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# Heat-not-Burn Products: Scientific Assessment of Risk Reduction

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*Tobacco Merchants Association 2015 Annual Meeting*

*Moira Gilchrist PhD  
Philip Morris International R&D  
May 20th 2015*

# The Objective is Harm Reduction

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## Offering adult smokers satisfying products that reduce risk

- Smoking is addictive and causes a number of serious diseases
- Worldwide it is estimated that more than one billion people will continue to smoke in the foreseeable future\*



- Successful harm reduction requires that current adult smokers be offered a range of Reduced Risk Products so that consumer acceptance can be best fulfilled

\*The Tobacco Atlas 3<sup>rd</sup> Edition. American Cancer Society, 2009  
Figure adapted from Clive Bates presentation to E-Cigarette Summit (19 Nov 2013)  
Note: Reduced-Risk Products ("RRPs") is the term we use to refer to products that have the potential to reduce individual risk and population harm in comparison to smoking combustible cigarettes

# A Range of Alternative Products That Appeal to Adult Smokers is Required



- **Exposure**  
*What level of reduction in exposure to harmful chemicals can be achieved compared to continued cigarette smoking?*
- **Risk**  
*What level of risk reduction can be achieved compared to continued cigarette smoking?*
- **Appeal**  
*Does the product appeal to adult smokers and not appeal to non-smokers?*
- **Behavior**  
*Are smokers willing to fully (or predominantly) switch to the product?*

# Developing Scientific Evidence: An Overview of PMI's Approach

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# Heat-not-Burn

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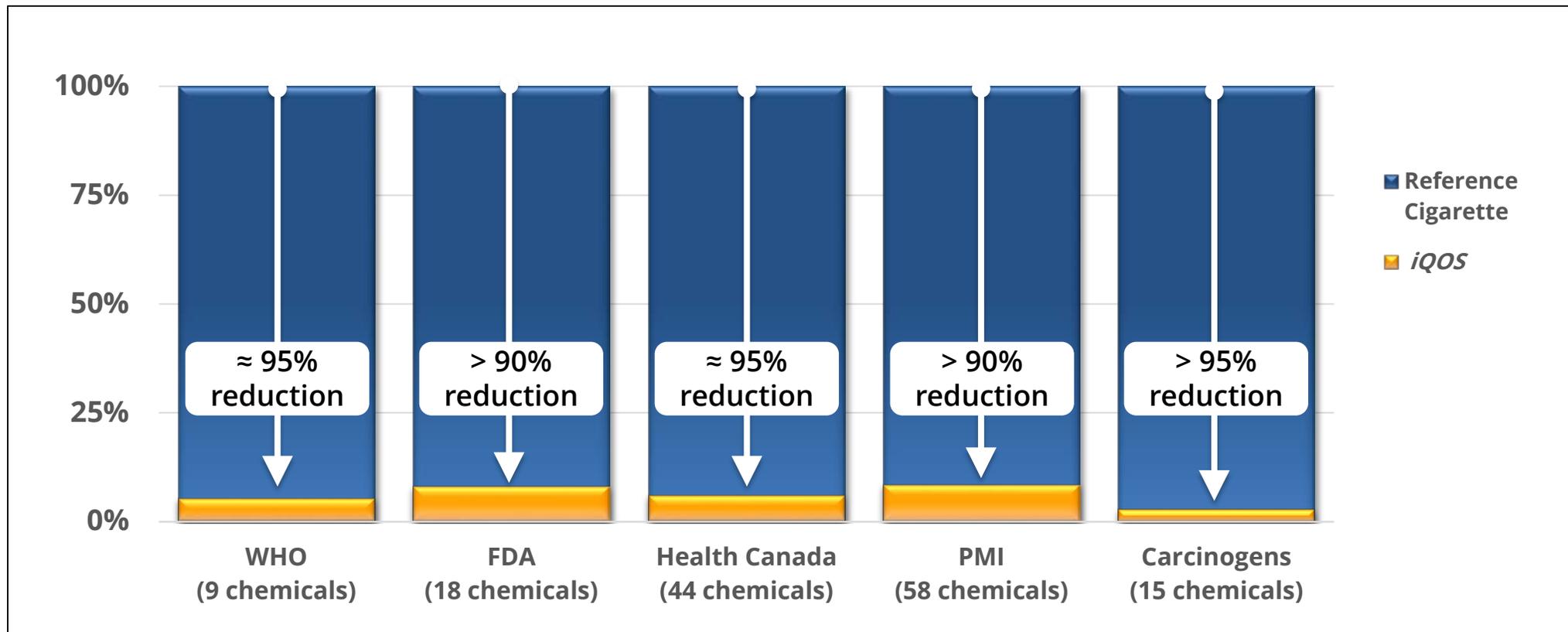
*Product-Specific iQOS Science*



