

## SCENIHR Opinion on the Health Effects of Smokeless Tobacco Products

### Results from the public consultation

#### **QUESTION 1**

##### **What are the adverse health effects of smokeless tobacco products?**

In answering this question, it must be recognised that marketed smokeless tobacco products (STP) vary considerably in form and content of toxicants, including nicotine, and thereby in associated health effects, which have been documented across countries.

All STP contain nicotine, a potent addictive substance. The major group of carcinogens in STP includes non-volatile tobacco-specific nitrosamines (TSNA) and N-nitroamino acids. During the last two decades the levels of TSNA in snus have been considerably lowered. One recent study documented total TSNA levels in one brand of Swedish snus to be 2.0 microgram/gram product wet weight, whereas total TSNA levels in 6 American brands varied from 1.3 to 9.2 microgram/gram. Levels of TSNA in STP from other regions such as India and Africa are higher. Nevertheless, STP including moist snuff have higher levels of carcinogenic nitrosamines than any consumer product used orally. Some forms of STP contain polycyclic aromatic hydrocarbons depending on curing.

Aqueous and organic extracts of American and Swedish moist snuff and Indian chewing tobacco cause mutations and chromosomal damage in bacterial and mammalian cell cultures. Increased micronuclei formation in oral epithelial cells as evidence of chromosomal damage, has been associated with moist snuff use.

Use of American and Swedish moist snuff results in localised lesions in the oral epithelium, where the snuff is placed. These changes are reversible, whereas gingival retractions caused by moist snuff are not reversible. Moist snuff in portion-bag sachets gives less severe epithelial changes than snuff in loose form.

There is sufficient evidence that the use of a wide variety of STP causes cancer in humans. The pancreas has been identified as a main target organ in two Scandinavian cohort studies. Furthermore, several studies from the USA have provided additional support for a causal association between the use of smokeless tobacco and pancreatic cancer. There is no evidence that STP cause lung cancer.

Risks of oral cancer were strongly associated with the use of American snuff in one large case-control study; however, a detailed characterisation of the product was not given. Four studies in India and Pakistan and one study from Sudan have reported large increases in the risk for oral cancers related to the use of various STP. In Swedish studies, an increased risk of oral cancer has not been proven in snus users. In one study from Sweden among users of moist snuff, an increased

overall risk of head and neck cancer was not detected. However, an increased risk of head and neck cancer has been found among the subgroup of never-smokers.

There are suggestions that nasal use of STP increases the risk for certain cancers, e.g. oral cancers.

Three large cohort studies show a statistically significant but weak effect on fatal myocardial infarction. In addition, animal experiments and human studies indicate that oral tobacco use has short-term effects resulting in an increase of blood pressure and heart rate. Whether long-term use increases the risk of hypertension is uncertain. These data indicate a potential effect on the risk of cardiovascular disease.

The data on reproductive effects in relation to oral tobacco use during pregnancy are too sparse to allow conclusions. Nonetheless, studies of reproductive effects in female Swedish users of moist snuff indicated an increased risk for prematurity and pre-eclampsia. Other studies indicate that the use of STP during pregnancy is associated with reduced birth weight and reduction in gestational age.

Various studies suggest that diabetes and other components of the metabolic syndrome might be associated with the use of moist snuff, but these findings must be interpreted with caution, in particular because of study design limitations.

Based on the available evidence it is difficult to identify overall relative risk estimates for the various adverse health effects from oral tobacco products as a whole because the products and conditions of use (e.g. frequency, duration, mode of use, other lifestyle factors) vary widely.

In conclusion, all STP contain nicotine, a potent addictive substance. They also contain carcinogenic tobacco-specific nitrosamines, albeit at differing levels. STP are carcinogenic to humans and the pancreas has been identified as a main target organ in American and Scandinavian studies. All STP cause localised oral lesions and a high risk for development of oral cancer has been shown for various STP but has not been proven for Swedish moist snuff (snus). There is some evidence for an increased risk of fatal myocardial infarction among STP users. Some data indicate reproductive effects of smokeless tobacco use during pregnancy but firm conclusions cannot be drawn.

## **QUESTION 2**

### **What is the addiction potential of smokeless tobacco products?**

It is widely accepted that nicotine is the primary addictive constituent of tobacco, and there is a growing body of evidence that nicotine demonstrates the properties of a drug of abuse. All commercially successful tobacco products, regardless of delivery mechanism, deliver psychoactive levels of nicotine to users. Denicotinised tobacco products are typically not widely accepted by or palatable to chronic

tobacco users and are of marginal commercial importance.

Smokeless tobacco contains and delivers quantities of nicotine comparable to those typically absorbed from cigarette smoking, although delivery of nicotine from STP lacks the high initial concentration that results from inhalation of tobacco smoke. Nicotine levels obtained from STP are generally higher than those typically obtained from nicotine replacement therapy.

The time course and symptoms of withdrawal from smokeless tobacco are generally similar to those of cigarette smokers. It seems also that symptoms of withdrawal are stronger with some brands of smokeless tobacco delivering higher levels of nicotine compared to other brands with lower levels.

There is a lack of evidence from animal models for the addictive potential of STP, given the conceptual difficulty in developing an animal self-administration model of smokeless tobacco. There is also a lack of evidence relating to the effects of additives introduced to tobacco in the manufacturing process on the initiation of use of STP and subsequent dependence.

In conclusion, smokeless tobacco is addictive and withdrawal symptoms are similar to those seen in smokers.

### **QUESTION 3**

**Does the available data support the claim that smokeless tobacco may constitute a smoking cessation aid comparable to pharmaceutical nicotine replacement products?**

No randomized trial has been conducted on smokeless tobacco as an aid to smoking cessation and no randomized trial has compared smokeless tobacco to pharmaceutical nicotine replacement products in this respect.

A small number of studies have looked at the use of smokeless tobacco in relation to smoking habits and one of those also includes nicotine replacement products. The results of these studies are inconsistent. Due to this and methodological limitations no conclusions can be drawn.

Aggregate data on smokeless tobacco product use and cigarette smoking show that particularly in Swedish men, there is a clear trend over the last decade for smoking prevalence to decrease and for use of the oral tobacco snus to increase. It has been suggested that the greater decline in smoking prevalence in men compared to women in Sweden is explained by the availability of snus. However, the trend in smoking prevalence in males could also be due to successful non-smoking programs or other socio-cultural factors. Smoking prevalence in Norway has decreased at the same rates in men and women during the last decade, whereas a marked increase in snus use during this time period has only occurred in men. In general, aggregate data provide inadequate evidence to make any causal inference.

Due to insufficient evidence it is not possible to draw conclusions as to the relative effectiveness of smokeless tobacco as an aid to clinical smoking cessation in comparison with established therapies.

#### **QUESTION 4**

##### **What is the impact of smokeless tobacco use on subsequent initiation of smoking?**

The association between smokeless tobacco use and cigarette smoking initiation is likely to be confounded by socio-demographic factors. In addition, across countries there are possible differences in risk for which the determinants are not fully understood. The associations observed may be due to an increased likelihood of all substance use (including STP and cigarettes) as part of a broader spectrum of risky and impulsive behaviours in adolescence. There is some evidence from the USA that smokeless tobacco use may lead to subsequent cigarette smoking. The Swedish data, with its prospective and long-term follow-up do not support the hypothesis that smokeless tobacco (i.e. Swedish snus) is a gateway to future smoking. The marked social, cultural and product differences between North America and Europe suggest caution in translating findings across countries, also within Europe.

#### **QUESTION 5**

##### **Is it possible to extrapolate the information on the patterns of smokeless tobacco use, smoking cessation and initiation from countries where oral tobacco is available to EU-countries where oral tobacco is not available?**

The only smokeless tobacco product, as defined in the Tobacco Products Directive (2001/37/EC) (i.e. 'tobacco for oral use' means all products for oral use, except those intended to be smoked or chewed, made wholly or partly of tobacco, in powder or in particulate form or in any combination of those forms, particularly those presented in sachet portions or porous sachets, or in a form resembling a food product) that is available in some European countries, but not all, is the oral tobacco snus, which is available in Sweden but not allowed to be sold in other EU-countries. As discussed in the answer to Question 3, the smoking prevalence in Swedish men has declined over the last decade while the use of snus has increased during the same period. However, while smoking prevalence has decreased also in Swedish women during this period, the prevalence of snus use in women has increased to a smaller degree than in men. In Norway, smoking cessation rates are similar in both genders, however, increased prevalence of smokeless tobacco use is observed only in men. In California both the prevalence of smoking and smokeless tobacco use have decreased concurrently. These data imply that the association between patterns of smokeless tobacco use and smoking cessation differ from one population to the other and are affected by cultural and societal factors. As was also discussed in the answer to Question 3, available scientific data are inadequate to determine if there is any causal relation between the trends in smoking prevalence and prevalence of use of STP.

In conclusion, it is not possible to extrapolate future patterns of tobacco use across countries. In particular, it is not possible to extrapolate the trends in prevalence of smoking and use of oral tobacco if it were made available in an EU-country where it is now unavailable due to societal and cultural differences.

**Submission: 1**

**Name**

Inger Wahlberg IWG Consulting (Individual)

**Question 1**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Other

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Errors/Inconsistencies on Products, Tobacco and Chemistry in the SCENIHR Preliminary Report It is recognised that marketed STP products vary considerably in form and toxicant content and their associated health effects. A comprehensive section of the report (Section 3.3) details these product differences. There are however a number of errors/inconsistencies that should be addressed: Table 1 (starting on page 16):

- The heading 'Constituents' should be replaced by 'Ingredients'. A constituent is commonly used as a synonym for a chemical component of a product. Ingredients are added to a product. Nicotine is described as a constituent in moist snuff, snus, but in no other product. Nicotine is not added to snus and is hence not an ingredient; this compound is a constituent of the in-going tobaccos. Nicotine is also a constituent of all other products in the table.
- Under the heading 'Constituents'(Ingredients): except for tobacco, no ingredients are listed for Dry snuff and Nicotine gum.
- Under the heading 'Where used, Brand names' for Moist snuff, snus: Gellivare and Landströms snus are manufactured by Gellivare Snusfabrik, Metropol, Granit and Mocca by Fiedler & Lundgren, and Roots by Snusab. Kicks and Rocker are no longer on the market.
- Under 'Processing' for Moist snuff, snus: "The product is heated and kept cool to avoid fermentation" should be replaced by ...."The product is pasteurised by heating and kept cool to avoid ageing."
- Under the heading 'Processing' for Dry snuff: Should read Tobacco is fire-cured or air-cured, then fermented or simply mixed with other ingredients and processed into a dry, powdered form.
- Under the heading 'Common name' for Nicotine gum. Should read Tobacco gum.
- Under the heading 'Who uses': very limited or no data are given throughout the table.

3.3.2.1 2nd para: Ammonia is not added to STP. 6th para: Flue-cured tobacco, which has very low levels of PAH, is used to a very small extent in STP. By contrast, fire-cured tobacco, which is mixed with other types of tobacco in American moist snuff, has elevated levels of PAH. Swedish snus is prepared from air- and sun-cured tobaccos and has very low levels of PAH. Flue-cured tobacco is mistaken for fire-cured tobacco in the text. 3.3.2.3 Table 3. This table is misleading in the sense that for some products only recent levels of TSNA are available and given. For other products historic and recent data are listed, giving a wide range of contents. This style of presentation makes comparisons between products difficult or impossible.

**Submission: 2**

**Name**

Cynthia Callard

**Organisation**

Physicians for a Smoke-Free Canada (NGO)

**Question 1**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Agree

**Question 5**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

We have prepared a background document comparing the experience of Canada (where smokeless tobacco is available, but not much used, Norway and Sweden (where smokeless tobacco use is widespread) and Australia (where smokeless tobacco is not much used). This analysis suggests that the "Swedish Experience" is no better than other countries and, in some areas, worse. Claim: WHEN MORE PEOPLE USE SNUS, FEWER PEOPLE SMOKE. Our finding: Sweden is not in a better situation than Canada with respect to cigarette smoking. Norway is in a much worse situation. Although Sweden has a slightly lower rate of daily smoking among men than Canada, the overall rates of smoking are almost one-fourth higher in Sweden than in Canada (19% in Canada, 25% in Sweden), and almost twice as high in Norway (19% in Canada, 35% in Norway). Snus has not protected Swedish nor Norwegian men and women from high rates of current smoking than in countries where oral tobacco is not used. See section 2.2 Over the past decade, Canada has reduced smoking at a faster pace than Sweden, Norway and Australia. (Section 2.3) Claim: WHEN MORE PEOPLE USE SNUS, ADDICTION IS TRANSFERRED FROM SMOKING TO SNUS, BUT IS NOT INCREASED. Our finding: Sweden and Norway are in much worse situations than Canada with respect to the number of people who are addicted to tobacco. The prevalence of tobacco use is much higher in Sweden and Norway than in Canada. Establishing the extent to which tobacco use in Canada, Sweden and Norway is 'addictive' is not straightforward. However, data does exist for daily use. Daily use of tobacco by men is more than twice as high in Sweden (at 37%) and Norway (at 36%) than in Canada (at 15%). Among women, daily use of tobacco products is 1.6 higher in Sweden (at 21%) and Norway (24%) than in Canada (13%). (Section 2.4) Claim: WIDESPREAD SNUS USE DOES NOT LEAD TO HIGHER LEVELS OF YOUTH SMOKING. Our finding: Sweden and Norway have much higher rates of youth tobacco use than Canada Addiction to tobacco is much higher among young people in Norway and Sweden than in Canada. Among those aged 16-24 Daily use of tobacco products among men is 2.5 times higher in Sweden (at 37%) and Norway (at 36%)

than it is in Canada (at 15%). Among women, daily use of tobacco products is 1.6 higher in Sweden (at 21%) and Norway (24%) than it is in Canada (13%). (Section 2.4) Sweden is not in a better situation than Canada with respect to protecting people from becoming smokers. The rates of 'never smoking' in are roughly the same in Canada as in Sweden. Canada has been equally able to protect its population from the onset of smoking as Sweden. It has also protected them from addiction to smokeless tobacco. (Section 2.6) Claim: WIDESPREAD SNUS USE LEADS TO MORE SUCCESSFUL QUITTING AMONG SMOKERS. Our finding: Canadians who smoke have been more successful at quitting than their Swedish counterparts. Swedish men—even though snus is widely available and accepted as a smoking alternative — have had less success in quitting than Canadian men, on a population level. Canadian women have been more successful in quitting than Swedish women. (Section 2.7) In recent years, Sweden has made much slower progress than Canada in reducing the amount of tobacco consumed. Unlike Sweden, Canada is experiencing a decline in per capita consumption in all forms of tobacco. Sweden is one of the few developed countries where total tobacco consumption is not falling. Claim: WHEN MORE PEOPLE USE SNUS, DEATHS FROM TOBACCO ARE LOWER. Our finding: Sweden has lower rates of mortality from smoking than Canada, but is making slower progress. Canada—without snus use—is making faster progress against smoking related deaths among both men and women — than Sweden is. Sweden's current rate of progress against tobacco related disease is slower than that of England, Australia, New Zealand, the United States . (Section 3.1) Sweden's success is more likely due to early tobacco control than to snus use. Sweden's exemplary comprehensive tobacco control policies, implemented in the 1970s, helped prevent rates of tobacco consumption from ever growing to the high levels in other countries. Sweden's current low rates of smoking-related mortality is a continuing benefit of effective primary prevention policies implemented in the 1970s. Since then, however, Sweden has experienced some tobacco control policy reversals (after joining the European Union, the number of and size of warnings was reduced). Sweden is now making slower progress than other countries in reducing tobacco consumption and consequent tobacco-related mortality. (Section 4.2)

### **References**

The Snus Experience. Lessons from Norway, Sweden and Canada on the public health consequences of widespread oral tobacco use. Physicians for a Smoke-Free Canada. [www.smoke-free.ca](http://www.smoke-free.ca). [ccallard@smoke-free.ca](mailto:ccallard@smoke-free.ca)



**Submission: 3**

**Name**

Florence Berteletti Kemp

**Organisation**

The Smoke Free Partnership (NGO)

**Question 1**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

A very clear distinction needs to be made between the various types of oral tobacco and great care used in defining which particular products are being discussed in any particular context. Thus the products currently generating the greatest interest are those prepared to the Gothiatek standard, such as Swedish snus and some newer moist snuff products being introduced into the markets of the US, South Africa and elsewhere. Swedish snus is pasteurised and stored at a low temperature, and this seems to reduce the levels of nitrosamines. However, some other forms of moist snuff still available e.g. in the USA, (and similar to those products that were starting to be introduced into Europe some 15 years ago) contain high levels of nitrosamines and carry a considerable risk e.g. of oral cancer. Also, the various types of chewed and sucked tobacco used traditionally by South Asian communities also carry a far higher risk of cancer than snus. In the answers below, we restrict our comments to products such as Swedish snus that are manufactured to Gothiatek-type standards. A recent systematic review of the literature was produced by the New Zealand Health Technology Board. This supports the conclusions of the EU SCENHIR report and confirmed that snus carries a far reduced risk of cancer and other diseases than smoked tobacco. Thus while there may be increased risks of cardiovascular disease and pancreatic cancer due to the long-term use of snus, and risks to pregnant women also need to be assessed, the use of snus is many orders of magnitude less harmful than that of smoked tobacco.

**References**

1 - Gray N, Henningfield JE, Benowitz NL et al. Towards a comprehensive long term nicotine policy. Tobacco Control, 2005; 14: 161-165  
2 - McNeil A, Bedi R, Islam S et al, Levels of toxins in oral tobacco in the UK. Tobacco Control 2006; 15:64-67  
3 - Broadstock M, Systematic review of the health effects of modified smokeless tobacco products. New Zealand Health Technology Assessment Report 2007; 10(1)  
4 - Gartner C, Hall W, Vos et al. Assessment of Swedish snus for tobacco harm reduction: an epidemiological modelling study. The Lancet, 2007; 369: 2010-2014  
5- Chapman S, Public Health Advocacy and Tobacco Control, Blackwell Publishing, Oxford, 2007

**Question 2**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The NZ review<sup>3</sup> confirms the addictiveness of oral tobacco products. Snus delivers a nicotine 'hit' that more closely resembles that from smoked tobacco, and might therefore be more

effective, than currently available NRT products. We do not believe that addictiveness in itself should impede use of a product that could potentially help many thousands of people to quit smoking. What is in greater question here is whether indeed smokers would switch from cigarettes to snus or whether a new cohort of snus-users would be created if it became available on the market (see also Qu 4). Therefore what is crucial is how snus would be controlled and made available. In our view, it should initially be solely for quitting purposes, and on prescription, if shown in RCTS to be an effective cessation aid. If full, independent regulation of all tobacco and nicotine products was introduced, then (following careful behavioural and social marketing research) it could be considered for wider use, if research indicated that smokers would switch. However, messages and availability would both need to be tightly controlled by the public health authorities. This could lead to the interesting situation, whereby government agencies were 'promoting' a tobacco product<sup>5</sup> - such a scenario would need to be preceded by professional and public awareness campaigns.

### **References**

3 - Broadstock M, Systematic review of the health effects of modified smokeless tobacco products. New Zealand Health Technology Assessment Report 2007; 10(1) 5- Chapman S, Public Health Advocacy and Tobacco Control, Blackwell Publishing, Oxford, 2007

### **Question 3**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

It is a matter of considerable public health interest that RCTs on snus as a cessation aid are undertaken. The Smoke Free Partnership knows that Cancer Research UK was considering such a trial but due to the dual difficulties of snus a) being a tobacco product and b) illegal, the trial proposal has not as yet gone to peer review. We believe that discussions about such a RCT are also being held in France. It would be very helpful if the EC sanctioned the use of snus in RCTs, i.e. provided a special license to overcome the illegality of snus for this research. It should however be recognised that there are already effective non-tobacco treatments for nicotine addiction. Therefore public health interest can be served even more by encouraging a) greater use of these treatments and b) the development of more effective cessation aids, especially those that mimic more closely the nicotine 'hit' delivered by cigarettes<sup>1</sup>. Therefore, it would be preferable if the use of snus, within the spectrum of treatment options, would be targeted to those for whom other treatments have failed (especially as it now seems that there may be other addictive substances in tobacco besides nicotine).

### **References**

1 - Gray N, Henningfield JE, Benowitz NL et al. Towards a comprehensive long term nicotine policy. Tobacco Control, 2005; 14: 161-165

### **Question 4**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

We have no idea how snus would be perceived or used in other countries. A small study conducted by the University of Nottingham by Professor Ann McNeil showed that, in the UK, people could not see the point of snus unless it was as a cessation aid<sup>6</sup>. Clearly if allowed to

be promoted by tobacco companies as a 'safer alternative' to cigarettes, people might take it up, but as it is also in these companies' interests to continue promoting smoked tobacco as well, we cannot allow them to have any active part in such promotion or to make any claims about smokeless tobacco products. We agree that there is no good evidence that snus might lead to smoking initiation, but, as noted above, nor is there any evidence that, if snus were introduced to the market, smokers would switch to using it, rather than a new group of solely snus users being created. The EC could take a leadership role in this evidence vacuum by funding social marketing research into perceptions of snus in different cultural settings across the EU.

### **References**

6 - McNeil A, Scott K, McIntyre D, Smokers' Perceptions of Relative Harm based on Package Information. Unpublished Report April 2007

### **Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

In conclusion We need to understand how snus might be perceived and used in different EU countries. We especially need to know whether it might be an effective cessation aid via RCTs. And most importantly the EU must ensure that snus can only become available under tightly regulated conditions that prohibit the tobacco industry from making any claims or promotion. If research indicated that it could have a role in smoking cessation (outside of Sweden), snus could be made available on prescription. This should be in the context of making the most harmful form of nicotine – smoked tobacco, the least accessible, affordable and attractive and the least harmful – NRT, the most available and affordable .

### **References**

7 - The Leuven Consensus On 3-4 May 2007, more than 50 members of the tobacco control and scientific community met to discuss tobacco and nicotine product regulation within the European Union. What emerged from the meeting is the 'Leuven Consensus'. THE LEUVEN CONSENSUS · There is a spectrum of harm and toxicity of tobacco and nicotine products. Smoked tobacco is the most dangerous form. Smokeless tobacco products are less harmful, some of these products being less hazardous than others. Medicinal nicotine products are by far the least harmful. · Greater regulatory consistency is needed on tobacco and nicotine products, including price and availability. The regulatory process should include an assessment of the harm and regulate accordingly. As it currently stands, tobacco product regulation is very weak and should be strengthened. The most dangerous form of nicotine containing products (cigarettes) is the least regulated and least dangerous (NRT) is heavily regulated. · Current NRT products are much less addictive than tobacco. NRT should be more accessible for cessation of smoking and appropriate use should be encouraged. Evidence that is still needed · Harm of smokeless tobacco on health · Impact of SNUS on public health · Research for novel products, based on emerging evidence of all aspects of tobacco dependence Where do we want to be within 15 years Our vision is zero tobacco use. The following are steps towards this: · The public health community to have completely taken back control of the Regulatory agenda on tobacco and nicotine products · EU Regulation to remove the misleading product yield info on cigarette packets and replace with appropriate data · Tobacco products out of the consumer price index · A price differential between tobacco and non-tobacco nicotine products. Tax and price increases are the most effective mechanism to reduce sales and consumption. This should be part of the regulatory approach. · Reduced Ignition Propensity (RIP) cigarettes within 3 years · Effective graphic warnings on tobacco packaging within 3 years · Plain cigarette packages within 10 years · Tobacco products are 'under the counter' - not visible at point of sale · Smokers are part of the picture and they need to be taken into account but not through the front groups funded by the tobacco industry · Access to internal documents from the Tobacco industry · Effective

cessation treatments available through health systems and insurance (no price barrier to quit) · No tobacco industry involvement in decision-making and regulation but they should contribute to the cost · At least full and strong implementation of the Framework Convention for Tobacco Control (FCTC) based on the best available evidence · Greater funds and commitment to tobacco control and prevention, particularly training for tobacco control advocates · A Tobacco and Nicotine Regulatory Authority

**Submission: 4**

**Name**

Olli Simonen

**Organisation**

Ministry of Social Affairs and Health (Public authority)

**Question 1**

**Do you agree with the response given ?**

Agree

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

It is wellknown, that both nicotine replacement products and smokeless tobacco products include nicotine, but only smokeless tobacco products deliver psychoactive level of nicotine and cause "nicotine kick" to users and only smokeless tobacco products include several other toxic and health hazardous life perilous substances. On the basis of these negative effects of smokeless tobacco it cannot constitute a smoking cessation aid comparable to pharmaceutical nicotine replacement products.

**Question 4**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The Swedish figures on the use of tobacco products show, that half of the users of smokeless tobacco products smoke and are at the same time also smokers. Whether they were earlier former smokers or former users of smokeless tobacco is not known. This Swedish information on it available in the Swedish Public Health Institute should be considered and discussed in the report.

**Question 5**

**Do you agree with the response given ?**

Agree

**Submission: 5**

**Name**

Clive Bates (Individual)

**Question 1**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

In characterising the risk associated with STP, the only useful scientific advice would position STPs in a continuum of risk associated with nicotine delivery products. Furthermore, risk information is of no value unless quantified. Many everyday items pose health risks of some sort and meaningful risk assessment demands quantification. The conclusions presented are not quantified and there is no positioning of the health effects of STP in a spectrum of risk with other nicotine products. Though almost half the report is devoted to this question, the scientific advice provided is worthless. Though most of the statements are technically correct, they are summarised in a way that will mislead.

**Question 2**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The conclusions regarding addictiveness are correct but insufficient and poorly framed. A credible scientific assessment would compare the psychoactive properties with smoking, and recognise that for STP to be a viable nicotine substitute for smoking, the product would need to provide nicotine delivery similar to smoke inhalation. The main concern about smokeless tobacco is that it may not be addictive enough to be a viable alternative to smoking. The report simply states what is already known and uncontested, and adds nothing useful.

**Question 3**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

3. This conclusion is incorrect and highly misleading. There is plenty of evidence to suggest that snus has played an important role in smoking cessation. The experience of Sweden convincingly demonstrates the use of STP as an exit route from smoking. Foulds et al

(2003)[1] concluded: "Snus availability in Sweden appears to have contributed to the unusually low rates of smoking among Swedish men by helping them transfer to a notably less harmful form of nicotine dependence. The Norwegian tobacco statistics report [2] is used to conclude (erroneously) that snus does not reduce smoking, the following observation about the importance of snus in quitting in Norway would be lost on most readers of the Committee's conclusions: " [...] nicotine gums, nicotine patches and Zyban were used by ten, four and three per cent, respectively, as part of the last and successful attempt to quit smoking. Very few had sought help using the national telephone helpline (Røyketelefonen), whereas 17 per cent reported that they used snus during their last attempt to quit. The product is not a medicine and its users don't see themselves as making a medicalised attempt to quit, so there is a basic error in the assumptions about how the product works and therefore how its effect on cessation should be tested. The conclusions are an example of the very weak approach to communication of knowledge where there is uncertainty. Just because there are no randomised controlled trials does not mean there is no evidence or that nothing scientifically useful can be said. Again, the report fails as a scientific assessment.

#### **References**

1. Foulds J, Ramstrom L, Burke M and Fagerström K, Effect of smokeless tobacco (snus) on smoking and public health in Sweden, *Tobacco Control* 2003;12:349-359 2. Norwegian National Institute for Alcohol and Drug Research (SIRUS), *Tobacco Statistics 1973-→2006, 2007 figure 24.* (for the Norwegian Directorate for Health and Social Affairs)

#### **Question 4**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The conclusion that the Swedish data "do not support the hypothesis that smokeless tobacco (i.e. Swedish snus) is a gateway to future smoking" conceals that important conclusion that the data do support the opposite hypothesis – that Swedish snus is an 'exit' gateway out of smoking - and there is abundant evidence for that [1]. There is also reasonable evidence that it displaces smoking initiation. A further conjecture, not explored or recognised in the report, is that snus use in men may have an effect on women's smoking prevalence through 'denormalising' smoking in the home and the tendency of cohabitants to adopt similar smoking behaviours. This 'inconclusive' conclusion misleads the reader about the considerable volume of evidence that is available and that does support more relevant hypotheses. The summary of section 3.3.3.2 included at Section 3.8 is incorrect: "If, on the other hand, the availability of snus has little impact on smoking prevalence but adds further tobacco users to the existing population, as appears to have occurred in Norway (chapter 3.3.3.2), there would be no benefit, but an adverse impact on public health from allowing snus use This does not accurately reflect the discussion in 3.3.3.2 or the real Norwegian experience. The originators of the Norwegian data argue in evidence to the Committee: These findings clearly demonstrate that users of snus are significantly more likely to quit than non-users. This result is consistent with several Swedish studies already cited in the report.[...] In order to address the third and fifth question, the SCENIHR-report has applied inadequate (and unpublished) data for Norway in chapter 3.3.3.2. If more adequate data is to be used, a revised conclusion may be drawn [2]

## **References**

[1] Ramström LM, Foulds J. Role of snus in initiation and cessation of tobacco smoking in Sweden. *Tobacco Control* 2006;15:210–214 [2] Evidence submitted to the Committee by Dr Karl Lund, Norwegian Institute for Alcohol and Drug Research, September 2007. E-mail communication 28 September 2007.

## **Question 5**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

By stating that it is not possible to extrapolate Swedish experience to other countries, the Committee states the obvious, but presents no evidence to support the more implausible hypothesis that the impact on smoking would be different to Sweden. Of course, one cannot assume that Sweden's experience can be replicated everywhere. But a reasonable working hypothesis would be that the effects would be similar in other countries, at least in direction, if not in magnitude, unless there was some evidence to the contrary. No evidence is presented in the report that other countries would be completely different. In fact, this argument forms an evidential 'Catch 22' because the only way to gather evidence about the impact of STP outside Sweden would be to liberalise it and record what happens to smoking prevalence as snus consumption rises. But if a regulator demands certainty in advance of liberalisation, then the product will never be liberalised and the data never gathered. This is another case of an unrealistic evidential hurdle being used to argue that nothing is known or can be known. In fact, it would be impossible to generalise from the past at all, because an introduction of snus as a harm reduction strategy would happen in a way that hasn't been done anywhere, but we should expect the policy-driven approach to favour better outcomes and to respond to and correct policies if adverse trends develop. If the mis-statement of the Norwegian experience is corrected as discussed in question 4, then both countries show a consistent impact and that should strengthen a working hypothesis that the Swedish success could be exported, at least until confounding evidence can be produced.



