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Effects of prototype nicotine pouches on acid production in dental plaque, salivary pH, and oral mucosa

Submission date 08/12/2025	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 09/12/2025	**Overall study status** Ongoing	
Last Edited 04/02/2026	**Condition category** Other	

Plain English summary of protocol

Background and study aims:
Snus, a tobacco product used in Sweden for over 200 years, exposes users to nicotine but not to the harmful combustion compounds in tobacco smoke, making it widely regarded as significantly less harmful than smoking.
Nicotine pouches (NPs) have been on the US market for just over 10 years. They contain similar levels of nicotine as snus and are intended to be placed under the upper lip in the same way. Since NPs do not contain tobacco leaves, they have non-measurable levels of tobacco-specific nitrosamines and polycyclic hydrocarbons – two major classes of harmful substances found in snus.
Previous studies have shown that snus does not increase the risk of dental caries, and that the number of filled teeth is comparable to non-users. It has also been reported that tobacco snus may protect against dental caries by reducing acid production from oral bacteria, leading to less plaque formation. Two clinical studies involving snus users found that NP products did not negatively affect acid production in dental plaque, either after a single dose or after four weeks of daily use.
There are two types of NP: dry and moist, both available in various flavors and nicotine strengths. Dry NPs require moistening by saliva before the flavor becomes noticeable, which some consumers find unfavorable. Modifications of the pouch paper may help to trigger an initial flavor release. However, whether these modifications affect oral and dental health remains to be investigated.
The aim of the study is therefore to examine how the specific modifications to the pouch paper of dry NPs affect acid production in dental plaque and other oral variables, including saliva buffering capacity, saliva pH, oral mucosal condition (redness and mechanical irritation), perceived saliva-stimulating effect, and the overall safety profile of the study products.

Who can participate?
Healthy male or female volunteers aged 21 to 55 years who have used NPs or tobacco-based snus for ≥1 year, with a minimum weekly consumption of three cans

What does the study involve?
The study consists of four visits to the research laboratory (approximately 1.5 hours per visit), the first of which is a screening visit. The subsequent visits (visits 2-4) will occur on three separate days, with at least three days between each. Thus, each subject will participate in the study for approximately two weeks, excluding the screening period (the time between visit 1 and visit 2, which may be up to 4 weeks).
Before each usage visit (Visits 2-4), subjects will refrain from approximal tooth cleaning for 24 hours and toothbrushing for 12 hours prior to the visit. At each usage visit, one pouch of the study product will be placed under the upper lip and kept for 45 minutes. Acid production in dental plaque will be assessed before and during usage using an electrode or a pH strip. Unstimulated saliva (collected via passive drooling) will also be sampled before and during usage to assess buffering capacity and pH value. Effects on the oral mucosa, including redness and mechanical irritation, will be visually assessed and photographed before and after use. The perceived saliva-stimulating effect will be rated on a scale, and adverse events (AEs) will be recorded through subject interviews, including any spontaneously reported AEs, starting from the initiation of IP use (visit 2) and continuing until the last usage visit (visit 4).

What are the possible benefits and risks of participating?
In analogy with a regular Phase I study in healthy volunteers, there is no direct benefit for the participants, aside from a brief oral examination, which may provide them with information on their general state of oral health. Hence, the safety and wellbeing of the subjects are of utmost importance. Only adult participants who are well acquainted with and used to the effects of nicotine can participate in the study. The potential AEs of the study procedures are expected to be minor and clinically insignificant, based on experience from clinical studies on similar products. Notably, previous clinical studies with similar products have reported no AEs other than those likely attributed to nicotine exposure, such as salivation, nausea, and dyspepsia.

Where is the study run from?
Sahlgrenska Academy (Sweden)

When is the study starting and how long is it expected to run for?
May 2025 to March 2026

Who is funding the study?
Swedish Match North Europe AB (Sweden)

Who is the main contact?
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Contact information

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Public

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Study information

Scientific Title
Risk assessment of dental plaque acidogenicity following short-term exposure to prototype nicotine pouches

Acronym
SM25-02

Study objectives
Primary objective:
To compare the effects on dental plaque acidogenicity after short-term exposure to three different Dry 3 mg NPs.

