SCIENTIFIC UPDATE

PMI SCIENCE – PHILIP MORRIS INTERNATIONAL

JUNE 2022 | ISSUE 15

DELIVERING A SMOKE-FREE FUTURE

THE PEOPLE **BEHIND OUR SCIENCE**

OUR PRODUCT **PORTFOLIO**

CONTENTS

04
Events

06
Delivering a smoke-free future

10
The people behind our science
We have over 980 scientists, engineers, technicians, and support staff at PMI, each working in different, complex areas and all playing a role in helping us to deliver a smoke-free future.

14
Our product portfolio
At PMI, we have come a long way since our inception as a manufacturer of cigarettes.

18
PMI publications

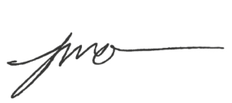
19
Independent studies

INTRODUCTION

Philip Morris International has transformed from being just a cigarette company. We've developed a portfolio of smoke-free products with the potential to reduce the risk of harm for adult smokers who would otherwise continue smoking. We rigorously assess our smoke-free alternatives with a comprehensive scientific assessment program. Our practices are inspired by the pharmaceutical industry and aligned with the U.S. Food and Drug Administration's Draft Guidance for Modified Risk Tobacco Product Applications (2012).

More than 980 scientists, engineers, technicians, and support staff who have brought us this far are determined to carry us forward towards our goal of a smoke-free future by continuing to innovate, advancing our smoke-free product portfolio for adults who would otherwise continue to smoke, developing and improving research methods, and exploring long-term opportunities in the health and wellness sectors. We invite you to learn about our smoke-free product portfolio, the people behind our research, and how we're advancing towards a smoke-free future.

Dr. Jana Olson
Managing Editor and Scientific Writer



Manuel C. Peitsch, Prof.
Chief Scientific Officer

Editorial Team:

Dr. Ann Riley, Head of Scientific Writing (ann.riley@pmi.com)
Dr. Jana Olson, Scientific Writer, Managing Editor (jana.olson@pmi.com)
Moyette Gibbons, Scientific Writer
Dr. Heike Schramke, Scientific Integrity Editor
Michi Nozaki, Science Editorial and Digital Analyst
Liina Vallimaa, Social Media Content Producer

Scientific Team:

Prof. Manuel Peitsch, Chief Scientific Officer
Dr. Moira Gilchrist, VP Strategic & Scientific Communications
Dr. Gizelle Baker, VP Global Scientific Engagement

You can contact us here:

For press inquiries:
jana.olson@pmi.com
+41 (0)58 242 4500

For scientific inquiries:
contact@pmiscience.com

You can also follow us on:

Twitter
@PMIScience

LinkedIn
PMI Science

Facebook
PMI Science

EVENTS

The 1st AOP Community of Practice Symposium

Online

February 15-22, 2022

The 1st AOP Community of Practice Symposium focused on topics centered on Adverse Outcome Pathways (AOPs) which are a conceptual framework for portraying scientifically credible, causal, linkages between perturbations of biological systems at the molecular, cellular, biochemical levels of organization and their resulting adverse effects on human health or the environment.

PMI scientists co-authored the presentation on “An Adverse Outcome Pathway for Decreased Lung Function Focusing on Mechanisms of Impaired Mucociliary Clearance Following Inhalation Exposure”.

AOPs are a knowledge synthesis and aggregation tool with a wide range of applications in environmental safety assessments of chemicals and radiation, environmental health and human medicine, life sciences research, and regulatory and policy arenas that rely on science-based decision-making. The sessions were open to all and held entirely on zoom.

Society of Toxicology Annual Meeting + ToxExpo

San Diego, California, Online

March 27-31, 2022

This year’s meeting included more than 2,000 scientific sessions, continuing education courses, poster sessions, and exhibitor-hosted sessions, networking, and other events, as well as over 250 exhibitors at ToxExpo.

PMI scientist Bjoern Titz presented on “The Omics of the X-Species DILI Validation Consortium” and Ee Tsin Wong focused on the “Evaluation of chronic inhalation toxicity of e-vapor aerosols in 18-month study in A/J mice”. Justyna Szostak presented on “Regional Airway Dosimetry of Hydroxychloroquine for Oral, Intratracheal and Nose-Only Rat Exposures”.

Most scientific and featured sessions were also available for registrants to watch live online and via on-demand video recordings through the SOT Event App or Online Planner until July 31.

Advances in Science + Therapy

Barcelona and Online

March 15-20, 2022

The hybrid conference provided opportunities for international medical and scientific professionals to discuss the latest breakthroughs in treatment, early diagnosis, translational R&D, drug development, and clinical trials in Alzheimer’s, Parkinson’s and other related neurological disorders.

PMI scientist Melinda Barkhuizen participated with a poster on “Comparing astrocyte and microglial signaling in LPS-induced neuroinflammation with causal biological network models”.

A key theme of the conference was advancing innovative strategies in therapy and prevention, clinical trials, and diagnostic markers, and fostering collaborations among industry and academia.