**Submission: 6**

**Name**

Ari Haukkala, PhD, University Lecturer (Individual)

**Question 1**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

I agree with the statement but there is other reason not mentioned in the answer for Q1. Combined use of more dangerous cigarettes and oral snuff has been very common in many studies (Galanti et al. 2001; Tomar 2002). In Finland approximately only 10% of STP users are currently using only oral snuff. Therefore it is really difficult to assess independent health consequences of STP because smoking is causing earlier health problems that might hide consequences of STP.

**References**

Galanti, M.R, Wickholm, S., Giljam, H. (2001). Between harm and dangers. Oral snuff use, cigarette smoking and problem behaviours in a survey of Swedish male adolescents. *European Journal of Public Health*, 11, 340-345. Tomar, S.L. (2002). Snuff use and smoking in U.S. men: implications for harm reduction. *American Journal of Preventive Medicine*, 23, 143-149.

**Question 2**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

This section of answer does not address psychological aspect of addiction that is causing as severe withdrawal symptoms and could be bigger barrier for quitting than physiological aspect of addiction. In a study by Haukkala et al (2006) we show that the combined use of oral snuff and cigarettes among adolescent weekly smokers increased nicotine addiction even after adjustment for the amount of smoking among boys.

**References**

Haukkala, A, Vartiainen, E, de Vries H. (2006). Progression of oral snuff use among Finnish 13 to 16 year old students and its relation to smoking behaviour. *Addiction*, 101, 581-589.

**Question 3**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

First there are no proven studies to show the effects of STP in cessation. This is related to smoking initiation as well. As earlier studies have suggested (Karvonen et al. 1995; Galanti et al. 2001), among adolescents oral snuff is not used as a substitute; it is added health risk behaviour to try during adolescence. The higher addiction level among boys, who are using both oral snuff and cigarettes (haukkala et al 2006), will be a barrier to future smoking

cessation attempts among them. Henningfield, Rose and Giovino (2002) suggest that there could also be similar problems among adult smokers who are using smokeless tobacco products.

### **References**

Galanti, M.R, Wickholm, S., Giljam, H. (2001). Between harm and dangers. Oral snuff use, cigarette smoking and problem behaviours in a survey of Swedish male adolescents. *European Journal of Public Health*, 11, 340-345. Haukkala, A, Vartiainen, E, de Vries H. (2006). Progression of oral snuff use among Finnish 13 to 16 year old students and its relation to smoking behaviour. *Addiction*, 101, 581-589. Henningfield, J.E., Rose, C.A. & Giovino G.A. (2002). Brave new world of tobacco disease prevention: Promoting dual product use? *American Journal of Preventive Medicine*, 23, 226-228. Karvonen, S, Rimpelä A.H., & Rimpelä, M. (1995). Do sports clubs promote snuff use: trends among Finnish boys between 1981 and 1991. *Health Education Research*, 10, 147-154.

### **Question 4**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

There exist other studies have found that STP is predicting oral snuff use in USA (Ary et al. 1987; Haddock et al. 2001; Tomar 2003). We also found In Finnish study that both weekly smoking predicted later snuff experimentation and that snuff use predicted weekly smoking, in all assessments (Haukkala et al 2006).

### **References**

Ary, D.V., Lichtenstein, E., & Severson, H.H. (1987). Smokeless tobacco use among male adolescents: patterns, correlates, predictors, and the use of other drugs. *Preventive Medicine*, 16, 385-401. Haddock, C.K., Vander Weg, M., DeBon, M., Klesges, R.C., Talcott, G.W., Lando, H. & Peterson, A. (2001). Evidence that smokeless tobacco use is a gateway for smoking initiation in young adult males. *Preventive Medicine*, 32, 262-267. Haukkala, A, Vartiainen, E, de Vries H. (2006). Progression of oral snuff use among Finnish 13 to 16 year old students and its relation to smoking behaviour. *Addiction*, 101, 581-589. Tomar, S. L. (2003) Is use of smokeless tobacco a risk factor for cigarette smoking? The U.S. experience. *Nicotine & Tobacco Research*, 5, 561-569.

### **Question 5**

**Do you agree with the response given ?**

Agree

**Submission: 7**

**Name**

Linda Cuthbertson, Secretary to the Royal College of Physicians, Tobacco Advisory Group

**Organisation**

Royal College of Physicians (Professional membership organisation representing the concerns of over 22,000 Fellows and Collegiate Members worldwide)

**Question 1**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Other

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

We agree that Smokeless Tobacco Products have very different contents and therefore the health effects from usage also differ appropriately. It would be more helpful for the different types of STP to be listed along with their specific health effects. This would make it much clearer and avoid the current confusion in the document. We agree that STP may have an effect on cardiovascular disease but the evidence on myocardial infarction is not so compelling. On 10 October 2007 The Royal College of Physicians will be publishing a report – 'Harm reduction in nicotine addiction', which will cover this subject in more detail.

**Question 2**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

We partially agree with the response given. The rate of absorption of nicotine from STP is lower than from smoked tobacco, so the extent of addictiveness is likely to be less.

**Question 3**

**Do you agree with the response given ?**

Disagree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

We are persuaded by the observational data from Sweden, again summarised in the forthcoming RCP report, that the availability of snus has contributed positively to a decline in smoking prevalence among men in Sweden, and that many smokers in that country have used snus as a cessation aid or long-term substitute for smoking. This accounts in part for the greater decline in smoking prevalence in men than in women in recent years in Sweden, a point that does not appear to be discussed in the report.

**Question 4**

**Do you agree with the response given ?**

Disagree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

In our view the use of smokeless tobacco is likely to be linked with subsequent smoking, as both are manifestations of risk-taking and rebellious behaviour among young people but we are not convinced that more people start to smoke in societies in which smokeless is available than in those where it is not. We were surprised to see this issue raised in this consultation, whose remit is the science of smokeless tobacco, and question whether it is appropriate in this context.

**Question 5**

**Do you agree with the response given ?**

Disagree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

We are disappointed that the report pays only minimal attention to the role of smokeless tobacco as a potential harm reduction alternative to cigarettes. This is their main potential application. It has been recognised for years that smokeless products are harmful, some more than others, but what matters is whether they can provide a substitute for smoking tobacco, which is much more harmful. It is always difficult to extrapolate with any confidence but if the Swedish pattern of use of snus could be replicated in other EU countries, that would lead to massive improvements in public health. The report largely ignores this, and instead dwells in inordinate detail in the recognised adverse effects. We see this as a major wasted opportunity to explore the potential use of smokeless to reduce harm from smoking, and to explore and quantify the potential risks to society of this option. The forthcoming RCP report will examine these issues in great detail, and promote in particular the medicinal forms of smokeless tobacco that have a lower risk profile than existing widely used smokeless tobacco products such as snus as a way forward to improve public health.

**Submission: 8**

**Name**

Randi Selmer

**Organisation**

Norwegian Institute of Public Health (Public authority)

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Comments from the Division of Epidemiology, Norwegian Institute of Public Health, prepared by Randi Selmer (PhD), Aage Tverdal (PhD) and Liv Grøtvedt (MSc). We limit our comments to studies of smokeless tobacco as a risk factor of different diseases and mortality. In the judgement of epidemiological evidence it is important to have valid and precise information about exposure (snus/other smokeless tobacco), confounders and health outcome. In addition it is important to assess if the available studies have sufficient power to detect important health effects. Pancreatic cancer. The conclusion of an effect on pancreatic cancer is mainly based on two Scandinavian studies (1,2). In the study by Boffetta et al there was an increased risk associated with STP use when adjusted for smoking, but only three persons with pancreatic cancer had used snus only. This number is too small to draw conclusions about the effect of smokeless tobacco alone. It is problematic to fully adjust for smoking when most STP users are smokers. It was also a limitation that tobacco use was assessed only at start of follow-up. The other study by Luo et al was published in 2007. The strength of this study was the possibility to analyse the effect of snus in never smokers. It was also possible to analyse the effect of misclassification by including updated information at each visit. A limitation, as mentioned by the authors, is the scarcity of information about possible confounding covariates. They suggest that additional studies in other populations are desirable. Cardiovascular disease. The report concludes that there is some evidence of an increased risk of fatal myocardial infarction among users of smokeless tobacco. The cohort study of Swedish construction workers (3) includes more than 30 000 nonusers of tobacco and more than 6000 users of STP only. The relative risk of mortality from ischemic heart disease was 2.0 (1.4-2.9) and from stroke mortality 1.9 (0.6-5.7) in men under 55 years. Thus we cannot preclude an effect on stroke mortality. More studies on the effect of STP on non fatal myocardial infarction and stroke, with sufficient power to detect a moderate effect are needed. As cardiovascular disease is common, even a moderate increased risk may have big public health consequences. Osteoporosis Osteoporosis is not mentioned in the report. We have become aware of a publication which shows that use of smokeless tobacco accelerates age-related loss of bone mineral density among older women (4) Minor corrections and comments Legend to Figure 18 should be corrected to : Daily use of cigarettes (upper lines) and snus (lower lines) among 14 and 15 year old boys in Norway (The Directorate for Health and Social Affairs and TNS Gallup, Oslo Norway 2007). It would be helpful to the reader if an overview of the epidemiological studies had been presented in tables, including reported design, size, number of cases, power, reported effects with confidence intervals, and adjustment for confounders. Conclusion The report concluded that users of smokeless tobacco had increased risk of pancreatic cancer, that use of various STPs was associated with high risk of oral cancer, but not for Swedish moist snuff, and that there is some evidence of an increased risk of fatal myocardial infarction. But does this mean that we can preclude an effect on stroke, non fatal myocardial infarction or other cancer forms? We agree on the reported health effects from the epidemiological studies, but we miss a discussion of the power of the studies and the lack of good studies with sufficient power to detect moderate increased risk of various diseases. The problem with multivariate adjustment for smoking when most users of STP also smoke tobacco, could also be

discussed. More studies are desirable even for pancreatic cancer.

**References**

1. Boffetta P, Aagnes B, Weiderpass E et al. Smokeless tobacco use and risk of cancer of the pancreas and other organs. *Int J Cancer* 2005; 114: 992-5. 2. Luo J, Ye W, Zendejdel K 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: 2015-20. 3. Bolinder G, Alfredsson L, Englund A et al. Smokeless tobacco use and increased cardiovascular mortality among Swedish construction workers. *Am J Public Health* 1994; 84: 399-404. 4. Quandt SA, Spangler JG, Case LD et al. Smokeless tobacco use accelerates age-related loss of bone mineral density among older women in a multi-ethnic rural community. *J Cross Cult Gerontol* 2005; 20: 109-25.

**Submission: 9**

**Name**

STIVORO: Fleur van Bladeren, policy advisor

**Organisation**

STIVORO for a smoke free future, on behalf of Dutch Cancer Society, Dutch Heart Association and Netherlands Asthma Foundation (NGO)

**Question 1**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

General Comment The conclusions in the report are, for us, not convincing to increase the availability of STP in other European countries. The report however does not focus on this issue. Even though STP seem to cause less health damage than other tobacco products, especially concerning ETS, the question whether it is desirable to extend the availability is not discussed. We also wonder why the tobacco industry is progressively involved in this issue and lobbying in all countries in favour of STP. We hope you will consider concluding this matter in the overall conclusion and recommendations that will be given in the report. This response is supported by the Dutch Cancer Society, Netherlands Asthma Foundation, Dutch Heart Association and advise has been given by the Netherland Insitute for Public Health and Environment (rivm)

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Comment: When STP is viewed as possible aid for smoking cessation, as NRT is, it should follow an extensive clinical research process. As this has not yet been the case for STP, it is impossible to consider STP a proper smoking cessation aid. We recommend investigating this possibility of using STP as NRT thoroughly as it might safe lives and burden of disease. The question is also, however, if it is desirable to consider STP as cessation aid in general, as NRT is as effective and not harmful.

**Question 4**

**Do you agree with the response given ?**

Agree

**Question 5**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment**

**(with complete references).**

Comment: Even when comparing countries is not 100% reliable, the culture (mentality, attitude) in some western European countries is relatively similar. Therefore comparison is difficult and possibly not complete but not impossible.



**Submission: 10**

**Name**

Francis Grozna

**Organisation**

ENSP - European Network for Smoking Prevention (NGO)

**Question 1**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

ENSP agrees with the response given. In addition, as mentioned by ASH Scotland in their contribution to the present consultation, it is important to underline that a recent study has found that users of smokeless tobacco products were exposed to similar levels of the powerful carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) than smokers [1]. Furthermore, data are missing regarding effects of oral smokeless tobacco use on conditions that are well known in smokers such as disc degeneration, reduced sexual potency and impaired night vision.

**References**

[1] Hecht, S., et al. Similar Exposure to a Tobacco-Specific Carcinogen in Smokeless Tobacco Users and Cigarette Smokers. *Cancer Epidemiology Biomarkers & Prevention* 16: 1567-1572, August 1, 2007.

**Question 2**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

All forms of smokeless tobacco, including snus, have nicotine as a major constituent, and are therefore dependence forming in the same way as other forms of tobacco consumption [1,2]. Over time, many users increase amounts they consume [2]. Cessation is difficult, as it is for smoking tobacco. Users of both smokeless and smoking products find tobacco cessation even more difficult to achieve than those who use only smokeless tobacco or only smoke (2,3). Tobacco manufacturers encourage use of smokeless tobacco products by smokers on occasions when they are not permitted to smoke [4] and thereby promote individuals to adopt smokeless tobacco use in conjunction with continued smoking.

**References**

[1] Henningfield, J.E., Fant, R.V and Tomar, S.L. Smokeless tobacco: an addicting drug. *Advances in Dental Research* 11 (3): pp.330-335, 1997. [2] Hatsukami, D.K. and Severson H.H. Oral spit tobacco: addiction, prevention and treatment. *Nicotine and Tobacco Research* 1 (1): pp.21-44, 1999. [3] Tomar S. Snuff use and smoking in U.S. men. Implications for harm reduction(1). *American Journal of Preventive Medicine*, 2002, 23: 143. [4] Henningfield JE, Rose CA, Giovino GA. Brave new world of tobacco disease prevention: promoting dual product use? *American Journal of Preventive Medicine*, 2002, 23: 226-228.

**Question 3**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

As commented under question 1, converging scientific evidence today show that the use of oral smokeless tobacco causes reversible as well as irreversible oral lesions, that it is cancerogenic, it increases the risk of cardiovascular diseases and it is independently associated with development of the metabolic syndrome. Other potential health effects associated with the use of snus remain unclear, and the potential for long-term harm cannot at this stage be clearly quantified. On the other hand, there is insufficient evidence as to the relative effectiveness of smokeless tobacco as an aid to clinical smoking cessation in comparison with established therapies to support the designation of snus as a legal harm reduction product at present. Because many of the harms of smoking are associated with inhalation, it has been suggested that Swedish snus and other forms of smokeless tobacco use are associated with lower health risks than those with smoking cigarettes. A recent study systematically reviewed the literature in order to compare the data on health risks associated with smoking and Swedish snus use across a range of health conditions. Only seven studies were identified, which addressed eight health outcomes. The results suggested that for certain health outcomes, the health risks associated with snus use are lower than those associated with smoking. The authors suggest this is so for cardiovascular disease, lung cancer, gastric cancer, and for all-cause mortality, but each of these assertions are based on review of one study only, with the exception of heart disease outcomes, which were based on review of 'three or four' studies. It is worth noting that this research was funded by the North Europe Division of Swedish Match [1]. Finally, as quoted by the WHO Scientific Advisory Committee on Tobacco Products Regulation (SACTob) [2]: "There are several reasons that argue against endorsing the use of smokeless tobacco products for the purpose of harm reduction. They are as follows: Benefits have not been demonstrated · Smokeless tobacco products have not been shown to be more effective smoking cessation aids than other cessation strategies · It has not been shown that people substitute smokeless tobacco for smoking or that they will not relapse to smoking · Smoking prevalence has not been shown to be decreased by substitution of smokeless tobacco for smoking Potential for harm exists · Promoting smokeless tobacco products may encourage individuals to adopt smokeless tobacco use in addition to continuing smoking · Use of smokeless tobacco products has been reported to increase the chances of subsequent initiation of smoking (49) · People who may have quit tobacco use altogether will not do so (37) · Children who might not have started smoking may start smokeless tobacco use · Health effects from the use of smokeless tobacco products remain unclear, and the potential for long term harm cannot be ruled out · All smokeless tobacco products are addictive (35) · The designation of smokeless tobacco products as harm reducing agents may promote a false perception of safety A lower risk of adverse health outcomes is achieved by reducing smoking and not by substituting another form of tobacco use."

**References**

[1] Roth, H.D., Roth, A.B. and Lui, X. Health risks of smoking compared to Swedish snus. *Inhalation Toxicology*, 17 (13): pp.741-748, 2005. [2]WHO Scientific Advisory Committee on Tobacco Products Regulation: Recommendation on Smokeless Tobacco Products: pp.3, 2003 ([http://www.who.int/tobacco/global\\_interaction/tobreg/brisbane\\_2002\\_smokeless/en/](http://www.who.int/tobacco/global_interaction/tobreg/brisbane_2002_smokeless/en/) )  
(35) Henningfield JE, Fant RV, Tomar SL. Smokeless tobacco: an addicting drug. *Advances in Dental Research*, 1997, 11: 330-5. (37) Tomar S. Snuff use and smoking in U.S. men. Implications for harm reduction(1). *American Journal of Preventive Medicine*, 2002, 23: 143. (49) Haddock CK, Weg MV, DeBon M, Klesges RC, Talcott GW, Lando H, et al. Evidence that smokeless tobacco use is a gateway for smoking initiation in young adult males. *Preventive*

Medicine, 2001, 32: 262-267.

#### **Question 4**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

As quoted by ASH Scotland in their position paper "Should the EU ban on Snus be lifted?" [1], "There is some debate as to whether or not snus and other forms of smokeless tobacco could become a gateway product, with young people becoming addicted to nicotine from a cheaper and more easily concealed product, before they move on to more addictive, and more harmful products, such as cigarettes." However, ENSP would like also to underline the following paragraphs, which strengthen our reply to question 1 and invites to extreme cautiousness: "b. The development of nicotine dependence All forms of smokeless tobacco, including snus, have nicotine as a major constituent, and are therefore dependence forming in the same way as other forms of tobacco consumption. [2] Research has suggested that experimenting with smokeless tobacco in adolescence often develops into a pattern of daily use, and that over time, users may increase the amounts they consume [2,3]. Adolescents have often not stabilised their tobacco use, and as already outlined, research has demonstrated that the use of cigarettes and snus in parallel is fairly common. [4,5,6,7,8] There is some evidence that snus users develop cravings and withdrawal symptoms when attempting to abstain, find it difficult to quit, and report similar levels of subjective dependence on tobacco [9,10]. Initial evidence also suggests that users of both smokeless tobacco and smoking products may find smoking cessation even more difficult to achieve than those who use only smokeless tobacco or only smoking products. [3,11] The website of the Scandinavian Tobacco Companies group, which manufactures snus products, states that "the use of snus involves a health risk and is habitual...In our opinion nobody under the age of 18 should use snus." [12] "

#### **References**

[1] <http://www.ashscotland.org.uk/ash/3368.html#position>, pp.15, 2007 [2] Henningfield, J.E., Fant, R.V and Tomar, S.L. Smokeless tobacco: an addicting drug. *Advances in Dental Research* 11 (3): pp.330-335, 1997. [3] Hatsukami, D.K. and Severson H.H. Oral spit tobacco: addiction, prevention and treatment. *Nicotine and Tobacco Research* 1 (1): pp.21-44, 1999 [4] Galanti, M.R. et al. Early gender differences in adolescent tobacco use - the experience of a Swedish cohort. *Scandinavian Journal of Public Health*, 29 (4): pp.314-317, 2001. [5] Galanti, M.R., Wickholm, S and Gilljam, H. Between harm and dangers. Oral snuff use, cigarette smoking and problem behaviours in a survey of Swedish male adolescents. *European Journal of Public Health*, 11 (3): pp.340-345, 2001. [6] Wickholm, S. et al. Cigarette smoking, snuff use and alcohol drinking: coexisting risk behaviours for oral health in young males. *Community Dentistry and Oral Epidemiology* 31 (4): pp.269-274, 2003. [7] Tomar, S.L. Is use of smokeless tobacco a risk factor for cigarette smoking? The U.S. experience. *Nicotine and Tobacco Research*, 5 (4): pp.561-569, 2003. [8] Tomar SL. Smokeless tobacco is a significant predictor of smoking when appropriately modeled. *Nicotine and Tobacco Research* 5 (4): pp.571-573, 2003. [9] Holm, H. et al. Nicotine intake and dependence in Swedish snuff takers. *Psychopharmacology* 108 (4): pp.507-511, 1992. [10] Fant, R.V. et al. Pharmacokinetics and pharmacodynamics of moist snuff in humans. *Tobacco Control* 8 (4): pp.387-392, 1999. [11] Tomar, S. Snuff use and smoking in U.S. men. Implications for harm reduction. *American Journal of Preventive Medicine* 23 (3): pp.143-149, 2002. [12] Scandinavian Tobaks-kompagni. STs view on Snus [online]. [no date] Available from: <http://www.st.dk/sw17126.asp> [accessed 16 July 2007]

### **Question 5**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

ENSP agrees with the response given. However, as explained in our answer to question 1, there is sufficient evidence that the use of a wide variety of smokeless tobacco products causes cancer and other diseases to humans. Also, the focus on snus as a harm reduction agent is disproportionate, given that many of the health hazards associated with snus use remain uncertain, and given that snus is known to be an addictive substance. Therefore, it is the opinion of ENSP that the European Commission precautionary principle [1] should definitely be applied: "The precautionary principle may be invoked where urgent measures are needed in the face of a possible danger to human, animal or plant health, or to protect the environment where scientific data do not permit a complete evaluation of the risk. It may not be used as a pretext for protectionist measures. This principle is applied mainly where there is a danger to public health. For example, it may be used to stop distribution or order withdrawal from the market of products likely to constitute a health hazard." Finally, ENSP would like to draw the attention on the fact that the tobacco industry is financing several of the studies behind the use of snus. This can have an influence on the conclusions. Unfortunately, ENSP does not have the resources to investigate to what extent the science referred to has been financed by the tobacco industry. ENSP encourages the SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks) to do this.

### **References**

[1] <http://europa.eu/scadplus/leg/en/lvb/l32042.htm>

**Submission: 11**

**Name**

Ruth Dempsey, Vice President Product Risk Management, PMI

**Organisation**

Philip Morris International (Business)

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The Committee's risk assessment is based on a comprehensive analysis of data on a range of STP sold around the world, which it notes "vary considerably...in associated health effects." However, the Committee acknowledges that "use of STP in Europe is significant only in the form of snus" – the STP to which it had been asked to pay "particular attention." The Committee's response to this question, therefore, would have been clearer and more relevant had it focused on snus. For example, greater weight should have been given to the "mounting epidemiological evidence" (see Foulds and Kozlowski 2007) from Sweden. As Kozlowski et al (2003) stated, no data including "clinical trial[s] in another country can provide...better evidence on the possible...effects of snus." To be clear, snus contains toxins and carcinogens and is not a harmless substitute for smoking. Nevertheless, the data suggest that snus has fewer health effects than smoking and some other STP, particularly those in developing countries. Given the space limitations, we provide below only key points where we believe the Committee's assessment on snus could have been stronger. The quotes are examples and are not intended to suggest all researchers share the same views. ? Studies have consistently not found a causal relationship between head and neck cancer, including oral cancer, and snus. See Luo et al 2007 (no "excess risk" for oral cancer); Hatsukami et al. 2007 (Swedish studies suggest head and neck cancer risk "is not significantly elevated"); Rosenquist et al 2005 ("no effect on the risk" of oral cancer). ? The combined evidence from studies in Sweden does not demonstrate that snus increases the risk of cardiovascular disease. See Wennberg et al. 2007 ("no risk for myocardial infarction" without previous history of smoking); Gartner et al. 2007b (Sweden studies "have so far failed to detect any increase" in cardiovascular disease rates). ? There is sufficient evidence to infer a causal relationship between snus and oral leukoplakia, but little evidence that lesions progress to cancer. See Larsson et al. 1991. There is insufficient evidence to infer a causal relationship between snus and periodontal diseases and dental caries. Rolandsson et al. 2005. (Some Swedish studies find no effect (Rolandsson, et al. 2005) while others find a small effect (Andersson and Axell 1989). There are too few studies for a meta-analysis.) ? The evidence, while suggestive, is not sufficient to infer a causal relationship with pancreatic cancer or to support the Committee's statement, based on two cohort studies, that the pancreas is "a main target organ" of snus. Commenting on one of those studies, Foulds and Kozlowski 2007 state, "Most snus users who developed pancreatic cancer in Luo's study had used snus before the 1980s" prior to reductions in carcinogens in Swedish snus. And the other study, Boffeta et al 2005, notes that residual confounding by risk factors such as alcohol intake and poor diet "cannot be completely ruled out." As Nilsson 2006 states, "Sweden has the lowest incidence of pancreatic cancer in Europe" suggesting any causative effect of snus "is bound to be modest." Moreover, there is a clear difference between the results of cohort studies and case-control studies, the most recent of which, Hassan et al. 2007, a US study, shows no association. Finally, adverse effects from snus must be examined in the context of the harm caused by smoking. As the Committee says, "It is undeniable that for an individual substitution of tobacco smoking by the use of moist snuff would decrease the incidence of tobacco related diseases." Its answer to this question should have made this point. We also note that while dual usage of snus and cigarettes is

rare in Sweden (approximately 2%) (Ramstrom and Foulds 2006), its impact on reported health effects of snus and the potential for an increase in dual usage as a result of public smoking restrictions warrant further investigation.

## **References**

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## **Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

We agree with the Committee that STP, including snus, are addictive.

## **Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

It is evident that pharmaceutical nicotine replacement therapies (NRT) are safer smoking cessation aids than snus. However, while the data do not permit a definitive response to this question, several studies have concluded that snus may be as effective, if not more effective, than NRT. Fagerstrom and Schildt 2003 stated, "In Sweden it seems that snus is used as least as often as [NRT] for quitting smoking and is also at least as effective...." See also Furberg et al 2005 ("Consistent with recent studies, we observed that snus use was associated with smoking cessation, not initiation.") Ramstrom and Foulds 2006 postulated

that snus may be more effective than NRT because it “deliver[s] boosts of venous nicotine” comparable to smoking and is usually used for longer periods of time than NRT: “While the association between use of snus as a smoking cessation aid and success in quitting smoking may not be causal, it is impressively consistent across the sexes, age groups, and levels of education.” Gartner et al. 2007a stated, “Snus might be more attractive to smokers than pharmaceutical nicotine as a long-term alternative to cigarettes because the nicotine delivery and social aspects are much closer to that of smoking.”

### **References**

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### **Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

There is a legitimate public health concern that people who begin tobacco use with snus may subsequently start smoking cigarettes, i.e., the “gateway” theory. However, the Committee acknowledges that the “Swedish data, with its prospective and long-term follow-up do not support the hypothesis that smokeless tobacco (i.e., Swedish snus) is a gateway to future smoking.” This appears to be accurate. Ramstrom and Foulds 2006 state that snus is more of a gateway out of smoking than into it. Furberg et al 2006 similarly report, “Among men who reported using both cigarettes and snus during their life-time, it was far more common to quit cigarettes and currently use snus than to quit snus and currently use cigarettes.” Gartner et al 2007b state, “[I]ncreased snus use in Sweden did not impede smoking cessation efforts. In fact, smoking prevalence and tobacco-related mortality have both declined in Sweden as snus use has increased.” Kozlowski et al 2003 stated emphatically “that a dramatic increase in snus use in Sweden did not lead to increased smoking.” Bates et al 2003 urge a lifting of the EU ban on snus in part because “the Swedish data suggest that uptake of snus use prevents rather than promotes smoking and therefore contributes a net public health benefit.”

### **References**

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### **Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The Committee states that it is not possible to conclude with any degree of certainty the reaction of consumers outside of Sweden to snus both in terms of relative risk and relative rate of uptake. However, as the Committee notes, some researchers have attempted to

extrapolate from the Swedish experience. For example, Gartner et al. 2007a, using modeling based on Swedish snus use, suggest that the introduction of snus in Australia could have an overall positive effect on public health. In another study, Levy et al 2006 estimate that “under strict regulations but with relevant health claims [wider availability of Swedish snus in the United States] would not impede the decline in overall smoking prevalence.” On the contrary, they opined that more widely available snus would “likely accelerate the decline in smoking prevalence.” Foulds et al. 2003 state that while one could not “assume” that the benefits of the Swedish experience with snus would “automatically transfer to other countries,” Sweden provides “a concrete example in which availability of a less harmful tobacco product has probably worked to produce a net improvement in health....” Thus, while it may be difficult and not precise, the impact of introducing snus in other Member States can be extrapolated from the Swedish experience using appropriate modeling, adjusting for social and cultural factors, and limiting the extent of any conclusions drawn from the extrapolation.

### **References**

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**Submission: 12**

**Name/Organisation**

HOUSE OF OLIVER TWIST A/S (Business)

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Comments to Table 1: House of Oliver Twist recognised that ST products vary considerably in form and toxicant content and their associated health effects. Section 3.3 of the report details these product differences. There are, however, some errors that should be addressed. A list has also been forwarded directly to SCENIHR for the attention of Mrs. Katja Bromen. Part 3.3.1 Table 1 is incomplete and contains errors. Oliver Twist is not a moist snuff product but a chewing tobacco product. Oliver Twist is also sold in Europe especially in the Nordic countries. These are the grounds for our following comments to table 1. Table 1, page 17: Add the following text under "Chewing tobacco" in Column 1 – Common name - under the category "Europe" with the following wording: Column 2 - Where used, Brand names: Oliver Twist. Primarily used in the Nordic countries. Column 3 - Constituents: Tobacco, water, flavouring Column 4 - How used: Chewed. Column 5 - Who uses: No data. Column 6 - Processing: Pieces of twisted tobacco used orally. Handmade in Denmark from unfermented tobacco. Tabel 1, page 18 Column 2: Oliver Twist must be deleted in Column 2 – Where used, Brand names - in the row "Moist snuff ". Oliver Twist is neither moist snuff, a moist plug, a plug chew nor a twist roll but a chewing tobacco as mentioned under the category "Europe" above. Therefore, add a new row between "Moist snuff" and "Plug chew" with the following wording: Column 1 – Common name: Chewing tobacco Column 2 - Where used, Brand names: Oliver Twist. USA. Column 3 - Constituents: Tobacco, water, flavouring Column 4 - How used: Chewed. Column 5 - Who uses: No data. Column 6 - Processing: Pieces of twisted tobacco used orally. Handmade in Denmark from unfermented tobacco. Further comments to the preliminary opinion: Section. 3.3.2.3 Table 2: It is not appropriate that the report refers to data from The IARC report which has not yet been published. The article, Brad Rodu (2004), should be used as reference in connection with the description of NNN, NNK and TSNA which is contained in different tobacco products. The content is measured for products in 2003.

