



PMI SCIENCE
PHILIP MORRIS INTERNATIONAL

Heated Tobacco Technology: Science, Behavior and Avoiding Unintended Consequences

Global Forum on Nicotine 2017

*Moir Gilchrist PhD
Philip Morris International
June 16th 2017*

Important Information



PMI SCIENCE
PHILIP MORRIS INTERNATIONAL

Reduced-Risk Products (“RRPs”) is the term we use to refer to products that present, are likely to present, or have the potential to present less risk of harm to smokers who switch to these products versus continued smoking.

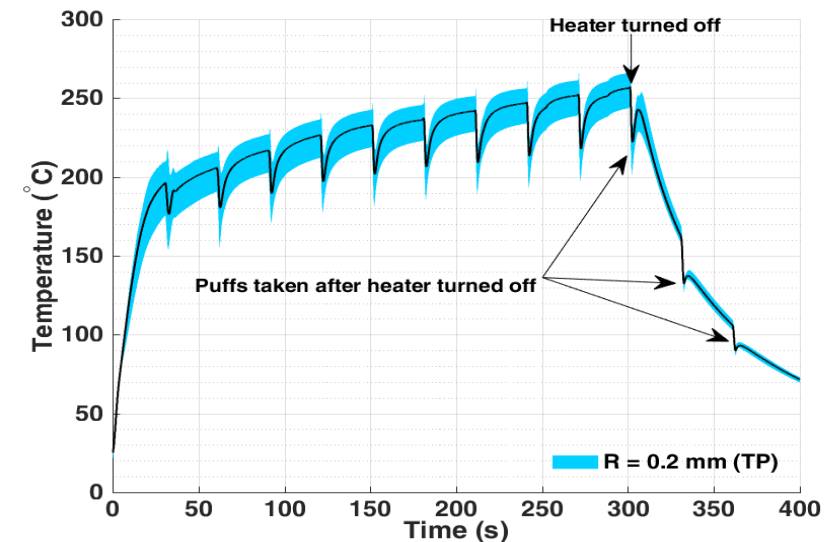
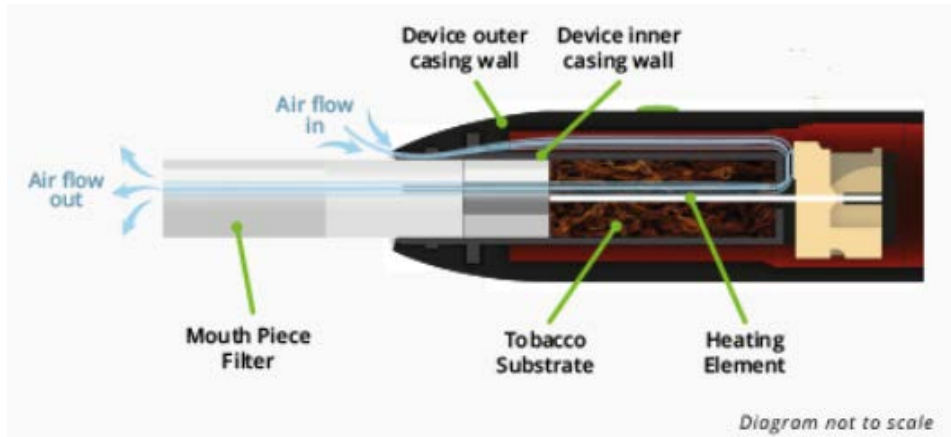
We have a range of RRP s in various stages of development, scientific assessment and commercialization.

Because our RRP s do not burn tobacco, they produce far lower quantities of harmful and potentially harmful compounds than found in cigarette smoke.

