JATC2 Task 7.4 / Information sheet 2:

Factors contributing to health impact and abuse liability of tobacco and nicotine products

Factors contributing to attractiveness

Attractiveness encompasses factors that stimulate the initiation and continuation of tobacco and nicotine product (TNP) use. Factors contributing to attractiveness can be product related, such as sensory properties and design, or situational, such as accessibility and marketing.

Tobacco and nicotine products (TNPs) are designed to be attractive, in order to encourage initiation and sustain use. The factors that stimulate TNP use can generally be categorized into two types: product-related and situational (Table 1).

Product related factors encompass the sensory properties of TNPs such as taste and odor. For example, substances such as menthol are commonly added to improve the taste and reduce harshness of the product. Flavors also play a significant role in TNP appeal. Access to a variety of flavors is associated with higher appeal and abuse potential and of vaping products. Flavors such as fruit and candy were also associated with greater user satisfaction and enjoyment. Additionally, nicotine content is an important factor; certain nicotine levels may be attractive to people seeking a substitute for traditional tobacco cigarettes, to satisfy their nicotine cravings. Higher nicotine concentrations in vaping products are often linked to higher abuse potential and appeal.

Manufacturers of TNPs develop a broad range of products with various attractive design features to target specific user groups. Some are colorful, compact and easy to carry, while other devices allow for extensive personalization, refills or accessories. Certain designs enable discreet use in smoke and aerosol free environments, which may appeal to some users. Moreover, product packaging can enhance appeal through the use of vibrant colors and sleek designs, or conversely, reduce appeal by incorporating plain packaging and prominent health warnings. Other product-related factors that influence TNP attractiveness are affordability and experienced or expected health consequences.

Situational factors that may increase the appeal of TNPs include accessibility (i.e., how easy it is to obtain a product) and marketing efforts, both on- and offline. Public health institutes and governments may also disseminate information via public channels to shape public perception and raise awareness of the risks associated with TNP use. Finally, particularly among young individuals, there may be strong influence of peers in their personal social network as well as from online communities.

It is important to note that attractiveness is subjective, varying across consumer groups and potentially changing over time. Cultural differences and legislative actions can also influence factors contributing to the attractiveness of TNPs.

When evaluating the population risk associated with TNPs, it is crucial to consider their attractiveness, as this significantly influences both the initiation and continuation of use. To prevent and discourage TNP initiation and use, regulators may consider implementing several measures aimed at reducing their attractiveness:

- Banning the use of ingredients that enhance the sensory experience, such as flavoring agents and substances that reduce harshness of smoke or vapor, including those that activate the TRPM8 receptor (also see partial guidelines on article 9 an 10 of FCTC)
- Banning all flavors

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- Standardizing product designs to ensure a uniform and plain appearance across each product type
- Requiring plain packaging and clearly visible health warnings (also see guidelines on article 11 of FCTC)
- Implementing a minimum price for TNPs and increasing tax rates on a regular basis, taking into account inflation and income growth developments (also see guidelines to article 6 of FCTC)
- Increasing age restrictions for purchase and implement effective monitoring and enforcement strategies.
- Reducing the number of points of sales
- Expanding Smoke and Aerosol-Free Environment (SAFE) legislation to include more spaces and all types of TNPs (also see guidelines to article 8 of FCTC and the EU proposal for a council recommendation on SAFE)
- Implementing a comprehensive ban on all forms of marketing for TNPs and their devices, including online and on social media (also see guidelines to article 13 of FCTC)
- Providing an infrastructure to raise public awareness of health risks associated with TNP use and discourage use, for example by means of launching information campaigns (also see guidelines to article 12 of FCTC)

Table 1. Product related and situational factors contributing to attractiveness of TNPs.

Product related factors	Situational factors
Sensory properties, palatability	Accessibility
	- Points of sale
	- Age restriction
	- Bans in public places
Availability and variety of flavors	Marketing and advertising
	- Health claims
	- Social media
Nicotine content	Public information/education
Design of the product, device and packaging	Social network
- Aesthetics	- Use and reputation among peers
- Concealability	- Social media
- Functionality	
Affordability	
Experienced health effects	

Factors contributing to addictiveness

Use of TNPs can cause and sustain addiction. Factors contributing to their addictiveness are the amount and form of nicotine they contain, the route of exposure and rate of nicotine delivery to the user, and the presence of other addiction enhancing substances.

The main addictive substance in TNPs is nicotine. Nicotine stimulates the release of dopamine in the brain, a chemical associated with pleasure and reward. This leads to cravings and reinforces the desire to use tobacco. Over time, changes in neural pathways increase cravings and reduce sensitivity to nicotine's effects. As a result, the brain becomes dependent on nicotine to maintain a sense of normalcy, making it difficult to quit due to withdrawal symptoms and persistent cravings. Nicotine's effects can be more pronounced during adolescence, potentially leading to future substance abuse, reduced social

skills, aggressive or impulsive behavior, poor sleep, lower academic performance, and even symptoms of depression or suicidal thoughts.

Higher nicotine content typically leads to a stronger activation of the brain's reward system. For e-liquids, the Tobacco Products Directive (TPD) sets a maximum allowable nicotine concentration of 20 mg per milliliter. However, other nicotine products are not subject to such concentration limits. The actual amount of nicotine a user takes in depends on both the product's characteristics and how it is used. For example, factors such as the device's electrical power and the user's behavior influence the amount of nicotine released in the inhalable aerosol (emissions). Users can also modify e-cigarettes to deliver higher nicotine concentrations, for example by changing the wick material or increasing power settings.