Online February 24, 2022

In February this year, we hosted our Open Science in Brief event. Three of our leading scientists, Moira Gilchrist, VP Strategic & Scientific Communications, Maurice Smith, Senior Scientific Advisor, and Catherine Goujon-Ginglinger, Head of Chemistry Research, discussed the analysis of both targeted and untargeted screening of toxicants in the aerosols of smoke-free products and other alternatives. The 30-minute session was hosted on our Open Science platform and simultaneously broadcasted on PMIScience LinkedIn.

Learn more about Open Science:
Open Science- PMI Scientific Update | PMI Science

Event page: watch the replay:
Open Science in Brief February 2022 | PMI Science

DELIVERING A SMOKE-FREE FUTURE

Delivering a smoke-free future

At Philip Morris International (PMI), we are transforming our company and focusing on a portfolio of smoke-free alternatives to replace cigarettes as soon as possible. For over 20 years, we've been working on developing and scientifically assessing products that are better alternatives to cigarettes. Products that do not burn tobacco or create cigarette smoke and, therefore, generate significantly lower levels of toxic substances compared with cigarettes.

In 2020, we issued our Statement of Purpose, reaffirming our 2016 commitment to delivering a smoke-free future. Since 2008, we have invested more than USD 9 billion to develop, scientifically substantiate, and commercialize smoke-free products for adults who would otherwise continue to smoke, with the goal of completely ending the sale of cigarettes. Of that amount, USD 120 million went into the construction of our R&D facility, the Cube. This facility is located in Neuchâtel, Switzerland, and is focused exclusively on smoke-free alternatives.

And our investments don't stop there. We are also investing in our people: more than 980 scientists, engineers, technicians, and support staff work on our smoke-free portfolio.

2009

Opening of a **new R&D center**, the Cube, in Switzerland, focusing exclusively on smoke-free products.

2010

Opening of a new research laboratory in **Singapore.**

2014

Launch of **tobacco heating system (THS)** in Nagoya **(Japan)** and Milan **(Italy).**

2015

In 2015, we launched **PMIScience.com** to publicly share with the scientific community the methods and findings related to our smoke-free products.

2016

THS was launched nationally **in Japan** in April 2016.

In December 2016, the **U.S. Food and Drug Administration (FDA) received** our Modified Risk Tobacco Product (MRTP) application for THS.

2018

Opening of an **R&D center in Armenia** - the third in the company's global network of R&D centers.

2020

In 2020, we issued **PMI's Statement of Purpose**.

On July 7, 2020, the **FDA** authorized the marketing of the *IQOS Tobacco Heating System* as an MRTP.

2021

Our acquisitions in 2021 of **Fertin Pharma, Vectura, and OtiTopic** provide a base for building critical respiratory and oral product development capabilities, in tandem with our existing expertise.

Sharing our science

In 2015, we launched PMIScience.com to publicly share with the scientific community the methods and findings related to our smoke-free alternatives. However, smoke-free products are not risk-free, and they contain nicotine, which is addictive. To identify the extent of reduction in risk compared to continued smoking, we are evaluating the risk profile of our smoke-free products using a robust scientific assessment program.

Our smoke-free portfolio

Our smoke-free portfolio includes heat-not-burn, e- vapor, and oral nicotine products. We have three smoke-free products in various stages of development. These products do not involve combustion of tobacco, so they generate significantly lower levels of harmful compounds compared with cigarettes. Several of our smoke-free products use, but do not burn tobacco. Two other products generate nicotine vapor through different technical solutions and do not involve tobacco. Following feedback from the 2021 consumer test of our carbon tip product, the design of our current technology has been discontinued. We are assessing alternative designs for this consumer segment.

In line with our commitment to provide smokers who would otherwise continue to smoke with a broader range of better alternatives to cigarettes, we have launched a newly formulated nicotine pouch, which does not contain tobacco.

Tobacco heating systems

We have developed several heated tobacco products (HTPs) that are commercialized as *IQOS* in various markets. HTPs, also known as tobacco heating systems (THS) and heat-not-burn products, heat the tobacco at a temperature that allows the release of a nicotine-containing tobacco aerosol but without burning the tobacco. Because tobacco is heated and not burned, there is no smoke. The levels of harmful chemicals in the generated aerosols are significantly reduced compared to cigarette smoke.

Initial generations of our HTPs use blade heating technology, and these are designed to be used with specific heated tobacco units. The latest addition to our HTP devices uses induction rather than a blade to heat tobacco and is commercialized as *IQOS ILUMA.*