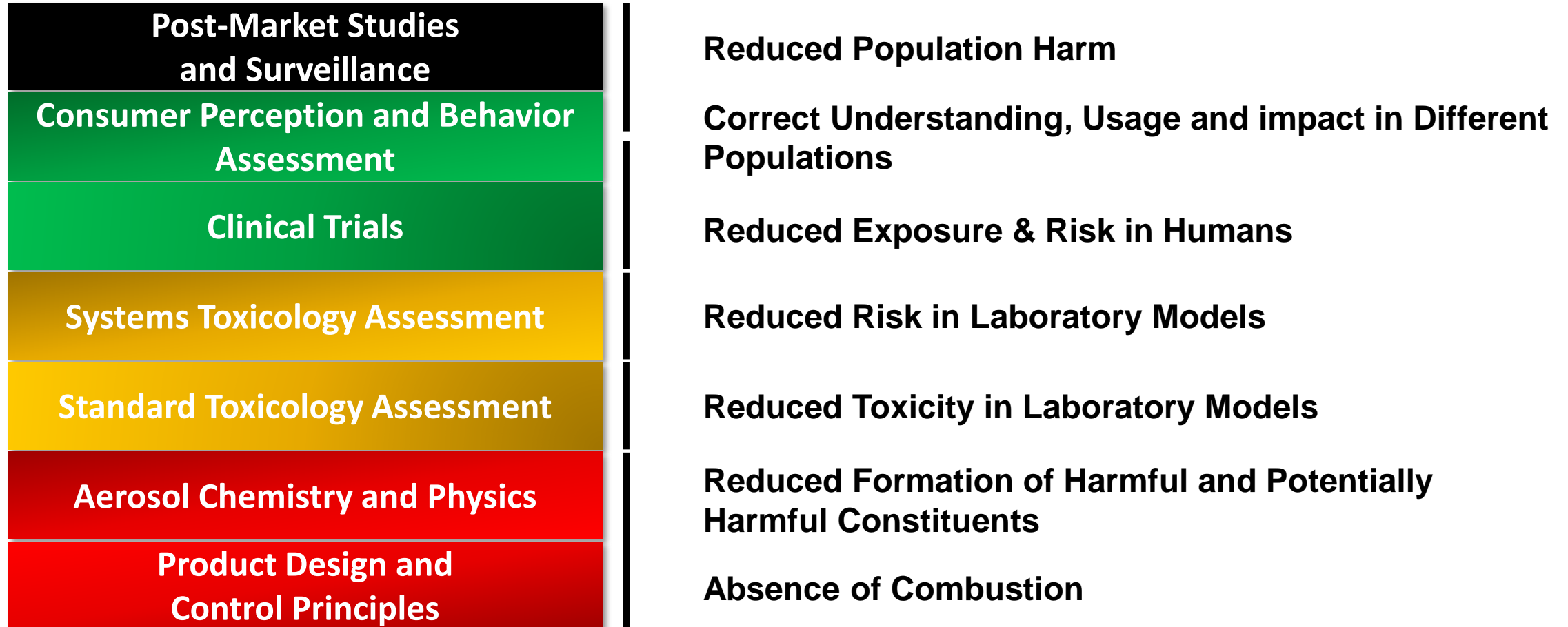
Heating Tobacco Rather than Burning It

The Tobacco Heating System 2.2 (THS2.2, currently commercialized as *IQOS* in >25 countries) is designed and has been demonstrated to:

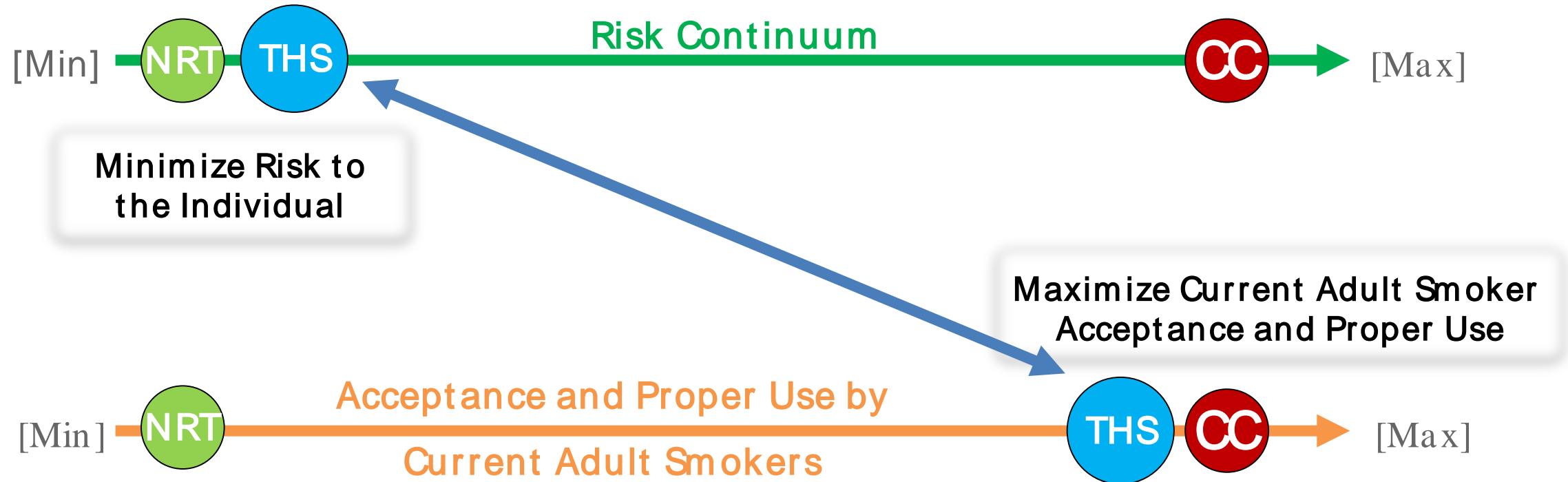
- Heat tobacco without combustion
- Preserve elements of the taste, sensory experience, nicotine delivery profile and ritual characteristics of cigarettes



