

Response to the Netherlands' Tobacco and Smoking Products Act Proposal

Broughton Life Sciences Ltd. (herein referred to as Broughton) would like to submit the following in response to the Dutch Government's proposal to ban oral nicotine pouches in the Netherlands. Broughton is a contract research organisation that provides scientific and regulatory consulting services, and our company vision is to accelerate life-enhancing products to market. Our core services include the analytical, toxicological, clinical, and behavioural assessment of next-generation nicotine-based products. We do not engage in the evaluation of combustible tobacco products nor facilitate new combustible products to market. Given our experience of risk-assessing a vast number of multi-category, less-risky alternatives to combustible cigarettes, Broughton felt it necessary to respond to this consultation as an independent body with no financial or other interests in combustible cigarettes.

Nicotine pouches offer the opportunity to deliver nicotine without inhalation and without the use of tobacco. We acknowledge that youth use of these pouches may be implicit in driving this proposal. However, the overall health benefits these products could offer current adult smokers would be expected to heavily outweigh the potential uptake and associated risk to naïve nicotine users. This risk could be mitigated by exploring options to limit sales to smokers only.

Based on the current scientific literature and client data that we have reviewed, we believe this proposal, if carried forward, may *delay* the achievement of the Government's "Smoke-Free Generation" goal by 2040, and remove the significant harm-reduction opportunity presented by smokeless products for current smokers in the Netherlands.

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Aiming to cut smoking while banning safer, alternative nicotine products is counter-intuitive

We categorically support and are culturally aligned with the Dutch Government's "Smoke-Free Generation" initiative and believe that all nicotine-and tobacco-based products should be regulated to ensure only high-quality, compliant products are permitted to market. However, we are concerned by the proposal to ban non-tobacco nicotine pouches, as these products have been established as a safer alternative to combustible tobacco¹. Many Public Health bodies state smokers' best choice is to quit nicotine and smoking. However, for those struggling to quit, we believe that a wide range of reduced-risk alternatives should be available.

A recent review by Public Health England² (PHE) found that in 2020, 27.2% of smokers in the United Kingdom (UK) used a vaping product in a quit attempt in the previous 12 months, compared with 15.5% who used nicotine replacement therapy (NRT) over the counter, or on prescription (2.7%), and 4.4% who used varenicline. All methods were positively associated with smoking cessation, and the authors concluded, "***this shows how important it is for people who smoke to have access to a wide choice of cessation aids.***" Although this research did not include oral nicotine pouches, presumably because they only became available in the United Kingdom (UK) in 2019, the conclusion is still applicable since oral nicotine pouches represent an additional choice for current smokers.

Broughton believes it is counterintuitive to ban oral nicotine pouches while allowing the riskiest nicotine products to remain on the market, especially as a range of safer alternatives have all been positively associated with facilitating smoking cessation.

¹ Committee on Toxicity. First draft statement on the bioavailability of nicotine from the use of oral nicotine pouches and assessment of the potential toxicological risk to users. 2022. [First draft statement on the bioavailability of nicotine from the use of oral nicotine pouches and assessment of the potential toxicological risk to users | Committee on Toxicity \(food.gov.uk\)](#) Accessed 13 Jan 2023.

² McNeill, A., Brose, L.S., Calder, R., Simonavicius, E. and Robson, D. (2021). Vaping in England: An evidence update including vaping for smoking cessation, February 2021: a report commissioned by PHE. London: PHE.

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Swedish snus has helped cut smoking and improve public health in Sweden

It is widely recognised that most of the harm from combustible tobacco is caused by the toxicants in smoke, inhaled into the lungs, rather than nicotine³. “Smokeless” products, which generally refer to oral pouched tobacco products and the relatively new oral nicotine pouches, are not combusted and present no harmful exposure to chemicals via the lungs, as is the case for some NRTs which include gums, lozenges, and tablets. **The data presented below relate to pouched tobacco products, but Broughton believes the findings are likely to apply to oral nicotine pouches since both are smokeless.**

The composition of oral tobacco pouches is distinct for different geographical regions and defined as either European (Swedish) snus; American; or Asia, Middle East, and Africa (AMEA). A recent systematic review⁴ of smokeless tobacco products found no excess mortality (overall, cardiovascular disease, or from cancers) or morbidity (ischemic heart disease, stroke, oral, head and neck, pancreatic, or colon cancers) associated with the use of European (Swedish) snus. However, elevated risk profiles were reported for American smokeless tobacco with significantly worse outcomes associated with using AMEA tobacco products (with odds ratios up to 38.7). **If studies on smokeless tobacco products are reviewed without considering the country of origin, risk profiles may be over or under-estimated, with the potential for such profiles to misinform policy and regulation.** The data presented below refer specifically to Swedish snus.

