

## **GINIES Celine (SANCO)**

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**From:** SCHNICHELs Dominik (SANCO)  
**Sent:** 23 December 2011 00:03  
**To:** AMPELAS Anna Eva (SANCO); GINIES Celine (SANCO); MAUNU Antti (SANCO)  
**Subject:** TR : Follow-up of meeting with ESTOC  
**Attachments:** Final paper.pdf; FINAL ARTICLE NTR.pdf; Meta-analysis protocol.pdf; End Note 8633 (Fagerstrom).pdf; Final article on GothiaTek in HRJ.pdf; Bertuccio et al. 2011.pdf; End Note 8630 (Gustafsson on metabolic syndrome 2010).pdf; Lee snus overview 2011.pdf; Nilsson TSNA-ADDUCTS 2011.pdf; Lunell & Curvall.pdf

**Follow Up Flag:** Follow up  
**Flag Status:** Flagged

FYI and registration. Dominik

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**De:** Rutqvist Lars-Erik (STO) [mailto:Lars-Erik.Rutqvist@swedishmatch.com]  
**Date:** mer. 21/12/2011 17:05  
**À:** SCHNICHELs Dominik (SANCO)  
**Objet :** VB: Follow-up of meeting with ESTOC

Dear Mr Schnichels,

Thank you for our recent meeting that gave me the opportunity to present scientific data about Swedish snus that have a bearing on the ongoing revision of the Tobacco Products Directive. I am delighted that the objectives of the revision includes measures that could decrease tobacco-related morbidity and mortality. Clearly, Swedish snus has a role to play in that regard.

You invited me to submit additional data that may be relevant to your work. Below, I have briefly summarized the most widely publicized scientific developments about snus during 2011 as well as the Bertuccio paper (showing no association between risk of pancreatic cancer and use of mainly US smokeless tobacco products). I have also enclosed the referenced articles in pdf-format. However, as the formal review and meta-analysis of the clinical trials on snus and smoking cessation has not yet been published I can only send the protocol for that analysis, not the paper including the final results. I will submit that to you as soon as they are published, which I expect will happen in the near future.

Sincerely,

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

### **Significant scientific developments 2011 about snus & related issues:**

#### **Smoking cessation**

The SM sponsored clinical trials in Serbia and the US have both been published. Both trials showed that smokers allocated to snus were 2-3 times more likely to quit cigarettes completely compared to those allocated to a placebo-product. A systematic review and meta-analysis of the two studies have been conducted and the results have been submitted for publication.

*Joksić G, Spasojević-Tišma V, Antić R, Nilsson R, Rutqvist LE: Randomized, placebo-controlled, double-blind trial of Swedish snus for smoking reduction and cessation. Harm Reduct J 2011*

*Fagerström K, Rutqvist L, Hughes J: Snus as a smoking cessation aid: a randomized, placebo-controlled trial [E-publication ahead of print]. Nicotine Tob Res 2011*

## **Nicotine, addiction**

It has sometimes hypothesized that nicotine addiction among snus users is more profound than among cigarette smokers as a result of a notion that snus delivers more nicotine. This hypothesis was refuted in the 2008 SCENIHR report but continues to come up in the public debate. Several lines of evidence have recently emerged that provide further support to the SCENIHR conclusion. For instance, a randomized trial of vareniclin (Chantix, Champix) for snus cessation has been published showing that snus users allocated to active treatment were 1.4-1.6 times more likely to give up snus than those allocated to placebo. However, the cessation rate among the placebo-allocated participants was substantially higher (35-40%) than in similar trials among smokers. This observation prompted the researchers to conclude: "The response rate in the placebo group...was high, suggesting a population less resistant to treatment than smokers".

*Fagerström et al. Stopping smokeless tobacco with varenicline: randomized, double blind, placebo controlled trial. BMJ, 20110*

Also, a nicotine uptake study comparing 1.0 g snus pouches to a 4 mg Nicorette chewing gum showed similar uptake with the two products. Time to C<sub>max</sub> was slightly shorter with snus, but AUC (Area Under the Curve), which is an indicator of the total uptake, slightly higher with the chewing gum.

*Lunell & Curvall: Nicotine delivery and subjective effects of Swedish portion snus compared with 4 mg nicotine polacrilex chewing gum. Nicotine Tob Res. 2011 Jul;13(7):573-8.*

## **GothiaTek, TSNAs**

A scientific report on the development of SM's GothiaTek standard was published in Harm Reduction Journal.

*Rutqvist et al: Swedish snus and the GothiaTek standard. Harm Reduction J, 2011*

A review was published on the molecular basis for induction of human cancers by tobacco-specific nitrosamines. It was concluded that the levels of TSNAs in modern Swedish snus are so low that they are not expected to appreciably affect the "background" levels of the types of DNA adducts that are associated with exposure to TSNAs. These findings support and provides a preclinical rationale for the lack of increased cancer risks observed in the epidemiological studies on Swedish-type snus.

*Nilsson R: The molecular basis for induction of human cancers by tobacco specific nitrosamines. Regulatory Toxicology Pharmacology (In press), 2011, doi:10.1016/j.yrtph.2011.02.014*

## **Health effects**

A systematic overview and meta-analysis of health effects of Swedish snus has been published which essentially debunks claims that snus is associated with major health effects. On the issue of pancreatic cancer the conclusion was that the available data on an association are weak, statistically non-significant, and only "indicative" at the most.

*Lee PN: Summary of the epidemiological evidence relating snus to health. Regul Toxicol Pharmacol. 2011 Mar;59(2):197-214.*

A study from the University of Umeå of 1,071 individuals followed from age 16 to 43 years showed that the risk of metabolic syndrome (MB) was related to hazardous metabolic profile during childhood, adolescent socioeconomic deprivation, and obesity. No relationship was found with snus use which contradicts previous claims (mainly based on cross-sectional surveys) of an association between snus use and MB.

*Gustavsson et al: Life course origins of the metabolic syndrome in middle-aged women and men: the role of socioeconomic status and metabolic risk factors in adolescence and early adulthood. Am J Epidemiol, 2011*

### **Other significant publications**

A meta-analysis of several case-control studies of pancreatic cancer (PC) showed no association between use of different smokeless tobacco products and risk of (PC). Although none of the studies included snus users, the negative findings cast serious doubt on the alleged association between PC and snus use. The authors concluded that the discrepancy between their findings and the Scandinavian studies could be due to the lack of information on potential confounders, such as, alcohol use and diabetes in the latter two studies.

*Bertuccio et al. Cigar and pipe smoking, smokeless tobacco use and pancreatic cancer: an analysis from the International Pancreatic Cancer Case Control Consortium (PANC-4). Annals of Oncology, 2011*

/ler, 2011-12-21