**References**

Brad Rodu. Smokeless tobacco and oral cancer: A review of risk and determinants. Crit Rev Oral Biol Med 2004; 15(5): 252-263

**Submission: 13**

**Name**

Karl Erik Lund, Research Director (Individual)

**Question 3**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The dataset on which (prior to this unpublished) prevalence figures in section 3.3.3.2 are based, also contain data on quit rates in Norway. Time series analysis on gender specific quit rates shows an increasing discrepancy between men and women, this is paralleled by the steep rise in the use of snus by men. In 2001 the quitting rate of both sexes was 0.43; in 2006 it had increased to .56 among men but remained at .46 among women. An even more valid measure of the likely impact of snus on smoking prevalence is the quit rate for different categories of tobacco-use (again, using the same dataset). These findings clearly demonstrate that users of snus are significantly more likely to quit than non-users. This result is consistent with several Swedish studies already cited in the report. Published results on smoking quit rates in a population of University students in Oslo, Norway, (Tefre et al 2007; <http://www.sirus.no/files/pub/367/sirusrap.4.07> ) also found higher quitting rates among daily users (.53) and former users of snus (.64) compared with non-users (.34). In order to address the third and fifth question, the SCENIHR-report has applied inadequate (and unpublished) data for Norway in chapter 3.3.3.2. If more adequate is to be used, a revised conclusion may be drawn.

**Question 5**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The dataset on which (prior to this unpublished) prevalence figures in section 3.3.3.2 are based, also contain data on quit rates in Norway. Time series analysis on gender specific quit rates shows an increasing discrepancy between men and women, this is paralleled by the steep rise in the use of snus by men. In 2001 the quitting rate of both sexes was 0.43; in 2006 it had increased to .56 among men but remained at .46 among women. An even more valid measure of the likely impact of snus on smoking prevalence is the quit rate for different categories of tobacco-use (again, using the same dataset). These findings clearly demonstrate that users of snus are significantly more likely to quit than non-users. This result is consistent with several Swedish studies already cited in the report. Published results on smoking quit rates in a population of University students in Oslo, Norway, (Tefre et al 2007; <http://www.sirus.no/files/pub/367/sirusrap.4.07> ) also found higher quitting rates among daily users (.53) and former users of snus (.64) compared with non-users (.34). In order to address the third and fifth question, the SCENIHR-report has applied inadequate

(and unpublished) data for Norway in chapter 3.3.3.2. If more adequate is to be used, a revised conclusion may be drawn.

**References**

<http://www.sirus.no/files/pub/367/sirusrap.4.07>

**Submission: 14**

**Name/Organisation**

THE SWEDISH NETWORK FOR TOBACCO PREVENTION (NGO)

**Question 1**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

There is a tendency in the debate to underestimate how the evolution of knowledge repeatedly shows that all effects are not known in the beginning of an era of research. By the time lung cancer was acknowledged as a cause of smoking the academic community was not too aware of that cardiovascular disease was to be one of the main killers among smokers. Passive smoking was in a BMJ editorial in 1978 considered as an aesthetic rather than a health risk problem (ref). The light cigarette lesson is another example... As the Scientific Committees report outlines, converging scientific evidence today show that use of STP cause reversible as well as irreversible oral lesions, that it is carcinogenic, increases the risk of mortality from CVD and is independently associated with development of the metabolic syndrome, a risk which seem greater in middle age men than in elderly. Insufficient data or inconclusive results exist regarding the risk of hypertensive disease, stroke, diabetes and effects in pregnancy. Furthermore, data are missing regarding effects of STP use on conditions that are well known in smokers such as disc degeneration (1), reduced sexual potency (2) and impaired night vision (3). Next, there is data missing on the association with snus taken by breastfeeding mothers and nicotine that is passed to the infant (4). It is important to remember that even a small increase in risk is of concern from a population-based perspective. Lastly there are other side effects of STP promotion recognizable in Sweden: Nicotine dependence in Sweden is substantial. Every third man and every fifth woman is dependent on nicotine on a daily basis due to their use of cigarettes and/or STP (5). The STP pattern reinforces the socioeconomic inequality pattern of smoking, one of the most challenging aspects in tobacco control. The substantial use in adults increases the use in minors. Like father like son demonstrates that sons of men who snus repeat this behaviour (6). The growing evidence for the interaction on the brain by nicotine and alcohol is also a cause for concern – if we are concerned for our childrens' drinking habits we feel we should not be liberal on nicotine use. It is known among youth in Sweden that those heaviest drinkers are also smokers and snusers (7).

**References**

(1) Fogelholm RR, Alho AV. Smoking and intervertebral disc degeneration. *Med Hypotheses*. 2001 Apr;56(4):537-9. (2) Millett C, Wen LM, Rissel C, Smith A, Richters J, Grulich A, de Visser R. Smoking and erectile dysfunction: findings from a representative sample of Australian men. *Tob Control*. 2006 Apr;15(2):136-9. (3) Havelius U, Hansen F. Ocular vasodynamic changes in light and darkness in smokers. *Invest Ophthalmol Vis Sci*. 2005 May;46(5):1698-705 (4) Dahlström A, Ebersjö C, Lundell B. Nicotine exposure in breastfed infants. *Acta Paediatr*. 2004;93(6):810-16. (5) "Minskat bruk av tobak – var står vi idag?" Augusti 2007. National Institute of Public Health, Sweden (FHI). The statistics are based on Centrum för Alkohol och Narkotika (CAN), FHI, Socialstyrelsen och Statistiska centralbyrån. Available at: [www.fhi.se](http://www.fhi.se) (6) Rosendahl, KI, Galanti MR, Gilljam H and Ahlbom A. Smoking mothers and snuffing fathers: behavioural influences on youth tobacco use in a Swedish cohort. *Tobacco Control* 2003;12:74-78. (7) Wickholm S, Galanti MR, Söder B, Gilljam H. Cigarette smoking, snuff use and alcohol drinking: coexisting risk behaviours for oral health

in young males. *Community Dent Oral Epidemiol.* 2003 Aug;31(4):269-74.

**Question 2**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Nicotine also interacts with alcohol in the brain – see comment to Q1...

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Other factors that must be listed to completely answer this question are first of all the availability of STP in a society and the marketing of the product which creates a “need” within the potential consumer. Speaking from experience in Sweden, there have been cases where tobacco vendors have encouraged youth to buy a package of snus as opposed to cigarettes. With the good intentions that they would rather see the youth with the less harmful product, they increase the young person's risk for addiction. Next, in Sweden 50%-60% of youth still buy tobacco products from retailers (1). This demonstrates that the product although legislated to be sold to those 18 and over still gets in the hands of youth. Secondly, marketing of snus in Sweden is still a challenge. Although Sweden passed legislation calling for a comprehensive advertising ban on tobacco products, advertising for tobacco products still exists at point of placement. Specifically related to snus in Sweden, this point of placement advertising includes placement of ads at the point of purchase and a large display of snus products available for sale. There have also been cases where tobacco advertising has made its way to the mainstream in terms of exhibits at cultural events and print advertising in newspapers.

**References**

1) Centralförbundet för Alkohol och Narkotika- och narkotikaupplysning (CAN) 2005. Available at: [www.can.se](http://www.can.se)

**Question 5**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

A most relevant question in the debate on “harm reduction by snus” must be: To what extent has oral smokeless tobacco actually had an impact on Swedish smoking behaviours? There are several reasons to question the often repeated statement from the manufacturer and some researchers that STP is the main explanatory cause of the decrease of smoking in Swedish men. Smoking in most western countries have continuously decreased during the last decades, most notably in states where substantial investments in tobacco control strategies have been made. Relevant examples are Canada and California where smoking

rates now are in the same order as in Sweden – without the “help” of STP (1 & 2). A majority of smokers have quit without switching to STP. Much larger and more recent surveys performed by the National Institute of Public Health show that of today’s regular STP users 36% smoke daily or occasionally concomitantly with their STP use and 39% have not smoked at all prior to their STP use. If all Swedish men are considered, only 5 % at the most, may have had some help from STP in quitting smoking (3). There are still no longitudinal data proving to what extent STP in the individual case has played a major part in the quitting process or what the smoker would have done had STP not been available. There is an important gender aspect regarding the issue of STP. Women in Sweden have diminished their smoking to a level close to that of male – without more than a marginal increase in STP use – in spite of an apparent marketing of STP to women in the last few years. Only 1% of women use STP and are former smokers (ref FHI same as above). The STP manufacturers have declared that Swedish women are their main target today – and the product development certainly verifies this strategy. We are therefore much concerned over a rise in STP use among 15 years old Swedish girls in recent years (ref same as above ). The marketing strategy/efforts of the STP manufacturers will naturally play an important role in the next few years. It is naive to believe that STP could and would be marketed only for smokers experiencing a difficulty to quit. The tobacco industry has already demonstrated their intention to target new groups. The tobacco industry (TI) is strongly supporting the “harm reduction by snus” process in various ways. Swedish Match, as the main manufacturer of STP, has coined the expression “The Swedish Experience”, implying that the existence of STP is the major reason for low smoking rates in Swedish men. One of the most productive authors, Brad Rodu, received a 5-year unrestricted research grant from the TI via the University of Alabama at Birmingham from 1999 to 2004 ([http://www.smokersonly.org/financial\\_support/financial\\_support\\_landing.html](http://www.smokersonly.org/financial_support/financial_support_landing.html)). Eudoxa, a TI sponsored think tank in Stockholm which has a harm reduction forum named Eudoxa Science, financed by an unrestricted grant from International Smokeless Tobacco Company, Inc., an affiliate of U.S. Smokeless Tobacco Company (<http://www.eudoxascience.com/?q=node/1>). BAT sponsored South African parliamentarians’ “study tour” in July 2007 to Sweden to learn about the “blessings” of Swedish STP. One of the basic problems in tobacco control is the “perverse public health policy that makes an addictive drug widely available in its most harmful forms” (Foulds, Lancet) while less hazardous forms are either more restricted, less available or more expensive. A regulation according to harmfulness is crucial. However, it is not the least hazardous products that need less restriction. It is obviously the biggest killer, cigarettes, that should – at last - be appropriately regulated. How do we deal with products that kill every other user even when used according to the producer’s instructions? And the ultimate question being: How do we handle a substance with an addictive capacity equivalent to many illegal drugs? Because snus is an unregulated tobacco industry product it does not go through the rigorous testing methods that say for example products of the pharmaceutical industry. It is therefore unethical at the present moment and in the future to place a label on this product that it aids in curing smoking addiction. Next, there are a wealth of tested smoking cessation products which have demonstrated with varying degrees of success to aid in smoking prevention. Among these, nicotine replacement therapy has been developed as a clean form of nicotine for those smokers experiencing withdrawal symptoms. An international tobacco control strategy which has proved effective is comprehensive tobacco control programming which involves a multi-faceted approach that when actually implemented, as in for instance in California and Canada, smoking behaviours have been reduced to levels comparable to or under the Swedish levels. Thus, STP is not a prerequisite for smoking reduction. The strategy includes legislation (of for instance marketing restrictions, smoke-free environment), enforcement, information and opinion building, primary prevention (support of minors from all adults) and secondary prevention (increased and improved cessation support including pharmacologic aid). In summary, to implement

this broad and long-term strategy - that is sound public health policy. On account of society's failure to tackle the tobacco industry and its deadly products, we will not be able to save all today's smokers – in the same way as we can't help many people that die from their alcoholism or drug addiction. But to use STP (snus or other forms of STP) to conceal our long time failure to help smokers would be a great mistake for which future generations will pay a prize.

**References**

(1) Canadian Tobacco Use Monitoring Survey (CTUMS). 2006 statistics. Health Canada. Available at: [http://www.hc-sc.gc.ca/hl-vs/tobac-tabac/research-recherche/stat/ctums-esutc/index\\_e.html](http://www.hc-sc.gc.ca/hl-vs/tobac-tabac/research-recherche/stat/ctums-esutc/index_e.html) (2) County and Statewide Archive of Tobacco Statistics. 2005 statistics. California Department of Health Services. Available at <http://www.cstats.info/> (3) National Institute of Public Health, Sweden. 2006

**Submission: 15**

**Name**

Professor Carl V Phillips, MPP PhD (Individual)

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

I have chosen to focus my remarks on issues of interpretation of epidemiologic evidence and related epistemology, my primary area of professional expertise. Epidemiologic evidence is both fundamentally important (because it is the only way to observe actual health effects on actual people) and notorious (because of study errors, publication biases, and other uncertainties that mean that most conclusions are overstated). This means that some critical analysis is necessary. But the report seems to uncritically accept the conclusions stated by the authors of various studies in their article abstracts, without attempting to critically evaluate the results. Such headline conclusions are often biased or inaccurate portrayals of the results. It is impossible to go into detail about every study in this comment process, but it is surprising that it was not done as part of the report. There are hundreds of critical analysis that have been written about articles you cite, in letters to the editor, subsequent articles, and other forums, but these were ignored. To note just one particularly well-known example, the Winn et al. (1981) study that is probably the most often cited found a very low relative risk for black women, and so only the famous relative risk of 4.2 for non-black women (usually mis-identified as white women) was emphasized by the authors. Even though you presumably do not think that black people are fundamentally different or do not count, you repeat this biased reporting. The only critical questioning of the conclusions that study authors presented and emphasized that I could identify in the report was with regard to Schildt et al. (1998). This is the one case I am aware of where the authors stated a conclusion of no elevated risk, but others have published assessments that show that the data can be interpreted to conclude otherwise. (This contrasts with at least a dozen of the studies that claim that modern Western smokeless tobacco (ST) causes disease, where later published assessments show that the data can be interpreted as showing otherwise.) The singling out of this study for critical comment suggests a motivational bias in this report. Part of the comment about Schildt et al. is, "The relatively weak effect of smoking is noteworthy," and yet the assessment of Winn et al. did not mention the strangely low relative risk from smoking reported in that study. The simple acceptance of whatever happens to have been written is particularly problematic in the case of pancreatic cancer. Epidemiologic publication tends to follow a predictable cycle. Because there are so many possible exposure-disease associations, there is little interest in a paper that says "E did not seem to cause D in our data" until there are articles that claim that E does cause D. Thus, the first few papers published on an exposure-disease association will almost inevitably claim there is an association. It is often the case that a decade of null results will then follow, showing that the original publications were outliers in the inevitable distribution of results across studies. You chronicle exactly this phenomenon in the literature on ST and oral cancer, and come to the conclusion that the science does not support the claim of association. But as recently as 10 years ago, many who looked at only what had been published at the time would have insisted otherwise. It is currently premature to conclude that ST causes pancreatic cancer, let alone with the definitiveness and finality that appears in the answer to the question. The reasons for this include: the aforementioned incentives and arc in publication; the low relative risks reported in the studies that claim to demonstrate an effect, combined with the failure to adequately control for known pancreatic cancer risk factors; and the critiques that have been written about some of the studies (particularly Bofetta et al. 2005 and Alguacil and Silverman, 2004). This is not to suggest that we should ignore the possibility that ST cause pancreatic cancer in



research and policy. But the evidence of the claim is similar to what existed regarding oral cancer in the 1980s, and the research publication arc has now proven rather embarrassing for those who stated emphatic conclusions back then. In addition, to the extent that tentative conclusions are drawn, a simple qualitative statement of "increased risk" is not terribly informative; the absolute health risk caused by ST, even if there is a relative risk of 1.7 for pancreatic cancer, is quite small. Regarding the claim that TSNAs are human carcinogens: It is worth noting that there is no direct evidence of this and it must be inferred from a variety of very indirect sources. Subjecting non-human animals to exceptionally high doses of these chemicals has induced cancer in some cases, but there are few chemicals for which this is not true. We can reason by analogy, considering other nitrosamines where there is convincing epidemiologic evidence of carcinogenicity. But these are only suggestive of possible human carcinogenicity from TSNAs in doses/quantities that are actually experienced. The only direct evidence that TSNAs in ST are carcinogenic comes from comparing studies of older or non-Western products (which have much higher levels of TSNAs) to studies of modern products. This is the only source of a contrasting exposure to TSNAs, holding most other things (in particular, exposure to smokeless tobacco) equal. Some studies of older or non-Western products show an association with oral cancer, whereas modern studies of modern products do not. Thus, if one believes that the older and non-Western studies sometimes show positive associations because of genuine different effects (and not poorer methodology or publication bias), the reasonable conclusion is that TSNAs cause cancer in high concentrations, but the concentrations in current products do not cause measurable levels of cancer. It is important to recognize what constitutes evidence of a claim and what is related by tangential. There is something of a double standard about such inference in the report, wherein social/economic evidence from Sweden is very strongly suggestive of the potential of ST in reducing smoking, but in the report much of that evidence is treated as uninformative because it requires inferences beyond what is directly observed. And yet TSNA exposure from ST use is declared to be carcinogenic, when this requires a quite tenuous inference from indirect evidence. Finally I note that though the report offered some answers to this question in its most relevant form – i.e., what are the health effects as compared to the existing, popular substitute product, cigarettes – but the summarized answer made the much less informative comparison of the health effects of ST versus the unrealistic scenario of no tobacco use at all.

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In direct response to the answer to this question, it should be noted that it is not standard scientific epistemology to draw comparative conclusions only if a direct comparative study has been conducted. That is, the lead statement that notes that there has not been a randomized trial comparing smokeless tobacco to pharmaceutical products is literally true, but rather disingenuous, since a reader would likely conclude that there has been no clinical trial of smokeless tobacco as a smoking cessation tool, but as you note in your text, there has been such a study (Tilashalski et al. 1998). Moreover, when citing that study, you fail to cite the seven-year followup of it (Tilashalski et al. 2005). These studies, which constitute useful information about the question as asked, suggested that smokeless tobacco is much more effective in aiding smoking cessation than studies of pharmaceutical products suggest that those products are. More important, however, are two observations that must be made about this question. First, any assessment of past switching to a highly-reduced-harm alternative to cigarettes must be considered in the context of what consumers believed about different products' health risks. People cannot be expected to change their behavior to improve their health if they do not know that the new behavior is health-improving. In the case of smokeless tobacco, very few people in Europe, outside of Sweden, or in North America know that smokeless tobacco poses approximately 1/100th the risk of smoking. There is a substantial literature about the efforts made by anti-tobacco activists to misinform

people about smokeless tobacco, and these have succeeded in convincing most people that smokeless tobacco poses a health risk similar to that from cigarettes (see references below). Thus, past observations about decisions to switch, outside of Sweden, provide very little information about what would happen if people knew the truth. The only thing we can conclude from observing people who mostly do not know the comparative risk is that however many of them switched products, more people would use smokeless tobacco as an effective means to quitting smoking if everyone were given access to the products and accurate information. Second, it is sometimes the case that literally answering a question, rather than responding to its underlying premise, can distract us from what is most useful to know. Asking whether smokeless tobacco provides an alternative to smoking that is comparable to pharmaceutical nicotine products implicitly assumes (a) that the effectiveness of pharmaceutical products presents a worthy target and (b) that comparability is relevant to decision making. A large body of research shows that the effectiveness of existing pharmaceutical products in smoking cessation is quite poor, usually barely better than unassisted quit rates. It is likely that most advocates of tobacco harm reduction would find it a substantial (and unexpected) disappointment if a population of smokers were educated about the low risks from smokeless tobacco, but their rate of smokeless-tobacco-aided smoking cessation were no higher than the rate of successful quitting using pharmaceutical products. Moreover, it is not clear why comparability to the effectiveness of pharmaceutical products is relevant to anything. When proposing a new safety feature for cars, we do not ask if its benefits are comparable to those of side air bags. If there are benefits, it does not matter whether they are larger or smaller than the benefits of some other intervention unless the two interventions compete in an either-or manner. If the interventions do not crowd each other out, then from a health perspective the net benefits of the new option add to the benefits that have already been provided by the existing option. There is no reason to expect that smokeless tobacco (whose public health niche would be to provide a long-term source of nicotine in doses comparable to those from smoking for those who do not quit entirely) and existing pharmaceutical products (whose niche is to assist the transition to nicotine abstinence) would compete. Indeed, given the over-hyped messages about the benefits of using pharmaceutical products, it is likely that few smokers who consider switching to smokeless tobacco would not have already tried (and failed with) the pharmaceutical products. (Note that in this context, competition refers to whether one product might crowd out the health benefits from the other. From a corporate profits standpoint, anything that is effective at getting people to quit smoking is a competitor for pharmaceutical stop-smoking products. Thus, pharmaceutical companies presumably are interested in the comparison that was posed and concerned about smokeless tobacco because of the effect it might have on their profits, but this is not relevant to a public-spirited analysis of health effects.) It would be possible to create pharmaceutical products that occupied the same niche as smokeless tobacco in smoking cessation efforts. A high-peak-dose, competitively-priced pharmaceutical nicotine products would directly compete with smokeless tobacco in all ways. However, even then the introduction of smokeless tobacco would still have net benefits if there is anyone who would not switch to long-term-substitute pharmaceutical products, but would switch to smokeless tobacco. There would be no measurable health advantage of one product over the other, since there is no reason to believe that the pharmaceutical product would have higher or lower health effects than smokeless tobacco but there is every reason to believe that both would be very low. (Why is that? We have never observed a large population of long-term pharmaceutical nicotine users, so the only scientific basis we have for concluding the risks from it would be low is that the risks from smokeless tobacco are so low. Thus we have absolutely no basis for concluding that the risks would be different.) Therefore even if smokeless tobacco were competing with some hypothetical pharmaceutical product in the future, the competition would only represent a cost to the pharmaceutical companies; there would be no measurable public health cost from the competition.

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## **Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The question of whether the existence or popularity of smokeless tobacco might cause an increase or decrease in smoking is of critical importance since, due to the very minor direct health effects of using smokeless tobacco, this is the only potential source of substantial health impacts. The question is phrased without reference to whether the impact is an increase or decrease in smoking initiation, though the answer emphasizes only a potential increase. This may not be entirely appropriate since, in addition to the expectation that some current smokers would switch to a lower risk product, the culturally accepted use of smokeless tobacco might cause some people who otherwise have started smoking to never do so, but only use smokeless tobacco instead. However, in a culture where the overwhelmingly dominant form of tobacco use is cigarette smoking, there are likely to be few people who are inclined to use tobacco regularly who do not meet the "100 cigarettes ever" threshold for being called a smoker. Thus, even when smokeless tobacco provides a substitute for long term use of cigarettes, it may prevent few nicotine users from crossing the "ever smoker" threshold (which is not to say that it will prevent them from smoking so much that it kills them, which it likely will in many cases). In assessing whether there is a "gateway" effect, it is important to clarify what causation means in this context. For the gateway concept to have meaning we have to consider cause and effect (or "impact", as phrased in the question). Smokeless tobacco availability causing smoking initiation means that someone who would never have smoked if smokeless tobacco were not available becomes a smoker when smokeless tobacco is available (probably after trying smokeless tobacco and switching, though this need not be the mechanism). It is only people who fit that causal scenario that are prevented from smoking by maintaining a ban on smokeless tobacco. There is no reason to believe that there is any substantial population that fits that description. Someone with an inclination to use nicotine and who is willing to risk the health impact of smoking will smoke if there is no other satisfying source of nicotine available. (The persistence of smoking in spite of extreme anti-smoking efforts in some jurisdictions suggests that about 20% of the population finds nicotine sufficiently appealing to meet this description. It is very unlikely that such individuals will never even try nicotine, and thus could be kept a nonsmoker by hiding the appeal of nicotine.) Who, then, might use smokeless tobacco but would not use tobacco at all if it were not available? This must be people who like nicotine, but not enough to suffer the health consequences of smoking. But why would such a smokeless tobacco user switch to cigarettes, which still have the health risk that they were trying to avoid? Most anyone who would be willing to do that would probably have just smoked in a world that lacked smokeless tobacco. The logic of this assessment is important because simplistic empiricism is of little value when it is ignored. For example, if someone would have taken up smoking anyway then the fact that they used

smokeless tobacco first is not a case of causation, though many of the claims about a gateway effect simply look at the order of use. Nor is it surprising that people who use one product are more likely to use the other product, either in the past, the future, or concurrently; this just reflects the fact that some people quite like to consume nicotine while others do not. The U.S. studies that are cited in the report provide no actual evidence of a gateway effect. All just provide evidence that the same people who are inclined to use nicotine from one source are more inclined than others to later use nicotine from another source. The report and the answer to this question emphasize cultural differences (between Sweden and other countries) in arguing that we cannot extrapolate the data we have. But much more important than cultural difference are knowledge differences. If there is currently a gateway effect in North America, there is no reason to expect that it would persist if consumers were given honest information. North American consumers are currently the victim of misinformation about smokeless tobacco, and generally believe its use is at least as unhealthy as smoking. Thus, if after becoming a nicotine user they discover they like smoking a bit more than smokeless tobacco use, they see no reason to not switch. I have dubbed this the "you might as well smoke" message to smokeless tobacco users, and it is undoubtedly responsible for killing some people who would not have switched to smoking if they knew the truth. Completing the analysis, the people who are true gateway cases in a population that receives honest information are those few who: - would not have smoked if that were the only source of nicotine, -but use nicotine when a much less harmful form is available (which, incidentally, could be pharmaceutical as much as smokeless tobacco), -though they still like cigarettes better, -and then decide that nicotine/tobacco has become so much more appealing that the risk from cigarettes is now worth the marginal benefit that cigarettes offer above that from smokeless tobacco. That is quite a conjunction. It is basically impossible for us to empirically determine how many people would fit that description, and so the studies that get cited are largely a smokescreen for empirical ignorance. But the logic of the situation is much more compelling than the observational evidence: it is difficult to imagine very many true gateway cases once people knew the comparative risks.

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

If interpreted quantitatively, the answer to this question seems accurate but relatively uninteresting. That is, we cannot predict how many smokers will switch to smokeless tobacco, and in what communities, by a particular time. There are too many economic, sociologic, and educational issues that are left as unknowns in a scenario that merely describes the changing availability of smokeless tobacco. However, if interpreted qualitatively, the answer given to this question in the report borders on scientific nihilism, suggesting a belief that we can never predict anything that we have not already seen (a attitude that translates into not predicting anything in public health since the social situation always differs). Fundamental and empirically well-established economic theory predicts that when a much-lower-cost substitute for a product is offered, many consumers of the existing product will switch to it. In this case, the much lower cost is the health cost, not the purchases price. The existing product has a roughly 1-in-3 chance of substantially hastening a user's death, while the substitute product has about 1/100th that risk; it is difficult to imagine a deeper discount. Of course it is always reassuring to have at least one direct empirical observation to back a theory, no matter how compelling that theory is, and no matter how well supported it is by analogous experiences. This is the value of the Swedish experience, as a confirmation of something that we have every reason to believe is true. Epistemically, this is quite different from the Swedish data being the only reason to believe that people would switch upon learning of the comparative risks. If we had just a few empirical findings, based on limited data, and not backed by any theory, then it would be appropriate to say "this is not really enough to go on; there might be something odd about

this population". For example, that would be the appropriate response to the epidemiologic claims that smokeless tobacco causes pancreatic cancer, even though it does not cause cancer at more proximate sites. But a single example that shows that an overwhelmingly convincing theory is borne out is a good reality check, and so it does not need to be extrapolated to be informative. The Swedish phenomenon is confirmation that a near-universally accurate economic prediction applies in the particular case of smokeless tobacco. While switching patterns in Sweden now may have social forces driving them, before smokeless tobacco became socially popular, first-movers were apparently motivated by the lower cost. Again, social factors – including cultural history of tobacco use, the social role of smoking, attitudes toward environmental tobacco smoke and other perceptions of what is clean and dirty, and most importantly education about and attitude toward health risks – will clearly influence the pace at which smokers switch products. In particular, if no one is willing or able to educate the public about the fact that Western-style smokeless tobacco poses about 1/100th the risk of smoking, then consumers will not realize that the product is much less costly and have no reason to switch. The rate at which the experience in other places comes to replicate the experience in Sweden is not some uncontrollable feature of the populations; it is largely within the control of the same authorities who currently discourage/ban smokeless tobacco. In summary, the answer to "is it possible to extrapolate" is, perhaps, "no", if we pretend that we know nothing about human behavior other than the observations about Swedish tobacco use. But the more informative answer is that we do not need to extrapolate, because other sources of knowledge provide much more convincing evidence that that experience can be replicated if people are given accurate information.

**Submission: 16**

**Name**

James E. Dillard III Senior Vice President

**Organisation**

International Smokeless Tobacco Company Inc. (Business)

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The Preliminary Report and Opinion do not discuss a definition of causation or the criteria the Committee utilized to reach a judgment that STP cause cancer in humans. (See, by comparison, the discussion of such issues in the 2004 report of the US Surgeon General on smoking and health (SG '04)). Also, there is no synthesis of the studies identified or any discussion of the scientific weight given to each study. Further, the Opinion uses inconsistent and undefined terminology such as "strongly associated" and "increased risk," which is the type of terminology SG '04 specifically avoids because it lacks clarity and creates ambiguity. The judgments reached regarding oral cancer distinguish between American and Swedish snuff. There is no basis to make this distinction. (See, e.g., SG '86, which included in its analysis, without distinction, studies from Sweden, Norway and the UK). To the extent such a distinction is based on manufacturing differences between modern Swedish and American snuff, there is no basis for that distinction when evaluating STP epidemiology. Sweden did not change to its current manufacturing process until the 1980s, decades after the majority of people studied in Swedish studies began using snuff. Indeed, the data in Lewin, et al. 1998 and Schildt, et al. 1998 show that the majority of snuff consumed was not of the modern variety, but was manufactured in the 1930s through the 1970s. If a geographic distinction is to be made among smokeless tobacco products, it should be made between Western (American and Western European) and non-Western (e.g., Asian, African, Indian, Sudanese) products because non-Western products incorporate other materials. The Opinion recognizes this distinction and excludes products with betel quid, but inexplicably discusses products with lime. Even if American snuff is distinguished from Swedish snuff, the majority of American studies discussed in the Report do not report a statistically significant association between American snuff and oral cancer, and therefore there is insufficient basis to reach the judgment that American snuff causes oral cancer. The Opinion focuses on Winn, et al 1981. Winn states that the product used was "[a]lmost exclusively dry snuff" (Banbury Report 1986), whereas moist snuff is the primary product used in America and Sweden. Further, Winn was conducted almost 30 years ago and studied a non-representative population of elderly women in an isolated geographic area. Its results have never been replicated. Inconsistent with its oral cancer judgment, the Opinion does not distinguish between American and Swedish snuff in its pancreatic cancer judgment. Nevertheless, an evaluation of the two Scandinavian and five American studies discussed in the Report does not support a causal judgment. The majority of the studies do not find a statistically significant association. The relative risks in the two Scandinavian studies are of borderline statistical significance and have methodological limitations acknowledged by the authors and criticized by other researchers. (See, e.g., letters to the editor on Boffetta, et al. 2005). If the Opinion continues to distinguish between Swedish and American snuff with respect to oral cancer, it should make the same distinction with respect to pancreatic cancer and state that American studies do not support a causal judgment. Four of the five American studies report no statistically significant association between snuff and pancreatic cancer. The single study that reports a statistically significant association (Alguacil, et al. 2004) did not find such an association in the overall population studied, but rather only reports it in a single subgroup of the study (consumers who used

more than 2.5 oz/week). That association is of borderline statistical significance and is not adjusted for alcohol consumption. Therefore, there is an insufficient basis to reach the judgment that American snuff causes pancreatic cancer.