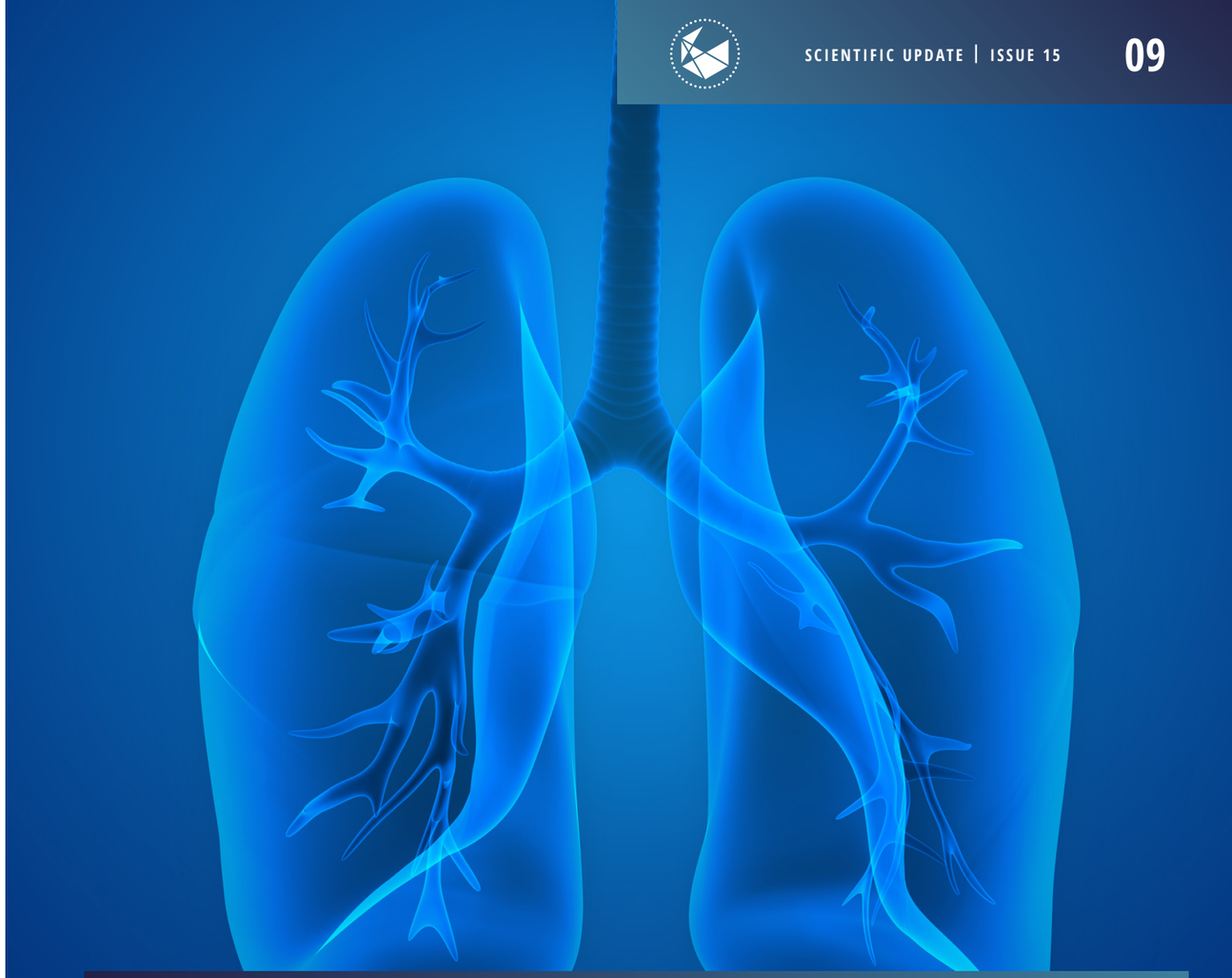
OUR STUDIES TO DATE SHOW THAT OUR LEADING TOBACCO HEATING SYSTEM, WHILE NOT RISK-FREE:

- Generates **no combustion** and **no smoke.**
- The THS aerosol has on average **90 to 95 percent lower levels** of harmful and potentially harmful constituents (**HPHCs**) and is less toxic than cigarette smoke in laboratory models.
- **No adverse effect on** the overall **indoor air quality** when used in an indoor environment.
- Two 90-day clinical studies conducted in the United States and Japan respectively, reported that adult smokers who **switched** completely **to the THS reduced** their **exposure to** selected **HPHCs** (based on the measurements of biomarkers of exposure).
- Clinical findings from a six-month study on biomarkers of potential harm indicate that **switching** completely **to the THS has a positive impact on** adult smokers' **health.**
- Our research shows **negligible interest in the THS among people who have never smoked** or who have quit smoking.
- **70 percent** of adult smokers who switch to the THS **use it exclusively or together with other smoke-free products.**
- The THS aerosol **discolors teeth significantly less** than cigarette smoke.

A historic decision

On July 7, 2020, the U.S. Food and Drug Administration (FDA) authorized the marketing of a version of the *IQOS Tobacco Heating System* as a Modified Risk Tobacco Product (MRTP) with reduced exposure information. It's the first and, so far, the only electronic nicotine product to receive such authorization. In doing so, the agency found that the issuance of the MRTP orders with reduced exposure information would be "appropriate to promote public health and is expected to benefit the health of the population as a whole."

> *"appropriate to promote the public health and is expected to benefit the health of the population as a whole."*



Moving beyond nicotine: Respiratory drug delivery, health, and wellness

At PMI, we have developed a rigorous scientific assessment program to assess our smoke-free products. And in the process, we've developed skills, facilities, and experience that we can apply to a wider range of technologies and industries, such as respiratory drug delivery, and health and wellness. Our acquisitions in 2021 of Fertin Pharma, Vectura, and OtiTopic provide a base for building critical respiratory and oral product development capabilities, in tandem with our existing expertise.

