Designing a Smoke-Free future

How long will the world's leading cigarette company be in the cigarette business?

We've built the world's most successful cigarette company, with the world's most popular and iconic brands.

Now we've made a dramatic decision.

We will be far more than the leading cigarette company. We're building PMI's future on smoke-free products that are a much better choice than cigarette smoking.

Indeed, our vision – for all of us at PMI – is that these products will one day replace cigarettes. Why are we doing this?

Because we should...

We understand the millions of men and women who smoke cigarettes. They are looking for less harmful, yet satisfying, alternatives to smoking. We will give them that choice.

We have a commitment to our employees and our shareholders. We will fulfill that commitment by pursuing this long-term vision for success.

Society expects us to act responsibly. And we are doing just that by designing a smoke-free future.

... and because we now can.

Success in the cigarette business gives us the resources to pursue our ambitious vision.

Thanks to the imagination and perseverance of thousands of people at PMI, we have developed breakthrough products that are smoke-free and enjoyable.

And, we are selling them today. Over a million people have already given up smoking and switched to our new products, and this is just the beginning.

We're investing to make these products the Philip Morris icons of the future.

A future PMI that's known for replacing cigarettes with a portfolio of revolutionary products.

In changing times you can always choose to do nothing. Instead, we've set a new course for the company. We've chosen to do something really big.

Products With Reduced-Risk Potential: An innovative way to address the harm caused by smoking?

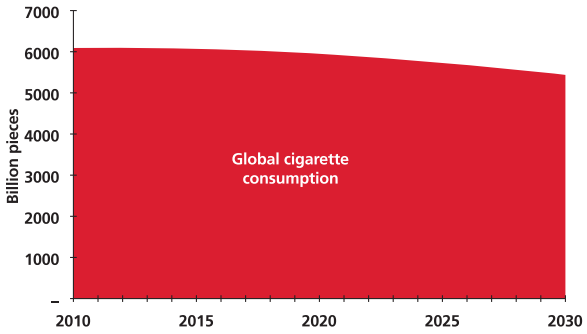
The Problem

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

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

An approach for these smokers is the development of non-combustible products that are proven to be less harmful and are acceptable alternatives to cigarettes.

Cigarette global consumption trend projection to 2030



Consumption 2010–2030 on parabolic trend projection from 1908–2012 data from Ng M, Freeman MK, Fleming TD, et al. Smoking prevalence and cigarette consumption in 187 countries, 1980–2012. JAMA 2014; 311: 183–92.

In addition to projections by public health experts showing limited declines in cigarette consumption, the World Health Organization's projections of worldwide smoking prevalence, when combined with population growth projections, show that there will be more than one billion smokers for the foreseeable future despite declining smoking prevalence. Based on these projections, the expected toll of smoking-related disease will remain constant.

National data show similar trends: even in countries with declining prevalence, the number of smokers is likely to remain flat or increase due to population trends, leading tobacco control experts to conclude that many tobacco control policies have reached either a limit on what can be done, or at least a state of greatly diminishing marginal returns.

So the question is…

Can reduced-risk tobacco products help those who continue smoking?

The results so far are promising and show that:

The levels of harmful and potentially harmful constituents in the aerosol of iQOS,[1] PMI's flagship reduced risk product, are reduced by more than 90% on average compared to smoke from a standard research cigarette

Premarket research and post-market data show very little interest in iQOS among adult nonsmokers and former smokers with substantial potential for full switching among current adult smokers

Exposure to harmful and potentially harmful constituents measured in smokers who switched to iQOS approached the effect observed in smokers who quit smoking for the duration of clinical studies

To date, more than one million adult smokers worldwide have quit smoking and switched to iQOS. In six countries where iQOS is sold, between 66% and 73% of iQOS users have fully or predominantly switched to it.

1. iQOS is one of several products in Philip Morris International's portfolio of Reduced-Risk Products ("RRPs"), which are products with the potential to reduce individual risk and population harm in comparison to smoking cigarettes. PMI's RRPs are in various stages of development and commercialization, and we are conducting extensive and rigorous scientific studies to determine whether we can support claims for such products of reduced exposure to harmful and potentially harmful constituents in smoke, and ultimately claims of reduced disease risk, when compared to smoking cigarettes. Before making any such claims, we will rigorously evaluate the full set of data from the relevant scientific studies to determine whether they substantiate reduced exposure or risk. Any such claims may also be subject to government review and authorization, as is the case in the United States today.

