



SCIENTIFIC UPDATE

PMI SCIENCE – PHILIP MORRIS INTERNATIONAL

SEPTEMBER 2020 | ISSUE 11

HISTORIC DECISION



***IQOS* authorized under
U.S. MRTP pathway**

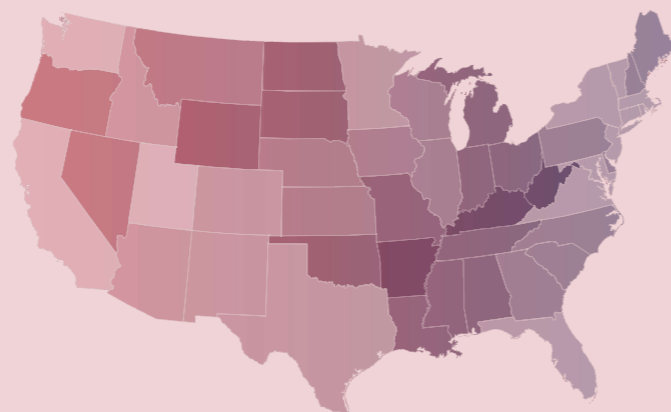


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INTRODUCTION

The U.S. Food and Drug Administration (FDA) really put science at the center of their decision-making this year as they authorized the *IQOS Tobacco Heating System* as a Modified-Risk Tobacco Product with Reduced Exposure Information.

How can an adult smoker know that something is a better choice unless you tell them? It's not intuitive.

One thing that is unique in the approach by the U.S. is the ability of the FDA to authorize the passing of messages to adult smokers to help guide their choices. We really hope that other countries look to the FDA's approach and learn from their decision in the context of their own country. To likewise put science at the center of their decision-making processes to help consumers and guide their choices.



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EVENTS

Congratulations: sbvIMPROVER MEDIC winners

 August 27, 2020

sbvIMPROVER is a collaborative initiative led and founded by PMI. The program hosted a computational competition entitled the Metagenomics Diagnosis for Inflammatory Bowel Diseases Challenge (MEDIC), in which participants were challenged to use machine learning to classify patients with Inflammatory Bowel Disease (IBD) and non-IBD subjects based on metagenomics data. The competition was divided into two sub-challenges: "MEDIC RAW" and "MEDIC PROCESSED" to ensure that even participants with no access to metagenomics analysis pipelines can solve the challenge successfully. Participants were scored by an independent scoring review panel that included experts in metagenomics and systems biology. The winners were announced August 27, 2020, and won a cash prize, earned the chance to collaborate with the top biologists and data scientists of today, as well as the opportunity to publish their findings in peer-reviewed journals.

More on this challenge and the winners: <https://www.pmscience.com/whats-new/winners-of-sbv-improver-machine-learning-diagnostic-challenge-announced>

FDA Authorization for IQOS in US

 July 7, 2020

The U.S Food and Drug Administration (FDA) authorized the marketing of the *IQOS Tobacco Heating System* as a Modified Risk Tobacco Product (MRTP) with Reduced Exposure Information. This is the first electronic nicotine product to gain such authorization and the second nicotine product ever recognized as an MRTP. This decision acknowledges that our leading heated tobacco product is fundamentally different from combusted cigarettes, and a better choice for adults who would otherwise continue smoking. The MRTP review process started back on December 5, 2016, when the FDA received MRTPAs for the *IQOS* device and three HeatStick variants. It was an ongoing process that included PMI presenting to FDA's Tobacco Products Scientific Advisory Committee on January 24-25, 2018.

Learn more about this milestone: <https://www.pmscience.com/smoke-free/regulation/fda-mrtpa>



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Open Science

 Online  September 15, 2020

On September 15, 2020, we hosted our second Open Science online webinar, focusing on the problem of burning tobacco. The webinar explored some of our fundamental research regarding the aerosol of our leading heated tobacco product. We hosted three different sessions to cater to different time zones. Each session included pre-recorded videos of our scientists walking us through their selected topics and was followed by a live Q&A. Just like our last webinar, the event was free and open to registered individuals.

Dr. Tom McGrath discussed why the absence of combustion was so important. Dr. Markus Nordlund gave us a breakdown of the fundamental differences between smoke and aerosol. Mark Bentley explained the chemistry behind our product's aerosol, while Dr. Catherine Goujon assessed the impact of the aerosol on indoor air. And Dr. Maurice Smith spoke about what we know from independent studies our product's aerosol.

Hosting webinars for the scientific community is an excellent way for us to remain transparent with our latest results. With this year's incredible turnout, we were able to share our findings and open a discussion with the scientific community. We look forward to our next session, whether it be online or in person.

Learn more about Open Science: www.pmscience.com/open-science



Historic decision made as *IQOS Tobacco Heating System* is authorized under U.S. MRTP pathway

