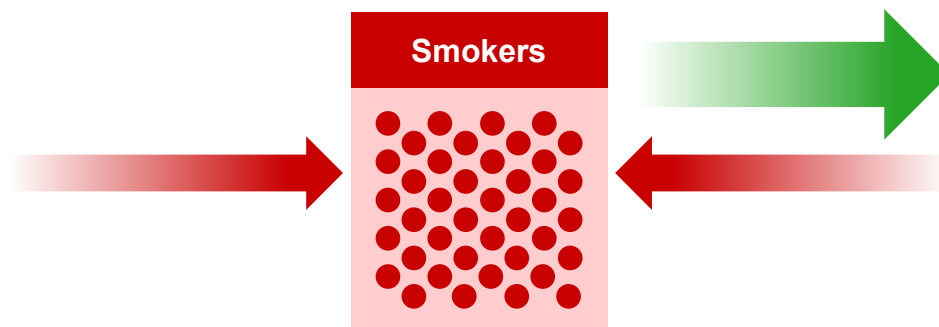
Introduction

Moira Gilchrist, PhD

Vice President Scientific and Public Communications
Philip Morris International

CC-2

The Status Quo



CC-3

Risk Continuum



Highest Risk

Lowest Risk

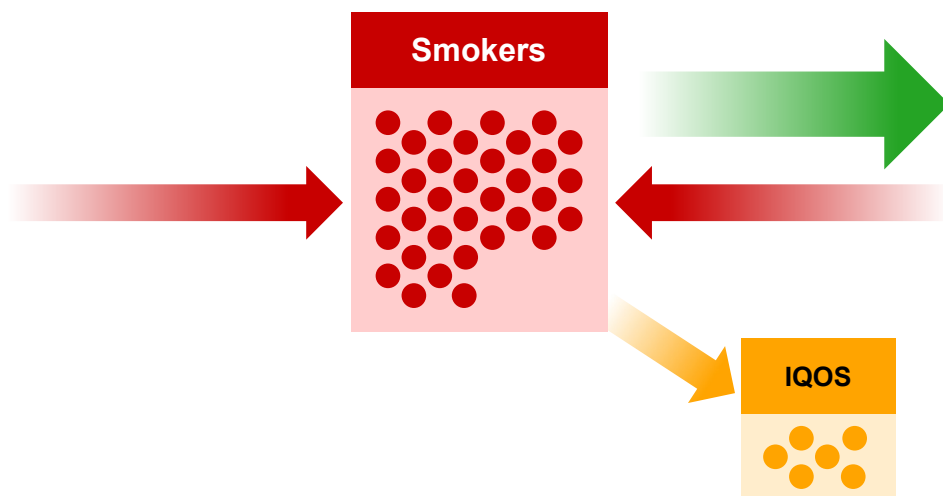
CC-4

The IQOS Heating System



CC-5

The IQOS Opportunity



CC-6

911(g)(1) Modified Risk Products

...the applicant has demonstrated that such product, as it is actually used by consumers, will—

A

Significantly reduce harm and the risk of tobacco-related disease to individual tobacco users

B

Benefit the health of the population as a whole taking into account both users of tobacco products and persons who do not currently use tobacco products

CC-7

911(g)(1) Modified Risk Products

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CC-8

911(g)(1) Modified Risk Products

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Significantly reduce harm and the risk of tobacco-related disease to individual tobacco users

B

Benefit the health of the population as a whole taking into account both users of tobacco products and persons who do not currently use tobacco products

CC-9

Product Messages



AVAILABLE EVIDENCE TO DATE:

- The IQOS system heats tobacco but does not burn it. This significantly reduces the production of harmful and potentially harmful chemicals.
- Scientific studies have shown that switching completely from conventional cigarettes to the IQOS system can reduce the risks of tobacco-related diseases.

SURGEON GENERAL'S WARNING:
Smoking Causes Lung Cancer, Heart Disease,
Emphysema, And May Complicate Pregnancy.

1

Switching completely from cigarettes to the IQOS system can reduce the risks of tobacco-related diseases.

CC-10

Product Messages



AVAILABLE EVIDENCE TO DATE:
Switching completely to IQOS presents less risk of harm than continuing to smoke cigarettes.

SURGEON GENERAL'S WARNING:
Smoking Causes Lung Cancer, Heart Disease, Emphysema, And May Complicate Pregnancy.

1

Switching completely from cigarettes to the IQOS system can reduce the risks of tobacco-related diseases.

2

Switching completely to IQOS presents less risk of harm than continuing to smoke cigarettes.

CC-11

Product Messages



AVAILABLE EVIDENCE TO DATE:

- The IQOS system heats tobacco but does not burn it.
- This significantly reduces the production of harmful and potentially harmful chemicals.
- Scientific studies have shown that switching completely from conventional cigarettes to the IQOS system can reduce the risks of tobacco-related disease.

SURGEON GENERAL'S WARNING:
Smoking Causes Lung Cancer, Heart Disease, Emphysema, And May Complicate Pregnancy.

1

Switching completely from cigarettes to the IQOS system can reduce the risks of tobacco-related diseases.

2

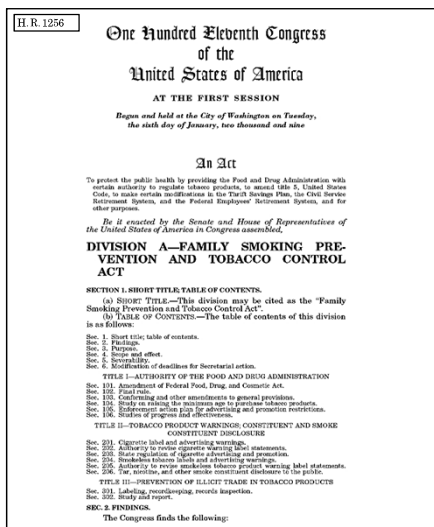
Switching completely to IQOS presents less risk of harm than continuing to smoke cigarettes.

3

Switching completely from cigarettes to the IQOS system significantly reduces your body's exposure to harmful and potentially harmful chemicals.

CC-12

Family Smoking Prevention and Tobacco Control Act



“... to provide new and flexible enforcement authority to ensure that there is effective oversight of the tobacco industry’s efforts to develop, introduce, and promote less harmful tobacco products”

-Sec. 3 (4) Purpose

CC-13

Presentation Agenda

Moira Gilchrist, PhD VP Scientific & Public Communications Philip Morris International	IQOS System and Heating Technology
Manuel Peitsch, PhD Chief Scientific Officer Philip Morris International	Scientific Assessment of IQOS
Antonio Ramazzotti VP Human Insights and Behavioral Research Philip Morris International	Perception and Behavior
Sarah Knakmuhs VP Heated Tobacco Products Philip Morris USA	U.S. Commercialization and Controls
Moira Gilchrist, PhD VP Scientific & Public Communications Philip Morris International	Population Modeling and Conclusion

CC-14



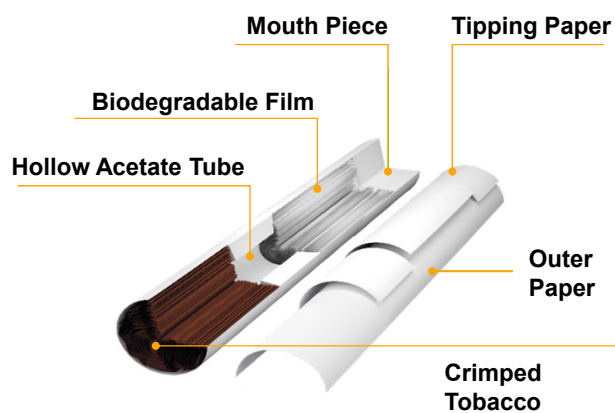
IQOS System and Heating Technology

Moira Gilchrist, PhD

Vice President Scientific and Public Communications
Philip Morris International

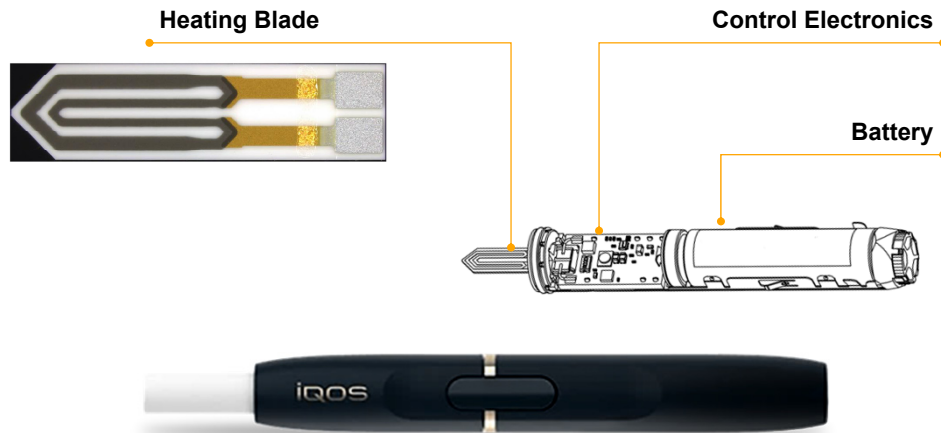
CC-15

HeatStick Construction



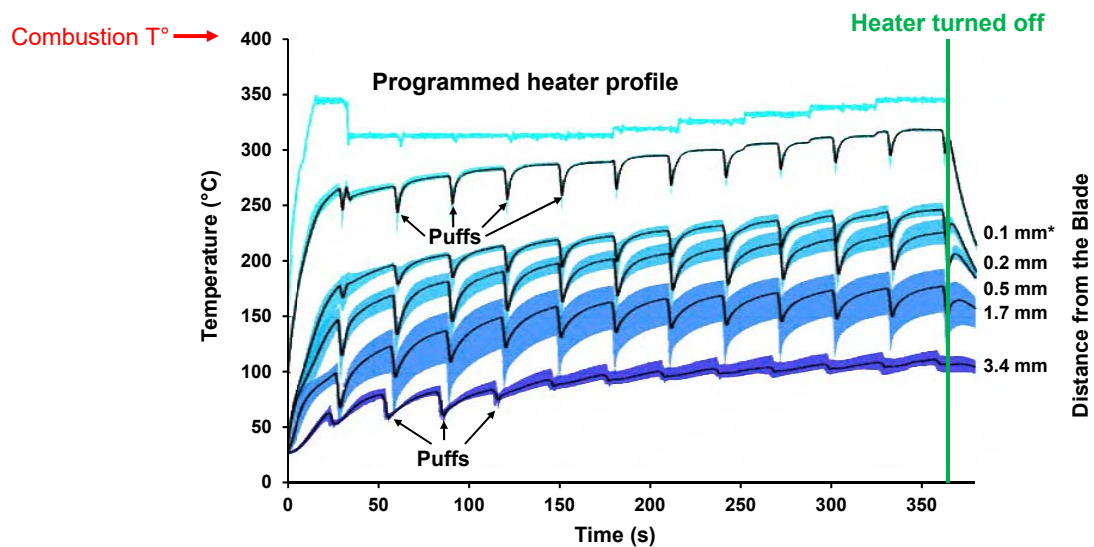
CC-16

IQOS Holder and Heating Blade



CC-17

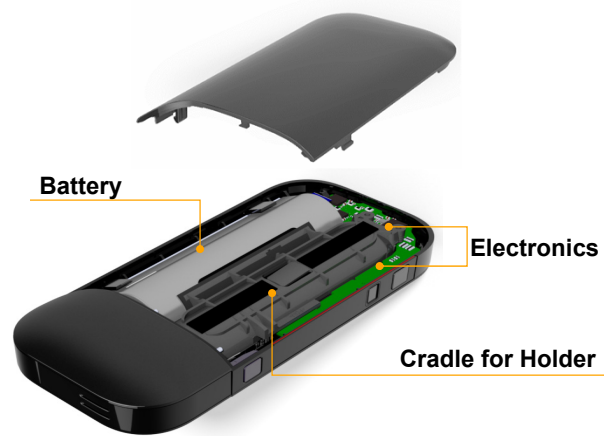
IQOS Temperature Profile



* Radial position of thermocouple relative to the surface of the heater

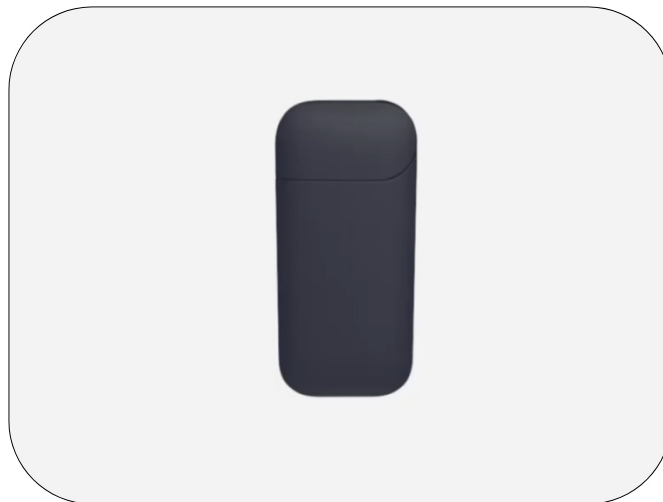
CC-18

IQOS Charger



CC-19

IQOS Operation



CC-20



Scientific Assessment of IQOS

Manuel Peitsch, PhD

Chief Scientific Officer
Philip Morris International

CC-21

911(g)(1) Modified Risk Products

...the applicant has demonstrated that such product, as it is actually used by consumers, will—

A

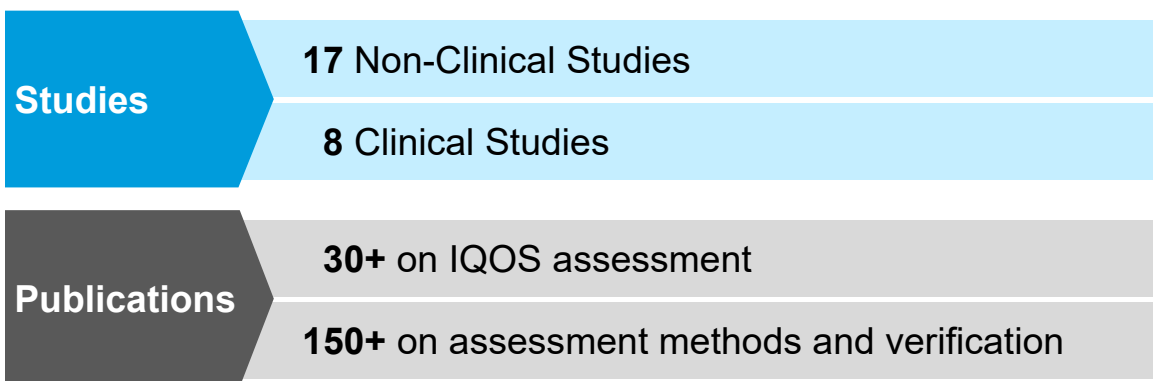
Significantly reduce harm and the risk of tobacco-related disease to individual tobacco users

B

Benefit the health of the population as a whole taking into account both users of tobacco products and persons who do not currently use tobacco products

CC-22

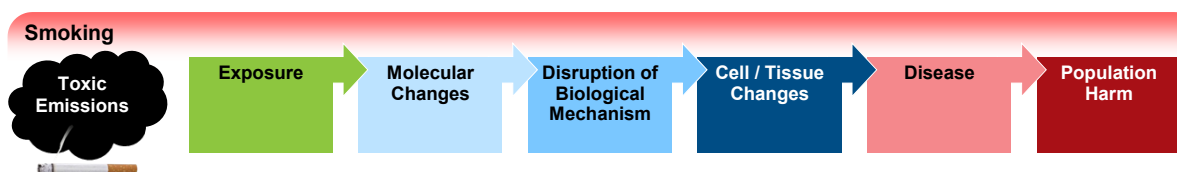
Scientific Assessment



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-23

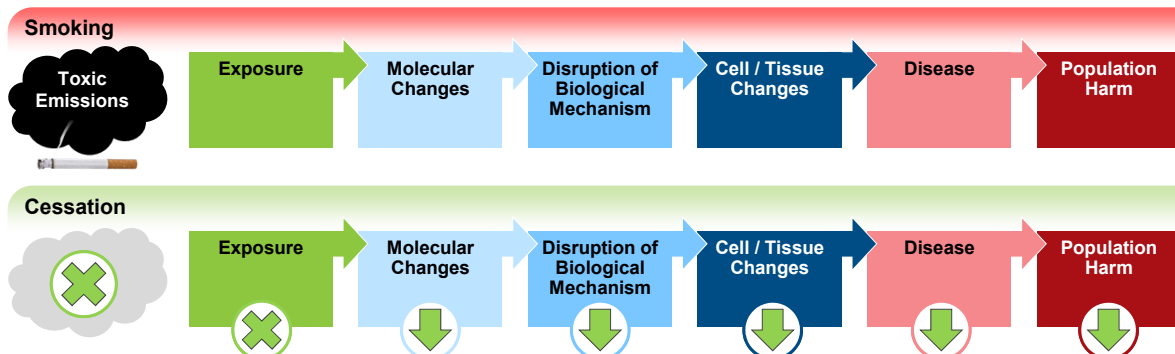
Assessment Framework: Informed by Epidemiology



The health risks of **smoking** are well established and supported by epidemiological evidence (IARC 2004, 2007)