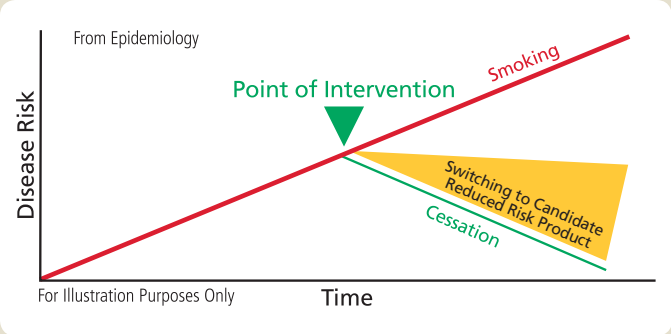
The Challenge

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

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

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

Philip Morris International's comprehensive assessment program is designed to address these challenges and follows relevant scientific precedents. Clinical and scientific assessment methods are similar to those used by the pharmaceutical industry, including product design controls, a range of toxicological tests, clinical studies, premarket consumer perception and behavior studies and post-market assessments.



The Goal: A Risk Profile Approaching Cessation

Philip Morris International's goal is to demonstrate that switching fully to its potentially reduced risk products has a risk reduction profile approaching that of cessation, referred to by the United States Institute of Medicine (IOM) as the "gold standard" for assessing risk reduction.

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

Philip Morris International's Assessment of Reduced Risk Tobacco Products

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

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

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

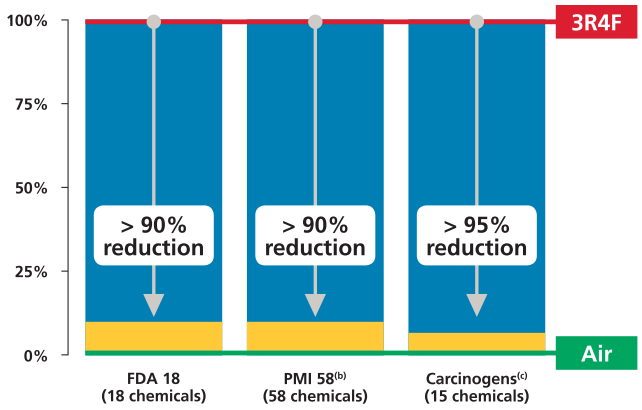
Premarket perception and behavior research is conducted to determine consumer understanding of the product's attributes and communications (including risk perception) and the extent to which marketing of the reduced-risk product will encourage adult smokers to switch as well as the likely impact on non-smokers and former smokers initiating tobacco use.

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

Philip Morris International's studies on iQOS, a heat-not-burn tobacco product, are well-advanced.

iQOS
Results Summary

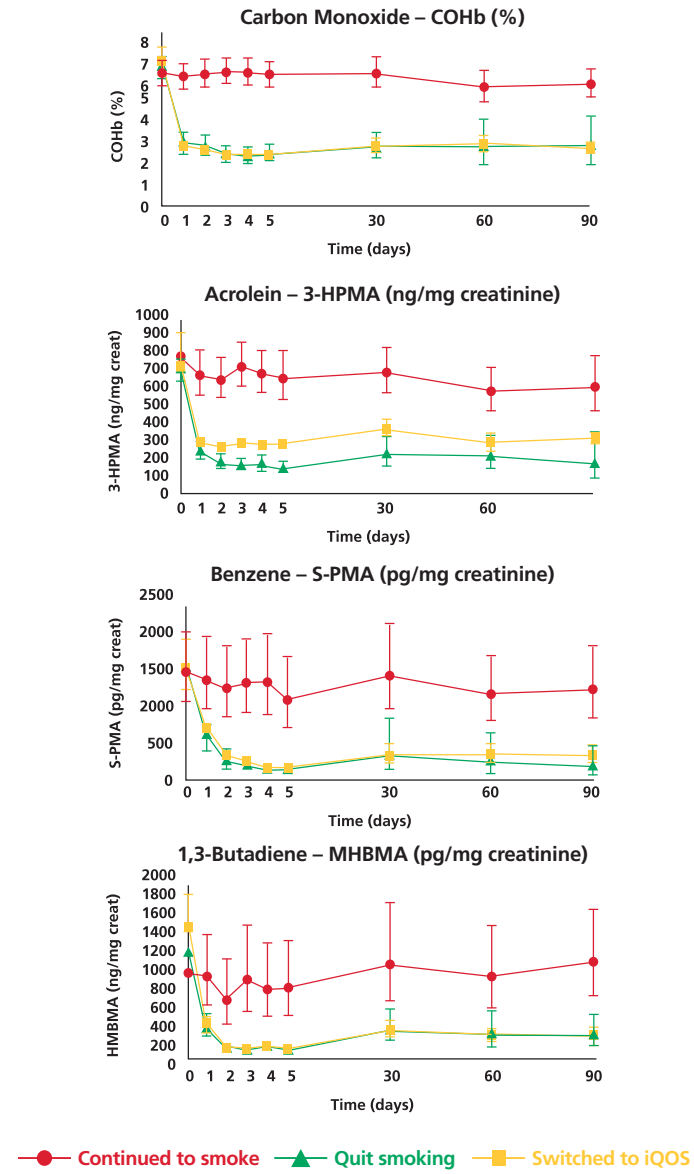
- The levels of chemicals classified by the International Agency for Research on Cancer (IARC) as Group 1 carcinogens are reduced on average by more than 95% compared to a standard research cigarette (3R4F).[2] Similar reductions are found among the HPHCs designated by the U.S. Food and Drug Administration and among the 58 chemicals monitored by PMI.



