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How a single controlled use of a nicotine pouch affects the body in daily users

Submission date
11/02/2026

Recruitment status
Recruiting

Registration date
13/02/2026

Overall study status
Ongoing

Last Edited
10/03/2026

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Tobacco harm reduction focuses on lowering the health risks for people who use tobacco or nicotine, especially for those who do not want to stop using nicotine. One way to reduce harm is to switch from combustible cigarettes (which burn tobacco and produce many harmful chemicals) to alternatives that may pose fewer risks, such as Swedish snus or nicotine pouches (NPs). These products can still deliver nicotine, but with potentially lower health risks. Nicotine itself is addictive and not risk-free, but it is not the main cause of the diseases linked to smoking. Most smoking-related harm comes from the toxic substances created when tobacco burns.
NPs have been sold in the U.S. for just over 10 years. They are placed under the upper lip, similar to snus, and contain comparable nicotine levels. However, because 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 tobacco products like snus.
When comparing different nicotine-delivery products, it is important to understand that people do not absorb nicotine the same way from each product. Nicotine extraction and uptake can differ depending on whether the product contains tobacco or not, as well as on how the pouch is made (for example, its size, pH, water content.). There are also large differences between individuals, partly because saliva production varies from person to person. This results in a wide range of nicotine extraction among users.
The flavor of a NP may influence how it tastes and how satisfying or pleasant users find it. This can affect how likely people are to use a certain product and may indirectly influence how much nicotine they take in.

This study aims to measure how the body absorbs nicotine (pharmacokinetic, PK) and how the body responds to it (pharmacodynamic, PD) when using NP products under controlled conditions. The main goal is to assess the similarity in nicotine exposure (by comparing baseline-adjusted AUC0-inf values) between an unflavored NP product (Smooth, 1.5 mg) and a flavored NP product (Wintergreen, 1.5 mg) to determine whether flavoring significantly changes overall nicotine exposure. The study also includes several secondary objectives:
• Nicotine extraction: Understanding how much nicotine is released from the pouches helps show both the amounts of nicotine subjects are exposed to and how efficiently the product delivers nicotine.
• PK comparisons: Looking at all three NP products makes it possible to identify differences in

how quickly and how much nicotine is absorbed.
• PD assessments: Measuring pulse rate and collecting user-reported experiences (such as craving, satisfaction, product liking, and intent to use again) helps evaluate physiological and behavioral responses.
• Safety and tolerability: Monitoring adverse events ensures that using one pouch of the study products is safe for people who regularly use NPs.
Together, these objectives provide a comprehensive understanding of nicotine uptake, user experience, and safety. This information supports product development and helps meet regulatory requirements.

Who can participate?
Healthy volunteer adults aged 21 to 60 years who have used NPs for ≥1 year, with a minimum daily consumption of 5 pouches and users of other nicotine products are eligible.

What does the study involve?
The study consists of four visits to the study site, the first of which is a screening visit. The subsequent visits (visits 2-4) will take place on three separate days. 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 last up to 4 weeks).
Before each usage visit (Visits 2-4), subjects will refrain from all nicotine products for at least 12 hours. At each usage visit, one pouch of the study product will be placed under the upper lip and kept there for 30 minutes. Afterward, each used pouch will be collected and frozen at -20°C for later analysis of residual nicotine content.
Blood samples for assessing nicotine plasma concentrations and pharmacokinetic (PK) parameters will be collected at predefined timepoints, from pre-use up to 6 hours after administration. The pharmacodynamic (PD) effects of the investigational products (IPs) will be evaluated using pulse rate measurements and subjective assessments (visual analog scale questions) at the same predefined timepoints, along with a multiple-choice question 30 minutes after IP administration.
Adverse events (AEs) will be recorded through subject interviews and will include any spontaneously reported AEs, beginning at the start of IP use (visit 2) and continuing through the last usage visit (Visit 4).

What are the possible benefits and risks of participating?
Analogous to regular phase 1 clinical studies in healthy volunteers, there is no direct benefit for the subjects to participate in the study, aside from a brief medical examination, which may provide them with information on their general state of 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?
Clinical Trial Consultants AB, Sweden.

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

Who is funding the study?
Swedish Match North Europe AB

Who is the main contact?
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Study information

Scientific Title
Pharmacokinetics and pharmacodynamics of nicotine pouches following controlled single-dose administration in daily nicotine pouch users

Acronym
SM26-01

Study objectives

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 02/02/2026, Swedish Ethical Review Authority (Box 2110, Uppsala, SE-75002, Sweden; +46104750800; registrator@etikprovning.se), ref: 2025-09064-01

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Dose comparison

Assignment
Crossover

Purpose
To ensure that nicotine exposure does not substantially differ between a flavored and an unflavored 1.5 mg nicotine pouch product after 30 minutes of use.

