Swedish Match

Swedish Match response to public consultation on the proposed ban on nicotine pouches in the Netherlands

Swedish Match welcomes the opportunity to provide comments to the proposed ban of tobacco free nicotine pouches, which is proposed in the Dutch government's amendment "to regulate non-tobacco nicotine products and nicotine devices" to the Dutch Tobacco and Smoking Products Act.

Swedish Match is a pioneer in providing smokers with substantially less harmful products and has spearheaded the steep decline in smoking prevalence in countries such as Sweden and Norway.

Swedish Match was recently acquired by Philip Morris International to accelerate our joint endeavor to achieve a smokefree future.

Introduction

In line with the ambitious target of the Dutch government to create a tobacco and nicotine free generation and bringing down smoking to less than 5% amongst the adult population by 2040, it has been proposed to ban the marketing of oral tobacco free nicotine pouches. In our view the proposed ban does not only constitute a breach against the internal market rules as it lacks any convincing scientific justification. It also deprives the approximate 2.8 million Dutch smokers of a viable alternative to cigarettes. A robust regulation of nicotine pouches is a more proportionate action, one which will also enhance the protection of public health.

What is a nicotine pouch

Tobacco-free nicotine pouches is a category of products aimed at smokers and other tobacco and nicotine users who are unwilling or unable to quite using nicotine/tobacco. They come in small pouches, containing pharma-grade nicotine, often together with one or more fillers, flavorings, and other food grade ingredients. Nicotine pouches are placed between the lip and the gum where it delivers nicotine through the oral mucosa to the blood stream, resulting in a systemic nicotine exposure (1, 2). Nicotine poches have been shown to have significantly fewer toxicants and reduced toxicological effects as compared with cigarette smoke and tobacco-based snus (2-5). The reduced toxicological profile of nicotine pouches translates in to actual exposure to users, as nicotine pouch users have considerably lower levels of several biomarkers of exposure (BoE) and biomarkers of potential harm (BoPH) to tobacco toxicants as compared with current smokers (6). In fact, most BoEs and BoPHs, apart from nicotine and its degradation products, are comparable to those of non-users of nicotine products.

As nicotine pouches do not contain tobacco and are consumed without combustion or inhalation, - which is the overwhelming cause for tobacco related morbidity and mortality –the use of nicotine pouches is substantially less harmful than many of products regulated by the current Dutch tobacco legislation,.

A number of Member States have introduced specific product regulation (Sweden, Denmark, Czech Republic, Slovakia, Hungary) balancing the availability of nicotine pouches for smokers and other nicotine/tobacco users with the protection of young people and non-users.

The category is subject to excise tax in a number of countries (Estonia, Latvia, Hungary, Sweden, Denmark) and from our understanding it is likely that nicotine pouches will be included as an excisable category in the forthcoming revision of the European Union's Tobacco Excise Directive.

Proportionality and non-discrimination are two fundamental principles governing the function of the internal market. As nicotine pouches were not on the market when the EU's latest Tobacco Products Directive (TPD) was adopted in 2014, they are not part of this specific legislation. However, as the product category can be compared to other product categories regulated by the TPD and cater to the same consumers using products currently regulated under the TPD, it would be logical to also include this category in the upcoming revision of the TPD, being treated in the same manner as other similar product categories.

Nicotine pouches do not contain tobacco, the closest other category in the TPD is electronic cigarettes. The regulation in the TPD concerning electronic cigarettes was deemed appropriate by the EU's legislators in 2014 to both ensure a high level of public health protection as well as the functioning of the internal market.

The Dutch government argues that the proposed ban is necessary to protect public health. In order for the ban to be justified however, the government would have to prove that the ban doesn't *"constitute a means of arbitrary discrimination or a disguised restriction on trade between Member States"* (7).

Based on the current scientific knowledge around nicotine pouches there is no evidence calling for a harsher treatment of nicotine pouches compared to similar product categories already regulated by the TPD.

The Dutch government has not provided any convincing scientific arguments why an outright ban of this category would be a more appropriate measure than to regulate the product category with a view to ensure a high level of public health protection whilst at the same time ensuring a proper functioning of the internal market. Below, we will outline the main areas where the Dutch government has failed to properly assess the scientific evidence around the use of nicotine pouches.

The science behind nicotine

In a letter sent to Maarten van Ooijen the State Secretary for Prevention at the Ministry of Public Health on the 18 March 2022, Swedish Match provided data aimed at informing the debate on nicotine pouches that was held in the Parliament on 24 March 2022.

We have taken the liberty to provide you with letter again (Annex 1) for your reference. The letter was intended to provide some further scientific evidence above what was captured in the RIVM assessment (8).

As with any society that prides itself with a regulatory culture where legislation is created based on robust scientific evidence, we trust that all relevant science is taken into account when assessing the future regulatory regime for nicotine pouches.

With regards to the arguments in the explanatory memorandum we would like to make the following points.

Nicotine, the common, but not decisive denominator

There are many hazardous substances that people are exposed to on an every-day basis. Nicotine is one of them. Other examples are alcohol, drugs, chemicals, waste etc. The modern society have mitigated the risk with these hazardous substances by regulating them, which is also the case for products used by people who consume nicotine. From a risk perspective, and in order to protect public health, there is a logic to regulate different products according to their risk profile.

The nicotine in nicotine pouches does not differ in any way from the nicotine found in products such as e-cigarettes, heated tobacco, smokeless tobacco, combustible tobacco products, or pharmaceutical nicotine replacement therapies for that matter. Whilst most parts of tobacco related morbidity and mortality stems from lung cancer, respiratory disease, and cardiovascular disease (9), nicotine is not the predominant

chemical in cigarette smoke responsible. Consumers of Swedish snus are exposed to the same levels of nicotine as cigarette smokers, but use of Swedish snus has not been associated with an increased risk of lung cancer, respiratory disease, or cardiovascular disease, clearly indicating that it is not the exposure of nicotine that causes the major smoking-related diseases (10-12).

