OVERVIEW OF INDEPENDENT RESEARCH ON IQOS

Over the last few years, numerous independent studies have already confirmed different elements of our research on *IQOS*.

STUDIES ON IQOS CONDUCTED BY GOVERNMENT BODIES

Many government bodies have conducted literature reviews or performed research on heated tobacco products, finding that they expose users to significantly lower levels of harmful chemicals.

On July 7, 2020, the U.S. Food and Drug Administration (FDA) <u>issued decisions</u> on Modified Risk Tobacco Product (MRTP) applications for <i>IQOS</i> and three HeatSticks variants ("the <i>IQOS</i> tobacco heating system") submitted by Philip Morris International (PMI) in December 2016. In doing so, the agency found that the issuance of the modified risk tobacco product orders with reduced exposure claims would be "appropriate to promote the public health and is expected to benefit the health of the population as a whole." This decision follows a <u>review</u> of the extensive scientific evidence package PMI submitted to the FDA in December 2016 to support its MRTP applications.
On May 12, 2020 The Dutch National Institute for Public Health and the Environment (RIVM) published the findings of its <u>research</u> on "A Method for Comparing the Impact on Carcinogenicity of Tobacco Products: A Case Study on Heated Tobacco Versus Cigarettes." RIVM research is new and is not a review of PMI's findings. RIVM developed a method to estimate risk—or assess the potential magnitude of the health impact—between tobacco products. In their publication they assessed eight carcinogens to understand the likely health impact on individuals who switch to <i>IQOS</i> , compared to those who continue smoking. In their conclusions they state that—while <i>IQOS</i> is not risk-free—it is associated with 10 to 25 times lower exposure to these carcinogens, and that this could translate into a substantially improved risk profile.
Public Health England (PHE) <u>published a review</u> of the evidence on e-cigarettes and heated tobacco products, and stated that heated tobacco products likely reduce users' and bystanders' exposure to harmful compounds compared to cigarettes. PHE also stated that the available evidence suggests that heated tobacco products may be considerably less harmful than tobacco cigarettes and more harmful than e-cigarettes.
The U.S. Food and Drug Administration (FDA), in a <u>briefing document</u> , reviewed PMI's data supporting <i>IQOS</i> and the available independent literature about <i>IQOS</i> . The briefing document included a section explaining the results of the FDA's <i>IQOS</i> aerosol chemistry measurements.
On April 30, 2019, following a comprehensive assessment of PMI's premarket tobacco product applications, the U.S. FDA confirmed that <i>IQOS</i> is appropriate for the protection of public health and

has authorized it for sale in the United States. "Appropriate for the protection of public health" means that looking at population as a whole, new products cannot pose the same or greater harm to public health as smoking (i.e., they must pose less harm than combustible cigarettes). The FDA published a

	<u>detailed report</u> describing their assessment and their conclusions including results on aerosol chemistry, toxicology and unintended use.	
	The U.K. Committee of Toxicity conducted a <u>review of available evidence</u> on two heated tobacco products, one of which is <i>IQOS</i> , and concluded that these products "are likely to reduce risks for smokers."	
	The Dutch National Institute for Public Health and the Environment (RIVM) published a <u>fact sheet on novel tobacco products that are heated</u> and an <u>English-language summary</u> . They concluded that "The use of <i>Heatsticks</i> with the <i>IQOS</i> is harmful to health, but probably less harmful than smoking tobacco cigarettes," based on their aerosol chemistry measurements, which are "of the same order of magnitude as in the data of Philip Morris."	
	The German Federal Institute for Risk Assessment (BfR), published <u>laboratory studies</u> in Archives of Toxicology, finding that reductions in selected toxicants measured by the institute "are likely to reduce toxicant exposure."	
	Two government-commissioned studies were conducted by independent scientists in Russia, confirming that <i>IQOS</i> aerosol contains an average of 90 percent reduced levels of harmful chemicals compared to cigarette smoke, and that <i>IQOS</i> has a minimal effect on biological processes in people compared to smoking. This report is not published yet, though the researchers have made some public statements. (Rossiyskaya Gazeta)	
ОТ	HER STUDIES ON IQOS	
To date, around 43 studies from independent laboratories have results that are in line with our findings on IQOS. Listed below is a selection of those publications:		
	Researchers working for the <u>American Cancer Society</u> (Michal Stoklosa et al., 2019) confirms that the introduction of <i>IQOS</i> is the only likely cause of cigarette sales decline in Japan. A backgrounder, key messages and Q&A can be found <u>here</u> .	
	Research by Japanese Department of Environmental Health, National Institute of Public Health, compared selected chemicals in the aerosol generated by <i>IQOS</i> and in smoke from reference cigarettes. The research shows significant reductions in the levels of several chemicals, in line with those found by PMI's research. (Bekki et al, 2017)	
	The China National Tobacco Quality Supervision and Test Centre, a member of the WHO Tobacco Laboratory Network, published an independent study comparing the harmful chemicals present in <i>IQOS</i> aerosol and cigarette smoke, which generally agree with PMI's results. (<u>Li et al, 2018</u>)	
	One of Ukraine's leading research institutes conducted a six-month clinical study on <i>IQOS</i> , which was published in prominent national medical periodical Ukrainian Health, showing no significant adverse effect on users of smoke-free products. (Kvasha et al, 2018)	

Research by cardiologist and leading e-cigarette researcher Dr. K. Farsalinos on <i>IQOS</i> was published in the journal Addiction, showing that <i>IQOS</i> emits lower levels of carbonyls than a commercial cigarette, but higher levels than an e-cigarette. (Farsalinos et al, 2018)
Researchers at the University of St. Andrews, Scotland calculated that <i>IQOS</i> aerosol has "lower cancer potencies than tobacco smoke by at least one order of magnitude, but higher potencies than ecigarettes." (Stephens et al, 2018)
The first independent study investigating eCO levels after use of two recently marketed HTPs was conducted by Pasquale Caponnetto, Marilena Maglia, Gaetano Prosperini, Barbara Busà and Riccardo Polosa and was published in Respiratory Research. The aim of this randomized cross-over study was to measure the exposure levels of the combustion marker, carbon monoxide in the exhaled breath (eCO) of subjects after use of two HTPs and to compare these levels with participants' own brand of cigarettes. The study found no eCO elevations during inhalational testing with HTPs under investigation in any of the study participants.