Study type(s)

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

Interventions
Interventions:
Investigational products (IPs):
• Nicotine pouch 1 (NP1) – Smooth 1.5 mg
• NP2 – Wintergreen 1.5 mg
• NP3 – Smooth 3 mg

Administration and assessments:
Subjects will report to a study site for a screening visit, followed by three IP use visits held on separate days (preferably with at least 24 hours between visits). Each subject will participate in the study for approximately two weeks, excluding the preceding screening period. The screening visit (Visit 1) will occur within 4 weeks prior to Visit 2 and will include an eligibility check, including evaluation of prior nicotine use, collection of medical history, a brief physical examination, serology tests, electrocardiogram (ECG), vital signs (pulse rate and blood pressure), and assessments of height, weight, and body mass index (BMI).

Before each use visit (Visits 2-4), subjects will abstain from all nicotine products for 12 hours. All IP use visits will be conducted in the morning (08:00-12:00) to facilitate abstinence. Eligibility confirmation, randomization, drug and alcohol screening, and pregnancy testing for female subjects of childbearing potential will occur on Visit 2. Subjects will then be randomized to one of six sequences:
Sequence 1: A B C
Sequence 2: B C A
Sequence 3: C A B
Sequence 4: C B A
Sequence 5: A C B
Sequence 6: B A C
where
A = NP1 – Smooth 1.5 mg
B = NP2 – Wintergreen 1.5 mg
C = NP3 – Smooth 3 mg

As this is an open-label study, the assigned IP sequence will be recorded in the eCRF. Randomization will be stratified by site. Each randomization list, generated by CTC, will include site, randomization number, randomization sequence, visit, and product. The original randomization list will be retained by the randomizer, and copies will be provided to each site and to Swedish Match North Europe AB as the IP packing company.

During IP use sessions at Visits 2-4, subjects will keep the pouch between the upper lip and gum for 30 minutes. Subjects will be instructed not to manipulate the pouch with the tongue or lips, and to refrain from drinking, chewing gum, or brushing their teeth for 30 minutes before use, during use, and for 30 minutes after IP removal. Blood samples for the determination of nicotine plasma levels and subsequent calculation of pharmacokinetic (PK) parameters will be collected pre use (within -10 minutes to -1 minute prior to start of IP use) and at 5, 10, 15, 20, 30, 40, 60, 90 minutes, 2 hours, 4 hours, and 6 hours post use.

Pharmacodynamic (PD) effects will be assessed by measuring pulse rate using a pulse oximeter and by collecting subjective outcome parameters via visual analog scale (VAS) questions and a multiple-choice question (MCQ), at predetermined timepoints. Pulse rate will be measured at pre use (-15 minutes) and at the same post-use timepoints as PK sampling. Subjective outcomes will include “craving”, “satisfaction”, “product liking”, and “intent to use again”. “Craving” and “satisfaction” will be assessed at the same post-use timepoints as PK sampling, whereas “product liking” and “intent to use again” will be assessed at the 30-minute timepoint. Additionally, “product liking” vs. the subjects’ usual NP product of choice will be assessed using a 3-point scale questionnaire at 30 minutes post-use.

Used pouches will be collected after 30 minutes of use and stored at -20°C pending determination of residual nicotine. The extracted amount (mg/unit) and extracted fraction (%) of nicotine will be assessed. Unused pouches from the same batches will serve as references and

will be stored at -20°C pending analysis. Adverse events (AEs) will be collected through subject interviews and will include any AEs reported spontaneously by subjects, beginning from the start of IP use at Visit 2 until the end of Visit 4. Any prior and concomitant medications use will also be recorded. Visits 3 and 4 will follow the same schedule as Visit 2, except for certain admission procedures described above. The date of the final IP use visit (Visit 4) will be considered the subject's end-of-study date.

Intervention Type
Other

Primary outcome(s)
1. Similarity between NP1 and NP2 based on the geometric least squares means (LSMeans) ratio of baseline-adjusted AUC0-inf within the range of 0.8 to 1.25. measured using nicotine concentrations in plasma collected at pre-use, 5, 10, 15, 20, 30, 40, 60, 90 minutes, 2 hours, 4 hours, and 6 hours post use, determined by a validated LCMS/MS method at the end of the study at 0-infinitity

Key secondary outcome(s))
1. In vivo extracted amounts (mg/unit) and extracted fractions (%) of nicotine for each of the three NP products measured using collected and frozen IP pouches prior to analysis using GC-MS at the end of the study. The in vivo extraction of nicotine will be calculated by subtracting the residual amount of nicotine after 30 minutes of usage of the pouches from the mean of 10 unused pouches, at 30 minutes

2. Non-adjusted and baseline-adjusted PK parameters AUC0-inf, AUC0-last, AUC0-1.5h, Cmax, Tmax, and T1/2 for each of the three NP products measured using nicotine concentrations in plasma collected at pre-use, 5, 10, 15, 20, 30, 40, 60, 90 minutes, 2 hours, 4 hours, and 6 hours post use, determined by a validated LCMS/MS method at the end of the study at 0-infinity

3. Similarity between NP1 and NP2 based on the geometric LSMeans ratio of baseline-adjusted Cmax within the range of 0.8 to 1.25 measured using nicotine concentrations in plasma collected at pre-use, 5, 10, 15, 20, 30, 40, 60, 90 minutes, 2 hours, 4 hours, and 6 hours post use, determined by a validated LCMS/MS method at the end of the study at Cmax

