

Assessment of the Tobacco Heating System (THS) 2.2, A Candidate Modified Risk Tobacco Product: From Concept to Early Clinical Data

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Harm Reduction



- 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?

Acceptability Is the product acceptable to adult smokers and

<u>not</u> appealing to non-smokers?

- Behavior

Are smokers willing to fully (or predominantly) switch to the product?

PHILIP MORRIS INTERNATIONAL

Offering Adult Smokers Acceptable Products that Reduce Risk



Developing Scientific Evidence: An Overview of PMI's THS 2.2 and Scientific Approach



Smoking Cessation as a Benchmark





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

Reduced Formation

Average reductions in formation of harmful or potentially harmful constituents for *THS* compared to levels measured in smoke from the 3R4F reference cigarette^{*}



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



*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

Systems Biology

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*



* Systems toxicology analysis of cardiovascular and respiratory endpoints from ApoE-/- 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).

Mechanistic studies also show a halting or regression of disease genesis following switching from conventional cigarettes to THS2.2* Gene expression changes measured in lung tissue show changes similar to cessation



Reduced Exposure

Clinical Studies

Smokers used the products ad libitum Smokers randomized to cigarettes or THS 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

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Reduced Risk

Does a measurable reduction in exposure to harmful and potentially harmful constituents lead to a potential reduction in the risk of developing smoking related diseases?

To determine the likelihood of risk reduction, we have selected a number of risk endpoints associated with respiratory disease, cardiovascular disease, inflammation and genotoxicity, as well as with indicators of general health.

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 smokingrelated 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



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

Consider Evidence for Reduced Risk <u>and</u> 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**





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 RRPs 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.



Source: Philip Morris International R&D

Data generated by:

Aerosol Chemistry Team Toxicology and Systems Toxicology Teams Clinical Team Perception and Behavioral Assessment Team

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