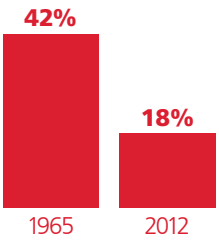
The Problem

Cigarette smoking is one of the leading preventable causes of death and illness in the world.

The best way for people to eliminate the adverse health consequences of smoking is to never start, and, for smokers, to stop. However, many smokers either do not want to quit or find it very difficult to quit, and thus continue to consume a dangerous product.

An approach for these smokers is the development of novel products that are scientifically substantiated to be less harmful and are acceptable alternatives to cigarettes.



Since 1965, smoking rates have decreased by more than half, BUT...

>42 million
Americans still smoke.

The 2014 U.S. Surgeon General's Report, *The Health Consequences of Smoking — 50 Years of Progress*, says that successes in tobacco control have cut smoking rates more than half since the 1964 Surgeon General's report; from 42% in 1965 to 18% in 2012. But the report also points out that more than 42 million Americans still smoke and that "the burden of death and disease from tobacco in the U.S. is overwhelmingly caused by cigarettes and other combusted tobacco products; rapid elimination of their use will dramatically reduce this burden."

The picture is consistent around the world; there will be more than one billion smokers around the globe for the foreseeable future, and millions of them in the United States. From a public health perspective, however, the only policy approach to tobacco use traditionally offered to American smokers has been cessation.

So the question is...

Can reduced-risk tobacco products be relied upon as tools to help those who continue smoking?

The U.S. Has a Pathway Forward

The science is promising, and the U.S. Congress and the Food and Drug Administration (FDA) have prepared the way. The Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act) — which passed with overwhelming bipartisan support in both houses of the U.S. Congress in 2009 — gives FDA a powerful tool to improve public health by ensuring that tobacco products marketed with claims of reduced harm or risk of tobacco-related disease actually do reduce harm or risk of disease. FDA has issued guidance[1] with a 360-day timeframe for review of applications for Modified Risk Tobacco Products (MRTP) under section 911 of the Federal Food, Drug, and Cosmetic Act, as modified by the Tobacco Control Act.

Philip Morris International (PMI) submitted applications to FDA in December 2016 for authorization to market its novel IQOS tobacco heating system (THS), a product that heats but does not burn tobacco, as a Modified Risk Tobacco Product (MRTP).

Although FDA is in the process of reviewing PMI's MRTP applications and has not yet reached conclusion, the results so far show that:

- **The levels of harmful and potentially harmful chemicals (HPHCs) in the IQOS aerosol can be reduced by more than 90% on average compared to smoke from a standard research cigarette**
- **The exposure to harmful and potentially harmful chemicals measured in smokers who switched to IQOS approached the levels observed in smokers who quit smoking for the duration of the clinical studies**
- **Premarket research shows negligible interest in IQOS among adult nonsmokers and former smokers with substantial potential for full switching among current adult smokers**
- **Real-life results from countries where IQOS is available confirm the potential indicated in premarket research data — almost 5 million adult smokers have stopped smoking and switched to IQOS**

1. FDA: Modified Risk Tobacco Product Applications: Draft Guidance for Industry, March 2012.

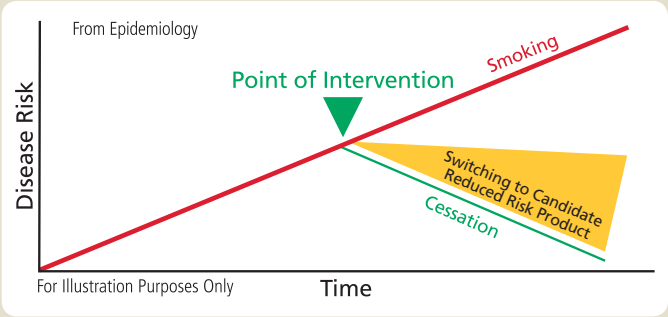
The Challenge

It is one thing to make a tobacco product that is less hazardous; it is quite another to do so while making the product acceptable and appealing so that adult smokers will want to switch to it from cigarettes. Less harm without appeal will generate little in the way of public health benefits. These are big challenges, but, if met, can produce significant benefits for public health.

Reduced-Risk Product X **Product Acceptance and Usage** = **HARM REDUCTION**

MRTPs must also be marketed in a manner that conveys their benefits to adult smokers without encouraging never smokers, former smokers and especially youth to begin using them.

PMI's comprehensive assessment program is designed to address these challenges and follows relevant scientific precedents and the FDA's Draft Guidance for MRTP Applications. Clinical and scientific assessment methods are similar to those used by the pharmaceutical industry, including product design controls, a range of toxicological tests, clinical studies, premarket consumer perception and behavior studies, and postmarket assessments.



The Goal: A Risk Profile Approaching Cessation

PMI's goal is to demonstrate that switching fully to its candidate reduced risk products has a risk reduction profile approaching that of cessation, referred to by the U.S. Institute of Medicine (IOM) as the "gold standard" for assessing risk reduction.