PMI's Scientific Assessment Approach

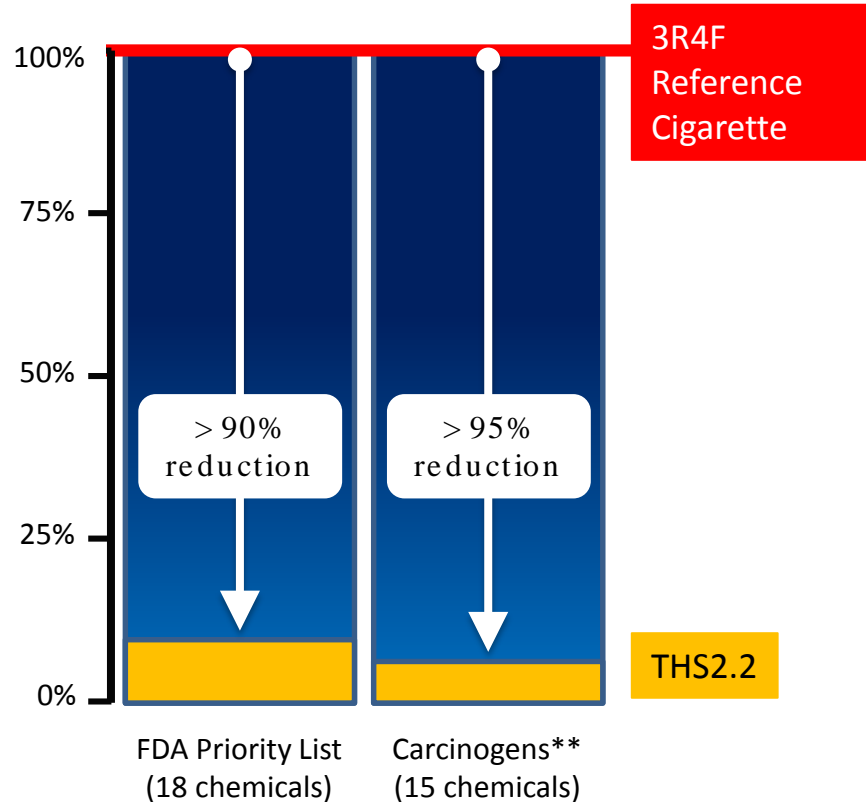


Reduced Harm / Risk Concept: What We Need to Demonstrate for Tobacco Heating System