Further, in a memorandum summarizing the epidemiological literature on oral tobacco products (including nicotine pouches) the Center for Tobacco Products found that "The overall epidemiological literature supports that cigarette smokers who completely switch to SLT products are likely to substantially lower their risks of cardiovascular disease, lung cancer, and respiratory disease compared to smoking."(13).

Acute toxicity – a matter of dose

Nicotine is not risk free and is toxic when ingested or absorbed at high doses. Excessive amounts of nicotine can cause acute poisoning, and in worst case resulting in respiratory failure and death. However, this is at nicotine doses beyond those in nicotine pouches or regulated smoking/ vaping products, under reasonably foreseeable use.

The acute toxicity of nicotine does not differ based on the nicotine delivery system. In other words, the nicotine in the products regulated under the EU's TPD is the same as the nicotine found in nicotine pouches. Therefore, there is no apparent reason to arbitrarily discriminate against nicotine pouches based on the risk of acute toxicity.

In fact, there is published scientific reports on intoxications following ingestion of e-cigarette liquids, the outcomes were linked to the nicotine exposure, assessed as plasma nicotine levels, and not due to the route of administration of the nicotine intake (oral or intravenous). This case report describes patients who suffered from e-liquid intoxications, see graph below (14). The mean plasma nicotine concentration among the survivors was 307 ± 312 ng/mL and among the patients that died, the mean plasma nicotine concentration was 3360 ± 1692 ng/mL. The lowest lethal dose was almost 100 times higher compared to the maximum plasma exposure (C_{max}) after use of a nicotine pouch or a cigarette or vaping product (C_{max} <20ng/mL) (1, 15-17).

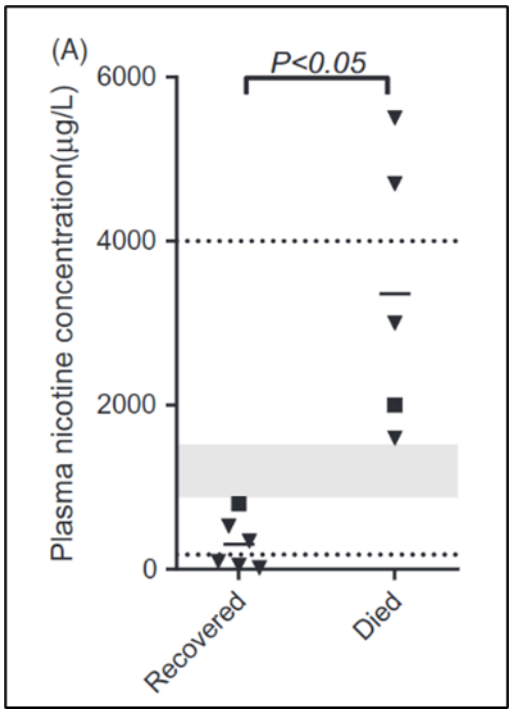

Figure 1. Graph from Maessen et al (14) displaying individual and mean nicotine concentration in the plasma in µg/L (1 µg/L = 1 ng/mL) in cases with acute e-liquid poisoning subdivided in the outcome recovered or death. Symbols: triangle, oral intake; squares, intravenous intake. Black horizontal dotted lines (at 180 and 4000µg/L) indicate levels of lethal value as found in literature (18). Grey horizontal bar indicates Maessen's lethal value range. The mean is displayed by the short black lines (at 307 and 3360µg/L)

If the plasma nicotine concentrations from a nicotine pouch or a cigarette were added to the graph, the data points would be close to 0 on the y-axis (<20 ng/mL).

Furthermore, the commonly referenced lethal dose of 60 mg (corresponding to 1 mg/kg body weight (bw) for a 60 kg person) is lower than the harmonized classification for the acute toxicity estimates (ATE) for oral nicotine of 5 mg/kg bw (19) (corresponding to 300 mg for a 60 kg person). The oral ATE is based on the estimated oral LD50 of nicotine in mice (3.34 mg/kg and 24 mg/kg) and LD50 of nicotine in dogs (9.2 mg/kg) as the most sensitive species both fit best within the range of >5 mg/kg and ≤50 mg/kg, The Committee for Risk Assessment (RAC) is of the opinion that nicotine warrants a classification as Acute Tox. 2 (oral) with the hazard statement H300: Fatal if swallowed (20). After reviewing fatal nicotine intoxications, Mayer (18) has suggested that the lower limit for a lethal blood nicotine concentration is about 2000ng/mL, correlating to an estimated lethal dose of nicotine in humans of about 500mg to 1g (or 8 - 16 mg/kg for a 60 kg adult). This estimation is similar to the LD50 in dogs.

While there are no published reports on lethal intoxication from ingestion of nicotine pouches or snus. The pouch format prevents ingestion of very high doses of nicotine due to nausea and vomiting following swallowing of several pouches which protect the individual from absorbing lethal doses of nicotine. In contrast, swallowing two vials, (20ml) of e-cigarette liquid (20mg/ml, 10ml) is doable and could result in a lethal nicotine dose for an adult person.

Nicotine addiction – nicotine pouches vs. combustible products

As nicotine consumer products are allowed in the Netherlands it is relevant to assess if data indicate that nicotine pouches are more addictive than cigarettes and e-cigarettes. The abuse potential of nicotine is largely a function of how fast nicotine is delivered to the brain and which peak levels of nicotine are reached (21). It has been widely recognized that nicotine absorption in the lung is the most effective means of delivery, and nicotine reaches the brain within seconds while smoking a cigarette, which is even faster compared to intravenously administrated nicotine. The peak plasma levels are reached somewhat later, within 5-7 minutes. In comparison, the plasma peak levels using a nicotine pouch is reached considerably slower, within 30 – 60 minutes. The peak levels following cigarette smoking and nicotine pouch use are

dependent on nicotine strength, but in general quite similar. As a consequence, data indicate that nicotine pouches are less addictive compared to conventional cigarettes (22, 23).