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**Submission: 17**

**Name**

Brad Rodu, Professor of Medicine (Oncology) School of Medicine University of Louisville (Individual)

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

This submission contains technical/scientific evidence that will improve the overall assessment of the SCENIHR preliminary report on "Health Effects of Smokeless Tobacco Products." Section 3.3.1 (Table 1, pp 17-18) of the preliminary report incorrectly and inadequately describes smokeless tobacco use in the United States. First, the U.S. federal government categorizes smokeless tobacco products as: chewing tobacco (including plug, twist and loose leaf), dry snuff and moist snuff (1). Second, the brand names for dry snuff are incorrect, as these brands are from other countries. American brand names include Bruton, Garrett, Honest Scotch, Railroad Mills and Red Seal. The section "How Used" describes American dry snuff as "inhaled up the nostril," which is incorrect. In the U.S. dry snuff is not inhaled, but is used in the oral cavity, primarily by women, whereas chewing tobacco and moist snuff are used primarily by men (2). Table 1 describes no data for the U.S. in the section "Who uses." In fact, a recent publication provided a detailed description of smokeless tobacco use in the U.S. (3) Section 3.3.2.3 (Table 3, p 27) lists studies of TSNA levels in smokeless tobacco products. Another study provides additional information on TSNA levels in American, Swedish and Danish products (4). The TSNA analyses in this study were performed by a scientist at the Swedish National Food Administration. Section 3.6.2.1 (p 76) refers to a study by Wynder et al., 1957. However, there is no citation for this study (5) in the reference list. In fact, Wynder et al. published a second study of smokeless tobacco and oral cancer in 1957 using American data (6), which was not discussed in the report. Section 3.6.2.1 (pp 75-83) omitted six studies of smokeless tobacco and oral cancer (7,8,9,10,11,12). These studies should be discussed. Section 3.6.2.1 (p 79) discussed the 1981 New England Journal of Medicine study by Winn et al. but inadequately described the smokeless tobacco exposure as "snuff." In fact, Winn clearly described the exposure as "dry snuff" in two scientific publications (13,14). Therefore, the SCENIHR report should describe the smokeless tobacco exposure in the 1981 Winn study as "dry snuff." Four passages in the report make the following statement: "Risks of oral cancer were strongly associated with the use of American snuff." (Executive summary, p 9; Section 3.6.2.3, p 89, Section 3.6.7, p 99; Opinion, p 112). The latter three occurrences, in an obvious reference to Winn et al., refer to "one large case-control study," adding that "a detailed characterisation of the product was not given." This is inaccurate (see previous paragraph). In all cases the passages should be corrected to read "American dry snuff." Section 3.6.6.1 (p 98) discusses the association of snus use with diabetes. One published study (15) was omitted from this discussion. Section 3.8.2 (pages 108-110) describes the potential health impact of the availability of snus on the tobacco market in the EU but provides no EU-specific data. In 2004 a published study (16) constructed a set of age-, gender- and smoking-specific mortality rates to estimate the current number of smoking-attributable deaths in the (15-member) EU, compared to estimates if each country had the smoking prevalence of Sweden. The results from this study provide specific information about the scope of smoking-related mortality in the EU, and about the potential health impact of tobacco harm reduction. References 1. Capeheart T (2007). Tobacco Outlook. Economic Research Service, U.S. Department of Agriculture. Available at: <http://usda.mannlib.cornell.edu/usda/ers/TBS//2000s/2007/TBS-04-24-2007.pdf> (Accessed 8 August 2007) 2. Rodu B, Cole P. Smokeless tobacco use and cancer of the upper respiratory tract. Oral Surgery 2002; 93: 511-515. 3. Nelson DE, Mowery P, Tomar S,



Marcus S, Giovino G, Zhao L. Trends in smokeless tobacco use among adults and adolescents in the United States. *Am J Public Health* 2006; 96: 897-905. 4. Rodu B, Jansson C. Smokeless tobacco and oral cancer: a review of the risks and determinants. *Crit Rev Oral Biol Med* 2004; 15: 252-263. 5. Wynder EL, Hultberg S, Jacobsson F, Bross IJ. Environmental factors in cancer of the upper alimentary tract: a Swedish study with special reference to Plummer-Vinson (Patterson-Kelly) syndrome. *Cancer* 1957; 10: 470-487. 6. Wynder EL, Bross IJ, Feldman RM. A study of the etiological factors in cancer of the mouth. *Cancer* 1957; 10: 1300-1323. 7. Peacock EE, Greenberg BG, Brawley BW. The effect of snuff and tobacco on the production of oral carcinoma: an experimental and epidemiological study. *Ann Surg* 1960; 151: 542-550. 8. Vogler WR, Lloyd JW, Milmore BK. A retrospective study of etiological factors in cancer of the mouth, pharynx, and larynx. *Cancer* 1962; 15: 246-258. 9. Vincent RG, Marchetta F. The relationship of the use of tobacco and alcohol to cancer of the oral cavity, pharynx or larynx. *Am J Surg* 1963; 106: 501-505. 10. Martinez I. Factors associated with cancer of the esophagus, mouth, and pharynx in Puerto Rico. *JNCI* 1969; 42: 1069-1094. 11. Wynder EL, Stellman SD. Comparative epidemiology of tobacco-related cancers. *Cancer Res* 1977; 37: 4608-4622. 12. Browne RM, Camsey MC, Waterhouse JAH, Manning GL. Etiological factors in oral squamous cell carcinoma. *Comm Dent Oral Epidemiol* 1977; 5: 301-306. 13. Winn DM. Tobacco chewing and snuff dipping: an association with human cancer. In O'Neill IK et al. *N-Nitroso Compounds: Occurrence, Biological Effects and Relevance to Human Cancer*. IARC Scientific Publications No. 57, Lyon, France, 1984. 14. Winn DM. Smokeless tobacco and oral/pharynx cancer: the role of cofactors. In Hoffmann D, Harris CC. *Mechanisms in tobacco carcinogenesis*. Cold Spring Harbor Laboratory (Banbury Reports 23), 1986. 15. Eliasson M, Asplund K, Nasic S, Rodu B. Influence of smoking and snus on the prevalence and incidence of type 2 diabetes amongst men: the northern Sweden MONICA study. *J Int Med* 2004; 256: 101-110. 16. Rodu B, Cole P. The burden of mortality from smoking : Comparing Sweden with other countries in the European Union. *Europ J Epidemiol* 2004; 19: 129-131. Note: PDF versions of these references have been sent by email to: [Sanco-sc1-secretariat@europa.eu](mailto:Sanco-sc1-secretariat@europa.eu)

**Submission: 18**

**Name**

Dr Justine Williamson, Chairman of the ESTOC Scientific Committee

**Organisation**

European Smokeless Tobacco Council (Industry Association)

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

ESTOC is a trade association of tobacco companies, and recognises that the public should rely upon public health bodies as the main source of information on the health risks of tobacco products, including smokeless tobacco (ST) products. One general observation we have is that the Executive Summary ("Summary") of the SCENIHR preliminary report ("Report") does not always reflect the generally balanced scientific analysis in the body of the Report and, in some cases, the body of the Report does not consider all of the available scientific information. We agree that ST products vary considerably in form, toxicant content and their associated health effects. Section 3.3 of the Report provides some details of these product differences, but there are some omissions upon which we will be writing separately to the Committee. The Report (Section 3.3.2.3, paragraph 4) compares the exposure of an average smoker and an average snus user to TSNA, but does not consider that the absorption of TSNA from the mainstream smoke in the lungs of the smoker is most likely to be substantially different from the degree of extraction and absorption of TSNA from snus in the mouth of the snus user. The conclusion in the Report that the exposure to TSNA is 6 times higher in ST users than in cigarette smokers is not consistent with findings from Hecht et al. (2007), who reported similar exposures to NNK in smokers and users of the US oral tobaccos and the findings of Hatsukami et al. (2004) who reported that the levels of urinary total NNAL in users of Swedish snus were significantly lower than the levels of urinary total NNAL in smokers. Regarding genotoxicity, the Report suggests that Swedish moist snuff causes mutations and chromosomal damage in culture by reference to an IARC monograph that as of late September 2007 was 'in preparation' not 'in press'. It is not possible to comment on data that is not published. The Summary does note the scarcity of positive in vivo toxicological studies. In respect of cardiovascular disease ("CVD"), it should be noted that a recent review by Broadstock (2007), commissioned by the New Zealand Ministry of Health, concluded that "Five of six studies investigating risks for fatal and/or non-fatal cardiovascular disease (CVD) outcomes in men, including three case-control studies, a nested case-control study and a cohort study, found no significantly increased prevalence of CVD for snus users compared with no tobacco use" and that "The excess risks found in the construction worker study may be associated with population and exposure characteristics specific to the cohort, and findings may be less applicable to snus products currently on the market." The construction worker cohort does not seem to have taken potential confounders into account. In Sweden, treatment of myocardial infarction ("MI") has changed considerably over the past 15 years and become much more active, and this has corresponded with a substantial decrease in CVD mortality. There is considerable heterogeneity between different hospitals in how these newer treatment regimens have been implemented. This is evidenced by the reports from the Swedish nationwide register of MI that has been active since the mid 1990s ([www.ucr.uu.se/rikshia](http://www.ucr.uu.se/rikshia).) For instance, in their report from 2000 it can be found that among 67 hospitals, use of reperfusion varied between 15-65%, use of iv betablocker 10-85%, sc/iv anticoagulant therapy 18-90%, and lipid-lowering treatment after discharge 15-70%. Broadstock also highlighted the need for "additional, high quality research" on snus use and CVD mortality "to further understand the potential association". While ESTOC believes that SCENIHR should not dismiss the potential risks of pancreatic cancer, the

Committee's draft view on pancreatic cancer does not reflect the inconsistency found between some of the studies. For example, Boffetta et al. (2005) reported only an increase in smokers using snus. Luo et al. (2007) reported only an increased pancreatic cancer risk and a significant trend by the amount of snus consumed, but did not observe an effect in both ever and never smokers. The Report determines that there is a dose-response trend of increasing pancreatic cancer risk by amount of snus consumed per day, but this conclusion does not reflect the comments of the authors of the Luo et al study who noted "the point estimates for the two dose categories above zero (1-9g and =>10g snus per day) did not differ greatly from each other." While Zheng et al. (1993) reported a relative risk of 1.7 in US smokeless tobacco users, Alguacil et al. (2004) found little or no relationship (OR1.1, 95% CI 0.4 -3.1) and Farrow et al.(1990), studying chewing tobacco use, reported a relative risk of 0.8. The Report also did not note three further studies all of which report no increase in pancreatic cancer risk associated with smokeless tobacco use: Williams et al. (1977), Falk et al. (1988), Ghadirian et al. (1991). As with CVD and snus use, additional high quality research on ST use and pancreatic cancer would be desirable to help clarify the reported inconsistencies.

### References

Q1. References cited but not included in the preliminary report. These have been emailed in pdf form to the SCENIHR Secretariat: Stephen S. Hecht et al, Similar Exposure to a Tobacco-Specific Carcinogen in Smokeless Tobacco Users and Cigarette Smokers. *Cancer Epidemiol Biomarkers Prev* 2007;16(8):1567-72 Dorothy K. Hatsukami et al, Evaluation of Carcinogen Exposure in People Who Used "Reduced Exposure" Tobacco Products. *J Natl Cancer Inst* 2004;96:844-52 Marita Broadstock, Systematic Review of the Health Effects of Modified Smokeless Tobacco Products. New Zealand Health Technology Assessment Report, Feb 2007 Volume 10 Number 1 ([www.ucr.uu.se/rikshia](http://www.ucr.uu.se/rikshia).) Register of Information and Knowledge about Swedish Heart Intensive Care Admissions 2000 report. Roger R. Williams, and John W. Horm, Association of Cancer Sites with Tobacco and Alcohol Consumption and Socioeconomic Status of Patients: Interview Study from the Third National Cancer Survey. *J Natl Cancer Inst* 1977;58:525-547 Roni T. Falk et al, Life-Style Risk Factors for Pancreatic Cancer in Louisiana: A Case-Control Study. *American J of Epidemiol* Vol.128, No.2 p324-336 Parviz Ghadirian et al, Tobacco, Alcohol, and Coffee and Cancer in Quebec, Canada. *Cancer* 1991 67:2664-2670

### Question 2

**Do you agree with the response given ?**

Mostly agree

### Question 3

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

It is important to state that ST products are not designed for use as smoking cessation aids. All ESTOC members' ST products are potential harm reduction products. Such products offer consumers a tobacco use alternative to smoking, whereas pharmaceutical nicotine replacement products are expressly marketed for cessation. It is for governments to determine whether ST products should be included in tobacco health policy for this purpose based on all of the available evidence including both clinical and observational data. The

terms of reference asks whether "...smokeless tobacco may constitute a smoking cessation aid comparable to pharmaceutical....", whereas the abstract and the Summary are focused on efficacy and conclude that there are no randomized trials and, therefore, no conclusions can be drawn. However, the terms of reference do not specifically mention "efficacy", they state "comparable to", in which case there is observational data from both Sweden (e.g. Ramström & Foulds, 2006) and Norway (Tall om Tobakk 1973-2006) which report that snus is, in fact, used much more often in those countries as a successful smoking cessation aid than pharmaceutical products. There is a discrepancy between the Report and the Summary in how the available scientific data are described. The Report correctly states (p103) that "Observational data from Sweden indicate that snus has been used more often than pharmaceutical nicotine products by some men as an aid to stop smoking. The data are consistent in demonstrating these male snus users are more likely to quit smoking than non-users". The Summary (p10), on the other hand, describes the same set of scientific data as "The results of these studies are inconsistent", thus failing to reflect the Committee's conclusions in the body of the Report. The following published papers, while relevant, are either not mentioned in the Report or some of their results have not been fully considered\*:

- \*Lindström et al (2002): A cohort of c. 12,000 individuals was followed for one year to assess determinants of smoking reduction/cessation among baseline smokers. Snus users were more likely to quit or substantially decrease their smoking than non-users. The authors also concluded that snus use may explain part of the increase in smoking cessation among men as opposed to women in Sweden.
- \*Furberg et al (2005): This cross-sectional survey was based on c. 15,000 male twins from the Swedish Twin Registry. Regular use of Swedish snus was strongly associated with being a former smoker (OR: 3.7, 95% C.I. 3.3-4.2).
- Hjalmarsson & Saloojee (2005): A national survey of 1,000 Swedish psychologists provided evidence that snus use was associated with smoking cessation among male psychologists
- Stratelis et al (2006): This was a prospective smoking cessation study among c. 500 smokers screened for COPD. The protocol intervention consisted of counselling and nicotine replacement therapy and/or bupropion. Despite this intervention, the most common cessation aid among those who actually managed to quit was non-protocol Swedish snus.
- Sosial- och helsedirektoratet (Norwegian Board of Health and Welfare): Tall om tobakk 1973-2006 (2007): This compilation of annual, national surveys on tobacco use in Norway showed that among smokers who managed to quit between 1990 through 2006, snus was the most commonly reported cessation aid (17%), compared to nicotine gum (10%), nicotine patch (4%), bupropion (3%), and contact with a telephone quit line (1%), (p 29, Figure 24).

In discussing the Helgason study (p. 103) the Report fails to mention that the atypical results for snus are probably explained by the fact that the telephone helpline through which the informants were recruited actively discouraged smokers from using snus as an aid in smoking cessation ([www.sluta-roka-linjen.org](http://www.sluta-roka-linjen.org)). As a down-side of using snus as a quitting aid, the Report mentions that a proportion of those who quit smoking with the aid of snus become long-term users (p. 104). However, the Report fails to acknowledge that the same holds true also for nicotine replacement therapy. For example, in the Lung Health Study (Murray et al, 1998), 40% of those who quit using nicotine gum continued to use the product beyond 12 months, and 15% beyond five years.

## **References**

Q3 References cited but not included in the preliminary report. These have been emailed in pdf form to the SCENIHR Secretariat: Sosial- och helsedirektoratet (Norwegian Board of Health and Welfare): Tall om tobakk 1973-2006 (2007); Agneta Hjalmarsson & Yussuf Saloojee, Psychologists and tobacco: attitudes to cessation counselling and patterns of use. *Prev Med*, 2005; 41; 291-294 Georgios Stratelis et al, The impact of repeated spirometry and smoking cessation advice on smokers with mild COPD. *Scand J Prim Health Care*, 2006; 24:133-139 Robert P. Murray et al, Levels of cotinine associated with long-term ad-libitum nicotine polacrilex use in a clinical trial. *Addictive Behav*, 1998, 23;4;529-535

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The report from Norway (Tall om tobakk, 1973-2006) includes data that is of relevance to this question. Fig 16 on p 18 illustrates that despite the rapid increase in snus use during the last 10-15 years in Norway, the proportion of users of any tobacco product has actually decreased since the late 1990s. This illustrates that availability of snus does not necessarily mean that overall tobacco use will increase.

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The Summary states that "societal and cultural differences" precludes extrapolations of the results from one European country to another. The report does not however provide detail of these differences. The findings from the epidemiological modelling study performed by Gartner et al. (2007), to assess the role Swedish snus might play for tobacco harm reduction in the Australian population should be considered in the context of answering a question on extrapolating patterns of ST use. Australians could be considered as having many "societal and cultural differences" to people from Sweden and yet Gartner's study concluded that there are substantial health gains to be had by smokers who switched to snus rather than continuing to smoke and that this could result in a net benefit to the population if enough inveterate smokers did so. Specifically, the study stated that "for net harm to occur 14-25 ex-smokers would have to start using snus to offset the health gain from every smoker who switched to snus rather than continuing to smoke. Likewise, 14-25 people who have never smoked would need to start using snus to offset the health gain from every new tobacco user who used snus rather than smoking". The magnitude of these figures are in line with those extrapolated from the 'Risk/Use Equilibrium' of Kozlowski et al. (2001). Using this equilibrium it can be calculated that for a product such as Swedish snus which has been estimated as having at least a 90% lower risk than cigarettes, for every individual that uses cigarettes, 10-19 times the number of individuals would have to use Swedish snus to achieve an equal level of population risk. Extrapolations are possible but not necessarily reliable. The only way to determine the effect oral tobacco products, such as snus, will have on tobacco use patterns in EU Member States where the product is not available is by making it available with stringent post-market surveillance in place. This would allow governments to monitor the product's effects and make their decisions for tobacco health policy based on the predicted public health impact from the surveillance.

**References**

Q5 References cited but not included in the preliminary report. These have been emailed in pdf form to the SCENIHR Secretariat: Lynn T. Kozlowski et al, Applying the risk/use equilibrium: use medicinal nicotine now for harm reduction. *Tob. Control*, 2001; 10; 201-203

**Submission: 19**

**Name**

Mark Beamish

**Organisation**

Council of European Dentists (European Professional Association, ASBL)

**Question 1**

**Do you agree with the response given ?**

Agree

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The CED agrees with the answer given but would like to make the following comments: Smokeless tobacco is not appropriate for smoking cessation, because the nicotine dose from it is much higher than from nicotine replacement therapy: ST leads to stronger nicotine addiction, when the purpose of therapy should be tobacco cessation. Nicotine replacement therapy can be used even for smokeless tobacco cessation. Individual and group counselling by health personnel, and pharmaceutical products, like nicotine replacement therapy, bupropion and varenicline, are well documented aids for smoking cessation. They contain no carcinogenic or other toxic compounds like smokeless tobacco. Policies supporting smoking prevention and cessation have decreased significantly the smoking prevalence in western countries. Marketing smokeless tobacco in European Union countries to decrease smoking lacks scientific evidence. EU should support proven, safe means for tobacco prevention and cessation.

**Question 4**

**Do you agree with the response given ?**

Agree

**Question 5**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The CED mostly agrees with the answer given but would like to make the following comments: There are claims that in Sweden wide use of smokeless tobacco is in connection with decreased smoking prevalence among men. In Finland smoking prevalence among men has decreased from 33 % in 1988 to 26 % in 2005. In Sweden, if both smokers and snuff users are counted, 43 % used tobacco in 1988-89 and 37 % in 2004-05. This suggests less tobacco use in Finland than in Sweden. Anyhow, the data are not fully comparable. There is a possibility that free availability of smokeless tobacco in EU could increase consumption of

tobacco products as a whole.

**References**

1. Health Behaviour among the Finnish Adult Population, National Public Health Institute, 1979-2005. [www.ktl.fi](http://www.ktl.fi)
2. Use of alcohol and tobacco. Statistics Sweden 2007. <http://www.scb.se/statistik/publikationer>.

**Submission: 20**

**Name**

Kurt Aigner, M.D.

**Organisation**

Austrian Council on Smoking and Health (NGO)

**Question 1**

**Do you agree with the response given ?**

Agree

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Agree

**Question 5**

**Do you agree with the response given ?**

Agree



## **Submission: 21**

### **Name**

Pekka Puska, Director General KTL Kristiina Patja, MD, PhD, tobacco and health coordinator, senior researcher

### **Organisation**

National Public Health Institute, KTL Finland (Public Authority)

### **Question 1**

#### **Do you agree with the response given ?**

Mostly agree

#### **Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Scientific committee on emerging and newly identified health risks (SCENIHR) has produced a preliminary report on health risks of smokeless tobacco products (STP). The health impact of STP will depend on multiple uncontrolled factors including marketing of tobacco products within the country, cultural acceptability of the product, abuse of tobacco industry in the marketing of tobacco products, price and within the products: addictive capacity and harm profile of different STP. In this report, public health gains are stated possible, but many uncertainties remain and a large number of studies referred are low quality. The report concentrates on chemical constituents of STP, which are indeed large in magnitude. Toxins are numerous and potential health harms numerous. Therefore it is interesting, that there are only few prospective cohorts available and special caution needs to be taken, when judging public health effects of STP. Finland is a neighbouring country of Sweden, where STP is sold legally. Questions relevant to Finland when estimating the opening the market to STP are: • Does STP harm health? • Who will be the users of STP? • What is the impact of STP on smoking among the general population, in sexes, age groups and socio-economic groups? • Specifically, what is the impact of STP on three main domains of tobacco use prevalence: initiation, cessation and tobacco use patterns of successive cohorts • How consumers will be able to make judgements on STP when research is conflicting? • Consumers and communication: How the differences between products will be outspoken and understood? • Will STP increase tobacco consumption? We want to comment upon the methodology used in the report. Public health decisions rely in large on scientific research. In current last decades, there has been a request for more transparent evaluation of scientific evidence in clinical settings in a systematic way: evidence based medicine (EBM) (1). This statement would have clearly benefited from methodology of EBM opening the search strategies, stakeholders and grading the quality of studies. There are widely used tools for this purpose like e.g. <http://www.agreetrust.org/instrument.htm> of [www.cocnhrane.org](http://www.cocnhrane.org). Typically, strength of recommendation is communicated by a scale from A to D, drawn from the level of evidence and "considered clinical judgement". This includes the size and consistency of the body of evidence, its applicability, clinical impact (including economic factors) and generalisability (which takes the values of the target population into account (Scottish Intercollegiate Guidelines (SIGN), a brief description of the SIGN approach) <http://www.sign.ac.uk/>. Grading the quality of studies would have given the public health decision makers, clinicians and the general public guidance in their interpretations of weight of the studies in their decisions. We propose that transparent evaluation methods would be used in judgements on public health items in the future.

### **References**

Montori VM, Guyatt GH. What is evidence-based medicine and why should it be

practiced? Respir Care. 2001 Nov; 46(11): 1201-14.

### Question 2

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

No comment on this matter. Nicotine is addictive in all forms.

### Question 3

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Impact on quitting smoking and STP Cessation interventions of STP have been very few with mixed results both in quit rates and withdrawal symptoms. However, tobacco users are not only smokers or only STP users, but switching between products and simultaneous use many tobacco products is common. Moreover, our understanding of STP addiction is yet limited even in defining and measuring the components of specific areas of STP addiction. (12). In countries, where STP use is legal, there is a need for high quality research evaluating interventions to promote cessation of smokeless tobacco use (13). There are no randomised controlled trials on quitting snuff or using snuff as tool for quitting smoking and tobacco use. In Sweden, policy seems to have lead into dichotomy situation, where males switch to snus and women either quit or do not start, but in the end there has been a slow increase in tobacco consumption in Sweden. As women in Sweden are decreasing smoking via both not initiating and quitting, without mixed message of snuff, this could have been possible for Swedish males too. Most likely STP will undermine tobacco cessation efforts. Conclusion: STP products have not shown efficacy in promoting quitting tobacco use or smoking cessation.

### References

Eg. 12. Thomas JL, Ebbert JO, Patten CA, Dale LC, Bronars CA, Schroeder DR. Measuring nicotine dependence among smokeless tobacco users. Addict Behav. 2006 Sep; 31(9): 1511-21.

### Question 4

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Impact of tobacco use on subsequent initiation of smoking There is one study in Sweden looking the impact of snuff on initiations of STP and smoking. Statement quotation: "Order of initiation with snus or cigarettes is a predictor of progression of tobacco use among female adolescents, but not among male adolescents. Young age and initiation with both tobacco types very close in time predict escalation of use" is based on one cohort study. The risk of becoming a daily smoker among boys was 2.54, 95% CI=1.68-3.91 fro those using both snus and cigarettes and from cigarette starters 1.42, 95% CI=0.98-2.10 (6). In this cohort, every fifth boy was using both snus and cigarettes during one year follow up. One has to keep in mind, that STP use studies from US have reported later initiation of STP than smoked tobacco (7). In Finland, snus has become alternative for athletes willing to use

tobacco (13) and there is some indications, that some part of this population will smoke later in their life (13, 14). Two retrospective studies conducted in Sweden on Swedish snus, arrive at a different conclusion, but there are several methodological problems in using retrospective smoking status at the population setting. Generally retrospective studies produce more positive results than prospective studies or randomised control trials, which was learned in the case of hormone replacement therapy and mortality (8, 9) with extensive number of cohort studies showing benefit, but later shown opposite by RCT studies with thorough follow up. Conclusion: At this point, there is some evidence on impact of initiation of STP at adolescence on later daily smoking in adulthood from US (10, 11), which does imply, that STP markets should not be opened in new countries. STP use starts in adolescence and as tobacco use habits are not stable, it may later lead to use of smoked tobacco too.

### **References**

7. Riley WT, Kaugars GE, Grisius TM, Page DG, Burns JC, Svirsky JA. Adult smokeless tobacco use and age of onset. *Addict Behav.* 1996 Jan-Feb;21(1):135-8. 8. Kunz R, Oxman AD. The unpredictability paradox: review of empirical comparisons of randomised and non-randomised clinical trials. *BMJ.* 1998 Oct 31;317(7167):1185-90. 10. Tomar SL, Asma S. Smoking-attributable periodontitis in the United States: findings from NHANES III. National Health and Nutrition Examination Survey. *J Periodontol.* 2000 May;71(5):743-51. 11. Tomar SL, Winn DM. Chewing tobacco use and dental caries among U.S. men. *J Am Dent Assoc.* 1999 Nov;130(11):1601-10. 13. Alaranta A, Alaranta H, Patja K, Palmu P, Prattala R, Martelin T, Helenius I. Snuff use and smoking in Finnish olympic athletes. *Int J Sports Med.* 2006 Jul;27(7):581-6. 14. Huhtala HS, Rainio SU, Rimpela AH. Adolescent snus use in Finland in 1981-2003: trend, total sales ban and acquisition. *Tob Control.* 2006 Oct;15(5):392-7. 15. Karvonen JS, Rimpela AH, Rimpela MK. Modernization and smoking-regional differences in adolescent smoking in Finland in 1977-1987. *Scand J Soc Med.* 1993 Sep;21(3):188-96.