The Swedish snus risk profile is substantiated by long-term epidemiological evidence. During the 1970s and 1980s, there was a substantial shift from cigarette smoking to snus use, particularly among Swedish males. **The epidemiological data indicate that the use of snus has contributed to a faster decline in smoking, and a corresponding reduction in the incidence of smoking-related disease and death in Sweden, compared to other countries in the European Union (EU), where snus is banned.** The lower prevalence of smoking-related diseases in Swedish men reportedly correlates with the switch from smoking to snus, considering disease pathogenesis⁵. Studies indicate that Swedish males have the lowest rate of lung cancer and the lowest rate of tobacco-related mortality in Europe⁶. **These findings are especially compelling since total tobacco use in Sweden is higher than in most other European countries, see Figure 1.**

³ Royal College of Physicians (2016) Nicotine without smoke: Tobacco harm reduction. [Nicotine without smoke_0.pdf](#) Accessed 14 Jan 2023.

⁴ Hajat, C., Stein, E., Ramstrom, L., Shantikumar, S., & Polosa, R. (2021). The health impact of smokeless tobacco products: a systematic review. *Harm reduction journal*, 18(1), 123. <https://doi.org/10.1186/s12954-021-00557-6>

⁵ Foulds, Jonathan, et al. “Effect of smokeless tobacco (snus) on smoking and public health in Sweden.” *Tobacco control* 12.4 (2003): 349-359.

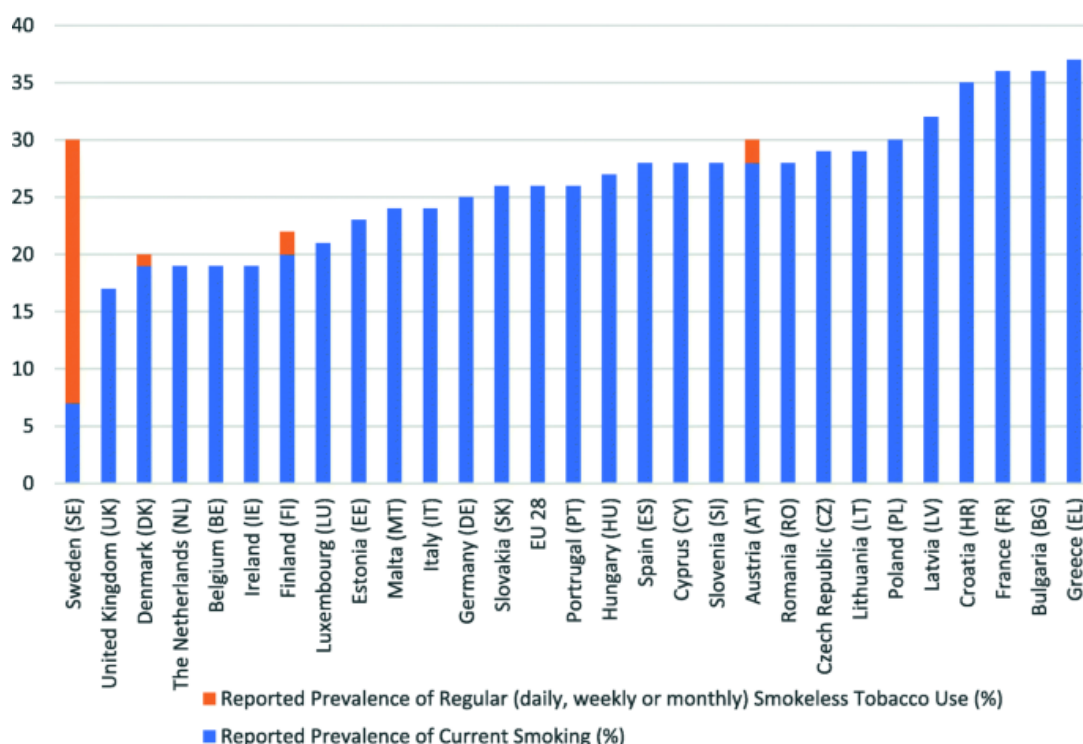
⁶ Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2018). Global Cancer Observatory: cancer today. Lyon, France: International Agency for Research on Cancer. <http://gco.iarc.fr/today/home>. Accessed 11 Jan 2023.