- These reductions in the formation of HPHCs translate into significantly reduced toxicity compared to cigarette smoke as demonstrated in well recognized *in vitro* and *in vivo* tests and significantly reduced impact on disease mechanisms and disease progression relative to cigarette smoke as modeled through innovative systems toxicology assessments.

- The real life results in countries where iQOS is being sold are encouraging. In Italy and Portugal, 68% of iQOS purchasers have fully or predominantly switched to it. In Romania, a full or predominant conversion rate of 71% was achieved among iQOS purchasers. The conversion rate in Japan is even higher at 73%. PMI estimates that more than one million adult smokers worldwide have quit smoking and switched to iQOS.
- Premarket assessments show negligible interest in iQOS among adult never smokers and former smokers and substantial potential for full switching among adult smokers. In one study conducted in the United States. 0% of never smokers aged 18-25 said they intended to use iQOS, while up to 39% of adult smokers stated a high intention to use the product.
- At the same time, initial post-market cross-sectional population studies conducted in Japan and Italy suggest that iQOS generated negligible rates of initiation among adult never smokers (less than 1%) and relapse among adult former smokers (less than 2%).

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



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

2. Average yield reductions of an investigational variant of iQOS compared to the 3R4F reference cigarette, calculated as an average of the reductions of individual HPHCs, which could be reliably quantified in the study. Aerosol collection with Intense Health Canada's Smoking Regime. All yields were taken on a mass per stick basis. Reduction calculations exclude nicotine.

Products With Reduced-Risk Potential: An innovative way to address the harm caused by smoking?

Philip Morris International's current portfolio of potentially reduced-risk products is aimed at addressing different adult consumers' preferences and includes:

iQOS Platform 2 — Heat-not-burn tobacco products

Platform 3 E-cigarettes — Nicotine-containing products that contain tobacco-derived nicotine but no tobacco

Each of PMI's product platforms is designed to significantly reduce the formation of the chemicals which are widely recognized as the primary probable causes of smoking-related diseases, while providing acceptable alternatives to cigarettes for adult smokers. PMI intends to file an application with the U.S. FDA in 2016 to market iQOS in the United States as a Modified Risk Tobacco Product (i.e. less risky than a cigarette).

Philip Morris International's iQOS

How iQOS Works

- The tobacco mixture in the HeatStick is heated to a maximum temperature of approximately 300°C, well below the temperature required for combustion. By contrast, cigarettes burn at temperatures of between 600°C to 800°C, exceeding 900°C during puffs.
- iQOS generates an aerosol and not smoke.
- The aerosol is composed mainly of water, glycerol and other vaporized substances (including nicotine and flavors) present in the original tobacco mixture.

Commitment to Science

PMI is committed to making innovative products that will benefit public health and transform the tobacco industry.

Since 2008, PMI has invested over $3 billion in the development of a portfolio of innovative products that seek to replicate the sensorial and taste attributes of cigarettes, while delivering an aerosol that is significantly less harmful than cigarette smoke.

PMI has assembled a team of over 400 world-class scientists and engineers in key disciplines with state-of-the-art facilities in Switzerland and Singapore. It also has established a global network of research and technology partners. Since 2011, PMI has published over 160 peer-reviewed scientific publications and book chapters on the scientific assessment of products with reduced-risk potential, and all our clinical studies are registered on the public website ClinicalTrials.gov. To date, the company has over 1,000 patents granted and over 2,000 pending applications on new product developments related to candidate reduced-risk products.

PMI is committed to transparent sharing of its reduced risk product science for unbiased verification by qualified scientists. We are confident that such evaluations of our data will support the encouraging results obtained for PMI's products so far.

Visit PMIScience.com to learn more.

Nicotine and harm reduction

The goal at Philip Morris International is to develop a portfolio of reduced risk products containing nicotine that are satisfying to adult smokers and significantly less harmful than smoking cigarettes — all based on rigorous scientific standards and assessment.

Tobacco-related diseases are primarily associated with exposure to toxic substances in smoke generated by burning tobacco, not by exposure to nicotine per se. As the United Kingdom's National Institute for Health and Care Excellence stated: "It is primarily the toxins and carcinogens in tobacco smoke — not the nicotine — that cause illness and death."