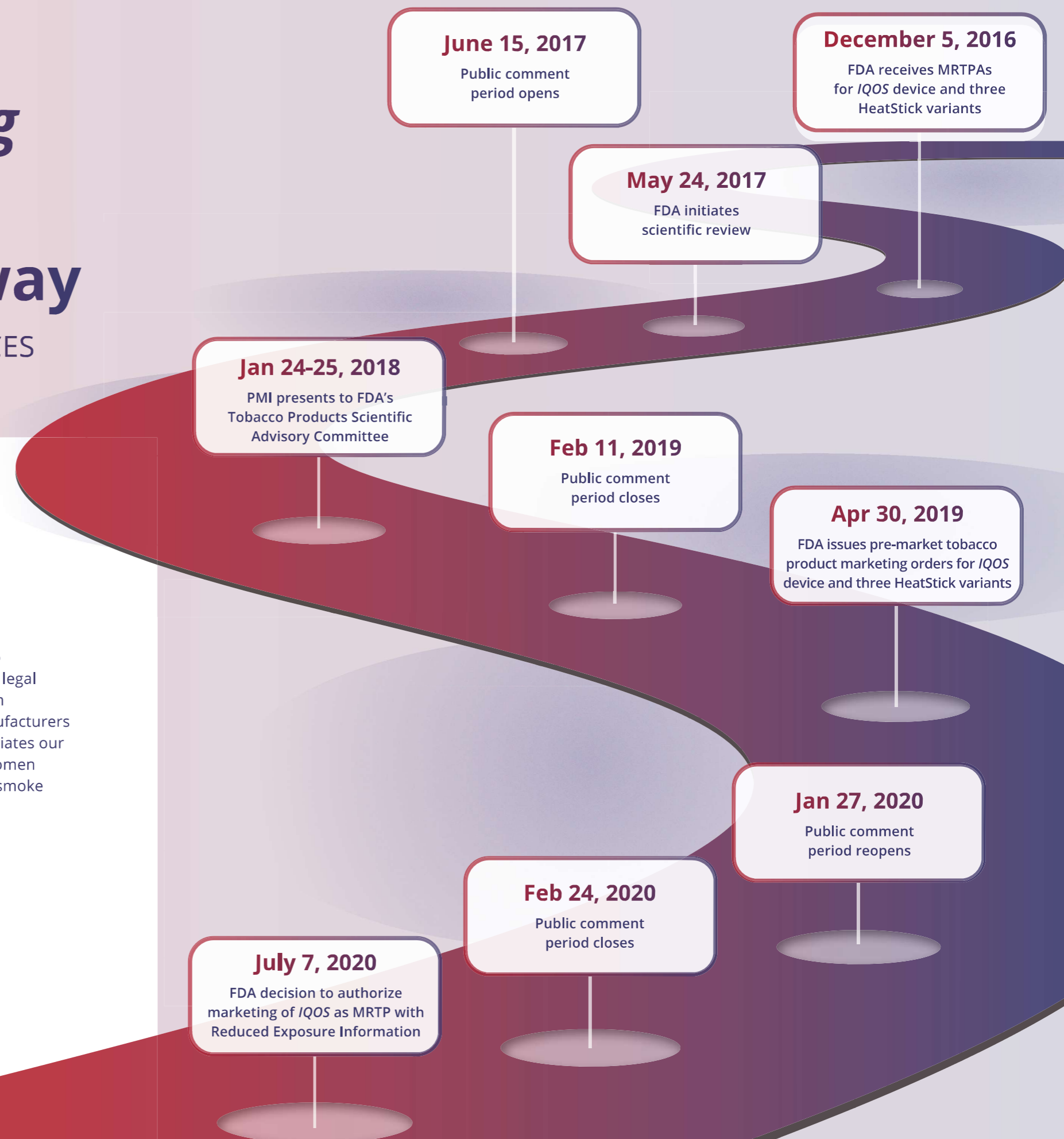
U.S. FDA RECOGNIZES FUNDAMENTAL DIFFERENCES BETWEEN *IQOS* SYSTEM AND CIGARETTES

The U.S. Food and Drug Administration (FDA) announced on July 7, 2020 authorization to market the *IQOS Tobacco Heating System with Reduced Exposure Information*. This is the second set of products ever to be authorized as Modified Risk Tobacco Products (MRTPs), and the first electronic nicotine product to receive such authorization.

The FDA's decision provides an important example of regulation of smoke-free alternatives to differentiate them from combusted cigarettes in order to promote the public health. The U.S. legal framework and FDA policy recognizes that tobacco products exist on a continuum of risk, with combusted cigarettes being the most harmful, and provides a regulatory framework for manufacturers to inform consumers about products with different risk profiles. The decision clearly differentiates our leading heated tobacco product from combusted cigarettes and allows American men and women who smoke to receive information about a product that is a better choice than continuing to smoke cigarettes. But first, a quick review on how we got to where we are now.

Timeline of the MRTP review process

The MRTP application review process began with several meetings between PMI and the FDA to discuss plans to submit an MRTP application. With the initial submission of the application in December 2016, FDA then determined whether the product fell under the jurisdiction of the Center for Tobacco Products and that legal requirements for the application were met. With the application in hand, FDA reviewed the filing to ensure the application contained all the necessary content, and then began scientific review of the application.