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Figure 1: Reported Prevalence of Total Tobacco Use in the EU (%)⁷



The prevalence findings reported in the Special Eurobarometer 458⁷ broadly correlate with those from the most recent Special Eurobarometer 506 report⁸, which found that Sweden had the lowest prevalence of daily cigarette use at 7%, followed by 12% in the UK and the Netherlands, and 15% in Finland. As per previous reports, the most recent EU data indicated that smokeless tobacco products were used predominantly in Sweden, with minimal regular use reported in a few other EU member states. This is expected given that oral tobacco is illegal in the EU, except in Sweden. Data from Swedish respondents found that 18% reported using oral tobacco at least monthly, with 16% reporting daily use (compared to 20% in 2017). **This is significant as the data show continued low levels of smoking in Sweden and a reduction in the use of Swedish snus, indicating its availability is not associated with an upward trend of smokeless tobacco use.** Neither Eurobarometer study specifically investigated the prevalence of oral nicotine pouch use.

⁷ The European Commission. Special Eurobarometer 458. Attitudes of Europeans towards tobacco and electronic cigarettes. 2017. <http://ec.europa.eu/commfrontoffice/publicopinion/index.cfm/Survey/getSurveyDetail/instruments/SPECIAL/surveyKy/2146>

⁸ The European Commission. Special Eurobarometer 506. Attitudes of Europeans towards tobacco and electronic cigarettes. 2021. https://gecp.pt/wp-content/uploads/2021/02/ebs_506_en.pdf. Accessed 10 Jan 2023.

A literature review⁹ investigating the harm reduction potential of Swedish snus reported the following conclusions from public health bodies and other investigators:

- The use of snus indicates it is substantially less harmful to health than smoking (based on epidemiology)^{10,11} and it is estimated that snus confers only 5% of the harm of cigarettes¹².
- In 2007, the Royal College of Physicians (RCP) stated there are no clearly established causes of premature death associated with snus use¹³.
- Literature reviews have estimated that users of snus have at least 90–95% less smoking-related mortality, with minimal reduction in life expectancy, if any at all^{14,15}.
- The health benefits for smokers who completely transition to snus use are similar to those reported for smoking cessation¹⁶.
- The Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)¹⁷ concluded that snus use carried an overall risk reduction close to 100% for respiratory disease (lung cancer, chronic obstructive pulmonary disease, and pneumonia), at least 50% for cardiovascular disease and at least 50% for oral and pharyngeal, oesophageal, and pancreatic cancers compared to cigarette smoking.

We want to highlight that the referenced studies relate to Swedish snus, which contains tobacco. It should be emphasised that since snus contains tobacco, it may also contain harmful tobacco-related compounds (such as tobacco-specific nitrosamines, lead, and aflatoxins). However, these have been substantially reduced over the past two decades due to advances in production and processing techniques¹⁰. **Consequently, as tobacco-free nicotine pouches do not contain tobacco and harmful tobacco-related constituents, this category is likely to offer an even greater harm reduction opportunity for smokers who switch compared to snus.**

⁹ Clarke, E., Thompson, K., Weaver, S. et al. Snus: a compelling harm reduction alternative to cigarettes. *Harm Reduct J* 16, 62 (2019). <https://doi.org/10.1186/s12954-019-0335-1>

¹⁰ Scientific Committee on Emerging and Newly Identified Health Risks. Health effects of smokeless tobacco products. 2008. http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_013.pdf. Accessed 11 Jan 2023.

¹¹ Lee PN. Epidemiological evidence relating snus to health - an updated review based on recent publications. *Harm Reduct J*. 2013;10:36.

