

REGULATIONS on HEATED TOBACCO PRODUCTS and GLOBAL PRACTICES

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This study has been prepared based on the Consultancy Service Procurement Agreement signed between Ankara Yıldırım Beyazıt University and Philip Morris Pazarlama ve Satış A.Ş. in 2020.

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Introduction

Novel smoke-free tobacco products are increasingly being used all over the world as an alternative to cigarettes. Extensive debate continues about the public health implications of their use together with concerns about their increased promotion. The fact that the number of smokers is declining very slowly, despite the constantly increasing regulations encouraging smokers to quit, the government policies that make tobacco products less attractive for smokers and campaigns aiming to prevent non-smokers from starting smoking makes it necessary to consider the implementation of other public health policies. There are nearly 1 billion smokers all around the world, and the World Health Organization states that this number will be similar by 2030¹.

Epidemiological data gathered throughout decades indicate that smoking causes various serious diseases such as cardiovascular diseases, lung cancer and chronic obstructive pulmonary diseases, and nearly eight million deaths per year are attributed to tobacco smoke^{2,3}. It is widely accepted that the adverse health effects caused by smoking are primarily triggered by toxic substances formed during the combustion of tobacco, not the nicotine content⁴.

Quitting smoking is the best choice to be made for reducing the harm of smoking but is difficult for many smokers. On average, across countries where the Global Adult Tobacco Survey has been conducted, over 60% of smokers indicated that they intend to quit, and over 40% had attempted to quit in the 12 months preceding the survey. Without cessation assistance, 4% of attempts to quit tobacco succeed. Proven cessation medications and professional support can double a tobacco user's chance of successfully quitting.⁵

As mentioned before, while there have been treatment options such as Nicotine Replacement Therapy (NRT) for a long time to support smoking cessation, these treatment options fail to be effective for many smokers. Researchers from the Institute of Social and Preventive Medicine in Switzerland identified all randomized placebo-controlled trials of NRT that lasted longer than 12 months. In both the treatment and placebo groups, 30% of volunteers relapsed after the 12-month point. NRT showed

significant benefits in six of the 12 trials, and no benefit in the other six. But when all the data were combined and analyzed, NRT almost doubled the rate of successfully quitting beyond 12 months. However, since the rate of success was quite low, even a doubling of this rate meant success for only about 7% of the 2,408 participants receiving NRT in this meta-analysis⁶.

There are frequent debates about the newly developed smoke-free tobacco products nowadays, and the idea that they are reduced-risk alternatives is becoming highly popular among the public. There is increased consensus among the public that these products are significantly less harmful compared to conventional cigarettes, and some of these products (e-cigarettes) are actively supported in some countries such as the United Kingdom in terms of tobacco control and tobacco harm reduction strategies. According to National Statistic Institution smoking prevalence in Turkey is 31.4% (2019) and when we look at the 10-year trend we can see it is not declining⁷. Considering the high smoking prevalence in our country, we believe other strategies in addition to prevent initiation and encourage cessation should be added to public health policies.

In this printed opinion paper, we primarily and fundamentally wanted to examine the global regulations and applications of heated tobacco products. In addition, we secondarily evaluated the independent publications that we come across using some key words.

Searches were made on databases related to public health published after 2017 (PubMed, Medline, and Web of Science) with a view to conducting efficient research on heated tobacco products. Searched terms include 'systematic reviews', 'meta-analysis', 'heat- not-burn', 'heat-not-burn products' and "HnB" tobacco products.

Summary of scientific evidence on heated tobacco products

Summarizing current information on heated tobacco products (HTP), it is worth analyzing the current publications comparing levels of toxicants between ordinary cigarette smoke and HTP aerosol. We also believe that is of vital importance to consider the potential impact of the use of HTPs on public health.

HTPs are intended to reduce the exposure of smokers to hazardous substances found in cigarette smoke and reduce the likelihood of tobacco-related diseases. Compared with cigarettes, HTPs delivered comparative nicotine levels and decreased levels of harmful and potentially harmful toxicants and particulate matter namely tar, carbonyls, VOCs, CO, free radicals, or nitrosamines and thus may diminish health risks⁸.

