SCIENTIFIC UPDATE

PMI SCIENCE – PHILIP MORRIS INTERNATIONAL

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10 YEARS OF SAFETY SURVEILLANCE

CONTENTS

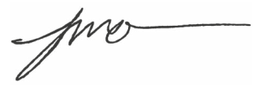
INTRODUCTION

Postmarket safety surveillance is an integral part of our comprehensive assessment program, and it is fundamental to our product safety and quality assessment. Over the last decade, Philip Morris International (PMI) has developed an extensive postmarket safety surveillance system for our smoke-free products. This system was designed to exceed regulatory standards for the tobacco industry and set new benchmarks for industry transparency and consumer protection. By proactively monitoring adverse events and integrating advanced technologies, PMI aims not only to comply with global requirements but to lead in responsible product stewardship.

In this issue, we interview PMI's safety surveillance team, who discuss the strategies and tools used for safety signal detection and regulatory reporting. We also summarize 10 years of safety data for our leading heated tobacco product, which show a stable safety profile even as user numbers and markets grow. Common adverse events like cough, headache, and throat irritation align with those seen in nicotine replacement therapies, reinforcing the reliability of our products.

We encourage you to take a look through this issue and explore the insights and data that guide our pursuit of a smoke-free future and our ongoing commitment to consumer safety.

Dr. Jana Olson
Manager Scientific Writing



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SCIENTISTS BEHIND THE ISSUE

Special THANKS to the entire PMI Product Safety Surveillance team—N. Blanc, G. Caccia, T. Djurovic, K. Kowa, Z. Lampropoulou, L. Leroy, R. Moore, N. Nuic, D. Peric, P. Quesada, V. Schaub Ferreira, and C.T. Tran—for their continuous dedication and contributions to the data presented in this Scientific Update.

Brindusa Taranu

Head Product Safety Surveillance

Provides oversight for the revision and optimization of processes related to safety monitoring, safety signal detection, and documentation of safety cases. Oversees all critical activities related to high-profile safety concerns, emerging safety issues, and litigation-relevant safety topics. Serves as the most senior safety point of contact for other departments during the issue escalation process.

Nicolas Blanc

Principal Medical Safety Officer

Provides medical interpretation of case-level information and performs medical risk assessments, starting with the design and control principles of the products and extending throughout the commercialization phase.

Nicolina Nuic

Manager Safety Databases

Oversees the safety surveillance platforms to ensure optimal performance, compliance with data integrity guidelines, and effective system vendor management.

FEATURED SCIENTIST: Kamila Kowa

Kamila Kowa is Sr. Safety Lead, Product Safety Surveillance at PMI. She joined the company in 2021 as a Sr. Product Safety Scientist, and was responsible for collecting adverse events from market research studies, analyzing scientific literature, and preparing safety aggregate reports. After joining she transitioned into her current position, which focuses on two key areas: safety data analysis and detection and management of safety signals.

In her work in safety data analysis, Kamila prepares safety aggregate reports and contributes to premarket tobacco applications required by local authorities (e.g., the U.S. Food and Drug Administration). These reports are vital in ensuring regulatory compliance and provide critical insights into the safety profile of PMI smoke-free products. She also oversees the detection and management of safety signals, including conducting qualitative assessments to determine signal validity and presenting findings at internal Product Safety Management Board meetings.

Kamila studied cell biology at the University of Geneva, where she investigated the mechanisms responsible for the establishment and maintenance of cell polarity and the link between polarity and cell cycle progression. Prior to joining PMI, she worked in the pharmaceutical industry, gaining experience in adverse event reporting and preparation of safety reports.

Her role at PMI includes presenting on safety surveillance activities at key scientific events, such as the 34th Pharmacovigilance UK & EU in January 2024 and the 78th Tobacco Science Research Conference in September 2025. Kamila's work in safety surveillance is instrumental in supporting the launch of new products and substantiating the claim that PMI smoke-free products are better alternatives for adult smokers who would otherwise continue to smoke.

FROM DATA **COLLECTION TO GLOBAL IMPACT**

An interview with PMI's safety surveillance team

PMI has a robust and highly specialized postmarket safety surveillance system in place. We conducted an interview with members of the safety surveillance team to find out how this system works and how it is used to monitor the safety of PMI smoke-free products.

What is postmarket safety surveillance for smoke-free products?

Brindusa: Postmarket safety surveillance is the practice of monitoring the safety of a product after it has been released on the market. In order to improve consumer safety, we conduct systematic collection, analysis, and communication of health-related events—known as **adverse events (AEs).** These are events that are not necessarily caused by product use but are associated with it.

PMI launched its safety surveillance system alongside the initial release of the Tobacco Heating System (THS), in 2014. We currently conduct postmarket safety surveillance for all our smoke-free products, which include heated tobacco products, e-vapor products (aka e-cigarettes or vapes), and nicotine pouches.

This system is used to ensure timely detection and regulatory-compliant handling of safety signals to protect consumer well-being, support responsible innovation, and contribute to product improvement.

