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A study to assess and compare health effect indicators in users of Vype vaping products, smokers, former smokers and never-smokers

Submission date 14/01/2021	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 14/01/2021	**Overall study status** Completed	
Last Edited 20/06/2023	**Condition category** Other	

Plain English summary of protocol

Background and study aims
The aim of this study is to compare 'health effect indicators' in healthy adult volunteers who use Vype e-pen3 and/or ePod with healthy adult volunteers who smoke, and to compare these results with volunteers who have quit smoking and those who have never smoked.

Who can participate?
Healthy males or non-pregnant, non-breastfeeding females between the ages of 19 and 55 who:
- Have been cigarette smokers for at least the one year prior to participating; or
- Have used the Vype ePen 3 and/or ePod vapour products for at least the 6 months before participating; or
- Are ex-smokers, who quit all tobacco and nicotine use for at least the 6 months before participating; or
- Have never smoked

What does the study involve?
On the morning of arrival at the clinic (Day 1), participants will be screened to ensure they are healthy and that they fit the criteria (e.g. in terms of tobacco and nicotine product use history, based on responses to a short questionnaire) for the study group into which they are planned to be enrolled. Eligible participants will be enrolled in the study the same afternoon/evening, and the urine they produce over the next 24 hours will be collected. Participants will stay in the clinic overnight. To the extent possible (e.g. when this does not interfere with the timing of study assessments), participants in the smoking group will be allowed to smoke their own cigarettes and participants who vape will be allowed to vape their own product, which they must supply themselves, during their stay in the clinic. Blood samples will be taken for 'health effect indicator' (biomarker) assessments, a test to show how much air the participant can breathe out in one forced breath (spirometry) will be performed, a further assessment of levels of a specific gas (nitric oxide) in participants' breath will be performed, an ultrasound of the neck will be carried out to capture images of the carotid artery (CIMT assessment), and participants will complete a quality of life questionnaire. Participants will be discharged from the clinic in the afternoon/evening of Day 2, after completing the 24-hour urine collection period and

assessments to ensure they are safe to discharge (including blood pressure, heart rate and blood test). About 1 week after leaving the clinic, participants will have a follow-up telephone call.

What are the possible benefits and risks of participating?
There are no direct benefits to participants. However, participants will undergo a general health examination, which may provide them with information on their state of health. Participants will be able to ask for advice on completely stopping using tobacco and nicotine products. This study may help doctors, scientists and manufacturers learn things about tobacco and nicotine products that could help others to quit smoking.
The risk that participants develop clinical symptoms is low, as they will be using their own products, which they will have been using consistently for at least the past 6 months before enrolment in the study. The only risks to the participants will be related to the trial procedures (blood pressure measuring, blood sampling, electrocardiograms [ECGs] and neck ultrasound scans). These are all extremely mild.

Where is the study run from?
Richmond Pharmacology (UK)

When is the study starting and how long is it expected to run for?
September 2020 to August 2021

Who is funding the study?
British American Tobacco (UK)

Who is the main contact?
Nathan Gale
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
291542

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
BAT4120026, C20034, IRAS 291542

Study information

Scientific Title
A cross-sectional study to assess biomarkers of exposure and biomarkers of potential harm in solus users of Vype ePen 3 and ePod products

Study objectives
The purpose of this study is to compare selected biomarkers of exposure, biomarkers of potential harm and physiological measures in suitable adult subjects who use Vype vapour products with suitable adult subjects who smoke, and to assess the findings in context of subjects who have quit smoking and those who have never smoked.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/03/2021, South Central - Berkshire B Research Ethics Committee (Level 3, Block B, Bristol HRA Centre, Whitefriars, Lewin Mead, Bristol, BS1 2NT, UK; +44 (0)207 1048226; berkshireb.rec@hra.nhs.uk), REC ref: 21/SC/0005

Study design
Single-centre cross-sectional cohort study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Biomarkers of toxicant exposure, biomarkers of potential harm and physiological measures in subjects who smoke, use Vype vaping products, have quit smoking or have never smoked

Interventions
This study does not involve the testing of any investigational medical products. The study involves collection of blood and urine samples to analyse ‘health effect indicators’ in four different populations: Vype ePen 3 and/or ePod users, smokers, former smokers or never smokers.

