The IQOS Heating System

Tobacco Products Scientific Advisory Committee

January 24, 2018
Introduction

Moira Gilchrist, PhD
Vice President Scientific and Public Communications
Philip Morris International
The Status Quo

Smokers
Risk Continuum

Combustibles  Cessation

Highest Risk  Lowest Risk

Institute of Medicine, Clearing the Smoke, Assessing the Science Base for Tobacco Harm Reduction, 2001.
The IQOS Heating System
The IQOS Opportunity
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
911(g)(1) Modified Risk Products

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Product Messages

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

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.
Product Messages

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

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

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.

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- 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.
“... 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
<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Company</th>
<th>Topic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moira Gilchrist, PhD</td>
<td>VP Scientific &amp; Public Communications</td>
<td>Philip Morris International</td>
<td>IQOS System and Heating Technology</td>
</tr>
<tr>
<td>Manuel Peitsch, PhD</td>
<td>Chief Scientific Officer</td>
<td>Philip Morris International</td>
<td>Scientific Assessment of IQOS</td>
</tr>
<tr>
<td>Antonio Ramazzotti</td>
<td>VP Human Insights and Behavioral Research</td>
<td>Philip Morris International</td>
<td>Perception and Behavior</td>
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<tr>
<td>Sarah Knakmuhs</td>
<td>VP Heated Tobacco Products</td>
<td>Philip Morris USA</td>
<td>U.S. Commercialization and Controls</td>
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<td>Moira Gilchrist, PhD</td>
<td>VP Scientific &amp; Public Communications</td>
<td>Philip Morris International</td>
<td>Population Modeling and Conclusion</td>
</tr>
</tbody>
</table>
IQOS System and Heating Technology

Moira Gilchrist, PhD
Vice President Scientific and Public Communications
Philip Morris International
HeatStick Construction

- **Mouth Piece**
- **Tipping Paper**
- **Biodegradable Film**
- **Hollow Acetate Tube**
- **Outer Paper**
- **Crimped Tobacco**
IQOS Holder and Heating Blade

Heating Blade

Control Electronics

Battery
IQOS Temperature Profile

Combustion $T^\circ$

Heater turned off

Programmed heater profile

Distance from the Blade

* Radial position of thermocouple relative to the surface of the heater
Scientific Assessment of IQOS

Manuel Peitsch, PhD
Chief Scientific Officer
Philip Morris International
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
# Scientific Assessment

<table>
<thead>
<tr>
<th>Studies</th>
<th>17 Non-Clinical Studies</th>
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<tr>
<td></td>
<td>8 Clinical Studies</td>
</tr>
<tr>
<td>Publications</td>
<td>30+ on IQOS assessment</td>
</tr>
<tr>
<td></td>
<td>150+ on assessment methods and verification</td>
</tr>
</tbody>
</table>

The health risks of smoking are well established and supported by epidemiological evidence (IARC 2004, 2007)
The health risks of smoking and the reversal of risks after quitting smoking are well established (IARC 2004, 2007)
The health risks of smoking and the reversal of risks after quitting smoking are well established (IARC 2004, 2007)
The health risks of switching should be lower than those of smoking. Cessation is the ‘gold standard’ for risk reduction (IOM, 2012)
Differences Between IQOS Aerosol and Cigarette Smoke

Smoke and aerosol were collected on a Cambridge filter pad using Health Canada Intense smoking regime.

- Water and glycerin form 50% of smoke mass
- Toxicants
- Contains Carbon-based solid particles

- Water and glycerin form 90% of aerosol mass
- Toxicants reduced by >90%
- **No** Carbon-based solid particles

Water and glycerin form 50% of smoke mass

Toxicants

Contains Carbon-based solid particles

Water and glycerin form 90% of aerosol mass

Toxicants reduced by >90%

**No** Carbon-based solid particles
IQOS Does Not Emit Carbon-Based Solid Particles

Cigarette smoke
Carbon-based nanoparticles
Median diameter = 75 nm
Amount: $6 \times 10^{11}$ particles $\approx$ 0.7 mg*

Blank
(Air)

IQOS aerosol
No solid particles

* Under the Health Canada’s Intense Smoking Regime.