Protecting children from nicotine

There are many products in society that children should not be exposed to and nicotine containing products is one example. It is Swedish Match's firm belief that children – born and un-born - should be protected against nicotine in all forms. The products that we manufacture and sell are intended for adult users with a previous history of tobacco and/or nicotine use. The RIVM survey referenced in the explanatory memorandum points to the fact that nicotine pouches only have a very limited use amongst younger age-groups. What is more reassuring is the fact that close to 70% of those how have used nicotine pouches are smokers or have previously smoked (24). Moreover, another study found that 95% of never users of tobacco or nicotine products had very little interest in purchasing nicotine pouches and therefore the likelihood of use in that group was considered low (25).

The protection of children is one of the key reasons that this product category needs a robust regulatory framework. Banning the product will create another set of challenges, including less control of the quality of the illegal products ending up on the market. We note that even though nicotine pouches are de-facto banned, media has reported that children are using the product and possibly also are recruited by criminals who are offering nicotine pouches as a payment for criminal activities (26). This should serve as an indication of the challenges that come with prohibition.

Long-term use

Nicotine is known to have a short-term cardiovascular effect leading to transient increase in blood pressure and heart rate. Hypertension is a risk factor leading to manifestation of arteriosclerosis such as ischemic heart disease, stroke, and peripheral artery disease (PAD). Further, it is well established that cigarette smoking leads to arteriosclerosis, ischemic heart disease, stroke, and PAD. It is therefore reasonable to assume that nicotine is the cause of the cardiovascular risk seen in smoking and consequently assume that the use of nicotine pouches would lead to an increased risk of cardiovascular disease, However, numerous epidemiology studies have addressed this question and neither ischemic heart disease, stroke, or PAD is associated with snus use (27-29), and as the nicotine exposure from snus is similar to that of nicotine pouches, it is clear that the long-term use of nicotine pouches would not increase the risk of developing cardiovascular disease.

Possible other harmful constituents

From a toxicological perspective, products produced by responsible companies contains minimal amount of toxic substances. Below is an overview comparing the content of unwanted constituents in Swedish Match's nicotine pouch ZYN with levels in normal food. The list if constituents stems from Swedish Match's internal standard (Gothiatek®) which caps unwanted constituents in our oral tobacco products.

Constituent in Swedish Match's Gothiatek standard for snus	**ZYN Pouch 0.4g/0.8g (mean)**	**Quantification Limit (per gram ZYN)**	**Levels in normal food (100 gram)**
Acetaldehyde (µg/unit)	BQL	0.5 µg	1000 µg in bananas
Arsenic (µg/unit)	BQL	0.05 µg	9.4 µg in un-boiled rice
Benzo(a)pyrene (B(a)P) (ng/unit)	BQL	0.6 ng	190 ng in grilled meat
Cadmium (µg/unit)	BQL	0.05 µg	18 µg fish and seafood

Chromium (µg/unit)	BQL	0.15 µg	28.2 µg in fats/oils
Crotonaldehyde (µg/unit)	BQL	0.1 µg	50 µg in wine (100 ml)
Formaldehyde (µg/unit)	1.03 - 2.65	0.25 µg	4900 µg in pear
Lead (µg/unit)	BQL	0.10 µg	4 µg in salad
Mercury (µg/unit)	BQL	0.02 µg	13 µg in fish and seafood
Nickel (µg/unit)	BQL	0.10 µg	30 µg in bread
Nitrite ion (µg/unit)	BQL	1 µg	300 µg in broccoli
Sum NNN+NNK (µg/unit)	BQL	0.03 µg	Tobacco specific (not found in food)
Aflatoxin Sum (ng/unit)	BQL	2.1 ng	20 ng in pistachio nuts
Ochratoxin (ng/unit)	BQL	0.5 ng	260 ng in raisins
NDMA (ng/unit)	BQL	0.6 ng	120 ng in fried bacon

BQL = below quantification limit, µg = microgram, ng = nanogram

No evidence supporting the gateway theory

The concern that the introduction of nicotine pouches in the Netherlands would lead to increasing use of cigarette smoking based on the "gateway" theory. To our knowledge this theory is not substantiated in the scientific literature. A recent publication (30) clearly shows that the countries with high uptake of reduced risk tobacco/nicotine products demonstrate a steeper slope in smoking prevalence compared to countries which have restricted these products. A proportional and reasonable regulation rather enables the conditions for the opposite i.e.; a gateway away from cigarettes.

The ban on snus is not supported by science

In the explanatory memorandum accompanying the bill, we note the comparison between nicotine pouches and snus and the reference to the fact that the European Court of Justice (EJC) has upheld the ban twice (as opposed to several as stated in the explanatory memorandum).

Suffice to say, Swedish Match does not agree with neither the ban on oral tobacco nor the ECJ's decision and we would like to draw your attention to the following points:

The European Commission's Impact Assessment (IA) accompanying the proposal for a revised TPD (31) was an illustration of how the science was massaged to support a predetermined policy conclusion. The IA included selective evidence and incorrect or misleading assessment of data that fundamentally distorted the debate around snus. Swedish Match would like to make the following points:

- The impact assessment tried to establish that oral tobacco is associated with various diseases, but mostly without quantifying risk or harm. No-one argues that snus is perfectly safe, but how unsafe is important. What should have mattered to a regulator or legislator is the following:
    - that the excess risk of prolonged snus use compared to being a non-tobacco user is small and comparable with other lifestyle risks;
    - that the relative risk compared to smoking, for which it is a viable alternative, is very low, and thus, presents opportunities for harm reduction and health benefits – and these are strongly evident in Sweden.

- The relative risk of use of oral tobacco in the form of Swedish snus is substantially less than for cigarette smoking and at the low end of the spectrum of risk arising from smokeless tobacco products. In this context it can be pointed out that the Swedish National Board of Health and Welfare ranks the negative impact of smoking as great to very great, and the impact of using snus as small to moderate (32).