The form of nicotine used in a product can also impact its addiction potential. E-liquids containing nicotine salts generally have higher concentrations of nicotine and flavorings compared to those with free-base nicotine. Nicotine salts are believed to increase nicotine absorption in the lungs and reduce the harshness perceived by users, making them potentially more addictive than free-base nicotine.

TNPs deliver nicotine through various routes, which also affects their addictive potential. For inhaled products like e-cigarettes, nicotine is rapidly absorbed through the lungs, reaching the brain within seconds and strongly reinforcing addiction. In contrast, nicotine pouches and smokeless tobacco deliver nicotine through the oral mucosa or digestive system, resulting in slower delivery to the brain and thus, possibly, a lower addiction potential.

Lastly, other substances can enhance addictiveness through various mechanisms. For instance, (synthetic) nicotine analogs and minor alkaloids present in tobacco can mimic the effect of nicotine. Substances that facilitate inhalation, such as menthol and its analogs, increase nicotine bioavailability and intake. Other substances may affect nicotine absorption by altering pH levels or contribute to inhibition of nicotine breakdown in the brain, further contributing to its addictive potential.

When evaluating the population risk of TNPs, it is important to consider their addictive potential, as addiction leads to sustained use and associated health risks. While, a complete ban on nicotine or nicotine containing products seems to be the ultimate solution to mitigate harm, such a ban could face legal challenges. These include arguments about personal freedom, property rights, and economic impacts. Even if it is legally feasible, implementing such a ban would involve navigating complex legal, economic, and social factors.

As an alternative, regulators may consider other measurers to reduce the addictive potential of TNPs, such as:

- Lowering the maximum allowed nicotine and nicotine salt concentrations to levels that are minimally addictive. These levels likely vary between product types, and further research is needed to determine appropriate thresholds for all TNPs
- Supporting the enforcement of the ban on additives that facilitate inhalation or nicotine uptake in tobacco products and e-liquids (TPD art. 7.6). To this end, some Member States (MS), including Belgium, Germany and the Netherlands, have established lists of substances meeting these definitions.
- Extending the forementioned ban to include all substances in ingredients or emissions that in any way may enhance the addictive potential of a TNP. To support enforcement, MS are encouraged to create and periodically update lists of substances that meet these criteria, incorporating the latest research and insights.
- Implementing regulations to restrict user-adjustable device settings that increase nicotine delivery. Standardizing the physical design features of devices will likely also reduce their appeal to current and potential users.

Identification of potential harm (hazard assessment) of novel tobacco- and nicotine products

A hazard is a source of potential harm. Ingredients and emissions from TNPs can contain harmful substances that can be classified based on the type of harm they may cause, such as cancer or skin irritation. The types and quantities of these substances may vary depending on the product type. In addition to chemical hazards, products may also present risks associated with their use, such as poisoning from accidental ingestion or exposure to harmful substances due to improper mixing of ingredients. Additionally, hazards can arise from product malfunctions, such as overheating or explosions. To identify potential health risks, it is important to characterize both the harmful substances and other dangers associated with use of TNPs.

TNPs such as e-cigarettes and heated tobacco products (HTP) may contain harmful substances that can cause cancer, genetic mutations, or reproductive harm (known as CMR properties). These harmful substances can be present in the ingredients as well as in the inhalable aerosol (emissions) of these products. If there is a suspicion or confirmation that these substances are present, they should be given high priority for characterization, quantification, hazard evaluation and regulation. Besides substances with CMR properties, TNP may also contain other harmful substances that can affect the lungs, heart, hormones, or contribute to addiction potential.

Another hazard arises when e-cigarette users mix substances themselves, engaging in do-it-yourself (DIY) practices. Impropriate mixing can alter the amount and type of hazardous substances in the emissions from a product. Device settings, such as temperature of the coil in the e-cigarette, can also influence the level of harmful substances in the aerosol. In addition, TNP can pose other risks, such as e-cigarette battery explosions and accidental ingestion of e-liquids by children, which may cause poisoning. Furthermore, small parts, such as metal components in HTPs, can be dangerous if swallowed, as reported in cases involving young children.

When evaluating the health risks of TNPs, it is important to identify the potential hazards associated with these products. This involves identifying potentially harmful substances present in ingredients and emissions, as well as other product-related dangers. To achieve this, regulators may consider the following actions:

- Strengthening the enforcement of existing bans on harmful substances, such as CMR substances. MS are encouraged to create and periodically update lists of banned ingredients according to article 7 (6) e and Article 20 (3) e TPD. Competent authorities and independent academic research should collaborate to identify harmful and potentially harmful substances that an be included on such lists.
- Establishing limits on the concentration of certain harmful substances in the emissions produced by TNP.
- Launching public information campaigns to raise awareness of health risks associated with DIY practices and other dangers related to TNP use.

General recommendations for tobacco and nicotine product regulators

To safeguard the public from the harmful effects of TNP use, regulators need to establish a climate conducive to effective tobacco and nicotine product regulation. To achieve this, they should consider the following actions:

- Fund and promote independent academic research to better understand how various product characteristics influence the attractiveness, addictiveness and harmful health consequences of TNPs.
- Stay vigilant and anticipate industry strategies to manipulate product characteristics in response to

regulatory measures.

- Build and foster sustainable partnerships between different governmental agencies, civil society and NGOs to increase awareness as well as prevent and discourage TNP use.
- Harmonize legislation and enforcement practices across EU countries and across TNP types to help prevent cross-border trade and product switching.
- Implement uniform and detailed reporting requirements for manufacturers of all types of TNPs to ensure transparency and accountability.