### **Question 5**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Impact on tobacco consumption Tobacco products are all addictive and consist of toxic substances. Tobacco use has been bound into culture, thus there is a rapid change going in the use of tobacco in the EU region: tobacco use decreases steadily. Smoked cigarettes are vast the most dangerous form of tobacco and tobacco industry is constantly building also new smoked and non-smoked products to confuse consumers about health risks of tobacco products. The concept of risk in health is difficult to communicate with the general public if message is unclear and competing messages are most likely to overpower. This has been the case in tobacco marketing and counter marketing throughout the short history of tobacco. Impact of this can be seen in Sweden, where older age groups have quit smoking equally to other countries neighbouring them, but younger generations have adopted a new form of tobacco use, marketed to them freely until 1994. As report states at page 11. it is not possible to assess future patterns of tobacco use across countries, but opening markets to a new product will cut the decrease of tobacco products. For instance, there has been a constant decrease of 1.5 grams per year per every 15-year-old in Finland (Figure 1.), which has not happened in Sweden (Figure 3, page 32). More over, there is indications, that lower socio-economic groups are more keen to STP than higher (Figure 13, page 36). This report does not present any other data on trends of tobacco use in the different subpopulations. Figure 1. Smoking prevalence in Finland and tobacco consumption in tons per every 15-

year-old from 1950 to 2007. In Finland in 1959 76% of men smoked, 13% of women and consumption per every 15-year-old was 19,6 tons. In 1980 figures were 35%, 17% and 21,29tons. In 2004 27,1% , 19,5% and 11,65 tons. This trend did not occur in Sweden. Conclusion: Bringing a new tobacco product to market will most likely increase the tobacco consumption or at least cut the ongoing decrease. In Sweden, new users have been young never-smoking males and middle-aged males switching products. There is no data on trends socio-economic, but price policy in Sweden has favoured snuff, which seems to attract more low SES groups to tobacco use. Consumer communication The society does not have moral obligations to engage itself to evidence for all tobacco industry's innovations to market tobacco products. The basic principle of consumer safety notes, that responsibility of proof for safety and efficacy lies on the producer, but not on the public health policy and society. Marketing of the tobacco industry is aimed at future generations and in Sweden they have succeed in this by increasing the use of tobacco among younger age cohorts of males. It is very difficult to discuss about health risks and when STP is marketed even in the public discussion as less harmful that will be interpreted by a certain part of public as non-harmful. Tobacco industry has been skilful in using conflicting research for its purposes and there is no indication, that it will not be able to do it again. Recent development with so-called PREPS (with lower amounts of carcinogens) and light and ultra-light cigarettes in the 1970s and 1980s have been using the same technique (14). STP will offer a great vehicle for misleading marketing and perhaps lowering a threshold for PREPS. One suggestion has been tighter control of nicotine and tobacco products, but lessons learned from light-cigarette hoax have not been encouraging. Investing into large scale prevention, cessation promotion and decreasing availability and increasing price has been shown to be most effective tools in tobacco prevention (15, 16). Conclusion: Mixed consumer messages will foil the aim of reducing tobacco use and burden of disease. In conclusion STP do harm health. They will tempt new users without a smoking history. A particular concern is their potential to have new generations of Finns addicted to nicotine and thus also as potential new smokers. There is limited information of the impact of STP on smoking among the general population and different parts of population (sex, age groups and socio-economic groups). They have the potential to reduce quitting of tobacco products and abate willingness to cessation. STP have not shown efficacy in promoting quitting tobacco use or smoking cessation. New products will tempt new users. There is some evidence on impact of initiation of STP at adolescence on later daily smoking in adulthood. Bringing a new tobacco product to market will most likely increase the tobacco consumption or at least cut the ongoing decrease. Tobacco products, their price and sales should be regulated more strictly with EU. All marketing needs to be banned. New products entering the market are not favoured if old products remain. There is no safe form of tobacco and public should not be exposed to tobacco industry. The tobacco free society is our long term aim.

## **References**

[http://www.stat.fi/til/tup/index\\_en.html](http://www.stat.fi/til/tup/index_en.html)

**Submission: 22**

**Name**

Kurt AIGNER, MD, FCCP (Individual)

**Question 1**

**Do you agree with the response given ?**

Agree

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Agree

**Question 5**

**Do you agree with the response given ?**

Agree

**Submission: 23**

**Name**

Prof. Manfred Neuberger, M.D. (Individual)

**Question 1**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

<http://www.aerzteinitiative.at/Oraltabak040425.pdf>

**References**

Neuberger M, Aigner K, Dittrich P, Götz M, Maurer G, Mlczoch J, Oberfeld G, Schulte-Hermann R. Schäden durch Oraltabak. Österreichische Ärztezeitung 2004; 8: 44-45.

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Agree

**Question 5**

**Do you agree with the response given ?**

Agree

**Submission: 24**

**Name**

Dr Ian A. Bailey

**Organisation**

Imperial Tobacco Ltd (Business)

**Question 1**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

As a new entrant to the market, Imperial Tobacco appreciates the measured and scientific approach taken by SCENIHR in their analysis of smokeless tobacco. While we had no proprietary or unpublished information to submit to your review process, we would point out that relying on peer review as the only quality standard for admissibility of data and for the quality of the work assessed can result in the exclusion of high quality data for which publication may not have been sought, and the inclusion of poor quality data in journals where the standard of peer review is more political or based on nepotism than on sound science. Furthermore, a recent court case stressed the paramount importance of careful, expert sifting of the evidence rather than simple summarising of what exists [McTear vs Imperial Tobacco 2005, Court of Session, Edinburgh – Sections 6.160 & 6.161]. Scientific advice to Governments and Competent Authorities should be based on critical review of the primary literature and its evaluation by experts, rather than an uncritical gathering of publications. Imperial Tobacco sees the main difference between the various forms of tobacco as offered to consumers as the fact that in some cases human exposure is directly to tobacco and in others it is to smoke. Smoke contains many of the constituents present in tobacco. As the component or combination of components [as found in cigarette smoke] which may cause human disease remain unidentified despite decades of laboratory research, it is not yet possible to make comparative judgements relating the chemistry of different formats of tobacco product to disease causation. Specifically, the attention drawn by SCENIHR to TSNAs may not be adequately based. In their joint statement on the re-assessment of the toxicological testing of tobacco products in 2004, three authoritative advisory committees to the UK Department of Health (the Committee On Toxicology, Committee On Carcinogenicity and the Committee On Mutagenicity) commented “that tobacco smoke was a highly complex chemical mixture and that the causative agents for smoke induced diseases (such as cardiovascular disease, cancer, effects on reproduction and on offspring) were unknown. The mechanisms by which tobacco induced adverse effects were not established.” [www.advisory\_bodies.doh.gov.uk/cotnonfood/tobacco]. A similar situation applies to smokeless tobacco. We would point out that the reported effects of snus in relation to pancreatic cancer are unusual and inconsistent. Luo et al (2007) show inconsistent results in ever- and never-smokers and there is no real evidence of a dose response relationship. Oddly, Boffetta et al (2005) demonstrate an increase in pancreatic tumours in smokers using snus but not in non-smokers using snus. No increase in odds ratios, or a non-significant increase, was observed in six other studies named below. We agree that “on the available evidence it is difficult to identify overall relative risk estimates for the various adverse health effects from oral tobacco products as a whole because the products and conditions of use...vary widely.”

## References

Alguacil J, Silverman DT. Smokeless and other noncigarette tobacco use and pancreatic cancer: a case-control study based on direct interviews. *Cancer Epidemiol Biomarkers Prev* 2004;13:55-8. 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;114:992-5. Falk RT, Pickle LW, Fontham ET, Correa P, Fraumeni JF, Jr. Life-style risk factors for pancreatic cancer in Louisiana: a case-control study. *Am J Epidemiol* 1988;128:324-36. Farrow DC, Davis S. Risk of pancreatic cancer in relation to medical history and the use of tobacco, alcohol and coffee. *Int J Cancer* 1990;45:816-20. Ghadirian P, Simard A, Baillargeon J. Tobacco, alcohol and coffee and cancer of the pancreas. *Cancer* 1991;67:2664-70. Williams RR, Horm JW. Association of cancer sites with tobacco and alcohol consumption and socioeconomic status of patients: interview study from the Third National Cancer Survey. *J Natl Cancer Inst* 1977;58:525-47. Muscat JE, Stellman SD, Hoffmann D, Wynder EL. Smoking and pancreatic cancer in men and women. *Cancer Epidemiol Biomarkers Prev* 1997;6:15-9.

## Question 2

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Imperial Tobacco believes that the use of tobacco products can be characterised as addictive as the term is commonly used today. Some people find it difficult to stop, but we believe that it is important for them to realise that they are able to stop if they choose to do so. Millions of people have stopped smoking, the majority without assistance. Nicotine is one component of tobacco products which is thought to stimulate the central 'Reward' pathway, providing a pleasurable experience of tobacco usage [Wonnacott et al (2005) *Current Opinion in Pharmacology* 5:53-59]. However, there may not be a simple relationship between the quantity of nicotine and addiction, even allowing for the pharmacokinetics of different routes of exposure [Frenk H and Dar R 2000, *A critique of Nicotine Addiction*, Kluwer academic Publishers, Boston]. There is 'non-peer-reviewed' evidence that smokers prefer to smoke products with a tar to nicotine ratio close to ten to one. Products which vary far from that ratio tend not to be successful. The unpopularity or un-palatability of de-nicotinised products may be a result of this effect.

## Question 3

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Nicotine replacement therapies are by no means universally successful smoking cessation aids; studies show poor efficacy; measurement of their effectiveness has been cursory. For example, the efficacy of nicotine replacement therapy has been estimated to be less than 20% in Rose JE (2006) [Nicotine and non-nicotine factors in cigarette addiction. *Psychopharmacology* 184:274-285], and 7% above baseline in Silagy C et al (2003). [in Silagy C et al. Nicotine replacement therapy for smoking cessation. *Cochrane Database of Systematic Reviews* 2004, Issue 3.]. The UK experience in its National Health Service indicates that "long term quit rates for the services [NRT and Zyban] show about 15% of people remain quit at 52 weeks, which is comparable with earlier clinical trials" [NHS Stop Smoking Services, 30 July 2007 [www.dh.gov.uk/en/Policyandguidance/Healthandsocialcaretopics/Tobacco/Tobaccogeneralinf](http://www.dh.gov.uk/en/Policyandguidance/Healthandsocialcaretopics/Tobacco/Tobaccogeneralinf)



ormation/DH\_4002192. There is even less data on smokeless tobacco. It is therefore difficult to see how such a comparison can be made with any rigour. We therefore agree that "Due to insufficient evidence it is not possible to draw conclusions as to the relative effectiveness of smokeless tobacco as an aid to clinical smoking cessation in comparison with established therapies".

**Question 4**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

This is an extraordinarily complex question, encompassing a wealth of difficult to interpret studies on the initiation of smoking behaviour. We regard the results of these studies as indicating that individual adults choose to smoke for a variety of reasons within the complexities of culture and lifestyle. We therefore agree with the suggestion of "caution in translating findings across countries". However, we do support the freedom of adults to choose whether or not to smoke or to use other tobacco products.

**Question 5**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

We agree that "it is not possible to extrapolate future patterns of tobacco use across countries".

**Submission: 25**

**Name**

Lars E, Rutqvist, MD, Ph D Vice President - Scientific Affairs Swedish Match AB

**Organisation**

Swedish Match AB (Business)

**Question 1**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

It is unacceptable that the conclusions about genetic toxicology are based on unpublished documents with no references whatsoever to published studies. The conclusion in the Executive Summary "...Swedish moist snuff...cause mutations and chromosomal damage in bacterial and mammalian cell cultures..." (p. 9) thus lacks support from referenced data. Since the committee had access to the pending IARC report, appropriate references (if such exist) should have been given. This is particularly troublesome since the conclusions about carcinogenesis in experimental animals to a large extent is based on these alleged genotoxic effects. The animal data themselves are essentially negative or equivocal aside from the lip canal studies which the Committee itself finds methodologically dubious (p. 66). As it stands, the conclusion about carcinogenic effects in animals (p. 67) is based on a circular argument the elements of which are not supported by referenced data. There are several key elements in demonstrating causality in observational studies. Some of the most important is strength, consistency and biologic gradient (which the Committee itself acknowledges in the section on Methodology, p 14). Against this background, it is inconsistent that the report does not acknowledge that the associations between snus and pancreatic cancer in the Bofetta and Luo studies fail to demonstrate these elements. For example, the reported relative risks with snus are not very high (which indicates that different types of bias cannot be ruled out to explain the observed associations), in the Bofetta study an association was only observed among smokers whereas the Luo study found an association among non-smokers, and there were no clear dose-effect relationships. Given these observations, it is unreasonable to describe the studies as having conclusively demonstrated pancreas to be "a main target organ" (p 9). This wording also implies that there are other "target" organs, whereas the no association between Swedish snus and any other cancer site is concluded in the report. The statement that one Swedish study has demonstrated an increased risk of head-neck cancer associated with snus among never-smokers is a misrepresentation of science. The Lewin et al (1998) study presented odds ratios for this subset, but those figures were only published to illustrate the lack of statistical power in such analyses. The estimates were based on only nine exposed cases (of which three were oral cancer cases), and they were not adjusted for alcohol intake (which was a confounder in the Lewin study) or any other potential confounder. Given these methodological problems, the Lewin study cannot be quoted as unequivocal evidence of an association between snus and any type of head-neck cancer among never-smokers. It is inconsistent that the committee does not cite the absence of randomized trials as an obstacle to firm conclusions about causality. In the section about snus as a smoking cessation aid the lack of randomized trials is described as a significant impediment to such conclusions. Randomized trials may be needed to reliably

distinguish small (although clinically worthwhile) effects of clinical interventions because of the risk of different types of bias in observational studies. But with Swedish snus, the quoted health effects are also small (relative risks <1.5-2), so the risk of bias is reasonably not materially different compared to the smoking cessation setting. The report concludes that there is a statistically significant but weak effect on fatal myocardial infarction (MI), that is, that snus usage is a negative prognostic factor among MI patients. However, the Committee itself points out that the presence or absence of statistical significance should only be one factor in the evaluation of different studies. Reliable identification of prognostic factors in MI patients requires data on potential confounders, whereas no data on such factors are available from the Construction Worker Cohort which is the only data set for which a significant increase of fatal MI have been reported. The report should acknowledge that, in contrast to smoked tobacco products, health effects related to environmental tobacco smoke or smoking-related fires are not issues with smokeless tobacco products. The Committee goes beyond the Terms of Reference when it concludes that "STP... have higher levels of carcinogenic nitrosamines than any consumer product used orally" (p 111). The Terms of Reference does not ask for comparisons to be made with "any consumer product". If such comparisons of health effects are considered relevant, it would seem reasonable to use cigarettes as a comparator. The Report also fails to provide any scientific documentation to support the statement and does not acknowledge the fact that the levels of many other potentially toxic and/or carcinogenic substances in snus are lower than in many commonly used food-stuffs.

**Question 2**

**Do you agree with the response given ?**

Mostly agree

**Question 3**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

There is an inconsistency between the Report and the Executive Summary. The Report correctly states (p. 103) that "Observational data from Sweden indicate that snus has been used more often than pharmaceutical nicotine products by some men as an aid to stop smoking. The data are consistent in demonstrating these male snus users are more likely to quit smoking than non-users". However, in the Executive Summary (p. 10) the same data are described as "The results of these studies are inconsistent". The report should acknowledge that there is a plausible biologic rationale for snus as an effective smoking cessation aid: it delivers nicotine (more so than nicotine replacement therapies, fig 27, p. 47) and self-administration of pharmaceutical nicotine has been shown to improve long-term smoking quit rates in randomized trials. The nicotine in nicotine replacement therapies is produced from tobacco leaves so there is no biologic difference between the nicotine in such therapies and in snus. The following published papers are not mentioned or are referenced in a biased way in the report. They further support Swedish snus as an effective aid in smoking cessation: Lindström et al (2002): A cohort of c. 12,000 individuals was followed for one year to assess determinants of smoking reduction/cessation among baseline smokers. Snus users were more likely to quit or substantially decrease their smoking than non-users. The authors also concluded that snus use may explain part of the increase in smoking cessation among men as opposed to women in Sweden. The text on p 102

describing the study is obscure and it might erroneously be interpreted as providing no support for snus as an effective quitting aid. Furberg et al (2005): This cross-sectional survey was based on c. 15,000 male twins from the Swedish Twin Registry. Regular use of Swedish snus was strongly associated with being a former smoker (odds ratio: 3.7, 95% C.I. 3.3-4.2). Hjalmarsson & Saloojee (2005): A national survey of 1,000 Swedish psychologists provided evidence that snus use was associated with smoking cessation among male psychologists Stratelis et al (2006): This was a prospective smoking cessation study among c. 500 smokers screened for COPD. The protocol intervention consisted of counselling and nicotine replacement therapy and/or bupropion. Despite this intervention, the most common cessation aid among those who actually managed to quit was non-protocol Swedish snus. Socialstyrelsen (Swedish National Board of Health and Welfare): Folkhälsorapport 2005. The national survey on public health, p302. The survey quotes population-based data indicating that for every snus user who starts to smoke, there are four smokers who quit smoking with the aid of snus. Sosial- och helsedirektoratet (Norwegian Board of Health and Welfare): Tall om tobakk 1973-2006 (2007): This compilation of annual, national surveys on tobacco use in Norway showed that among smokers who managed to quit between 1990 through 2006, snus was the most commonly reported cessation aid (17%), compared to nicotine gum (10%), nicotine patch (4%), bupropion (3%), and contact with a telephone quit line (1%), (p 29, Figure 24). The report states that the lack of randomized clinical trials of snus as a smoking cessation aid precludes firm conclusions about its efficacy. However, most smoking cessation occurs outside of clinical settings for which results of observational studies may be more relevant. In discussing the Helgason study (p. 103) the report fails to mention that the atypical results for snus, probably were affected by the fact the telephone helpline through which the informants were recruited actively discourages smokers from using snus as an aid in smoking cessation ([www.sluta-roka-linjen.org](http://www.sluta-roka-linjen.org)). As a down-side of using snus as a quitting aid, the report mentions that a proportion of those who quit smoking with the aid of snus become long-term users (p. 104). However, the report fails to acknowledge that the same holds true also for ad libitum nicotine replacement therapy. For example, in the Lung Health Study (Murray et al, 1998), 40% of those who quit using nicotine gum continued to use the product beyond 12 months, and 15% beyond five years. Given the chronic nature of nicotine addiction, it is perhaps necessary in some quitters to continue nicotine treatment for an extended period of time in order to prevent smoking relapse. This implies that long-term use may have beneficial effects in some individuals.

## **References**

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2. Furberg H, Bulik CM, Lerman C, et al. Is Swedish snus associated with smoking initiation or smoking cessation. *Tobacco Control* 2005; 14: 422-424
3. Hjalmarsson A, Saloojee Y. Psychologists and tobacco: Attitudes to cessation counselling and patterns of use. *Prev Med* 2005; 41: 291-294
4. Stratelis G, Mölsted S, Jakobsson P, Zetterström O. The impact of repeated spirometry and smoking cessation advice on smokers with mild COPD. *Scand J Primary Health Care* 2006; 24: 133-139
5. Socialstyrelsen (Swedish National Board of Health and Welfare): Folkhälsorapport 2005. Stockholm, 2006
6. Sosial- och helsedirektoratet (Norwegian Board of Health and Welfare): Tall om tobakk 1973-2006. Oslo, 2007
7. Murray RP, Nides MA, Istvan JA, et al. Levels of cotinine associated with long-term ad libitum nicotine polacrilex use in a clinical trial. *Addiction Behaviors* 1998; 23: 529-535

## **Question 4**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The report correctly notes that the Swedish data are consistent in showing that snus is not a gateway to smoking, rather a gateway from smoking. This is further reinforced by the Swedish National Survey on Public Health 2005 which quotes population-based data indicating that for every snus user who starts to smoke, there are four smokers who quit smoking with the aid of snus (p 302). The Norwegian Board of Health and Welfare's compilation of annual, national surveys on tobacco use in Norway (Tall om tobakk 1973-2006, 2007) also illustrates that despite the rapid increase of snus use during the past 5-10 years in Norway, the overall prevalence of tobacco users is going down. This observation contradicts the speculation about snus as a gateway to smoking and increased overall population tobacco use in a setting where snus is available. The statement in the Abstract's general conclusions (p 4) "...data on progression from STP into smoking are inconsistent" is a biased description of the available science and is not consistent with the Executive Summary or the Report itself. The Swedish data are fully consistent which is correctly noted. It is only the American data which are inconsistent with some authors claiming STP to be a gateway to smoking (e.g. Haddock et al, 2001 and Tomar et al 2003) and some refuting this hypothesis (e.g. O'Connor et al 2003). The description of the O'Connor data on p 101 is unscientific: "...reduced the number of observations.....Hence (the results) did not reach statistical significance...". If an observation is not statistically significant, this should be interpreted to mean that it may have occurred simply by the play of chance alone with no underlying difference between the populations or data sets being compared. It is impossible to know beforehand what the point estimate and corresponding confidence interval will be if a data set is expanded. As it stands, the text erroneously implies that O'Connor's result would have been statistically significantly positive had the numbers been greater.

**Question 5**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

While it is, in a strict sense, not possible to accurately predict the future of any cultural phenomenon, it would have been appropriate by the Committee to reference more extensively the experiences from Norway. In that country snus use was uncommon until 10-15 years ago, but has increased quite rapidly in recent years. In the compilation of annual tobacco statistics for 1973-2006 (Tall om Tobakk), the Norwegian Health and Welfare Authority reports that snus was the most common cessation aid among smokers who quit between 2000 through 2006. In this respect, Norway emulates the Swedish experience as reported by Ramström & Foulds (2006). The Norwegian report also notes that (p 18), despite the increase in snus use since the mid 1990s, the overall proportion of adult tobacco users in the population is decreasing. This is the case also in Sweden ([www.statveca.com](http://www.statveca.com)). These observations should be mentioned in conjunction with the Report's speculations about the possible uptake of snus among new tobacco users who would otherwise never have smoked (p. 108). The committee fails to mention which "societal and cultural differences" it believes precludes extrapolations of tobacco trends between Sweden and neighbouring countries such as Finland and Denmark. In fact, the report provides no scientific rationale for

this conclusion. The committee should acknowledge the fact that there are several examples from the past where cultural patterns, for instance, dietary habits and patterns of alcohol usage, have changed in Europe as a result of influences from other countries.

**References**

1. Sosial- och helsedirektoratet (Norwegian Board of Health and Welfare): Tall om tobakk 1973-2006. Oslo, 2007 2. VECA-HB. Nordic Tobacco Statistics 1970-2004. Smoking and snus prevalence, consumption of smoking tobacco and snus, price movements and consumer spending in Sweden, Norway, Denmark, Finland and Iceland. Statistical Bureau VECA-HB, Statistical report 2005-09-30, Stockholm, [www.statveca.com](http://www.statveca.com).

**Submission: 26**

**Name**

Margarida Silva

**Organisation**

European Respiratory Society (Medical and scientific society)

**Question 1**

**Do you agree with the response given ?**

Disagree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

We agree with the opening statement in the summary that STP vary considerably in their content and associated health effects. In these circumstances, scientific convention is to summarise effects within the main different subgroups, and we suggest that this should be done in this report. The most widely used groups of STP are probably the oral products used in Asia (which often include other non-tobacco products, such as betel or areca nut, which may also have adverse effects on health); North American STP; and Swedish snus. The adverse health effects of Asian products are substantial; those of Swedish snus much less so 1. We found the statement in the summary that STP have a statistically significant but weak effect on myocardial infarction misleading. The INTERHEART study shows a substantial (more than twofold) risk of myocardial infarction associated with what, in the context of the study, was predominantly Asian STP use 2, and although some of this effect could be due to betel or areca, it is clearly an important risk. In contrast, the highest estimates of relative risk of infarction with Swedish STP are around 1.4 (see section 3.6.3.1), so are lower than for Asian STP. Many of the studies of Swedish STP listed in that section show no significant effect. The reported effects of Swedish STP on fatal infarction, which have been chosen for highlighting in the summary, have in some cases seemingly arisen from post-hoc subgroup analyses (and are therefore of doubtful validity), and sometimes in the context of a reduced overall risk of myocardial infarction. For example, Huhtasaari et al report an adjusted odds ratio for fatal myocardial infarction of 1.5, which is non-significant (95% CI 0.5-5.0), but for all myocardial infarction of 0.6, which was a significant (95% CI 0.4-0.9) reduction 3. Hergens reported odds ratios of 1.0 for both fatal and non-fatal myocardial infarction in one study 4 (a higher odds ratio was observed in further subgroup analysis, but as section 3.6.3.1 correctly points out, this observation was based on only three deaths), and in a more recent cohort study report a significant effect on fatal infarction only in the subgroup with the highest use of snus, in a table that alone includes 21 different hypothesis tests 5. No adjustment appears to have been made in these papers for the multiple tests carried out. We therefore question the statistical significance of these observations, and wonder why this result has been chosen to be highlighted with this statement in the summary. Section 3.6.3.1 however provides an informative overview of the evidence, on the basis of which we would suggest that if this concern is to be highlighted at all, a more dispassionate synthesis such as that by Broadstock 6, that "a slightly increased risk of sudden death cannot be excluded" would be more appropriate. We are surprised that the summary does not comment on the risk of stroke. We are also surprised that the health effects of commonly used additives, such as betel and areca, are not discussed in section 3.4.2.2.

**References**

- 1 Critchley JA, Unal B. Health effects associated with smokeless tobacco: a systematic

review. *Thorax* 2003; 58:435-443. 2 Teo KK, Ounpuu S, Hawken S, Pandey MR, Valentin V, Hunt D, Diaz R, Rashed W, Freeman R, Jiang L, Zhang X, Yusuf S. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. *Lancet* 2006; 368:647-658. 3 Huhtasaari F, Lundberg V, Eliasson M, Janlert U, Asplund K. Smokeless tobacco as a possible risk factor for myocardial infarction: a population-based study in middle-aged men. *J Am Coll Cardiol* 1999; 34:1784-1790. 4 Hergens MP, Ahlbom A, Andersson T, Pershagen G. Swedish moist snuff and myocardial infarction among men. *Epidemiology* 2005; 16:12-16. 5 Hergens MP, Alfredsson L, Bolinder G, Lambe M, Pershagen G, Ye W. Long-term use of Swedish moist snuff and the risk of myocardial infarction amongst men. *J Intern Med* 2007; 262:351-359. 6 Broadstock M. Systematic review of the health effects of modified smokeless tobacco products. Christchurch: New Zealand Health Technology Assessment; 2007.

### **Question 2**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

STP deliver nicotine much more slowly, so are likely to be less powerfully addictive than smoked tobacco. Section 3.6.1.2 reflects this, and the summary should do the same. The summary also states that "withdrawal symptoms are similar to those seen in smokers", which is not entirely true since in the report this same sentence (page 73) ends with "with the exception of depressed mood or negative affect", which is an important point to consider in relation to addictiveness.

### **Question 3**

**Do you agree with the response given ?**

Disagree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

We agree that without appropriate randomised controlled trial data, this question is difficult to answer. However the cohort data from northern Sweden reported by Rodu et al provide very strong observational evidence that Swedish snus has been used by men in that cohort as a substitute and/or cessation product by many male smokers 7. Ramstrom and Foulds have also reported observational data on smoking cessation, also from Sweden, showing that "Among men who used snus as a single aid, 66% succeeded in quitting completely, as compared with 47% of those using nicotine gum (OR 2.2, 95% CI 1.3 to 3.7) or 32% for those using the nicotine patch (OR 4.2, 95% CI 2.1 to 8.6)" 8. We think these studies provide strong evidence that Swedish STP have been used effectively as cessation products and are surprised that the conclusion instead reports only 'aggregate' data on national smoking trends. We also point out that the decline in smoking prevalence in Swedish men described in the report is substantially greater than that in women, which discounts the given explanation that the decline in both sexes is due to other tobacco control measures. If so the decline would be expected to be similar in both sexes. In Sweden it is not, and the used of snus is the only recognised alternative explanation for the greater reduction in men. The data from Norway however do show similar declines in prevalence in men and women, despite the availability of snus, but uptake of snus by Norwegian men is low in relation to that in Sweden. This is not discussed. We do not consider that the Norwegian data provide conclusive evidence that the availability of STP will not have a beneficial effect on smoking prevalence.



## **References**

7 Rodu B, Stegmayr B, Nasic S, Asplund K. Impact of smokeless tobacco use on smoking in northern Sweden. *J Intern Med* 2002; 252:398-404. 8 Ramstrom LM, Foulds J. Role of snus in initiation and cessation of tobacco smoking in Sweden. *Tobacco Control* 2006; 15:210-214.

## **Question 4**

**Do you agree with the response given ?**

Disagree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The Swedish data outlined in the report indicate that snus is far more likely to be used as an exit than an entry product in relation to smoking, and an example of this evidence is provided by Ramstrom and Foulds 8. The answer given in the report prevaricates with a section on risk behaviours, acknowledges the Swedish data, and comments on the need for caution in translating findings across other countries. The remit of the committee and of this consultation is stated clearly to be to deal with the science, not policy or risk management, so the final sentence of the summary of the response to this question (and related sections in the report) should be removed.

## **References**

Ramstrom LM, Foulds J. Role of snus in initiation and cessation of tobacco smoking in Sweden. *Tobacco Control* 2006; 15:210-214.

## **Question 5**

**Do you agree with the response given ?**

Disagree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The existence of different patterns of use of STP in general, and particularly their use by smokers, is likely to reflect different cultural attitudes to tobacco, and different perceptions of the relative risks of these products. If a product is made available in society with harsh warnings on risk it is likely to be much less widely used than if it is perceived to be and endorsed as an acceptable and safe alternative to smoking. The latter appears to be the case in Sweden. None of the likely explanations for the different patterns of use of STP in different countries and cultures are discussed or addressed in any detail. We perceive this to be a major failing of the report. Extrapolation, like all prediction, is by nature subject to error but the committee could have done a great deal more to explain and estimate the likely impacts of the introduction of STP on public health in countries with no major past STP use. The point of this argument, and the reason for the interest of the ERS in this debate, is that tobacco smoking causes more respiratory disease, and causes more deaths from respiratory disease than any other known avoidable factor. Preventing or reducing the harm caused by smoking is therefore a major priority for us. We therefore support the principle of applying harm reduction strategies to smoking in the EU and acknowledge, with serious reservations, that smokeless tobacco products may have a role to play in this approach since the two biggest killers from respiratory disease caused by smoking (lung cancer and COPD) are not caused by STP. Given that it is also clear that STP are not safe, the only logic for allowing more widespread use would be if they prove to be effective harm reduction agents with a net benefit to public health. There is a substantial scientific literature on this harm reduction debate which is not extensively reviewed in the report. Finally, any changes in the regulation of STP in the EU should only be carried out following a comprehensive review of

the regulation of all tobacco and nicotine products and within a framework in which such products are regulated according to the level of harm they cause.

**Submission: 27**

**Name**

Mrs Gaëlle Labet

**Organisation**

Association of the European Self-Medication Industry (AESGP) (NGO)

**Question 1**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Concerning the carcinogen exposure, a very recent paper by Hecht and al. focused on the urine tobacco-specific carcinogen content in US smokeless tobacco users, in comparison with smokers. This real-life study provided very strong evidence ( $p < 0.0001$ ) for significantly higher nitrosamine levels in the urine of smokeless tobacco users. Some papers were also published very recently on the cardio-vascular associated risks of smokeless tobacco use. Their conclusions were that increased risk of CV disease is associated with tobacco use, regardless of the source (smokeless or cigarettes). In two studies (Hergens et al 2007, Wennberg et al 2007) about Swedish snuff use, the overall risk for myocardial infarction was not modified in the snuff using group, but the risk for fatal myocardial infarction was significantly increased. Finally, considering the effect on reproductive life, some additional studies not mentioned in the full text report, but in line with the overall conclusions are provided (England 2003, Gupta 2004, Gupta 2006).