"This system is used to ensure timely detection and regulatory-compliant handling of safety signals to protect consumer well-being, support responsible innovation, and contribute to product improvement."

PMI's postmarket safety surveillance process

Intake: Data are collected from different sources, including call centers, poison control centers, local campaigns, and clinical studies, and logged into the GVP-compliant LifeSphere® MultiVigilance database.

Translation: Reports are collected in local languages and translated into English.

Review: Includes validity and duplication checks.

Medical review: Assessment of the seriousness and likelihood of an AE. This includes the following steps:

- **Identification of the AE**
- **Coding:** Application of a standardized code from the Medical Dictionary for Regulatory Activities (MedDRA). This enables easier information sharing across platforms.
- **Seriousness assessment:** Determination of the seriousness of the AE based on International Council for Harmonization (ICH) criteria and the European Medicines Agency (EMA) list for the definition of important medical events.
- **Expectedness:** Determination of how likely it is for the AE to occur.
- **Causality narrative:** Description of the individual AE.

Submission to regulatory authorities: Depending on the market, different reporting requirements will apply.

What guidelines and regulations does PMI's safety surveillance system follow?

Kamila: In 2019, the U.S. Food and Drug Administration (FDA) authorized the marketing of the THS 2.2 under the premarket tobacco product application (PMTA) pathway. Under the PMTA, it is a legal requirement that any novel, tobacco-containing product introduced into the U.S. market must be supported by scientific data demonstrating that the product is appropriate for the protection of public health. We are also obliged to collect all AEs that occur with the usage of our smoke-free products and perform signal detection activities. In our annual report to the FDA, we include an update and analysis of any safety signals and risks that were identified for our smoke-free products. So, our safety surveillance system ensures we meet these requirements.

Brindusa: Data from our smoke-free products are collected from more than 80 markets, and some of these markets have their own reporting requirements. Greece, for example, requires the reporting of all serious AEs, while Canada requires only reporting of life-threatening AEs and deaths. In addition to the U.S., our safety data help us meet reporting requirements in around 35 countries where our products are marketed.

Can you tell us a bit about how PMI tracks health-related complaints?

Nikolina: To track health-related events, we use a database called LifeSphere® MultiVigilance (LSMV), which is a common tool used in the pharmaceutical industry for safety surveillance. There are many ways that information on AEs can come to us, but around 90% of all AEs come through PMI's call centers. What often happens is that a consumer calls to ask a question, maybe about how to use the product, and during the call they mention an AE, for example, headache after product use. The call center agents are trained to recognize AEs, so when they hear that someone has experienced a health-related event, they open LSMV and fill out the special form that we have created for them.

Brindusa: LSMV is a validated system that incorporates advanced technology and follows pharmaceutical industry standards inspired by the EU Good Pharmacovigilance Practices (GVP). We continuously evaluate and enhance the system with new tools and technology to improve efficiency. For example, we recently integrated the LifeSphere® Signal and Risk Management (LSSRM) tool. This is an end-to-end platform for the definition, identification, management, and communication of safety risks throughout the lifecycle of a product. This platform enhances our ability to rapidly identify signals and respond appropriately, further supporting consumer protection.

Do you use AI or automation in this process?

Nikolina: Artificial Intelligence (AI) is used to extract specific information about events from the AE reports. The LSMV system also uses intelligent coding, which automatically assigns AEs to a standardized classification system and applies criteria for determining their seriousness and expectedness. Approximately 80% of our cases are processed automatically.

Brindusa: The identification of discrepancies or missing information is also partially automated: the system will suggest questions for the call center to ask, and the team will verify whether those questions are relevant to a particular query and issue the final instructions to the call center.

What tools and techniques do you use when looking for data patterns?

Kamila: We perform both quantitative and qualitative analysis on the data we receive. In our qualitative review we focus on specific cases that meet one or more of the seriousness criteria, and we conduct a medical review to determine if our product was causally related to a serious AE. We also analyze cases quantitatively, in aggregate, to look for patterns. For example, if we notice a spike in the numbers of a specific AE, we conduct a deeper quantitative analysis to try and understand what has caused the observed increase. We then use statistical analysis to verify if that increase was statistically significant.

Nicolas: We also examine the data for signals. A signal is an event which represents either a potential or an identified risk whose occurrence is likely enough to justify further analysis and verification. Signals may include an unexpected event that might be linked to a product but for which we lack confirmed evidence, or a previously identified risk where there is enough evidence to show a link with the product.

How do you decide when a signal is serious enough to warrant mitigation measures?

Nicolas: When we have identified a signal, we conduct a risk assessment, taking into account the severity of the situation and the likelihood of it occurring. This will produce a score that tells us the seriousness of this risk.

Kamila: The level of seriousness will affect the action taken. For example, it will help us determine if placing a warning on the product is adequate to mitigate the risk, or if the risk is sufficiently severe and likely to occur that we need to consider a withdrawal of the product from the market. Generally, we put standard mitigation measures in place to limit the risk, no matter the severity. Even if it is something relatively minor, we want to make sure our consumers are aware of it.