Subjects will be selected for enrolment into the study itself based on clinical laboratory evaluations, medical history, tobacco and nicotine use status and history, physical examination, vital signs, drugs of abuse and alcohol consumption screening. Pregnancy testing will be performed on female subjects. During this visit, informed consent will take place and subjects' eligibility for inclusion will be determined. Nicotine use status will be determined using a one-step urinary cotinine test kit, and smoking status will be confirmed via an exhaled breath carbon monoxide test. Tobacco and nicotine use history will be assessed using a questionnaire. Blood biochemistry, haematology, virology, urinalysis and urinary drugs of abuse screening will also be performed. All screening assessments will be performed on the morning of Day 1 prior to enrolment the same afternoon/evening.
Enrolled subjects will have all urine which they produce over the next 24-hours collected, aliquots of which will be analysed for the urinary biomarker outcome measures. Participants will stay in the clinic overnight. To the extent possible (e.g. when this does not interfere with the timing of study assessments), participants in the smoking group will be allowed to smoke their own cigarettes and participants who vape will be allowed to vape their own product, which they must supply themselves, during their stay in the clinic. Blood samples will be taken for analysis for the blood biomarker outcome measures, a spirometry assessment will be performed, nitric oxide in exhaled breath will be measured, carotid intima-media thickness will be assessed via an ultrasound of the neck, and participants will complete the quality of life questionnaire (SF-36). Participants will be discharged from the clinic in the afternoon/evening of Day 2, following completion of their 24-hour urine collection period and assessments to ensure they are safe to discharge (including blood pressure, heart rate and blood test). Approximately 1 week after leaving the clinic, participants will have a follow-up telephone call.

Intervention Type
Other

Primary outcome(s)
Measured at a single timepoint:
1. Total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (Total NNAL) is measured in 24-hour urine void using a validated LC-MS/MS method
2. Nitric oxide is measured in exhaled breath (FeNO) using a handheld monitor containing an electrochemical sensor
3. 8-epi-prostaglandin F2α Type III (8-Epi-PGF2α Type III) is measured in 24-hour urine void using a validated LC-MS/MS method
4. Carboxyhaemoglobin (COHb) is measured in blood using a validated GC-MS method
5. Total white blood cell count (WBC) is measured in blood using an automated haematology sampling procedure
6. Soluble intercellular adhesion molecule-1 (s-ICAM1) is measured in blood using a validated ELISA/CLIA method
7. High-density lipoprotein (HDL) is measured in blood using a homogenous enzymatic colorimetry method

Key secondary outcome(s))
Measured at a single timepoint:
1. 11-dehydrothromboxane B2 (11-dTX B2) is measured in 24-hour urine void using a validated LC-MS/MS method
2. Total nicotine equivalents (nicotine, cotinine, 3-hydroxycotinine and their glucuronide conjugates) (TNeq) is measured in 24-hour urine void using a validated LC-MS/MS method
3. Monohydroxybutenylmercapturic acid (MHBMA) in 24-hour urine void using a validated LC-MS /MS method

4. 3-hydroxy-1-methylpropylmercapuric acid (HMPMA) in 24-hour urine void using a validated LC-MS/MS method
5. 3-hydroxypropylmercapturic acid (3-HPMA) in 24-hour urine void using a validated LC-MS/MS method
6. Total N-nitrosonornicotine (Total NNN) in 24-hour urine void using a validated LC-MS/MS method
7. 3-hydroxybenzo[a]pyrene (3-OH-B[a]P) in 24-hour urine void using a validated LC-MS/MS method
8. Forced Expiratory Volume in 1 second as % of predicted (FEV1%pred) is measured using a spirometer
9. Carotid intima-media thickness (CIMT) is measured using ultrasonography
10. Quality of life is measured using the validated RAND 36-Item Health Survey 1.0 Questionnaire Items (SF-36)

Added 20/08/2021:
11. S-phenylmercapturic acid (S-PMA) in 24-hour urine void measured using a validated LC-MS /MS method

Completion date
15/08/2021

Eligibility

Key inclusion criteria
All Subjects:
1. Subjects will be:
1.1. Males or females
1.2. 19 to 55 years of age, inclusive, demonstrated by appropriate proof of identification
2. Subjects will have a:
2.1. Body mass index (BMI) of 18.5 to 30.0 kg/m^2, inclusive
2.2. Body weight exceeding 52 kg (males) or 45 kg (females)
3. Subjects will be in good health, as judged by the PI or the appropriately qualified designee based on:
3.1. Medical history (confirmed by volunteer)
3.2. Physical examination
3.3. Vital signs assessment
3.4. 12-lead ECG
3.5. Clinical laboratory evaluations
3.6. Lung function tests/spirometry at screening
4. Subjects will have given their written informed consent to participate in the study and will have agreed to abide by the study restrictions
5. Subjects must demonstrate the ability to comprehend the informed consent form (ICF), be able to communicate well with the PI or the appropriately qualified designee, understand and comply with the requirements of the study, and be judged suitable for the study in the opinion of the PI or the appropriately qualified designee
6. Subjects will refrain from consuming alcohol within 24 hours prior to Screening
7. Subjects will refrain from consuming cruciferous vegetables, and grilled, fried or barbequed food, and avoid being in the presence of the cooking of cruciferous vegetables, and grilled, fried or barbequed food for 48 hours prior to Screening

Additional criteria for Arm A subjects only:
8. Subjects will be regular (daily) users of the Vype ePen 3 and/or Vype ePod vaping devices
9. Subjects will have used the Vype ePen 3 and/or Vype ePod vaping devices for a minimum of 6 months prior to Screening
10. Subjects will have a urine cotinine level > 200 ng/mL and an exhaled breath CO level < 7 ppm at Screening