The existing reviews support the idea that the potential risk for people is reduced when they use HTP products compared to traditional cigarettes based on reduced levels of exposure to toxicants, confirmed by measuring biomarkers of exposure⁹¹. Biomarkers of exposure chosen as primary endpoints (total NNAL, COHb, MHBMA, 3-HPMA, and S-PMA) in the mTHS group compared with the mCC group using one-sided tests with 2.5% alpha level. All biomarkers of exposure surveyed were lower for HTP users. Thus, HTP products are potentially reduced-risk products, considering the potential indirect impact on chronic diseases, which are traditionally linked to conventional cigarettes.

While these results support tobacco producers' claims to have less harmful products compared to continued smoking, survey of limited number of biomarkers and methodological heterogeneity of reviews require more independent studies to confirm that HTP products are safer alternatives compared to conventional cigarettes. As far as we are concerned, findings were largely similar for independent and industry-funded studies except secondhand exposure. Future longitudinal studies are needed to evaluate the long-term usage of heated tobacco products and impact on smoking related diseases prevalence. In the next section, we reviewed how novel smoke-free products are being regulated in different countries and provide a summary status.

Consideration from worldwide public health bodies on novel smoke-free products

USA Food and Drug Administration (FDA)

The Family Smoking Prevention and Tobacco Control Act (TCA) of the US has granted the authority to regulate all tobacco products including Modified Risk Tobacco Products to the Food and Drug Administration (FDA). A marketing authorization should be obtained from the FDA for the marketing of all “new tobacco products” (i.e., tobacco products introduced to the US market or modified after 15 February 2007). Any new tobacco product not commercially marketed in the US or modified as of 15 February 2007 should be subject to the Pre-Market Tobacco Application Process (PMTA) and obtain a marketing order.

In addition, TCA defines Modified Risk Tobacco Product as “any tobacco product that is sold or distributed for use to reduce harm or the risk of tobacco-related disease associated with commercially marketed tobacco products”.¹⁰

Tobacco producers are not allowed to market their products with the claim that they are “modified risk tobacco products” without explicit authorization by the agency, which requires prior review and assessment of all available supporting scientific data and analysis substantiating any claim.

In addition, as regards “modified risk” and “modified exposure” authorization orders, the FDA requires that all advertisements and labelling related to these products should allow the public to accurately understand the claim of modified risk or exposure, considering the impact on the general population and appropriateness of marketing these products for the protection or promotion of public health. PMI has applied to the FDA in December 2016 for the marketing of IQOS system and consumables as “modified-risk products” in the US.

The FDA’s novel tobacco strategy involves two main components: reducing the addiction-potential of combustible cigarettes and introducing and clarifying the role of potentially



reduced-risk tobacco products in improving public health¹¹.

FDA Center for Tobacco Products (CTP) has authorized the marketing of PMI's IQOS tobacco heating system in the US market in April 2019.

The FDA has confirmed that “the aerosol generated by said product contains fewer toxic chemicals compared to cigarette smoke” and that “toxins found in the aerosol are at much lower levels compared to those in the cigarette smoke”. Acrolein and formaldehyde levels for this product are 89-95% and 66-91% lower than those in conventional combustible cigarettes, respectively. Carbon monoxide (CO) levels are reduced by 98% in IQOS compared to cigarette smoke.

In PMTA application the FDA recommended the removal of the surgeon's general warning: “Cigarette Smoke Contains Carbon Monoxide” from the heatsticks. It was stated “the IQOS device does not pose any CO-related risks. Accordingly, the required CO warning is misleading with respect to IQOS products.”¹²

In July 2020, the FDA has authorized the marketing of IQOS as a modified-risk tobacco product (“MRTP”) with reduced exposure information:

1. IQOS System heats tobacco but does not burn it.
2. This significantly reduces the generation of harmful and potentially harmful chemicals; and
3. Scientific studies have shown that switching completely from conventional cigarettes to the IQOS system reduces your body's exposure to harmful or potentially harmful chemicals¹³⁻¹⁶.