We believe that there are significant unmet patient needs for fast and effective treatments for cardiovascular diseases, such as myocardial infarction, and neurology, such as migraine, which can be served via innovative solutions. In the health and wellness sector, we have several initiatives looking at focus, sleep, energy, pain, and calm, notably through oral delivery. We see opportunities to deliver the positive effects of existing wellness and healthcare molecules in a fast and effective manner.

PMI will continue to leverage science and technology to develop, assess, and commercialize less harmful alternatives to cigarettes for adults who would otherwise continue smoking. To achieve our vision of replacing cigarettes with science-based smoke-free products as soon as possible, we're shifting our resources and have fundamentally changed both our purpose and our operations.

THE PEOPLE BEHIND OUR SCIENCE

Our scientific approach

We have more than 980 scientists, engineers, technicians, and support staff at PMI, each working in different, complex areas and all playing a role in helping us to deliver a smoke-free future.

Our goal is to develop and scientifically substantiate smoke-free products that are less harmful than continued smoking, with the aim of completely replacing cigarettes as soon as possible. For these smoke-free alternatives, we've implemented a rigorous scientific assessment program.

The best way to avoid the harm of smoking is to not start in the first place. For someone who already smokes, quitting tobacco and nicotine altogether is the best thing they can do to reduce their risk. And if an adult smoker won't quit, then switching to a product that doesn't burn tobacco is a better choice than continuing to smoke cigarettes. This is because most of the harmful chemicals found in cigarette smoke and linked to smoking-related diseases are generated by the burning process.

Our scientific assessment program covers a wide spectrum of activities from initial product development to the monitoring of these products once they are on the market.

Our practices are inspired by the pharmaceutical industry and aligned with the draft guidance from the U.S. Food and Drug Administration for a Modified Risk Tobacco Product Application (MRTPA). We conduct our research in accordance with Good Laboratory Practice (GLP), Good Clinical Practice (GCP) and other international standards and practices.

Here is a closer look at the five steps in our assessment program: Platform Development, Toxicological Assessment, Clinical Assessment, Perception and Behavior, and Long-term Assessment, and the work conducted by some of our scientists and R&D experts.

PLATFORM DEVELOPMENT

TOXICOLOGICAL ASSESSMENT

CLINICAL ASSESSMENT

PERCEPTION AND BEHAVOIR

LONG-TERM ASSESSMENT

Platform Development

Assessing the risk reduction potential of a smoke-free product relies on the quality of the initial product design and on strict manufacturing controls to ensure it delivers a consistent aerosol. Our heated tobacco products (HTPs), for example, are designed with the aim of eliminating or reducing the levels of Harmful and Potentially Harmful Constituents (HPHCs) found in their aerosol, compared to those found in cigarette smoke.

"Building and leveraging our knowledge in chemistry research can support innovation, product development, scientific claim substantiation, and regulatory submissions, and plays a key role in facilitating consumer acceptance.

Another key area of focus is to enhance capabilities related to liquid chromatography (LC), and gas chromatography (GC)xGC high-resolution mass spectrometry (MS), which serves to characterize the chemical space of smoke-free alternatives and detect any new constituents in aerosols. In this context, customized chemical databases are designed to support data interpretation and facilitate toxicological assessment. Learnings acquired in recent years have proved critical in developing new methodologies and processes to accelerate the assessment of smoke-free products."

Catherine Goujon-Ginglinger
Head of Chemistry Research

Joanne Chua
Global Head of Preclinical Science and Toxicology

Toxicological Assessment

Toxicological assessment aims to confirm whether the reduced formation of HPHCs, for example, leads to reduced toxicity and reduced risk of smoking-related diseases in laboratory models. We also take an innovative systems toxicology-based approach to risk assessment.

"In Preclinical Science and Toxicology, our scientists from various areas of biology, pharmacology, toxicology, aerosol science, biostatistics, and computational modeling, dedicate their time to preclinical scientific assessment of all PMI's smoke-free products. Our laboratories are ISO 17025, GLP, and GCP accredited to ensure all data generated is of the highest quality standard and withstands external scrutiny by regulatory authorities and the global scientific community."

Clinical Assessment

Clinical studies help show the extent to which adult smokers would find the product an acceptable alternative to cigarettes. They investigate whether a reduction in the formation of HPHCs measured in the laboratory leads to a reduction in HPHC exposure under real-world conditions and if switching from cigarettes to a smoke-free product has a beneficial effect on a smoker's health profile.

"In my current position, my role involves contract/agreement execution with external suppliers, collaboration with internal and external stakeholders on budget and contracts, vendor management, and budget management for all the clinical studies and projects within Clinical Research. Previously, I was Manager of Translational Research, and worked on bridging nonclinical and clinical data in clinical studies in terms of biomarkers of potential harm."

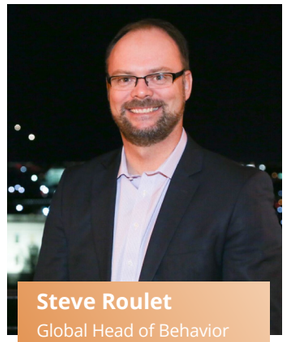
Ashraf Elamin
Manager, Study Outsourcing

Perception and Behavior

We conduct perception and behavior studies to better understand a smoke-free product's potential to benefit public health. These studies include research into how smokers perceive a product's risk and how they adopt and use the smoke-free alternative under real-life conditions.