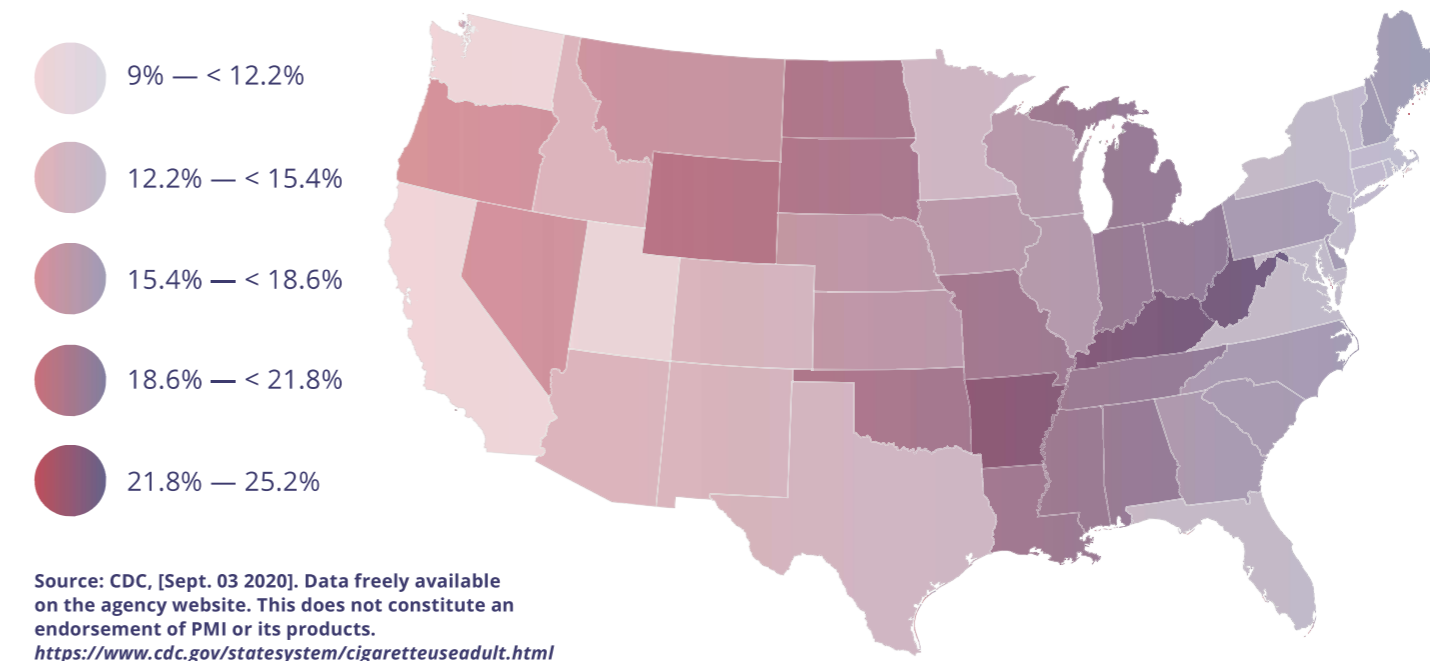


PMI's requested MRTP claims

The FDA has authorized the marketing of *IQOS Tobacco Heating System* in the U.S. as an MRTP with Reduced Exposure Information. The *IQOS* system is the name under which our Electronically Heated Tobacco Product (EHTS) is marketed. The agency found that the issuance of the modified risk tobacco product orders with reduced exposure information would be *"appropriate to promote the public health and is expected to benefit the health of the population as a whole."*

The FDA also concluded that the totality of evidence presented suggests that a measurable and substantial reduction in morbidity or mortality among individual tobacco users is reasonably likely to be established in subsequent studies.

Cigarette use among adults in the USA 2018



Available evidence to-date:

1 The *IQOS* system heats tobacco but does not burn it.

2 This significantly reduces the production of harmful and potentially harmful chemicals.

3 Scientific studies have shown that switching completely from conventional cigarettes to the *IQOS* system significantly reduces your body's exposure to harmful or potentially harmful chemicals.

These are the MRTP claims authorized by FDA regarding the *IQOS Tobacco Heating System*.



There are two types of modified risk orders the FDA is authorized by statute to issue: a “risk modification” order or an “exposure modification” order. PMI had requested both types of orders for EHTS. In its Technical Project Lead (TPL) summary review of the decision, the FDA determined that the evidence that has been submitted by PMI did not support issuing risk modification orders at this time—according to the FDA’s interpretation of the Tobacco Control Act standard for issuance of such orders—but that the evidence submitted did support issuing exposure modification orders for these products. This determination included a finding that issuance of the exposure modification orders is appropriate to promote public health and is expected to benefit the health of the population as a whole, taking into account both users of tobacco products and persons who do not currently use tobacco products.

In particular, the agency determined that PMI demonstrated that EHTS heats tobacco and does not burn it, and that this significantly reduces the production of harmful and potentially harmful chemicals compared to cigarette smoke. The FDA also concluded that the totality of evidence presented suggests that a measurable and substantial reduction in morbidity or mortality among individual tobacco users is reasonably likely to be established in subsequent studies.

While we are convinced that the totality of evidence demonstrates that switching completely to EHTS presents less risk of harm compared to continued smoking, we will continue to work closely with the agency to determine what information would allow the FDA to conclude that the specific and statutory requirements in the U.S. are met, and therefore to authorize us to communicate reduced risk or harm information.

This decision follows the agency’s April 2019 authorization of the marketing of the *IQOS Tobacco Heating System* as “appropriate for the protection of public health” pursuant to the Premarket Tobacco Product Application (PMTA) pathway.

Our assessment program for the EHTS was presented to the FDA in our applications. This simplified, 5-step version represents the different levels of evidence we can obtain from our product assessment. Step 1 examines the product and its aerosol, Step 2 understands its effects using laboratory models, Step 3 learns about the effects in smokers who switch, Step 4 studies how people perceive and use the product, and Step 5 observes its impact on population health and/or over the long term.



“The FDA’s decision to authorize the marketing of the IQOS Tobacco Heating System as a Modified-Risk Tobacco Product with Reduced Exposure Information demonstrates the fundamental difference between this product and cigarettes. The FDA has set a high standard, and we look forward to working with them to implement the order so that IQOS is reaching the right audience.”

The science behind reduced exposure

The high temperature process of burning is known to create thousands of chemicals in smoke, many of which are harmful or potentially harmful. By not burning tobacco in EHTS, we significantly reduce, in some cases even eliminate, harmful chemicals compared to cigarettes. Using clinical studies, we confirmed that the reduced formation of harmful chemicals translated to reduced exposure among those who switched from cigarettes to EHTS. The FDA reviewed this evidence, together with research conducted by independent scientists, and found it to be sufficient to allow this information to be communicated to those adult men and women in the U.S. who smoke.

In addition to the scientific evidence supporting the reduced exposure profile of the product, consumer understanding of the message also matters. The FDA found that our consumer perception studies show that consumers generally comprehend the modified risk information in the context of total health. In particular, the results indicate that consumers understand that the product is not without risks and that it is more harmful than quitting smoking. Consumers also generally perceive the product as less harmful than combusted cigarettes, which is in line with the relative health risks of the product that are reasonably likely.