Scanning Electron Microscopy images of the collected smoke/aerosol after passing through a thermodenuder set at 300º C to remove the volatile portion / collected material characterized by Electron Diffusive X-ray.
IQOS Releases Less Toxicants than Cigarettes

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

**3R4F**
- ca. 4330 constituents ≥ 100 ng/stick
- 3 constituents unique to IQOS aerosol
- 50 constituents more abundant in IQOS than 3R4F
- Abundance equivalent to, or lower than, 3R4F

**IQOS Regular**
- ca. 750 constituents ≥ 100 ng/stick
- 50 constituents more abundant in IQOS than 3R4F

Constituents of toxicological concern:
- Glycidol (IARC 2A)
- 2-Furanemethanol (IARC 2B)
- 3-Monochloro-1,2-propanediol (IARC 2B)
- Furfural (IARC 3)

Exposure from IQOS is below the level of concern.
Reductions of Toxicants by Disease Category

<table>
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<th>Category</th>
<th>% of Reference Cigarette</th>
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<tbody>
<tr>
<td>Carcinogens in IARC Group 1</td>
<td>97%</td>
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<tr>
<td>Carcinogens (FDA)</td>
<td>93%</td>
</tr>
<tr>
<td>Cardiovascular toxicants (FDA)</td>
<td>92%</td>
</tr>
<tr>
<td>Respiratory Toxicants (FDA)</td>
<td>92%</td>
</tr>
<tr>
<td>Reproductive and Developmental Toxicants (FDA)</td>
<td>94%</td>
</tr>
</tbody>
</table>

Number of toxicants

- Carcinogens in IARC Group 1: 12
- Carcinogens (FDA): 29
- Cardiovascular toxicants (FDA): 8
- Respiratory Toxicants (FDA): 18
- Reproductive and Developmental Toxicants (FDA): 7

Note: Intense Health Canada’s Smoking Regime; Comparison on a per-stick basis; Excludes Nicotine
Study Design
Reduced Exposure in Healthy Human Subjects

Ad libitum Use

Confinement

Ambulatory

Continued Cigarette Smoking (n=40)

Switching to IQOS (n=80)

Smoking Abstinence (n=40)

Safety Follow-up Period

Study Day

Day -2

Day -1

Day 1 to 5

Day 6 to 90

Sample Collection

-1

1 2 3 4 5

30

60

90

Measurements: 16 Biomarkers of Exposure; Nicotine and its metabolites
Smoker Acceptance of IQOS is Similar to Cigarettes
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
Changes in Exposure to HPHCs with IQOS Use
Reduced Exposure in Healthy Human Subjects

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Leads to

Exposure is Significantly Reduced After Switching to IQOS

* On equivalent nicotine basis
Changes in Exposure to HPHCs with IQOS Use
Reduced Exposure in Healthy Human Subjects

HPHCs are Drastically Reduced in IQOS Aerosol

Exposure is Significantly Reduced After Switching to IQOS

- 98.6%*

Cigarette
IQOS
Smoking Abstinence

* On equivalent nicotine basis
Changes in Exposure to HPHCs with IQOS Use
Reduced Exposure in Healthy Human Subjects

HPHCs are Drastically Reduced in IQOS Aerosol

Exposure is Significantly Reduced After Switching to IQOS

- Acrolein (µg/stick)
  - Cigarette: 161, Reduced to 9.32 (94.2%*)
  - IQOS: 33.3, Reduced to 0.48 (98.6%*)

- Carbon monoxide (mg/stick)
  - Cigarette: 100, Reduced to 2 (98.6%*)
  - IQOS: 5, Reduced to 0.02 (99.8%*)

- 3-HMA (ng/mg creat)
  - Cigarette: 900, Reduced to 20 (99.8%*)
  - IQOS: 30, Reduced to 1 (99.7%*)

* On equivalent nicotine basis
Changes in Exposure to HPHCs with IQOS Use
Reduced Exposure in Healthy Human Subjects

HPHCs are Drastically Reduced in IQOS Aerosol

Exposure is Significantly Reduced After Switching to IQOS

- 97.2%*

- 98.0%*

Leads to

Leads to

* On equivalent nicotine basis
Reduced Exposure Compared to Cigarettes
Reduced Exposure in Healthy Human Subjects

Percent of Cigarette Exposure

IQOS

Cigarettes

Reduced Exposure Compared to Cigarettes
Reduced Exposure in Healthy Human Subjects

Percent of Cigarette Exposure

IQOS

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Reduced Exposure Compared to Cigarettes
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Reduced Exposure Compared to Cigarettes
Reduced Exposure in Healthy Human Subjects

Percent of Cigarette Exposure

IQOS

Cigarettes
Reduced Exposure Similar to Smoking Abstinence
Reduced Exposure in Healthy Human Subjects

<table>
<thead>
<tr>
<th>Compound</th>
<th>IQOS</th>
<th>Smoking Abstinence</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - to 1</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td>1 - 0.3</td>
<td>10%</td>
<td>7%</td>
</tr>
<tr>
<td>2 - 0.5</td>
<td>15%</td>
<td>12%</td>
</tr>
<tr>
<td>Total</td>
<td>35%</td>
<td>21%</td>
</tr>
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</table>

IQOS: Reduced Exposure in Healthy Human Subjects
Smoking Abstinence: IQOS

Graph showing the percent of cigarette exposure with 95% CI.
Switching to IQOS achieves almost 95% of the reduction achieved by smoking abstinence.
Demonstrated Reduced Exposure