Once you have identified a signal, how do you solve issues at the product level?

Nicolas: There are two main ways in which our work informs product development. For products that are already on the market, we notify the product development teams when a new signal is identified. If it is a serious risk, they will investigate the feasibility of making changes at the product level. In addition to this, we will change the safety warnings to inform consumers of the risk. For products not yet on the market, we can use the experience we gained from conducting safety surveillance on existing products to advise product development teams during the design phase.

PMI's signal detection process

Signal detection: Analysis of the reported AE data to identify any potential safety signals.

Signal validation and prioritization: Evaluation of the data to verify if there is sufficient evidence of a potentially causal association between an AE and a product, or a new aspect of a known association, to justify further investigation. Safety signals are categorized as urgent or nonurgent, based on their seriousness, severity, clinical relevance, and the need for immediate action.

Assessment: Additional research is performed to further evaluate the significance and potential risk of a validated signal.

Recommendation for actions: The likelihood of the signal occurring is determined, along with any actions that need to be taken to mitigate the risk.

Risk communication: The new safety signal is communicated to consumers by making changes to the safety warnings and instructions. The analysis of the signal is also included in the annual reports submitted to competent regulatory authorities and the information is shared with relevant PMI's stakeholders.

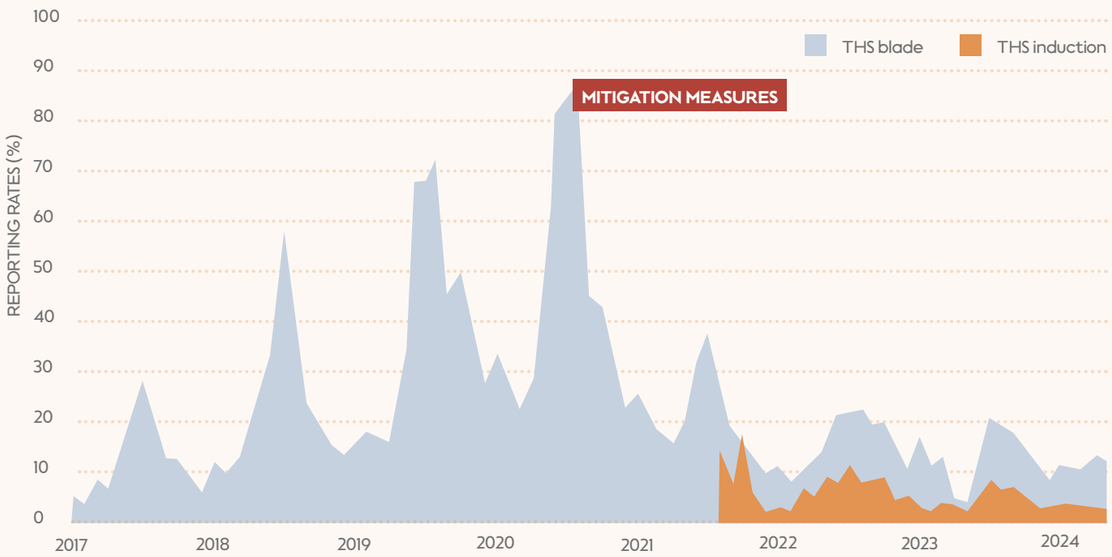
Signal case study: Thermal burn

In 2016, safety surveillance data indicated an increase in cases of thermal burns being reported to PMI's call centers. Complaints mainly included burns to the lips, fingers, or hands while using THS.

The safety surveillance team reviewed and analyzed the reports and determined that thermal burn was in fact a safety signal related to product use. Further analysis determined that the physical perception of thermal burn was driven by an increase in aerosol mass, which occurred when tobacco rods absorbed more moisture after being stored in humid conditions. The increase in aerosol mass can raise the temperature by 3 °C or more, causing the aerosol to reach temperatures hot enough to be perceived as mildly-to-moderately painful. The team concluded that most of the cases of thermal burn were reports of this burning sensation rather than tissue damage.

Quantitative examination of the AE reports found that thermal burn complaints tended to spike during periods of hotter and more humid weather. These spikes were due to the consumables absorbing more water, increasing the aerosol mass and the subsequent number of thermal burn reports.

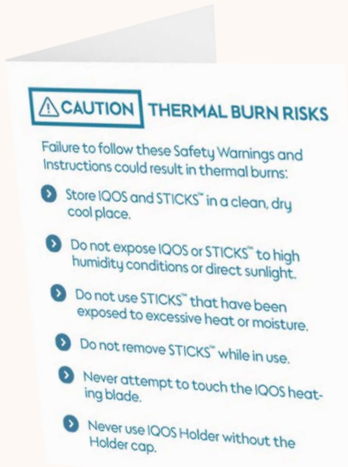
Thermal Burn Reporting Rates Over Time



Reporting rates were calculated by dividing the number of cases by the number of estimated consumers in millions.

Once the cause of the signal was determined, actions were taken to warn consumers and mitigate the risk. This included redesigning the consumables to increase airflow, subsequently decreasing the temperature of the aerosol.