Authorization by FDA of IQOS as a MRTP does not mean that the product is “safe” or “FDA-approved”.

European Union (EU)

In the European Union (EU), novel tobacco products (including smoke-free tobacco products and electronic cigarettes) are regulated by Articles 19 and 20 of the European Union's Tobacco Products Directive ("TPD") requiring a notification or authorization application and data submission.

Heated Tobacco Products are subject to different regulations than combustible tobacco products under the TPD. For example, health warnings for these products are different than those applicable to cigarettes in terms of both size and content. The TPD provides that Member States should follow a notification or authorization process that requires manufacturers or importers to submit required or available scientific data, including a risk/benefit assessment, before they introduce a product into the market¹².


German Federal Institute for Risk Assessment (BfR) –

The German Federal Institute for Risk Assessment (BfR) has analyzed IQOS aerosol (tobacco smoke released by the product) and observed significant reduction (nearly by 80-99%) in selected toxic substances and carcinogens compared to those in cigarette smoke in parallel to the producers' data¹⁷⁻¹⁸.

The German Cancer Research Center (DKFZ) has confirmed these results in its 2020 report by saying that "the aerosol from tobacco heating systems contains lower toxin levels than tobacco smoke and that consumers are exposed to lesser toxin levels compared to cigarettes"¹⁹.

In addition, the Federal Health Education Center (BZgA) published a survey on heated tobacco products and underlined that the rate of use among the youth and young adults is low (0.5% in adolescents and 4.5% in young adults)²⁰.

"Our study confirms that main carcinogen levels in the emissions of the analyzed Heated Tobacco Product are significantly lower than those in conventional tobacco cigarettes. Smoking machines standardized for these emission measurements provide reliable and replicable data, and thus provide a useful basis allowing the assessment of these risks to human health and exposure".



The German Federal Institute for Risk Assessment confirmed in its report that the Tobacco Heating System selected for the previous study significantly reduces the levels of toxic substances in 2017 with the foregoing statements.

Substantial overall reduction of toxicants, in addition to benzene and 1,3-butadiene, is expected to affect health risks, if people abstain completely from other tobacco products. Nicotine levels are still in the range of conventional cigarettes, limiting the risk to switch back to conventional smoking tobacco.²¹

Public Health England

Smoking prevalence has significantly decreased in the UK in the last several decades, however cigarettes continue to be the leading preventable cause of diseases and early deaths, as well as one of the major causes of health inequalities. The smoking prevalence among adults in the UK fell from 19.9% in 2010 to 15.5% in 2016.

The Department of Health and Social Care published a new Tobacco Control Plan in 2017 with the aim of achieving a “smoke-free generation” with a smoking prevalence of 5% or lower. In this plan, the Department states that less harmful alternatives could make contributions, and that Public Health England would update the studies that offer evidence on e-cigarettes and other nicotine delivery systems every year until the end of 2022.

Public Health England reaffirmed that vaping plays an important role in helping smokers to quit and consequently, health professionals need training in the use of vaping devices.

E-cigarettes are particularly specified to a part of the vision of the Department of Health to achieve a smoke-free generation by 2030²².

Sajid Javid, Secretary of State for Health and Social Care, stated that vaping products and other nicotine delivery products could be prescribed to smokers in the National Health Service in the UK to help them quit according to the decision dated 29 October 2021. Medicines and Healthcare Products Regulatory Agency (MHRA) announced that they would publish an updated guide to pave the way for the prescription of medicinally licensed vaping products to the smokers wishing to quit. This may mean

that the UK is the first country to prescribe licensed vaping products as a medicinal product.

E-cigarettes contain nicotine and are not risk-free, but the reviews made by the experts from the United Kingdom and the US reveal that regulated vaping products are less harmful than smoking. It is strongly emphasized that a medically- licensed vaping product should be subjected to stricter security checks, and that non-smokers and children should not initiate the use of vaping products.