Authorization: An ongoing process

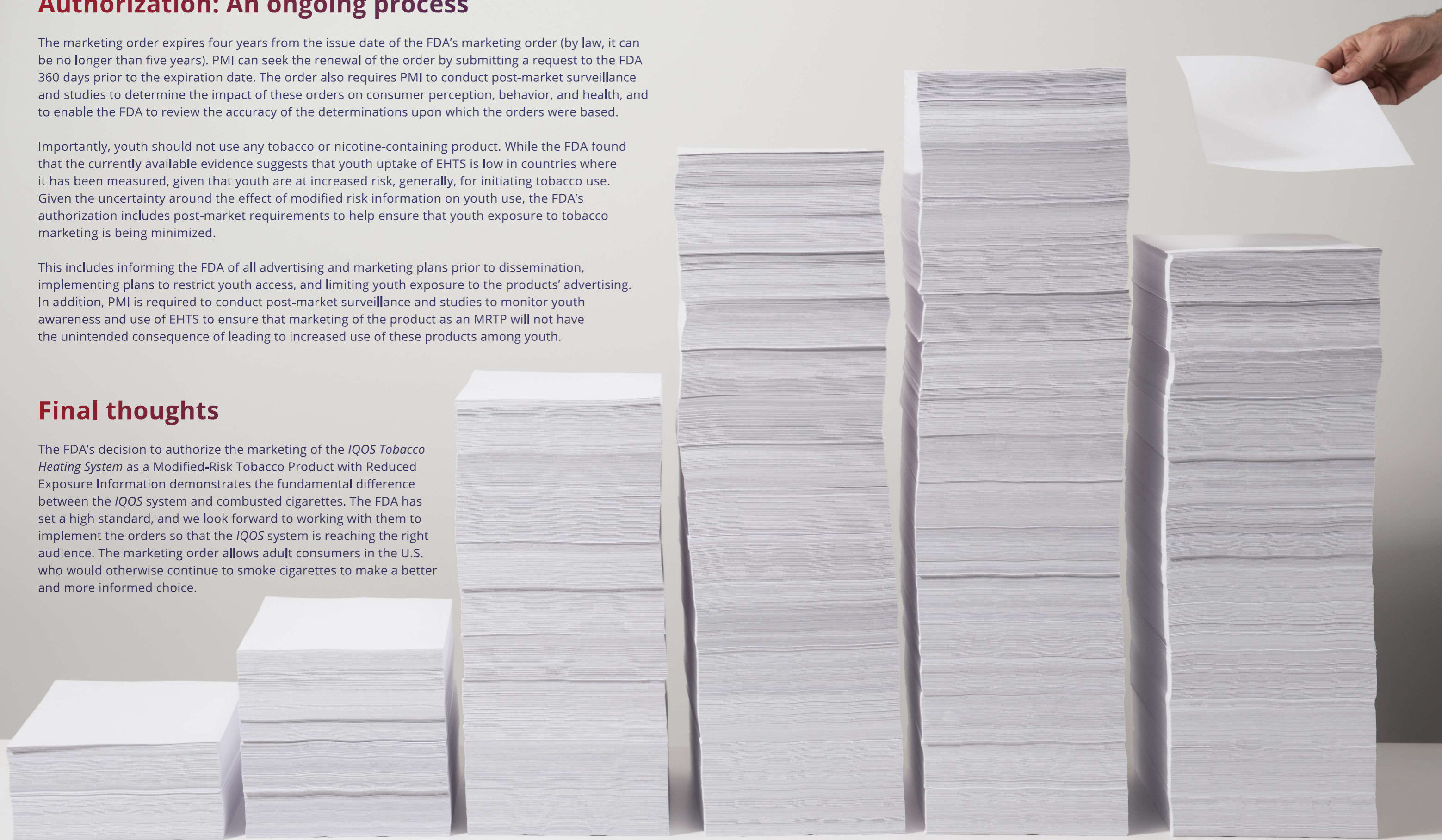
The marketing order expires four years from the issue date of the FDA's marketing order (by law, it can be no longer than five years). PMI can seek the renewal of the order by submitting a request to the FDA 360 days prior to the expiration date. The order also requires PMI to conduct post-market surveillance and studies to determine the impact of these orders on consumer perception, behavior, and health, and to enable the FDA to review the accuracy of the determinations upon which the orders were based.

Importantly, youth should not use any tobacco or nicotine-containing product. While the FDA found that the currently available evidence suggests that youth uptake of EHTS is low in countries where it has been measured, given that youth are at increased risk, generally, for initiating tobacco use. Given the uncertainty around the effect of modified risk information on youth use, the FDA's authorization includes post-market requirements to help ensure that youth exposure to tobacco marketing is being minimized.

This includes informing the FDA of all advertising and marketing plans prior to dissemination, implementing plans to restrict youth access, and limiting youth exposure to the products' advertising. In addition, PMI is required to conduct post-market surveillance and studies to monitor youth awareness and use of EHTS to ensure that marketing of the product as an MRTP will not have the unintended consequence of leading to increased use of these products among youth.

Final thoughts

The FDA's decision to authorize the marketing of the *IQOS Tobacco Heating System* as a Modified-Risk Tobacco Product with Reduced Exposure Information demonstrates the fundamental difference between the *IQOS* system and combusted cigarettes. The FDA has set a high standard, and we look forward to working with them to implement the orders so that the *IQOS* system is reaching the right audience. The marketing order allows adult consumers in the U.S. who would otherwise continue to smoke cigarettes to make a better and more informed choice.