Consumer safety warnings and instructions in the user guide were updated to highlight the specific risk and advise users to keep consumables in a cool, dry place. An analysis of the thermal burn risk was also included in annual reports submitted to relevant authorities, and ongoing monitoring of thermal burn reports continues through PMI's safety surveillance system.



How is PMI aligning our postmarket surveillance practices with emerging industry standards?

Brindusa: PMI participates in a number of initiatives through CORESTA (Cooperation Center for Scientific Research Relative to Tobacco), an international organization promoting global scientific cooperation in tobacco research. As the tobacco industry has no current guidelines for conducting postmarket safety surveillance, PMI, together with other tobacco manufacturers, are working to put this in place under the CORESTA umbrella.

Through CORESTA, PMI is working to address the lack of standardized guidelines for postmarket surveillance of smoke-free products. The initiative, which was proposed by PMI and approved in April 2024, will develop best practices and guidelines inspired by pharmaceutical pharmacovigilance systems.

This effort aims to harmonize AE management across the tobacco industry, support regulatory compliance, and enhance product safety through a phased approach that includes guideline development and industry-wide training. The proposal aligns with both CORESTA's mission and our own Product Science team's 5-year plan, and includes key industry stakeholders.

Nikolina: While all tobacco companies are conducting safety surveillance, the level at which we do it is significantly more advanced. That's why PMI's participation in CORESTA is important, it's an opportunity to work together with other tobacco companies to improve safety surveillance across the industry.

A DECADE OF SAFETY DATA **SUPPORTING THE TOBACCO HEATING SYSTEM**

PMI collects postmarket safety surveillance data on all of our smoke-free products and has collected more than 10 years of data on our THS, a heated tobacco product (HTP) which comes in various versions commercialized as *IQOS*. Read more to find out what we have learned about the overall safety profile of our leading HTP.

What data does PMI collect on its smoke-free products?

PMI collects safety data related to AEs. This includes information on the type of event (thermal burn, headache, cough, etc.), type of device, and the location, gender, and age of the reporter.

As part of the medical review process, AEs collected from various sources are categorized by level of seriousness based on ICH and EMA criteria.

According to these criteria, a serious AE is one which could result in one or more of the following:

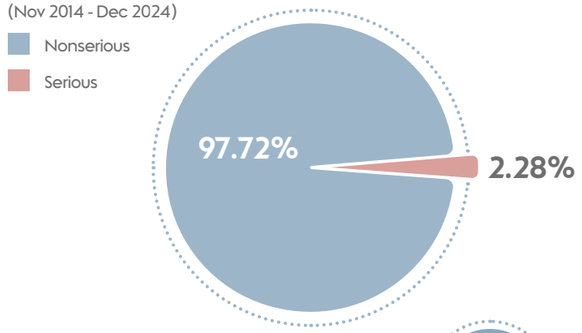
- Inpatient hospitalization or prolongation of existing hospitalization
- Persistent or significant disability/incapacity
- Congenital anomaly/birth defects
- Is life threatening
- Death
- Is assessed as an important medical event

What do the data show about the overall safety of THS?

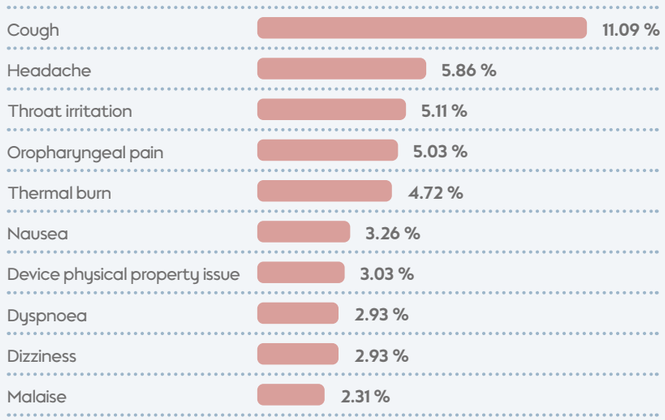
Our postmarket safety surveillance data show that, between 2014 and the end of 2024, THS has shown a steady safety profile, even as the number of markets where it is available expanded from two to more than 80 and the number of users increased from 5,000 (2014) to 32.2 million (end of 2024).

Throughout the past 10 years, the total number of AEs has been influenced by factors such as the number of markets, number of users, and events such as COVID-19. However, the percentage of AEs meeting the criteria for seriousness has remained stable at an average of 2.28% of the total number of AEs recorded. **This is close to the safety profile for nicotine replacement therapies (NRTs), which serves as a reference for evaluating the safety of THS products.** It is important to note that the number of serious events has also remained consistent across different devices, indicating that all PMI smoke-free products share a similar safety profile.