- Oral tobacco can substitute for cigarette use and provide a substantial health benefit for those who switch. The health benefit arising from 'harm reduction' is unambiguously clear in Sweden. More specifically and uncontested is the fact that the risk of a man dying from a tobacco-related illness is less in Sweden than in any other EU country, although tobacco consumption is on a comparable level with that of other countries in Europe (33, 34). This phenomenon is referred to as "the Swedish Experience" and is explained by the unique form of tobacco use among Swedish men, which largely takes the form of snus. Total daily tobacco consumption is about equal in comparable countries, but Swedish men smoke substantially less. The smoking prevalence in Sweden is 7%, the lowest in Europe whereas the daily tobacco consumption prevalence is 20% (35).

  The positive effect of this phenomenon is the very low tobacco-related morbidity and mortality rates in Sweden. This unique situation is documented in a large number of epidemiological studies, which, inter alia, note that Sweden shows the lowest risk of lung cancer among industrial countries (36).

  While the public health benefits from substituting cigarette smoking with snus or other reduced-risk nicotine products will not be detectable in health statics for several years it is of interest to notice that "the Swedish Experience" has more recently been replicated in Norway where snus also has substituted cigarettes.

- During the last decade (2011 to 2021) smoking prevalence in Norway has dropped from 17% to 8%, and snus use has increased from 8% to 15%, resulting in the total daily use of cigarettes + snus has gone from 25% to 23% during the same period of time. Of special interest is the dramatic substitution seen among youth where cigarette smoking has become almost obsolete with a decrease from 11% in 2011 to 1% in 2021 among 16 – 24 years old, while smoking + snus has decreased from 29% to 22%. As data from Statics Norway show, it is clear that the uptake of snus has not led to an increase of total tobacco consumption, but that snus has substituted cigarettes (37).

- In US, Food and Drug Administration's (FDA) assessment of Swedish Match regulatory application (PMTA) for General Snus, the Technical Project Lead (TPL) recommended that a marketing authorization letter should be issued based on data showing that "*The proposed products contain significantly lower levels of NNN and NNK compared to over 97% the smokeless-tobacco products currently on US market. Since NNN and NNK are among the most carcinogenic constituents in tobacco products, reduction of NNN and NNK levels in smokeless tobacco (ST) products could reduce the cancer risk for consumers using ST products. Assuming persons who would have used other US ST products use these products instead, an individual using these products with reduced NNN levels could decrease the excess cancer risk by 90% compared to use of moist snuff (market share: 82%), 67% compared to use of chewing tobacco (market share: 15%), 38% compared to use of United States (US)-style snus, and 92% compared to use of dry snuff. Even further reductions in excess cancer risk could occur with the corresponding reductions in NNK; however, a quantitative contribution cannot be determined at this time due to the absence of a NNK cancer slope factor*." (38).

Further, the Swedish Match General Snus is to date the only tobacco/nicotine product that has been granted a Modified Risk Tobacco Order under section 911 of the Federal Food, Drug, and Cosmetic (FD&C) Act (39) which allows General Snus to be marketed by the following claim *"Using General Snus instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis."*

The TPL concluded that the claim was scientifically accurate and pointed specifically at the long-term epidemiological studies at hand.

Conclusion

Swedish Match questions if the smoke-free generation goal by 2040 is attainable without scientifically proven alternatives to cigarettes. In both Sweden and Norway, alternative reduced risk tobacco and nicotine products have played a crucial role to accelerate the steep decline in smoking prevalence. There are no other countries where the smoking rates have declined so rapidly. This success cannot be explained without taking availability of reduced risk products into account.

Banning nicotine pouches in the Netherlands is a far more restrictive measure than the current treatment of similar product categories such as e-cigarettes and heated tobacco products. The Dutch government has so far not presented a sufficient justification why a ban would be a more appropriate measure to protect youth and non-users, than regulating this category in the same way as other comparable product categories such as e-cigarettes and heated tobacco products. Especially considering that there is no meaningful difference in nicotine intake compared to the aforementioned categories compared to nicotine pouches.

Banning a product category like nicotine pouches, especially since they are available and regulated in other EU Member States will lead to a fragmented internal market. It will also be negative for the protection of public health. Firstly it deprives smokers of a potentially life-saving alternative to cigarettes and secondly a ban will lead to limited means to control which products are consumed on the market and by whom, as well as the quality of the products.

By moving forward with this ban the legislators and regulators will abdicate their responsibility to ensure the functioning of the internal market and their responsibility to protect public health.