¹² Nutt DJ, Philips LD, Balfour D, Curran HV, Dockrell M, Foulds J, Fagerstöm K, Letlape K, Milton A, Polosa R, Ramsey J, Sweanor D. Estimating the harms of nicotine-containing products using the MDCA approach. *Eur Addict Res*. 2014;20:218–25.

¹³ Royal College of Physicians. Harm reduction in nicotine addiction: helping people who can't quit. 2007. <https://cdn.shopify.com/s/files/1/0924/4392/files/harm-reduction-nicotine-addiction.pdf?15599436013786148553>. Accessed 11 Jan 2023.

¹⁴ Levy DT, Mumford EA, Cummins KM, Gilpin EA, Giovino EA, Hyland A, Sweanor D, Warner KE. The relative risks of a low-nitrosamine smokeless tobacco product compared with smoking cigarettes: Estimates of a panel of experts. *Cancer Epidemiol Biomarkers Prev*. 2004;13:2035–42.

¹⁵ Gartner CE, Hall WD, Vos T, Bertram MY, Wallace AL, Lim SS. Assessment of Swedish snus for tobacco harm reduction: an epidemiological modelling study. *Lancet*. 2007;369:2010–4.

¹⁶ Ramström L, Borland R, Wikmans T. Patterns of smoking and snus use in Sweden: implications for public health. *Int J Environ Res Public Health*. 2016;13:E1110.

¹⁷ Scientific Committee on Emerging and Newly Identified Health Risks. Health effects of smokeless tobacco products. 2008. http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_013.pdf. Accessed 11 Jan 2023.

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Snus and oral nicotine pouches are not risk-free but offer enormous harm reduction potential for current smokers

The previously cited literature review⁹, which investigated the harm reduction potential of snus, reported no correlation between snus use and increased risk of cancer (lung, pancreatic and oral), cardiovascular disease, and diabetes. Non-neoplastic oral disease endpoints were also reviewed, and the key findings have been included for consideration.

- Oral mucosal lesions are associated with the use of snus but are generally reported as reversible upon cessation^{18, 19}.
- The data regarding snus use and gingival diseases are contradictory. However, the majority of studies have shown no correlation between snus use and gum infection, inflammation, bleeding^{20,21,22,23} and receding gums^{21,22,24,25}. In addition, the most extensive publication that encompassed three epidemiological, cross-sectional studies²⁶ reported that using snus did not seem to be a risk factor for periodontitis. None of the referenced studies showed a link between snus use and periodontal disease.

The association of snus use with oral mucosal lesions could be due to the skin irritant effects of nicotine, other tobacco-related constituents, or a combination of both. It is likely that heavy snus use or consistent buccal positioning of the pouch would carry a greater risk of developing oral mucosal lesions. **If oral mucosal lesions are due to the presence of nicotine, this will also be a risk for oral nicotine pouches. However, recent research has indicated improved oral mucosal lesions in snus users who switched to oral nicotine pouches²⁷.**

¹⁸ Kallischnigg G, Weitkunat R, Lee PN. Systematic review of the relation between smokeless tobacco and non-neoplastic oral diseases in Europe and the United States. *BMC Oral Health*. 2008;8:13.

¹⁹ Neville BW, Day TA. Oral cancer and precancerous lesions. *CA Cancer J Clin*. 2002;52(4):195–215.

²⁰ Wickholm S, Söder PO, Galanti MR, Söder B, Klinge B. Periodontal disease in a group of Swedish adult snuff and cigarette users. *Acta Odontol Scand*. 2004;62:333–8.

²¹ Rolandsson M, Hellqvist L, Lindqvist L, Hugoson A. Effects of snuff on the oral health status of adolescent males: a comparative study. *Oral Health Prev Dent*. 2005;3:77–85.

²² Bergström J, Keilani H, Lundholm C, Rådestad U. Smokeless tobacco (snuff) use and periodontal bone loss. *J Clin Periodontol*. 2006;33:549–54.

²³ Montén U, Wennström JL, Ramberg P. Periodontal conditions in male adolescents using smokeless tobacco (moist snuff). *J Clin Periodontol*. 2006;33:863–8.

²⁴ Andersson G, Axéll T. Clinical appearance of lesions associated with the use of loose and portion-bag packed Swedish moist snuff: a comparative study. *J Oral Pathol Med*. 1989;18:2–7.