Smoking
- Toxic Emissions
- Exposure
- Molecular Changes
- Disruption of Biological Mechanism
- Cell / Tissue Changes
- Disease
- Population Harm

Cessation
- Exposure
- Molecular Changes
- Disruption of Biological Mechanism
- Cell / Tissue Changes
- Disease
- Population Harm

IQOS
- Toxic Emissions
- Exposure
- Molecular Changes
- ?
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

**Group**
- Cigarette
- IQOS Switching
- Cessation
- IQOS
- Reference: Air

**Exposure**
- 3R4F
- IQOS at equivalent nicotine concentration
- Fresh Air

## Reduced Molecular Changes in the Lung

### Gene Expression in Lung Tissue at Month 8

<table>
<thead>
<tr>
<th>Proteins in Bronchoalveolar Lavage Fluid</th>
<th>Reference Cigarette</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgA</td>
<td>* * * * *</td>
</tr>
<tr>
<td>IL_1_alpha</td>
<td>* * * * *</td>
</tr>
<tr>
<td>IL_1_beta</td>
<td>* * * * *</td>
</tr>
<tr>
<td>IL_6</td>
<td>* * * * *</td>
</tr>
<tr>
<td>IL_7</td>
<td>* * * * *</td>
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<tr>
<td>IL_10</td>
<td>* * * * *</td>
</tr>
<tr>
<td>IL_11</td>
<td>* * * * *</td>
</tr>
<tr>
<td>IL_12p70</td>
<td>* * * * *</td>
</tr>
<tr>
<td>IL_18</td>
<td>* * * * *</td>
</tr>
<tr>
<td>Insulin</td>
<td>* * * * *</td>
</tr>
<tr>
<td>IP_10</td>
<td>* * * * *</td>
</tr>
<tr>
<td>KC_GRO</td>
<td>* * * * *</td>
</tr>
<tr>
<td>Leptin</td>
<td>* * * * *</td>
</tr>
<tr>
<td>LIF</td>
<td>* * * * *</td>
</tr>
<tr>
<td>Lymphotactin</td>
<td>* * * * *</td>
</tr>
<tr>
<td>M_CSF_1</td>
<td>* * * * *</td>
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<tr>
<td>MCP_1</td>
<td>* * * * *</td>
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</tr>
<tr>
<td>MMP_9</td>
<td>* * * * *</td>
</tr>
<tr>
<td>MPO</td>
<td>* * * * *</td>
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</table>

* p-value <0.05

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Reduced Molecular Changes in the Lung

<table>
<thead>
<tr>
<th>Proteins in Bronchoalveolar Lavage Fluid</th>
<th>Reference Cigarette</th>
<th>IQOS Switch</th>
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<tbody>
<tr>
<td>IgA</td>
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Reduced Molecular Changes in the Lung

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<table>
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<tr>
<th></th>
<th>Reference Cigarette</th>
<th>IQOS Switch</th>
<th>Cessation</th>
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<tbody>
<tr>
<td>Time (months)</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
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<td>*</td>
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<tr>
<td>MCP_5</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>MDC</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>MIP_1_alpha</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>MIP_1_beta</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>MIP_1_gamma</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>MIP_2</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>MIP_2_beta</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>MMP_9</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>MPO</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

* p-value <0.05

Reduced Molecular Changes in the Lung

<table>
<thead>
<tr>
<th>Proteins in Bronchoalveolar Lavage Fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference Cigarette</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>IgA</td>
</tr>
<tr>
<td>IL_1_alpha</td>
</tr>
<tr>
<td>IL_1_beta</td>
</tr>
<tr>
<td>IL_6</td>
</tr>
<tr>
<td>IL_7</td>
</tr>
<tr>
<td>IL_10</td>
</tr>
<tr>
<td>IL_11</td>
</tr>
<tr>
<td>IL_12p70</td>
</tr>
<tr>
<td>IL_18</td>
</tr>
<tr>
<td>Insulin</td>
</tr>
<tr>
<td>IP_10</td>
</tr>
<tr>
<td>KC_GRO</td>
</tr>
<tr>
<td>Leptin</td>
</tr>
<tr>
<td>LIF</td>
</tr>
<tr>
<td>Lymphotactin</td>
</tr>
<tr>
<td>M_CS1</td>
</tr>
<tr>
<td>MCP_1</td>
</tr>
<tr>
<td>MCP_3</td>
</tr>
<tr>
<td>MCP_5</td>
</tr>
<tr>
<td>MDC</td>
</tr>
<tr>
<td>MIP_1_alpha</td>
</tr>
<tr>
<td>MIP_1_beta</td>
</tr>
<tr>
<td>MIP_1_gamma</td>
</tr>
<tr>
<td>MIP_2</td>
</tr>
<tr>
<td>MIP_2_beta</td>
</tr>
<tr>
<td>MMP_9</td>
</tr>
<tr>
<td>MPO</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IQOS Switch</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cessation</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IQOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
</tbody>
</table>