ABOUT HEALTH & FUNCTIONING

To assess the perception and behavior of adults who may use PMI's smoke-free products we built the ABOUT Toolbox – a robust portfolio of self-report instruments, which support our regulatory submissions and MRTP applications. This article outlines the latest instrument in the Toolbox which focuses on measuring the perceived health status of adult smokers who switch to our smoke-free products. The ABOUT Toolbox team is Esther Afolalu, Emilie Clerc, and Christelle Chrea. Special thanks to our intern Giulia Penone.

How we assess behavioral outcomes related to tobacco and nicotine products

The number of individuals switching from cigarette smoking to using smoke-free Tobacco and Nicotine-containing Products (TNPs) is growing. Existing self-reporting measures for evaluating perceived health and quality of life are often not sensitive enough to provide a complete picture of the situation and assess impact of TNPs on the perceived health and functioning status of users.¹

For this reason, since 2012, we have been working on new outcome measures to specifically assess people's perceptions, attitudes, and behaviors towards smoke-free products in a scientifically robust manner. This is the purpose for which the [ABOUT Toolbox](#) has been created: to evaluate and assess the public health impact of tobacco harm reduction strategies on consumer perception and behavior.

The ABOUT Toolbox instruments are relevant to the whole spectrum of TNPs and they are designed using best

measurement and development practices in order to facilitate the comparison of perception and behavior data across academic, industry, and public health research communities.

Developing a new outcome measure to assess the impact of tobacco and nicotine-containing products on health and functioning

Aiming to assess the impact of TNPs on consumers' health and functioning, we strive to build one of the five key priority domains included in the ABOUT Toolbox (as displayed to the right) with a precise purpose. Since February 2018, we have worked on the Health and Functioning instrument, aiming to make it a comprehensive tool for the evaluation of smoke-free products' impact on public health.

The Health and Functioning instrument is currently being developed to accurately reflect the health status of individuals who use TNPs, with a particular focus on healthy adult smokers who switch to smoke-free products.

Theoretical framework and main development phases

To reach this goal while remaining scientifically robust, the instruments development has been underpinned by theoretical conceptual frameworks from health authorities such as: WHO's International Classification of Functioning, Disability,² and Health (ICF); the Revised Wilson and Cleary Model for Health-Related Quality of Life;³ and the US Food and Drug Administration's (FDA) Guidance on Patient-Reported Outcome (PRO) Measures.⁴ Based on these and other frameworks, we organized the development process of the new self-reporting measures into three main phases:

A. PREPARATION

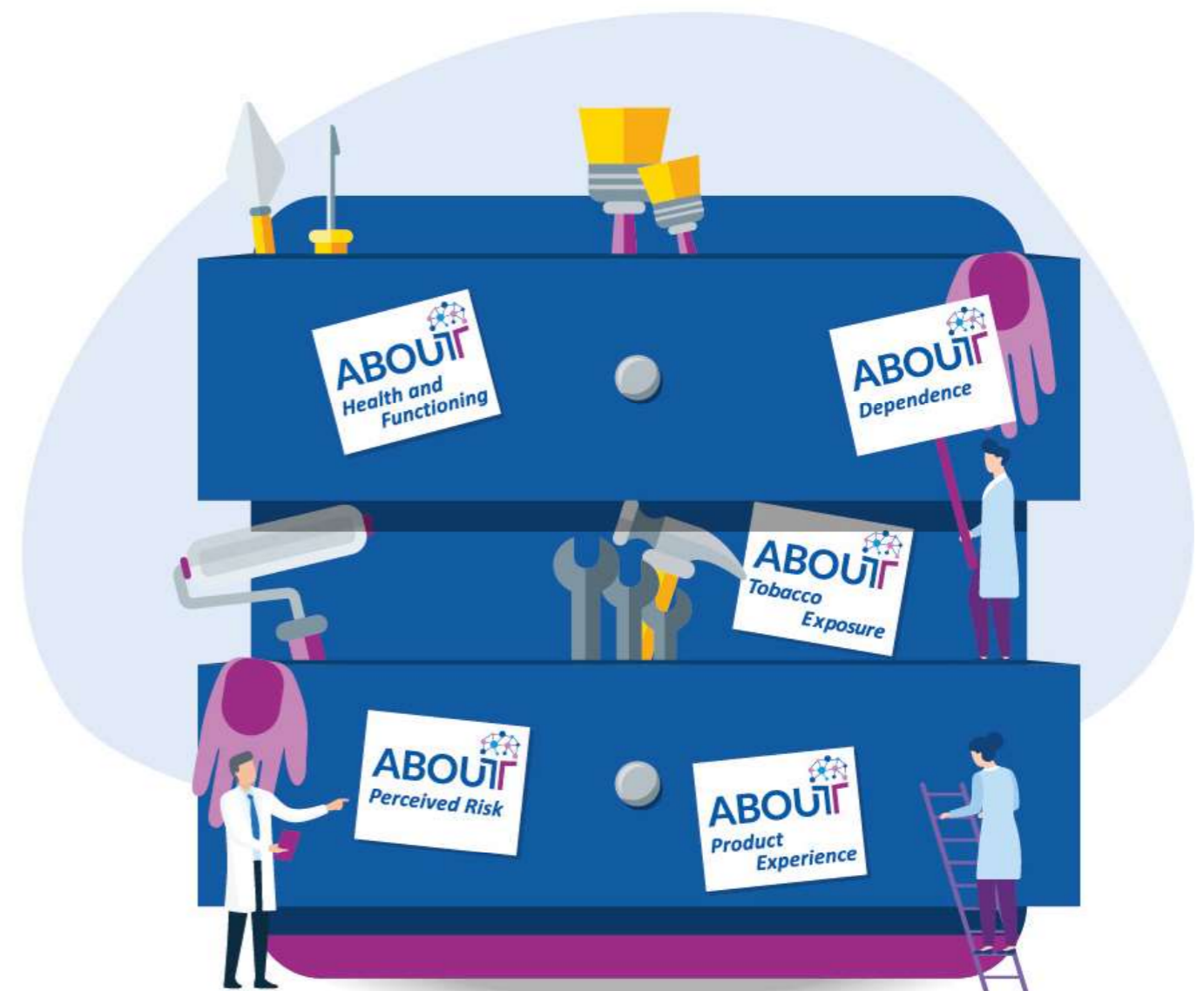
This phase incorporates background research and consultations with subject matter experts to guide the selection of methodologies for identifying relevant concepts in this context. This phase started in early 2018 with a comprehensive literature review of 97 existing publications, aiming at identifying both the positive and negative impacts that TNP use could have on users' health and functioning. Later, we reanalyzed data from focus groups on risk perception and individual interviews on perceived dependence in TNP users, in order to extract meaningful

