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A study to assess nicotine uptake to the bloodstream after use of six different oral nicotine products in adult smokers

Submission date 25/11/2025	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 26/11/2025	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 02/02/2026	**Condition category** Other	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
The main purpose of this clinical study is to learn how much nicotine is in the blood of adult smokers after using each of the six oral nicotine products measured by blood sampling. The other purpose of this clinical study is to learn, by collecting questionnaires, about product liking, flavour, positive/negative effects the study products have on you and how the study products affect your urge to smoke and mood.

Who can participate?
Smokers aged 19-55 years

What does the study involve?
1. Staying at the research site for 8 days.
2. Undergo a training session for how to correctly use the different nicotine products.
3. Following a successful training session, participants will be randomly assigned an order to use the study products.
On each product test session (6 in total), an oral nicotine product will be used in the morning following going without nicotine or tobacco products for 24 hours and without food for 8 hours. During the test session, blood samples will be collected regularly and questionnaires completed.

What are the possible benefits and risks of participating?
There are no positive health benefits from participating. This study is for research purposes only.

Where is the study run from?
Celerion (UK)

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

Who is funding the study?
1. British American Tobacco (Investments) Limited (UK)
2. Nicoventures Trading Limited (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific, Public

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Type(s)
Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
362705

Study information

Scientific Title
Single exposure, randomised, crossover study to assess the pharmacokinetics of six oral nicotine products in adult smokers under fasting conditions

Study objectives

This single exposure study is designed in accordance with regulatory guidelines, with the aim of characterising the bioavailability of nicotine in the six products in adult cigarette smokers. As this is a comparative bioavailability study where each participant will receive each study product in a crossover fashion, a control group is not included.

The primary objective of this study is to compare the nicotine PK parameters between the Test products and each of the three Reference products after a single administration under fasting conditions.

The secondary objectives are to compare the nicotine pharmacokinetic parameters between the Test product(s) and the appropriate Reference products, to assess multiple subjective measures via questionnaires, and to evaluate the safety and tolerability of a single use of the three Test and the three Reference products.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 29/10/2025, Wales Research Ethics Committee 2 (Health and Care Research Wales Floor 4 Crown Building Cathays Park, Cardiff, CF10 3NQ, United Kingdom; +44 (0)2922941119; Wales.REC2@wales.nhs.uk), ref: 25/WA/0296

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Uncontrolled

Assignment
Crossover

Purpose
To assess the nicotine uptake in the blood of six oral nicotine products

Study type(s)

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

Interventions
Participants:
1. Stay at the research site for 8 days.
2. Undergo a training session for how to correctly use the different nicotine products.
3. Following a successful training session, participants will be randomly assigned an order to use the study products.

On each product test session (six in total), an oral nicotine product will be used in the morning following going without nicotine or tobacco products for 24 hours and without food for 8 hours. During the test session, blood samples will be collected regularly and questionnaires completed.

2 mg Nicotine Pouch (Test)
2 mg Mini Nicotine Pouch (Test)
4 mg Mini Nicotine Pouch (Test)
2 mg Nicotine Lozenge (Reference)
4 mg Nicotine Pouch (Reference)
2 mg Nicotine Gum (Reference)

The randomisation approach for this study is the William Design/Latin Square.

Intervention Type
Other

Primary outcome(s)
1. Plasma nicotine uptake parameters using blood samples following the use of an oral nicotine product measured using Cmax and AUC0-T of nicotine at 12-hour test session

Key secondary outcome(s))
1. Nicotine pharmacokinetic (PK) parameters of the Test product(s) and the appropriate Reference products measured using Cmax and AUC0-T of nicotine at 12-hour test session

2. Subjective measures of Overall Product Liking and Flavour Longevity after the intended use period of the study products measured using Overall Product Liking and Flavour Longevity questionnaires at the end of product use

3. Subjective measure of Product Effects 1 hour after the start of study product use measured using Product Effects questionnaire at 1 hour after the start of study product use

4. Subjective measures of Urge to Smoke and a Visual Analogue Mood Scale before and 1 hour after the start of study product use and the change from baseline measured using Urge to Smoke and a Visual Analogue Mood Scale questionnaires at before and 1 hour after the start of study product use

Completion date
26/01/2026

Eligibility

Key inclusion criteria
1. Able to read, understand, and willing to sign an informed consent form (ICF) and complete questionnaires written in English
2. Stated willingness to comply with all study procedures and availability for the duration of the study
3. Adult male or female
4. If female, and is of childbearing potential and agrees to use one of the accepted contraceptive regimens from at least 28 days prior to the first study product administration through to at least 30 days after the last use of study product.
5. Aged at least 19 years but not older than 55 years