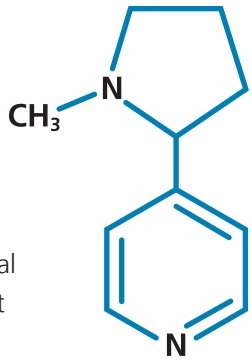
Therefore, progress towards the above stated public health objective requires that fewer people use combustible tobacco, even if nicotine use persists through use of alternative products. In fact, allowing adult smokers to continue using nicotine-containing products, with the nicotine delivered by less harmful means, has the potential to switch smokers away from conventional cigarettes.

For alternative products to benefit public health, three conditions need to be met:

- Smokers must find these products satisfying as alternatives to smoking conventional cigarettes. Nicotine plays an essential part in achieving this necessary consumer acceptance.
- Actual reduction in risk promised by these alternative products must be scientifically substantiated — from product development and analysis through clinical evaluations in realistic use conditions — applying assessment methods that meet recognized scientific standards.
- Alternative products should not be appealing to persons who would otherwise not smoke, particularly minors, nor should they encourage continued tobacco use by those who would otherwise quit. Pre-market assessment must be complemented by post-marketing surveillance to confirm these products achieve these objectives.

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

What is nicotine?



Nicotine occurs naturally in tobacco and at significantly lower levels in some other plant varieties.

Nicotine used in pharmaceutical products (nicotine replacement therapies; NRTs) as well as in e-cigarettes is usually extracted from tobacco. It is possible to produce synthetic nicotine, but the process is costly.

When tobacco smoke is inhaled, nicotine is absorbed through the lungs into the bloodstream, and reaches the brain in about 10–20 seconds. There, nicotine binds to specific receptor molecules, mimicking the actions of a naturally occurring brain chemical, acetylcholine. In turn, these activated receptors influence the brain's "pleasure center," which may explain the subjective pleasurable effects associated with smoking, but also relates to the desire for nicotine and potential for addiction.

Nicotine also affects other parts of the body such as the heart and blood vessels.

Through other routes, such as absorption through the skin when using a nicotine patch, or through the mouth and stomach when chewing nicotine gum, the nicotine is absorbed more slowly and takes longer to reach the brain.

Nicotine is addictive and not risk free. Minors, pregnant or breast feeding women, and people with heart disease, severe high blood pressure or diabetes should not use tobacco or nicotine containing products. Minors in particular should not have access to nicotine containing products.

"Preventable morbidity and mortality has overwhelmingly been related to combusted tobacco smoking, not to nicotine itself. Decoupled from combustion or other toxic modes of delivery, nicotine, by itself, is much less harmful."

— Truth Initiative, America's largest non-profit public health organization dedicated to tobacco control

How safe is nicotine use?

Experts, including the U.S. Surgeon General and the U.K. Royal College of Physicians, agree that nicotine, while addictive, is not the primary cause of smoking-related diseases. Smoking-related diseases, such as lung cancer, cardiovascular disease and emphysema, are caused primarily by inhaling harmful compounds formed when tobacco is burned.

As stated by the UK Royal College of Physicians: "Nicotine is not, however, in itself a highly hazardous drug… it is inherently unlikely that nicotine inhalation itself contributes significantly to the mortality or morbidity caused by smoking. The main culprit is smoke and, if nicotine could be delivered effectively and acceptably to smokers without smoke, most if not all of the harm of smoking could probably be avoided."

What are the health risks associated with nicotine?

Researchers have concluded that while nicotine has not been shown to cause the chronic diseases associated with tobacco use, there are risks associated with nicotine:

- Nicotine can be acutely toxic at levels much higher than those consumers are exposed to when using tobacco or nicotine-containing products.
- Nicotine can harm your baby if you are pregnant or nursing.
- Nicotine exposure can increase your heart rate and blood pressure.

To learn more about PMI's efforts to develop less harmful tobacco products, visit PMIScience.com.

Additional resources

Raymond Niaura, PhD, Truth Initiative, Re-thinking nicotine and its effects (2016)

Royal College of Physicians, Harm reduction in nicotine addiction: helping people who can't quit (2007)

Royal College of Physicians, Nicotine without smoke, Tobacco harm reduction (2016)

Surgeon General's Report: The Health Consequences of Smoking — 50 Years of Progress (2014)

National Institute for Health and Care Excellence, Tobacco: harm-reduction approaches to smoking, NICE public health guidance no. 45 (2013)

Modifications to Labeling of Nicotine Replacement Therapy Products for Over-the-Counter Human Use, A Notice by the Food and Drug Administration, 78 FR 19718 (2013)

Ramstrom L, Wikmans T. Mortality attributable to tobacco among men in Sweden and other European countries: an analysis of data in a WHO report. Tob Induc Dis 2014;12:14. doi:10.1186/1617-9625-12-14

Most smoking-related harm comes from combustion, *not nicotine*

"The burden of death and disease from tobacco use in the United States is overwhelmingly caused by cigarettes and other combusted tobacco products; rapid elimination of their use will dramatically reduce this burden."