**References**

Gupta PC, Subramoney S. Smokeless tobacco use and risk of stillbirth. A cohort study in Mumbai, India. *Epidemiology*, 2006; 17 (1): 47-51  
Hecht SS, Carmella SG, Murphy SE, Riley WT, Le C, Luo X, Mooney M, Hatsukami DK. Similar exposure to a tobacco-specific carcinogen in smokeless tobacco users and cigarette smokers. *Cancer Epidemiol Biomarkers Prev*, 2007; 16 (8): 1567-72  
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**Question 2**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

In further support of the conclusion, it is worth noting that, when taking into account the total kinetic curve of nicotine from ST, the total quantity of nicotine absorbed is generally similar, if not superior, to that obtained through smoking (Benowitz 1997). This is because, with the gradual absorption of nicotine and the longer time needed to consume one unit,

high concentrations are sustained over a longer period (Savitz et al 2006). In fact, a very recent study, dosing cotinine in urine (a method commonly used to estimate nicotine exposure) provided evidence that, globally, the nicotine exposure of smokeless tobacco users was significantly higher than in smokers ( $p < 0.001$ ) (Hecht 2007). This is generally considered one of the reasons why ST induces strong addiction. Consider, for example, the high NRT doses needed to efficiently substitute ST users who wish to quit ST (Ebbert JO, Dale LC et al 2007).

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### **Question 3**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

There is no clinical evidence that ST is a viable option for becoming totally tobacco free. In addition to the evidence from Sweden and Norway, it is worth noting the following: - There have been greater decreases in smoking prevalence levels in Iceland, UK, Norway, Ireland and Malta than in Sweden between 1985 and 2003 (Joossens L. 2004 Graphic 3). - In the UK where no ST products are allowed, but where there has been strong involvement of the health services in smoking cessation related activities, between 1980 and 2002 the smoking prevalence for men (above 15 years of age) fell from 42% to 27% (-15%) and for women from 37% to 25% (-12%). Also in the UK, the number of cigarettes/year/capita was 2 987 in 1970, falling to 1 374 in 2000, a 54% decrease. - In the United States, the states with the lowest smoking prevalence also tend to have the lowest prevalence of ST use (Tomar S 2006). Furthermore, data on ST use in combination with smoking should be considered. For instance, some data on combined use of snus + tobacco suggests that for many users snus is not a way to stop smoking but only a way to address their craving in places where smoking is forbidden (Patja et al 2006). Among snus users 12% smoke daily and 24% occasionally, meaning that at least a third of snus users do not consider snus as a way to stop smoking but only as a way to supplement cigarette smoking and adapt tobacco consumption to environmental regulations. Finally, in support of the sentence "the trend in smoking prevalence in males could also be due to successful non-smoking programs or other socio-cultural factors", it is worth noting that the similar drop observed in the rates of smoking women – without a large increase in ST consumption – is a strong indicator in favour of this "environmental changes" effect.

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- <http://www.heatstats.org/datapage.asp?id=4661>

#### **Question 4**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

It is indeed difficult to translate findings across countries. Apart from the social and cultural differences, the Swedish data is based on studies initiated twenty years ago when: - smoking prevalence in Sweden was much higher than is the case now in most of European countries; - ST products were not marketed to the same extent as cigarettes. This historic situation could be one of the reasons why in the Swedish surveys there are many more people switching from cigarette to ST than the other way around. Any future trend in Europe could be much closer to what is happening in the US, with an overall level of smoking much lower than the initial one in Sweden, and sport champions exposing ST quite openly.

#### **Question 5**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Based on the present level of evidence, no conclusion can be drawn on this question. It is not only a question of extrapolating across countries, but also of extrapolating the past to the future. Twenty years ago when the first Swedish surveys started, very few people were starting a tobacco addiction with ST.

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**Submission: 28**

**Name**

PETER N LEE (Individual)

**Question 1**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

I am an epidemiologist/statistician who over the last few years has spent a considerable time reviewing the evidence relating to use of smokeless tobacco products (STP) in Western populations (mainly US and Scandinavia) to a variety of health endpoints. I have recently published a review on STP and circulatory disease<sup>1</sup>, have a paper on STP and oral cancer submitted, and a paper on STP and non-neoplastic oral disease almost ready for submission. My website [www.pnlee.co.uk/Reports.htm](http://www.pnlee.co.uk/Reports.htm) also contains a number of unpublished detailed reviews, which the Committee are invited to access. I found the SCENIHR draft report very good in many ways and the comments below are aimed at improving it further. I feel that the answer to question 1 should mention the considerably lower adverse health effects of STP users compared to smokers, which is made clear in the body of the report. It is surely worth emphasising that the evidence suggests strongly that overall death rates would be reduced if the whole population used STP (as currently used in the West) and no one smoked cigarettes. I note that the literature considered is far from comprehensive – compared to reviews I conducted at about the same time I noted that a number of references are missed for oral cancer<sup>2-19</sup>, stroke<sup>20</sup>, diabetes<sup>21</sup>, blood pressure<sup>22-30</sup>, other risk factors for circulatory disease<sup>31-38</sup>, and non-neoplastic oral lesions<sup>39-58</sup>, and also for cancer of the oesophagus<sup>3,12,14,15,59-63</sup>, stomach<sup>14,59,62,64,65</sup>, pancreas<sup>14,60,62,66,67</sup> and lung<sup>14,15,62,68,69</sup>. There are also some other more recent references related to health effects, not considered in the report<sup>70-78</sup>. I have particular reservations about the conclusions on pancreatic cancer, which I feel are vastly overstated. The evidence from the two pivotal Scandinavian studies when meta-analysed (random-effects) shows no significant relationship either in never smokers (RR 1.61, 95% CI 0.77-3.34), based on individual RRs of 0.85 (0.24-3.07) and 2.0 (1.2-3.3), or in all subjects (1.20, 0.66-2.20), based on individual RRs of 1.67 (1.12-2.50) and 0.9 (0.7-1.2). However the report does not even present the RRs less than 1 for never smokers in one study<sup>79</sup> or for all subjects in the other<sup>80</sup>. The five US studies are cited as “providing additional support” but in fact none show a significant increase in STP users and there are also four other uncited studies<sup>14,66,67,81</sup> showing no significant association. For pancreatic cancer (and also for oral cancer) the report would be much improved by presentation of meta-analyses. For MI I note that the evidence of an increased risk actually derives mainly from two large US studies<sup>82</sup>. It should be made clear that the combined evidence from all the Swedish studies actually provide little evidence of an increase for either heart disease (1.06, 0.83-1.37, n=5) or stroke (1.17, 0.80-1.70, n=2)<sup>1</sup>. For other cancers (i.e. not oral cavity, oesophagus, stomach, pancreas or lung) the Committee may find it useful to reference my website for a review by Thornton and myself (download THORNT2007). This may be regarded as a more accessible source of information to the reader than “IARC in press”. The conclusions we reach for these other cancers are, however, the same. Though I received financial support from Philip Morris Products SA for my work on STP and have done so in the past from BAT, all opinions expressed are my own and do not necessarily represent the views of my sponsors.

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### Question 3

#### Do you agree with the response given ?

Uncertain

#### Please provide the technical/scientific evidence to improve the overall assessment (with complete references).

I am not an expert on the effects of smoking cessation via pharmaceutical nicotine replacement products so cannot usefully comment. However I have looked at some of the papers relating to smokeless tobacco as a gateway for cessation and initiation. For convenience this is considered together in the reply to question 4.

### Question 4

#### Do you agree with the response given ?

Mostly agree

#### Please provide the technical/scientific evidence to improve the overall assessment (with complete references).

I have not assessed the full literature on STP as a gateway to initiation or cessation of smoking, but I have studied in detail two of the Swedish papers<sup>1,2</sup>. The data considered by Ramström and Foulds<sup>1</sup> would have been better analyzed by retrospectively constructing cohorts of subjects born at different times and using life-table methods to test whether previous use of snus affects the probability of initiation, with adjustment for cohort, attained age and other relevant confounding variables. The unadjusted nature of this analysis should be pointed out, and perhaps the Committee should encourage proper analysis as the basic approach seems appropriate. However the sheer strength of the associations suggests the conclusions are right. Thus those who had previously used snus had an almost four times lower chance of initiating cigarettes (OR = 0.28, 95% CI 0.22-0.36) than those who had not, and cigarette smokers who had ever used snus had over a four times higher chance of quitting (4.36, 3.25-5.83) than those who had never used snus. [The second probability was calculated from Figure 1 of the source –  $371/438 = 85\%$  quit vs  $497/888 = 56\%$ .] The same limitations of analysis apply to the data of Furberg et al<sup>2</sup> and they do not even calculate the relevant probabilities. This can be done (albeit unadjusted for age or other factors) for men based on the data in Figure 2 of the source. I estimate that the probability of initiating cigarettes was  $291/1327 = 22\%$  if one first used snus and  $8490/12727 = 67\%$  if one had never used snus, an odds ratio of 0.14 (0.12-0.16). I also estimate that the probability of quitting if one had previously used snus was  $2415/3083 = 78\%$  and  $3652/6068 = 62\%$  if one had never done so, an odds ratio of 2.39 (2.16-2.64). Presenting the results in a consistent way helps to make it clearer that in these studies in Sweden previous snus use was associated with markedly lower initiation and higher quitting rates. I also note that there are a number of references related to the gateway hypothesis that do not appear in the report<sup>3-13</sup>.

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order of product use to evaluate causation in a national US sample. *Addiction* 2003;98:1077-85. 7. Merne MET, Tiekso JT, Syrjänen SM. Snuff use and smoking among senior high school students: effects of a snuff sales ban. *Oral Dis* 1998;4:207-12. 8. Ramström LM. Smokeless tobacco - a potential gateway to smoking. In: Durston B, Jamrozik K, editors. *Tobacco & health 1990. The global war*, Seventh World Conference on Tobacco and Health, Perth, Western Australia, 1-5 April 1990. 189 Royal Street, East Perth, Western Australia 6004: Organising Committee of the Seventh World Conference on Tobacco and Health, 1990;451-2. 9. Ramström L. Snuff - an alternative nicotine delivery system. In: Ferrence R, Slade J, Room R, Pope M, editors. *Nicotine and Public Health*. Washington DC: American Public Health Association, 2000;159-78. 10. Rolandsson M, Hugoson A. Changes in tobacco habits. A prospective longitudinal study of tobacco habits among boys who play ice hockey. *Swed Dent J* 2003;27:175-84. 11. Tillgren P, Haglund BJ, Lundberg M, Romelsjö A. The sociodemographic pattern of tobacco cessation in the 1980s: results from a panel study of living condition surveys in Sweden. *J Epidemiol Community Health* 1996;50:625-30. 12. Tomar SL. Snuff use and smoking in US men - implications for harm reduction. *Am J Prev Med* 2002;23:143-9. 13. Tilashalski K, Rodu B, Cole P. Seven year follow-up of smoking cessation with smokeless tobacco. *J Psychoactive Drugs* 2005;37:105-8.

**Submission: 29**

**Name**

Anne Pietinalho

**Organisation**

Filha (NGO)

**Question 1**

**Do you agree with the response given ?**

Agree

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Question 4**

**Do you agree with the response given ?**

Mostly agree

**Question 5**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Submission: 30**

**Name**

Tore Sanner (Individual)

**Question 1**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Musculoskeletal injuries should be included after 3.6.4 Suggested new text Musculoskeletal injuries A study has been carried out in Norway among infantry conscripts undergoing a physical training programme. The population consisted of 480 male conscripts in the Army. Data was obtained for height and weight measurements from a questionnaire and from a 3,000 metre run test prior to ten weeks of basic military and physical training. Physicians attached to the training camp registered injuries. Every fourth conscript sustained one or more musculoskeletal injuries during the training period. Of these, certain groups (subjects aged 22 years or more; those who were the least active before call-up; those who thought they were less fit than the average person; the slowest finishers in the 3,000-metre run test; smokers of more than 10 cigarettes a day; and snuff-takers) suffered more injuries, according to univariate analyses. Seventy-two of the conscripts were snuff users and their relative risk for musculoskeletal injuries was 1.75 (1.18-2.58) compared to non-snuff users. For conscripts smoking more than 10 cigarettes a day, the relative risk was 1.53 (1.06-2.21) compared to non-smokers (Heir and Eide, 1997). These results are of particular interest in relation to the previous findings of Bolinder et al. (1992) that the use of snuff increased the odds ratio for disability pension, due to musculoskeletal diagnoses. Table 2 should be updated. IARC has now classified benzo(a)pyrene as a group 1 carcinogen <http://monographs.iarc.fr/ENG/Classification/crthgr01.php> Suggested addition to response to Question 1 (at the end of the paragraph starting with "Various studies...") Two studies suggest that the use of snuff increase the risk of musculoskeletal injuries.

**References**

Bolinder GM, Ahlborg BO, Lindell JH. Use of smokeless tobacco: blood pressure elevation and other health hazard found in a large-scale population survey. *J Intern Med* 232: 327-334, 1992. Heir T, Eide G. Injury proneness in infantry conscripts undergoing a physical training programme: smokeless tobacco use, higher age and low levels of physical fitness are risk factors. *Scand J Med Sci Sports* 7: 304-311, 1997.

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment**

**(with complete references).**

Suggested new text in section 3.7.1. Smokeless tobacco and smoking initiation Insert in second last paragraph at the end: Tomar has since .... However, the small study of STP users make results imprecise. "The study of Tomar has recently been supported by Severson et al. (in press). They studied nearly 2,300 7th and 9th graders controlled for known smoking initiation risk factors and found that STP use was independently associated with a more than 2.5-fold higher risk of smoking two years later (fig. 1)" [The figures attached have been taken from a presentation by Scott Tomar at the Tobacco or Health World Congress in Washington DC 2006]." Suggested deletion to response Question 4 (in the beginning of the second paragraph) There is some evidence from the USA .....

**References**

Severson HH, Forrester KK, Biglan A. Use of smokeless tobacco is a risk factor for cigarette smoking, *Nicotine and Tobacco Research* 2007 (in press).

**Question 5**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Suggested new text after 3.3.3.3. Initiation of snuff use among middle age men may primarily take place in relation to smoke cessation or in addition to cigarette smoking due to restriction of places where smoking is permitted. The possible role of snuff use in smoking cessation in Sweden and Norway has been discussed previously. Snuff has been used for a long time in USA and is available in all 50 US states. When comparing daily smoking and daily snuff use among males in the 50 US states, one might have expected a negative correlation if use of snuff had any role in smoking cessation. The results indicate, however, slight positive correlation (Fig. 2). A major concern if snuff is introduced to new markets is that the use of snuff may come in addition to smoking or that the use of snuff may initiate smoking (discussed in section 3.7.1). As discussed earlier the majority of snus/snuff users in Sweden and Norway up to about 1960 appeared to be relative old working-class men. After the Swedish snuff industry launched an intensive marketing campaign around 1970, it was primarily young men that started to use snuff. Fig 3 (reference given in legend to figure) show that in 1955, the majority of the snuff users in Sweden were more than 45 year old men, while 30 years later the majority of the Swedish snuff users were younger than 45 years. In Norway the use of snuff was reintroduced some years later than in Sweden. Fig 4 (reference given in legend to fig) shows that as late as 1985 the group 56-74 old men had the highest prevalence of snuff use, while in 2003 the highest prevalence was in the age group 16-24 years. The trend in USA was similar when 1970 and 2000 are compared. In 1970 the majority of snuff users were men older than 45 years, while in 2000, the highest prevalence of snuff use were among men younger than 35 years (Fig. 5). The conclusion is that both in Sweden and Norway, as well as in USA, the increase in snuff use has primarily occurred among young men. In USA the use of STP by youth has declined since the record high rates during the mid-1990s. Alarmingly, however, in 2004-2005 rates of use by 10th and 12th graders climbed, possibly reflecting the introduction of numerous new snuff products specifically targeting youth (Promoting Healthy Lifestyles, 2007). Another major concern is due to the fact that that new products specifically targeting young women have been introduced on the market. This has resulted in an increased use of snuff among women. Thus the number of women using snuff in Sweden tripled during the last ten years. Suggested addition to response Question 5 (first and last paragraph) First paragraph, insert: The only smokeless tobacco product, .... affected by cultural and societal factors. "It should be noted that after the snuff industry increased their marketing efforts, the use of

snuff has particularly increased among young men both in Sweden, Norway, and USA. More recently the snuff industry has introduced products specifically targeting women" As was also discussed in the answer to Question 3, available scientific data are inadequate to determine if there is any causal relation between the trends in smoking prevalence and prevalence of use of STP. In conclusion, although it is difficult ( it is not possible) to extrapolate future patterns of tobacco use across countries increased use of snuff has particularly occurred among young men in countries where snuff are available. In particular, it is however difficult (it is not possible) to extrapolate the trends in prevalence of smoking and use of oral tobacco if it were made available in an EU-country where it is now unavailable due to societal and cultural differences.

### **References**

Promoting Healthy Lifestyles. Policy, Program, and Personal Recommendations for Reducing Cancer Risk. 2006-2007 Annual report. President's cancer panel, Washington DC, 2007 <http://deainfo.nci.nih.gov/ADVISORY/pcp/pcp07rpt/pcp07rpt.pdf>

**Submission: 31**

**Name**

Lars Ramström

**Organisation**

Institute for Tobacco Studies (Independent scientific research institute)

**Question 1**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The question on adverse health effects of smokeless tobacco products has different answers for different STPs and particular attention should be given to Swedish snus, the product that appears to be the least harmful kind of STP. The SCHENIR answer to Question 1 fails to address the product-related distinctions as thoroughly as would have been desirable. The question on adverse health effects of smokeless tobacco products includes both disease-specific aspects and aspects regarding all-cause mortality. The SCENIHR answer to Question 1 fails to give thorough attention to epidemiological aspects regarding the magnitude of excess all-cause mortality associated with human use of different STPs. Further, the adverse health effects of STPs have to be put in context both in relation to risk levels of "No tobacco" and those of smoking. Therefore the analysis has to include these two key issues: - comparison between death risks of cigarette smoking and those of using different STPs. - comparison between death risks for those who switch from smoking to snus use and those who stop using tobacco altogether. While these issues are not addressed in the SCENIHR answer, the scientific literature cited in the body of the SCENIHR report does provide a basis for such comparisons so as commented upon below. STP use vs smoking: The report of The Royal College of Physicians (2002) estimates that "As a way of using nicotine, the consumption of non-combustible tobacco is of the order of 10–1,000 times less hazardous than smoking, depending on the product." (page 5). This is not mentioned in the SCENIHR report's representation of this source. The study by Levy et al (2004b) is referred to on page 107 of the SCENIHR report by saying that it "estimated the relative hazard of snus and concluded that the product was likely to be approximately 90% less harmful than smoking." The actual wording in that study is, however, more specific: "For total mortality, the estimated median relative risks for individual users of LN-SLT were 9% and 5% of the risk associated with smoking for those ages 35 to 49 and, >49 respectively." These estimates do suggest that use of LN-SLT (LowNitrosamine SmokeLess Tobacco) and particularly Swedish snus (containing less of nitrosamines than other LN-SLT) is associated with death risk levels that are not just lower, but substantially lower than those of cigarette smoking and, consequently, closer to those of no tobacco use than to those of smoking. Switching to STP vs quitting all tobacco use: The recent study by Henley et al (2007) compared death rates of those who switched from cigarettes to STP and those who stopped using tobacco completely. This study is referenced in the SCENIHR report, but it does not mention its finding that the death risk of switchers appeared to be just slightly higher than that of smokers who quit tobacco use completely ("HR 1.08, 95% confidence interval (CI) 1.01 to 1.15"). Consequently, death risk levels of switchers appear to be substantially lower than



those of continuing smokers and, consequently, closer to that of people stopping tobacco use altogether than to that of people continuing to smoke. Conclusions: Since the most important toxicants in cigarette smoke are combustion products not present in unburned tobacco, use of STP must be expected to be less harmful than cigarette smoking. Some Asian and African kinds of STP do still entail very serious adverse health risks, while Western types of low-nitrosamine STP, particularly non-fermented Swedish snus, appear to be associated with death risk levels much closer to the one of "No tobacco" than to the one of cigarettes. Switching from cigarette smoking to STP use reduces the death risk to a level that is close to the one of quitting all tobacco and far below the one of continued smoking.

### **Question 2**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The SCENIHR report's answer to Question 2 does correctly state that STPs are addictive. However, it fails to make a comprehensive discussion of one key issue, the comparison between the addiction potential of different STPs and that of other nicotine delivery systems with respect to characteristics of nicotine delivery speed. The delivery speed aspects are recognized in the body of the report as major determinants of the addictiveness of a nicotine delivery system. The text in section 3.6.1.2. recognizes the contrast between the delivery speed from pulmonary absorption of nicotine in cigarette smoke (producing "arterial boli") and oral or transdermal absorption from NRT, but it fails to point out that STP belongs to the same "non-pulmonary-absorption" category as NRT. Thereby, the SCENIHR report unduly exaggerates the quite modest difference in delivery speed between STP and oral NRT instead of emphasizing the major difference, the one between pulmonary absorption (cigarettes) and any oral or transdermal delivery system (STP and NRT). Although the dependence potential of most NRT products is low, it should not be seen as a priori non-existent. These matters are also discussed in a recent paper by Hajek et al (full citation, see below) arriving at the conclusion: "Long-term use of nicotine replacement treatment is not uncommon. Its occurrence seems positively related to speed of nicotine delivery of individual products." With respect to nicotine delivery speed characteristics the dependence potential of nicotine delivery systems can be assumed to vary along a wide scale, lowest for NRT products, slightly higher for STP and substantially higher for systems with pulmonary absorption, for example cigarettes.

### **References**

Hajek P et al. Dependence potential of nicotine replacement treatments: Effects of product type, patient characteristics, and cost to user. Preventive Medicine, 2007; 44: 230-234.

### **Question 3**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The SCENIHR answer to Question 3 focuses on the issue of clinical trials. But this is not the most relevant aspect of cessation effectiveness in "the real world", i.e. outside clinical settings, where the vast majority of quit attempts take place. In his recently published book Professor Simon Chapman demonstrates some data extrapolated from Zhu et al (full citations, see below) by saying (p. 138): "...those who quit for at least 12 months after receiving counselling (n=7290) constitute only 9.3% of long term quitters." With respect to the above reality the key issues are those about the nature and effectiveness of quit procedures actually prevailing in the population at large so as can not be investigated by clinical trials, only by large population representative studies. Such studies have been carried out in Sweden and published in peer reviewed scientific journals. These articles are referenced in the SCENIHR report but the evidence from the studies in question has not been thoroughly represented in the SCENIHR report, just briefly mentioned. They provide solid evidence that: - among men who try to quit smoking snus is the most commonly used cessation aid. - among those, men and women, who use snus as cessation aid the success rate is significantly higher than among those using other aids or no aid. - among men who are primary smokers the smoking cessation rate is substantially higher among those who have started secondary snus use than among those who have not. Section 3.3.3.1. of the SCENIHR contains a number of diagrams which claim to present adult prevalence data for Sweden from 1980 to 2004 (Figures 4-9). These diagrams do, however, present partially false data. It is stated that these diagrams show data from "Statistics Sweden 2007". This is only partially true. Table B12 on page 71 in the referenced document does contain the data presented on daily snus use in the years 1988, 1996 and 2004, but it does not contain the data plotted for daily snus use in the year 1980 (simply because the underlying surveys did not measure daily snus use in 1980). The 1980 data that are plotted in these diagrams are obviously picked up from a different, unrecognized source, and the 1980 figures given there are NOT measures of daily snus use but measures of the sum of daily and occasional use. In the referenced document from Statistics Sweden there is a Table B13 showing data for this sum in the years 1988, 1996 and 2004. This makes it possible to calculate prevalence figures for occasional use in each one of those years and hence to estimate the occasional use prevalence rate for 1980 by extrapolation backwards. Subtracting these estimates from the observed sum could give reasonable estimates of the rate of daily snus use in 1980. Substituting such figures for the false ones in the current diagrams would entail a substantial change of the overall graphical picture of the development over time, where the snus use prevalence would more clearly show a continuous increase that mirrors the continuous decrease of smoking. This clear pattern is obscured in the current diagrams. Since this pattern is part of the background for assessment of the Swedish development, it is urgent to make corrections in the final report. Section 3.3.3.1. also contains a false statement in the text saying: "There are no national data on occasional use (of snus)." Even if none of the above mentioned tables B12 and B13 does explicitly spell out the numerical data in question, such figures can easily be derived by simple subtraction of data in the one Table from those in the other one. Consequently it is not correct to say that such data are unavailable. When discussing the above time series from Sweden, and analogous ones from Norway, the SCENIHR answer focuses on comparisons between men and women. This is inappropriate as a primary methodological approach, since that comparison is confounded by differences in many gender specific variables other than snus use, so that meaningful conclusions cannot be drawn. The only meaningful observations are those regarding men only and comparing developments of prevalence of smoking and prevalence of snus use. These patterns are quite similar in both these countries. Summary: While the above mentioned prevalence time series, both the Swedish and the Norwegian ones, do suggest an association between snus use and decrease of smoking, it is correct to point out that these data alone do not provide proof of causal inference. But, as pointed out above, the Swedish population studies provide strong evidence of such an association by demonstrating that snus is being used as a cessation aid by a large number of (predominantly male) smokers

achieving high success rates (higher than those using NRT) in quit attempts and that the proportion of ex-smokers is substantially higher among men with than among men without a history of snus use. The evidence that snus use enhances smoking cessation is further supported by the observation that snus use can mimic the nicotine uptake from cigarettes a little bit better than currently available NRT products (Ramström/Foulds 2006 p. 214). Conclusion: Available data do provide evidence that smokeless tobacco may constitute a smoking cessation aid comparable to pharmaceutical nicotine replacement products.

#### **References**

Chapman S. Public Health Advocacy and Tobacco Control. Oxford, Blackwells, 2007. Zhu S et al. Smoking cessation with and without assistance: a population-based analysis. *Am J Prev Med*, 2000;18(4):305-11.

#### **Question 4**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The SCENIHR answer to Question 4 can mostly be agreed upon, but a few supplementary points could be added. At the same time as there is "some evidence from the USA that smokeless tobacco use may lead to subsequent smoking", there are studies from the USA referenced in the body of the SCENIHR report (O'Connor et al, 2003, O'Connor et al 2005) having found evidence of the opposite. The data from Sweden does not only reject the idea that snus were a gateway to smoking. It has been found that primary snus use by an individual is actually associated with a significant reduction of the likelihood of subsequent initiation of smoking. Looking at a population perspective it has been found that, when we go from older to younger birth cohorts initiation of smoking is going down more than initiation of snus use is going up. Consequently, total initiation of tobacco use has been going down along with increased initiation of snus use (Ramström/Foulds 2006 p. 211).

#### **Question 5**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The SCENIHR answer to Question 5 repeats the inappropriate focus on gender comparison commented upon in relation to Question 3 and, here again, it is not justifiable to use it as a basis for conclusions. The overall point that existing data are insufficient to draw causal conclusions is quite trivial under current conditions, particularly in Europe. But this makes it even more urgent to discuss the pieces of suggestions that can actually be found in published Swedish data. The referenced source STATISTICS SWEDEN 2007 contains a Table B12 that makes it possible to see how snus use has changed over time in different subgroups. In 1988 snus use among women was virtually unknown and not readily accepted (prevalence 0.6 %). Later snus has started to gain acceptance and overall female prevalence in 2004 was more than four times as high as in 1988. In males 1988 snus use was not widely accepted among those with high education (prevalence of daily use being just 9.3% compared to 18.1% among those with low education) but in 2004 prevalence had almost doubled thereby becoming nearly as high as among low educated men, among whom the

increase was slower. The association between education and increased acceptance of snus is visible among women also, snus use being more common among those with high than among those with low education during the whole period of observation. Similar patterns are being reported from Norway as well. Conclusion: While there is no formal evidence on possibilities to extrapolate information on the patterns of smokeless tobacco use from one country to another, some published data from Sweden and Norway suggest that snus has a potential to gain acceptance and be used in population groups with no or minimal previous experience of snus use.

**Submission: 32**

**Name**

Lars Ramström (Individual)

**Question 1**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The question on adverse health effects of smokeless tobacco products has different answers for different STPs and particular attention should be given to Swedish snus, the product that appears to be the least harmful kind of STP. The SCENIHR answer to Question 1 fails to address the product-related distinctions as thoroughly as would have been desirable. The question on adverse health effects of smokeless tobacco products includes both disease-specific aspects and aspects regarding all-cause mortality. The SCENIHR answer to Question 1 fails to give thorough attention to epidemiological aspects regarding the magnitude of excess all-cause mortality associated with human use of different STPs. Further, the adverse health effects of STPs have to be put in context both in relation to risk levels of "No tobacco" and those of smoking. Therefore the analysis has to include these two key issues: - comparison between death risks of cigarette smoking and those of using different STPs. - comparison between death risks for those who switch from smoking to snus use and those who stop using tobacco altogether. While these issues are not addressed in the SCENIHR answer, the scientific literature cited in the body of the SCENIHR report does provide a basis for such comparisons so as commented upon below. STP use vs smoking: The report of The Royal College of Physicians (2002) estimates that "As a way of using nicotine, the consumption of non-combustible tobacco is of the order of 10–1,000 times less hazardous than smoking, depending on the product." (page 5). This is not mentioned in the SCENIHR report's representation of this source. The study by Levy et al (2004b) is referred to on page 107 of the SCENIHR report by saying that it "estimated the relative hazard of snus and concluded that the product was likely to be approximately 90% less harmful than smoking." The actual wording in that study is, however, more specific: "For total mortality, the estimated median relative risks for individual users of LN-SLT were 9% and 5% of the risk associated with smoking for those ages 35 to 49 and, >49 respectively." These estimates do suggest that use of LN-SLT (LowNitrosamine SmokeLess Tobacco) and particularly Swedish snus (containing less of nitrosamines than other LN-SLT) is associated with death risk levels that are not just lower, but substantially lower than those of cigarette smoking and, consequently, closer to those of no tobacco use than to those of smoking. Switching to STP vs quitting all tobacco use: The recent study by Henley et al (2007) compared death rates of those who switched from cigarettes to STP and those who stopped using tobacco completely. This study is referenced in the SCENIHR report, but it does not mention its finding that the death risk of switchers appeared to be just slightly higher than that of smokers who quit tobacco use completely ("HR 1.08, 95% confidence interval (CI) 1.01 to 1.15"). Consequently, death risk levels of switchers appear to be substantially lower than those of continuing smokers and, consequently, closer to that of people stopping tobacco use altogether than to that of people continuing to smoke. Conclusions: Since the most important toxicants in cigarette smoke are combustion products not present in unburned tobacco, use of STP must be expected to be less harmful than cigarette smoking. Some

Asian and African kinds of STP do still entail very serious adverse health risks, while Western types of low-nitrosamine STP, particularly non-fermented Swedish snus, appear to be associated with death risk levels much closer to the one of "No tobacco" than to the one of cigarettes. Switching from cigarette smoking to STP use reduces the death risk to a level that is close to the one of quitting all tobacco and far below the one of continued smoking.