CC-24

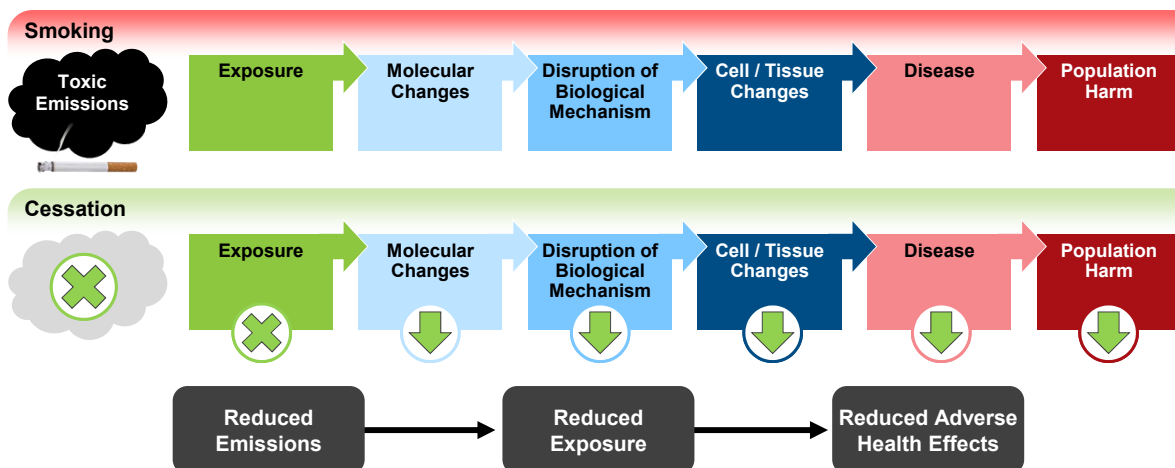
Assessment Framework: Informed by Epidemiology



The health risks of **smoking** and the **reversal** of risks **after quitting smoking** are well established (IARC 2004, 2007)

CC-25

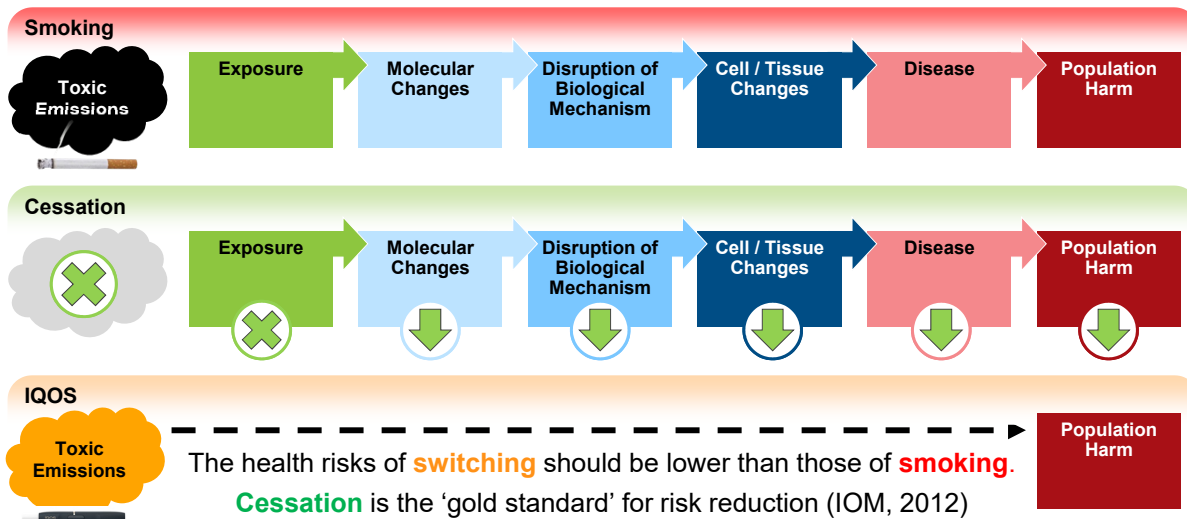
Assessment Framework: Informed by Epidemiology



The health risks of **smoking** and the **reversal** of risks **after quitting smoking** are well established (IARC 2004, 2007)

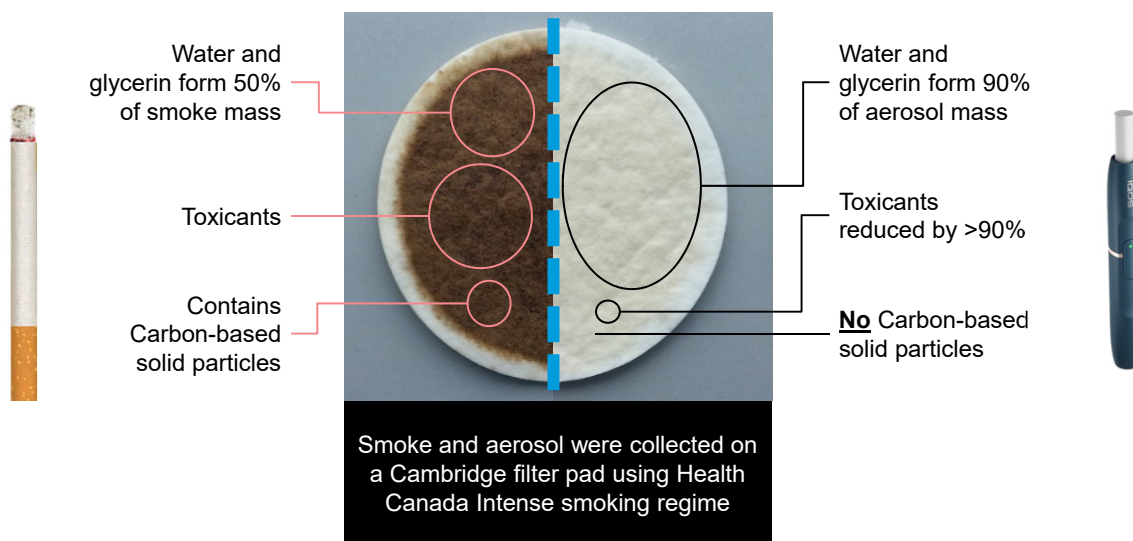
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Assessment Framework: Informed by Epidemiology



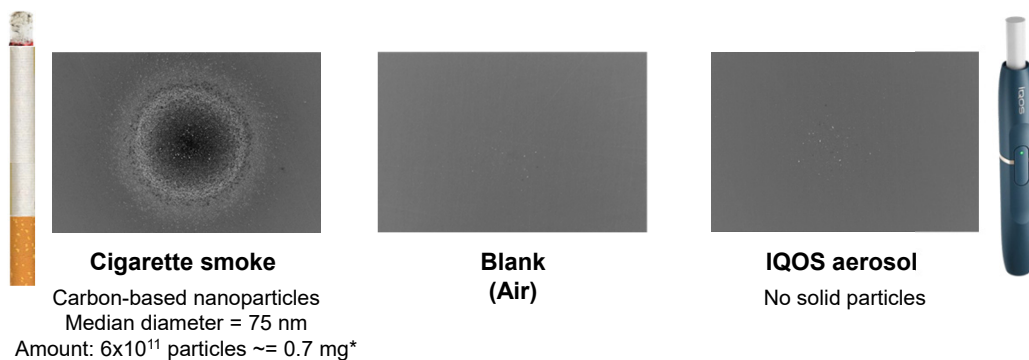
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Differences Between IQOS Aerosol and Cigarette Smoke



CC-28

IQOS Does Not Emit Carbon-Based Solid Particles

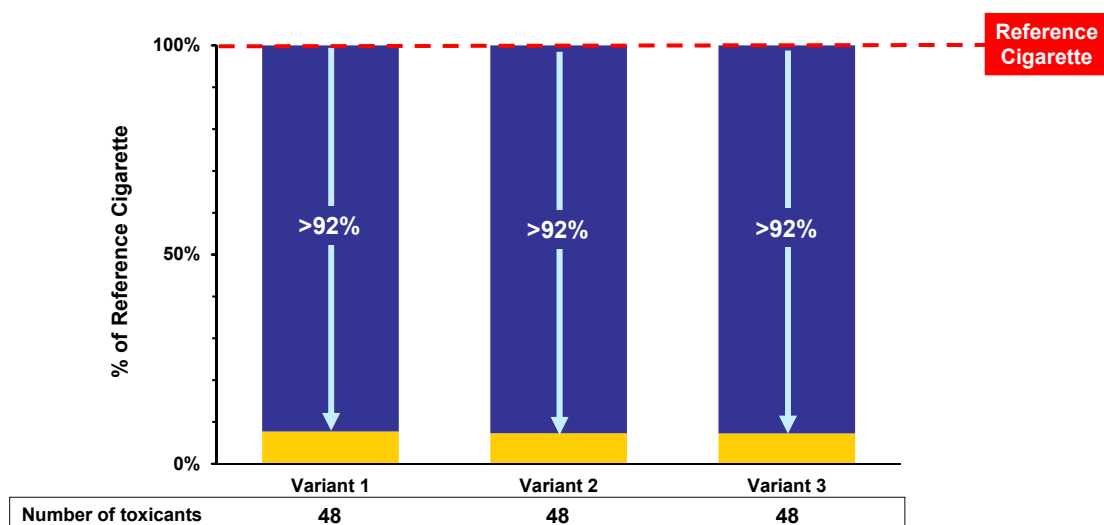


Scanning Electron Microscopy images of the collected smoke/aerosol after passing through a thermodenuder set at 300° C to remove the volatile portion / collected material characterized by Electron Diffusive X-ray.

* Under the Health Canada's Intense Smoking Regime.

Pratte et al. Investigation of solid particles in the mainstream aerosol of the Tobacco Heating System THS2.2 and mainstream smoke of a 3R4F reference cigarette. *Hum. Exp. Toxicol.* 2017; 36:1115-1120
Cohen et al. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. *Lancet* 2017; 1907-1918. **CC-29**

IQOS Releases Less Toxicants than Cigarettes

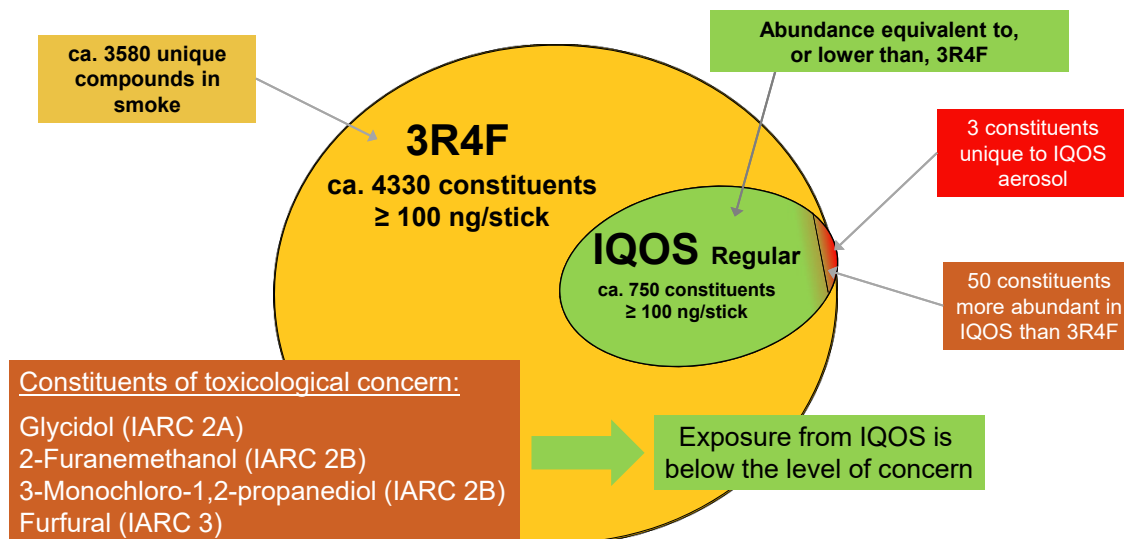


Health Canada's Intense Smoking Regime; Comparison on a per-stick basis; Excludes Nicotine

CC-30

Non-targeted Differential Screening

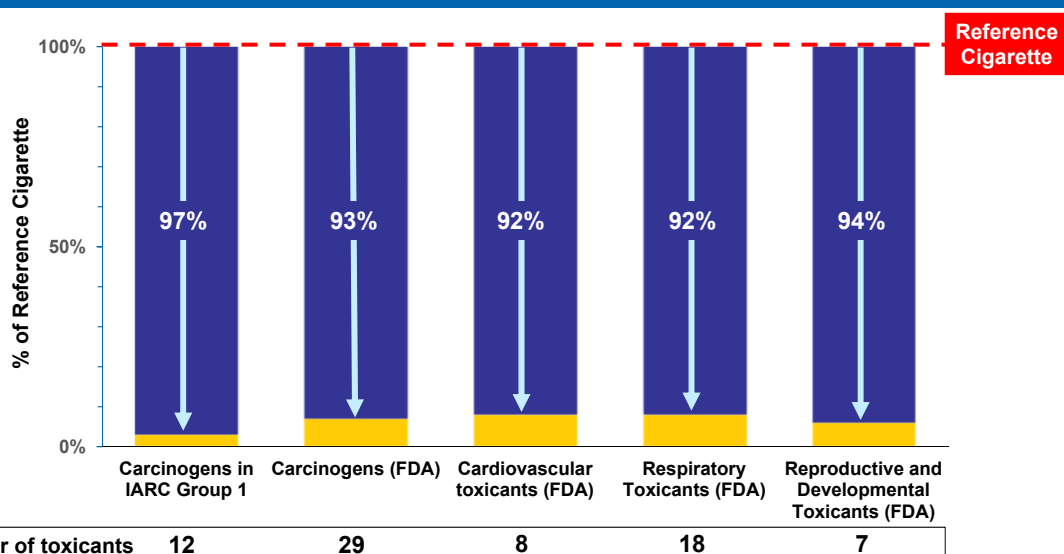
Comparison of IQOS Aerosol and 3R4F Smoke



This slide presents the results for the regular variant of the IQOS HeatStick characterization

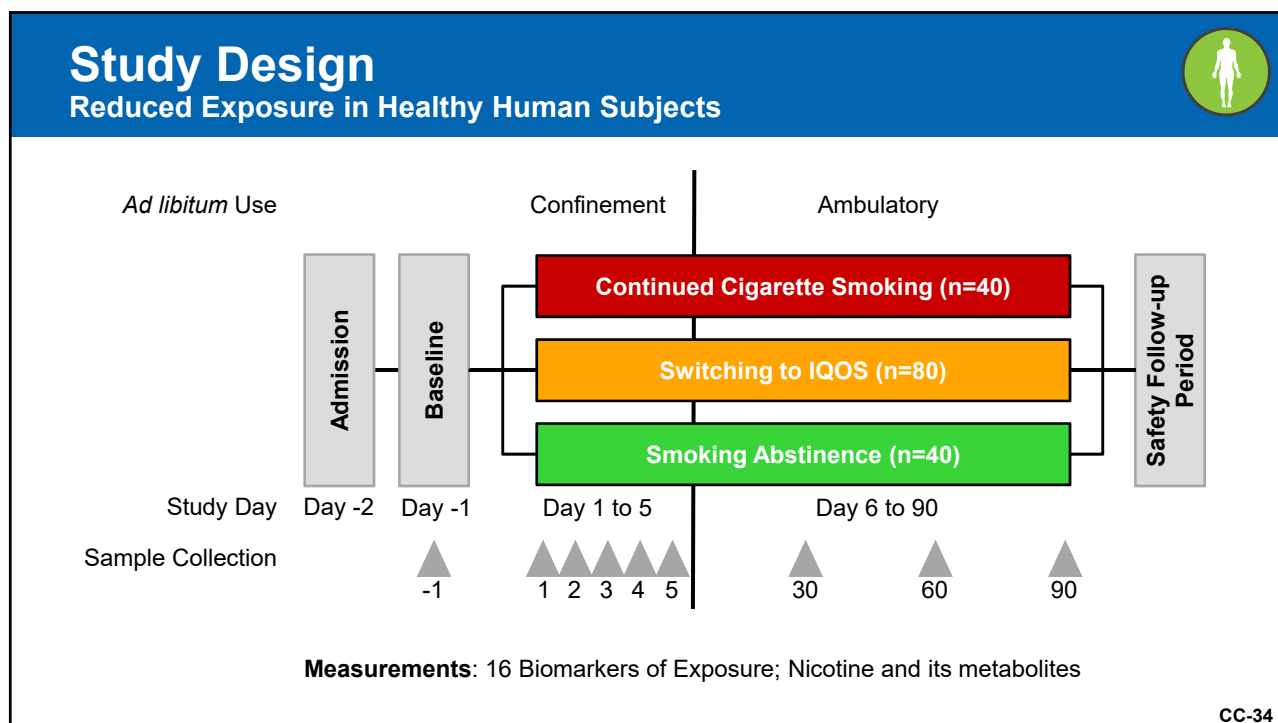
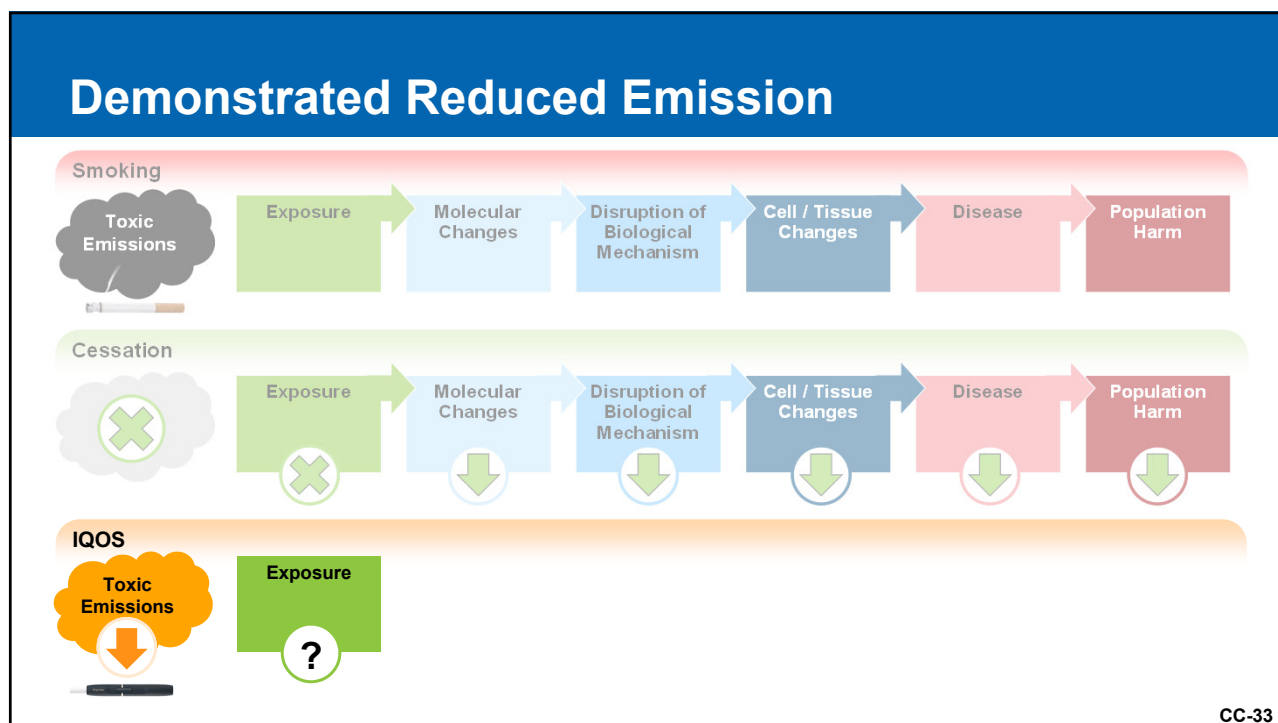
CC-31