For Illustration Purposes Only

Reduced Formation: Rationale and Results

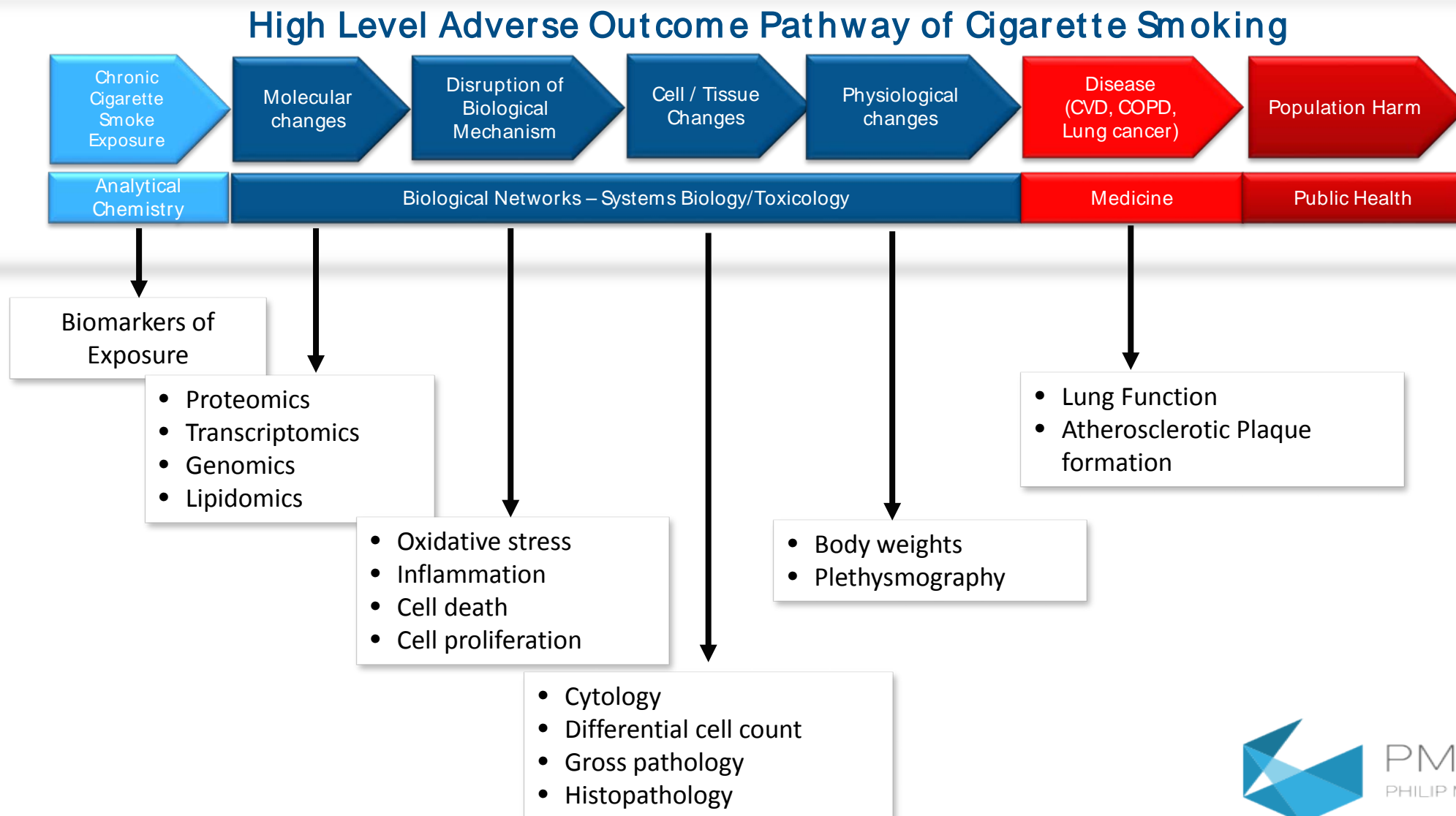


Measured 54 harmful and potentially harmful constituents and 4 additional analytes using validated methods in accredited facilities, both internally and at an independent laboratory.

Health Canada list (total 47)	47
Smoke Constituents with established Biomarkers of Exposure	+2
Smoke Constituents formed < 400°C	+4
Smoke Constituents formed > 400°C	+5

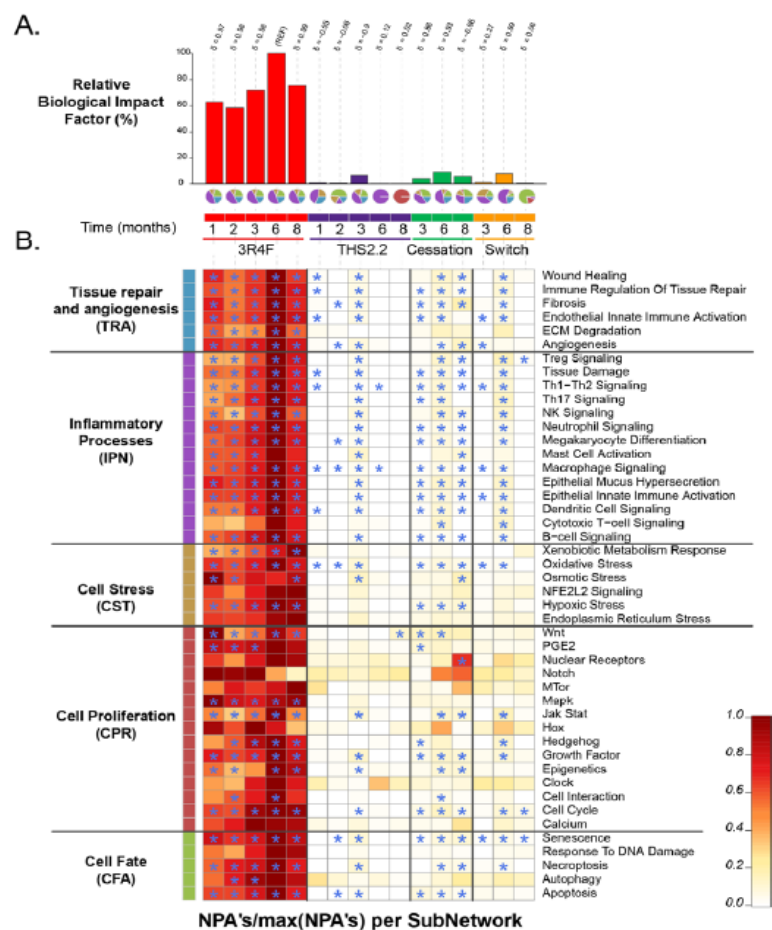
THS2.2 produces an aerosol that contains on average **90-95% lower levels of harmful and potentially harmful chemicals than a reference cigarette.**