* p-value <0.05

Demonstrated Reduced Molecular Changes

**Smoking**

- Toxic Emissions
- Exposure
- Molecular Changes
- Disruption of Biological Mechanism
- Cell / Tissue Changes
- Disease
- Population Harm

**Cessation**

- Exposure
- Molecular Changes
- Disruption of Biological Mechanism
- Cell / Tissue Changes
- Disease
- Population Harm

**IQOS**

- Toxic Emissions
- Exposure
- Molecular Changes
- Disruption of Biological Mechanism
- ?
Reduced Effects on Disease Mechanisms

Lung Inflammation

Mechanism Disruption (% ± SEM)

Time (months) 1 2 3 6 8

Cigarette
Reduced Effects on Disease Mechanisms

**Lung Inflammation**

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>Mechanism Disruption (% ± SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td>80</td>
</tr>
<tr>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>8</td>
<td>100</td>
</tr>
</tbody>
</table>

- **Cigarette**
- **IQOS Switch**
- **Cessation**
Reduced Effects on Disease Mechanisms

Lung Inflammation

Mechanism Disruption (% ± SEM)

Time (months)

1 2 3 6 8 3 6 8 1 2 3 6 8
Cigarette  IQOS Switch  Cessation  IQOS
Specific Markers of Lung Inflammation

Reduced Effects on Disease Mechanisms

Cell Stress

Cell Fate & Apoptosis

Cell Proliferation

Tissue Repair & Angiogenesis

Mechanism Disruption (% ± SEM)
Clinical Changes After 90 Days of Cessation
Reduced Exposure in Healthy Human Subjects

<table>
<thead>
<tr>
<th>Disease Pathway</th>
<th>Endpoint</th>
<th>Abstinence Effect at 3m [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid Metabolism</td>
<td>HDL-C</td>
<td>$0.0 \text{ mg/dL} [-5.77; 5.84]$</td>
</tr>
<tr>
<td>Inflammation</td>
<td>WBC</td>
<td>$-0.94 \times 10^9/\text{L} [-2.00; 0.13]$</td>
</tr>
<tr>
<td>Airway Impairment</td>
<td>FEV$_1$</td>
<td>$2.0 % \text{ pred} [-3.37; 7.36]$</td>
</tr>
<tr>
<td>Endothelial Dysfunction</td>
<td>sICAM-1</td>
<td>$-9.9 % [-19.7; 1.1]$</td>
</tr>
<tr>
<td>Oxidative Stress</td>
<td>8-epi-PGF$_2\alpha$</td>
<td>$-8.5 % [-25.13; 11.8]$</td>
</tr>
<tr>
<td>Clotting</td>
<td>11-DTX-B$_2$</td>
<td>$-7.2 % [-37.7; 38.3]$</td>
</tr>
</tbody>
</table>

Smoking Abstinence:

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

Changes are in the expected direction upon cessation.
## Clinical Changes After 90 Days
Reduced Exposure in Healthy Human Subjects

<table>
<thead>
<tr>
<th>Disease Pathway</th>
<th>Endpoint</th>
<th>Abstinence Effect at 3m [95% CI]</th>
<th>Switching to IQOS Effect at 3m [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid Metabolism</td>
<td>HDL-C</td>
<td>0.0 mg/dL [-5.77; 5.84]</td>
<td>1.4 mg/dL [-2.3;5.0]</td>
</tr>
<tr>
<td>Inflammation</td>
<td>WBC</td>
<td>-0.94 10^9/L [-2.00; 0.13]</td>
<td>-</td>
</tr>
<tr>
<td>Airway Impairment</td>
<td>FEV₁</td>
<td>2.0 % pred [-3.37; 7.36]</td>
<td>0.53 % pred [-2.79; 3.85]</td>
</tr>
<tr>
<td>Endothelial Dysfunction</td>
<td>sICAM-1</td>
<td>-9.9 % [-19.7;1.1]</td>
<td>-10.6 % [-16.7; -4.0]</td>
</tr>
<tr>
<td>Oxidative Stress</td>
<td>8-epi-PGF₂α</td>
<td>-8.5 % [-25.13; 11.8]</td>
<td>-13.5 % [-23.6; -1.9]</td>
</tr>
<tr>
<td>Clotting</td>
<td>11-DTX-B₂</td>
<td>-7.2 % [-37.7; 38.3]</td>
<td>-3.6 % [-24.6; 23.3]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease Pathway</th>
<th>Endpoint</th>
<th>Abstinence Effect at 3m [95% CI]</th>
<th>Switching to IQOS Effect at 3m [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid Metabolism</td>
<td>HDL-C</td>
<td>6.4 mg/dL [2.5; 10.3]</td>
<td>4.5 mg/dL [1.17, 7.88]</td>
</tr>
<tr>
<td>Inflammation</td>
<td>WBC</td>
<td>-0.41 10^9/L [-0.95; 0.14]</td>
<td>-0.57 10^9/L [-1.04, -0.10]</td>
</tr>
<tr>
<td>Airway Impairment</td>
<td>FEV₁</td>
<td>1.94 % pred [-0.44; 4.31]</td>
<td>1.91 % pred [-0.14, 3.97]</td>
</tr>
<tr>
<td>Endothelial Dysfunction</td>
<td>sICAM-1</td>
<td>-10.9 % [-17.8; -3.4]</td>
<td>-8.7 % [-14.94; -2.05]</td>
</tr>
<tr>
<td>Oxidative Stress</td>
<td>8-epi-PGF₂α</td>
<td>-5.9 % [-17.1; 6.8]</td>
<td>-12.7 % [-21.81; -2.55]</td>
</tr>
<tr>
<td>Clotting</td>
<td>11-DTX-B₂</td>
<td>-19.4 % [-30.1; -7.0]</td>
<td>-8.98 % [-19.52, 2.94]</td>
</tr>
</tbody>
</table>
Demonstrated Reduced Disruption of Biological Mechanisms