Reductions of Toxicants by Disease Category

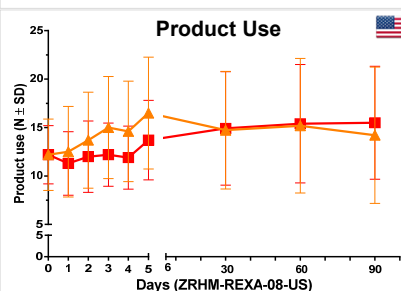
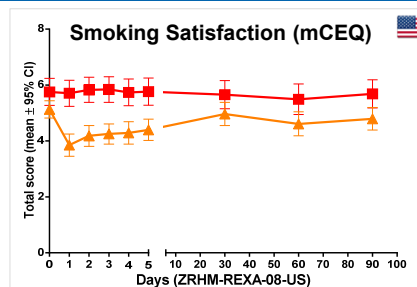
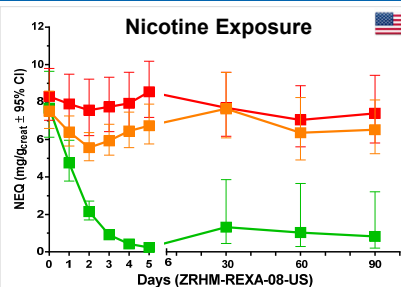


Note: Intense Health Canada's Smoking Regime; Comparison on a per-stick basis; Excludes Nicotine

CC-32



Smoker Acceptance of IQOS is Similar to Cigarettes



Cigarette
 IQOS
 Smoking Abstinence

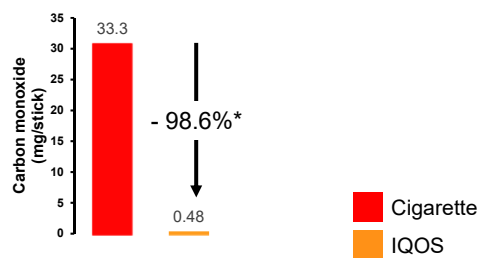
CC-35

Changes in Exposure to HPHCs with IQOS Use

Reduced Exposure in Healthy Human Subjects



HPHCs are Drastically Reduced in IQOS Aerosol



* On equivalent nicotine basis

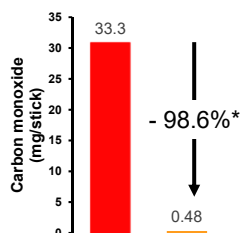
CC-36

Changes in Exposure to HPHCs with IQOS Use

Reduced Exposure in Healthy Human Subjects



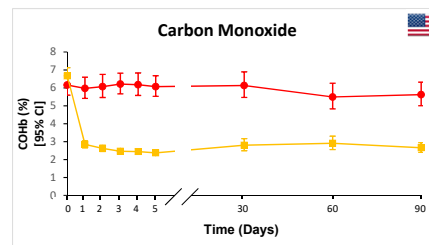
HPHCs are Drastically
Reduced in IQOS Aerosol



Leads to

■ Cigarette
■ IQOS

Exposure is Significantly Reduced
After Switching to IQOS



* On equivalent nicotine basis

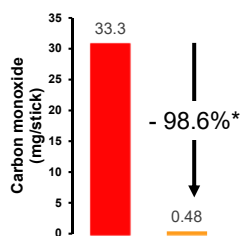
CC-37

Changes in Exposure to HPHCs with IQOS Use

Reduced Exposure in Healthy Human Subjects



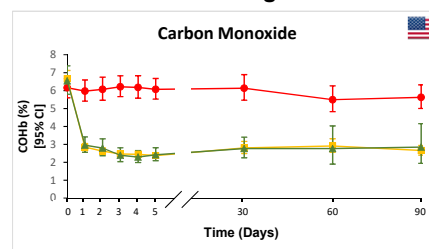
HPHCs are Drastically
Reduced in IQOS Aerosol



Leads to

■ Cigarette
■ IQOS
■ Smoking Abstinence

Exposure is Significantly Reduced
After Switching to IQOS



* On equivalent nicotine basis

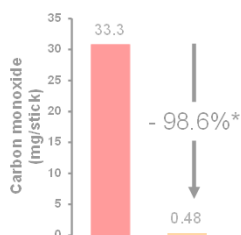
CC-38

Changes in Exposure to HPHCs with IQOS Use

Reduced Exposure in Healthy Human Subjects

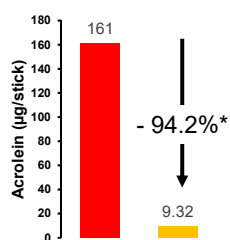


HPHCs are Drastically
Reduced in IQOS Aerosol



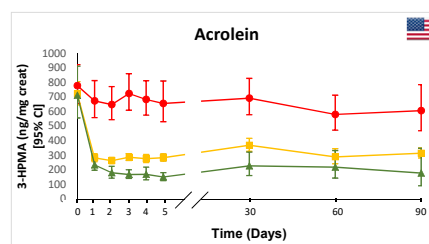
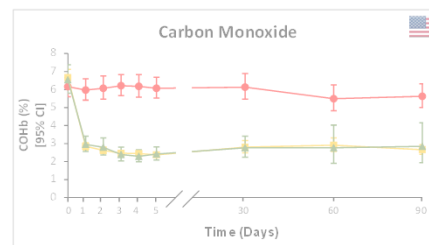
Leads to

- Cigarette
- IQOS
- Smoking Abstinence



Leads to

Exposure is Significantly Reduced
After Switching to IQOS



* On equivalent nicotine basis

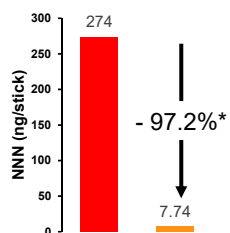
CC-39

Changes in Exposure to HPHCs with IQOS Use

Reduced Exposure in Healthy Human Subjects

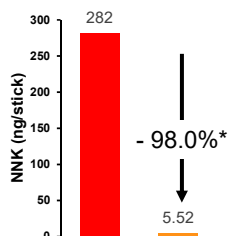


HPHCs are Drastically
Reduced in IQOS Aerosol



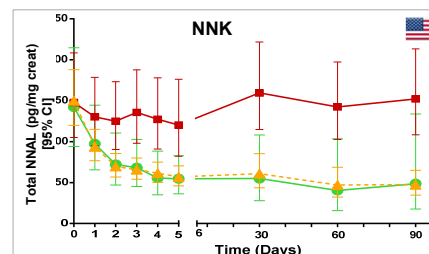
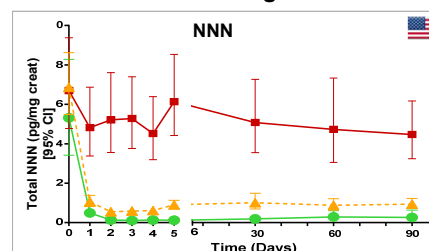
Leads to

- Cigarette
- IQOS
- Smoking Abstinence



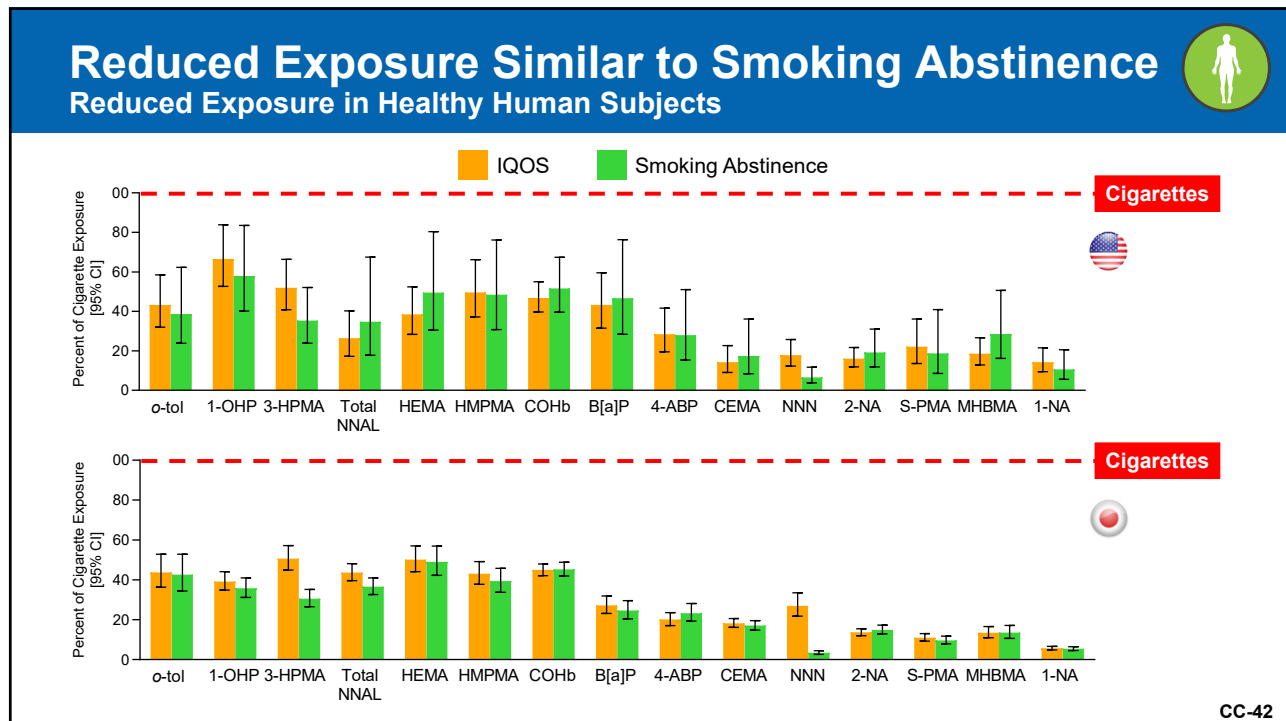
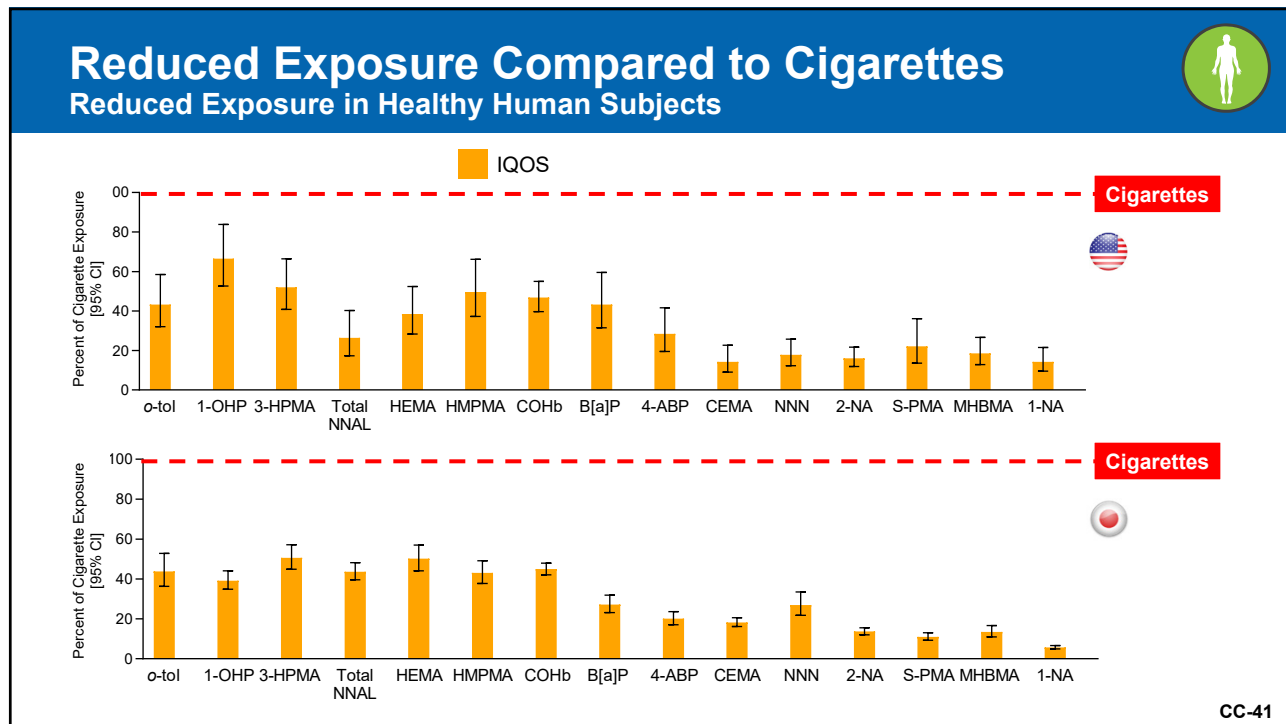
Leads to

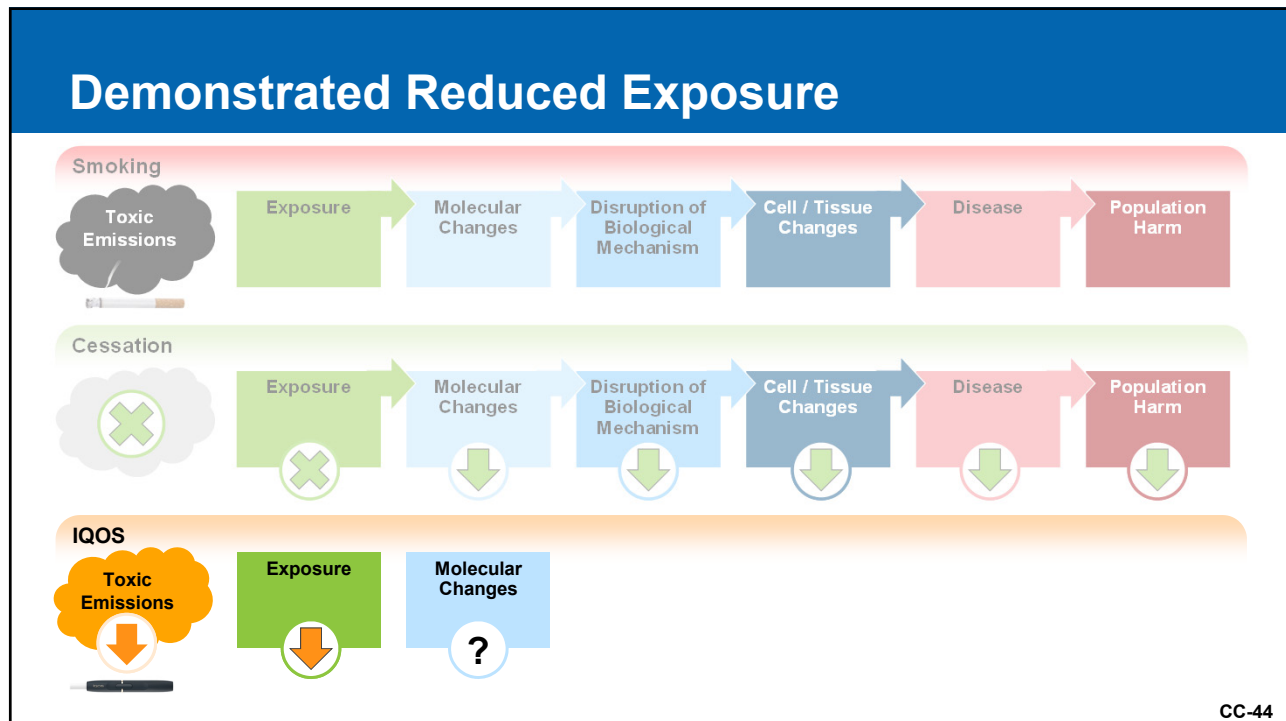
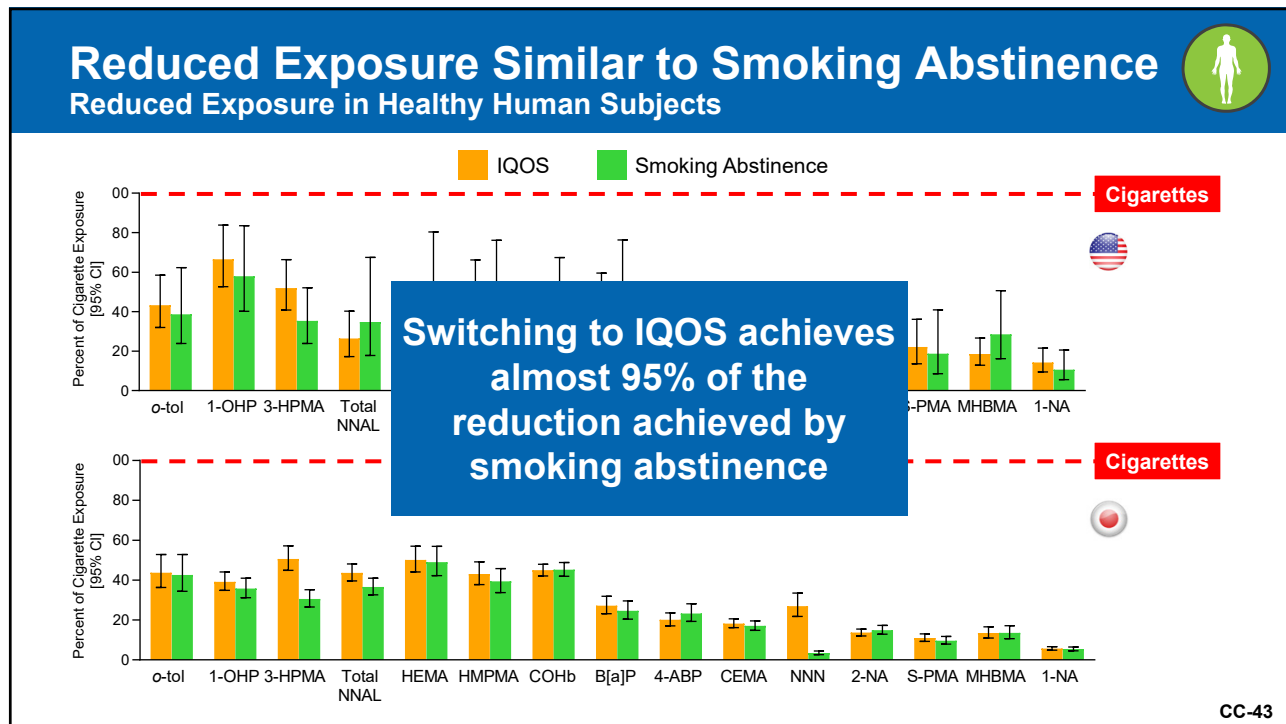
Exposure is Significantly Reduced
After Switching to IQOS