"At PMI, I lead the development and execution of PMI's Perception and Behavior Assessment (PBA) consumer research program on smoke-free products. The PBA program consists of premarket studies aiming at gathering scientifically robust evidence to measure a) the effect of smoke-free products on tobacco use in adult tobacco- or nicotine-containing product users, b) the effect of smoke-free products on tobacco initiation in adult non-tobacco or nicotine-containing product users, c) consumer understanding and perceptions.

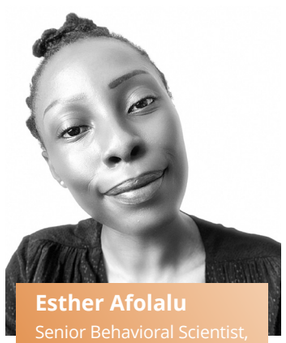
The PBA program also consists of post-market studies aiming at gathering scientifically robust evidence to measure the effect of the commercialization of smoke-free products on the population as a whole by measuring the effect of smoke-free products on tobacco- or nicotine-containing product use prevalence, use patterns, risk perception, initiation, relapse, re-initiation, and quitting."



Steve Roulet
Global Head of Behavior Research Insights

Long-term Assessment

The assessment of our smoke-free products continues after the products are placed on the market. Long-term assessment, including post-market studies, will confirm whether these products reduce the risk of smoking-related diseases, such as chronic obstructive pulmonary disease, cardiovascular disease, and lung cancer. We combine several approaches, including safety surveillance, clinical studies, and epidemiological studies, to obtain a progressively clearer picture of the risk-reduction potential of our products.



Esther Afolalu
Senior Behavioral Scientist, Life Sciences

"In the Behavioral Science team, we are working on the ABOUT™ Toolbox, which is a portfolio of self-report questionnaires that we refer to as Consumer Reported Outcomes Measures to support perception and behavior assessment related to the use of tobacco and nicotine products (TNPs). These measures are developed using best practices and are fit for purpose to accurately assess both combustible and smoke-free TNPs.

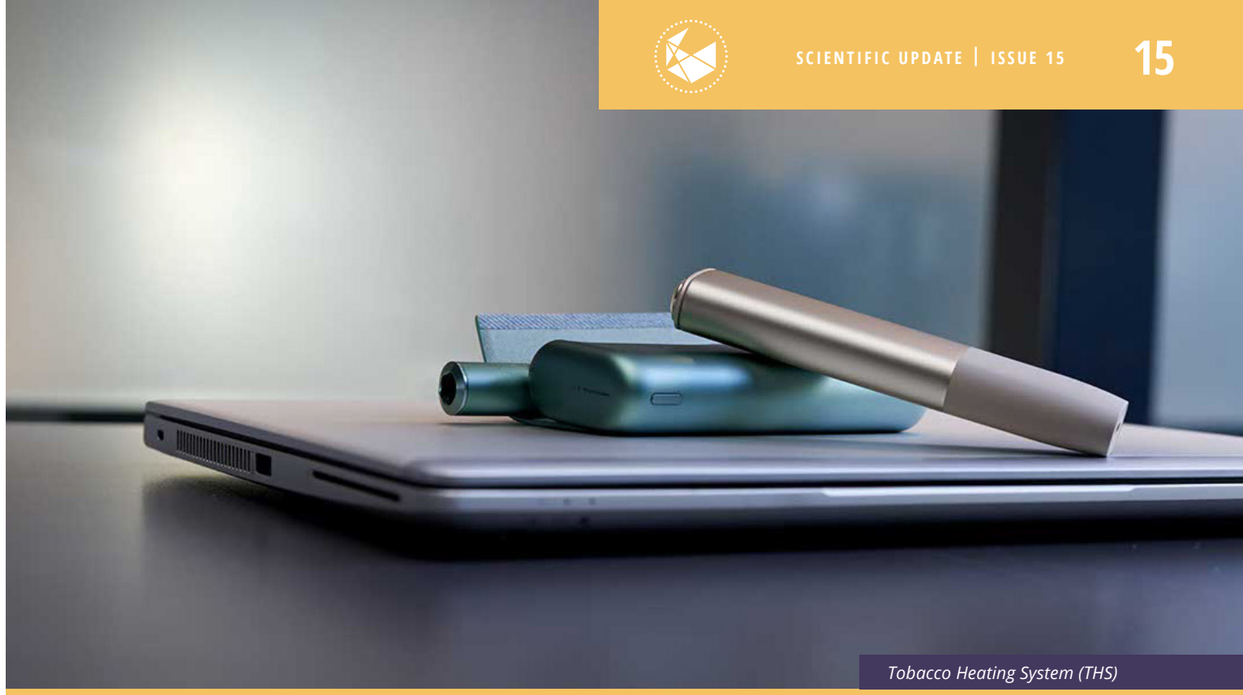
For example, we are currently validating a measure (ABOUT–Health and Functioning) to assess people's perceptions of how the use of different TNPs affects their health status and daily activities. My role involves providing scientific leadership to support behavioral research activities for the development and validation of these measures and their implementation in clinical and long-term assessment studies."