Smoking

Toxic Emissions

Exposure → Molecular Changes → Disruption of Biological Mechanism → Cell / Tissue Changes → Disease → Population Harm

Cessation

Exposure → Molecular Changes → Disruption of Biological Mechanism → Cell / Tissue Changes → Disease → Population Harm

IQOS

Toxic Emissions

Exposure → Molecular Changes → Disruption of Biological Mechanism → Cell / Tissue Changes → ?
Reduces the Effects on Cells

Inflammatory Lung Cells in Bronchoalveolar Lavage Fluid

- Fresh Air
- Cigarette
- IQOS Switch
- Cessation
- IQOS

Reduces the Effects on Tissues

Lung Tissue Destructive Index

Time (months) 1 2 3 6 8 1 2 3 6 8 3 6 8 3 6 8 1 2 3 6 8

Fresh Air Cigarette IQOS Switch Cessation IQOS

Demonstrated Reduced Cell & Tissue Changes

Smoking
- Toxic Emissions
- Exposure
- Molecular Changes
- Disruption of Biological Mechanism
- Cell / Tissue Changes
- Disease
- Population Harm

Cessation
- Exposure
- Molecular Changes
- Disruption of Biological Mechanism
- Cell / Tissue Changes
- Disease
- Population Harm

IQOS
- Toxic Emissions
- Exposure
- Molecular Changes
- Disruption of Biological Mechanism
- Cell / Tissue Changes
- Disease
- ?
Reduces the Risk of Disease *in vivo*

**Disease Endpoint for COPD**

**Lung Emphysema**

Data from Histology after 8 months

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>Fresh Air</th>
<th>Cigarette</th>
<th>IQOS Switch</th>
<th>Cessation</th>
<th>IQOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>6</td>
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<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Reduces the Risk of Disease *in vivo*

Disease Endpoint for CVD

Atherosclerotic Plaque in the Aortic Arch

Data from μCT at month 7

---

**Plaque surface area (mm²)**

- Fresh Air
- Cigarette smoke
- IQOS Switch
- Cessation
- IQOS

**Aorta mean occlusion (%)**

- Fresh Air
- Cigarette smoke
- IQOS Switch
- Cessation
- IQOS

**Plaque volume (mm³)**

- Fresh Air
- Cigarette smoke
- IQOS Switch
- Cessation
- IQOS

---


*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.*
How Cigarette Smoke Causes Cancer

Genetic damage
“the match that lights the fire”*

Carcinogens

Questions
Does switching from cigarettes to IQOS
1. Reduce Genetic damage?
2. Reduce Inflammation?
3. Reduce the risk of lung cancer?

Inflammation
“fuel that feeds the flames”*

Nanoparticles**
HPHCs

Tumor progression & Invasiveness***

Cancer

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 Genotoxicity
- Reduced DNA Damage

Reduced Genetic Damage

Nanoparticles Deposit in the Lung

Cigarette Smoke
Carbon-based nanoparticles
$6 \times 10^{11}$ particles $\approx 0.7$ mg*

IQOS Aerosol
No solid particles

Lung Deposition after 6 months

Cigarette smoke (600 mg/m$^3$ TPM)

Corresponding concentration of IQOS aerosol

Apoe/- mice exposed for 6 months, 3h/day and 5days/week.
Inflammatory Markers in Smokers’ Lungs