* On equivalent nicotine basis

CC-40

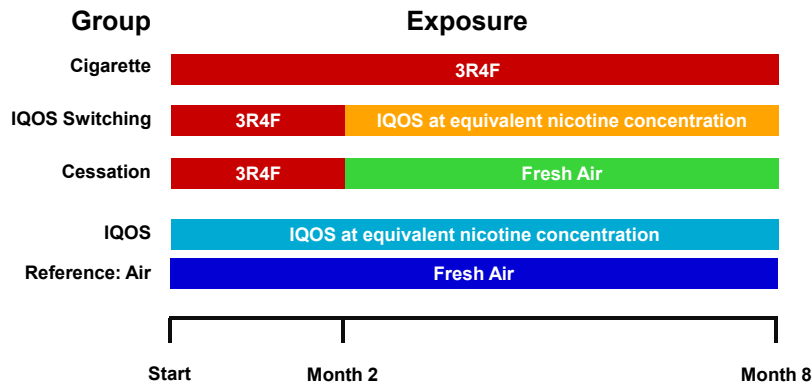




Switching Study in Apoe^{-/-} Mouse Model



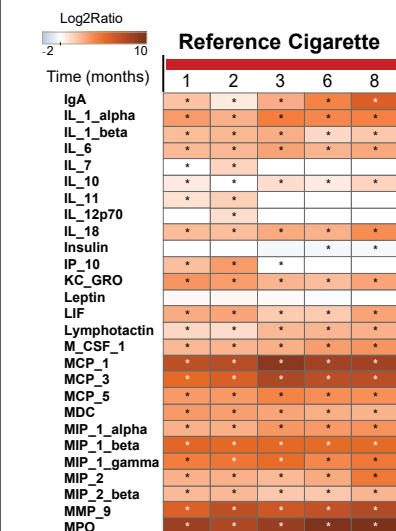
- 8 months duration (approximately 40% of lifetime)
- Concomitant analysis of CVD and COPD endpoints
- Comprehensive analysis of molecular changes and mechanistic impact
- Exposure dose corresponds to ~30 cigarettes per day in human comparison



Use of animal model reviewed in: Lo Sasso et al. The Apoe^{-/-} mouse model: a suitable model to study cardiovascular and respiratory diseases in the context of cigarette smoke exposure and harm reduction. *J. Transl. Med.*, 2016; 14:146.

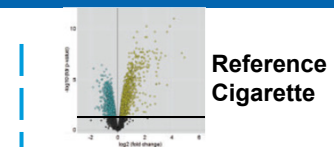
CC-45

Reduced Molecular Changes in the Lung



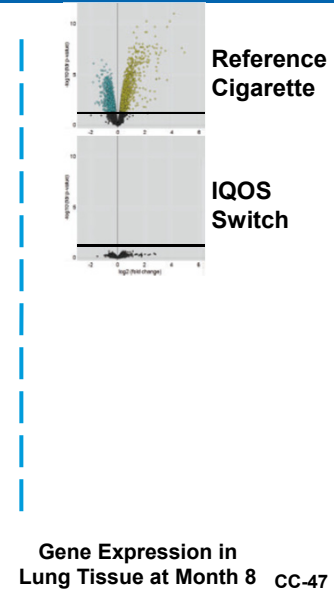
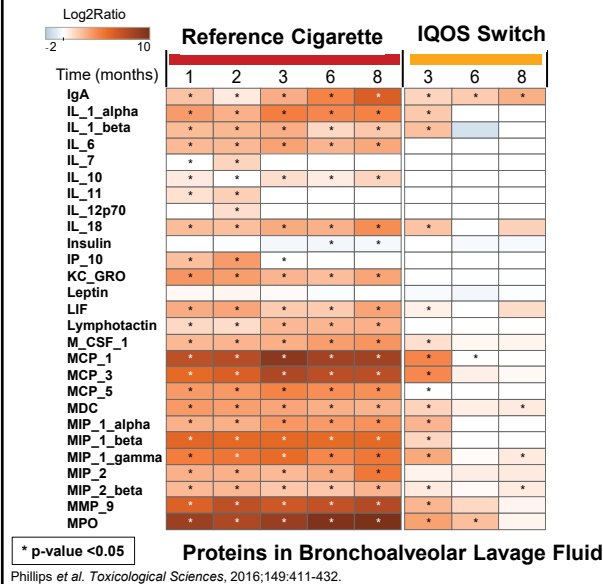
* p-value < 0.05

Proteins in Bronchoalveolar Lavage Fluid

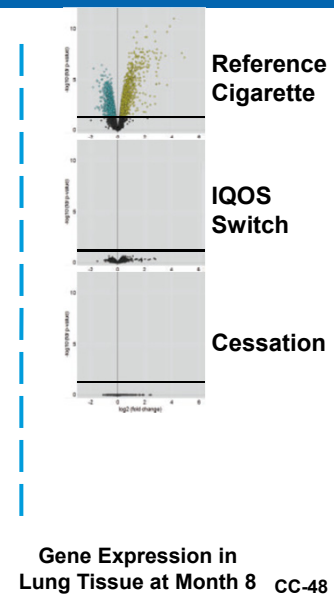
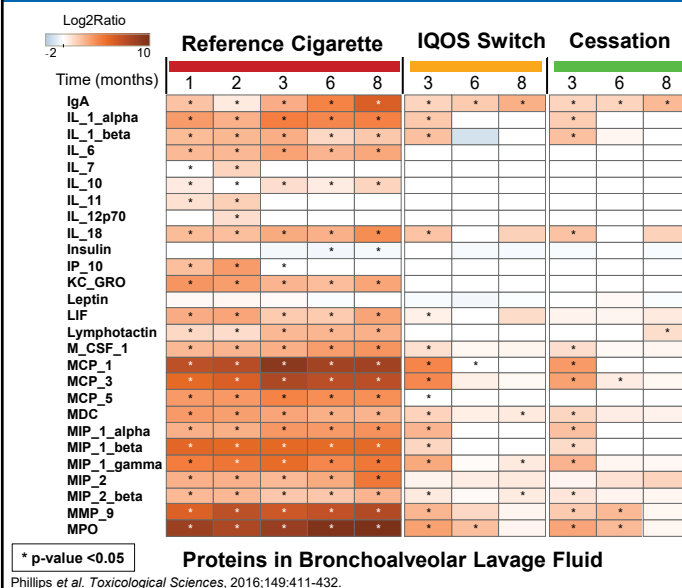
Phillips et al. *Toxicological Sciences*, 2016;149:411-432.

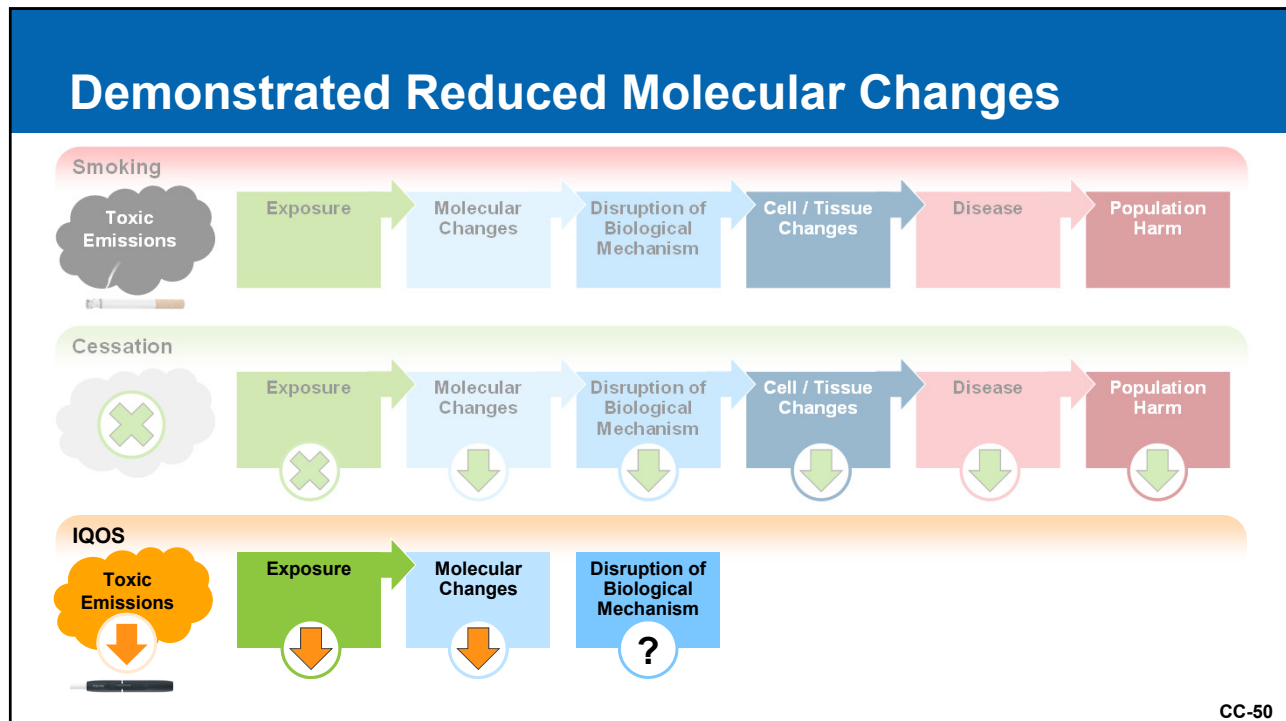
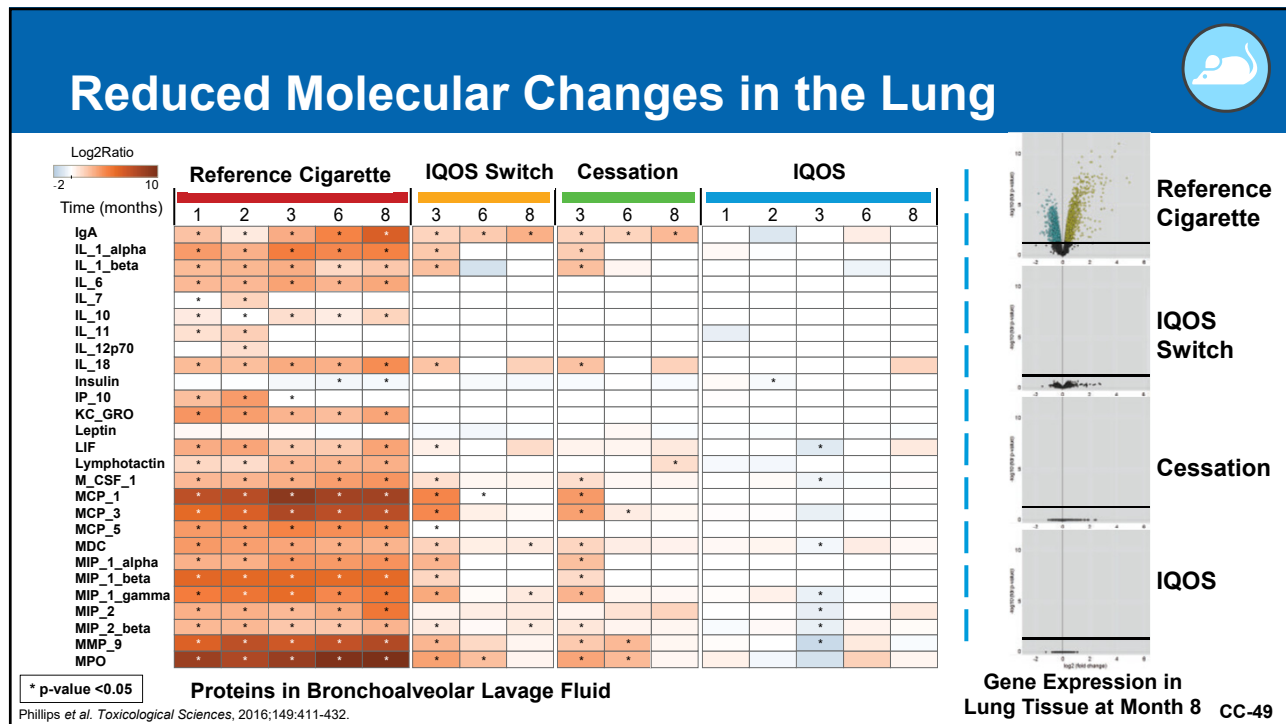
Gene Expression in Lung Tissue at Month 8 CC-46

Reduced Molecular Changes in the Lung



Reduced Molecular Changes in the Lung

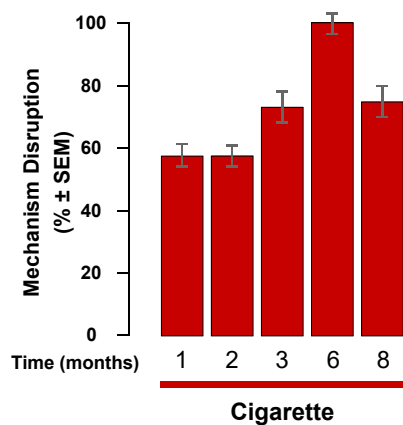




Reduced Effects on Disease Mechanisms



Lung Inflammation

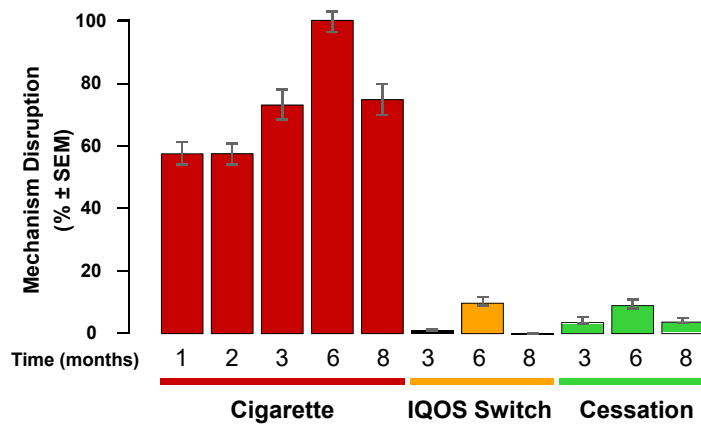


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Reduced Effects on Disease Mechanisms