CASE SERIOUSNESS
(Nov 2014 - Dec 2024)



TOP 10 ADVERSE EVENTS
(Nov 2014 - Dec 2024)



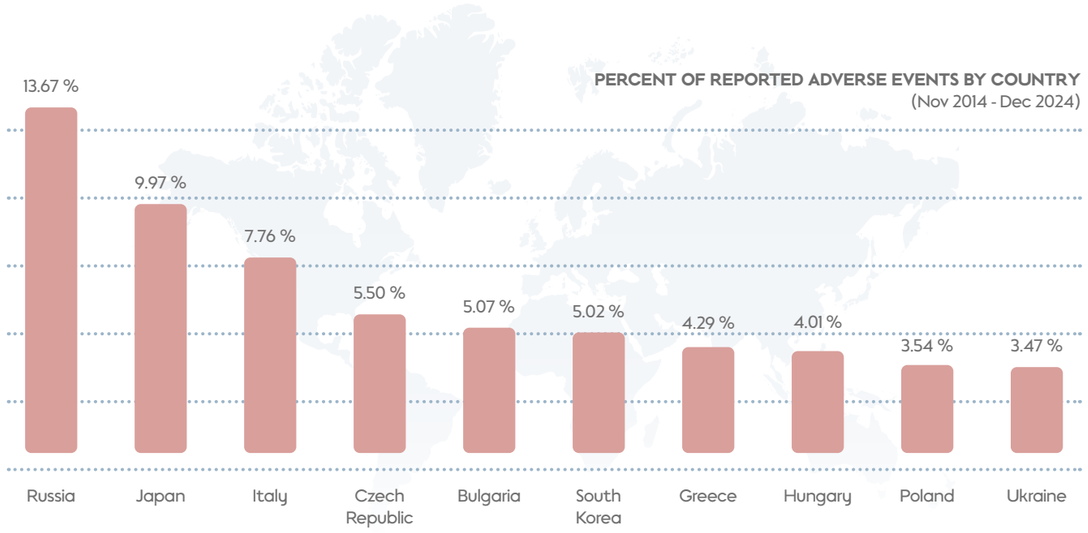
What are the most commonly reported AEs?

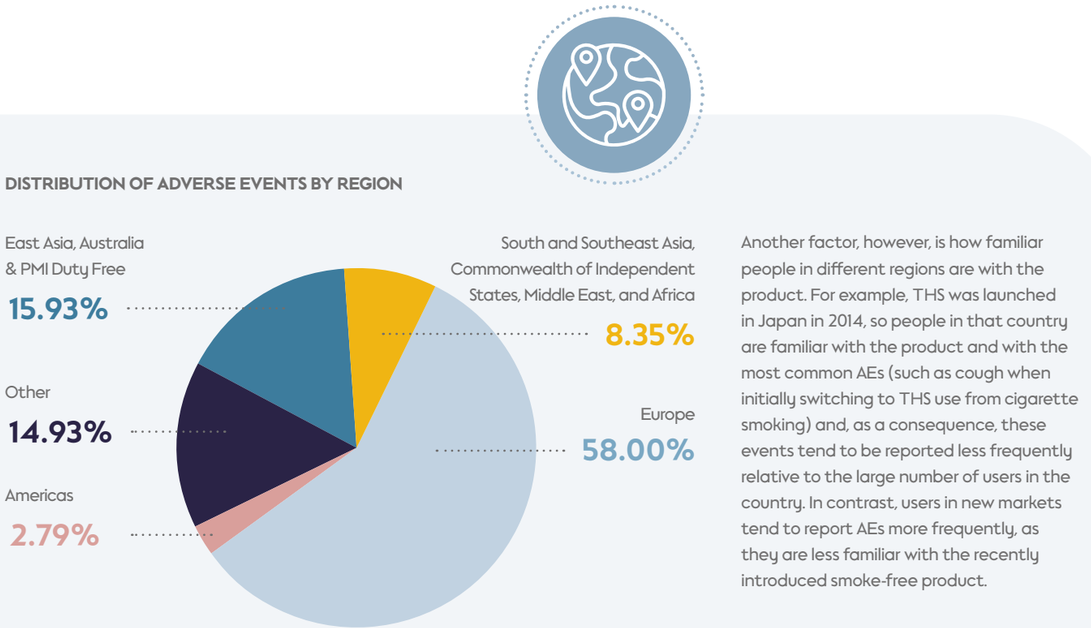
The overall data show that, for legal age consumers, the most frequently reported AEs for THS are similar to those most frequently reported with NRTs (the specific risks and frequency of reporting vary based on the type of NRT).

Cough is the most commonly reported AE for THS, representing just over 11% of AEs. Analysis of our postmarket safety surveillance data indicates that coughing tends to be most common in the first few days after switching from cigarette smoking to THS use. This might be related to the adaptation phase associated with the product. In addition to cough, headache, throat irritation, and oropharyngeal pain each account for more than 5% of reported AEs.

How do reported AEs for THS vary across countries?

As of the end of 2024, THS was available in more than 80 markets. We would expect to see a variation in the number of AEs reported in different markets. For example, we would expect countries with larger numbers of THS users to have more reports of AEs. In general, this is indeed the case.