— National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health, The Health Consequences of Smoking — 50 Years of Progress: A Report of the Surgeon General (2014)

"Most of the physiological harm attributable to cigarette smoking derives from the toxicants in tobacco and combustion products. Preventable morbidity and mortality has overwhelmingly been related to combusted tobacco smoking, not to nicotine itself. Decoupled from combustion or other toxic modes of delivery, nicotine, by itself, is much less harmful."

— Truth Initiative, Re-thinking nicotine and its effects (2016), TruthInitiative.org

"Although nicotine is addictive and can be toxic if ingested at high doses, it does not cause cancer — other chemicals are responsible for most of the severe consequences of tobacco use. Tobacco smoke is a mixture of chemicals such as carbon monoxide, tar, formaldehyde, cyanide and ammonia — many of which are known carcinogens."

— US National Institute on Drug Abuse, Cigarettes and Other Tobacco Products (2016)

"Nicotine is not, however, in itself a highly hazardous drug…it is inherently unlikely that nicotine inhalation itself contributes significantly to the mortality or morbidity caused by smoking. The main culprit is smoke and, if nicotine could be delivered effectively and acceptably to smokers without smoke, most if not all of the harm of smoking could probably be avoided."

— Royal College of Physicians, Nicotine without smoke: Tobacco harm reduction (2016)

"Nicotine does not cause smoking related disease, such as cancers and heart disease. These are caused by other chemicals found in tobacco smoke. Nicotine is addictive however and it is why people continue to smoke despite knowing about the harmful effects of tobacco."

— National Centre for Smoking Cessation and Training, Electronic cigarettes: A briefing for stop smoking services (2016), NCSCT.co.uk

"The evidence suggests a strong potential for VNP [Vaporized Nicotine Product] use to improve population health by replacing or displacing cigarette use in countries where cigarette prevalence is high and smokers are interested in quitting."

"The substantially lower levels of toxins than cigarettes make VNPs far less harmful, although by exactly how much is unclear."

"For dual users, VNP use may translate to a lower quantity and duration of cigarettes smoked."

— Levy, D.T., Cummings K.M., Villanti, A.C., Niaura, R., Abrams, D.B., Fong, G.T., Borland, R., "A framework for evaluating the public health impacts of e-cigarettes and other vaporized nicotine products." Addiction. 25 April 2016

"ASH believes, therefore, in line with the Royal College of Physicians, that in the interests of public health it is important to promote the use of e-cigarettes, NRT [Nicotine Replacement Therapy] and other non-tobacco nicotine products as widely as possible as a substitute for smoking in the UK. Vapourised tobacco may also be substantially less harmful as the tobacco is not combusted to produce smoke."

— Action on Smoking and Health UK, ASH reaction to new Philip Morris IQOS 'heat not burn' product, 30 November 2016

E-Cigarettes

"The best estimate is that e-cigarettes are around 95% less harmful than smoking."

— Public Health England, "E-cigarettes: an evidence update," August 2015

"E-cigarettes are a safer alternative, providing smokers with the nicotine to which they are addicted and the 'smoking ritual,' without the smoke, tar, carbon monoxide and other toxic chemicals that cause almost all the harm. E-cigarettes are not completely safe. Nothing is. However, even the most ardent opponents admit e-cigarettes are substantially safer than smoking."

— Mendelsohn, C., "Opinion: Ban will rob smokers of a chance to quit," Newcastle Herald, 17 February 2017

"Today, despite uncertainties on the level of benefits, it is possible to argue that e-cigarettes are much safer than traditional cigarettes and switching from tobacco smoking to e-cigarettes may result in harm-reduction, and health benefits."

— Dautzenberg, B., et al., Practical guidelines on e-cigarettes for practitioners and others health professionals. A French 2016 expert's statement, Revue des Maladies Respiratoires, 9 February 2017

"We all agree that e-cigarettes are significantly less harmful than smoking…All the evidence suggests that the health risks posed by e-cigarettes are relatively small by comparison but we must continue to study the long-term effects."

— Joint statement regarding e-cigarettes issued by Public Health England, Action on Smoking and Health, the British Lung Foundation, Cancer Research UK and the UK Center for Tobacco and Alcohol Studies and other UK public health organizations, July 2016

"Vapour from e-cigarettes contains substantially fewer toxicants than does smoke from regular tobacco cigarettes…"

— O'Leary, R., et al., Clearing the air: A systematic review on the harms and benefits of e-cigarettes and vapour devices, Centre for Addictions Research of BC, January 2017

"E-cigarette aerosol is not harmless 'water vapor' although it generally contains fewer toxicants than combustible tobacco products."