OUR PRODUCT **PORTFOLIO**

At PMI, we have come a long way since our inception as a manufacturer of cigarettes. For over 20 years, we've been working on developing and scientifically assessing less harmful alternatives to continued cigarette smoking that do not create smoke, because they do not combust tobacco.

Today, our smoke-free portfolio includes heated tobacco products, vapor, and oral nicotine products, at various stages of development, assessment, and commercialization.

Our product development is based on the elimination of combustion via tobacco heating and other innovative systems, which we believe are the most promising path to providing better consumer choice for those adults who would otherwise continue to smoke. We recognize that no single product will appeal to all adult smokers. Therefore, our approach is to develop a variety of smoke-free products, so that adults who would otherwise continue to smoke can find a suitable alternative that allows them to fully switch.



Tobacco Heating System (THS)

Our heated tobacco products

We have several heated tobacco products (HTPs) in our portfolio. Our HTPs, also known as tobacco heating systems and heat-not-burn products, heat the tobacco to release a nicotine-containing tobacco aerosol but without burning the tobacco. Because tobacco is heated and not burned there is no smoke, and therefore the levels of harmful chemicals in the generated aerosols are significantly reduced compared to cigarette smoke. HTPs, though, are not risk free, and provide nicotine, which is addictive.

Blade and induction devices

Initial generations of our HTPs use blade heating technology, and these are designed to be used with specific heated tobacco units. The latest addition to our HTP devices, uses induction to heat tobacco. These devices also use new specifically designed heated tobacco units. Despite the change in heating technology, the aerosol generated by our induction heating device remains comparable to the previous versions.

Our blade HTPs are available in two versions. The first version has three main components—a heated tobacco unit, a holder, and a charger. The second version is an integrated product that combines the holder and charger and allows multiple uses without recharging the battery. Both products contain an electronic system that heats the tobacco within a precisely controlled temperature range to avoid burning the tobacco. The system uses a heating blade, which acts as both a heater and temperature sensor.

When the heated tobacco unit is inserted into the tobacco holder, the heating blade is embedded in the tobacco. Once turned on, the heating blade heats the tobacco while also monitoring its temperature to ensure consistent taste and avoid burning.

The integrated version of our HTP works the same way. It combines the holder and charger into a single unit that must be charged after at least 10 uses. Unlike the original HTP, the integrated design allows for consecutive uses.

Our induction HTPs use induction rather than a blade to heat tobacco. This means there is no direct contact between the electronics and the heating element. The induction system relies on specially designed heated tobacco units, each with their own internal heating element at their core.

Rigorous scientific assessment

We have shown through testing our tobacco heating system, that if tobacco is heated above 250 °C, similar amounts of nicotine as those found in cigarette smoke, can be released. Keeping the temperature low enough, however, means the tobacco is not burned and the levels of harmful and potentially harmful chemicals generated and, therefore, inhaled are significantly reduced. Our studies have shown an average reduction of 90 to 95% in the levels of harmful and potentially harmful constituents (HPHCs) measured in the aerosol of our HTPs, compared to those found in the smoke of a standard research reference cigarette (3R4F).

Products without tobacco

Heating tobacco is just one possibility in developing alternatives to continued cigarette smoking. We are also developing products that contain nicotine but not tobacco. Instead of heating tobacco to release tobacco flavors and nicotine, our e-vapor and nicotine-based electronics-free products use nicotine that is extracted from tobacco leaves. Our products without tobacco produce a nicotine-containing vapor. They do this in distinctly different ways.

E-cigarettes redesigned

Our portfolio includes several next generation e-vapor products, which are battery-powered devices that produce an aerosol by vaporizing a nicotine-containing liquid. Our e-vapor products comprise devices using current generation technology and our new e-vapor mesh technology that addresses certain challenges presented by some e-vapor products currently on the market.