Lung Inflammation

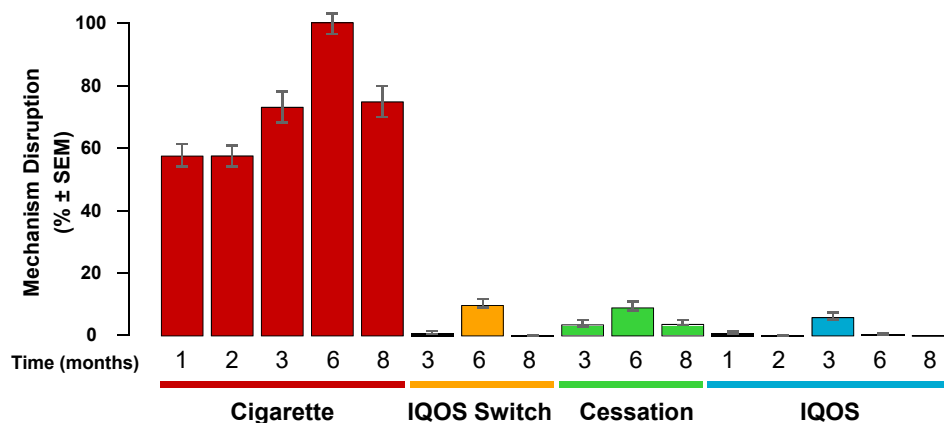


CC-52

Reduced Effects on Disease Mechanisms

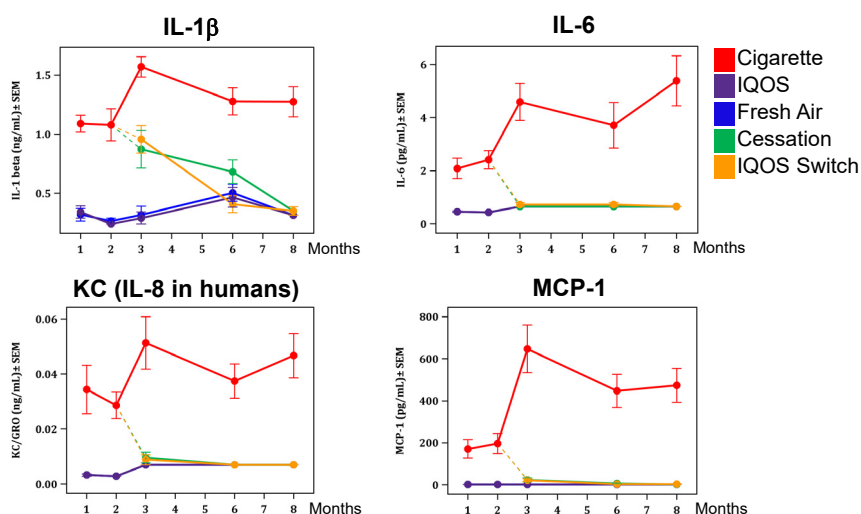


Lung Inflammation



CC-53

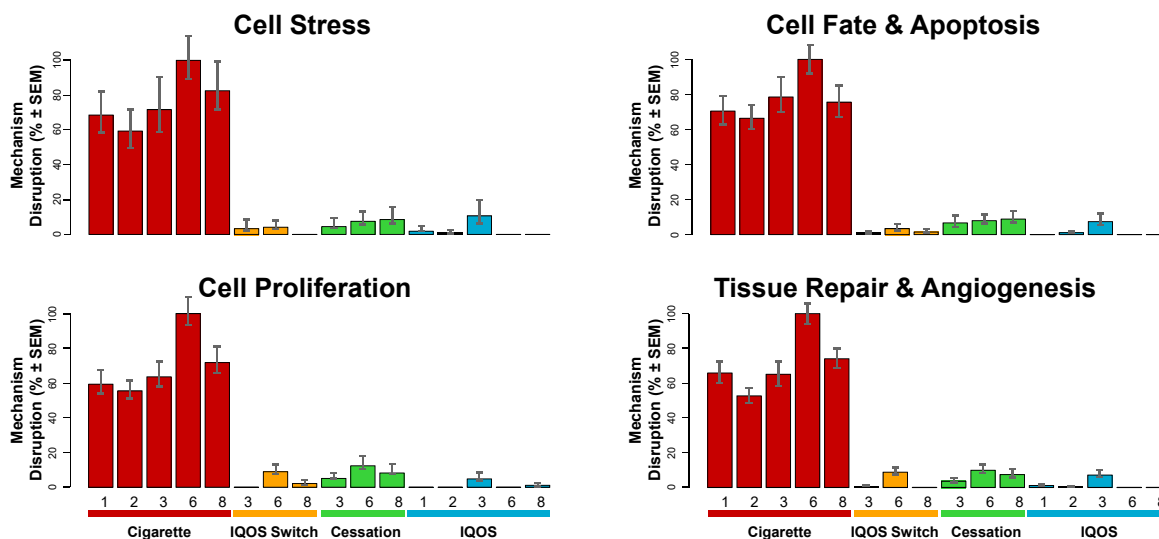
Specific Markers of Lung Inflammation



These changes in inflammation markers are all confirmed by the results from the A/J mouse dose response study at month 5.
Kuschnier *et al.* Dose-dependent cigarette smoking-related inflammatory responses in healthy adults. *Eur. Respir. J.*, 1996; 9:1989-1994.

CC-54

Reduced Effects on Disease Mechanisms



CC-55

Clinical Changes After 90 Days of Cessation

Reduced Exposure in Healthy Human Subjects



Disease Pathway	Endpoint		Abstinence Effect at 3m [95% CI]
Lipid Metabolism	HDL-C	↑	0.0 mg/dL [-5.77; 5.84]
Inflammation	WBC	↓	-0.94 10 ⁹ /L [-2.00; 0.13]
Airway Impairment	FEV ₁	↑	2.0 % pred [-3.37; 7.36]
Endothelial Dysfunction	sICAM-1	↓	-9.9 % [-19.7; 1.1]
Oxidative Stress	8-epi-PGF _{2α}	↓	-8.5 % [-25.13; 11.8]
Clotting	11-DTX-B ₂	↓	-7.2 % [-37.7; 38.3]

Smoking Abstinence:

Changes in Clinical Risk Endpoints after 3 months are small but relevant.

Changes are in the expected direction upon cessation.



Disease Pathway	Endpoint		Abstinence Effect at 3m [95% CI]
Lipid Metabolism	HDL-C	↑	6.4 mg/dL [2.5; 10.3]
Inflammation	WBC	↓	-0.41 10 ⁹ /L [-0.95; 0.14]
Airway Impairment	FEV ₁	↑	1.94 % pred [-0.44; 4.31]
Endothelial Dysfunction	sICAM-1	↓	-10.9 % [-17.8; -3.4]
Oxidative Stress	8-epi-PGF _{2α}	↓	-5.9 % [-17.1; 6.8]
Clotting	11-DTX-B ₂	↓	-19.4 % [-30.1; -7.0]

CC-56

Clinical Changes After 90 Days

Reduced Exposure in Healthy Human Subjects



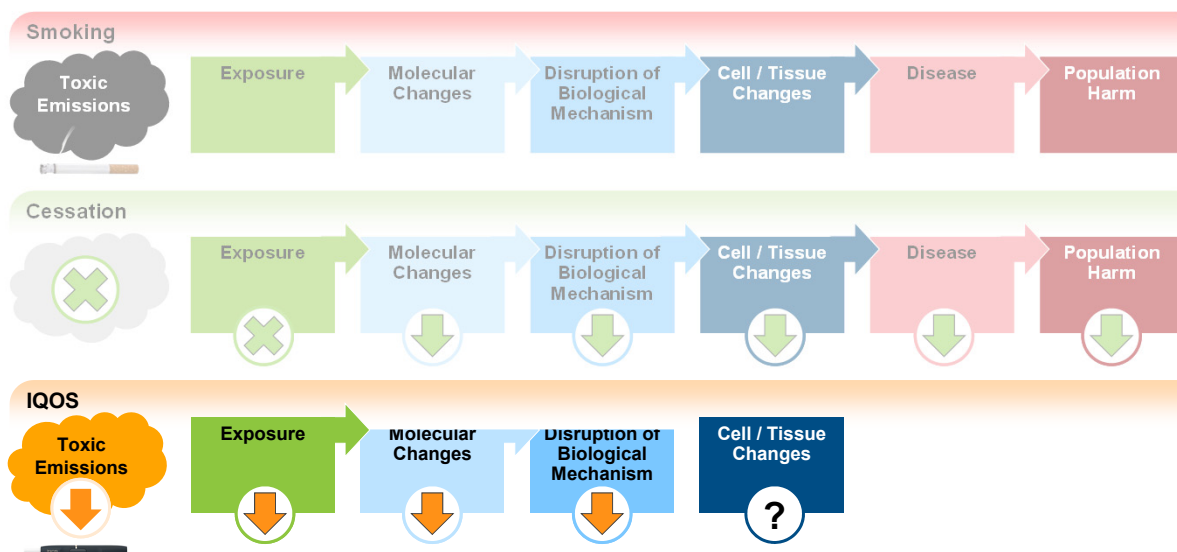
Disease Pathway	Endpoint	Abstinence Effect at 3m [95% CI]		Switching to IQOS Effect at 3m [95%CI]
Lipid Metabolism	HDL-C	0.0 mg/dL [-5.77; 5.84]	↑	1.4 mg/dL [-2.3;5.0]
Inflammation	WBC	-0.94 10 ⁹ /L [-2.00; 0.13]	-	0.17 10 ⁹ /L [-0.47; 0.81]
Airway Impairment	FEV ₁	2.0 % pred [-3.37; 7.36]	↑	0.53 % pred [-2.79; 3.85]
Endothelial Dysfunction	sICAM-1	-9.9 % [-19.7;1.1]	↓	-10.6 % [-16.7; -4.0]
Oxidative Stress	8-epi-PGF _{2α}	-8.5 % [-25.13; 11.8]	↓	-13.5 % [-23.6;-1.95]
Clotting	11-DTX-B ₂	-7.2 % [-37.7; 38.3]	↓	-3.6 % [-24.6; 23.3]



Disease Pathway	Endpoint	Abstinence Effect at 3m [95% CI]		Switching to IQOS Effect at 3m [95% CI]
Lipid Metabolism	HDL-C	6.4 mg/dL [2.5; 10.3]	↑	4.5 mg/dL [1.17, 7.88]
Inflammation	WBC	-0.41 10 ⁹ /L [-0.95; 0.14]	↓	-0.57 10 ⁹ /L [-1.04, -0.10]
Airway Impairment	FEV ₁	1.94 % pred [-0.44; 4.31]	↑	1.91 % pred [-0.14, 3.97]
Endothelial Dysfunction	sICAM-1	-10.9 % [-17.8; -3.4]	↓	-8.7 % [-14.94;-2.05]
Oxidative Stress	8-epi-PGF _{2α}	-5.9 % [-17.1; 6.8]	↓	-12.7 % [-21.81;-2.55]
Clotting	11-DTX-B ₂	-19.4 % [-30.1; -7.0]	↓	-8.98 % [-19.52, 2.94]

CC-57

Demonstrated Reduced Disruption of Biological Mechanisms

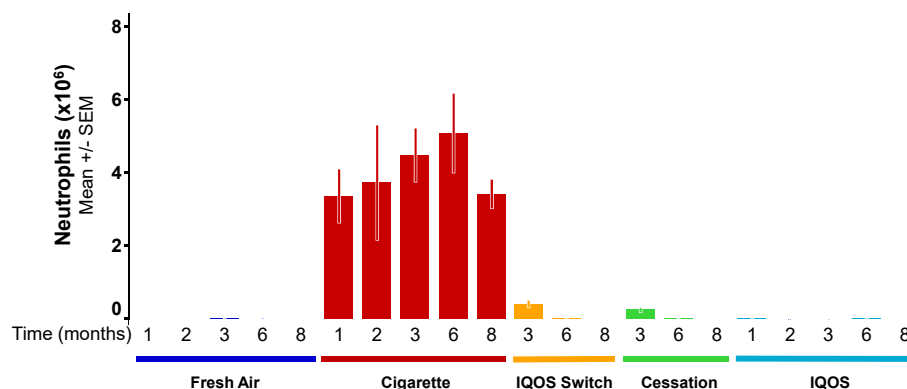


CC-58

Reduces the Effects on Cells



Inflammatory Lung Cells in Bronchoalveolar Lavage Fluid



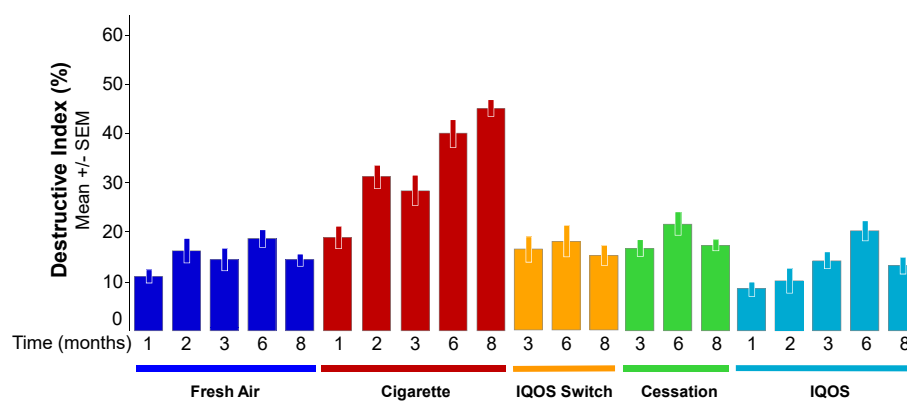
Phillips et al. *Toxicological Sciences*, 2016;149:411-432.

CC-59

Reduces the Effects on Tissues

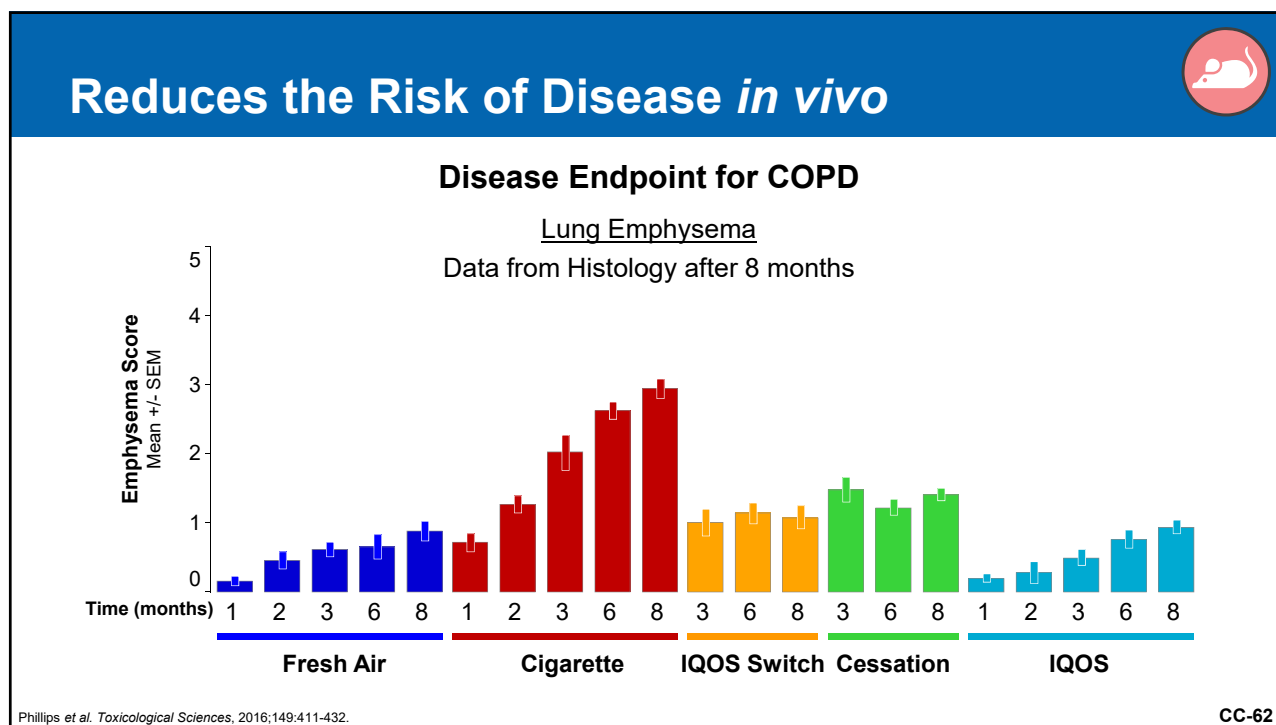
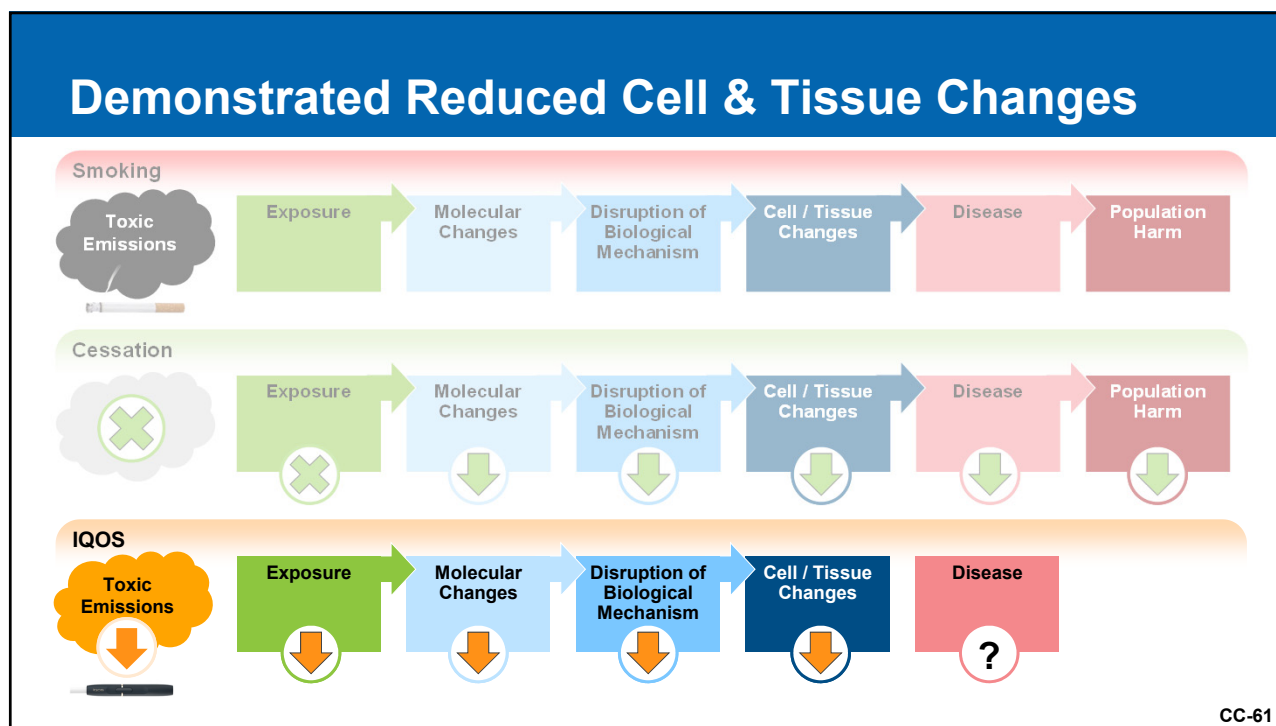


Lung Tissue Destructive Index



Phillips et al. *Toxicological Sciences*, 2016;149:411-432.

CC-60



Phillips et al. Toxicological Sciences, 2016;149:411-432.