# Reduced Formation

**We have demonstrated that the operation of *iQOS* does not result in the combustion of tobacco.**

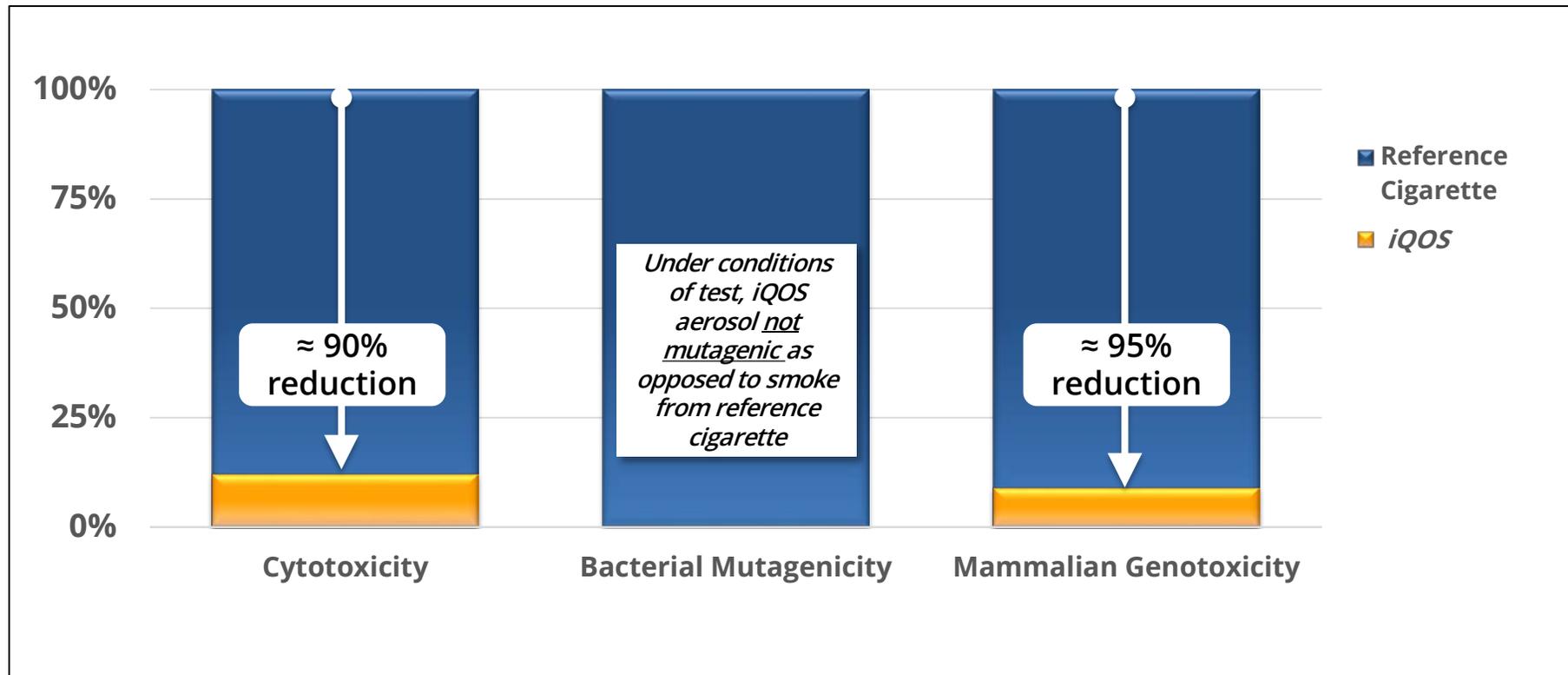
Average reductions in formation of harmful or potentially harmful constituents for *iQOS* compared to levels measured in smoke from the 3R4F reference cigarette\*



