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A study to examine the delivery of nicotine into the blood of people when they use Juul e-cigarettes with different pod designs

Submission date
30/07/2019

Recruitment status
No longer recruiting

Registration date
05/08/2019

Overall study status
Completed

Last Edited
03/03/2022

Condition category
Other

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
E-cigarettes (or ENDS, electronic nicotine delivery systems) are products which heat a liquid solution containing nicotine. This is unlike tobacco cigarettes, which burn tobacco to make nicotine inhalable. Because of the lack of burning of the tobacco leaves, it is generally accepted that vapour from e-cigarettes contains significantly lower levels of harmful inhaled chemicals. E-cigarettes do however enable the inhalation of nicotine at levels that smokers may find satisfying and which may mean they switch away from cigarette smoking. JUUL is an e-cigarette product. It generates vapour by heating a liquid containing nicotine and is intended to be an alternative to cigarette smoking for adult smokers. That said, it is not intended to be a product for smoking cessation or to alleviate the symptoms of nicotine withdrawal. JUUL is sponsoring this study because it wants to understand more about its current, future and other products, including how much nicotine people inhale when using JUUL and how this affects blood nicotine levels. The main aim of this study is to look at the levels of nicotine in the blood (nicotine pharmacokinetics) after the use of various JUUL e-cigarettes and regular cigarettes. Another aim is to get subject's opinions on the satisfaction associated with using JUUL e-cigarettes compared to their satisfaction with cigarette smoking.

Who can participate?
Healthy, adult, male or female smokers, 21 to 65 years of age

What does the study involve?
Participants are asked to use the JUUL e-cigarette device with different types of JUUL pods and with different nicotine levels, as well as to smoke their own-brand of regular cigarettes, in a randomly-allocated sequence. The two product use periods last for 5 minutes each. Blood samples are taken at various timepoints before, during and after product use, for blood nicotine level analysis.

What are the possible benefits and risks of participating?
The study will help the Sponsor understand how closely JUUL approximates to cigarette smoking, both in terms of user experience and perception and blood nicotine levels. The study is

not intended to assess the safety or efficacy of JUUL as a medicinal product or to treat any medical condition. Possible benefits for participants include obtaining a free medical assessment, and contributing to the scientific knowledge around how effectively e-cigarettes deliver nicotine when used by smokers. The main risk of participating is one of injury during blood draws. However, these will only be conducted by fully-trained clinic staff and this risk is minimal. A further risk is that tobacco and nicotine products are addictive and their consumption is associated with real risks of serious diseases. The best way to avoid the risks associated with tobacco and nicotine products is not to use them at all.

Where is the study run from?
Celerion (UK)

When is the study starting and how long is it expected to run for?
February 2019 to August 2019

Who is funding the study?
JUUL Labs Inc. (USA)

Who is the main contact?
Dr Josh Vose
jliscience@juul.com

Contact information

Type(s)
Public

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
JUUL-PROT-00015

Study information

Scientific Title
An open label, randomized, controlled, crossover study to measure nicotine pharmacokinetics using the JUUL ENDS with existing and new vaporization pods and a combustible cigarette in healthy adult subjects

Study objectives
Different e-cigarette wicking materials may modulate the delivery of nicotine into the blood of subjects when they use JUUL e-cigarettes.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/07/2019, Health and Social Care Research Ethics Committee B (HSC REC A), Office for Research Ethics Committees Northern Ireland (ORECNI) (Customer Care & Performance Directorate, Lissue Industrial Estate West, 5 Rathdown Walk, Moira Road, Lisburn, BT28 2RF, UK; Tel: +44 (0)28 95361407; Email: RECA@hscni.net), REC ref: 19/NI/0117, IRAS project ID: 265554

Study design
Randomised controlled crossover single-centre study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Use of e-cigarettes

Interventions
In a randomly-allocated sequence, on each assessment day subjects will either smoke combustible cigarettes of their usual brand or use one of the following JUUL e-cigarettes, for 2 brief use periods:

JUUL e-cigarette with current JUULpod with 59 mg/ml nicotine, Virginia Tobacco flavour
JUUL e-cigarette with current JUULpod with 18 mg/mL nicotine, Golden Tobacco flavour
JUUL e-cigarette with new JUULpod with 18 mg/mL nicotine, Golden Tobacco flavour
JUUL e-cigarette with new JUULpod with 9 mg/mL nicotine, Golden Tobacco flavour

The two product use periods last for 5 minutes and consist of either controlled puffing (10 puffs of 3-seconds duration, 30-seconds apart) or ad libitum puffing (no set number of puffs, puff interval or puff duration). Blood samples will be taken at various timepoints before, during and after product use, for blood nicotine level analysis.