— US Surgeon General, E-cigarette use among youth and young adults: A report of the Surgeon General, 8 December 2016

"E-cigarettes are one of the most popular cigarette replacement products, with a total market of around $2 billion per year. They have proven effective at helping smokers reduce their cigarette use or quit altogether and thus are expected to have significant public health benefits."

— Rodu, B., et al., "Vaping, e-cigarettes and public policy towards alternatives to smoking," The Heartland Institute, 20 February 2017

"Where a patient wants to quit smoking, and has not succeeded with other options, GPs should recommend and support the use of ENDS [electronic nicotine delivery systems]."

— UK Royal College of General Practitioners (RCGP), "To vape or not to vape? The RCGP position on e-cigarettes," November 2016

"The e-cigarette, for example, evaporates a liquid that usually contains nicotine. The user is not exposed to as many toxicants as when smoking a tobacco cigarette…"

— National Institute for Health and Environment (RIVM), "Alternative tobacco products: Harm reduction? Tobacco and related products that may possibly be less harmful than cigarettes." RIVM Letter Report 2016-0103. September 2016

"A growing body of evidence shows that e-cigarettes are much less harmful than tobacco."

— UK POSTnote, 9 August 2016

"By allowing smokers to transition to products that deliver nicotine without smoke's toxicity, MRTPs [modified risk tobacco products] could reduce the population's exposure to toxic combustion products inherent in smoking."

"A major strategy for potentially reducing population harm is to allow nicotine products...that would substitute for smoking, enabling smokers to get nicotine without exposing them to deadly combustion products."

"The available evidence so far suggests that levels of biomarkers of exposure to toxicants related to use of these devices [electronic nicotine delivery devices] is significantly lower than for smoked cigarettes."

— Truth Initiative, Truth Initiative: Re-thinking nicotine and its effects, 2016

"Large-scale substitution of e-cigarettes, or other non-tobacco nicotine products, for tobacco smoking has the potential to prevent almost all the harm from smoking in society. Promoting e-cigarettes, NRT and other non-tobacco nicotine products as widely as possible, as a substitute for smoking, is therefore likely to generate significant health gains in the UK."

"…the hazard arising from long-term vapour inhalation from e-cigarettes available today is unlikely to exceed 5% of the harm from smoking tobacco."

— UK Royal College of Physicians, "Tobacco Advisory Group, Nicotine without smoke: Tobacco Harm Reduction," 28 April 2016

"In conclusion, exclusive long-term NRT [nicotine replacement therapy] or EC [e-cigarette] use among ex-smokers is associated with substantially reduced levels of selected carcinogens and toxicants compared with cigarette smoking; however concurrent use with cigarettes appears not to be. We found no evidence that EC-only compared with NRT-only use is associated with greater carcinogen and toxicant levels measured in this study."

"While complete long-term switching to EC may produce a net benefit for the health outcomes of the smoking population, given the association with very low levels of dangerous constituents measured in this study similar in magnitude to NRT, it is only likely to be beneficial if complete cessation is achieved. Thus, dual users should be encouraged to cease using combustible products to reduce long-term health risks."

— Shahab, et al., Nicotine, carcinogen and toxicant exposure in long-term e-cigarette and nicotine replacement therapy users: a cross sectional study, Annals of Internal Medicine, 7 February 2017

Heated tobacco products

"We still need more research, but it's quite obvious that iQOS is far less dangerous than cigarettes. The health risk is significantly lower."

— "Smoke without fire: Philip Morris has developed a new way of smoking which the company's scientists claim is 90 percent less toxic," Andresseavisen, 2 December 2016 (unofficial translation)

"Heating tobacco at lower temperatures than combustible cigarettes allows nicotine to be delivered in ways that retain much of the ritual and experience of smoking. Comprehensive scientific programs have demonstrated that these products present significantly reduced risk when compared to traditional cigarettes. Collectively, they represent a new set of tools to reduce the harm of combustible tobacco."

— Anselm, E., "Tobacco harm reduction potential for 'heat not burn,'" R Street Policy Study, February 2017

"And now, a new type of less harmful cigarette — this time containing tobacco — has been developed by Philip Morris. iQOS, which heats tobacco instead of burning it (and therefore doesn't give off the carcinogenic substances produced by combustion), maintains the feeling that the smoker is actually smoking tobacco."

— Umberto Tirelli, quoted in La Verita, "Stop attacking electronic cigarettes. They really help those who want to quit smoking," 24 September 2016 (unofficial translation)

"We can lower by 50% the number of smokers, and as a consequence the tobacco related disease incidence by switching smokers to reduced risk products, such as e-cigarettes, snus, and most recently, iQOS."