\*Aerosol collection with Intense Health Canada's Smoking Regime (55 mL puff volume, 2 second puff duration, 30 second interval puff); Comparison on a per-stick basis  
Reduction calculations exclude Nicotine, Glycerin and Total Particulate Matter

# Reduced Toxicity

Average reductions in toxicity compared to levels measured for the 3R4F reference cigarette. Measured using Neutral Red Uptake, AMES and Mouse Lymphoma Assays

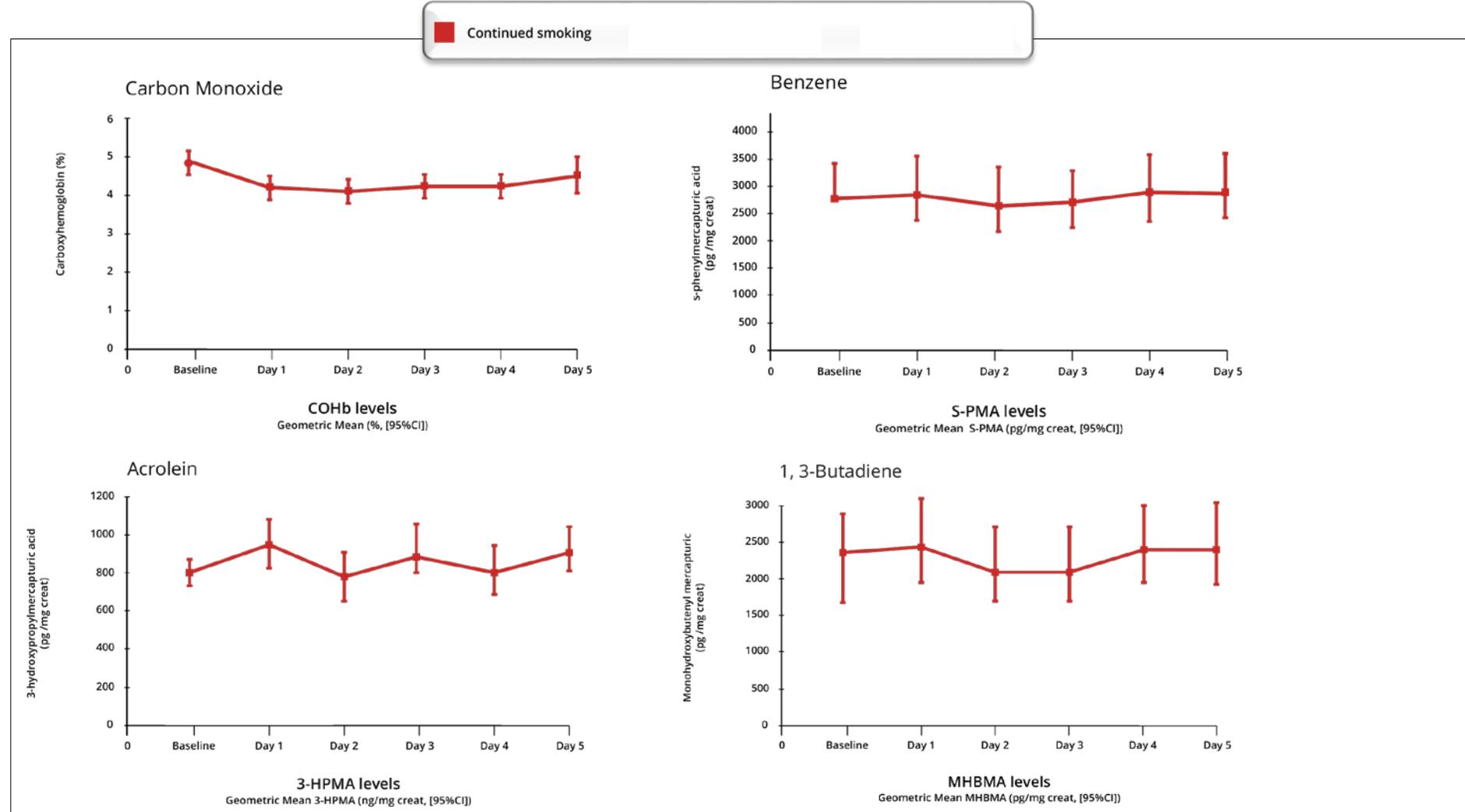


Comparison on a per-nicotine basis  
Note: These data alone do not represent a claim of reduced exposure or reduced risk.  
Source: PMI Research and Development

# Reduced Exposure

Clinical Studies

Smokers used the products *ad libitum*. Smokers randomized to cigarettes or iQOS were free to use the product as often as they wished.