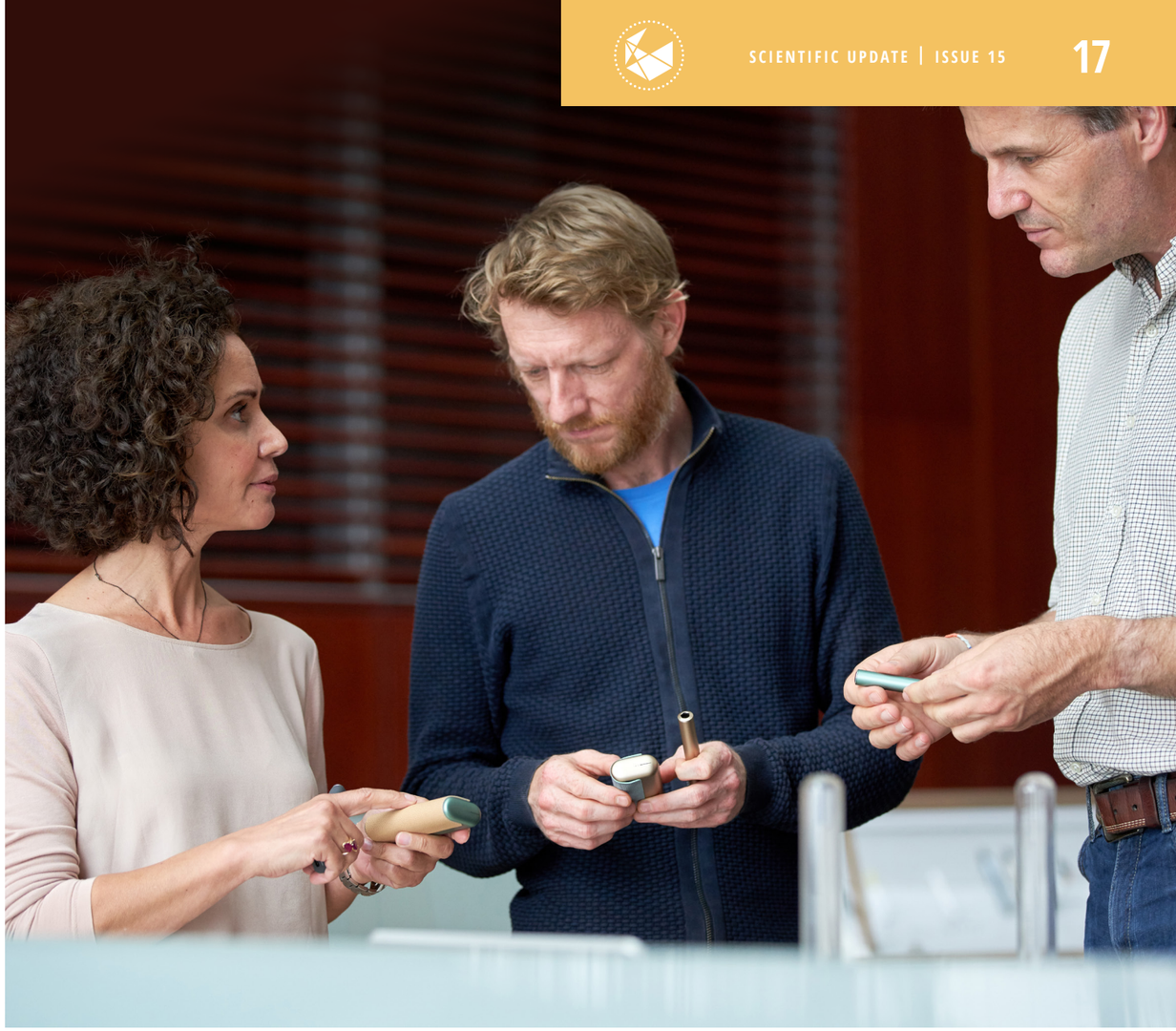
Our MESH vaping system (MVS) products are designed to improve upon traditional wick and coil designs and ensure the consistency and quality of the generated aerosol. They use closed-system e-liquid pods to prevent tampering and liquid leakage. The mouthpiece and a heating element are built into each replaceable pod to maintain product hygiene. The heating element is a metallic woven mesh with tiny holes to heat the pre-filled pre-sealed pod. Three main elements were further developed to make our latest e-vapor product a more acceptable smoke-free alternative: the mesh technology, the puff activated heating, and the low liquid detection system.

MESH vaping system (MVS)

Nicotine Salts Product (NSP)

A nicotine-based electronics-free product: NSP

We explored different technologies to mechanically produce a nicotine-containing aerosol without tobacco, combustion, or heating. The result is the nicotine salts product or NSP. This is a novel product that is composed of two parts: a consumable that contains a highly soluble encapsulated nicotine powder, and a non-electronic device that activates it. Once a consumable is inserted into the mechanical device, the nicotine powder is aerosolized and inhaled solely through the power of breath.



Oral pouches

No single product will address all adult smokers' or nicotine users' individual preferences. A range of alternatives is key to helping adults who otherwise continue to smoke to move away from cigarettes. Instead of producing an aerosol that is inhaled, these products are placed under the lip so that nicotine can be absorbed via the mouth. Our non-inhalable products include oral tobacco products, and oral nicotine products.

We have come a long way and are committed to further developing and scientifically substantiating innovative products that will one day replace cigarettes and deliver a smoke-free future. Explore our findings on our smoke-free products.

PMI PUBLICATIONS

Evaluating halitosis in cigarette smokers and alternative nicotine-delivery products users

This article reviews the existing literature on cigarette smoking and halitosis and proposes a framework for studying halitosis in the context of cigarette smoke and alternative tobacco product use. This three-layer approach combines the use of the most advanced breath analysis techniques and multi-omics analysis to define the interactions between oral bacterial species and their role in halitosis in vitro and in vivo. To date, only a few systematic studies have analyzed the effects of cigarette smoke on halitosis, and none has assessed the effects of the use of heated tobacco products and electronic vapor products on this condition.

The proposed framework also has the potential to quantify and mechanistically address the impact of alternative nicotine-delivery product use compared with cigarette smoke on halitosis. The results from such a comprehensive analysis could be used to design treatments for mitigating the potential side effects of alternative nicotine-delivery products on breath odor.