Secondary objectives:
1. To compare the effects on buffer capacity after short-term exposure to three different Dry 3 mg NPs.
2. To compare the effects on the oral mucosa after short-term exposure to three different Dry 3 mg NPs.
3. To compare the subjectively perceived salivary stimulation effect after short-term exposure to the three different Dry 3 mg NPs.
4. To evaluate the safety and tolerability of the three different Dry 3 mg NPs in current daily users of NPs or tobacco-based snus.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 01/12/2025, The Swedish Ethical Review Authority (Etikprövningsmyndigheten Box 2110, Uppsala, SE-75002, Sweden; +46 (0)10 475 08 00; registrator@etikprovning.se), ref: Ethics approval: 2025-05216-01; amendment approval: 2025-07630-02

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Dose comparison

Assignment
Crossover

Purpose
To ensure that the specific modifications to the pouch paper of 3 mg nicotine pouches do not result in a clinically relevant effect on acid production in dental plaque compared to reference pouches.

Study type(s)

Health condition(s) or problem(s) studied
Nicotine use

Interventions
Investigational products (IPs):
NP Dry (3 mg) – Reference
NP Dry (3 mg) – Prototype A
NP Dry (3 mg) – Prototype B

Subjects will report to the test laboratory for a screening visit, followed by three usage visits on separate days. These usage visits will be scheduled with a minimum interval of three days

between them, and each visit will last approximately 1.5 hours. Consequently, each subject is expected to participate in the study for about 2 weeks, excluding the screening period.
The screening (Visit 1) will take place within 4 weeks prior to the first usage visit and will involve an eligibility check, including evaluations of smoking and oral tobacco/nicotine use, a brief oral examination, urine pregnancy testing (for women of childbearing potential only), and collection of medical history. Additionally, the salivary secretion rate, buffer capacity, and the number of cariogenic bacteria (Streptococcus mutans and lactobacilli) will be assessed.
Before each usage visit (Visits 2-4), scheduled at the same time of day for each subject, the subjects will refrain from approximal tooth cleaning for 24 hours and toothbrushing for 12 hours prior to the visits. Additionally, subjects will be instructed not to eat, drink, chew gum, use nicotine-containing products (including smoking), or engage in any other mouth-related procedures 1 hour before the visits. Subjects will use their regular toothbrush, which may be manual or electric, throughout the study. Urinary pregnancy tests may be conducted at Visits 2-4 for women of childbearing potential.
On the first usage visit (Visit 2), subjects will be randomized to one of three usage sequences. The following sequences will be randomized:
Sequence 1: A B C
Sequence 2: B C A
Sequence 3: C A B
Where
A = NP Dry (3 mg) – Reference
B = NP Dry (3 mg) – Prototype A
C = NP Dry (3 mg) – Prototype B

As this is an open-label study, the IP sequence assigned to each subject will be recorded in the CRF. The randomization list will include the subject number, randomization sequence, visit, and product. It will be generated by Swedish Match North Europe AB. The original list will be retained by the randomizer, and a copy will be provided to the test laboratory.

During each usage visit (Visits 2-4), the subject will place the IP in their upper vestibulum, where they normally place their pouches, using their fingers. The IP will be kept in place for 45 minutes. Plaque acidogenicity will be assessed by measuring pH in the plaque at four different locations before placement (baseline) and up to 45 minutes afterwards. All pH assessments will be performed on the same side as the IP placement.

The salivary buffer capacity will be assessed at baseline (0 minutes), and at 15, 30, and 45 minutes. Unstimulated saliva will be collected at each time point.

The effects on the oral mucosa from the usage of each IP will be assessed before (baseline) and after 45 minutes of usage. The effects in the form of redness and mechanical irritation will be graded as: no effect, mild effect, and severe effect. Photos will be taken before and after usage of each IP to enable a more detailed comparison of the effects.