Non-Clinical Evidence: Approach and Rationale

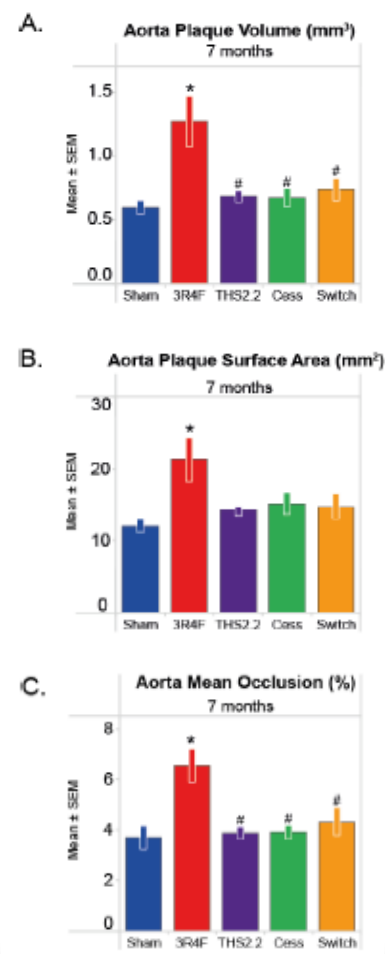


Non-Clinical Evidence: Snapshot of Results

Mechanistic Evidence for Reduced Harm to the Lung



Non-clinical Evidence for Reduced Cardiovascular Disease Risk



in situ aortic arch
plaque
measurements
(μ CT)