²⁵ Frithiof L, Anneroth G, Lasson U, Sederholm C. The snuff-induced lesion. A clinical and morphological study of a Swedish material. *Acta Odontol Scand*. 1983;41:53–64.

²⁶ Hugoson A, Rolandsson M. Periodontal disease in relation to smoking and the use of Swedish snus: epidemiological studies covering 20 years (1983-2003). *J Clin Periodontol*. 2011;38:809–16.

²⁷ Alizadehgharib, S., Lehrkinder, A., Alshabeeb, A., Östberg, A. K., & Lingström, P. (2022). The effect of a non-tobacco-based nicotine pouch on mucosal lesions caused by Swedish smokeless tobacco (snus). *European journal of oral sciences*, 130(4), e12885. <https://doi.org/10.1111/eos.12885>



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In addition, since oral nicotine pouches contain nicotine, which is addictive and a reproductive and developmental toxicant, this will also contribute to the risk profile of this product type. However, the overall risk should be contextualised against cigarettes and other combustibles. **Oral nicotine pouches contain only nicotine and none of the other harmful constituents of tobacco or tobacco smoke.**

A recent review by the Committee on Toxicity (COT)¹ on the use of oral nicotine pouches and assessment of the potential toxicological risk to users concluded that *“the use of oral nicotine pouches, as recommended by the manufacturer, as a replacement for combustible cigarette smoking is likely to be associated with a reduction in overall risk of adverse health effects, although the magnitude of the decrease will depend on the effect in question.”* **The COT further stated that nicotine pouches could be considered part of a harm-reduction strategy.**

Broughton’s position is that the considerable reduction in tobacco-related disease risk shown for snus is very likely to apply to oral nicotine pouches. We agree with the COT conclusions and believe that although oral nicotine pouches are not risk-free, they offer enormous harm reduction potential for current smokers, and should be included as part of a tobacco harm-reduction strategy.

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The U.S. FDA has recognised Swedish snus as a modified-risk tobacco product

A framework for a risk continuum of tobacco products has been acknowledged by various Public Health and Policy Organisations²⁸ based on epidemiological, clinical, and other scientific data generated using a range of nicotine-containing products. Although several iterations have been produced, Figure 2 shows the position of smokeless tobacco and nicotine products in relation to cigarettes.

Figure 2: The Continuum of Risk²⁹



The risk continuum is intended to show the comparative harm of alternative nicotine and tobacco products compared with cigarettes and other combustibles. Combustible tobacco products carry the highest risk of harm, while NRTs carry the lowest risk. Based on the weight of evidence from the scientific literature, and that smokeless tobacco avoids the inhalation of harmful constituents from tobacco smoke, smokeless tobacco has been positioned near NRTs, at the lower end of the risk spectrum²⁹. **The data for tobacco-free nicotine pouches indicate that this category should be placed even closer to NRTs than smokeless tobacco due to the absence of harmful tobacco-related constituents.**

In October 2019, Swedish Match was the first company to be issued a modified risk tobacco product (MRTP) marketing order granted by the United States (U.S.) Food and Drug Administration (FDA)³⁰. The FDA stated that the eight products named in the application “*will significantly reduce harm and the risk of tobacco-related disease to individual tobacco users and benefit the health of the population as a whole taking into account both users of tobacco products and persons who do not currently use tobacco products.*”

The eight named products are permitted to use the following modified risk information: “*Using General Snus instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.*” **Since tobacco-free nicotine pouches do not contain tobacco and harmful tobacco-**

²⁸ Speech by Scott Gottlieb M.D. (FDA Commissioner), Protecting American Families: Comprehensive Approach to Nicotine and Tobacco, 2017. [Protecting American Families: Comprehensive Approach to Nicotine and Tobacco - 06/28/2017 | FDA](#) Accessed 12 January 2023

²⁹ NATO comments on Copenhagen Snuff MRTP Application, 2019. <https://www.fda.gov/media/122016/download> Accessed 11 Jan 2023

³⁰ U.S. Food and Drug Administration, FDA grants first-ever modified risk orders to eight smokeless tobacco products, News Release, 22 October 2019, accessed November 2019

related constituents, this category is likely to offer an even greater harm reduction opportunity for smokers who switch compared to snus.