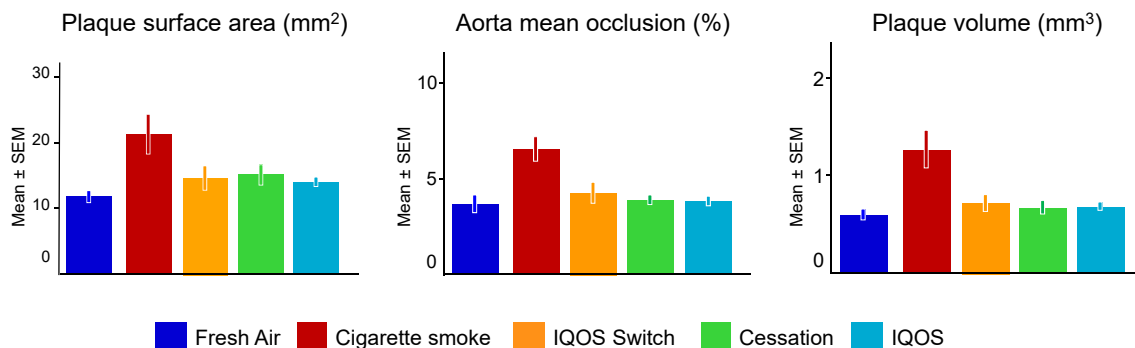
Reduces the Risk of Disease *in vivo*



Disease Endpoint for CVD

Atherosclerotic Plaque in the Aortic Arch

Data from μ CT at month 7

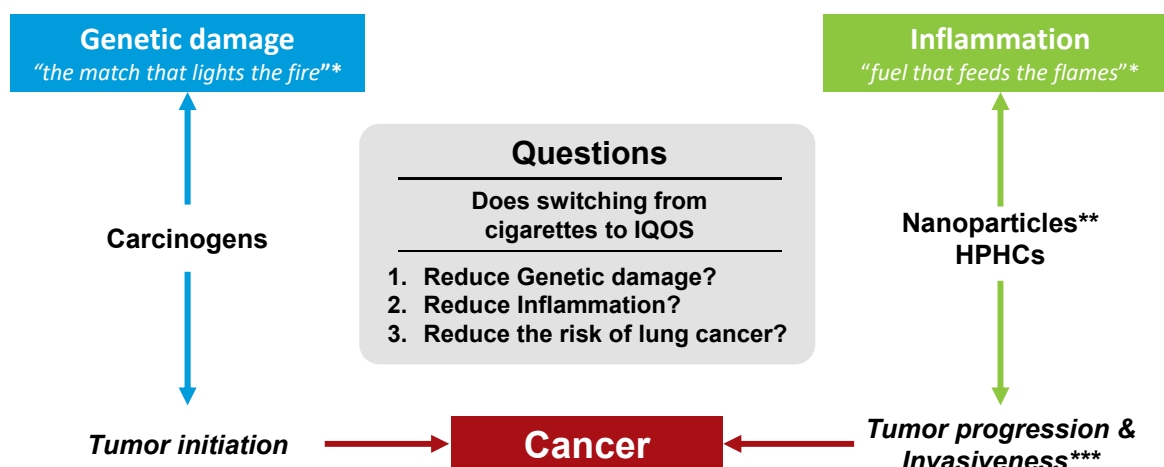


Phillips *et al. Toxicological Sciences*, 2016;149:411-432.

Poussin *et al. Systems toxicology-based assessment of the candidate modified-risk tobacco product THS2.2 for the adhesion of monocytic cells to human coronary arterial endothelial cells. Toxicology*, 2016; 339:73-86.

CC-63

How Cigarette Smoke Causes Cancer



* Balkwill F and Mantovani A. Inflammation and cancer: back to Virchow? *Lancet*, 2001, 357:539-45.

** You *et al.* Nanoparticulate carbon black in cigarette smoke induces DNA cleavage and Th17-mediated emphysema. *eLife* 2015; 4:e09623

*** Rothwell *et al.* Effect of daily aspirin on long-term risk of death due to cancer: analysis of individual patient data from randomised trials. *Lancet* 2011; 377:31-41.

CC-64

Genetic Damage is Reduced by IQOS

Does Switching to IQOS
Reduce Genetic damage?

Genetic damage

*"the match that lights the fire"**

Carcinogens

Tumor initiation

**Evidence from
IQOS Assessment**

Reduced Emission of Carcinogens



Reduced
Exposure to
Carcinogens



Reduced
Exposure
Response



Reduced
Genotoxicity



Reduced
DNA Damage



**Reduced
Genetic Damage**

* Balkwill F and Mantovani A. Inflammation and cancer: back to Virchow? Lancet, 2001, 357:539-45.

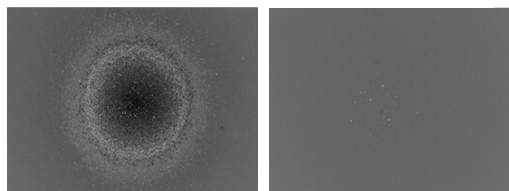
CC-65

Nanoparticles Deposit in the Lung



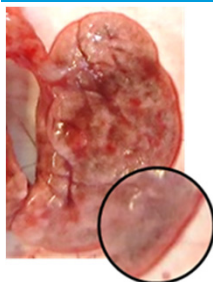
Cigarette Smoke

Carbon-based nanoparticles
 6×10^{11} particles \approx 0.7 mg*



Lung Deposition after 6 months

Cigarette smoke
(600 mg/m³ TPM)



IQOS Aerosol

No solid particles

Corresponding
concentration of
IQOS aerosol



Apoe^{-/-} mice exposed for 6 months, 3h/day and 5days/week.

You et al. Nanoparticle carbon black in cigarette smoke induces DNA cleavage and Th17-mediated emphysema. eLife 2015; 4:e09623

CC-66

Inflammatory Markers in Smokers' Lungs



Table 2. — Mean bronchoalveolar lavage (BAL) cell concentrations in smokers and nonsmokers

Cell type	BAL concentration $\times 10^3$ cells·mL ⁻¹		F statistic p-value	
	Smokers (n=14)	Nonsmokers (n=16)		
Macrophage	524±219	220±98	25.1	0.0001
Neutrophil	12.9±13.3	2.1±1.6	10.6	0.003
Lymphocyte	7.3±7.5	14.8±17.7	2.2	1.15
Eosinophil	0.9±1.7	1.1±1.3	0.1	0.75
Epithelial	1.5±1.4	2.1±2.1	1.0	0.33

Values are presented as mean±SD. Statistics quoted are by discriminant analysis. Overall model Hotelling's statistic = 1.7; p=0.0001. Critical Bonferoni alpha (n tests=5) = 0.01.

Table 3. — Bronchoalveolar lavage (BAL) supernatant cytokine and total protein (TP) concentration differences between smokers and nonsmokers

BAL constituent	Smokers (n=14)	Nonsmokers (n=16)	F statistic	p-value
IL-1 β pg·mL ⁻¹	1.2±0.7	0.5±0.4	14.3	0.0007
IL-6 pg·mL ⁻¹	5.3±3.2	1.9±1.0	17.3	0.0003
IL-8 pg·mL ⁻¹	32.8±15.9	18.2±11.5	8.4	0.007
TNF- α pg·mL ⁻¹	2.5±7.9	0.2±0.2	1.4	0.25
MCP-1 pg·mL ⁻¹	36.7±28.3	13.0±7.7	10.4	0.003
TP μ g·mL ⁻¹	75.8±27.7	87.2±56.5	0.4	0.50

Values are presented as mean±SD. IL-1 β : Interleukin-1 β (non-detectable in one nonsmoker); IL-6: interleukin-6 (detected in all subjects); IL-8: interleukin-8 (detected in all subjects); TNF- α : tumour necrosis factor- α (detectable in seven nonsmokers and two smokers); MCP-1: macrophage chemoattractant protein-1 (nondetectable in one nonsmoker and three smokers). Statistics quoted are by discriminant analysis. Overall model Hotelling's statistic=1.34; p<0.002. Critical Bonferoni alpha value (n tests=6) = 0.008.

Kuschner *et al.* Dose-dependent cigarette smoking-related inflammatory responses in healthy adults. *Eur. Respir. J.* 1996; 9:1989–1994.

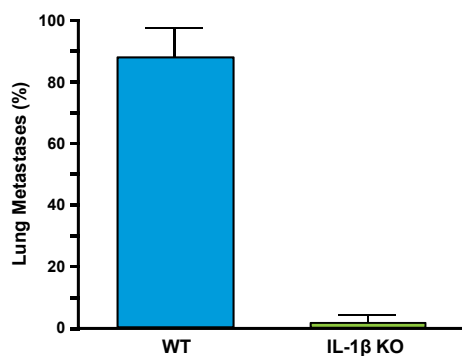
CC-67

Inflammation and Cancer

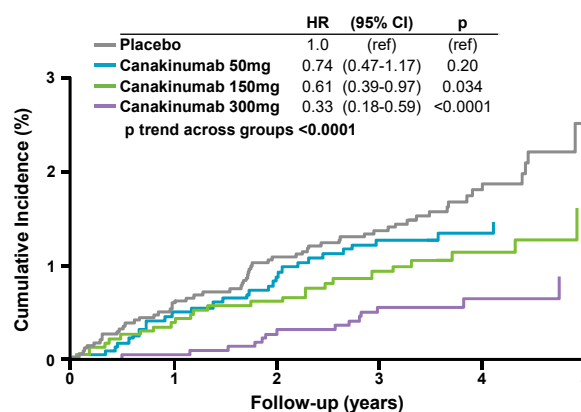
The Role of Interleukin-1 β in Cancer



Animal Studies* Lung Metastases (%)



Human Study (CANTOS)** Lung Cancer Cumulative Incidence (%)



* Voronov *et al.* IL-1 is required for tumor invasiveness and angiogenesis. *PNAS* 2002; 100:2645-2650.

** Ridker *et al.* Effect of interleukin-1 β inhibition with canakinumab on incident lung cancer in patients with atherosclerosis. *Lancet* 2017; 390:1833-1842.

Krelin *et al.* Interleukin-1 β -Driven Inflammation Promotes the Development and Invasiveness of Chemical Carcinogen-Induced Tumors. *Cancer Res.* 2007; 67:1062-1071.

CC-68

Inflammation is Reduced by IQOS

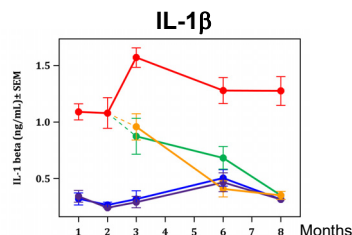
Evidence from IQOS Assessment

Reduced Emission of HPHCs and No carbon-based nanoparticles

Reduced Exposure to HPHCs

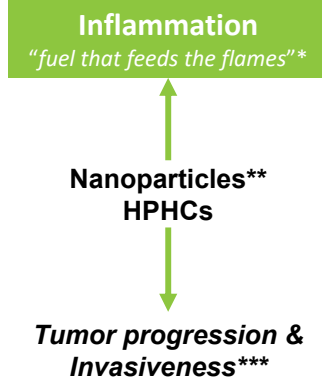
No Exposure to nanoparticles

Reduced Lung Inflammation



Reduced Inflammation

Does Switching to IQOS Reduce Inflammation?



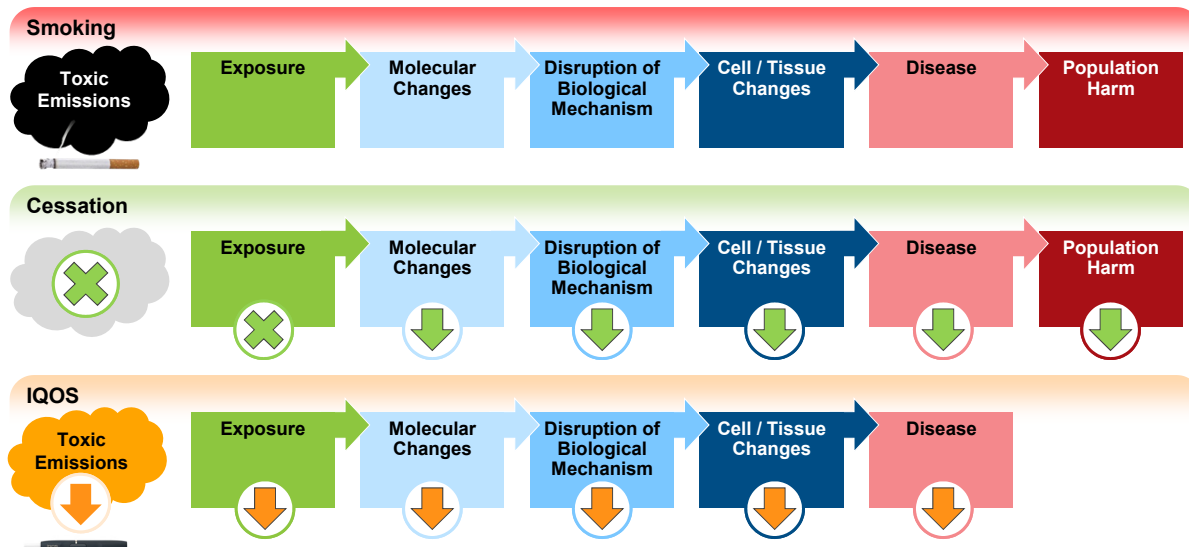
* Balkwill F and Mantovani A. Inflammation and cancer: back to Virchow? *Lancet*, 2001; 357:539–45.

** You *et al.* Nanoparticulate carbon black in cigarette smoke induces DNA cleavage and Th17-mediated emphysema. *eLife* 2015; 4:e09623.

*** Rothwell *et al.* Effect of daily aspirin on long-term risk of death due to cancer: analysis of individual patient data from randomised trials. *Lancet* 2011; 377:31–41.

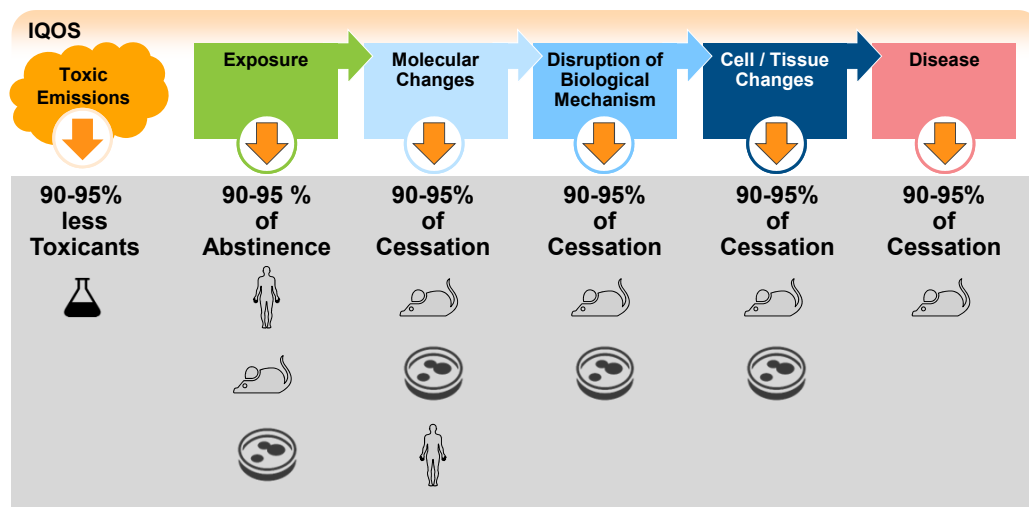
CC-69

Demonstrated Reduced Disease



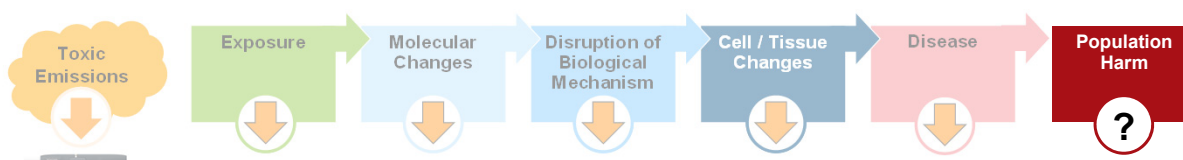
CC-70

Summary of Totality of Evidence



CC-71

Demonstrate a Benefit to the Health of the Population as a Whole ...



CC-72



Consumer Perception and Behavior

Antonio Ramazzotti

Vice President Human Insights and Behavioral Research
Philip Morris International

CC-73

911(g)(1) Modified Risk Products

...the applicant has demonstrated that such product, as it is actually used by consumers, will—

A

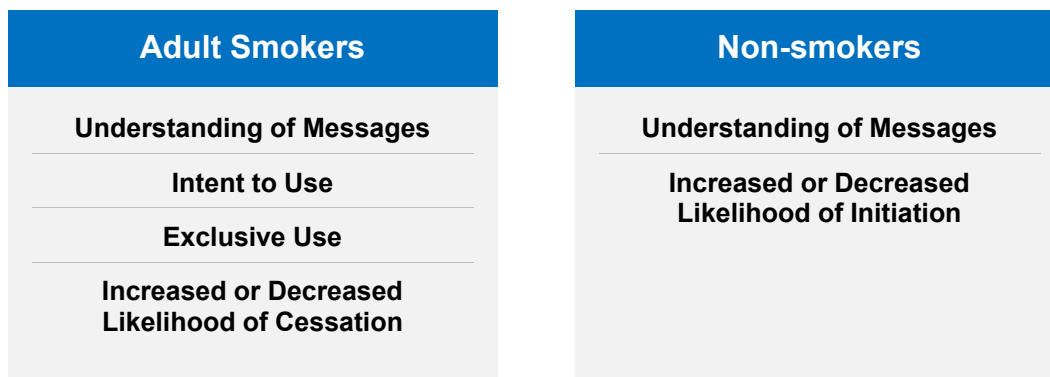
Significantly reduce harm and the risk of tobacco-related disease to individual tobacco users

B

Benefit the health of the population as a whole taking into account both users of tobacco products and persons who do not currently use tobacco products

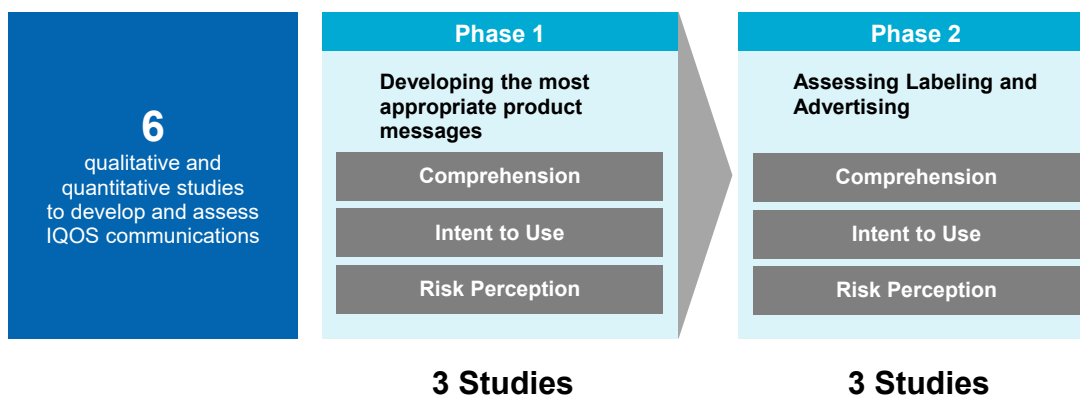
CC-74

Who Will Use IQOS and to What Degree?