— "GFN, Polosa: The MEF with taxes on e-cig drives people to traditional cigarettes." (Statement by Riccardo Polosa). Agivape News. 7 June 2015 (unofficial translation)

"There is plenty of data to show that heated tobacco products are much less hazardous than smoking, and it is irresponsible for public health activists to suggest otherwise. If tobacco is heated and its nicotine and flavours imparted to a neutral vapour rather than burnt, there are no particles of smouldering tobacco to inhale. It is these smoke particles that do the most of the health damage."

— Bates, C., "'Heat Stick' Safety." The Times. 9 April 2016

"These products, which now include electronic cigarettes, heat-not-burn tobacco products, snus, and vapor products, reduce user exposure to toxins associated with combusted tobacco, while maintaining nicotine content close to levels in traditional cigarettes."

— Core Team on Tobacco Control, "Ending Cigarette use by adults in a generation is possible: The views of 120 leaders in tobacco control," 2017 February

"E-cigarettes, as well as even newer products which heat but do not burn tobacco, allow those who are unable or unwilling to quit using nicotine to dramatically reduce their exposure to the deadliest components of cigarettes, the products of combustion in the smoke."

— Daren Bakst and Jeff Stier, "Rethinking tobacco policy: The federal government should stop blocking alternatives to smoking," The Heritage Foundation, 24 February 2017

"ASH believes, therefore, in line with the Royal College of Physicians, that in the interests of public health it is important to promote the use of e-cigarettes, NRT and other non-tobacco nicotine products as widely as possible as a substitute for smoking in the UK. Vapourised tobacco may also be substantially less harmful as the tobacco is not combusted to produce smoke."

— Action on Smoking and Health UK, ASH reaction to new Philip Morris IQOS 'heat not burn' product, 30 November 2016

"But on the face of it looks these products will be less hazardous than combusted tobacco but maybe more hazardous than vaping."

— Waugh, R., "New 'smokeless' cigarette goes on sale in the UK — here's what it does," Metro (quoting John Britton, director of the UK Centre for Tobacco and Alcohol Studies), 30 November 2016

"Examples of harm reduction products are oral tobacco, such as the so-called snus, the e-cigarette and tobacco that is heated but not burned (heat not burn). These products do not expose users to harmful combustion products. Heat not burn products also seem to be less harmful to health than conventional cigarettes."

— National Institute for Health and Environment (RIVM), "Alternative tobacco products: Harm reduction? Tobacco and related products that may possibly be less harmful than cigarettes." RIVM Letter Report 2016-0103

"Vaporized nicotine products (VNPs), including e-cigarettes and heat-not-burn cigarettes, represent a new generation of nicotine delivery products. Although the long-term health risks have yet to be thoroughly characterized, VNPs are likely to be much safer than cigarettes and are generally perceived by smokers as less risky than cigarettes."

— Levy, D.T., Borland R., Villanti, A.C., Niaura, R., Yuan, Z., Zhang, Y., Meza, R., Holford, T.R., Fong, G.T., Cummings, M.K., Abrams, D.B., "The application of a decision-theoretic model to estimate the public health impact of vaporized nicotine product initiation in the United States." Nicotine & Tobacco Research. 14 July 2016

"Reduced taxation than that imposed on cigarettes is justified considering the less impact on harm of the product compared to traditional cigarettes, thanks to lack of combustion therefore above all, without the production of tar and similar substances"

— Senate Legislative Decree, 15 December 2015, N. 106-bis (Italy) (unofficial translation)

"Fortunately, a number of innovations in the 21st century could reduce tobacco-related mortality to very low levels that existed before the emergence of manufactured cigarettes. These innovations include electronic cigarettes, vaporizers that heat tobacco without burning it, nicotine vaporizers that function with a propellant gas, and systems that use a chemical reaction (pyruvate) to vaporize nicotine."

— Etter, J.F., "New tobacco vaporizers: how to react?," Rev Med Suisse, June 2015 (unofficial translation)