preliminary consumer insights on health and functioning. Additionally, we brought together a panel of six experts, combining expertise in tobacco science, PRO development, FDA regulatory science, and health economics to provide guidance in all phases of development of the self-reported measure. In the preparatory phase, they helped in identifying the main concepts across key domains* impacted by TNP use to inform item generation and banking.

B. DEVELOPMENT

Carried out in 2019-2020, this aimed to implement mixed methods (qualitative and quantitative methodologies) to identify and develop suitable items to capture the relevant dimensions in this context. To do so, three qualitative studies have been conducted to elicit health- and functioning-related concepts in adult cigarette smokers who have switched to alternative smoke-free TNPs.

* These domains included core health and functioning domains (physical health symptoms [e.g., oral and respiratory], general physical appearance and hygiene, functional status [physical, sexual, cognitive, emotional, and social functioning]), and general health perceptions) and conceptually-related domains (worry about health risks of using TNPs, fear of withdrawal symptoms, and perceived benefits of TNP use)⁵.





First, we conducted some longitudinal interviews (with 45 participants completing the study) in an Exercise Capacity Clinical Study in Germany, with a sample of participants made by adult users who switched to EHTS, continued cigarette use, or abstained with or without a combined exercise training program.

Second, we carried out individual interviews for exploring changes in health and functioning in Japan with a sample of 35 Japanese healthy adults who switched from cigarette smoking to using EHTS (exclusively or dual use with cigarettes) and other smoke-free products.

Third, we conducted ten focus groups within a US population of adult smokers who switched from smoking cigarettes to exclusively using e-cigarettes, smokeless tobacco, or who used nicotine-replacement therapies (exclusively or dual use with cigarettes).

Following these three rounds of qualitative studies, we recruited some international healthcare providers to organize a global Delphi panel survey which ensured the clinical and cross-cultural relevance of the highlighted health and functioning concepts.

C. VALIDATION

The phase is still ongoing and expected to be completed in 2021. During this stage, we will conduct cognitive debriefing interviews to evaluate content validity, appropriateness, and understanding of draft items. Finally, we will field-test the pilot instrument to assess the reliability, validity and psychometric properties of the ABOUT Health and Functioning instruments across a range of TNPs and use types.

“The Health and Functioning instrument is currently being developed to accurately reflect the health status of individuals who use TNPs, with a particular focus on healthy adult smokers who switch to smoke-free products.”

Gathering data to develop the instrument



**GERMANY
LONGITUDINAL
INTERVIEWS**

Sample of adult users (a) switching to EHTS or (b) continued cigarette use or abstinence (c) with / (d) without a combined exercise training program.

51 participants at baseline, 45 participants at the end of the study.*

Interviews were conducted within the framework of the Exercise capacity clinical trial.



**JAPAN
INDIVIDUAL
INTERVIEWS**

Sample of healthy adult users who switched from cigarette smoking to using heated tobacco products (Glo, Ploom) and EHTS (exclusively or dual use with cigarettes).

35 participants.



**USA
FOCUS
GROUP**

Sample of adult smokers who switched from smoking cigarettes to exclusively using e-cigarettes, smokeless tobacco, or nicotine replacement therapies or dual use with cigarettes.

92 participants.