Swedish Match

References

1. Lunell E, Fagerström K, Hughes J, Pendrill R. Pharmacokinetic Comparison of a Novel Non-tobacco-Based Nicotine Pouch (ZYN) With Conventional, Tobacco-Based Swedish Snus and American Moist Snuff. Nicotine Tob Res. 2020;22(10):1757-63.
2. Azzopardi D, Liu C, Murphy J. Chemical characterization of tobacco-free "modern" oral nicotine pouches and their position on the toxicant and risk continuums. Drug Chem Toxicol. 2021:1-9.
3. Bishop E, East N, Bozhilova S, Santopietro S, Smart D, Taylor M, et al. An approach for the extract generation and toxicological assessment of tobacco-free 'modern' oral nicotine pouches. Food Chem Toxicol. 2020;145:111713.
4. Miller-Holt J, Baskerville-Abraham I, Sakimura M, Fukushima T, Puglisi A, Gafner J. In vitro evaluation of mutagenic, cytotoxic, genotoxic and oral irritation potential of nicotine pouch products. Toxicol Rep. 2022;9:1316-24.
5. Yu F, Rudd K, Pour SJ, Trelles Sticken E, Dethloff O, Wieczorek R, et al. Preclinical Assessment of Tobacco-Free Nicotine Pouches Demonstrates Reduced In Vitro Toxicity Compared with Tobacco Snus and Combustible Cigarette Smoke. Applied In Vitro Toxicology. 2022.
6. Azzopardi D, Haswell LE, Frosina J, McEwan M, Gale N, Thissen J, et al. Assessment of biomarkers of exposure and potential harm, and physiological and subjective health measures in exclusive users of nicotine pouches and current, former and never smokers. Biomarkers. 2022:1-12.
7. Consolidated version of the Treaty on the Functioning of the European Union, PART THREE - UNION POLICIES AND INTERNAL ACTIONS, TITLE II - FREE MOVEMENT OF GOODS, CHAPTER 3 - PROHIBITION OF QUANTITATIVE RESTRICTIONS BETWEEN MEMBER STATES, Article 36 (ex Article 30 TEC).
8. Rijksinstituut voor Volksgezondheid en Milieu (RIVM). Nicotineproducten zonder tabak voor recreatief gebruik, RIVM-briefrapport 2020-0152. 2021.
9. Rostron B. Smoking-attributable mortality by cause in the United States: revising the CDC's data and estimates. Nicotine Tob Res. 2013;15(1):238-46.
10. Rostron BL, Chang JT, Anic GM, Tanwar M, Chang CM, Corey CG. Smokeless tobacco use and circulatory disease risk: a systematic review and meta-analysis. Open Heart. 2018;5(2):e000846.
11. Boffetta P, Aagnes B, Weiderpass E, Andersen A. Smokeless tobacco use and risk of cancer of the pancreas and other organs. Int J Cancer. 2005;114(6):992-5.
12. Luo J, Ye W, Zendehdel K, Adami J, Adami HO, Boffetta P, et al. Oral use of Swedish moist snuff (snus) and risk for cancer of the mouth, lung, and pancreas in male construction workers: a retrospective cohort study. Lancet. 2007;369(9578):2015-20.
13. US Food & Drug Administration Center for Tobacco Products. Memorandum: Health effects of smokeless tobacco products. 2020.
14. Maessen GC, Wijnhoven AM, Neijzen RL, Paulus MC, van Heel DAM, Bomers BHA, et al. Nicotine intoxication by e-cigarette liquids: a study of case reports and pathophysiology. Clinical Toxicology. 2020;58(1):1-8.
15. Digard H, Proctor C, Kulasekaran A, Malmqvist U, Richter A. Determination of nicotine absorption from multiple tobacco products and nicotine gum. Nicotine Tob Res. 2013;15(1):255-61.
16. McEwan M, Azzopardi D, Gale N, Camacho OM, Hardie G, Fearon IM, et al. A Randomised Study to Investigate the Nicotine Pharmacokinetics of Oral Nicotine

Pouches and a Combustible Cigarette. Eur J Drug Metab Pharmacokinet. 2021(47):211-21.
17. Scherer G, Mütze J, Pluym N, Scherer M. Assessment of nicotine delivery and uptake in users of various tobacco/nicotine products. Curr Res Toxicol. 2022;3:100067.
18. Mayer B. How much nicotine kills a human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century. Arch Toxicol. 2014;88(1):5-7.
19. The European Chemicals Agency. Nicotine Harmonised classification - Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation), [Available from: https://echa.europa.eu/sv/information-on-chemicals/cl-inventory-database/-/discli/details/48724.
20. The European Chemicals Agency. Committee for Risk Assessment RAC Opinion proposing harmonised classification and labelling at EU level of Nicotine. 2015.
21. Hukkanen J, Jacob P, 3rd, Benowitz NL. Metabolism and disposition kinetics of nicotine. Pharmacol Rev. 2005;57(1):79-115.
22. Rensch J, Liu J, Wang J, Vansickel A, Edmiston J, Sarkar M. Nicotine pharmacokinetics and subjective response among adult smokers using different flavors of on!® nicotine pouches compared to combustible cigarettes. Psychopharmacology (Berl). 2021(238):3325-34.
23. Liu J, Rensch J, Wang J, Jin X, Vansickel A, Edmiston J, et al. Nicotine pharmacokinetics and subjective responses after using nicotine pouches with different nicotine levels compared to combustible cigarettes and moist smokeless tobacco in adult tobacco users. Psychopharmacology. 2022;239(9):2863-73.
24. Ministerie van Volksgezondheid Welzijn en Sport (RIVM). Explanatory Memorandum to the Bill amending the Tobacco and Tobacco Products Act regulating non-tobacco nicotine products and nicotine devices. 2022.
25. Sarkar M, Gogova M. Review of: "Nicotine Pouch Sales Trends in the US by Volume and Nicotine Concentration Levels From 2019 to 2022". Qeios.
26. Vlaanderen Katharina. Politie Amsterdam waarschuwt: criminelen ronselen schoolkinderen met verslavende snus. Het Parool. 2022.
27. Yuan S, Titova OE, Damrauer SM, Åkesson A, Larsson SC. Swedish snuff (snus) dipping, cigarette smoking, and risk of peripheral artery disease: a prospective cohort study. Scientific Reports. 2022;12(1):12139.
28. Hansson J, Galanti MR, Hergens MP, Fredlund P, Ahlbom A, Alfredsson L, et al. Use of snus and acute myocardial infarction: pooled analysis of eight prospective observational studies. Eur J Epidemiol. 2012;27(10):771-9.
29. Hansson J, Galanti MR, Hergens MP, Fredlund P, Ahlbom A, Alfredsson L, et al. Snus (Swedish smokeless tobacco) use and risk of stroke: pooled analyses of incidence and survival. J Intern Med. 2014;276(1):87-95.
30. Fagerström K. Can alternative nicotine products put the final nail in the smoking coffin? Harm Reduct J. 2022;19(1):131.
31. European Commission. IMPACT ASSESSMENT Accompanying the document Proposal for a DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL on the approximation of the laws, regulations and administrative provisions of the Member States concerning the manufacture, presentation and sale of tobacco and related products. Brussels, Belgium; 2012.