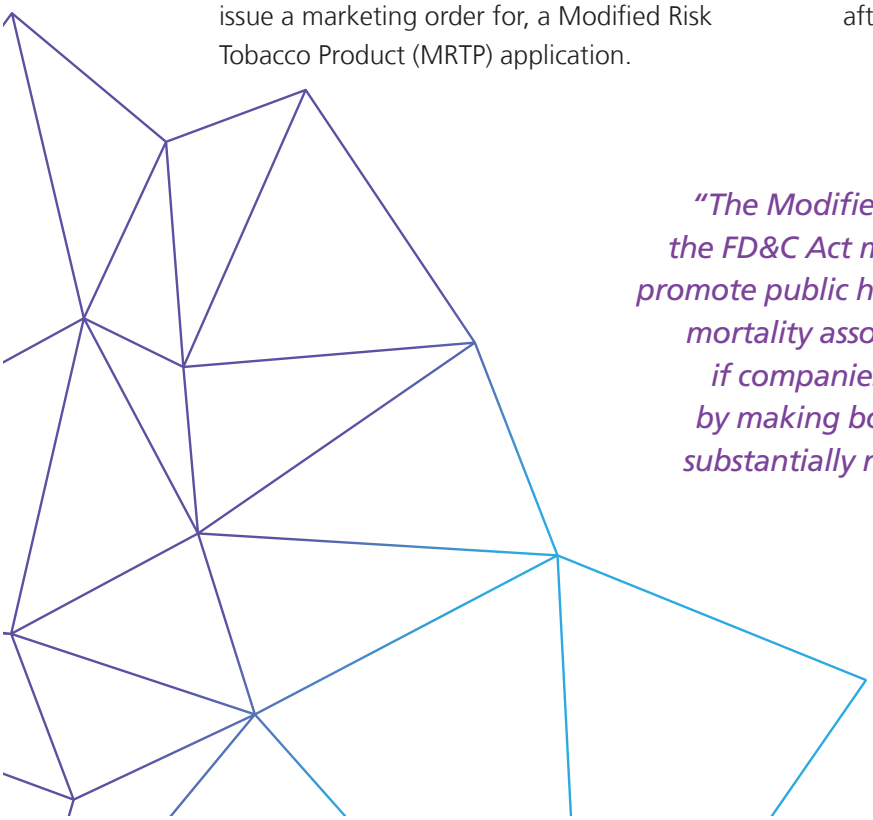
The U.S. FDA and potentially reduced risk tobacco products

The U.S. Food and Drug Administration (FDA) is responsible for reviewing and issuing marketing orders for new potentially reduced risk tobacco products, including e-cigarettes, smokeless tobacco for oral use, and heated tobacco products. Experts agree that scientifically substantiated risk-related information can encourage adult smokers to switch from cigarettes to less risky products. Conversely, denying adult smokers that information could prevent switching and "may cause more smoking."[1]

FDA review of potentially reduced risk tobacco products

In the U.S., bringing new and potentially reduced risk tobacco products to market involves two separate processes. Manufacturers must submit to the FDA a Pre-Market Tobacco Application (PMTA), which simply seeks a marketing order for a new tobacco product to be sold in the U.S. (without any claims of reduced risk). Separately, in order to market a product with claims of reduced exposure or reduced risk manufacturers must file, and the FDA must issue a marketing order for, a Modified Risk Tobacco Product (MRTP) application.

In evaluating a PMTA, the FDA determines whether the product is appropriate for the protection of public health in the U.S. The FDA also considers the relative health risks of the product and the likelihood of any changes in tobacco initiation and cessation rates once the product is introduced. The timing for FDA review and final determination of a PMTA is set by the underlying statute that requires the FDA to issue a decision "as promptly as possible, but in no event later than 180 days after the receipt of an application."



"The Modified Risk Tobacco Product provisions of the FD&C Act may be valuable tools in the effort to promote public health by reducing the morbidity and mortality associated with tobacco use, particularly if companies take advantage of these provisions by making bold, innovative product changes that substantially reduce, or even eliminate altogether, either the toxicity or addictiveness of tobacco products, or both."

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

In reviewing MRTP applications, the FDA aims to ensure that any reduced risk claims about the product are substantiated and supported by scientific evidence, and that the advertising and labeling of the product help the public understand these claims in relation to overall health.

The FDA also considers other potential impacts, including:

- The likelihood that consumers who would have otherwise quit tobacco will instead switch to the MRTP
- The likelihood that consumers will use the MRTP along with other tobacco products
- The likelihood that non-users of tobacco products will start using an MRTP

With respect to timing, FDA guidance indicates that the agency intends to make a final determination on MRTP applications within 360 days of its receipt, but this is merely a target and not a statutory requirement.

An FDA order permitting the marketing of an MRTP is not permanent; it is for a fixed period of time and manufacturers are required to seek approval by the FDA to renew the MTRP marketing order. In renewing these orders the FDA evaluates the actual experience in the marketplace as well as post-market surveillance data that is collected and submitted by the manufacturer.

PMI's PMTA and MRTP applications

Philip Morris International (PMI) submitted an application to the FDA in December 2016 for authorization to market IQOS in the U.S. as a Modified Risk Tobacco Product. In addition, the company filed a Pre-Market Tobacco Application with the FDA in March 2017.

PMI is committed to transparent sharing of its science. PMI's clinical studies are publicly available on the U.S. National Institutes of Health website ClinicalTrials.gov. Since 2011, PMI has published over 170 peer-reviewed scientific articles and book chapters describing its approaches, methods and product assessment studies.

Learn more at PMIScience.com.

1. Source: Sweanor, D. and Bates, C., Submission to New Zealand consultation on Policy Options for the Regulation of Electronic Cigarettes, 2016.