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

<table>
<thead>
<tr>
<th>Cell type</th>
<th>BAL concentration ( \times 10^3 ) cells \text{mL}^{-1}</th>
<th>Smokers (n=14)</th>
<th>Nonsmokers (n=16)</th>
<th>F statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrophage</td>
<td>524±219</td>
<td>220±98</td>
<td>25.1</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>Neutrophil</td>
<td>12.9±13.3</td>
<td>2.1±1.6</td>
<td>10.6</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>Lymphocyte</td>
<td>7.3±7.5</td>
<td>14.8±17.7</td>
<td>2.2</td>
<td>1.15</td>
<td></td>
</tr>
<tr>
<td>Eosinophil</td>
<td>0.9±1.7</td>
<td>1.1±1.3</td>
<td>0.1</td>
<td>0.75</td>
<td></td>
</tr>
<tr>
<td>Epithelial</td>
<td>1.5±1.4</td>
<td>2.1±2.1</td>
<td>1.0</td>
<td>0.33</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>BAL constituent</th>
<th>Smokers (n=14)</th>
<th>Nonsmokers (n=16)</th>
<th>F statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-1β pg\text{mL}^{-1}</td>
<td>1.2±0.7</td>
<td>0.5±0.4</td>
<td>14.3</td>
<td>0.0007</td>
</tr>
<tr>
<td>IL-6 pg\text{mL}^{-1}</td>
<td>5.3±3.2</td>
<td>1.9±1.0</td>
<td>17.3</td>
<td>0.0003</td>
</tr>
<tr>
<td>IL-8 pg\text{mL}^{-1}</td>
<td>32.8±15.9</td>
<td>18.2±11.5</td>
<td>8.4</td>
<td>0.007</td>
</tr>
<tr>
<td>TNF-α pg\text{mL}^{-1}</td>
<td>2.5±7.9</td>
<td>0.2±0.2</td>
<td>1.4</td>
<td>0.25</td>
</tr>
<tr>
<td>MCP-1 pg\text{mL}^{-1}</td>
<td>36.7±28.3</td>
<td>13.0±7.7</td>
<td>10.4</td>
<td>0.003</td>
</tr>
<tr>
<td>TP \mu g\text{mL}^{-1}</td>
<td>75.8±27.7</td>
<td>87.2±56.5</td>
<td>0.4</td>
<td>0.50</td>
</tr>
</tbody>
</table>

Values are presented as mean±SD. IL-1β: Interleukin-1β (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 chemotactic protein-1 (non-detectable 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.

Inflammation and Cancer
The Role of Interleukin-1β 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.


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


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

IL-1β

Does Switching to IQOS Reduce Inflammation?

Nanoparticles**

HPHCs

Tumor progression & Invasiveness***

Inflammation

“fuel that feeds the flames”*


Demonstrated Reduced Disease

Smoking
- Toxic Emissions
- Exposure → Molecular Changes → Disruption of Biological Mechanism → Cell / Tissue Changes → Disease → Population Harm

Cessation
- Exposure → Molecular Changes → Disruption of Biological Mechanism → Cell / Tissue Changes → Disease → Population Harm

IQOS
- Toxic Emissions
- Exposure → Molecular Changes → Disruption of Biological Mechanism → Cell / Tissue Changes → Disease
Summary of Totality of Evidence

IQOS
Toxic Emissions

Exposure

Molecular Changes

Disruption of Biological Mechanism

Cell / Tissue Changes

Disease

90-95% less Toxicants

90-95% of Abstinence

90-95% of Cessation

90-95% of Cessation

90-95% of Cessation

90-95% of Cessation
Demonstrate a Benefit to the Health of the Population as a Whole …
Consumer Perception and Behavior

Antonio Ramazzotti
Vice President Human Insights and Behavioral Research
Philip Morris International
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
## Who Will Use IQOS and to What Degree?

<table>
<thead>
<tr>
<th>Adult Smokers</th>
<th>Non-smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Understanding of Messages</strong></td>
<td><strong>Understanding of Messages</strong></td>
</tr>
<tr>
<td>Intent to Use</td>
<td>Increased or Decreased Likelihood of Initiation</td>
</tr>
<tr>
<td>Exclusive Use</td>
<td></td>
</tr>
<tr>
<td>Increased or Decreased Likelihood of Cessation</td>
<td></td>
</tr>
</tbody>
</table>
PBA Studies to Develop and Assess IQOS Messages

6 qualitative and quantitative studies to develop and assess IQOS communications

**Phase 1**
Developing the most appropriate product messages
- Comprehension
- Intent to Use
- Risk Perception

**Phase 2**
Assessing Labeling and Advertising
- Comprehension
- Intent to Use
- Risk Perception

3 Studies

CC-76
Switching completely from cigarettes to the IQOS system can reduce the risks of tobacco-related diseases.