32. The Swedish National Board of Health and Welfare (Socialstyrelsen). Adults who use snus daily – Advisory calls 2018 [Available from: https://roi.socialstyrelsen.se/riktlinjer/nationella-riktlinjer-for-prevention-och-behandling-vid-ohalsosamma-levnadsvanor/5/vuxna-som-snusar-dagligen-radgivande-samtal/5.6.
33. Ramström 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(1):14.
34. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019 (GBD 2019) Results. Seattle, United States: Institute for Health Metrics and Evaluation (IHME); 2020.
35. European Union. Special Eurobarometer 506, Attitudes of Europeans towards tobacco and electronic cigarettes2021.
36. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019 (GBD 2019) Results Seattle, United States: Institute for Health Metrics and Evaluation (IHME); 2020 [Available from: https://vizhub.healthdata.org/gbd-results/.
37. Statistics Norway. Tobacco, alcohol and other drugs 2022 [Available from: https://www.ssb.no/en/helse/helseforhold-og-levevaner/statistikk/royk-alkohol-og-andre-rusmidler.
38. U.S. Food & Drug Administration. Scientific Review of Modified Risk Tobacco Product Application (MRTPA) Under Section 911 (d) of the FD&C Act – Technical Project Lead 2014 [cited 2021 3 June]. Available from: https://www.fda.gov/media/131923/download.
39. U.S. Food & Drug Administration. FDA grants first-ever modified risk orders to eight smokeless tobacco products 2019 [cited 2021 2 June]. Available from: https://www.fda.gov/news-events/press-announcements/fda-grants-first-ever-modified-risk-orders-eight-smokeless-tobacco-products.

ANNEX 1

Dhr. Maarten van Ooijen
Staatssecretaris voor Preventie
Ministerie van Volks-gezondheid, Welzijn en Sport

CC:
Dhr. Victor Sannes, director Voeding, Gezondheids-bescherming en Preventie

Dhr. Herman Smits, Politiek adviseur Staatssecretaris

Debat inzake de Tabaks- en rookwarenwet op 24 maart 2022

Geachte Staatssecretaris,

Ik richt mij tot u namens Swedish Match, een Zweedse onderneming die actief heeft bijgedragen aan het terugdringen van het percentage rokers in Zweden en Noorwegen. In 1999 heeft de onderneming haar sigarettendivisie verkocht en is haar bedrijfsvisie "een wereld zonder sigaretten". Wellicht vindt u het interessant om te weten dat wij op de Nederlandse markt aanwezig zijn met het welbekende lucifermerk "De Zwaluw".

We volgen de aanhoudende discussie in Nederland over nicotinezakjes met grote belangstelling, aangezien dit een product is dat Swedish Match in Zweden en Denemarken fabriceert en in een aantal EU-landen op de markt brengt. Naar we begrijpen heeft uw voorganger de voorkeur uitgesproken om nicotinezakjes onder te brengen onder de Tabaks- en rookwarenwet, maar heeft hij het besluit daaromtrent overgelaten aan de nieuwe regering. We hebben ook begrepen dat op 24 maart 2022 een debat gevoerd zal worden in het parlement waarbij het onderwerp nicotinezakjes op de agenda staat. Graag willen wij met deze brief bijdragen aan dit debat.

Aangezien Nederland deze productcategorie op dit moment als levensmiddel ziet, kan de limiet voor het toegestane nicotinegehalte van 0,035 mg nicotine per zakje verstandig lijken. Het is echter duidelijk dat regelgevende instanties en het gros van de bevolking er sterk van overtuigd zijn dat nicotinezakjes geen levensmiddel zijn. Het ontwikkelen van regelgeving die Nederlandse rokers toegang zal bieden tot aanvaardbare, minder schadelijke alternatieven waarbij jongeren, kwetsbare groepen en niet-gebruikers beschermd worden tegen het product, moet welhaast de meest gepaste manier zijn om de huidige situatie aan te pakken.

We delen veel van de zorgen die tot nu toe in de Nederlandse discussies geuit zijn. We vinden dat er degelijke regelgeving voor nicotinezakjes moet komen teneinde een hoog niveau van volksgezondheid veilig te stellen en kwetsbare consumentengroepen en jongeren te beschermen. Wij kunnen ons volledig vinden in het onderbrengen van onze producten bij de Tabaks-en rookwarenwet in plaats van de Warenwet, zoals ook door het Rijksinstituut voor Volksgezondheid en Milieu (RIVM) wordt aanbevolen.

Gebruik van nicotinezakjes

Dit is ook logisch aangezien nicotinezakjes, een nicotineproduct dat aanzienlijk minder schadelijk is dan tabaksproducten die geconsumeerd worden via een proces van verbranding, gericht zijn op en vooral geconsumeerd worden door volwassen gebruikers die nu sigaretten en shag roken. Zoals ook door het RIVM wordt aangegeven, is bijna 70% van de ooit-gebruikers van nicotinezakjes (ex-)roker!

Deze bevinding is in overeenstemming met de eigen consumentgegevens van Swedish Match uit de Verenigde Staten (VS) zoals voorgeschreven door de US Food and Drug Administration (FDA) als onderdeel van onze vergunningsaanvraag voor het in de handel brengen van ons ZYN product. De resultaten toonden aan dat slechts 2-3% van de nooit-gebruikers en voormalige tabaksgebruikers interesse hadden in het kopen van ZYN. 96% van de ZYN-gebruikers waren reguliere tabaksgebruikers voordat zij ZYN gebruikten en de resterende 4% gebruikten allemaal andere tabaksproducten naast ZYN, waarvan 25% aangaf dat zij ZYN gebruikten om het gebruik van andere tabaksproducten te staken/verminderen. 43% van de ZYN-gebruikers had eerder tabaksproducten gebruikt en waren nu volledig overgestapt op ZYN. 26% gebruikte zowel ZYN als andere rookvrije producten en slecht 8% gebruikte zowel sigaretten als ZYN. De belangrijkste reden voor het gebruik van ZYN was "Het is minder schadelijk is voor mijn gezondheid dan andere tabaksproducten". Meer dan 60% van de rokers gaf aan dat zij ZYN gebruikten om met het gebruik van sigaretten te stoppen of dit te verminderen. [1]

Leeftijdsgrenzen en verantwoorde marketinggebruiken

In het verlengde van de aloude Nederlandse traditie van goede wettelijke normen is het van belang dat de toekomstige regelgeving gebaseerd wordt op dezelfde harde wetenschappelijke kennisbasis als andere productcategorieën die door dezelfde regelgeving beheerst worden, zoals tabaksproducten die geconsumeerd worden via een proces van verbranding.