## **Question 2**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The SCENIHR report's answer to Question 2 does correctly state that STPs are addictive. However, it fails to make a comprehensive discussion of one key issue, the comparison between the addiction potential of different STPs and that of other nicotine delivery systems with respect to characteristics of nicotine delivery speed. The delivery speed aspects are recognized in the body of the report as major determinants of the addictiveness of a nicotine delivery system. The text in section 3.6.1.2. recognizes the contrast between the delivery speed from pulmonary absorption of nicotine in cigarette smoke (producing "arterial boli") and oral or transdermal absorption from NRT, but it fails to point out that STP belongs to the same "non-pulmonary-absorption" category as NRT. Thereby, the SCENIHR report unduly exaggerates the quite modest difference in delivery speed between STP and oral NRT instead of emphasizing the major difference, the one between pulmonary absorption (cigarettes) and any oral or transdermal delivery system (STP and NRT). Although the dependence potential of most NRT products is low, it should not be seen as a priori non-existent. These matters are also discussed in a recent paper by Hajek et al (full citation, see below) arriving at the conclusion: "Long-term use of nicotine replacement treatment is not uncommon. Its occurrence seems positively related to speed of nicotine delivery of individual products." With respect to nicotine delivery speed characteristics the dependence potential of nicotine delivery systems can be assumed to vary along a wide scale, lowest for NRT products, slightly higher for STP and substantially higher for systems with pulmonary absorption, for example cigarettes.

## **References**

Hajek P et al. Dependence potential of nicotine replacement treatments: Effects of product type, patient characteristics, and cost to user. *Preventive Medicine*, 2007; 44: 230-234.

## **Question 3**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The SCENIHR answer to Question 3 focuses on the issue of clinical trials. But this is not the most relevant aspect of cessation effectiveness in "the real world", i.e. outside clinical settings, where the vast majority of quit attempts take place. In his recently published book Professor Simon Chapman demonstrates some data extrapolated from Zhu et al (full

citations, see below) by saying (p. 138): "...those who quit for at least 12 months after receiving counselling (n=7290) constitute only 9.3% of long term quitters." With respect to the above reality the key issues are those about the nature and effectiveness of quit procedures actually prevailing in the population at large so as can not be investigated by clinical trials, only by large population representative studies. Such studies have been carried out in Sweden and published in peer reviewed scientific journals. These articles are referenced in the SCENIHR report but the evidence from the studies in question has not been thoroughly represented in the SCENIHR report, just briefly mentioned. They provide solid evidence that: - among men who try to quit smoking snus is the most commonly used cessation aid. - among those, men and women, who use snus as cessation aid the success rate is significantly higher than among those using other aids or no aid. - among men who are primary smokers the smoking cessation rate is substantially higher among those who have started secondary snus use than among those who have not. Section 3.3.3.1. of the SCENIHR contains a number of diagrams which claim to present adult prevalence data for Sweden from 1980 to 2004 (Figures 4-9). These diagrams do, however, present partially false data. It is stated that these diagrams show data from "Statistics Sweden 2007". This is only partially true. Table B12 on page 71 in the referenced document does contain the data presented on daily snus use in the years 1988, 1996 and 2004, but it does not contain the data plotted for daily snus use in the year 1980 (simply because the underlying surveys did not measure daily snus use in 1980). The 1980 data that are plotted in these diagrams are obviously picked up from a different, unrecognized source, and the 1980 figures given there are NOT measures of daily snus use but measures of the sum of daily and occasional use. In the referenced document from Statistics Sweden there is a Table B13 showing data for this sum in the years 1988, 1996 and 2004. This makes it possible to calculate prevalence figures for occasional use in each one of those years and hence to estimate the occasional use prevalence rate for 1980 by extrapolation backwards. Subtracting these estimates from the observed sum could give reasonable estimates of the rate of daily snus use in 1980. Substituting such figures for the false ones in the current diagrams would entail a substantial change of the overall graphical picture of the development over time, where the snus use prevalence would more clearly show a continuous increase that mirrors the continuous decrease of smoking. This clear pattern is obscured in the current diagrams. Since this pattern is part of the background for assessment of the Swedish development, it is urgent to make corrections in the final report. Section 3.3.3.1. also contains a false statement in the text saying: "There are no national data on occasional use (of snus)." Even if none of the above mentioned tables B12 and B13 does explicitly spell out the numerical data in question, such figures can easily be derived by simple subtraction of data in the one Table from those in the other one. Consequently it is not correct to say that such data are unavailable. When discussing the above time series from Sweden, and analogous ones from Norway, the SCENIHR answer focuses on comparisons between men and women. This is inappropriate as a primary methodological approach, since that comparison is confounded by differences in many gender specific variables other than snus use, so that meaningful conclusions cannot be drawn. The only meaningful observations are those regarding men only and comparing developments of prevalence of smoking and prevalence of snus use. These patterns are quite similar in both these countries. Summary: While the above mentioned prevalence time series, both the Swedish and the Norwegian ones, do suggest an association between snus use and decrease of smoking, it is correct to point out that these data alone do not provide proof of causal inference. But, as pointed out above, the Swedish population studies provide strong evidence of such an association by demonstrating that snus is being used as a cessation aid by a large number of (predominantly male) smokers achieving high success rates (higher than those using NRT) in quit attempts and that the proportion of ex-smokers is substantially higher among men with than among men without a history of snus use. The evidence that snus use enhances smoking cessation is further supported by the observation that snus use can mimic the nicotine uptake from cigarettes a

little bit better than currently available NRT products (Ramström/Foulds 2006 p. 214). Conclusion: Available data do provide evidence that smokeless tobacco may constitute a smoking cessation aid comparable to pharmaceutical nicotine replacement products.

#### **References**

Chapman S. Public Health Advocacy and Tobacco Control. Oxford, Blackwells, 2007. Zhu S et al. Smoking cessation with and without assistance: a population-based analysis. *Am J Prev Med*, 2000; 18(4):305-11.

#### **Question 4**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The SCENIHR answer to Question 4 can mostly be agreed upon, but a few supplementary points could be added. At the same time as there is "some evidence from the USA that smokeless tobacco use may lead to subsequent smoking", there are studies from the USA referenced in the body of the SCENIHR report (O'Connor et al, 2003, O'Connor et al 2005) having found evidence of the opposite. The data from Sweden does not only reject the idea that snus were a gateway to smoking. It has been found that primary snus use by an individual is actually associated with a significant reduction of the likelihood of subsequent initiation of smoking. Looking at a population perspective it has been found that, when we go from older to younger birth cohorts initiation of smoking is going down more than initiation of snus use is going up. Consequently, total initiation of tobacco use has been going down along with increased initiation of snus use (Ramström/Foulds 2006 p. 211).

#### **Question 5**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The SCENIHR answer to Question 5 repeats the inappropriate focus on gender comparison commented upon in relation to Question 3 and, here again, it is not justifiable to use it as a basis for conclusions. The overall point that existing data are insufficient to draw causal conclusions is quite trivial under current conditions, particularly in Europe. But this makes it even more urgent to discuss the pieces of suggestions that can actually be found in published Swedish data. The referenced source STATISTICS SWEDEN 2007 contains a Table B12 that makes it possible to see how snus use has changed over time in different subgroups. In 1988 snus use among women was virtually unknown and not readily accepted (prevalence 0.6 %). Later snus has started to gain acceptance and overall female prevalence in 2004 was more than four times as high as in 1988. In males 1988 snus use was not widely accepted among those with high education (prevalence of daily use being just 9.3% compared to 18.1% among those with low education) but in 2004 prevalence had almost doubled thereby becoming nearly as high as among low educated men, among whom the increase was slower. The association between education and increased acceptance of snus is visible among women also, snus use being more common among those with high than among those with low education during the whole period of observation. Similar patterns are being reported from Norway as well. Conclusion: While there is no formal evidence on



possibilities to extrapolate information on the patterns of smokeless tobacco use from one country to another, some published data from Sweden and Norway suggest that snus has a potential to gain acceptance and be used in population groups with no or minimal previous experience of snus use.

**Submission: 33**

**Name**

Terhi Rokkanen

**Organisation**

Terveys ry (Health organisation)

**Question 1**

**Do you agree with the response given ?**

Agree

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Agree

**Question 5**

**Do you agree with the response given ?**

Agree

**Submission: 34**

**Name**

Jean King

**Organisation**

Cancer Research UK (NGO)

**Question 1**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

A very clear distinction needs to be made between the various types of oral tobacco and great care used in defining which particular products are being discussed in any particular context. Thus the products currently generating the greatest interest are those prepared to the Gothiatek standard, such as Swedish snus and some newer moist snuff products being introduced into the markets of the US, South Africa and elsewhere. Swedish snus is pasteurised and stored at a low temperature, and this seems to reduce the levels of nitrosamines (ref 1). However, some other forms of moist snuff still available e.g. in the USA, (and similar to those products that were starting to be introduced into Europe some 15 years ago) contain high levels of nitrosamines and carry a considerable risk e.g. of oral cancer (ref 2). Also, the various types of chewed and sucked tobacco used traditionally by South Asian communities also carry a far higher risk of cancer than snus (ref 3). In the answers below, we restrict our comments to products such as Swedish snus that are manufactured to Gothiatek-type standards. A recent systematic review of the literature was produced by the New Zealand Health Technology Board (ref 4). This supports the conclusions of the EU SCENHIR report and confirmed that snus carries a far reduced risk of cancer and other diseases than smoked tobacco. Thus while there may be increased risks of cardiovascular disease and pancreatic cancer due to the long-term use of snus, and risks to pregnant women also need to be assessed, the use of snus is many orders of magnitude less harmful than that of smoked tobacco. There is therefore a public health argument to be made for encouraging smokers to switch to snus (ref 5), but this needs to be weighed against several other key factors. Firstly, the tobacco industry must not be allowed to promote any such products or make any claims about them: messages must be public health-led, in order to prevent misconceptions about 'safe' or 'safer' tobacco and to avoid confusion about the very real harm of smoked tobacco (ref 2). Secondly, any promotion of snus may inhibit people from quitting tobacco use altogether which must remain the key public health goal given that there are some risks associated with snus, including possible reversion to smoking. It is possible however that, properly controlled, snus might be useful as a cessation aid (see qu 3 below). Thirdly, there are already available effective treatments for nicotine addiction, including medicinal or 'clean' nicotine (NRT), that do not carry the above risks, and these should be promoted first and foremost.

**References**

Ref 1 Gray N, Henningfield JE, Benowitz NL et al. Towards a comprehensive long term nicotine policy. *Tobacco Control*, 2005; 14: 161-165  
Ref 2 Chapman S, *Public Health Advocacy and Tobacco Control*, Blackwell Publishing, Oxford, 2007  
Ref 3 McNeil A, Bedi R, Islam S et al, Levels of toxins in oral tobacco in the UK. *Tobacco Control* 2006; 15:64-67  
Ref 4 Broadstock M, Systematic review of the health effects of modified smokeless tobacco

products. New Zealand Health Technology Assessment Report 2007; 10(1) Ref 5 Gartner C, Hall W, Vos et al. Assessment of Swedish snus for tobacco harm reduction: an epidemiological modelling study. *The Lancet*, 2007; 369: 2010-2014

## **Question 2**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The NZ review (ref 1) also confirms the addictiveness of oral tobacco products. Snus delivers a nicotine 'hit' that more closely resembles that from smoked tobacco, and might therefore be more effective, than currently available NRT products in helping to quit smoking. We do not believe that addictiveness in itself should impede use of a product that could potentially help many thousands of people to quit smoking. What is in greater question here is whether indeed smokers would switch from cigarettes to snus or whether a new cohort of snus-users would be created if it became available on the market (see also Qu 4). Therefore what is crucial is how snus would be controlled and made available. In our view, it should initially be solely for quitting purposes, and on prescription, if shown in RCTs to be an effective cessation aid. RCTs should target those for whom other cessation methods have failed. If full, independent regulation of all tobacco and nicotine products was introduced, then (following careful behavioural and social marketing research) it could be considered for wider use, if research indicated that smokers would switch. However, messages and availability would both need to be tightly controlled by the public health authorities. This could lead to the interesting situation, whereby government agencies were 'promoting' a tobacco product (ref 2) - such a scenario would need to be preceded by professional and public awareness campaigns.

## **References**

Ref 1 Broadstock M, Systematic review of the health effects of modified smokeless tobacco products. New Zealand Health Technology Assessment Report 2007; 10(1) Ref 2 Chapman S, Public Health Advocacy and Tobacco Control, Blackwell Publishing, Oxford, 2007

## **Question 3**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

It is a matter of considerable public health interest that RCTs on snus as a cessation aid are undertaken. Cancer Research UK was considering such a trial but due to the dual difficulties of snus a) being a tobacco product and b) illegal, the trial proposal has not gone to peer review. We understand that discussions about such a RCT are also being held in France. It would be very helpful if the EC sanctioned the use of snus in RCTs, i.e. provided a special license to overcome the illegality of snus, for this research. It should however be recognised that there are already effective non-tobacco treatments for nicotine addiction. Therefore public health interest can be served even more by encouraging a) greater use of these treatments and b) the development of more effective cessation aids, especially those that mimic more closely the nicotine 'hit' delivered by cigarettes (ref 1). Therefore, it would be preferable if the use of snus, within the spectrum of treatment options, would be targeted to those for whom other treatments have failed (especially as it now seems that there may be other addictive substances in tobacco besides nicotine). However this should only happen if RCT evidence showed effectiveness.

## References

Ref 1 Gray N, Henningfield JE, Benowitz NL et al. Towards a comprehensive long term nicotine policy. Tobacco Control, 2005; 14: 161-165

## Question 4

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

We have no idea how snus would be perceived or used in other countries. A small study conducted by the University of Nottingham by Professor Ann McNeil showed that, in the UK, people could not see the point of snus unless it was as a cessation aid (ref 1). Clearly if allowed to be promoted by tobacco companies as a 'safer alternative' to cigarettes, people might take it up, but as it is also in these companies' interests to continue promoting smoked tobacco as well, we cannot allow them to have any active part in such promotion or to make any claims about smokeless tobacco products. There is also the risk, already mentioned above, of generating confusion about the risk of tobacco overall. We agree that there is no good evidence that snus might lead to smoking initiation, but, as noted above, nor is there any evidence that, if snus were introduced to the market, smokers would switch to using it, rather than a new group of solely snus users being created. The EC could take a leadership role in this evidence vacuum by funding social marketing research into perceptions of snus in different cultural settings across the EU.

## References

Ref 1 McNeil A, Scott K, McIntyre D, Smokers' Perceptions of Relative Harm based on Package Information. Unpublished Report April 2007

## Question 5

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

We need to understand how snus might be perceived and used in different EU countries in order to assess any potential public health benefit. We especially need to know whether it might be an effective cessation aid via RCTs. And most importantly the EU must ensure that snus could only become available under tightly regulated conditions that prohibited the tobacco industry from making any claims or promotion. If research indicated that it could have a role in smoking cessation (outside of Sweden), snus could be made available on prescription. This should be in the context of making the most harmful form of nicotine – smoked tobacco, the least accessible, affordable and attractive and the least harmful – NRT, the most available and affordable (ref 1).

## References

Ref 1 [www.smokefreepartnership.eu/IMG/pdf/The\\_Leuven\\_Consensus.pdf](http://www.smokefreepartnership.eu/IMG/pdf/The_Leuven_Consensus.pdf)

**Submission: 35**

**Name**

Dr. Róbert Ochaba, MPH

**Organisation**

Public Health Authority of the Slovak Republic (Public Authority)

**Question 1**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

All STP products contain nicotine that is highly addictive substance. Dangerous is also carcinogenic content that leads to health damage results. We have recognized a lot of professional articles about this theme. Swedish snuss is by our opinion as well harmful as classic cigarettes.

**Question 2**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Smokeless tobacco is similarly addictive as smoking cigarettes. In spite of considerations smokeless tobacco is equally addictive as smoking cigarettes.

**Question 3**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

A small number of studies indicated that the use of smokeless tobacco leads to smoking cessation. For this reason discussion about cessation effect of smokeless tobacco is not appropriate.

**Question 4**

**Do you agree with the response given ?**

Uncertain

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

We have received different positions to initiation of smoking by smoking cigarettes. At the moment it is not exactly known whether smokeless tobacco can lead to initiation of smoking cigarettes.

**Question 5**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

To our opinion it is not possible to extrapolate patterns of tobacco use from other countries. Each country has its own particularity, conditions, social economics level, demographic trends and similarly.

**Submission: 36**

**Name**

Tuula Ojala

**Organisation**

The Finnish Health Association (NGO)

**Question 1**

**Do you agree with the response given ?**

Mostly agree

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Mostly agree

**Question 5**

**Do you agree with the response given ?**

Agree



**Submission: 37**

**Name**

Deborah Arnott, Director ASH (London)

**Organisation**

Action on Smoking and Health (London) (NGO)

**Question 1**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

To answer this question effectively it is necessary to put the answer in the context of other nicotine products as smokeless tobacco is an alternative to smoking, as is nicotine replacement therapy. As there are clearly significant differences between Swedish moist snuff (snus) and other STPs it is also important to spell out these differences in the Abstract and Executive Summary too and be very clear about which products are being discussed in which context. Therefore it should be spelt out in the Abstract and Executive Summary that: "There is no evidence that STP use causes an increased risk of lung cancer or other respiratory diseases, responsible for nearly half all deaths caused by smoking in the EU (Aspect Consortium 2004)." These sections should also spell out that: "There appear to be significant differences in the impact on cardiovascular disease of Swedish snus and other STPs, with higher risks from other STPs." Bolinder et al reported an overall relative increase in cardiovascular mortality of 1.4 in 12 years of follow-up (2.1 in those aged 35-54 at the outset), in a cohort of Swedish construction workers compared with respective increases of 1.9 and 3.2 in smokers (Bolinder et al. 1994). The Swedish MONICA study found no increase in risk of myocardial infarction in regular snus users (Huhtasaari et al. 1999; Huhtasaari et al. 1992), and this finding has since been confirmed in two further Swedish case-control studies (Hergens et al. 2005, Wennberg et al. 2007). The magnitude of the effect of snus thus appears lower than for other STP investigated in the recent INTERHEART study, which estimated an odds ratio for myocardial infarction of 2.23 (95% CI 1.41 to 3.52) in non-smoking users of chewing tobacco (Teo et al. 2006). In this study the users of chewing tobacco were predominantly from South Asian populations, so not directly comparable with the Swedish studies. The study did not estimate the risk associated with snus. The odds ratio of myocardial infarction in cigarette smokers in this study was significantly higher than that for STP, at 2.95 (95% CI 2.77 to 3.14) (Teo et al. 2006). In addition the statement pulled out of the report and highlighted in the Abstract and Executive Summary that there is "some evidence for an increased risk of fatal myocardial infarction among STP users" does not seem justified by the evidence, particularly as it does not make clear which type of STP is being referred to. The reported effects of Swedish snus on fatal infarction have either arisen from post-hoc subgroup analyses or arise in the context of a reduced overall risk of myocardial infarction. If any conclusion is to be included that reached in the New Zealand review (Broadstock 2007) that, "a slightly increased risk of sudden death cannot be excluded" would seem more justifiable. The health effects of commonly used additives, such as betel and areca, should also be included in section 3.4.2.2 Section 3.8.1 in the report spells out the overall reduction in hazard from STPs and particularly snus, compared to

cigarettes and it would be useful to include this in the executive summary section on adverse health effects. It would be useful to include in the Executive Summary the statement from section 3.8.1: "The magnitude of the overall reduction in hazard is difficult to estimate, but as outlined above, for cardiovascular disease is at least 50%, for pancreatic cancer at least 30%, for oral and other GI cancer at least 50% and probably more, and for lung cancer and chronic obstructive pulmonary disease, possibly 100%."

## **References**

Broadstock M. Systematic review of the health effects of modified smokeless tobacco products. Christchurch: New Zealand Health Technology Assessment; 2007. NB I have only added full references where they were not included in the original document.

## **Question 2**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

As in the answer to the first question it would be helpful to make the comparison with smoked tobacco use and NRT in the Executive Summary. For example to state that: "Like inhaled tobacco smoke, smokeless tobacco is addictive, but probably less so because of the slower rate of nicotine delivery (Benowitz 1999b), while in contrast NRT is considered to have a low potential for abuse (Hughes 1998)."

## **Question 3**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Section 3.7.2.3 states that there are some indicative findings from Sweden that amongst men, snus users are more likely to quit smoking than non-users, however, there is insufficient controlled data for a clear conclusion to be reached. If this is the case then, given the low rates of quitting among smokers currently, if there is a potential for snus to be effective in helping smokers quit then it is clear that more research is needed in this area, in particular randomised controlled trials testing snus against NRT to test whether it is effective and if so who it might be most effective for. This would be useful not just in Sweden but elsewhere in the EU. This would also test whether there are any likely cross cultural differences across Europe in use of the product as a smoking cessation aid. ASH would urge the EU to fund such research in order to ensure this hypothesis is properly tested since there are significant problems in trying to get such research funded in other ways. Independent researchers will quite understandably not wish to accept funding from the tobacco industry, while independent funding bodies have expressed concerns about funding research into tobacco products, particularly products which are not currently legally available in the majority of the EU. Currently we do not have the research evidence available to enable us to know whether Swedish snus is an effective smoking cessation aid which would add value in addition to NRT. Such research can and must be undertaken in order to enable us to weigh up more effectively the potential costs and benefits of introducing moist snuff on to the market in the EU. If research found it to be an effective quitting aid, given that it is addictive, care would still need to be used in introducing such a product on to the market.

An appropriate structure would need to be put in place for the effective regulation of all STPs, both in terms of their toxic constituents and their sales and marketing. ASH would be particularly concerned about issues like brand sharing between STPs and smoked tobacco products which open up new marketing opportunities for tobacco companies. Such comprehensive regulation of STPs would be an improvement on the current situation where effectively more hazardous forms of STP than Swedish snus are legal in the EU and their constituents remain unregulated.

#### **Question 4**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Given that Sweden is part of the EU so the regulatory framework for tobacco in Sweden conforms to the EU model, Sweden is more relevant to the EU context than the US. This is particularly critical when it comes to tobacco marketing that is to say advertising, sponsorship and promotion of tobacco products. It therefore does not seem appropriate to give the US evidence equal weight to that from Sweden, particularly given that even in the US the link between smokeless tobacco use and smoking initiation is contested (see 3.7.1). Therefore ASH would suggest that the Abstract and Executive Summary should state about the US data that: "The interpretation of US data is divergent and therefore it is not clear whether in the US smokeless tobacco use leads to subsequent smoking. Furthermore, the US does not have the same regulatory framework as the EU and therefore is less relevant to the EU context than Sweden."

#### **Question 5**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

As stated above the US context is less relevant to the EU than Sweden and we need to be very careful translating across from California to the EU. Furthermore the case of California is quoted without further reference to the evidence base in the body of the report and therefore it should be withdrawn or properly substantiated. While it may not be possible to extrapolate the future patterns of tobacco use across countries it would be possible, using an overall reduction in hazard for Swedish snus calculated from the percentages given in the report, to model the impact of possible changes in use of tobacco products if Swedish-snus style smokeless tobacco were introduced into the EU market and work out the critical point at which such a change switched from being beneficial to being detrimental. The assumption should be made that if any such change were to be introduced it could only occur alongside strict regulation of the content of currently legal smokeless tobacco products (chewing tobacco) to minimise the carcinogenic and toxic contents of all smokeless tobacco products on the market in the EU. This would in itself be a regulatory improvement as currently there are numerous chewing tobacco products on the market which contain higher levels of carcinogens and toxins than Swedish snus. (McNeill et al Tobacco Control. 2006). Lynn

Kozlowski set out such a model in his risk-reward ratio (Kozlowski et al Tobacco Control 2001). Using this model you can work out how much of an overall increase in smokeless tobacco would give you the same levels of harm as the current levels of smoked tobacco use. Given it is likely to be at least 50% probably more, you would need at least twice the levels of smokeless tobacco use as smoked tobacco use to lead to the same outcomes in terms of mortality and morbidity. This is assuming there is no increase in the level of smoked tobacco use as a result of oral snuff coming on to the market. This seems reasonable given the Swedish evidence (3.7.1), but would require a continued ban on advertising, promotion and sponsorship and in particular no brand sharing to be allowed between smoked and smokeless tobacco products. Using this graph, and assuming that the overall risk magnitude of Swedish snus is about 50% that of smoked tobacco, then at a rough estimate there would be no change in the overall hazard if for every smoker who switched to Swedish snus, one additional non-smoker started using the product, and it would be beneficial if fewer non-smokers than this took up snus. More work is needed to develop a more detailed model and to decide whether this is a likely scenario. For example, this rough model does not take account of the fact that a significant percentage of those switching to snus to quit smoking may go on to quit using tobacco altogether (see 3.7.2.3) as more research is needed on the use of snus as an aid to cessation. Graph from Kozlowski in Tobacco Control. <http://tobaccocontrol.bmj.com/cgi/content-nw/full/10/3/201/F1>

#### **References**

Kozlowski, L. Strasser, A. Giovino, G. Erickson P, Terza, J. Applying the risk/use equilibrium: use medicinal nicotine now for harm reduction. *Tob Control* 2001; 10: 201 - 203.

**Submission: 38**

**Name**

Joe Bloggs (Individual)

**Question 1**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Testing to see whether it is possible to attach documents to this submission Please ignore The name and address are fictitious but the email will reach me

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Agree

**Question 5**

**Do you agree with the response given ?**

Uncertain

**Submission: 39**

**Name**

Liisa Elovainio (Individual)

**Question 1**

**Do you agree with the response given ?**

Mostly agree

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Question 4**

**Do you agree with the response given ?**

Agree

**Question 5**

**Do you agree with the response given ?**

Agree

**Submission: 40**

**Name**

Harri Vainio

**Organisation**

Finnish Institute of Occupational Health (Research Institute, under the Ministry of Social Affairs and Health in Finland)

**Question 1**

**Do you agree with the response given ?**

Agree

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Agree

**Question 5**

**Do you agree with the response given ?**

Agree

**Submission: 41**

**Name**

Matti Rautalahti (Individual)

**Question 1**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

It is important to recognize that the studies of Swedish snus do not rule out the possibility of carcinogenic potential; i.e. they are NOT able to show that snus does NOT cause cancer.

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Mostly agree

**Question 5**

**Do you agree with the response given ?**

Agree



**Submission: 42**

**Name**

Mervi Hara

**Organisation**

Finland's ASH (NGO)

**Question 1**

**Do you agree with the response given ?**

Agree

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Mostly agree

**Question 5**

**Do you agree with the response given ?**

Agree

**Submission: 43**

**Name**

Rory Morrison, Research & Evaluation Officer

**Organisation**

Action on Smoking and Health (ASH) Scotland (NGO)

**Question 1**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

As the SCENIHR response notes, all STP expose the user to carcinogenic nitrosamines. Further to this, a recent study has found that users of smokeless tobacco products were exposed to similar levels of the powerful carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) than smokers [1]. As STP products are administered orally, a key area for investigation of the potentially harmful effects of STP is oral cancer. In the case of the most widely used STP in Europe, Swedish snus, research on its causal association with oral cancer, at present, lacks clarity. Although two case-controlled studies [2,3] found no increased risk of oral cancer associated with snus usage, it has been suggested [4] that these studies suffer from both small sample size and low statistical power, meaning that moderate positive associations cannot be ruled out. In addition, no studies conducted in this area have found that smokers that switch to snus have a lower risk for oral cancer than those that continue smoking. Given the inconsistencies in published studies to date, the possibility of increased risks of pancreatic cancer, diabetes and cardiovascular disease in snus users cannot currently be ruled out. As the SCENIHR preliminary report notes, the research body relating to the impact of STP usage on pregnancy is too sparse at present to draw firm conclusions. However, given that all commonly-used forms of STP administer high doses of nicotine (associated with attention-deficit/hyperactivity disorders [5]), ASH Scotland suggests it would be unwise to promote STP as safe for use during pregnancy. The clarity of findings concerning the health risks associated with snus use is also complicated by potential biases that are introduced when researchers have declared links with smokeless tobacco companies, or connections with the wider tobacco industry. Experience in the past has shown that the findings of researchers who have had overt or hidden links to the tobacco industry may be compromised by this relationship [6]. Thus, it is ASH Scotland's position that the areas of further research identified in the SCENIHR report should be investigated by wholly independent researchers in order to advance our future understanding of potential adverse health effects.

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Washington DC. 11th-15th July, 2006. [6] Smith, G. and Phillips, A. Passive smoking and health: should we believe Philips Morris's "experts"? *British Medical Journal* 313: pp.929-933, 1996.

## **Question 2**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

All forms of smokeless tobacco, including snus, have nicotine as a major constituent, and are therefore dependence forming in the same way as other forms of tobacco consumption [1,2]. Research has suggested that experimenting with smokeless tobacco in adolescence often develops into a pattern of daily use, and that over time, users may increase the amounts they consume [2]. Adolescents have often not stabilised their tobacco use, and as already outlined, research has demonstrated that the use of cigarettes and snus in parallel is fairly common [3,4,5,6,7]. There is some evidence that snus users develop cravings and withdrawal symptoms when attempting to abstain, find it difficult to quit, and report similar levels of subjective dependence on tobacco [8,9]. Initial evidence also suggests that users of both smokeless tobacco and smoking products may find smoking cessation even more difficult to achieve than those who use only smokeless tobacco or only smoking products [2, 10]. The website of the Scandinavian Tobacco Companies group, which manufactures snus products, states that "the use of snus involves a health risk and is habitual...In our opinion nobody under the age of 18 should use snus" [11]. Tobacco manufacturers encourage use of smokeless tobacco products by smokers on occasions when they are not permitted to smoke [12], and thereby promote individuals to adopt smokeless tobacco in conjunction with continued smoking [13]. Whilst it has been suggested that snus probably does not produce stronger nicotine dependence than smoking [14], the use of any form of tobacco, whether cigarettes or snus, contributes to the development of a dependence process. In conclusion, it is ASH Scotland's position that smokeless tobacco products are addictive in the same way as other forms of tobacco consumption are.