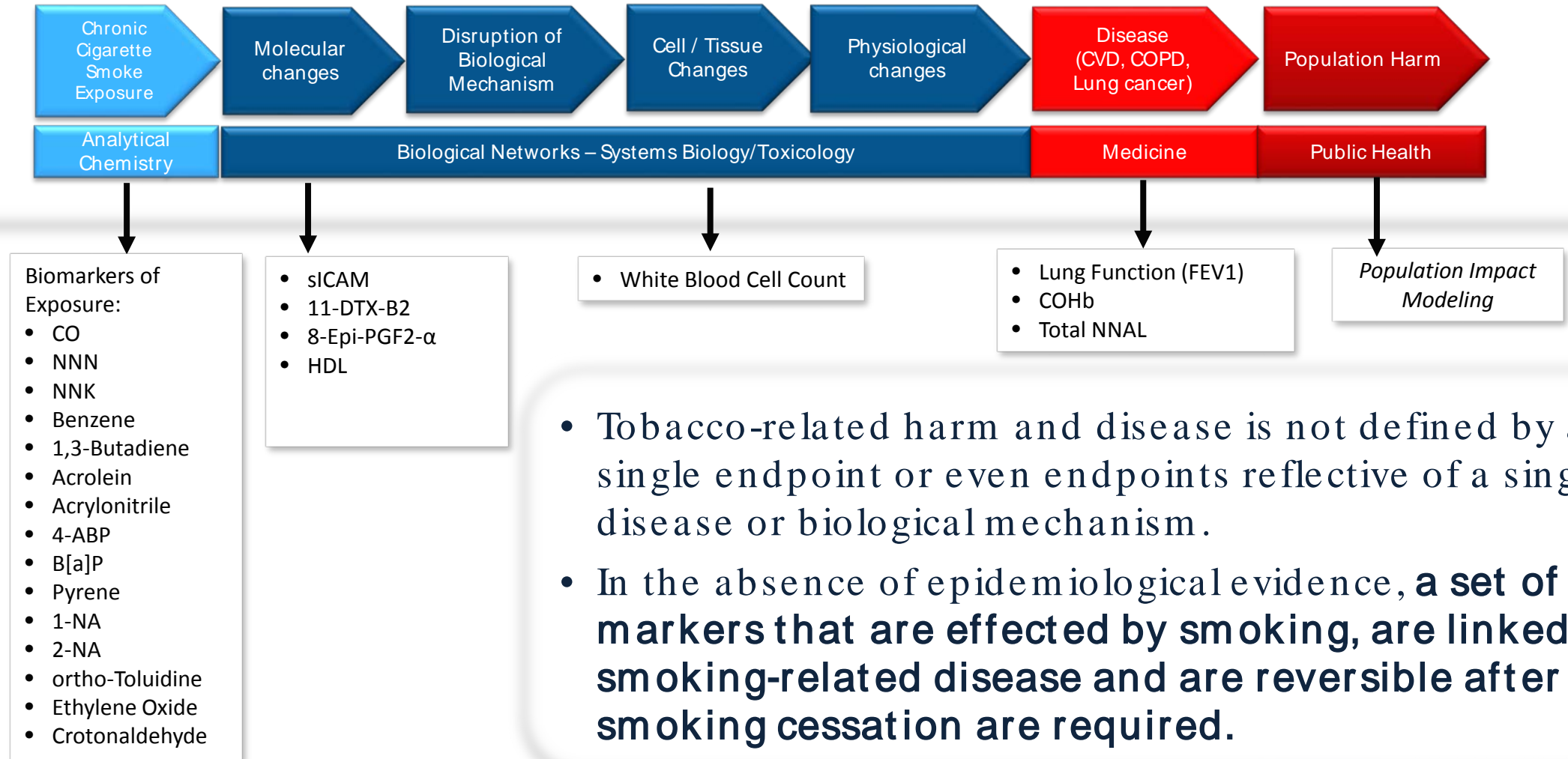
THS2.2 aerosol is over 10 times less active than reference cigarette smoke in key mechanisms leading to lung damage.

In animal models, switching to THS2.2 aerosol from cigarette smoke reduces levels of cardiovascular disease risk markers to levels similar to those seen in a model of smoking cessation.