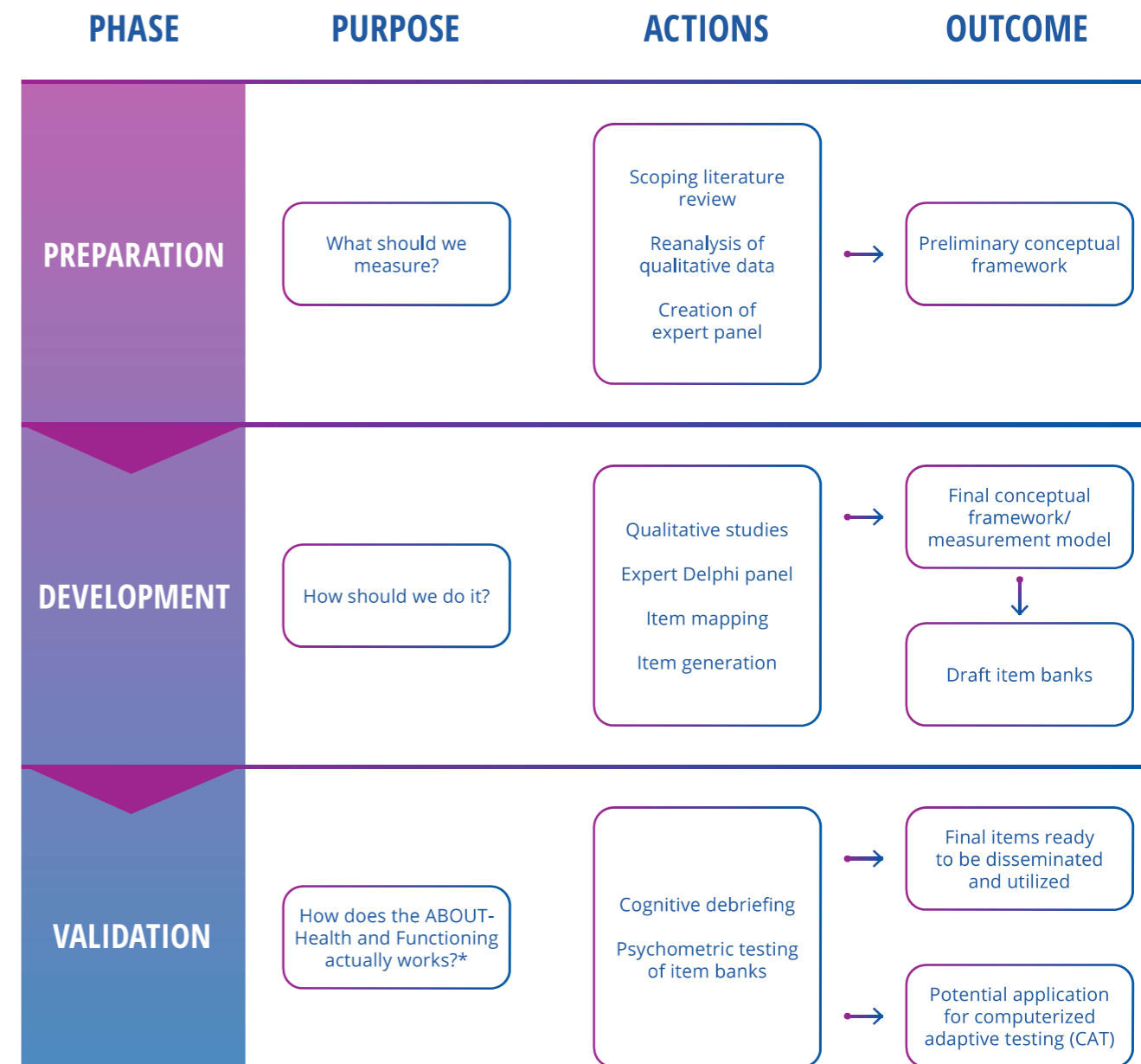
**WORLDWIDE
DELPHI
PANEL**

Three rounds of online survey (using MaxDiff ranking and an analytical approach) to gain consensus from 105 international experts on the most important health and functioning concepts impacted by switching from cigarette smoking to using an alternative smoke-free TNP.

* Continue smoking + training: N = 12; Abstinence + training N = 13; Switching to EHTS + training N = 14; Switching to EHTS only no training N = 6)



How ABOUT Health and Functioning was developed



* It is built on on the concepts of
- *validity*: it measures what it is meant to measure;
- *reliability*: it measures consistent and reproducible results between repeated assessments under several conditions.

What we expect to achieve with the ABOUT Health and Functioning instrument

By following reported best measurement practices and processes, the major aim of developing a new set of measures is to enable and facilitate an accurate assessment of TNP impact on individual health and quality of life. Moreover, we would also like to highlight the relevant personal and everyday dimensions that are impacted by TNP use, especially those that are more susceptible to change or remain stable when switching from cigarettes to TNP alternatives. By making the ABOUT Toolbox Health and Functioning instrument available to the tobacco research and public health communities, people can rapidly and properly expand their knowledge base on the topic. Furthermore, we pursue the goals of supporting consumer perception and behavior, enabling public health and regulatory communities to make better-informed decisions for future regulation of TNPs, and enhancing surveillance activities associated with the impact of TNPs on population health.

References can be found online at: www.pmiscience.com/SU11refs



INDEPENDENT RESEARCH

Position paper on e-cigarettes and health

In this position paper, members of the European Association of Preventive Cardiology (EAPC) review existing evidence and knowledge gaps in the prevalence of e-cigarette use, legislations, uptake of e-cigarettes in youth, cardiovascular effects, and effects of e-cigarettes in smoking cessation.⁶ The authors find a wide range in prevalence of e-cigarette use globally, possibly caused in part by regional legislative and social environments supporting or deterring use, though they do report an increasing trend of youth use. The authors state that observations from the National Health Interview Surveys of 2014 and 2016 suggested that e-cigarette users face higher risks for heart attacks than non-users, with an even higher risk for cigarette smokers. This analysis does not consider e-cigarette users' typical history of past smoking, though the authors do acknowledge there is no evidence from clinical trials or long-term studies for e-cigarettes and cardiovascular effects.

Assessing genotoxicity of tobacco heating products vs cigarette smoke with in vitro approaches

U.K.-based scientists aimed to assess the aerosol of a commercialized heated tobacco product (HTP) against cigarette smoke with a variety of in vitro cell analyses.⁷ They assessed total particulate matter (TPM) of the aerosol and smoke with concentrations up to 500 µg/ml. They were both tested on V79 and TK6 lines of lung cells with classic OECD 487 manual scoring, as well as CHO cells with contemporary TT21C high content screening approaches.

Results showed that the cells exposed to HTP aerosol were not negatively affected in regard to genotoxicity – specifically micronuclei formations – even when the HTP nicotine dose was ten times more than that of cigarette smoke, which elicited a genotoxic response in CHO and V79 cells. However, TK6 cells did not show this response to smoke in two of three test cases. The study concluded that high-throughput techniques can be used as part of HTP screening approaches, since they're in line with classic methods. Additionally, the researchers support the belief that HTPs are "less risky than conventional cigarettes."