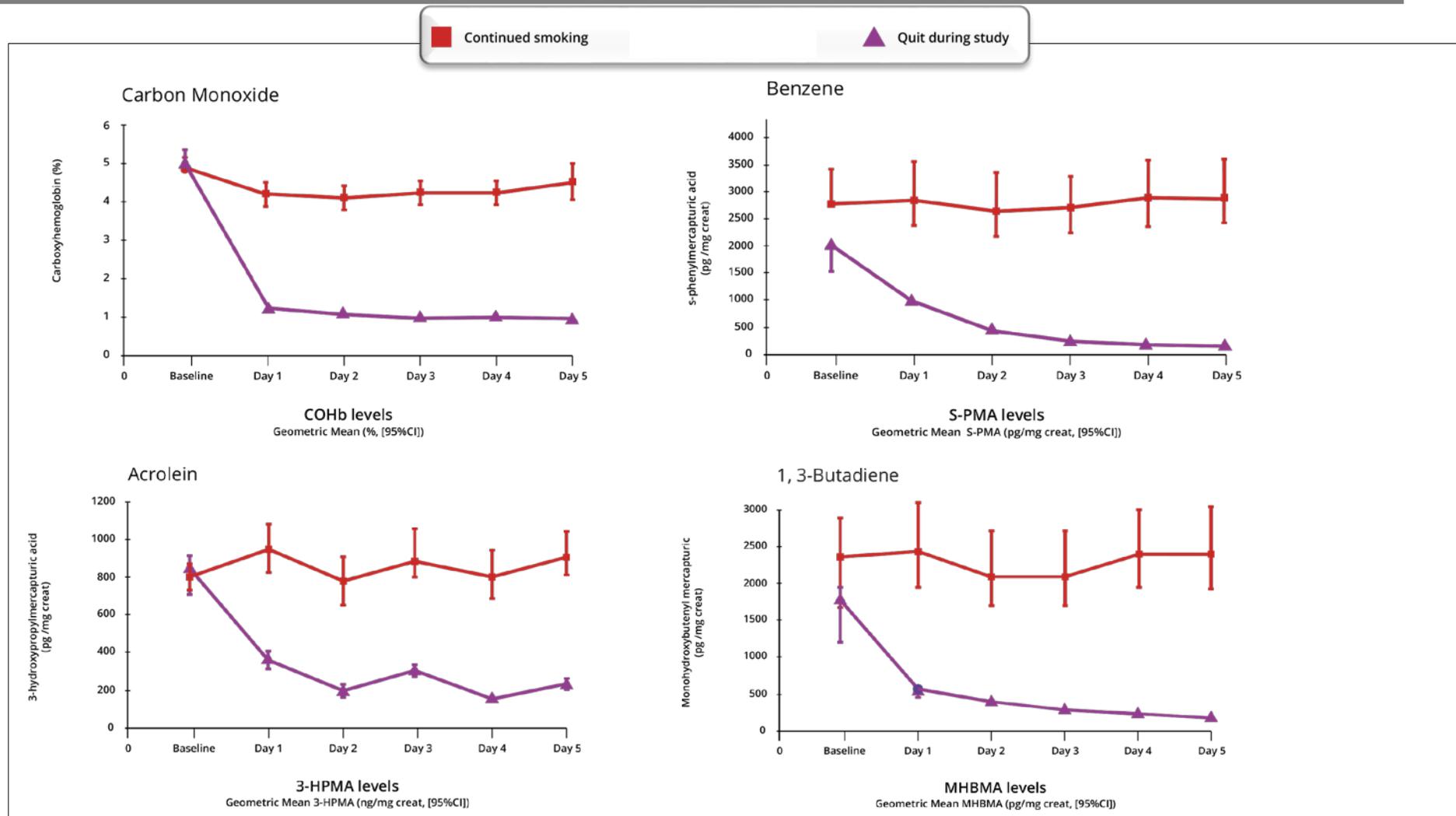


Note: These data alone do not represent a claim of reduced risk.  
Source: PMI Research and Development  
Registered on clinicaltrials.gov: NCT 01959932