Product Design and Control → Aerosol Chemistry and Physics → Pre-Clinical Toxicology Assessment → Systems Toxicology Assessment → Clinical Trials → Consumer Perception and Behavior Assessment → Postmarket Studies and Surveillance

PMI's Assessment of MRTPs

The first step in assessing the aerosol generated by a candidate reduced-risk product is to confirm a reduction in the levels of harmful and potentially harmful constituents compared to cigarette smoke. HPHCs are considered to be the primary cause of smoking related diseases.

The next step is to confirm that the reduction in HPHCs results in reduced toxicity in laboratory studies. PMI takes toxicological assessment one step further using a new area of science known as systems toxicology, which allows the use of non-clinical data to quantify the reduced impact of its products on the mechanisms leading to disease and thereby model their risk reduction potential compared with cigarettes.

Clinical studies are a cornerstone of the assessment program. They assess whether a reduction in the formation of HPHCs measured in the laboratory leads to a reduction in HPHC exposure under real use conditions when an adult smoker switches to the product; and they demonstrate whether switching from cigarettes to a candidate reduced-risk product has a beneficial effect on a smoker's health profile. Clinical studies also help determine the extent to which adult smokers would find the product an acceptable alternative to cigarettes.

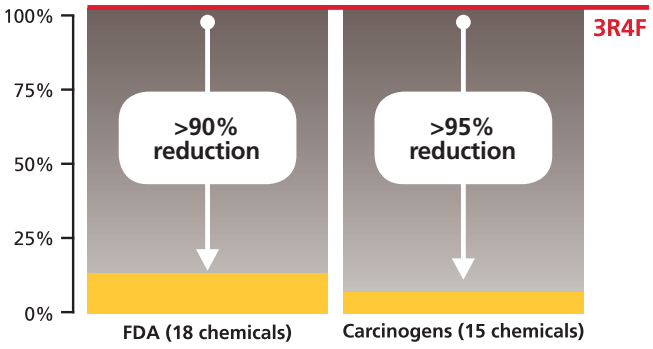
Premarket perception and behavior research is conducted to determine consumer understanding of the product's attributes and communications (including risk perception) and the extent to which marketing of the candidate reduced-risk product will encourage adult smokers to switch as well as the likely impact on nonsmokers and former smokers initiating tobacco use. This research is critical to help make a premarket determination of the overall public health impact of the product, and is a novel area of research designed and undertaken by PMI to meet the requirements established by the Tobacco Control Act's provisions on MRTPs.

PMI's assessment of candidate reduced-risk products continues after its products are placed on the market. Postmarket studies are important to verify how consumers use the product, longer term risk and the product's impact on health of the population as a whole.

PMI's studies on IQOS, a product that heats but does not burn tobacco, are well-advanced.
PMI submitted applications to FDA in December 2016 seeking FDA review of the science presented herein and authorization to market IQOS as a Modified Risk Tobacco Product.