4. Pharmacodynamic (PD) effects: a) The pulse rate parameters highest increase from baseline (Eimax), time to the first instance of Eimax (TEimax), the Emax from time 0 to 60 minutes (Emax0-60), and the time to reach Emax0-60 (TEmax0-60) measured using a pulse oximeter at pre-use (-15 minutes), 5, 10, 15, 20, 30, 40, 60, 90 minutes, 2, 4, and 6 hours post-use

5. Pharmacodynamic (PD) effects: b) The subjective "craving" parameters largest decrease from baseline (Edmax) and time to the first instance of Edmax (TEdmax) measured using a 100 mm visual analog scale (VAS) at pre-use (-10 minutes), 5, 10, 15, 20, 30, 40, 60, and 90 minutes, 2, 4, and 6 hours post-use

6. Pharmacodynamic (PD) effects: c) The subjective "satisfaction" parameters largest value (Evmax) and time to the first instance of Evmax (TEvmax) measured using a 100 mm VAS at 5, 10, 15, 20, 30, 40, 60, and 90 minutes, 2, 4, and 6 hours postuse

7. Pharmacodynamic (PD) effects: d) The subjective outcome parameters "product liking" and "intent to use again", measured using VAS questions at 30 minutes

8. Frequency, intensity, and seriousness of adverse events (AEs) measured using AEs collected through subject interviews, including any events reported spontaneously by subjects, starting from the first usage visit (Visit 2) and continuing through the last usage visit (Visit 4) at Visits 2-4

Completion date
10/04/2026

Eligibility

Key inclusion criteria
1. Be willing and able to provide written informed consent for participation in the study.
2. Be a user of NP products for ≥1 year, with a minimum daily consumption of five pouches, and be willing and able to use NP products while abstaining from all other nicotine products for at least 12 hours prior to and during Visits 2 to 4. Users of other nicotine products are eligible; however, subjects must primarily be users of NP products to be included.
3. Be a healthy male or female subject aged 21 to 60 years, inclusive
4. Be medically healthy, without clinically significant abnormalities in medical history, physical examination findings, vital signs, ECG, and/or laboratory results (including hepatitis B/C and human immunodeficiency virus [HIV]) at the time of the screening visit, as judged by the Investigator.
5. Female subjects of childbearing potential must either practice abstinence from heterosexual intercourse (if this reflects their preferred and usual lifestyle) or agree to use a highly effective method of contraception with a failure rate of <1%/year to prevent pregnancy for the duration of the study. Female subjects of childbearing potential with an exclusive male partner who has undergone vasectomy may choose not to use contraceptives. Acceptable methods of contraception include:
5.1. Combined (estrogen and progestogen-containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, transdermal),
5.2. Progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable), and
5.3. Intrauterine device or intrauterine hormone-releasing system.

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
21 years

Upper age limit
60 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. A history of diagnosed hypertension or any cardiovascular disease, or current manifestations of either, as judged by the Investigator.
2. Any surgical or medical condition, including abnormal salivation (including 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 due to study participation, influence the results, or impair the subject's ability to comply with the study.
3. A history of diagnosed severe allergy/hypersensitivity or current manifestations of severe allergy/hypersensitivity to aroma compounds (including fragrances and/or flavorings), as judged by the Investigator.
4. Poor venous access or fear of needles.
5. Any planned major surgery during the study period.
6. Pregnancy, currently breastfeeding, or intention to become pregnant during the course of the study.
7. Positive screening results for serum hepatitis B surface antigen, hepatitis C antibodies, and/or HIV.
8. Positive test results for drugs of abuse or alcohol at screening or upon admission to the study site prior to start of IP use. Positive results consistent with the subject's medical history and prescribed medications may be disregarded, as judged by the Investigator.
9. History of alcohol abuse or excessive alcohol intake, as judged by the Investigator.
10. Presence or history of drug abuse, as judged by the Investigator.
11. History of, or current use of anabolic steroids, as judged by the Investigator
12. Current, ongoing use of beta-adrenergic blocking agents (beta blockers) or central stimulant medications (psychostimulants), e.g., for the treatment of attention deficit hyperactivity disorder (ADHD), including pro re nata (as needed) use, at the discretion of the Investigator.
13. Plasma donation, blood donation or corresponding blood loss within 1 month prior to screening.
14. Intention to change nicotine consumption habits, including plans to stop using nicotine products, within the next 3 months of the screening visit, as judged by the Investigator.
15. The Investigator considers the subject unlikely to comply with study procedures, restrictions, and requirements.

Date of first enrolment
06/03/2026

Date of final enrolment
10/04/2026

Locations

Countries of recruitment
Sweden

Study participating centre
Clinical Trial Consultants AB
CTC Uppsala
Dag Hammarskjölds väg 10C
Uppsala

Sweden
SE-75237

Study participating centre
Clinical Trial Consultants AB
CTC EbbePark
Ebbegatan 3
Linköping
Sweden
SE-58213

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	17/02/2026	10/03/2026	No	No