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

Switching completely from cigarettes to the IQOS system significantly reduces your body’s exposure to harmful and potentially harmful chemicals.
Study Design
IQOS Communication Studies

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

IQOS Communication Study - Reduced Risk of Harm

<table>
<thead>
<tr>
<th>Correct Comprehension</th>
<th>Less risk of harm (correct)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HeatSticks Pack PMI Warning n=380</td>
<td>78%</td>
</tr>
<tr>
<td>HeatSticks Pack SG’s Warnings n=376</td>
<td>73%</td>
</tr>
</tbody>
</table>

0% 20% 40% 60% 80% 100%
Only 1% and 2% Misunderstood that IQOS Presents “No Risk of Harm”

IQOS Communication Study - Reduced Risk of Harm

<table>
<thead>
<tr>
<th>Correct Comprehension</th>
<th>Less risk of harm (correct)</th>
<th>HeatSticks Pack PMI Warning n=380</th>
<th>HeatSticks Pack SG’s Warnings n=376</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less risk of harm</td>
<td>78%</td>
<td></td>
<td>73%</td>
</tr>
<tr>
<td>The same risk of harm</td>
<td>11%</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>Greater risk of harm</td>
<td>1%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>No risk of harm</td>
<td>2%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>Don’t know</td>
<td>8%</td>
<td>11%</td>
<td></td>
</tr>
</tbody>
</table>

Correct Comprehension

- HeatSticks Pack PMI Warning n=380
- HeatSticks Pack SG’s Warnings n=376

Less risk of harm (correct) 78%

The same risk of harm 11%

Greater risk of harm 1%

No risk of harm 2%

Don’t know 8%
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.

HeatSticks Pack SG’s Warnings
- Definitely: 20%
- Very Likely: 15%

HeatSticks Pack PMI Warning
- Definitely: 28%
- Very Likely: 19%

n=94

n=96
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

- 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.

IMPORTANT WARNING: • Reduced risk does not mean no risk. The best way to reduce your risk of tobacco-related diseases is to completely quit tobacco use. • headtimes” ensures nicotine which is addiction. • Using the IQOS system can harm your health.
15% of U.S. Adult Daily Smokers Switched from Cigarettes to IQOS

IQOS and Cigarettes Use: Observational Period
Actual Use Study

% of Participants by Usage Categories

- **Exclusive Use:** [95-100]% IQOS
- **Predominant Use:** [70-95]% IQOS
- **Combined Use:** [30-70]% IQOS
- **Cigarette Use:** [0-30]% IQOS

Week 1 (n= 1,106)
- 7%
- 12%
- 39%

Week 2 (n= 1,061)
- 8%
- 9%
- 42%

Week 3 (n= 1,038)
- 9%
- 8%
- 52%

Week 4 (n= 1,009)
- 8%
- 8%
- 57%

Week 5 (n= 997)
- 7%
- 9%
- 60%

Week 6 (n= 968)
- 8%
- 7%
- 63%

15%
No Increase in IQOS and Cigarettes Consumption Between Baseline and Observational Period

Actual Use Study: IQOS + Cigarette Consumption

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Observational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exclusive or Predominant IQOS Use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=141</td>
<td>9.0</td>
<td>6.7</td>
</tr>
<tr>
<td>(Stick/Day–Total)</td>
<td>8.1</td>
<td>1.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Observational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined IQOS Use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=217</td>
<td>9.3</td>
<td>4.1</td>
</tr>
<tr>
<td>(Stick/Day–Total)</td>
<td>8.9</td>
<td>4.8</td>
</tr>
</tbody>
</table>

- '# of Cigarettes'
- '# of IQOS'
Between 12% and 30% of Participants Switched to IQOS

IQOS Usage Patterns

<table>
<thead>
<tr>
<th>Country</th>
<th>Cigarette Use: [0-30]% IQOS</th>
<th>Predominant Use: [70-95]% IQOS</th>
<th>Combined Use: [30-70]% IQOS</th>
<th>Exclusive Use: [95-100]% IQOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan</td>
<td>38%</td>
<td>32%</td>
<td>14%</td>
<td>16%</td>
</tr>
<tr>
<td>Italy</td>
<td>50%</td>
<td>38%</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>US</td>
<td>63%</td>
<td>22%</td>
<td>8%</td>
<td>7%</td>
</tr>
</tbody>
</table>

Japan (n=638), Italy (n=535), US (n=968)
Post-market Data Show Exclusive Use is the Most Common Behavior Among IQOS Purchasers

% of Participants by Usage Categories

Japan (n=6,925)
- Exclusive Use: 72%
- Predominant Use: 8%
- Combined Use: 9%
- Cigarette Use: 11%

Italy (n=4,197)
- Exclusive Use: 61%
- Predominant Use: 13%
- Combined Use: 11%
- Cigarette Use: 15%

Consumer Panels, August 2017
Increased Awareness and Repeated Communication Lead to Higher Switching Rates

Source: Consumer Panel Japan, March 2016

**Exclusive Use at Week 3 by Month of IQOS Purchase - Japan**

- **Sept 2015**: 35%
- **Nov 2015**: 49%
- **Jan 2016**: 56%
- **Mar 2016**: 61%

Source: Consumer Panel Japan, March 2016
Who Will Use IQOS and to What Degree?