Another factor, however, is how familiar people in different regions are with the product. For example, THS was launched in Japan in 2014, so people in that country are familiar with the product and with the most common AEs (such as cough when initially switching to THS use from cigarette smoking) and, as a consequence, these events tend to be reported less frequently relative to the large number of users in the country. In contrast, users in new markets tend to report AEs more frequently, as they are less familiar with the recently introduced smoke-free product.

Climate conditions can also have an impact. For example, reports of thermal burn are more common in hot climates, and at times of year with hotter weather. However, looking at the top AEs across different regions, the safety profile for THS shows similar patterns globally.

How is postmarket safety surveillance data used for regulatory purposes?

Our postmarket safety surveillance program is used to support regulatory submissions and authorizations of our smoke-free products, such as the U.S. FDA's premarket tobacco product applications (PMTAs) and modified risk tobacco product (MRTP) applications. The information we collect also helps us meet reporting requirements needed to maintain our products on the market.

Systematic analyses of aggregated reports are conducted to uncover emerging trends and potential risks, facilitating the timely identification of safety signals. PMI scientists compile safety update reports based on these analyses, and this information is communicated annually to regulatory authorities.

In the European market, postmarket safety surveillance is a critical component of the EU General Product Safety Regulation 2023/988 (EU GPSR). This regulation ensures that products sold within the EU, both online and offline, meet high safety standards to protect consumers. It requires manufacturers to establish a comprehensive safety surveillance system that includes monitoring product performance, product accident reporting to authorities by businesses, appropriate management of products found to be unsafe, and continuous communication with authorities for transparency and effective management of risks.

AE cases that satisfy criteria for reporting under this regime are escalated internally to the product safety surveillance team who coordinates the review of the package and collects all the different documents to perform the submission.

THS is not a medical device, but by committing to the same rigorous processes as those used for medical devices, PMI is demonstrating that product safety surveillance is a core part of our commitment to harm reduction.

How does PMI track incidents related to accidental ingestion?

The safety surveillance team monitors reports of accidental ingestion involving PMI smoke-free products and also uses data from poison control centers to look at general patterns for whole product categories, for example, for all nicotine pouches on the market. The data is analyzed to assess how reports of accidental ingestion evolve over time and how this compares with the internally tracked reporting patterns for PMI products.

While there have been cases reported of accidental ingestion of PMI's nicotine pouches, snus, e-vapor liquids, and THS consumables, no fatal or life-threatening acute nicotine toxicity cases have been reported so far.

Overall, the risk of lethal or life-threatening acute nicotine toxicity from accidental exposure to tobacco sticks, nicotine pouches, or portion-packed snus is considered highly unlikely. Our internal estimates indicate that, using conservative estimates for nicotine content and percentage of nicotine extraction, it would require more than 75 tobacco sticks or 40 nicotine pouches to be accidentally ingested at one time in order to produce serious or life-threatening effects in a 70 kg adult.

What is the overall safety profile of THS?

The data PMI collects on postmarket safety surveillance demonstrates that our THS has maintained a steady safety profile, even as the number of users and markets sees a large increase. These data cover 10 years of safety surveillance, from the launch of THS in 2014 until the end of 2024. Importantly, 97.7% of cases are nonserious, with the most common AEs reported (≥5%) being cough, headache, throat irritation, and oropharyngeal pain.

EVENT HIGHLIGHTS

GLOBAL FORUM ON NICOTINE **2025**

12th Global Forum on Nicotine

Warsaw, Poland

June 19-21, 2025

PMI participated in the 12th Global Forum on Nicotine. The theme for this year was "Challenging Perceptions - Effective Communications for Tobacco Harm Reduction." During this 3-day conference, PMI scientists gave four video presentations. Christoph Neubert, Manager Scientific and Medical Affairs at Philip Morris Germany, discussed the barriers to stopping smoking in Germany. Carrie Wade, Sr. Manager Scientific Engagement, and Gizelle Baker, VP Scientific Engagement, shared a conversation where they discussed common misunderstandings about nicotine delivery in pouches. Alexander K. Nussbaum, Head of Scientific and Medical Affairs at Philip Morris Germany, presented a study focusing on the reasons for oral nicotine product use among adults who smoke or use smoke-free products in Germany, and the results from PMI's survey on the main barriers for stopping smoking. Finally, Leanne Leroy, New Market Safety Support Scientist, Dariusz Peric, Medical Safety Scientist, and Cam Tuan Tran, Manager Medical Safety Operations, presented a video discussing a decade of safety insights from THS safety surveillance program.

See the presentations here.

INTERNATIONAL SOCIETY FOR PHARMACOECONOMICS AND OUTCOMES RESEARCH **2025**

International Society for Pharmacoeconomics and Outcomes Research (ISPOR)

Montreal, Canada

May 13-16, 2025

The theme for ISPOR this year was "Collaborating to Improve Healthcare Decision Making for All: Expanding HEOR Horizons," emphasizing the pivotal role of health economics and outcomes research (HEOR) in transforming healthcare systems. This year, PMI researchers presented a poster on a protocol for a real-world study that aims to evaluate the impact of switching from cigarette smoking to heated tobacco product use and the potential impact on the time to subsequent chronic obstructive pulmonary disease (COPD) hospitalizations compared with continued cigarette smoking. Our scientists also presented a poster which shared a protocol for a real-world retrospective study in Japan that looks at cardiovascular health outcomes. The study will examine whether switching from cigarettes to heated tobacco affects how long it takes for someone with cardiovascular disease to experience a major cardiovascular event.