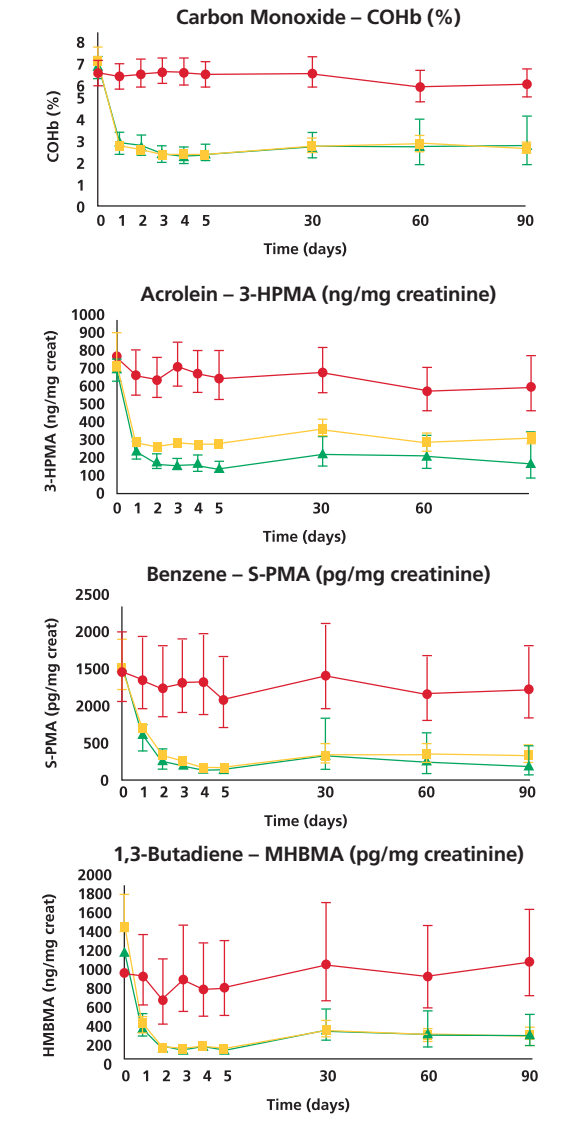
IQOS Results Summary

- The levels of the HPHCs required to be reported to FDA[2] were measured in the aerosol generated by IQOS and are over 90% lower, on average, than those in cigarette smoke from a 3R4F reference cigarette.[3] Similarly, the levels of chemicals classified by the International Agency for Research on Cancer (IARC) as Group 1 carcinogens are reduced on average by more than 95% compared to a standard research cigarette.
- Toxicological studies in a laboratory also indicate that reduced formation of HPHCs in the IQOS aerosol has the potential to translate into reduced disease risk for humans compared to continued cigarette smoking.



- Premarket assessments show very little interest in IQOS among adult never-smokers and former smokers and substantial potential for full switching among adult smokers. Less than 6.4% of adult former smokers and less than 1.1% of adult never smokers (including young adult never smokers below 25) expressed an intention to use IQOS, while a significant percentage of adult smokers — between 20% and 39% —intended to use IQOS, depending on the type of tested materials and modified risk message.
- Premarket data is corroborated by real-life results: In Japan, over 68% of IQOS purchasers have fully switched to the heated tobacco category as of December 2017. In other countries, a full or predominant switching rate exceeded 60% among IQOS users. PMI estimates that almost 5 million adult smokers have quit smoking and use IQOS exclusively.

- Three-month clinical trials recently carried out in the U.S. and Japan showed that smokers who switched to IQOS inhaled reduced levels of 15 harmful chemicals compared to smokers who continued to smoke. The exposure to HPHCs measured in smokers who switched to IQOS approached the levels observed in smokers who quit smoking for the duration of the study.
- Overall, product satisfaction and measured nicotine uptake were comparable to a cigarette, indicating that IQOS may be a viable alternative for adult smokers. The chart below shows the results for four primary biomarkers of exposure to HPHCs.



ClinicalTrials.gov Identifier: NCT01989156 | Results from a clinical trial conducted in the U.S. showing four biomarkers of exposure to HPHCs for adult smokers who continued to smoke, quit smoking and switched to IQOS over a 5-day period in confinement followed by 85 days in an ambulatory setting.

2. FDA: Draft Guidance for Industry: Reporting Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke Under Section 904(a)(3) of the Federal Food, Drug, and Cosmetic Act, March 2012.
3. Average yield reductions of an investigational variant of IQOS compared to the 3R4F reference cigarette, calculated as an average of the reductions of individual HPHCs, which could be reliably quantified in the study. Aerosol collection with Intense Health Canada's Smoking Regime. All yields were taken on a mass per stick basis. Reduction calculations exclude nicotine.

PMI's current portfolio of candidate reduced-risk products is aimed at addressing adult consumer preferences and includes four product platforms — two that heat tobacco instead of burning it and two that contain tobacco-derived nicotine, but no tobacco.

Each of PMI's product platforms is designed to significantly reduce the formation of the chemicals which are widely recognized as the primary probable causes of smoking-related diseases, while replicating as much as possible the taste, nicotine delivery, and ritual characteristics of cigarettes, which are important for adult smoker appeal and acceptance. PMI submitted an application to FDA in December 2016 to market THS, one of its heat-not-burn products, in the United States as a MRTP.

Philip Morris International's IQOS Tobacco Heating System

How IQOS Works

- The tobacco mixture in the tobacco stick is heated to a maximum temperature of approximately 570°F and does not result in the combustion of tobacco.
- By contrast, cigarettes reach temperatures of between 1110°F to 1470°F, exceeding 1650°F during puffs.
- IQOS generates an aerosol and not smoke.

Commitment to Science

Since 2008, PMI has invested over $4.5 billion in the development of a portfolio of innovative products that seek to replicate the sensorial and taste attributes of cigarettes, while delivering an aerosol that is significantly less harmful than cigarette smoke.

PMI has assembled a team of over 400 world-class scientists and engineers in key disciplines with state-of-the-art facilities in Switzerland and Singapore. It also has established a global network of research and technology partners. Since 2008, PMI has published over 250 peer-reviewed scientific publications and book chapters on the scientific assessment of products with reduced-risk potential, and all our clinical studies are registered on the public website ClinicalTrials.gov.

To date, the company has over 3,400 patents granted and over 5,000 pending applications on new product developments related to candidate reduced-risk products.

Learn more at PMIScienceUSA.com.

About PMI: Until March 28, 2008, Philip Morris International (PMI) was a wholly owned subsidiary of Altria Group, Inc. Since then, PMI has been an independent company, separately listed on the New York Stock Exchange (ticker symbol "PM"). This document is intended to provide information about PMI's efforts to develop modified risk tobacco products in accordance with federal regulatory requirements — it is not intended for consumers.

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