There is no evidence that smokeless products are a gateway to smoking

According to SCENIHR³¹, “the Swedish data do not support the hypothesis that smokeless tobacco (i.e., Swedish snus) is a gateway to future smoking.” The UK RCP³² has stated that there is data to support that Swedish snus appears to be an effective replacement for smoking, especially among men. Two other reviews also concluded that snus seemed to lead users away from smoking rather than towards it^{33,34}, and Swedish data generally show a low smokeless-to-cigarette transition^{35,36}. **By extension, it is not unreasonable to assume that tobacco-free oral nicotine pouches would not act as a gateway to smoking.**

The previously referencing Eurobarometer data has shown continued low levels of smoking in Sweden and a reduction in the use of Swedish snus (from 2017 to 2021), indicating its availability is not associated with either an increase in smoking or an upward trend of smokeless tobacco use. In addition, **oral nicotine pouches are widely available in several European countries where smoking rates are declining⁸.**

The availability of oral nicotine pouches must be tightly controlled to minimise uptake by youth

Broughton firmly believes that underage use of any nicotine product should be actively discouraged. Oral nicotine pouches are not for naïve nicotine users, and while the availability of this product type offers an additional opportunity for current adult smokers wanting to quit, **it is essential that sufficient safeguards are built to ensure youth access prevention.** This goes beyond marketing and sales practices and should be akin to the controls on alcohol and combustible cigarettes, where proof of age should be necessary to purchase. This could be further reinforced by potentially limiting the sale to specialist shops.

An alternative approach could be to restrict oral nicotine pouches as a prescribed medicinal product or over-the-counter via pharmacies for more effective enforcement of age verification.

³¹ European Commission’s Scientific Committee on Emerging and Newly-Identified Health Risks. Health Effects of Smokeless Tobacco Products (2008)

³² Royal College of Physicians. Nicotine without smoke: tobacco harm reduction. 2016.

<https://www.rcplondon.ac.uk/projects/outputs/nicotine-without-smoke-tobacco-harm-reduction-0>. Accessed 11 Jan 2023.

³³ Bates C, Fagerström K, Jarvis MJ, Kunze M, McNeill A, Ramström L. European Union policy on smokeless tobacco: a statement in favour of evidence based regulation for public health. Tob Control. 2003;12:360–7.

³⁴ Ramström L, Borland R, Wikmans T. Patterns of smoking and snus use in Sweden: implications for public health. Int J Environ Res Public Health. 2016;13:E1110.

³⁵ Ramström LM, Foulds J. Role of snus in initiation and cessation of tobacco smoking in Sweden. Tob Control 2006;15:210–14.

³⁶ Stenbeck M, Hagquist C, Rosén M. The association of snus and smoking behaviour: a cohort analysis of Swedish males in the 1990s. Addiction 2009;104:1579–85.

Key conclusions

1. Based on the epidemiological data, smokeless products as an alternative to cigarettes have the potential to deliver significant harm reduction benefits, as shown in Sweden. Smokeless tobacco products avoid the inhalation of harmful constituents from tobacco smoke, conferring a significant risk reduction compared to combustibles. Since tobacco-free nicotine pouches do not contain tobacco and harmful tobacco-related constituents, this category is likely to offer an even greater harm reduction opportunity for smokers who switch compared to snus.
2. Independent regulators and public health bodies recognise smokeless products as less harmful than combustible tobacco.
3. There is no evidence that the availability of smokeless products is a gateway to smoking.
4. Oral nicotine pouches should be available only to adult smokers, with strict safeguards to prevent youth access.
5. Broughton believes that the availability of oral nicotine pouches as an additional choice for current smokers who want to quit could deliver significant public health benefits, by reducing the incidence of tobacco-related diseases caused by the inhalation of tobacco smoke. A range of safer alternatives have all been positively associated with facilitating smoking cessation; therefore, banning tobacco-free nicotine pouches and removing this reduced-harm alternative from the market may delay the achievement of the Government's "Smoke-Free Generation" goal by 2040, and remove the significant harm-reduction opportunity presented by smokeless products for current smokers in the Netherlands.

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