Comparing indoor pollution from smoke-free products and cigarettes

The authors of this study present evidence from a small, randomized trial called the SUR-VAPES AIR trial on three types of smoke-free devices and cigarettes.⁸ Seven subjects were randomly assigned to use smoke-free products or cigarettes, and the particles in the resulting aerosol were measured in real time before, during, and after use using a DustTrak II Aerosol Monitor. The study found average PM₁ concentrations to be 28 µg/m³ for Glo, 25 µg/m³ for our own EHTS, and 73 µg/m³ for Juul – more than 10-fold less than PM₁ for cigarettes, which averaged more than 1000 µg/m³. Particle concentrations varied among subjects using the same type of smoke-free product, likely due to differences in the users' individual physical and behavioral characteristics. Though the study had a narrow scope and small sample size limited to healthy volunteers, it shows clearly how different products which burn tobacco (e.g., cigarettes) are from smoke-free products.

Quantifying wound healing in blood vessel lining

The endothelial layer is the one-cell-thick layer of flat cells that line the walls of blood vessels. Damage to it leads to dysfunction of the veins and arteries including atherosclerosis. Tools are needed to quantify and compare the effects of aerosols generated by smoking cigarettes and by using heated tobacco products on vascular function. The authors present a high-throughput assay that quantifies how exposure to aerosols generated by cigarettes or heated tobacco products affect the rate at which wounds heal in cultures of human umbilical vein endothelial cells.⁹ Cells grown in a 96-well culture plate were scratched simultaneously, exposed to different concentrations of extracts generated by cigarettes (3R4F) or a heated tobacco product, and monitored hourly. The authors report the relative wound density – the density of cells inside the wound compared with that of the outside of the wound – as the metric for wound healing. They found that aqueous extracts generated from the heated tobacco product tested here did not prevent wound healing while 20% extracts generated from cigarette smoke prevented wound healing. This study presents a useful way to investigate wound healing but requires further refinement to replicate realistic exposure conditions in vitro.

References can be found online at: www.pmiscience.com/SU11refs

Calibration is critical for indoor air quality monitors

Tools for monitoring indoor air quality are essential for assessing the effects of heat-not-burn tobacco products and cigarette smoke on indoor air quality and potential impacts on human health. The DustTrak DRX Aerosol Monitors measure the real-time concentration of micron-sized particles in air by measuring light scattering. This is an attractive option over gravimetric analysis, the current gold standard despite being labor-intensive and requiring days to obtain results after collecting samples. The DustTrak was designed to measure mineral dust, however, not heated tobacco aerosol and smoke. So, the device must be calibrated for this use to avoid overestimations as high as 150% compared to the true particle concentration.

We evaluated the suitability of the DustTrak DRX for measuring three types of aerosols in indoor air under non-default settings and changed the calibration factor from the default of 1.0 to 0.38.¹⁰ This reduced the overestimation of the concentration of particles in the smoke and aerosols. This working knowledge enables us to take advantage of the DustTrak DRX as a portable and economic means to track indoor air quality in real time.

Intestines-on-a-chip model to study inflammation

In this continued collaboration between PMI and Mimetas BV, a Leiden-based company specializing in organ-on-a-chip technologies, we expanded our high-throughput OrganoPlate-based model of human intestines to better mimic the complexity found in the human body and key features of intestinal inflammation.¹¹ In addition to the colon cells featured in the first OrganoPlate-based system, our new version includes a type of colon cell that secretes mucus and two types of immune cells involved in intestinal inflammation. Mucus is a critical physical barrier and a way to capture pathogens in the gut, so including mucus-secreting cells in this platform allows for predictions of the effects of drugs and pathogens close to what might occur in the human body. The immune cells here are activated during inflammation in humans, causing them to secrete substances called cytokines. We demonstrated that these organ models mimic the inflammation process by exposing them to TNF-α and 1L-1B, molecules typically elevated in patients with inflammatory bowel disease. Similar to the response in humans, these models showed loss of barrier function as measured by electrical measurements, and elevated levels of cytokines. With 40 independent intestinal cultures, this platform can support high-throughput efforts in drug discovery and personalized medicine.



PMI PUBLICATIONS

A/J mice exposure response to EHTS aerosol and cigarette smoke

In our latest inhalation study, complying with OECD Test Guideline 453, A/J mice were exposed to either EHTS aerosol or cigarette smoke (CS).¹² To evaluate chronic toxicity and carcinogenicity, our 18-month study focused on the histopathology. Compared to control mice, we found that mice exposed to CS showed increased heart weight, changes in red blood cell profiles and serum liver function parameters, increased pulmonary inflammation, altered lung function, and emphysematous changes. Mice exposed to EHTS aerosol did not have these changes.

The only commonalities between EHTS aerosol-exposed mice and CS-exposed mice were decreased thymus/spleen weights, blood lymphocyte counts, and serum cholesterol/triglyceride concentrations. But these were expected and attributed to high nicotine concentrations in the test environment.

Overall, these results show a lower impact of EHTS aerosol on toxicity, and reduced tumor incidence and multiplicity, compared to CS, which is consistent with a significant reduction in harmful and potentially harmful constituents supporting the risk reduction potential of existing adult smokers switching to EHTS.

Curating extensive tobacco plant databases

According to this database review, under the Solanaceae family of plants lies the Nicotiana genus – more commonly known as tobacco plants.¹³ Creating and curating metabolic databases with information on these plants is essential to keep up with the increasing swathes of omics-data being generated by high-throughput and next generation technologies.

SolanaCyc – for the Solanaceae family, and NicotianaCyc – for the Nicotiana genus, are the first manually curated metabolic databases for these specific taxons. First created in 2015 and 2016 respectively, SolanaCyc now houses 266 pathways of information and 36 'superpathways' while NicotianaCyc contains 143 pathways and 21 superpathways.

Due to the manually-curated nature of these databases – the gold standard of data collation – these databases have been widely accepted as efficient bioinformatics aids for analyses and visualizations of data.

References can be found online at: www.pmiscience.com/SU11refs



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.