The subjective salivary stimulation effect of each IP will be evaluated after 30 minutes of use using a 100 mm VAS, anchored with “no effect” to “extremely large effect”.

AEs will be collected by subject interview and those spontaneously reported by the subjects from the first usage visit (Visit 2) to the last usage visit (Visit 4).

Intervention Type
Other

Primary outcome(s)
1. Dental plaque acidogenicity, assessed by measuring pH in plaques measured using a microelectrode or a pH strip placed in the dental plaque at four different locations on the same side as the IP placement at baseline (time 0) and up to 45 minutes

Key secondary outcome(s))
1. Salivary buffer capacity measured using collection of unstimulated saliva through passive drooling at baseline (time 0) and up to 45 minutes

2. Effects on the oral mucosa in the form of redness and mechanical irritation measured using photographs visually graded as no effect, mild effect, or severe effect at baseline (time 0) and after 45 minutes

3. Subjectively perceived salivary stimulation effect measured using a 100 mm visual analogue scale (VAS) at 30 minutes of usage

4. Frequency, intensity, and seriousness of adverse events (AEs) measured using subject interviews and spontaneous reports at Visit 2 through Visit 4

Completion date
31/03/2026

Eligibility

Key inclusion criteria
1. Willing and able to give written informed consent for participation in the study
2. Subjects who have used NPs or tobacco-based snus for ≥1 year, with a minimum weekly consumption of three cans
3. Healthy male or female subject aged ≥21 to ≤55 years
4. Normal stimulated salivary secretion rate (>0.7 mL/min)
5. At least 24 own teeth remaining and overall good oral health, as judged by the Investigator
6. Women of child-bearing potential must practice abstinence from heterosexual intercourse (only allowed when this is the preferred and usual lifestyle of the subject) or must agree to use a highly effective method of contraception with a failure rate of <1% to prevent pregnancy for the duration of the study. The following are considered highly effective methods of contraception:
6.1. Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, transdermal)
6.2. Progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable)
6.3. Intrauterine device or intrauterine hormone-releasing system

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
21 years

Upper age limit

55 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. A history of diagnosed hypertension or any cardiovascular disease, or ongoing manifestations of hypertension or any cardiovascular disease as judged by the Investigator.
2. Any surgical or medical condition, including abnormal salivation (also pharmaceutically induced), or history thereof, which, in the judgment of the Investigator, might interfere with the absorption, distribution, metabolism or excretion of the IP or may either put the subject at risk because of participation in the study, influence the results, or the subject's ability to participate in the study.
3. Subjects who are pregnant, breastfeeding, or intend to become pregnant during the course of the study.
4. A history of diagnosed severe allergy/hypersensitivity or ongoing manifestations of severe allergy/hypersensitivity to aroma compounds (including fragrances and/or flavorings), as judged by the Investigator.
5. Subjects with severe oral conditions such as open caries lesions, severe periodontal health, lesions in soft tissues (apart from oral mucosal lesions related to the use of snus), or extensive prosthetic work (e.g., several implants, partial denture, dental veneers).
6. Any planned major surgery within the duration of the study.
7. Current or history of alcohol abuse and/or use of anabolic steroids or drugs of abuse, as judged by the Investigator.
8. Antibiotic use ≤4 weeks prior to the screening period.
9. Subjects who intend to change their nicotine consumption habit, including the intention to stop using nicotine products, within the next 3 months of the screening visit, as judged by the Investigator.
10. Subjects undergoing other dental treatment during the study period.
11. The Investigator considers the subject unlikely to comply with study procedures, restrictions, and requirements.

Date of first enrolment
02/02/2026

Date of final enrolment
16/03/2026

Locations

Countries of recruitment
Sweden

Study participating centre
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Sponsor information

Organisation
Swedish Match North Europe AB

Funder(s)

Funder type

Funder Name
Swedish Match North Europe AB

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.1	09/10/2025	21/01/2026	No	No