6. Body mass index (BMI) within 18.5 kg/m2 to 30.0 kg/m2, inclusively
7. Minimal body weight of 50 kg
8. Primary tobacco product used in the last 6 months is combustible cigarettes or roll your own cigarettes
9. A smoker of 10 cigarettes or more per day who has smoked for at least 6 months prior to the first study product administration, except for brief periods of abstinence due to illness, quit attempt (prior to 28 days of Screening), or clinical study participation (prior to 28 days of Screening) will be allowed at the discretion of an investigator
10. Response at Screening to the Fagerström Test for Nicotine Dependence (FTND) Question 1 ("How soon after you wake up do you smoke your first cigarette?") is either "Within 5 minutes" or "6-30 minutes".
11. Stated willingness to abstain from nicotine and tobacco products (except for the study products provided) from 24 hours prior to the first study product administration until the end of the study
12. Positive urine cotinine test (≥200 ng/mL) at Screening and prior to the first study product administration
13. Expired breath carbon monoxide (eCO) level is ≥10 ppm and ≤100 ppm at Screening and at check-in (Day -2)
14. Successful completion of the training session for study product use prior to the first study product administration (participant is able to follow the instructions and does not experience significant AEs during the training session)
15. Clinical laboratory values within the laboratory's stated normal range; if not within this range, they must be without clinical significance, as determined by an investigator
16. Have no clinically significant diseases captured in the medical history or evidence of clinically significant findings on the physical examination (including oral mucosa examination and vital signs) and/or ECG, as determined by an investigator

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
19 years

Upper age limit
55 years

Sex
All

Total final enrolment
34

Key exclusion criteria
1. Females who have a positive pregnancy test, are pregnant, breastfeeding, or intend to become pregnant during the course of the study
2. Presence of any tongue piercings or history of any tongue piercings in the last 90 days prior to the first study product administration
3. Presence of braces, partials, dentures or any dental work that could, in the opinion of an

investigator, affect the conduct of the study (including missing molars)
4. Presence or history of significant form of oral and/or pharyngeal inflammation, oral lesions and/or gum disease or temporomandibular joint dysfunction
5. Use of tobacco and/or nicotine containing products, other than combustible cigarettes, (e.g., e-cigarette/vapes pods, tanks, nicotine-containing pouches or disposables, or heated tobacco products) more than one day per week for the past 6 months prior to Screening or at any time in the last 28 days
6. History of significant hypersensitivity to any excipients of the formulations as well as severe hypersensitivity reactions (like angioedema) to any drugs
7. Presence or history of significant gastrointestinal, liver or kidney disease, or surgery that may affect drug bioavailability
8. History of significant cardiovascular, pulmonary, hematologic, neurological, psychiatric, endocrine, immunologic or dermatologic disease
9. Presence of clinically significant ECG abnormalities at the Screening visit, as defined by medical judgment
10. Maintenance therapy with any drug (with the exception of hormonal contraceptives or hormone replacement therapy)
11. Significant history of drug dependency or alcohol abuse (> 14 units of alcohol per week, intake of excessive alcohol, acute or chronic)
12. Any clinically significant illness in the 28 days prior to the first study product administration
13. Use of any prescription drugs (with the exception of hormonal contraceptives or hormone replacement therapy) in the 28 days prior to the first study product administration, that in the opinion of an investigator would put into question the status of the participant as healthy
14. Use of all formats of pseudoephedrine in the 7 days prior to the first study product administration
15. Use of any medication or substance that aids in smoking cessation, including but not limited to any nicotine replacement therapy (e.g., nicotine gum, lozenge, patch), varenicline (Chantix®), bupropion (Wellbutrin®, Zyban®), or Lobelia extract in the 28 days prior to the first study product administration
16. Any history of tuberculosis
17. Positive test result for alcohol and/or drugs of abuse at Screening or prior to the first product administration.
18. Positive Screening results for HIV Ag/Ab Combo, Hepatitis B surface Antigen (HBsAG (B) (hepatitis B)) or Hepatitis C Virus (HCV (C)) tests
19. Inclusion in a previous group for this clinical study
20. Intake of an Investigational Product in any other clinical trial in the 28 days prior to the first study product administration
21. Haemoglobin level is <12.5 g/dL for females or <13.5 g/dL for males at Screening
22. Donation of 500 mL or more of whole blood or lost blood or blood products in the 56 days prior to the first study product administration
23. Plasma donation within (≤) 7 days prior to signing the informed consent or between Screening and check-in Day -2
24. A postponement of a decision to quit using tobacco- or nicotine-containing products in order to participate in this study
25. Previously attempted to quit using tobacco- or nicotine-containing products in the 28 days prior to the first study product administration
26. Employed by a tobacco or nicotine company, the study site, or handles raw, unpackaged tobacco- or nicotine-containing products as part of their job

Date of first enrolment
12/11/2025

Date of final enrolment
06/01/2026

Locations

Countries of recruitment
United Kingdom

Northern Ireland

Study participating centre
Celerion
22-24 Lisburn Road
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BT9 6AD

Sponsor information

Organisation
British American Tobacco (United Kingdom)

ROR
https://ror.org/01znsh139

Organisation
Nicoventures Trading Limited

Funder(s)

Funder type

Funder Name
British American Tobacco

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Funder Name
Nicoventures Trading Limited

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available