Assessing an adverse outcome pathway for decreased lung function

This paper describes an adverse outcome pathway (AOP) for decreased lung function by focusing on mechanisms of impaired mucociliary clearance (MCC) following inhalation exposure. AOPs help to organize available mechanistic information related to an adverse outcome into key events spanning all organizational levels of a biological system. They can also help link exposures to eventual toxic effects.

MCC is an important aspect of the innate immune defense against airborne pathogens and inhaled chemicals. The AOP described in the paper links oxidative stress caused by inhalation exposure to toxicants to impaired lung function through a decrease in MCC. Having a greater understanding of the underlying mechanisms of this pathology is very important in the risk assessment of inhaled toxic chemicals.

Evaluating two methods of exposure: impact of cigarette smoke and THS aerosols on liver tissue

A study compared the effects of aqueous fractions (AF) from cigarette smoke (CS) and our tobacco heating system (THS) aerosols on cytochrome P450 (CYP) activity in liver spheroids.

Researchers used the data from the analysis to develop a physiological aerosol exposure system combining a multi-organs-on-a-chip (MOC), 3D lung tissues, liver spheroids, and a direct aerosol exposure system.

In this study, the physiological exposure system combines MOC technology, 3D human tissues, and a direct aerosol exposure system for studying CYP activity in liver tissues exposed to cigarette smoke. The preliminary study showed that the physiological exposure system provides data that corresponds better with the results observed in human smokers than the data obtained with CS AF exposure.

It also demonstrated that the effects of THS aerosol on the viability and CYP activity of lung and liver tissues were smaller than those of CS, even at doses more than 4 times higher than CS. The new exposure system can be used to test the effects of any type of aerosol—from air pollutants to respiratory drugs—on any type of airway derived from any human donor.

INDEPENDENT STUDIES

Assessing the effect of heat-not-burn tobacco products on indoor air quality

A preliminary study published in Environmental Research examined the effect of the use of heat-not-burn (HnB) tobacco products, also known as heated tobacco products, on indoor air quality compared to cigarette smoke.

Researchers analyzed and compared the concentrations of nicotine, propylene glycol, and vegetable glycerin (VG) emitted by HnB products with those from conventional cigarettes. They also measured the levels of volatile organic compounds (VOCs), aldehydes, nanoparticles, and particulate matter (PM) detected when HnB products were used in an exposure chamber to assess the impact on indoor air quality.

The results showed that the range of nicotine levels transferred by HnB products was lower than those from cigarettes, while the range of VG levels emitted by HnB products was higher than those emitted from cigarette smoke. They also indicated that users of HnB products are expected to use HnB products more frequently to receive the same amount of nicotine as smokers of conventional cigarettes.

The researchers also found that although the amounts of the VOCs, aldehydes, PM, and nanoparticles generated by HnB products were small compared to cigarettes, they still had an impact on indoor air quality.

According to the researchers, future studies should assess a broader range of HnB products and analyze smoking habits.

Examining associations between smokeless tobacco use and cardiovascular disease risk

A study published in Nicotine & Tobacco Research compared cardiovascular disease (CVD)-related biomarkers of potential harm and biomarkers of exposure among exclusive smokeless tobacco (ST) users and exclusive cigarette smokers—in relation to recent nicotine exposure—and never tobacco users.

Researchers used data from 4347 adults in the Population Assessment of Tobacco and Health Study (2013–2014), adjusting for age, sex, race/ethnicity, income, body mass index, and CVD. Biomarker levels among exclusive ST users, who were former established cigarette smokers, were compared with exclusive cigarette smokers.

The study found smokeless tobacco use is not associated with increases in biomarkers of CVD-related harm and exposure, compared with never smokers, despite exposure to nicotine at levels higher than those observed among cigarette smokers. Biomarkers of potential harm were all higher in exclusive smokers than exclusive smokeless tobacco users, but similar between smokeless tobacco users and never tobacco users. These findings support the notion that increases in CVD risk among cigarette smokers is caused primarily by constituents of tobacco smoke other than nicotine.

Japan study assesses knowledge of novel tobacco products among healthcare providers

A study published in Preventive Medicine Reports showed that healthcare providers in Japan lacked knowledge of heated tobacco products (HTPs) and self-efficacy to counsel patients about novel tobacco product use.

The cross-sectional study used data from a Japanese Association of Smoking Control Science (JASCS) online survey of 277 physicians, pharmacists, nurses, and public health practitioners.

The results showed that while over half the sample had received previous training in treating tobacco use, 62% of respondents had no knowledge of HTPs, and 80% of respondents indicated that they occasionally or always provide smoking cessation support.

The healthcare providers surveyed were mostly female (81%), primarily nurses (51%), and very few of them have been trained to support their patients to quit smoking (40% reported no training, and 35% reported training at a primary level training).

As healthcare providers are often consulted by their patients about tobacco product use, the results suggest they require additional training to address the changing landscape of tobacco products.

PMI SCIENCE

PHILIP MORRIS INTERNATIONAL

Important information

This Scientific Update provides an overview of the most recent scientific developments behind PMI's approach to achieving a smoke-free future through a range of alternatives to cigarettes that do not burn tobacco. The following pages include our product development and assessment efforts, our initiatives to share our methodologies and results, as well as independent research and government reports. More detailed information can be found at www.pmiscience.com.