World Health Organization


In the light of the belief that tobacco contains carcinogens even its natural form, the WHO recommends that Heated Tobacco Products should be subjected to the same policies and regulatory measures with those applicable to all other tobacco products under the Framework Convention on Tobacco Control (WHO, FCTC).

65 countries have authorized the sale of non-combustible tobacco products as of 2021. The first step in the effective monitoring of the market growth trend of these products is to develop measures to define the consumption patterns and positioning and sales dynamics for HTPs. These measures should assess various variables such as product consumption by different customer segments including pricing and sales generated via various channels.

Monitoring sales volumes by distribution channels, determining the demographic structure of users, and collecting information on rates of switching to different tobacco products and promotion budgets spent may be the key to anticipate the innovations and trends in this category.

Besides, coordinated efforts aiming to establish global supervision systems with the aim of examining market trends are valuable in terms of provision of the information that are highly needed by countries for their national regulatory framework, and should thus be encouraged. An infrastructure should be built to collect and catalogize data related to these measures, and this process may be supported alternative via user surveys¹.

181 state parties to the Framework Convention on Tobacco Control (FCTC) undertake to take measures to prevent and reduce tobacco consumption, nicotine addiction and exposure to tobacco smoke, and to inform everyone on the health results of tobacco



consumption, as well as its addiction-causing nature and the deadly threat posed by tobacco.

FCTC provides its parties with a strong and comprehensive support to allow them to protect the public against the harms of HTP products. The countries are free to choose various approaches that are in line with the objectives of the FCTC to regulate HTPs .

During the Conference of Parties (COP) held in November 2021, the representatives agreed on the need to regulate novel and emerging products, in particular heated tobacco products, which were being misleadingly marketed as less harmful and as aids for smoking cessation. Such products were also being heavily marketed to young people, which was of great concern. Speakers noted that regulations must be based on scientific evidence, and again highlighted the need for ongoing research during the intersessional period between COP9 and COP10.

Netherlands- National Environmental and Public Health Institute (RIVM)

In 2018, RIVM, an agency of the Ministry of Health, Welfare and Sport of the Netherlands, published a bulletin summarizing its own research and the existing scientific information on IQOS-branded tobacco heating system. According to this bulletin,

- * IQOS aerosol may be harmful for the health of users and the people around.
- * IQOS emits less harmful chemicals than cigarettes.
- * IQOS is highly unlikely to be more harmful than smoking.

Based on the chemical measurements for the aerosols in the same order of magnitude as in the data of Philip Morris, the RIVM has concluded that “IQOS use is harmful to health but is probably less harmful than cigarettes”²³.

The change in cumulative exposure (CCE) was estimated to be 10- to 25-fold lower when using HTPs instead of cigarettes. Such a change when switching to IQOS indicates a substantially smaller reduction in expected life span, based on available

dose-response information in smokers. However, this is a preliminary conclusion, as only eight carcinogens were considered so far. ²⁴

Japan Healthcare Institute

The usage data of Japan are of importance as Japan is the country in which these products have been on the market for the longest period. Research carried out by the Japan Environmental Health Department on IQOS aerosol demonstrates that HnB aerosol contains lesser concentrations of some harmful N-nitrosamines (~% 80) and lesser carbon monoxide levels (99%) compared to cigarette smoke despite having nearly the same nicotine level²⁵.


According to the Japan's National Health and Nutrition Survey conducted in 2018, whose results have been published in January 2020, while Tobacco Heating System sales are on the rise in the country, overall tobacco use continues to decrease in the country. Cummings et al. state in their published research that the reduction in cigarette sales that has accelerated starting from 2016 corresponds to the increase in the marketing and sales of Heated Tobacco Products²⁶.

Concerns related to the relapse of former smokers or initiation among non-smokers because of HTPs are not supported by the data coming from Japan. The adjusted odds ratio (AOR) related to IQOS use among current smokers intending to quit smoking is 13.3, whereas this rate is 6.74 for the current smokers not intending to quit, 1.79 for former smokers and 1.0 for non-smokers.