In this study, 20 subjects will use all 5 study products in a crossover fashion according to a randomisation schedule.

Intervention Type
Other

Primary outcome(s)
Baseline-adjusted and unadjusted plasma nicotine pharmacokinetic (PK) parameters following the 5-minute controlled product use sessions for each study product. The following PK parameters will be determined: AUC0-60, Cmax and Tmax (unadjusted only). These will be determined following the measurement of blood (plasma) nicotine levels in samples drawn at the following timepoints relatives to initiation of the first inhalation: -5, 1.5, 3, 5, 6, 7, 8, 10, 15, 30 and 60 minutes.

Key secondary outcome(s))
1. Baseline-adjusted and unadjusted plasma nicotine PK parameters following the 5-minute ad libitum product use sessions for each study product. The following PK parameters will be determined: AUC0-60, Cmax and Tmax (unadjusted only). These will be determined following the measurement of blood (plasma) nicotine levels in samples drawn at the following timepoints relatives to initiation of the first inhalation: -5, 1.5, 3, 5, 6, 7, 8, 10, 15, 30 and 60 minutes.
2. Subjective effects following use of the study products, assessed using the modified product evaluation scale (mPES) at a single timepoint on each assessment day, immediately after completion of the 30-minute blood draw

Completion date
24/08/2019

Eligibility

Key inclusion criteria
1. Healthy, adult, male or female smoker, 21 to 65 years of age, inclusive, at the Screening visit
2. BMI between 18 to 35 kg/m2, inclusive
3. Healthy based on medical history and screening assessments, in the opinion of the Investigator
4. Current smoker, for at least 12 months prior to the Screening visit. Brief periods of non-smoking (e.g., up to ~7 consecutive days due to illness, trying to quit, participation in a study or trial where smoking was prohibited) during that time will be permitted at the discretion of the PI
5. Currently smokes at least 10 manufactured combustible, non-menthol cigarettes per day (CPD), as self-reported at Screening visit. Subjects may also be dual-using cigarettes and ENDS products
6. Has a positive urine cotinine (≥ 200 ng/mL) at the Screening visit

7. Has an exhaled CO > 10 ppm at Screening visit
8. A female subject of childbearing potential must have been using one of the following forms of contraception and agree to continue using it through completion of
the study:
8.1. Hormonal (e.g., oral, vaginal ring, transdermal patch, implant, or injection) consistently for at least 3 months prior to Assessment Day 1
8.2. Double barrier method (e.g., condom with spermicide, diaphragm with spermicide) at screening
8.3. Intrauterine device for at least 3 months prior to Assessment Day 1
8.4. A partner who has been vasectomized for at least 6 months prior to Assessment Day 1
8.5. Abstinence beginning at least 6 months prior to screening
9. A female subject of non-childbearing potential must have undergone one of the following sterilization procedures at least 6 months prior to Assessment Day 1:
9.1. Hysteroscopic sterilization
9.2. Bilateral tubal ligation or bilateral salpingectomy
9.3. Hysterectomy
9.4. Bilateral oophorectomy
9.5. Or postmenopausal with amenorrhea for at least 1 year prior to Check-in and have follicle-stimulating hormone (FSH) levels consistent with postmenopausal status
10. Is willing to comply with the requirements of the study, including a willingness to use the study products during the study
11. Provides voluntary consent to participate in this study documented on the signed informed consent form (ICF)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
25

Key exclusion criteria
1. Clinically relevant medical or psychiatric disorder, in the opinion of the Investigator. This includes any clinically significant concomitant disease or condition that could interfere with, or for which the treatment of might interfere with, the conduct of the study, or that would, in the opinion of the investigator, pose an unacceptable risk to the subject in this study
2. Has a clinically significant abnormal finding on the physical examination, medical history, vital signs, ECG, or clinical laboratory results, in the opinion of an investigator
3. Has had an acute illness (e.g., upper respiratory infection, viral infection) requiring treatment within 28 days prior to Check-in