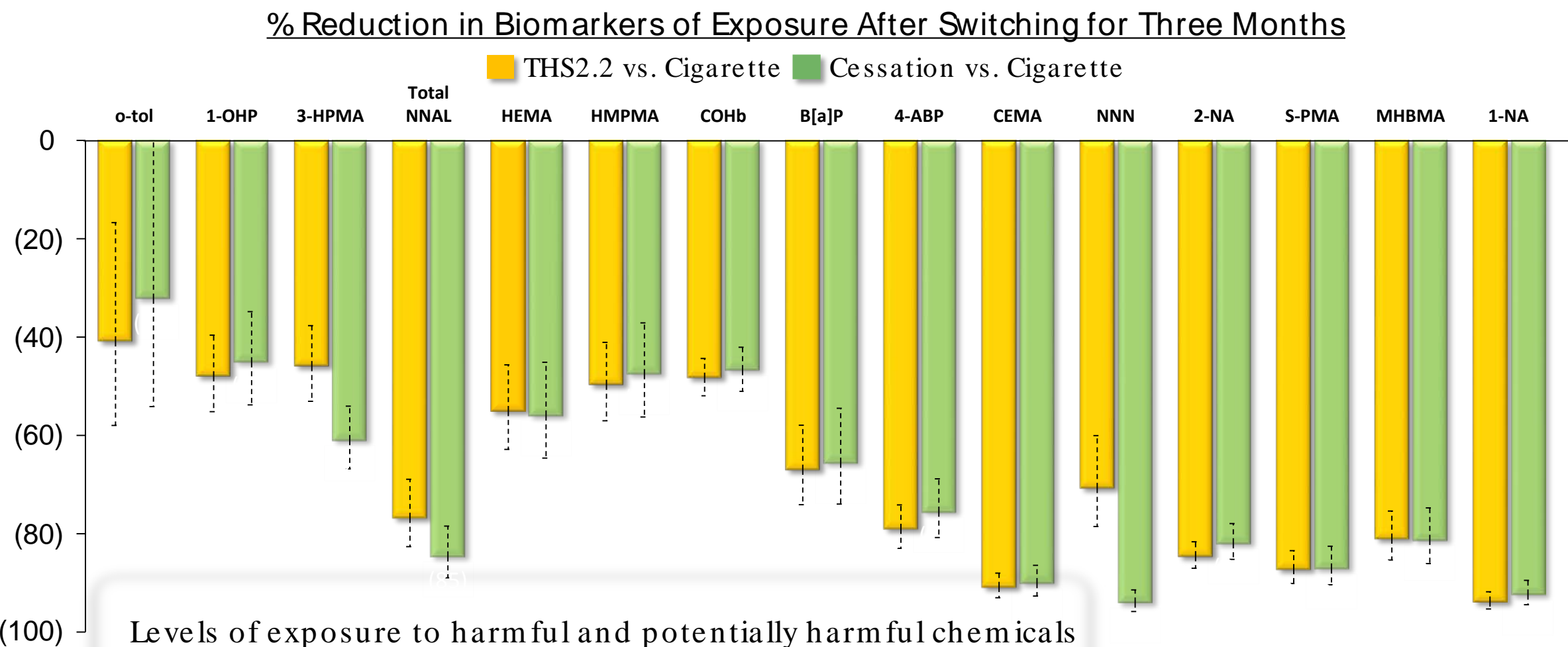


Clinical Evidence: Approach and Rationale

High Level Adverse Outcome Pathway of Cigarette Smoking



Clinical Evidence: Reduced Exposure



Levels of exposure to harmful and potentially harmful chemicals when smokers switch to THS2.2 **approach the levels observed in those who quit smoking during the study**

Note: These data alone do not represent a claim of reduced risk. Source: [PMI Research and Development](#); Registered on clinicaltrials.gov: NCT01970995

Clinical Evidence: Favorable Changes in Smoker's Health Profile in a 3-Month Study

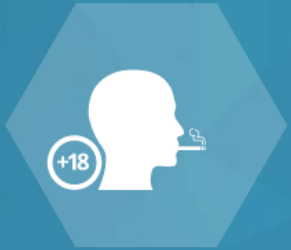
Disease Mechanisms	Expected Direction of Change	Effect of Cessation	Effect of Switching to THS2.2	Direction of Change
Lipid Metabolism (HDL-C)	Increase	6.4 mg/dL ↑	4.5 mg/dL ↑	Same direction as cessation
Inflammation (WBC)	Decrease	-0.40 10 ⁹ /L ↓	-0.57 10 ⁹ /L ↓	Same direction as cessation
Airway Impairment (FEV ₁)	Increase	1.93% pred ↑	1.9% pred ↑	Same direction as cessation
Endothelial Dysfunction (sICAM-1)	Decrease	10.9 % ↓	8.7 % ↓	Same direction as cessation
Oxidative Stress (8-epi-PGF _{2α})	Decrease	5.9 % ↓	12.7 % ↓	Same direction as cessation
Clotting (11-DTX-B ₂)	Decrease	19.4 % ↓	9.0 % ↓	Same direction as cessation

These studies measured the levels of 6 clinical risk markers closely associated with cardiovascular and lung disease.

Measurements of these markers in smokers who switched to THS2.2 showed that the **majority of beneficial effects that were seen in the smoking cessation arm were preserved.**

Adult Consumer Perception and Behavior: Approach and Results

Designed to measure Risk Perception, Comprehension and Intention to Use in a Pre-Market Setting:



Effect on Tobacco
Use Behavior Among
Adult Smokers



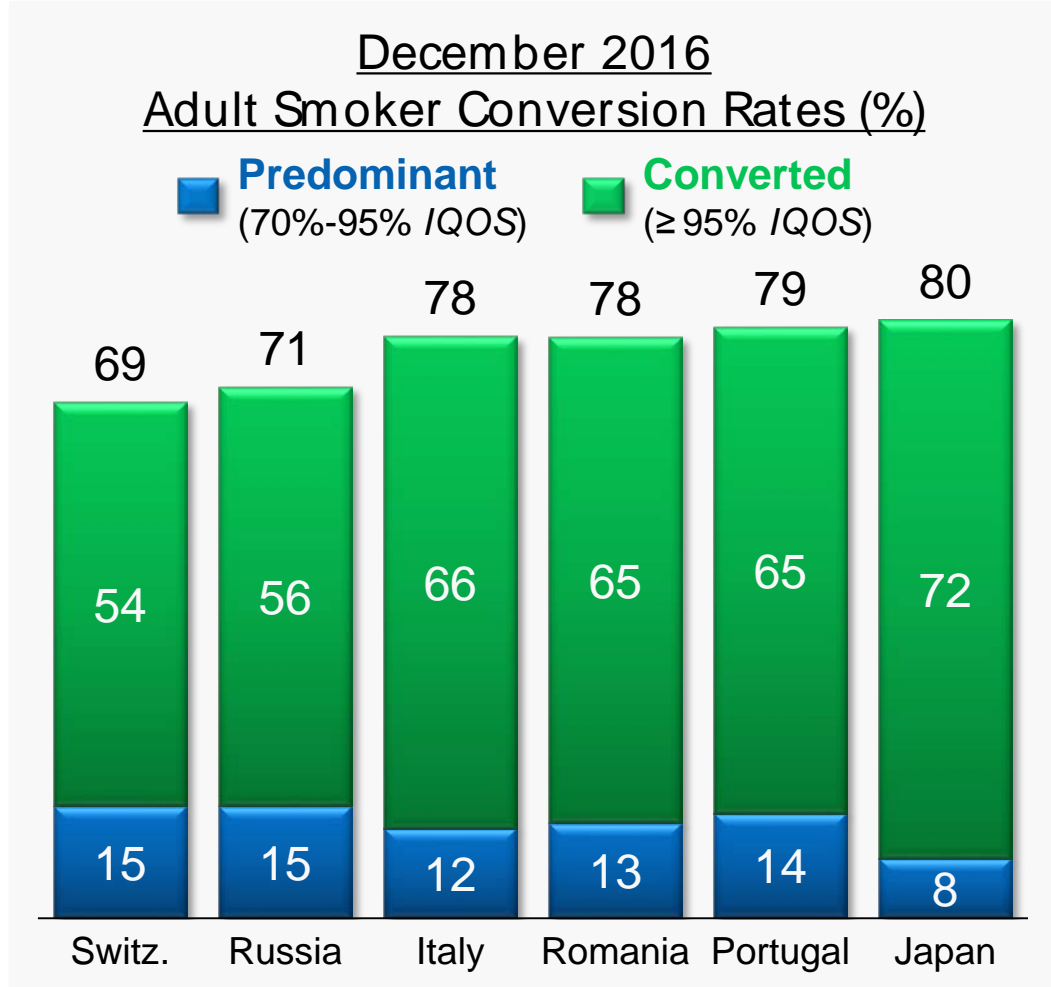
Effect on Tobacco
Use Initiation Among
Adult Non-Smokers



Effect on Consumer
Understanding and
Perceptions

- Non-intended audiences express negligible intention to use
- Adult smokers correctly understand the tested reduced risk communication
- Adult smokers correctly understand that THS2.2 is not without risk and is not an alternative to quitting
- Adult smokers react positively to the THS2.2 proposition and express sizeable intention to use

Avoiding Unintended Consequences: Dual Use, Never Smokers and Former Smokers



High rates of *IQOS* purchasers who have either fully or predominantly converted to the product

Negligible interest from unintended audiences

Results from our first launch markets show non-smokers and former smokers are not purchasing the product in large numbers

Avoiding Unintended Consequences: Principles for Engagement with Consumers

The data indicate that THS2.2 (*IQOS*) has the potential to provide a risk reduction benefit for adult smokers relative to the status quo – continued smoking. We are committed to responsible commercialization to ensure there is an overall benefit to public health. Our principles are:

Offer the product to adult smokers who want to continue enjoying tobacco products

- do not offer the product to people who have never smoked or who have quit smoking.

Support adult smokers in their conversion journey through education and guidance

Communicate accurately and clearly to adult smokers

- the product is **not an alternative to quitting**. The best choice for consumers concerned about the health risks of smoking is to quit tobacco products altogether.
- to experience the benefit of the product, adult smokers should **switch to it completely** and abandon cigarettes permanently.
- The product is **not risk free or a safe alternative to cigarettes**, but it is a much better choice than smoking



PMI SCIENCE
PHILIP MORRIS INTERNATIONAL

Source: Philip Morris International

Acknowledgements:

Aerosol Chemistry Team – Lead: Dr. Serge Maeder

Standard Toxicology Team – Lead: Dr. Patrick Vanscheeuwijck

Systems Toxicology Team – Lead: Dr. Julia Hoeng

Clinical Team – Lead: Dr. Frank Luedicke

Chief Scientific Officer – Dr. Manuel Peitsch

Market Research and Consumer Behavior Team – Lead: Antonio Ramazzotti