In summary, availability of HTPs in Japan has had a minimal impact on initiation or relapse to smoking among non-smokers and former smokers, respectively. Only 0.5% of the tobacco product users-initiated tobacco use through HTPs, and less than 0.1% of former smokers relapsed to the use of tobacco products with HTPs.

The data of the other countries are also similar. For example, in the UK, only 100,000 people (3%) were non-smokers when they initiated e-cigarette use among all vaping product users (3.2 million)²⁶.

Taxation of HTPs is performed by the Ministry of Finance in Japan. HTPs are considered as pipe tobacco according to Tobacco Taxation Law, and their sale to minors is restricted



under Article 5 of the Law Prohibiting the Sale of Cigarettes to Minors. In addition, heated tobacco products are governed by the Tobacco Trade Law, and mandatory health warnings are related to addiction, cigarettes, cigarette-related diseases, risks of smoking during pregnancy and health impacts of secondhand smoking.

Country Practices

An examination of the countries' general practices reveals that it is becoming increasingly accepted, including the leading countries in tobacco control, that product innovations such as Electronic Nicotine Delivery Systems and Tobacco Heating Systems can play an important role in decreasing smoking prevalence.

The regulatory framework for HTPs is becoming increasingly more differentiated from that applicable to conventional cigarettes, including issues related to taxation, health warnings and usage restrictions.

Marketing of HTPs are not allowed in limited number of countries like Australia, Singapore, Hong Kong.

HTPs have been introduced to the market as an alternative for cigarette smokers in more than 71 markets. While 30 of these countries are in the group of countries with low- and middle-income level, the number of the users of these products has exceeded 21.2 million all over the world, and the number of smokers who completely quit smoking and switched to HTPs has reached 15.3 million.

Of the 65 geographies in which HTPs are available, almost all – including EU countries, Eastern European countries, UK, Switzerland, Saudi Arabia etc. – require a simple text health warning, with a message like that applied in the EU “This tobacco product damages your health and is addictive.” This warning message is different from the one required on cigarettes.

Flavor restrictions for HTPs are rare. Most countries allow a wider range of flavors in HTPs than in combustible cigarettes, including the European Union. In some countries, the permitted flavors in HTPs are the same as for cigarettes (e.g., tobacco

and menthol in the US).

Age restrictions for purchase of ENDS and/or HTP are typically the same as those applied to other tobacco products. For example, in most European countries the minimum age for purchase is 18. In the United States, the minimum age varies by state, but a federal law adopted last year mandates that the minimum age is 21 for all tobacco products. In Japan, the minimum age of purchase is 20.

Most countries allow some form of e-commerce for ENDS and/or HTPs. Of more than 60 countries where IQOS is available, over 50 permit the sale of the device and/or consumables online, including 20 of the EU countries and the US.

Heated Tobacco Products are subject to different regulations than those applicable to conventional cigarettes, also with respect to taxation. For example, some cigarette bans do not apply to HTPs, and these products are taxed at a lower rate compared to conventional cigarettes in many countries where they are offered for sale²⁷. Japan, Italy, Belgium, UK among many other are examples of these countries.

Conclusion

Tobacco control is a strategy to reduce supply, demand and harm aiming to eliminate or reduce the consumption of tobacco products and exposure to tobacco smoke, and thus to improve public health.

Tobacco harm reduction approach is based on the fact that the harm is mainly caused by the combustion of tobacco although the primary reason for smoking is nicotine addiction. Thus, harm reduction policies encourage those who continue to smoke to switch to a reduced risk nicotine product.


Our literature review shows that, despite the need for long-term data, these products have the potential to be less risky than continuing to smoke. We see that these products, unlike cigarettes, are used in many countries of the world with close conditions and regulations.

Our country's high smoking prevalence does not show an effective decrease despite current measures. The presentation of novel smokeless tobacco products as an alternative to current smokers, may be considered as a new policy in addition to policies that prevent smoking initiation and encourage smoking cessation to protect public health.

This will be a significant achievement for public health if majority of those who fail to, or do not wish to, quit smoking can swiftly switch to an alternative nicotine product with reduced risk for health.

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