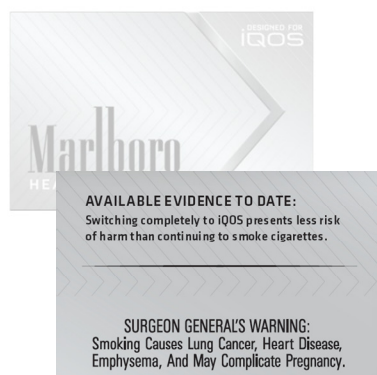
CC-75

PBA Studies to Develop and Assess IQOS Messages



CC-76

Product Messages (On a Tested Pack)



- 1 Switching completely from cigarettes to the IQOS system can reduce the risks of tobacco-related diseases.
- 2 Switching completely to IQOS presents less risk of harm than continuing to smoke cigarettes.
- 3 Switching completely from cigarettes to the IQOS system significantly reduces your body's exposure to harmful and potentially harmful chemicals.

CC-77

Study Design

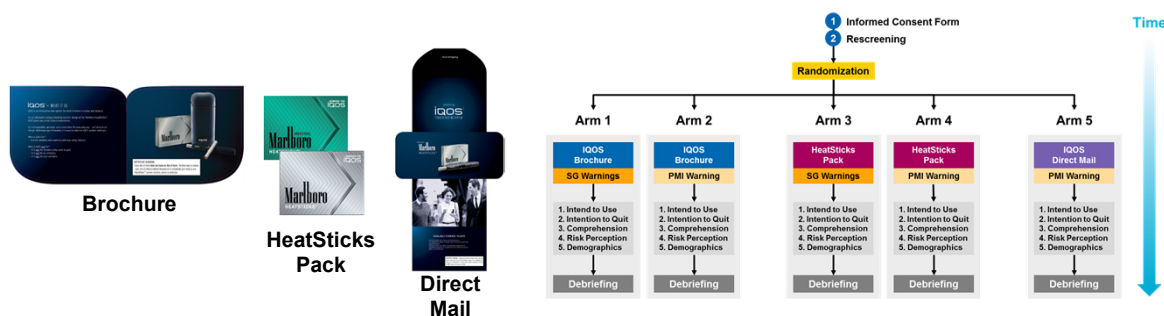
IQOS Communication Studies

Five arms, experimental studies, describing responses to materials on comprehension, intent to use, change in intention to quit and risk perception

≈ 2,200 enrolled participants in each study

- Five subject groups: adult smokers with and without intention to quit, adult former smokers, adult never smokers and LA-25 Adult Never Smokers
- Sample was balanced, by subject group, sex, age group and city

Conducted in 4 US cities



CC-78

Tested Product Message

Reduced Risk of Harm



HeatSticks Pack with SG's Warnings

AVAILABLE EVIDENCE TO DATE:
Switching completely to IQOS presents less risk
of harm than continuing to smoke cigarettes.

SURGEON GENERAL'S WARNING:
Smoking Causes Lung Cancer, Heart Disease,
Emphysema, And May Complicate Pregnancy.

HeatSticks Pack with PMI Warning

AVAILABLE EVIDENCE TO DATE:
Switching completely to IQOS presents less risk
of harm than continuing to smoke cigarettes.

IMPORTANT WARNING:
· Less risk of harm does not mean no risk of harm. The best way to reduce
your risk of tobacco-related diseases is to completely quit tobacco use.
· HeatSticks™ contain nicotine, which is addictive.

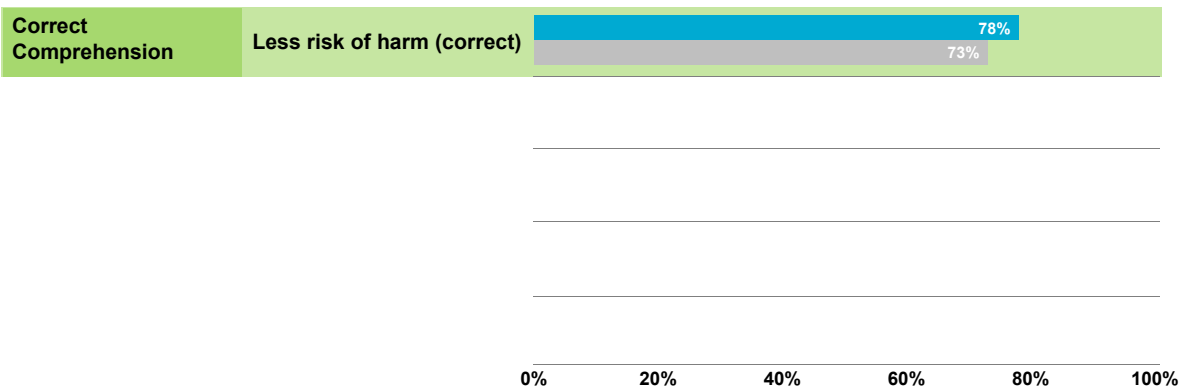
CC-79

The Majority Understood that IQOS Presents Less Risk of Harm, but is Not Risk Free

IQOS Communication Study - Reduced Risk of Harm

HeatSticks Pack PMI Warning n=380

HeatSticks Pack SG's Warnings n=376

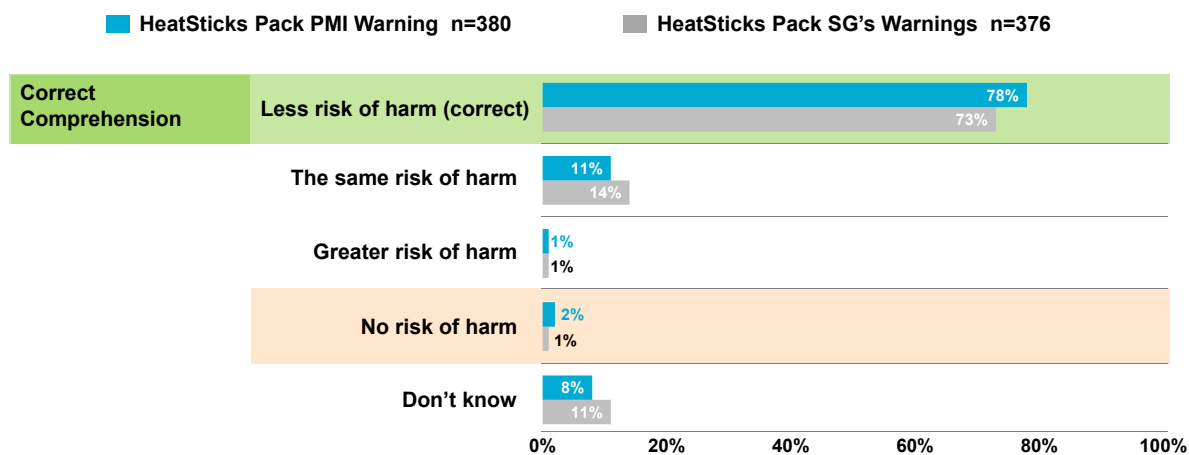


THS-PBA-05-RRC2-US

CC-80

Only 1% and 2% Misunderstood that IQOS Presents “No Risk of Harm”

IQOS Communication Study - Reduced Risk of Harm

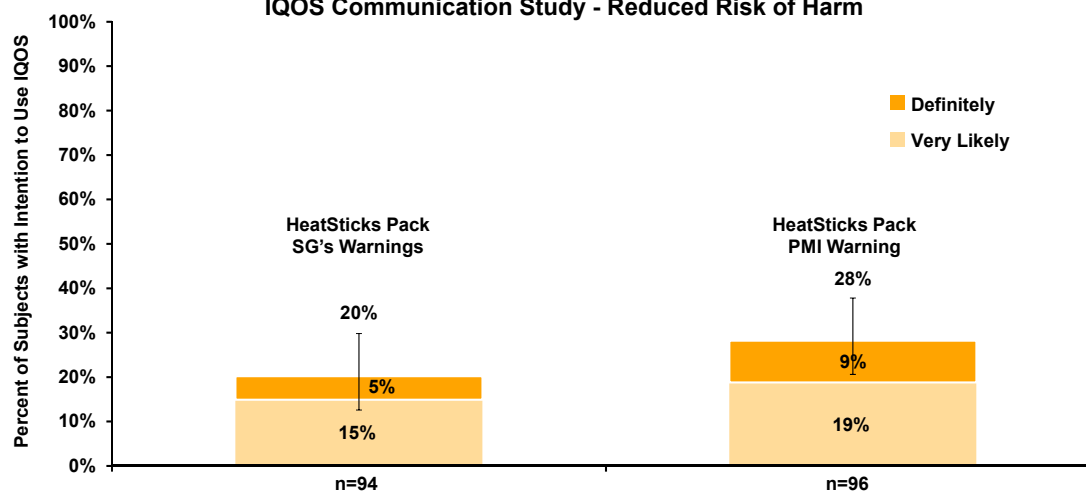


THS-PBA-05-RRC2-US

CC-81

Substantial Intention to Use IQOS Among Adult Smokers with No Intention to Quit

IQOS Communication Study - Reduced Risk of Harm



* Error bars show 95% confidence intervals for the 'very likely' and 'definitely' categories combined.
THS-PBA-05-RRC2-US

CC-82

Study Design

Actual Use Study

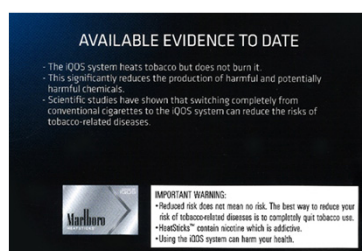
Single group, observational study, *ad libitum* use of IQOS and cigarettes, reported on a stick-by-stick basis

1,336 enrolled participants

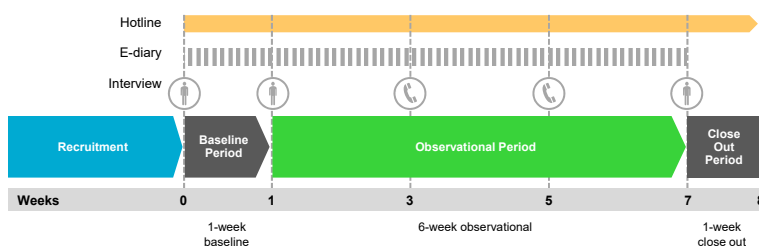
Quota sampling approximating the distribution of US adult smokers population by sex, age, race and income (CDC, 2012)