Het onderbrengen van deze categorie bij de Tabaks- en rookwarenwet heeft als duidelijk voordeel dat de leeftijdsgrens van 18 jaar direct ingevoerd wordt. Het behoeft geen betoog dat dit product niet gebruikt zou moeten worden door mensen onder de 18.

Er is een grote wetenschappelijke consensus over het verschil in schadelijkheid tussen producten die geconsumeerd worden via een proces van verbranding en producten waarbij bij consumptie geen verbranding plaatsvindt. Dankzij het feit dat bij consumptie van nicotinezakjes geen

[1] (Plurphanswat, N. Hughes, J.R., Fagerström, K. and Rodu, B. 2020: Initial Information on a Novel Nicotine Product.

verbranding plaatsvindt, is het risicoprofiel van dit product aanzienlijk lager dan dat van klassieke sigaretten, hetgeen ondersteund wordt door wetenschappelijke studies.[2][3][4] De schatting is dat het relatieve risico met tenminste enkele orden van grootte afneemt bij het gebruik van nicotinezakjes in plaats van sigaretten.

Een belangrijke factor in dit verband is dat ervoor gezorgd moet worden dat marketinggebruiken verantwoord zijn en dat alle tekst of illustraties op deze producten of hun verpakkingen geen elementen of kenmerken dienen te bevatten die:

- bedrieglijk of misleidend zijn,
- suggereren dat nicotinezakjes stimulerende, energetische, helende, verfrissende, natuurlijke, organische eigenschappen of gezondheidsvoordelen hebben,
- op een levensmiddel of cosmetisch product lijken,
- geassocieerd kunnen worden met jongerencultuur of situaties, omgevingen of voorwerpen die typisch zijn voor de leefwereld van kinderen en jongeren (zoals stripfiguren, speelgoed of snoep) of
- suggereren dat nicotinezakjes voordelen hebben voor het milieu.

Alternatieven bieden aan rokers

Jammer genoeg blijkt uit zeer recente gegevens van het CBS dat het aantal rokers sinds 2018 maar mondjesmaat is afgenomen[5]. Reden te meer om serieus te kijken naar alternatieven voor roken, zoals in Zweden, het Verenigd Koninkrijk en Nieuw-Zeeland is gebeurd.

In deze context wil Swedish Match graag het belang benadrukken van twee factoren die belangrijk zijn als een product erin moet slagen om rokers die niet geheel met nicotine kunnen of willen stoppen over te laten stappen:

- Besluiten om **smaakjes** te verbieden moeten op zorgvuldige overwegingen gebaseerd worden. Het spreekt voor zich dat alle smaakjes toxicologisch gezien veilig moeten zijn. Smaakjes spelen echter voor rokers een belangrijke rol bij de overstap van sigaretten op minder schadelijke alternatieven. Het is daarom raadzaam om eventueel beperkingen in te voeren m.b.t hoe smaakjes aan de consument aangeprezen mogen worden.

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2 McEwan, M., Azzopardi, D., Gale, N., Camacho, O. M., Hardie, G., Fearon, I. M., & Murphy, J. (2021). A Randomised Study to Investigate the Nicotine Pharmacokinetics of Oral Nicotine Pouches and a Combustible Cigarette. Eur J Drug Metab Pharmacokinet. doi:10.1007/s13318-021-00742-9

[3] Azzopardi, D., Liu, C., & Murphy, J. (2021). Chemical characterization of tobacco-free "modern" oral nicotine pouches and their position on the toxicant and risk continuums. Drug Chem Toxicol, 1-9. doi:10.1080/01480545.2021.1925691

[4] Yu, F., Rudd, K., Pour, S. J., Trelles Sticken, E., Dethloff, O., Wieczorek, R., . . . O'Connell, G. (2022). Preclinical Assessment of Tobacco-Free Nicotine Pouches Demonstrates Reduced In Vitro Toxicity Compared with Tobacco Snus and Combustible Cigarette Smoke. Applied In Vitro Toxicology. doi:10.1089/aivt.2021.0020

[5] Leefstijl en (preventief) gezondheidsonderzoek; persoonskenmerken (cbs.nl).

- Het **nicotinegehalte** moet hoog genoeg zijn om rokers een bevredigende nicotine-ervaring te geven. Als het nicotinegehalte te laag is, is de kans klein dat ze overstappen op dit alternatief met gering risico. Aan de andere kant zijn er tegenwoordig in sommige landen producten met extreem hoge nicotinegehaltes op de markt, wat schadelijk is voor de volksgezondheid. De serieuzere ondernemingen hebben – in afwachting van regelgeving – het gehalte vrijwillig gemaximeerd op 20 mg per zakje op basis van beschikbaar wetenschappelijk bewijs dat een dergelijke maximale hoeveelheid niet schadelijk is voor de volksgezondheid of individuele gezondheid van de doelgroep van dit product. Het Duitse Federale Instituut voor Risicobeoordeling (BfR) stelt een limiet van 16,7 mg per zakje voor[6]. De grondslag voor deze beoordeling wordt hieronder nader beschreven.