Find out more about PMI's presentations here.

SOCIETY OF TOXICOLOGY ANNUAL MEETING **2025**

64th Annual Meeting and ToxExpo

Orlando, Florida, USA

March 16-20, 2025

The annual meeting of the Society of Toxicologists (SoT) and the concurrent ToxExpo bring together leading toxicologists and industry experts with organizations that support toxicologists and the toxicology community. Researchers from PMI joined the conference with four posters. One poster was focusing on the use of gingival organotypic cultures as a tool to discriminate nicotine pouch formulation related oral biological effects. Another poster from Swedish Match (PMI affiliate) discussed the use of *in vivo* nicotine extraction in the risk assessment of snus and nicotine pouches. Conducted in collaboration with Altria, the last two posters focused on the evaluation of chronic toxicity and carcinogenicity of flavored e-vapor aerosol compared with cigarette smoke in laboratory models.

Find out more about these presentations here.

TOBACCO SCIENCE RESEARCH CONFERENCE **2025**

Tobacco Science Research Conference (TSRC)

Knoxville, TN, USA

September 14-17, 2025

The Tobacco Science Research Conference (TSRC) is an annual event dedicated to advancing scientific understanding of tobacco and tobacco-related products. It serves as a platform for academics, researchers, policymakers, and industry professionals to share the latest findings and foster collaboration across disciplines. The 78th edition of the conference opened with the theme "Collective Progress & Future Sustainability - Key Considerations, Shared Perspectives, and Common Ground." During the conference, PMI's Safety Surveillance team delivered a presentation covering 10 years of postmarket safety surveillance data for THS, and a poster on the management of safety signals related to THS. A second presentation, given by PMI's Real-World Evidence team, explored trends in tobacco and nicotine product use in Japan between 2016 and 2023, based on findings from repeated cross-sectional surveys. Additional findings from cross-sectional surveys were shared by PMI scientists through posters, including an analysis of nicotine pouch use characteristics and a study on the prevalence and usage patterns of tobacco and nicotine products in Italy from 2018 to 2023.

PMI PUBLICATIONS

A Comparative Assessment of the FDA List of 93 HPHCs in Aerosol Generated by Tobacco Heating System 2.2 versus 3R4F Reference Cigarette Smoke

In 2009, the U.S. Federal Food, Drug, and Cosmetic Act (FD&C Act) commissioned the FDA to establish a list of harmful and potentially harmful constituents (HPHCs) to be quantified in each tobacco product brand and sub-brand. This list (known as the FDA 93 and first published in 2012) comprises 93 compounds or classes of compounds linked to diseases such as cancer and cardiovascular disease, among others.

In a 2017 study, PMI examined the levels of HPHCs in THS aerosol and the smoke from a reference cigarette (3R4F). This found a 92% average reduction of HPHCs in THS aerosol compared with cigarette smoke. However, it did not include all HPHCs in the U.S. FDA 93 list as standardized methods for measuring some of the compounds had not yet been developed at the time of the study. Additional research was also needed to replicate and extend these findings.

A recent paper, published in 2025, details a study conducted by PMI researchers which leverages technological advances and new analytical methods to measure reductions in an expanded list of 108 HPHCs, which covers constituents listed in the FDA 93, in THS aerosol compared with 3R4F smoke.

Analysis was conducted on levels of HPHCs in aerosols emitted by THS 2.2, using two different THS heated tobacco units (HTUs) (regular and menthol), compared with 3R4F smoke. Of the 108 HPHCs tested, 105 showed an average reduction of >91.6% (regular) and >92.2% (menthol) in the THS aerosol, compared with 3R4F smoke. Of the three remaining constituents, two—nicotine and anabasine—are tobacco alkaloids and the remaining analyte, polonium-210, was near the limit of detection in THS aerosol. These results confirm that the elimination of combustion in THS results in a substantial reduction of HPHCs relative to cigarette smoke.