Conducted in 8 US geographic areas

IQOS brochure shown to participants contained a reduced risk product message



1-week baseline, 6-week observational and 1-week close out period

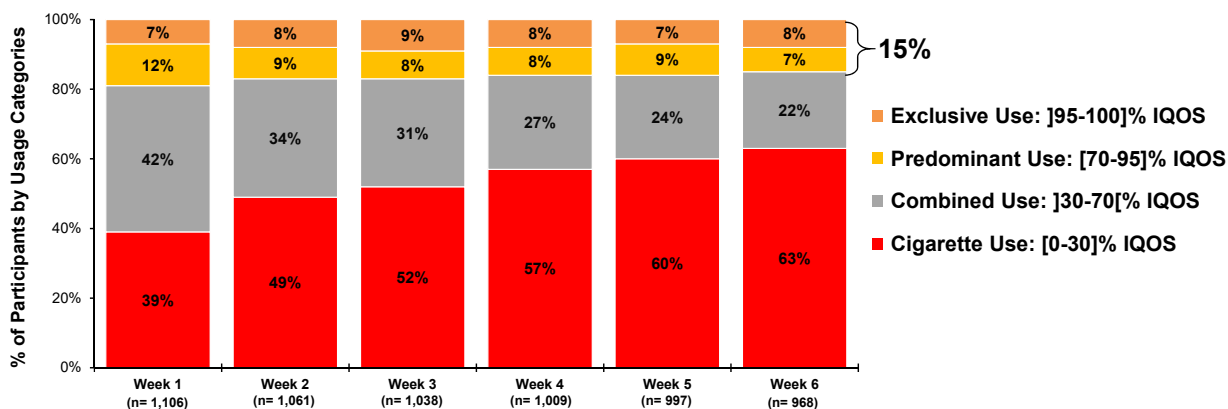


THS-PBA-07-US

CC-83

15% of U.S. Adult Daily Smokers Switched from Cigarettes to IQOS

IQOS and Cigarettes Use: Observational Period
Actual Use Study

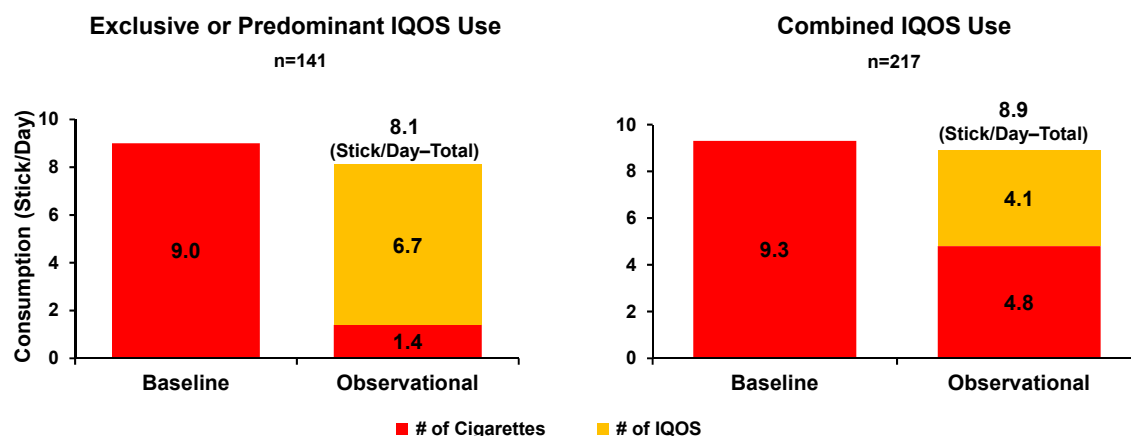


THS-PBA-07-US

CC-84

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

Actual Use Study: IQOS + Cigarette Consumption

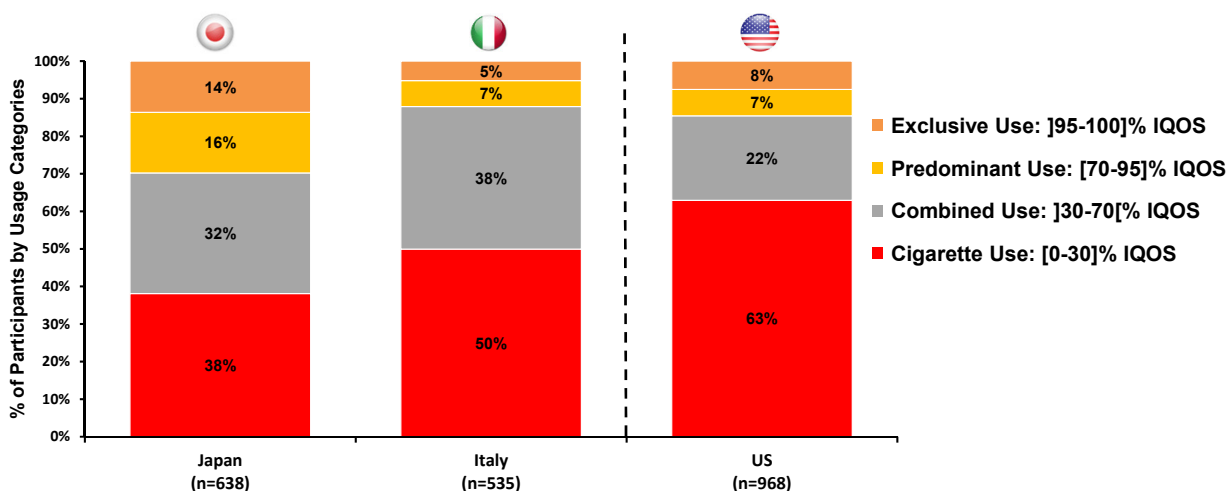


THS-PBA-07-US

CC-85

Between 12% and 30% of Participants Switched to IQOS

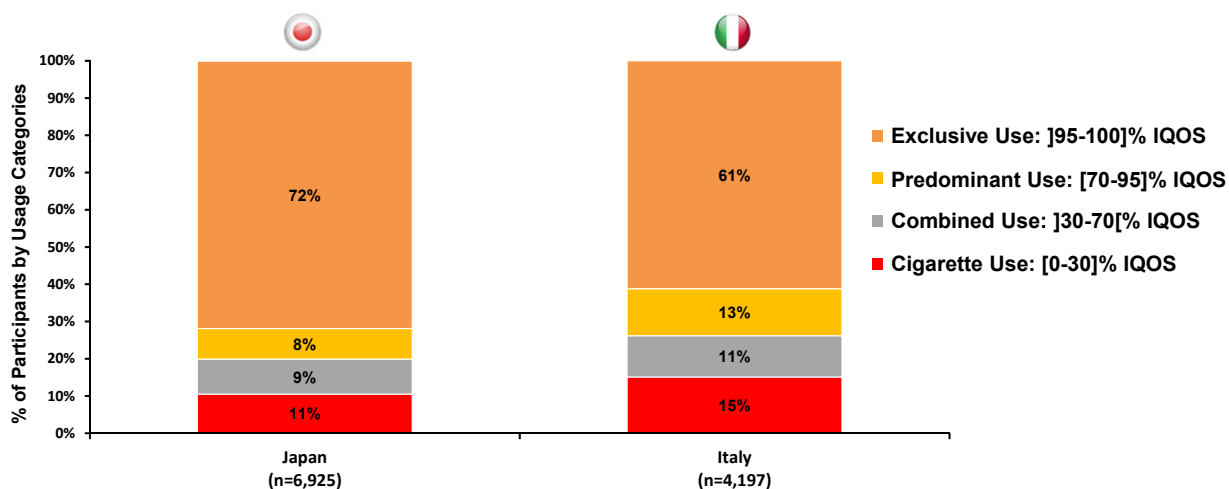
IQOS Usage Patterns



WOT

CC-86

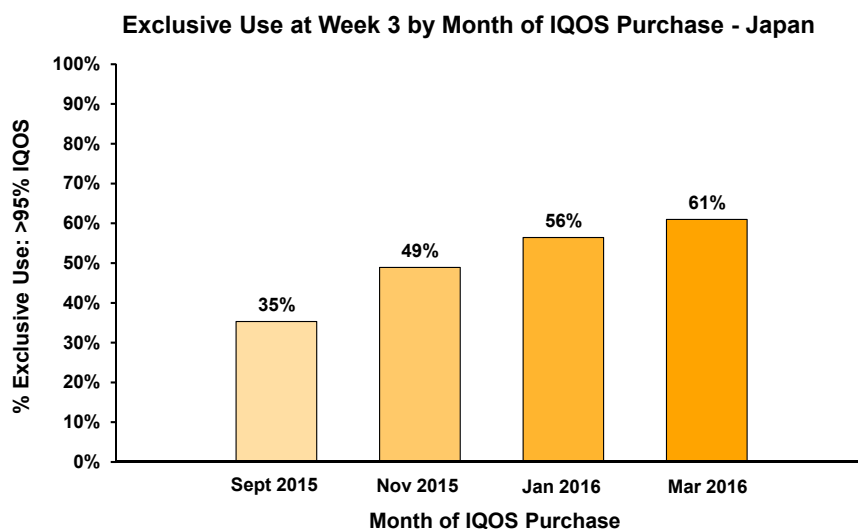
Post-market Data Show Exclusive Use is the Most Common Behavior Among IQOS Purchasers



Consumer Panels, August 2017

CC-87

Increased Awareness and Repeated Communication Lead to Higher Switching Rates



Source: Consumer Panel Japan, March 2016

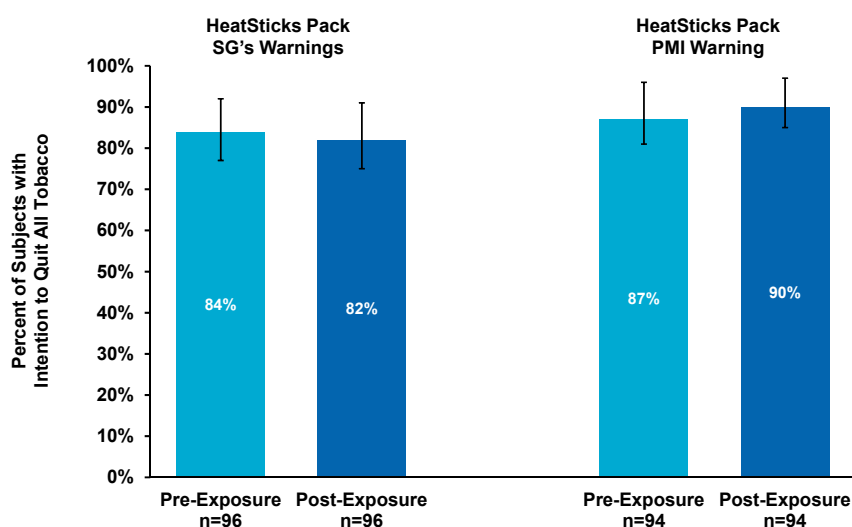
CC-88

Who Will Use IQOS and to What Degree?

Adult Smokers	Non-smokers
Understanding of Messages	Understanding of Messages
Intent to Use	Increased or Decreased Likelihood of Initiation
Exclusive Use	
Increased or Decreased Likelihood of Cessation	

CC-89

Minimal Interference on Intention to Quit All Tobacco among Adult Smokers with the Intention to Quit

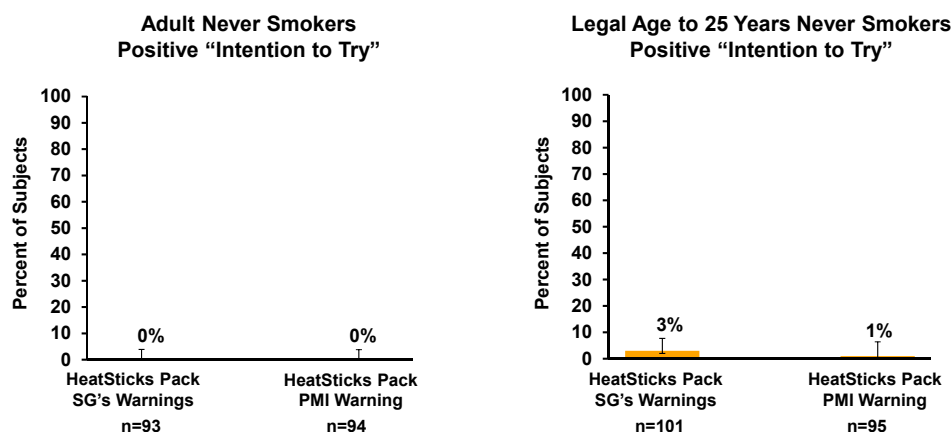


THS-PBA-05-RRC2-US

CC-90

Low Levels of Intent to Use Among Adult Never Smokers and LA-25 Never Smokers

IQOS Communication Study - Reduced Risk of Harm

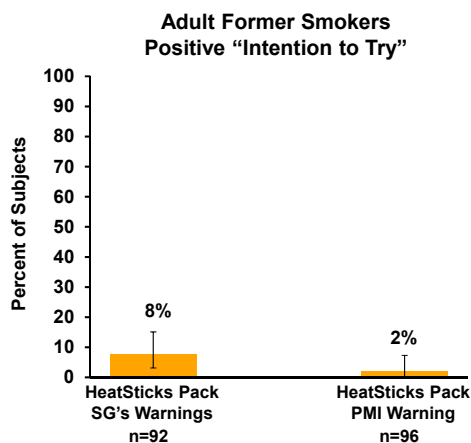


Positive Intention to Try IQOS is the sum of % *Very Likely* and % *Definitely* responses
 Error bars show 95% confidence intervals for the 'very likely' and 'definitely' categories combined
 THS-PBA-05-RRC2-US

CC-91

Low Levels of Intent to Use Among Adult Former Smokers

IQOS Communication Study - Reduced Risk of Harm



Positive Intention to Try IQOS is the sum of % *Very Likely* and % *Definitely* responses
 Error bars show 95% confidence intervals for the 'very likely' and 'definitely' categories combined
 THS-PBA-05-RRC2-US

CC-92

911(g)(1) Modified Risk Products

...the applicant has demonstrated that such product, as it is actually used by consumers, will—

A

Significantly reduce harm and the risk of tobacco-related disease to individual tobacco users

B

Benefit the health of the population as a whole taking into account both users of tobacco products and persons who do not currently use tobacco products

CC-93

U.S. Commercialization and Controls

Sarah Knakmuhs

Vice President, Heated Tobacco Products
Philip Morris USA

CC-94

Tobacco Harm Reduction in the U.S.



***“For the first time...the federal government
...is able to bring science-based regulation
to the manufacturing, marketing, and
distribution of tobacco products.”***

- Former FDA Commissioner Margaret A. Hamburg, M.D., September 19, 2013

CC-95

IQOS in the U.S.



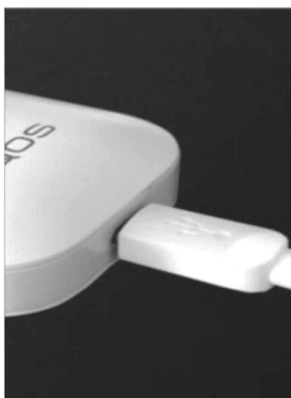
CC-96

Behavior Change – IQOS Use

Device Usability



Charging & Cleaning

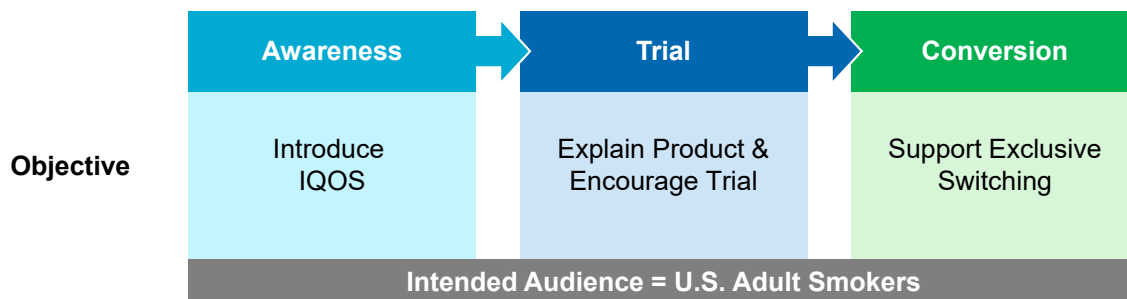


Taste & Experience



CC-97

PM USA Marketing Approach for IQOS



CC-98

Build Awareness for IQOS

Print Advertising

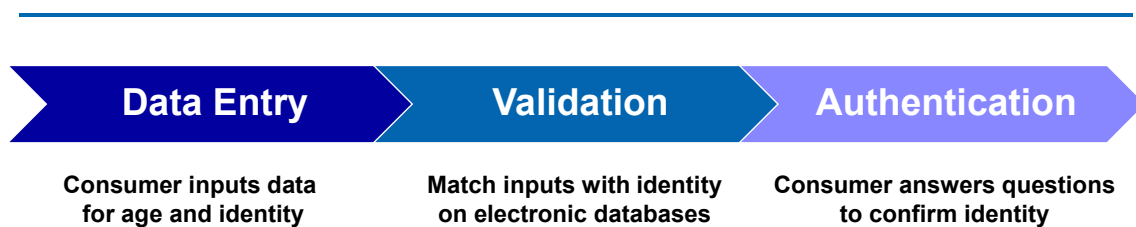
Direct Mail

Email



CC-99

Electronic Age Verification



CC-100

Opportunities for Trial of IQOS

Individual Engagements

Consumer Events

Retail



CC-101

Trial of IQOS

Verification



Confirm age and
identity via
government issued ID

Confirmation



Confirm
smoking status

Guided Trial



Provide overview
and perform
guided trial

CC-102

IQOS Support

Device Troubleshooting

HeatStick Availability

Personal Support



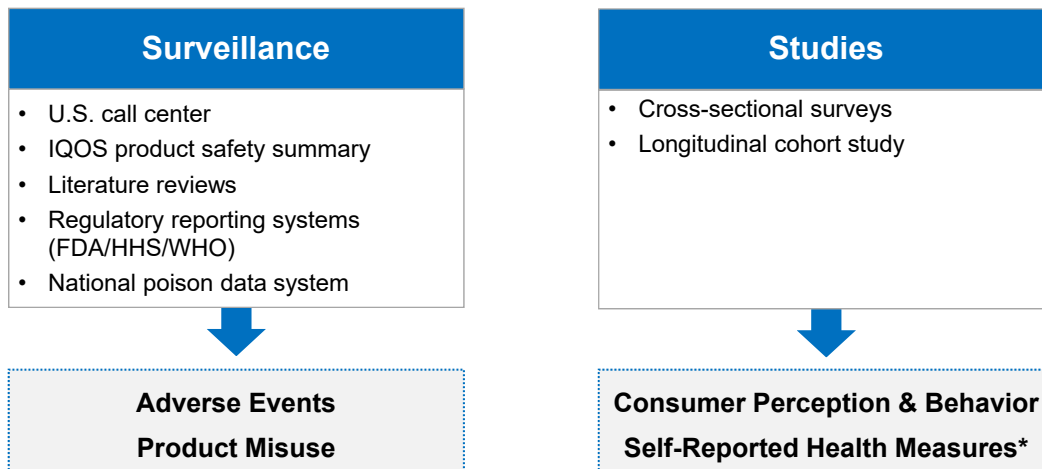
CC-103

PM USA Marketing Approach for IQOS

	Awareness	Trial	Conversion
Objective	Introduce IQOS	Explain Product & Encourage Trial	Support Exclusive Switching
Examples	Direct Mail Print Media	Consumer Events Retail Engagement	Customer Care Personal Support
Intended Audience = U.S. Adult Smokers			

CC-104

Post-market Surveillance



*For Longitudinal Cohort Study

CC-105

IQOS in the U.S.



CC-106

Population Modeling and Conclusion

Moira Gilchrist, PhD

Vice President Scientific and Public Communications
Philip Morris International

CC-107

The PMI Population Health Impact Model

Prevalence
Component

Epidemiological
Risk Component

Weitkunat R et al, A novel approach to assess the population health impact of introducing a Modified Risk Tobacco Product. *Regulatory Toxicology and Pharmacology* (2016).

Lee, P, et al, Estimating the effect of differing assumptions on the population health impact of introducing a Reduced Risk Tobacco Product in the USA. *Regulatory Toxicology and Pharmacology* (2017). CC-108

The Prevalence Component

Prevalence Component

Hypothetical population based on publicly
available databases and scientific literature

Transition probabilities



Validated

using published smoking statistics

CC-109

The Epidemiological Risk Component

Epidemiological Risk Component

Hypothetical population risk estimates

Ischemic heart disease, lung cancer,
stroke, and COPD

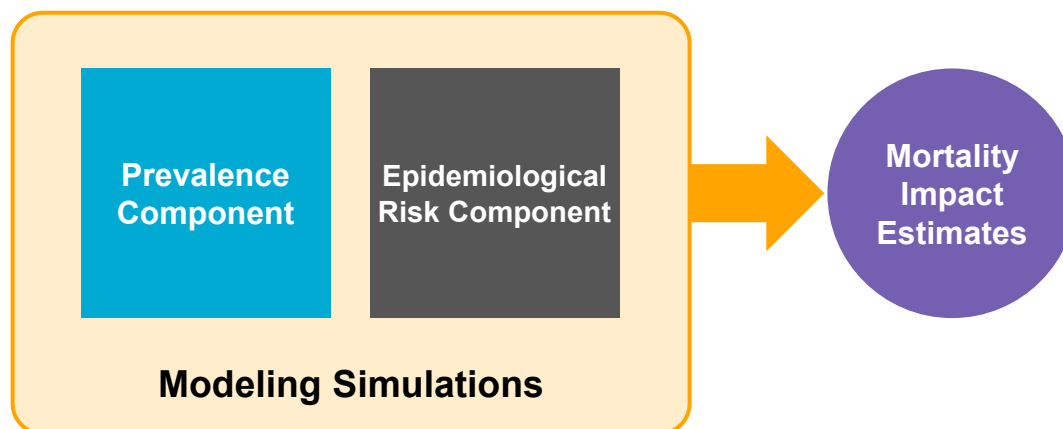


Validated

using estimates from the Surgeon General's Report

CC-110

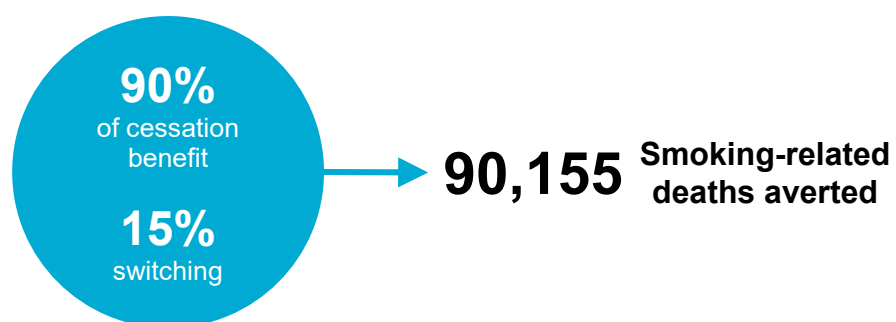
The PMI Population Health Impact Model



Weitkunat R et al, A novel approach to assess the population health impact of introducing a Modified Risk Tobacco Product. *Regulatory Toxicology and Pharmacology* (2016).
 Lee, P, et al, Estimating the effect of differing assumptions on the population health impact of introducing a Reduced Risk Tobacco Product in the USA. *Regulatory Toxicology and Pharmacology* (2017).

CC-111

Benefit to the U.S. Population as a Whole



CC-112

911(g)(1) Modified Risk Products

...the applicant has demonstrated that such product, as it is actually used by consumers, will—

A

Significantly reduce harm and the risk of tobacco-related disease to individual tobacco users

B

Benefit the health of the population as a whole taking into account both users of tobacco products and persons who do not currently use tobacco products

CC-113

The IQOS Opportunity



CC-114

The IQOS Opportunity

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

CC-115

The IQOS Heating System

Tobacco Products Scientific Advisory Committee

January 24, 2018

CC-116