# Reduced Exposure

Clinical Studies

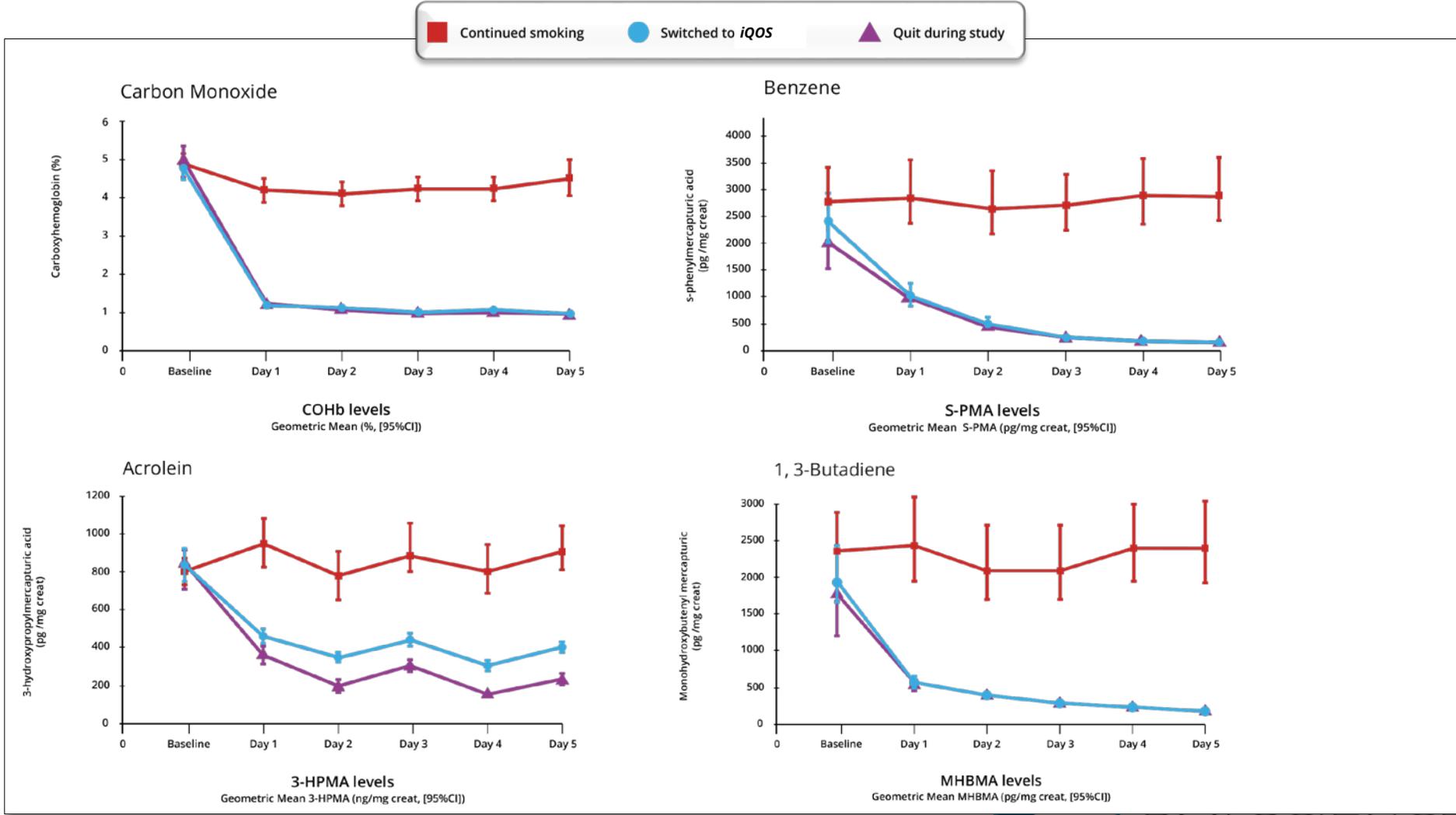
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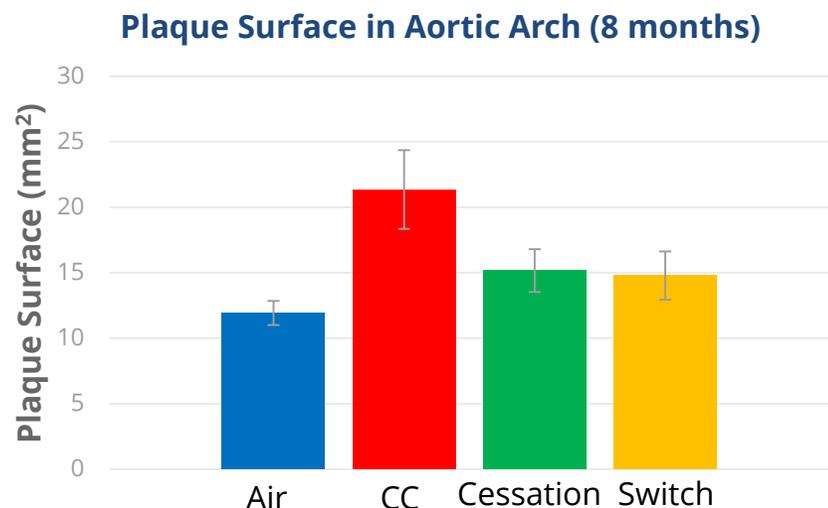
# Reduced Risk

Non-Clinical Studies

Clinical Studies

**Studies using animal models of disease show favorable changes in smoking-related disease endpoints\***

*Markers for Cardiovascular Disease and Chronic Obstructive Pulmonary Disease show changes similar to cessation*



**Human clinical studies verify results obtained in *in vitro* and *in vivo* models**

*Clinical studies provide pivotal data to show whether favorable changes in disease risk markers are achieved under realistic conditions of use*

**Clinical program is on-going**

*Markers known to be associated with smoking-related diseases (including Cardiovascular Disease, Chronic Obstructive Pulmonary Disease and others) are being measured over different timeframes up to 12 months in duration*

*ClinicalTrials.gov Identifiers:  
NCT01970995, NCT01970995, NCT02396381*

\* Systems toxicology analysis of cardiovascular and respiratory endpoints from ApoE<sup>-/-</sup> mice showed similar effects after switching to a candidate modified risk tobacco product, THS 2.2, or to smoking cessation. F1000Posters 2015, 6: 206 (poster).