Additional criteria for Arm B subjects only:
11. Subjects will be regular smokers of commercially manufactured filter cigarettes
12. Subjects will have smoked for at least one year prior to Screening
13. Subjects will typically smoke at least 10 CPD and must have a urine cotinine level >200ng/ml and an exhaled breath CO level ≥7 ppm at Screening

Additional criteria for Arm C subjects only:
14. Subjects will be former smokers of commercially manufactured filter cigarettes who quit smoking at least 6 months prior to Screening
15. Subjects will have a urine cotinine level < 200 ng/ml and an exhaled breath CO level <7 ppm at Screening

Additional criteria for Arm D subjects only:
16. Subjects will have never smoked (<100 cigarettes in their life and none within the six months prior to Screening)
17. Subjects will have a urine cotinine level < 200 ng/ml and an exhaled breath CO level <7 ppm at Screening

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
19 years

Upper age limit
55 years

Sex
All

Total final enrolment
222

Key exclusion criteria
All Subjects:
1. Female subjects who are pregnant or breastfeeding. This will be confirmed at Screening
2. Subjects who have donated:
2.1. ≥400 ml of blood within 90 days prior to screening

2.2. Plasma in the 7 days prior to screening
2.3. Platelets in the 6 weeks prior to screening
3. Subjects who have had an acute illness (e.g. upper respiratory tract infection, viral infection, etc.) requiring treatment within 4 weeks prior to screening
4. Subjects who have a significant history of alcoholism or drug/chemical abuse (apart from known smoking/vaping history) within 24 months prior to Screening, as determined by the PI or the appropriately qualified designee
5. Subjects who have a positive urine drugs of abuse or breath alcohol screen (confirmed by repeat) at Screening
6. Subjects who:
6.1. Have serum hepatitis/are carriers of the hepatitis B surface antigen (HBsAg)
6.2. Are carriers of the hepatitis C antibody
6.3. Have a positive result for the test for human immunodeficiency virus (HIV) antibodies
6.4. have a positive result in the COVID test at screening indicating current, active infection
7. Subjects who have used prescription or over-the-counter (OTC) bronchodilator medication (e. g. inhaled or oral β-adrenergic agonists) to treat a chronic condition within the 12 months prior to screening
8. Subjects who have received any medications or substances (other than nicotine) which:
8.1. Interfere with the cyclooxygenase pathway (e.g. anti-inflammatory drugs including aspirin and ibuprofen) within 14 days prior to Screening
8.2. Are known to be strong inducers or inhibitors of cytochrome P450 (CYP) enzymes within 14 days or 5 half-lives of the drug (whichever is longer) prior to Screening
9. Subjects who would need to take prescription medication during the period beginning with screening and ending with discharge
10. Subjects who are unwilling or unable to comply with the study requirements
11. Employees and immediate relatives of the tobacco industry or the clinical site
12. Subjects who have any clinically relevant abnormal findings on the physical examination, medical history, ECG, lung function tests or clinical laboratory panel, unless deemed not clinically significant by the PI or the appropriately qualified designee
13. Subjects who have been diagnosed with a significant history of urticaria or asthma (childhood asthma is acceptable)
14. Subjects who have, or who have a history of, any clinically significant neurological, gastrointestinal, renal (including urinary tract infection or nephrolithiasis), hepatic, cardiovascular, psychiatric, respiratory, metabolic, endocrine, haematological or other major disorder that, in the opinion of the PI or the appropriately qualified designee, would jeopardise the safety of the subject or impact on the validity of the study results
15. Subjects who have previously been diagnosed with any form of malignancy
16. Subjects who are currently participating in another clinical trial (including follow-up)
17. Subjects who, in the opinion of the PI or the appropriately qualified designee, should not participate in this study

Additional criteria for Arm A subjects only:
18. Subjects who have used any form of tobacco or nicotine-containing product, other than the Vype ePen 3 and Vype ePod, within the six months prior to Screening
19. Subjects who are self-reported non-inhalers (vapers/e-cigarette users who draw aerosol from their device into the mouth and throat but who do not inhale)

Additional criteria for Arm B subjects only:
20. Subjects who are self-reported non-inhalers (smokers who draw smoke from the cigarette into the mouth and throat but who do not inhale)

Additional criteria for Arm C and D subjects only:
21. Subjects who have used any form of tobacco or nicotine-containing product within the six months prior to Screening

Date of first enrolment
15/03/2021

Date of final enrolment
14/08/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Richmond Pharmacology Ltd
1A Newcomen Street
London Bridge
London
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SE1 1YR

Sponsor information

Organisation
British American Tobacco (United Kingdom)

ROR
https://ror.org/01znsh139

Funder(s)

Funder type
Industry

Funder Name
British American Tobacco

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Deidentified participant-level data will be available on request. This includes all data captured using the CRF, questionnaires and full bioanalytical reports available in SDTM format for at least 5 years. This data will be available immediately following publication. Data will be available to anyone who wishes access to the data and for any purpose. Requests for data should be made to clinical_info@bat.com and data requestors must sign a data access agreement.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		30/05/2023	20/06/2023	Yes	No
Protocol article		26/05/2022	14/07/2022	Yes	No