AeroSolved: Wall Boundary Conditions for Liquid Multispecies Aerosol Deposition at Transient and High-Humidity Flows

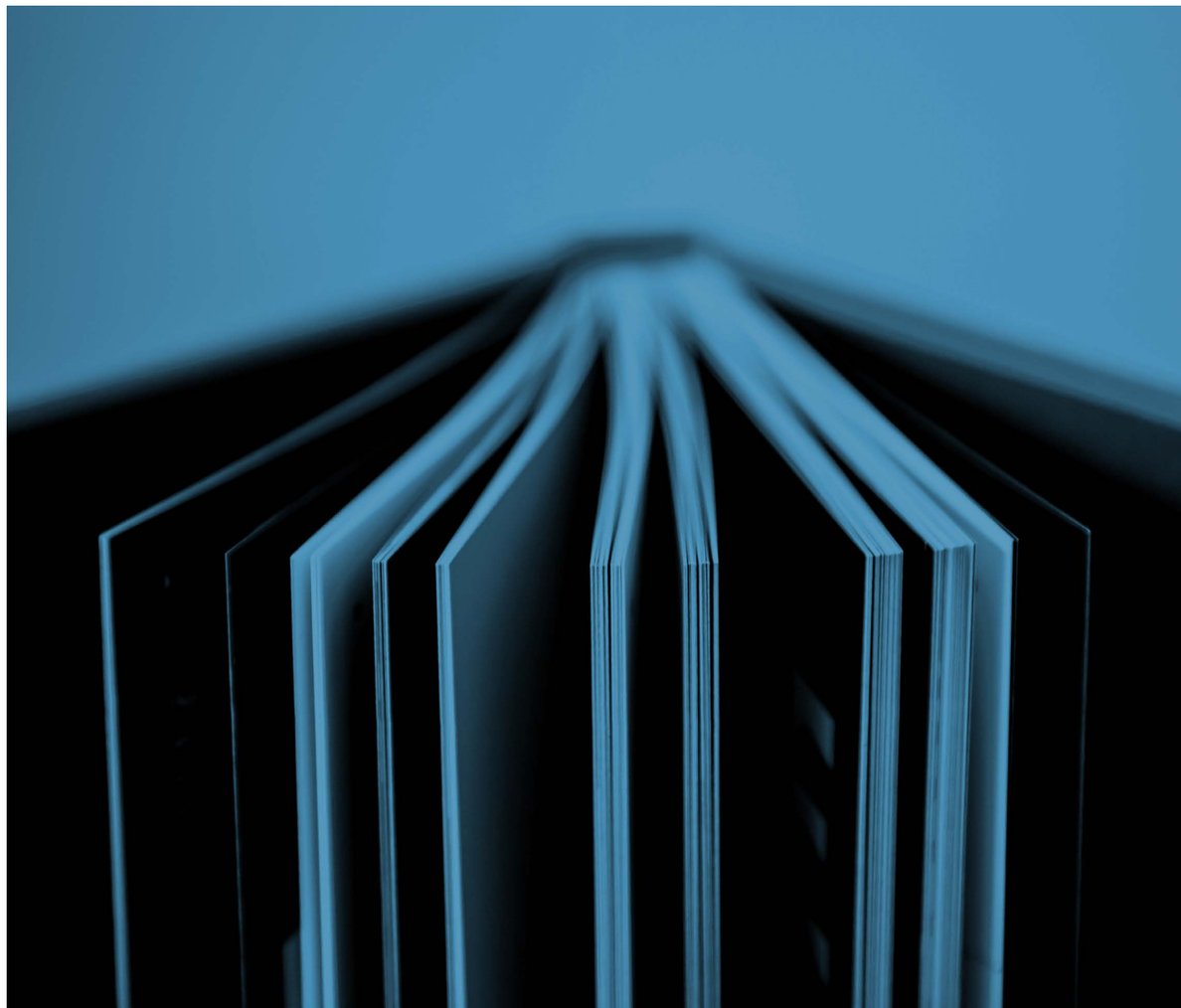
Aerosol studies are a critical part of PMI's assessment of our heated tobacco and e-vapor products. However, there are a number of challenges for conducting computational simulations of multispecies aerosols (i.e., aerosols containing a mix of substances that behave differently under changing conditions). This is due, in part, to the complexity of thermodynamic interactions and the diverse physical processes occurring during the inhalation of aerosols.

When studying how complex aerosols affect the lungs during product use, researchers routinely assume steady-state flow conditions. However, this does not allow them to take into account real-world conditions such as the effect of the inhalation profile on the aerosol evolution and how this affects aerosol interaction with the mucus interface.

PMI researchers developed advanced simulation methods to better understand how aerosols from e-vapor products behave inside the lungs. Using a specialized computational tool called AeroSolved™, they modeled how complex mixtures interact with airflow and lung surfaces during typical, real-world inhalation patterns.

In conducting the study, researchers introduced new boundary conditions which account for humidity and phase changes, allowing the simulation to reflect real-world conditions more accurately. To test the model, researchers simulated aerosol flow through a bent pipe, representing the upper airway. They analyzed how puffing, holding, and inhaling affect particle movement and deposition, showing that humidity and airflow patterns significantly influence aerosol deposition in the lungs.

The results provided insights into the dynamics of multispecies aerosol flow behavior in the airways under more realistic conditions. The researchers concluded that these types of investigations could enable simulation models to more closely mirror actual inhalation scenarios and help researchers obtain more accurate data than from models that assume steady state flow conditions.



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 text in these pages include our product development and assessment efforts, our initiatives to share our methodologies and results, as well as our publications.

More detailed information can be found at www.pmiscience.com.