Bepaling van een realistisch maximum nicotinegehalte

Swedish Match begrijpt het voornemen van het RIVM om een geschikt maximum nicotinegehalte voor nicotinezakjes vast te stellen. Graag maken we van deze gelegenheid gebruik om op een aantal wetenschappelijke overwegingen te wijzen die hopelijk als richtsnoer kunnen dienen bij de beoordeling van het juiste nicotinegehalte. Het RIVM lijkt zwaar te leunen op een EFSA rapport uit 2009 dat betrekking heeft op nicotine in wilde paddenstoelen dat gebaseerd is op een onderzoek uit 1999 waarin een verhoogde hartslag na nicotine-infusie werd gevonden, die echter van voorbijgaande aard was. Opgemerkt dient te worden dat EFSA zelf terughoudend is in het afleiden van richtwaarden voor de gezondheid op basis van de niet volledige toxicologische gegevens die zijn gebruikt.

De beoordeling van het RIVM dat een nicotinezakje slechts 0,035 mg nicotine per zakje mag bevatten komt in feite neer op een verbod van het product, waardoor Nederlandse rokers toegang wordt ontzegd tot een nicotine-houdend product dat veel veiliger is dan sigaretten.

In 2016 is de Europese Commissie tot een maximum gekomen van 5 mg nicotine per kg lichaamsgewicht (5 mg x 60 kg = 300 mg), dat veel hoger is dan het maximum van EFSA van 0,0035 mg/kg lichaamsgewicht (0,0035 mg x 60 kg = 0,21 mg).[7] De Commissie baseerde zich op de algemeen aanvaarde Risicobeoordelingsmethode van het Europees Agentschap voor chemische stoffen (ECHA).[8]

In een recent onderzoek naar het risicoprofiel van nicotinezakjes (2021), heeft het BfR het maximum nicotinegehalte per zakje vastgesteld op 16,7 mg. Het is zelfs zo dat het Duitse instituut de door EFSA vastgestelde referentiewaarden niet geschikt acht voor gebruik als referentiewaarden in risicobeoordelingen van nicotinezakjes. Het BfR baseert haar aanbeveling net als de Europese Commissie op de acute toxiciteitsschatting (ATE, 5 mg / kg lichaamsgewicht) voor orale inname van nicotine uit de eerder genoemde ECHA Risicobeoordelingsmethode.

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[6] Gesundheitlichen Bewertung des BFR 20-0203-03/002-11497361 Vorläufige gesundheitliche bewertung von nikotinbeutelchen Marz 2021.
[7] Verslag van de Commissie aan het Europees Parlement en de Raad over de potentiële risico's voor de volksgezondheid in samenhang met het gebruik van navulbare elektronische sigaretten, Brussel, 20.5.2016, COM (2016) 269.

[8] https://echa.europa.eu/documents/10162/23665416/clh_opinion_nicotine_5579_en.pdf/0103fadb-e945-4839-c4f4-17d20854adf0

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Opgemerkt dient te worden dat een hartslag in rust niet hetzelfde is als een tijdelijk verhoogde hartslag. Dit feit wordt benadrukt door het BfR in haar oordeel uit maart 2021 inzake nicotinezakjes.[9] In haar beoordeling concludeert het BfR dat het effect van nicotine op de hartslag van voorbijgaande aard is en afneemt ongeacht de aanhoudende hoge concentraties nicotine in het bloedplasma. Deze conclusie duidt erop dat tolerantie van het menselijk lichaam voor de cardiovasculaire effecten van nicotine snel optreedt, net zoals een aanzienlijke tolerantie voor de effecten van nicotine op de hartslag. Daarnaast valt de plasmablootstelling die voortvloeit uit het gebruik van nicotinezakjes binnen het "therapeutisch" bereik en heeft het product geen ernstige bijwerkingen of stopzettingen wegens bijwerkingen gekend in de onderzoeken van *Lunell et al. (2020)* [10] en *Rensch (2021)*[11].

Roken verhoogt het risico op het ontwikkelen van cardiovasculaire aandoeningen. Er zijn echter verschillende wetenschappelijke publicaties die poneren dat de inname van nicotine op zichzelf niet dezelfde nadelige invloed zou hebben op het ontwikkelen van cardiovasculaire aandoeningen. Het onderzoek van *Clark et al. (2019*) [12], bijvoorbeeld, stelt dat verschillende epidemiologische onderzoeken gemeld hebben dat er geen verband is tussen het gebruik van Zweedse "snus" en een verhoogd risico op een hartinfarct of ischemische hartziekte. Een onderzoek dat gegevens heeft gebruikt van het cohort van Zweedse bouwvakkers en dat zich richtte op onderzoek naar de incidentie van boezemfibrilleren constateerde dat het onwaarschijnlijk is dat het gebruik van snus leidt tot verhoging van enig risico.

Gezien het vorenstaande verzoeken wij u niet te snel definitieve conclusies te trekken en om rekening te houden met wetenschappelijk bewijs en praktische ervaringen uit andere EU-lidstaten en daarbuiten, in het bijzonder de definitieve risicobeoordeling van het BfR. We willen ook graag de aandacht vestigen op hoe deze categorie gereguleerd is in landen zoals Denemarken, Hongarije, de Tsjechische Republiek, alsmede de ontwerpregelgeving in Zweden.

Mocht u vragen hebben over de inhoud van deze brief of verdere vragen hebben inzake de relatieve veiligheid van nicotinezakjes verzoeken we u vriendelijk contact met ons op te nemen.Hoogachtend,

Cecilia Kindstrand Isaksson
Director
Public Affairs
cecilia.kindstrand-isaksson@swedishmatch.com

[9] Gesundheitlichen Bewertung des BFR 20-0203-03/002-11497361 Vorläufige gesundheitliche bewertung von nikotinbeutelchen Marz 2021.

[10] Lunell E et. al. Pharmacokinetic Comparison of a Novel Non-tobacco-Based Nicotine Pouch (ZYN) With Conventional, Tobacco-Based Swedish Snus and American Moist Snuff, Nicotine & Tobacco Research, 2020, 1–7.

[11] Nicotine pharmacokinetics and subjective response among adult smokers using different flavors of on!® nicotine pouches compared to combustible cigarettes | SpringerLink