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### **Question 3**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Sweden, at present the only E.U. country where snus is legal, have been the most successful of the European nations in reducing the daily smoking prevalence in their country (being the first to reach the reach the World Health Organisation goal of less than 20% daily smoking prevalence among adults by year 2000) [1]. Some researchers have suggested that, as part of Sweden's success, snus may be an effective aid to quitting for some smokers [2,3]. For example, in a recent retrospective study of 6752 Swedes, snus was the most commonly used cessation aid among men who made attempts to quit smoking. 58% of respondents had used snus, compared with 38% using NRT products. Among men who used snus as a single aid, 66% succeeded in quitting completely, as compared with 47% of those using nicotine gum, or 32% for those using the nicotine patch. Women using snus as a smoking cessation aid were also significantly more likely to quit smoking successfully than those using nicotine patches or gum [4]. This finding is supported by additional retrospective data, which demonstrated that having used snus at the latest attempt to quit increased the probability of being currently abstinent by approximately 50% [5]. However, in this study the mean duration of abstinence among former smokers did not appear to be influenced by snus use. The authors of this study note that it is possible that successful quitters who did not use snus could be better motivated, smoked less, or were otherwise different from those individuals who used snus to aid their successful quit attempt. Similar differences in outcome between groups have been observed in other work, where the authors have concluded that subgroups of more motivated and/or less addicted smokers do better with less help [6,7]. Additional studies have suggested a role for snus in smoking cessation, but the authors have noted that the cross-sectional data used is not sufficiently robust to establish a causal role for snus in smoking cessation [8,9]. It has been suggested that snus may be effective in reducing smoking because of its relatively efficient nicotine delivery. The nicotine values delivered by snus are comparable with those from smoking, and are approximately double those typically achieved by current NRT products (with the exception of the nasal spray nicotine replacement product, the strongest form of NRT) [10,11]. Another possible factor is that those who use snus for smoking cessation tend to use it for a long time after successfully quitting smoking. In one study, 76% of those who had successfully used snus as a single smoking cessation aid were still using snus at the time of the survey, as compared with only 12% of those who had successfully used NRT to stop smoking [4]. The authors of this study note that long-term use of snus as a nicotine maintenance and smoking relapse prevention product is possibly an additional reason for its potential effectiveness as an aid to smoking cessation, relative to short-term use of low dose NRT. To date, only one small pilot intervention study has been published examining the effects of smokeless tobacco as a means to quit smoking cigarettes. Sixty-three heavy smokers who had not been able to quit successfully using NRT were enrolled onto this study. Twenty-five percent of them achieved cessation at one year, but 13 out of the 16 abstainers

continued to use smokeless tobacco [12]. According to findings of a recent epidemiological study, almost 500,000 smoking-attributable deaths occur annually among men in the E.U. If men in all E.U. countries had the smoking prevalence of those in Sweden, it is estimated that about 200,000 deaths would be avoided at Swedish smoking rates. However, it is not clear whether 'the Swedish Experience' is directly transferable to countries that do not have Sweden's long tradition of snus use [13]. Furthermore, the proposed association between high snus consumption and low smoking prevalence in Sweden has been challenged. It has been argued that a larger proportion of men who quit smoking do so without using snus [5], suggesting that snus may not be a necessary component of smoking cessation at the population level. In addition, smoking among women in Sweden has fallen by almost 30% in the last 20 years [14]. Whilst longitudinal studies used to demonstrate larger declines in male daily smoking than in female daily smoking in Sweden [5,15,16], the most recent available data demonstrates that women are now quitting smoking at the same rate as men, and the vast majority of them do not use snus as a smoking cessation aid [17]. On this basis, ASH Scotland concludes that there is insufficient published research at present to demonstrate that snus is an effective aid to quitting smoking. Furthermore, it is our contention that, as of the time of writing, the full potential of NRT has not been explored. To ASH Scotland, the most logical approach would be to expand and support the use of NRT (a cessation aid that has minimal risk), rather than prematurely support the introduction STP as a substitute (which, as has been discussed, has conflicting evidence relating to its potentially harmful nature).

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#### **Question 4**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

There is some debate as to whether or not snus and other forms of smokeless tobacco could become a gateway product, with young people becoming addicted to nicotine from a cheaper, more easily concealed, and arguably more attractive product, before they move on to cigarettes. A recent survey of 84,472 Swedish boys and girls has shown that regular smoking prevalence rates among 15-16 year old boys in Sweden has declined over the past 14 years, from about 10% to under 4%. During this time, the prevalence of regular snus use among Swedish boys increased from about 10% to 13%. By contrast, the prevalence of regular smoking in girls remained almost double that of among boys over the study period, whilst the prevalence of snus use averaged at about 1% [1]. On this basis, the authors conclude that snus is not a gateway to smoking among Swedish youth, but instead is associated with low smoking prevalence among boys. Their findings are supported by a limited number of published studies that conclude that adolescent males who use snus regularly are less likely to ever smoke than adolescent males who do not use snus [2,3]. National statistics in Sweden suggest similar trends with regard to smoking and snus use among adolescent males and females. Smoking prevalence rates for 2003 demonstrate that 16% of boys aged 15-16 were daily snus users, compared to only 2% of girls aged 15-16. By contrast, only 7% of boys aged 15-16 were reported to be daily smokers, compared to 13% of girls aged 15-16. However, the statistical bureau VECA, which conducted the research, note that the figures for smoking prevalence among schoolchildren are difficult to interpret, and that published figures are reported for information purposes only [4]. It is very difficult to demonstrate gateway effects, because there is no way of quantifying whether, in the absence of smokeless tobacco, users would move straight to smoking cigarettes or would remain abstinent. Recent data from Sweden has suggested that among those adolescent boys starting tobacco use in the form of snus, 20% later go on to smoke cigarettes, while the same risk for those not starting with snus is 43% [5]. This data therefore suggests that a possible gateway effect may hold for some adolescent boys and not others. Other studies have been conducted which also suggest this may be a possibility. For example, research plotting the smoking patterns of a cohort of male fifth graders in Stockholm country found that 41% who used only snus in 1997 were smoking one year later [6]. Two recent studies among young boys (11-16 years) using snus have shown that parallel cigarette smoking is common [6,7]. Similarly, a recent Swedish study research reported that 20% of 9th grade male students surveyed used snus, and more than two thirds of snus users were also cigarette smokers [8]. In addition, findings from a four-year follow up study in the US demonstrated that 40% of youth took up cigarettes instead of, or in addition to, the use of oral tobacco [9,10]. It is ASH Scotland's position that the evidence regarding the extent to which snus may act as a gateway product to cigarettes remains inconclusive. Gateway effects are hard to demonstrate because there is no way of quantifying whether, in the absence of smokeless tobacco, users would move straight to smoking cigarettes or not. In this particular case, the cultural differences between the two most-studied nations (the U.S. and Sweden) make it very challenge to assess any 'gateway effect' within the evidence published at present.

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## Question 5

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

It is ASH Scotland's view that valid extrapolation of smokeless tobacco product prevalence data from countries where snus is currently available to E.U. countries where it is not currently available is not possible within the existing evidence-base. As discussed in the SCENIHR summary, we believe the conflicting patterns of smoking and STP increase and decline across the three principal countries of analysis (Sweden, Norway, and the U.S.A.) deny any straightforward causal predictions. Studies have shown in comparable research topics that prevalence of habits like drinking alcohol [1] vary substantially across different countries, so much so that comparisons are meaningless unless researchers have developed a deep understanding of each country's particular cultural characteristics. Within the context of smoking and STP prevalence, this might include factors such as: the role smoking/STP plays in everyday life, gender and age differences in smoking/STP usage, preference towards particular smoking/STP brands and types, smoking/STP usage contexts and patterns, differing approaches to prevention and intervention, and so on. Even once such 'baseline' data was collated for each country, there are numerous other confounding factors arising from continuing social change. For example, immigration has been shown to have a significant impact on patterns and cultures of alcohol use amongst Mexican men who emigrated to the United States [2]. If, as seems plausible, an effect also exists for smoking/STP use, this is likely to have an impact upon prevalence and cessation rates of the country in question. With the non-native-born population of Sweden rising from 7.5% in 1980 to 12.2% in 2004 [3], it would be wise to consider how factors like this may impact upon smoking/STP prevalence throughout the countries in question. In agreement with the SCENIHR response, ASH Scotland feels extrapolating evidence from one country to another can be an unsound practice if little attention is paid to culture and context. This is particularly pertinent given that Sweden has a long history of snus consumption, and often

acts as an 'outlier' when compared with other E.U. nations on social issues such as education and health care. Illustrative of this point was the first attempt by U.S. Tobacco to penetrate the U.K. market with its 'Skoal Bandits' product in 1985. A swift public outcry led by the medical and dental professions - fuelled by the suspicion that it was packaged and marketed towards British children - led to the abandonment of the plan, and the U.K. government's decision to ban the product outright (the ban coming into effect in 1990). Clearly U.S. Tobacco misjudged the culture in the U.K. when considering where to market smokeless tobacco products. ASH Scotland believes it is important that researchers avoid parallel mistakes while analysing evidence that is specific to a particular culture and context.

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**Submission: 44**

**Name**

Professor Martin Jarvis (Individual)

**Question 1**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The SCENIHR conclusions on cardiovascular risk are that "Three large cohort studies show a statistically significant but weak effect on fatal myocardial infarction." This conclusion is perplexing, and difficult to reconcile with the evidence cited in the text. The conclusion apparently relates to "oral tobacco", but this is unhelpful, as this covers a great diversity of products, as is acknowledged in the report. The Interheart study (Teo et al 2006) is not a cohort study and the reported findings relate to chewing tobacco, presumably largely reflecting oral tobacco of the type used in the Indian subcontinent. The more relevant form of smokeless tobacco use is moist snuff of the kind used in Sweden. Of the Swedish cohort studies, Bolinder et al (1994) reported RR1.4 (1.2-1.6) for 'cardiovascular mortality' (fatal myocardial infarction not separately identified). Hergens (2007, in press) apparently report RR 1.3(1.1-1.6) for fatal MI, and 0.9 (CI not given) for all MI. This was a later follow up of the Bolinder cohort, and therefore the results must be supposed to supersede Bolinder's. In any event, these are not 2 separate cohorts, but a single study. The principal finding here would seem to be the lack of an overall effect of snus on MI. Johansson et al (2005) reported RR1.4 (0.6-3.3) for 'heart disease'. Fatal MI does not appear to have been separately identified. Thus, there was only 1 cohort which found a significant effect on fatal MI. In addition some case-control studies have examined this risk. Huhtasaari et al (1999) reported OR 1.5(0.5-5.0); Hergens (2005) OR1.7(.48-5.5); Wennberg (2007) OR 1.1 (0.4-3.3). Thus no case-control study has found a significant effect on fatal MI. The more appropriate conclusion than that presently stated for cardiovascular diseases, which seems plain wrong, is that given in the introduction to Hergens et al (2005) "There are to date no definitive findings indicating that snuff users have increased morbidity or mortality from cardiovascular diseases".

**References**

as given in the SCENIHR report

**Submission: 45**

**Name**

John Britton (Individual)

**Question 1**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

I think the summary and the main report should distinguish the health effects of the different major groups of STP, should comment on the effects of STP on other diseases caused by smoking (COPD for example) and should compare the adverse effects of STP with those of smoking for the major outcomes. I disagree with the highlighting of the increased risk of fatal infarction in the summary, particularly as it is not clear to which form of STP this refers.

**Question 2**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The text of the report states It is likely that STP are less addictive, or perhaps less rapidly addictive, than smoked tobacco. The summary should say this.

**Question 3**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

I have argued throughout the meetings of the SCENIHR working group that the longitudinal data reported Rodu et al (J Intern Med 2002; 252:398-404) provide strong evidence that snus has been used in Northern Sweden as a de facto cessation agent. This observation is supported strongly by the paper by Ramstrom and Foulds (Tobacco Control 2006; 15:210-214). The answer to this question should therefore be much more reasoned and less dismissive. I also argued repeatedly at the working group meetings that if snus has no effect on smoking behaviour, the decline in smoking prevalence in men and women in Sweden should be similar. It is much greater in men. That snus has had an effect here is therefore a reasonable explanation for some of the greater reduction in men that certainly should not be discounted.

**Question 4**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Given the remit of the committee to deal with the science, not policy or risk management, I am surprised that the response to this question in the summary dwells on the caution necessary in translating findings across Europe, rather than discussing and addressing the facts. These are however summarised in the report, and provide emphatic evidence that in Sweden the availability of snus leads more people to quit smoking than to start.

**Question 5**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The simple answer to this question is yes, because extrapolation is always possible. However the relevance of the question lies in the likely impact of the availability of STP such as snus on public health. I argued strongly for a discussion of this in the report, and after substantial argument and opposition by some members of the working group, this was granted. I was the lead author of a section on harm reduction in the report. However substantial constraints were imposed on this section, preventing a comprehensive review of the harm reduction arguments. I was further disappointed to see that the final report put out for consultation does not include important sections of text that were agreed at the final meeting of the working group. In particular, section 3.8.1 has been completely rewritten, in poor English, and now comprises a restatement of the risks of STP rather than a summary of studies that provide a comparison of the risks of smoking. It needs to be substituted, as do all changes to the harm reduction section made since the draft report was submitted to SCENIHR, with the text agreed in my presence at the last working group meeting. The publication of the draft report with my name listed as an advisor implies that I endorse the contents of the report; as things stand this is not the case.

**Submission: 46**

**Name**

Jack E. Henningfield, Ph.D. (Individual)

**Question 1**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Although there has been considerable discussion regarding the differentiation of "Swedish snus" from other forms of "tobacco for oral use", even in Sweden, there is considerable variation in toxicant levels of snus products. Outside of Sweden, snuff or snus that is represented as "Swedish Snus" ( e.g., RJReynold's "Camel Snus - rhymes with Goose" allusions) can vary widely from snus typically sold in Sweden. So we have a problem of definition, is Swedish snus any snus sold in Sweden? Snus sold outside of Sweden by Swedish Match (which sells more toxic products outside of Sweden? or anything claimed be snus such as Camel Snus sold in the US - which is not refrigerated and contains higher levels of some toxicants. Furthermore, even in Sweden, what Swedish Match (the largest tobacco company) is making, and how they are marketing their products, may be considered an experiment in progress. I raise these issues by way of supporting the SCENIHR Report which states up front that the products vary widely. Until there is a clear means of identifying what Swedish snus is, with standards for form, handling (e.g., refrigeration or not), and levels of toxicants and nicotine, there is no objective basis for distinguishing these products. Furthermore, a report that appeared to endorse Swedish snus would inadvertently support the claims of products that differ widely from those typically sold in Sweden.

**References**

Henningfield, J.E. and Fagerstrom, K.O. Swedish Match Company, Swedish snus and public health: A harm reduction experiment in progress? Tobacco Control, 10: 253-257, 20

**Question 2**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Nicotine dependence and withdrawal appear to be fundamentally the same in oral smokeless users and cigarette smokers. However, severity of withdrawal symptoms generally appears somewhat weaker, perhaps due to the differences in onset and offset kinetics and/or smoke-specific substances. Whether, somewhat lower withdrawal (when approximately matched for nicotine intake) is of clinical significance is not clear and thus, even though, this difference should be recognized as a quantitative one, it is a matter of degree, not quality, and it should not be portrayed as implying easier cessation.

**References**

DK Hatsukami and HH Severson. Oral spit tobacco: addiction, prevention and treatment. Nicotine and Tobacco Research. 1(1):21-44, 1999. JE Henningfield, RV Fant and SL Tomar. Smokeless tobacco: An addicting drug. Advances in Dental Research, 11:330-335, 1997

**Question 3**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

I have to say that I find it absolutely amazing that there are some reputable scientists who at least imply that oral tobacco is effective treatment when there have been no trials of the sort that are routinely required for any medicine to determine that it is effective. Nor are there any of the fundamental resources that are expected for any pharmaceutical treatment (and the premis for treatment with oral tobacco is that it delivers nicotine) such as dose selection, dosing schedule, discontinuation schedule, warnings and cautions, behavioral guidance that is actually appropriate and empirically validated for the nature of the product etc. Such information can be seen to differentiate among products seemingly as closely related as nicotine gum, lozenges, patches, and inhalers. None of this has been done or is provided in the form of labeling for consumers so how could there possibly be endorsement. Another question is "Is it plausible that oral smokeless tobacco could be used to help people quit smoking?" The answer to this question is that the existing epidemiological data already discussed in the report, suggest that this is plausible, BUT proper trials need to be done to provide answers to the questions raised above. Then of course some way of determining the benefit risk and if perhaps such a treatment would be considered second line compared to nontobacco product, AND standards would be needed to allow consumers to identify which oral tobacco products were acceptable for smoking cessation - surely not products with vary high levels of toxicants. Whether products with 3-5 times the content of nicotine than is allowed in medicinals should be recommended is not clear but since many oral tobacco products do contain levels of nicotine that are several times higher than allowed in nicotine gum and lozenges, this is an important question to address as well.

**Question 4**

**Do you agree with the response given ?**

Agree

**Question 5**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Patterns of tobacco use differ widely within Sweden, let alone to other countries. Furthermore, as I mentioned above, the products differ widely across countries, and even Swedish Match products can differ widely when they are made for sale outside of Sweden (e.g., as in the US, South Africa and India). Finally, even in Sweden, this uncontrolled societal experiment is still in active progress as I mentioned in my comment on question 1 and in the referenced paper. As the fraction of dual tobacco users (smokers and oral smokeless rises and/or the fraction of past smokers now oral users rises - two apparent trends, will tobacco use and addiction escalate or decrease and will lung cancer rate fall then asymptote at higher levels than expected in other geopolitical regions in which all forms of tobacco use are discouraged, e.g., California (which by population and economic measures is substantially larger than Sweden). We don't know BUT the experiment in Sweden is not only of questionable generalizability, it may also prove to be one that would not be desired for export and may ultimately be regretted in Sweden. Care about current and future generations, thus, leaves me convinced that this is not the time to advocate the "Swedish" model with all its risks and uncertainties. It IS time to advocate models proving as effective if not more effective in reducing all forms of tobacco use (and already with signs of disease

reduction) in California, Massachusetts, Australia and elsewhere.

**References**

Henningfield, J.E. and Fagerstrom, K.O. Swedish Match Company, Swedish snus and public health: A harm reduction experiment in progress? *Tobacco Control*, 10: 253-257, 20

**Submission: 47**

**Name**

Karl Fagerstrom, Ph.D, Ass. Prof. (Individual)

**Question 3**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Unsatisfactory conclusion from the scientific point of view

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

It is correct that so far there are no controlled studies from clinical situations similar to what is the normal evaluation procedure for pharmaceutical drugs for smoking cessation. Among other things the legal/regulatory systems almost prohibits such a study in EU except Sweden. However most smokers who quit smoking do so by self-treatment. Sometimes they help themselves by prescription free products like nicotine replacement and as it seems in Sweden also with snus. A good body of data from the population studies in Sweden where snus and NRT has been compared (Ramstrom & Foulds, 2006) suggest that approximately as many use snus to aid their cessation attempt as pharmaceutical products. What is happening in the population with self-help is probably more important for public health than what occurs under medical treatment and supervision. Sometimes the external validity of controlled studies on e.g. nicotine replacement therapy (NRT) can be questioned as in US where there is a discussion as to whether NRT is effective as a self-help treatment only (Pierce & Gilpin, 2002). Others though find NRT effective under real life conditions (West & Zhou, 2007). Thus whether snus is a good product helping cigarette smokers to stop smoking is more complicated than showing efficacy in a clinical setting. What happens in the "real world" has not to be overlooked since that is where most smokers stop. What further adds weight is that the efficacy of snus in stopping smoking seem to be at least as good as NRT. In addition to the Ramstrom and Foulds (2006) data another study, commissioned by The Swedish Cancer Society and the Pharmacia Corporation (2001), 1000 ex-smokers were asked about their quitting methods. It was found that 50% had not used any help to stop, 33% had used Snus and 17% NRPs at some quit attempt. Twenty-eight per cent of men had used snus at the last quit attempt. In a more recent study (Ramstrom 2002) it was found that among males using a cessation aid at the last quit attempt, 55% used snus. For females the figure was 15%. The non-smoking rate after use of snus was 65% for males and 52% for females. For nicotine gum and patch the figures were 46% and 32% for males and 37% and 30% for females, respectively. Another issue that often comes up with snus is dual use of smoking and snus use. It has to be recognised not the "natural history" for smokers transferring to snus is different to those engaged in smoking cessation programs where abrupt quitting is prescribed. Often smokers interested in snus samples the product but finds the snus not being as satisfying immediately but gradually learn how to use it like it. This process can take anything from days to many months and throughout life a "former" cigarette smoker may allow him/herself to enjoy a cigarette at special occasions. The occasional cigarette is not a serious problem from a health point of view and the dual use in the beginning of the transition does most likely not mean more tobacco consumed. Whether daily dual use is more harmful than single use of cigarettes or snus is largely not known. Using a portion of snus may mean one less cigarette smoked rather than increasing the tolerance for nicotine leading to higher consumption. The long term use of snus that happens more often than with NRT is somewhat problematic. However most clinicians would

welcome long term use of NRT as long as it prevents relapse to smoking. The long term use of snus thus also has a positive side if continued use of snus makes the ex-smokers less likely to take up smoking again. Again the reality is more complex than how it is painted in the report.

### **References**

Ramström L & Foulds J. The role of snus in initiation and cessation of tobacco. *Tobacco Control*, 2006; 15: 210-214 Pirece JP & Gilpin EA. Impact of over the counter sales on effectiveness of pharmaceutical aids for smoking cessation. *JAMA*, 2002; 288: 1260-1264. West R. & Zhou X. Is nicotine replacement therapy for smoking cessation effective in the real world? *Thorax*, 2007; June 21 ahead of publication. TEMO (a public pool institute) (2001) *Rökare Och Slutare*[Smokers and Quitters]. Commissioned by the Cancer Society and Pharmacia Corporation. Snus better than nicotine preparations. Published in *Svenska Dagbladet*, Stockholm. Ramström, L. (2002) Patterns of use: a gate leading to smoking, or a way to give up. Proceedings of the 4th Annual Meeting of the Society for Research on Nicotine and Tobacco, Santander, Spain.

### **Question 5**

**Do you agree with the response given ?**

Disagree

**If you chose the option 'disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The conclusion is true in the sense that until we have tested whether snus can have an effect outside Sweden that is similar to what it has in Sweden we can of course not be certain that we can extrapolate to other cultures. That is by the way true for all other behaviours/habits we import from another country/culture. The natural scientific approach to such a situation would be to find out more under relatively controlled circumstances and possibly make small scale trials that are closely evaluated. A market status quo with, in practice, a "monopoly" for cigarettes is the worst of scenarios and is only benefiting the cigarette industry. There are numerous examples of where cultural habits have been exported. For example the diet and alcohol habits of Nordic people have been dramatically changed towards Mediterranean eating and drinking behaviour. Another example is how profoundly the American culture has influenced the European way of living. More relevant is perhaps to look at the history of tobacco use that has showed a change mainly from chewed, snuffed, pipe and cigar-smoked to today's cigarettes. There is no reason to believe that the current situation would just freeze for ever. For example is the muslim use of tobacco in the water-pipe gradually spreading into Europe. No convincing argument has been put forward why Europeans should not be able to use smokeless tobacco again or why Swedes would be so different to other Europeans. It may be interesting to make a comparison with how we look upon alcohol containing beverages and use of tobacco. A policy with alcohol beverages seem to be to stimulate use of alcohol-weaker alternatives such as beer and wine to the expense of stronger alternatives such as hard liqueur. This strategy has been one of the core pillars of alcohol control in the Nordic countries but is nowadays also making its way into the European Commission. To me it seems as the hard liqor is cigarettes and snus the beer or weine. Is beer and wine safe? The answer is a similar NO as for snus. In the ideal world we would need neither alcohol nor tobacco.



**Submission: 48**

**Name**

Herbert H. Severson Ph.D. (Individual)

**Question 1**

**Do you agree with the response given ?**

Mostly agree

**Question 2**

**Do you agree with the response given ?**

Agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Smokeless tobacco products vary widely in their bioavailable nicotine levels however many oral tobacco products have very high levels of nicotine. The addictive potential for smokeless tobacco products is high and we see very high levels of dependence among regular ST products users who seek cessation assistance.

**Question 3**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

There are no clinical trials that have demonstrated the efficacy of using smokeless tobacco products as a smoking cessation aid. Given that many other forms of nicotine substitution are available via pharmaceutical grade nicotine via patches, gum and lozenges it seems inappropriate to recommend the use of ST as a substitute or cessation aid for smokers.

**Question 4**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

we have published a research report that clearly shows that early use of smokeless tobacco by males is a strong risk for subsequent smoking two years later. The initial use of smokeless tobacco products increases by almost 4 fold the risk of subsequent smoking for youth in the 7th grade. This study included many other factors that are related to the onset of smoking and the use of smokeless tobacco is an independent and strong factor in increasing the likelihood of subsequent smoking.

**References**

Severson, H.H., Forester, K.A., & Biglan, A. (in press). Use of smokeless tobacco is a risk factor for cigarette smoking. *Nicotine & Tobacco Research*.

**Question 5**

**Do you agree with the response given ?**

Mostly agree

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The thing to remember is that marketing of smokeless tobacco products by companies will greatly increase the likelihood that these products will be used by a wide range of users and not limited to one demographic group. The experience in America shows that the companies will use restrictions of smoking and smoke free laws to encourage the use of smokeless products where smoking is restricted.

**Submission: 49**

**Name**

Dennis McChargue, PhD (Individual)

**Question 1**

**Do you agree with the response given ?**

Agree

**Question 2**

**Do you agree with the response given ?**

Agree

**References**

McChargue, D. E., Collins, F. L., & Cohen, L. M. (2002). Effect of non-nicotinic moist snuff replacement and lobeline on withdrawal symptoms during 48-hour smokeless tobacco deprivation. *Nicotine and Tobacco Research*, 4, 195-200. McChargue, D. E., & Collins, F. L. (1998). Differentiating withdrawal patterns between smokers and smokeless tobacco users. *Experimental and Clinical Psychopharmacology*, 6, 205-208.

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Agree

**Submission: 50**

**Name**

Scott L. Tomar, DMD, MPH, DrPH (Individual)

**Question 1**

**Do you agree with the response given ?**

Agree

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Agree

**Question 5**

**Do you agree with the response given ?**

Agree

**Submission: 51**

**Name**

John R Hughes, MD (Individual)

**Question 1**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The conclusions are flawed for two reasons. First, the report does not compare the risks of smokeless tobacco products (STP) to that of smoking. Given that many clinicians and adult smokers are considering using smokeless to stop smoking (e.g. this is why the commission addressed question 3 - see below), this comparison is as important, if not more so, than the question of whether any STP is worse than no STP. Second, the report has many statements about the effects of STP on health that are not true for snus. Lumping snus with other products is misleading.

**Question 2**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

The report is again flawed for not comparing the addiction potential of STP with smoking. Also, the studies cited as showing withdrawal symptoms are similar in STP users and smokers, are problematic because they compare STP users in the upper 20th percentile of heavy use with average daily smokers

**Question 3**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

Although I agree no randomized trials indicate efficacy of STP for smoking cessation, I think, here again, the wrong question is being asked. The correct question is whether STP use increases smoking cessation. This is because, even if STP were no better than NRT, it could be useful. For example, the text fails to cite the several reasons STP might be especially helpful for smoking cessation; i.e, delivery of high nicotine levels and low price. The latter is especially important for developing nations whose population or governments will not have the money to pay for NRT. STP may be a truly feasible option for them, rather than waiting

decades (and allowing millions of smokers to die) for them to develop to the point of being able to afford NRT.

**Question 4**

**Do you agree with the response given ?**

Agree

**Question 5**

**Do you agree with the response given ?**

Mostly disagree

**If you chose the option 'mostly disagree', please explain why :**

Relevant information missing from the analysis of the situation

**Please provide the technical/scientific evidence to improve the overall assessment (with complete references).**

This conclusion fails to recognize that perhaps one of the reasons for the STP associated decline in smoking in Sweden was the absence of false information that STP is as harmful as smoking (as is being stated in several EU countries). Also, even if STP only decreased smoking prevalence by 1-2%, this would greatly outweigh any potential harm from STP use. Here, as in other sections, the burden of proof appears to lie with those who wish to change EU regulations. An alternative is to state, that in order to ban consumer access to a product, governments must have solid data. The EU banned STP because it posited that, although snus has appeared to be beneficial in Sweden, it will be harmful in rest of Europe. This report shows the many gaps in our understanding of STP and, thus, it could be argued that it shows the basis for the EU position is weak. Finally, the report appears to ignore the urgency of the need to decrease smoking prevalence. Although smoking has declined somewhat in several EU countries, in many EU countries (and especially in new and applicant countries), it remains much higher than the rest of the developed world. Given that smoking cessation is the most important prevention behavior in developed countries, one would think the EU would be willing to allow innovative solutions to be tried – at least in some circumscribed, time-limited natural experiments.

**Submission: 52**

**Name**

Joey Bardell (Individual)

**Question 1**

**Do you agree with the response given ?**

Agree

**Question 2**

**Do you agree with the response given ?**

Agree

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Agree

**Question 5**

**Do you agree with the response given ?**

Agree

**Submission: 53**

**Name**

Manfred NEUBERGER

**Organisation**

Austrian Council on Smoking & Health (NGO)

**Question 1**

**Do you agree with the response given ?**

Agree

**References**

Neuberger M, Aigner K, Dittrich P, Götz M, Maurer G, Mlczoch J, Oberfeld G, Schulte-Hermann R (2004): Schäden durch Oraltabak. Österr. Ärztezeitung 8, 44-45.

**Question 2**

**Do you agree with the response given ?**

Agree

**References**

Ginzel KH, Maritz GS, Marks DF, Neuberger M, Pauly JR, Polito JR, Schulte-Hermann R, Slotkin TA 2007. Nicotine for the Fetus, the Infant and the Adolescent? Journal of Health Psychology 12, 2, 215-224

**Question 3**

**Do you agree with the response given ?**

Agree

**Question 4**

**Do you agree with the response given ?**

Mostly agree

**References**

Neuberger M. Recent recommendations endanger progress of tobacco control. (letter) BMJ 2007; 334: s16 [http://www.bmj.com/cgi/eletters/334/suppl\\_1/s16](http://www.bmj.com/cgi/eletters/334/suppl_1/s16)

**Question 5**

**Do you agree with the response given ?**

Agree