<table>
<thead>
<tr>
<th>Adult Smokers</th>
<th>Non-smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Understanding of Messages</strong></td>
<td><strong>Understanding of Messages</strong></td>
</tr>
<tr>
<td>Intent to Use</td>
<td>Increased or Decreased Likelihood of Initiation</td>
</tr>
<tr>
<td>Exclusive Use</td>
<td></td>
</tr>
<tr>
<td>Increased or Decreased Likelihood of Cessation</td>
<td></td>
</tr>
</tbody>
</table>
Minimal Interference on Intention to Quit All Tobacco among Adult Smokers with the Intention to Quit

<table>
<thead>
<tr>
<th></th>
<th>HeatSticks Pack</th>
<th>HeatSticks Pack</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SG’s Warnings</td>
<td>PMI Warning</td>
</tr>
<tr>
<td>Pre-Exposure</td>
<td>84%</td>
<td>87%</td>
</tr>
<tr>
<td>Post-Exposure</td>
<td>82%</td>
<td>90%</td>
</tr>
</tbody>
</table>

n=96 for both groups.
Low Levels of Intent to Use Among Adult Never Smokers and LA-25 Never Smokers

IQOS Communication Study - Reduced Risk of Harm

Adult Never Smokers
Positive “Intention to Try”

Legal Age to 25 Years Never Smokers
Positive “Intention to Try”

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
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

Low Levels of Intent to Use Among Adult Former Smokers

IQOS Communication Study - Reduced Risk of Harm

Adult Former Smokers
Positive “Intention to Try”

Percent of Subjects

<table>
<thead>
<tr>
<th>HeatSticks Pack</th>
<th>SG’s Warnings</th>
<th>n=92</th>
</tr>
</thead>
<tbody>
<tr>
<td>HeatSticks Pack</td>
<td>PMI Warning</td>
<td>n=96</td>
</tr>
<tr>
<td>8%</td>
<td>2%</td>
<td></td>
</tr>
</tbody>
</table>
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
U.S. Commercialization and Controls

Sarah Knakmuhs
Vice President, Heated Tobacco Products
Philip Morris USA
“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
IQOS in the U.S.
Behavior Change – IQOS Use

Device Usability

Charging & Cleaning

Taste & Experience
PM USA Marketing Approach for IQOS

Objective

- Awareness: Introduce IQOS
- Trial: Explain Product & Encourage Trial
- Conversion: Support Exclusive Switching

Intended Audience = U.S. Adult Smokers
Build Awareness for IQOS

- Print Advertising
- Direct Mail
- Email
Electronic Age Verification

- **Data Entry**: Consumer inputs data for age and identity
- **Validation**: Match inputs with identity on electronic databases
- **Authentication**: Consumer answers questions to confirm identity
Opportunities for Trial of IQOS

Individual Engagements

Consumer Events

Retail
Trial of IQOS

Verification

Confirm age and identity via government issued ID

Confirmation

Confirm smoking status

Guided Trial

Provide overview and perform guided trial
IQOS Support

- Device Troubleshooting
- HeatStick Availability
- Personal Support
PM USA Marketing Approach for IQOS

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
Post-market Surveillance

Surveillance

- U.S. call center
- IQOS product safety summary
- Literature reviews
- Regulatory reporting systems (FDA/HHS/WHO)
- National poison data system

Adverse Events
Product Misuse

Studies

- Cross-sectional surveys
- Longitudinal cohort study

Consumer Perception & Behavior
Self-Reported Health Measures*

*For Longitudinal Cohort Study
IQOS in the U.S.
Population Modeling and Conclusion

Moira Gilchrist, PhD
Vice President Scientific and Public Communications
Philip Morris International
The PMI Population Health Impact Model

Prevalence Component

Epidemiological Risk Component


The Prevalence Component

Prevalence Component

Hypothetical population based on publicly available databases and scientific literature

Transition probabilities

Validated using published smoking statistics
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
The PMI Population Health Impact Model

Modeling Simulations

Prevalence Component

Epidemiological Risk Component

Mortality Impact Estimates

Benefit to the U.S. Population as a Whole

90% of cessation benefit

15% switching

90,155 Smoking-related deaths averted
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
The IQOS Opportunity
The IQOS Opportunity

• Millions fewer smokers

• Reduced harm and tobacco-related disease

• An important step forward
The IQOS Heating System

Tobacco Products Scientific Advisory Committee

January 24, 2018