# Adult Smoker Behavior

## Home Usage Testing

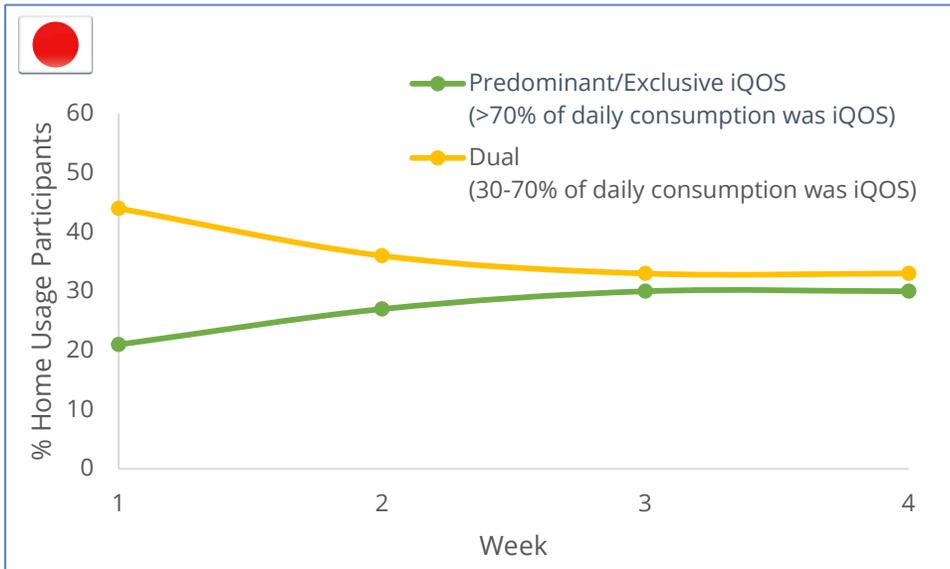


30%



12%

...of home usage participants adopted the product (replaced 70% or more of their daily cigarette consumption with *iQOS*)



**Switching patterns stabilized at 3 weeks**  
*Many smokers were willing to fully or predominantly switch to the product after an initial adjustment period*

# Assessing a Product's Potential to Contribute to Tobacco Harm Reduction

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Consider Evidence for Reduced Risk and Consumer Acceptability



Adult smokers should be informed on the different risk profiles of products, provided that these differences **are substantiated by robust, product-specific scientific evidence**



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Reduced-Risk Products (“RRPs”) is the term the company uses to refer to products with the potential to reduce individual risk and population harm in comparison to smoking combustible cigarettes. PMI’s RRP’s are **in various stages of development and commercialization**, and we are conducting **extensive and rigorous scientific studies** to determine whether we can support claims for such products of reduced exposure to harmful and potentially harmful constituents in smoke, and ultimately claims of reduced disease risk, when **compared to smoking combustible cigarettes**.

Before making any such claims, we will need to **rigorously evaluate the full set of data** from the relevant scientific studies to determine whether they substantiate reduced exposure or risk. Any such claims **may also be subject to government review and approval**, as is the case in the US today.



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## Source: Philip Morris International R&D

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### **Data generated by:**

*Aerosol Chemistry Team*

*Toxicology Team*

*Clinical Team*

*Perception and Behavioral Assessment Team*

### **Statistical and data analytics support:**

*Dr. Maxim Belushkin*