4. Has a fever (> 100.5°F) at the Screening visit or on Assessment day(s)
5. Positive result for urine drugs of abuse test or alcohol breath test at the screening visit. If a positive urine drug test is observed, and it is believed the positive urine test is due to prescription drugs, the PI should obtain documentation that;
5.1. Confirms the subject's use of the prescribed medication
5.2. The prescribed medication will cause a false positive drug test
6. Has or has a history of diabetes mellitus, asthma, or chronic obstructive pulmonary disease
7. Has a systolic blood pressure < 90 mmHg or > 150 mmHg, diastolic blood pressure < 40 mmHg or > 95 mmHg, or heart rate < 40 bpm or > 99 bpm at Screening
8. Has experienced an allergic reaction following previous e-cigarette use or with exposure to any primary components of the e-liquids (nicotine, flavor, benzoic acid, propylene glycol and glycerol)
9. Clinically significant abnormality in laboratory test results at screening, in the opinion of the Investigator
10. Has participated in a previous clinical study or trial for an investigational drug, device, biologic, or tobacco product within 30 days prior to Day 1
11. Has donated blood or blood products, > 500 mL, had significant blood loss, or received whole blood or a blood product transfusion within 3 months prior to Assessment Day 1
12. If female, the subject is pregnant, has a positive serum pregnancy test at screening, is lactating, breastfeeding, or intends to become pregnant during the time period from Screening through the end of study
13. Has used medications known to interact with cytochrome P450 (CYP) 2A6 (including, but not limited to, amiodarone, amlodipine, amobarbital, buprenorphine, clofibrate, clotrimazole, desipramine, disulfiram, entacapone, fenofibrate, isoniazid, ketoconazole, letrozole, methimazole, methoxsalen, metyrapone, miconazole, modafinil, orphenadrine, pentobarbital, phenobarbital, pilocarpine, primidone, propoxyphene, quinidine, rifampicin, rifampin, secobarbital, selegiline, sulconazole, tioconazole, tranylcypromine) within 14 days or 5 half-lives of the drug, whichever is longer, prior to Assessment Day 1
14. Has used any prescription smoking cessation treatments, including, but not limited to, varenicline (Chantix®) or bupropion (Zyban®) within 30 days prior to Assessment Day 1
15. Requires concomitant treatment with prescription or non-prescription products that contain pseudoephedrine (e.g., nasal/sinus decongestants)
16. Negative response (i.e., unwilling to use or unable to tolerate [e.g., experiences AEs during the product trial that will prevent the subjects from continuing to use the JUUL product as judged by the PI]) to any of the JUUL products at Screening
17. Is a self-reported puffer (i.e., adult smokers who draw smoke from the cigarette into the mouth and throat but do not inhale)
18. Is planning to quit smoking during the study or postponing a quit attempt in order to participate in the study
19. Unable to perform controlled puff sequence and draw down the pod weight by 20-60 mg after 3 attempts
20. Unwilling or unable to comply with study-related procedures including but not limited to; schedule of assessment, PK draws and placement of indwelling catheter
21. Is or has a first-degree relative (i.e., parent, sibling, child) who is a current employee of the study site or shareholder, or is member of the board of directors of JUUL Labs, Inc.
22. Has previously taken part in, has been excluded or withdrawn from, or has completed this study
23. Has previously been diagnosed with any form of cancer, except for basal cell or squamous epithelial carcinomas of the skin that have been resected at least 1 year prior to Screening
24. In the opinion of an investigator, the subject should not participate in this study

Date of first enrolment

10/07/2019

Date of final enrolment
19/07/2019

Locations

Countries of recruitment
United Kingdom

Northern Ireland

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

Sponsor information

Organisation
JUUL Labs Inc

Funder(s)

Funder type
Industry

Funder Name
JUUL Labs Inc

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available as the dataset may contain commercially-sensitive information.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		24/05/2021	03/03/2022	Yes	No
HRA research summary			26/07/2023	No	No