

CLINICAL STUDY REPORT:

**A Longitudinal Ambulatory Study to Assess Changes in Cigarette Consumption
Behavior and Biomarkers of Exposure during a 6-Week Switch to Very Low Nicotine
Cigarettes**

**Celerion Project No. CA24914
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Product Name: VLN™ Cigarettes

**First subject enrolled: 29 June 2018
Last subject completed: 08 March 2019**

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This study was conducted in compliance with Good Laboratory Practice and the International Council for Harmonisation Harmonized Tripartite Guideline regarding Good Clinical Practice.

Confidential

Nothing herein is to be disclosed in any way without the prior written permission of the study Sponsor.

2. SYNOPSIS

Click here for detailed [SYNOPSIS](#).

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4. LIST OF ABBREVIATIONS

1-OHP	1-hydroxypyrene
3-HPMA	3-hydroxypropylmercapturic acid
AE	Adverse event
ANOVA	Analysis of variance
AUC0-180	Area under the concentration-time curve from time 0 to 180 minutes
BLQ	Below the limit of quantitation
BMI	Body mass index
BoE	Biomarkers of exposure
CFR	Code of Federal Regulations
CI	Confidence interval
Cm	Centimeter
Cmax	The maximum observed concentration
CO	Carbon monoxide
COHb	S-phenylmercapturic acid
CPD	Cigarettes smoked per day
CRF	Case report form
CRU	Clinical research unit
CV	Coefficient of variation
ECG	Electrocardiogram
EU	European Union
FDA	Food and Drug Administration
FSH	Follicle-stimulating hormone
FTCD	Fagerström Test for Cigarette Dependence
g	gram
GCP	Good Clinical Practice
Geom CV	Geometric coefficient of variation
Geom Mean	Geometric mean
GMR	Geometric mean ratio
hr	Hour

HBsAg	Hepatitis B surface antigen
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
ICF	Informed Consent Form
ICH	International Council for Harmonisation
IRB	Institutional Review Board
ITT	Intent-to-treat
kg	Kilogram
kg/m ²	Kilogram per meter square
LC-MS/MS	Liquid chromatography-tandem mass spectrometry
LLOQ	Lower limit of quantitation
LSM	Least-squares means
MedDRA®	Medical Dictionary for Regulatory Activities
mg	Milligram
mL	Milliliter
MNWS-R	Minnesota Nicotine Withdrawal Scale-Revised
N;n	Sample size; number of observations
NNAL	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol
NNK	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone
NNN	total N-Nitrosornicotine
OECD	Organisation for Economic Cooperation and Development
PD	Pharmacodynamic
PI	Principal Investigator
PK	Pharmacokinetic
PP	Per protocol
PUEAE	Product use-emergent adverse event
QA	Quality Assurance
QSU-Brief	Brief Questionnaire of Smoking Urges
SAE	Serious adverse event
SAP	Statistical analysis plan

SD	Standard deviation
SEM	Standard error of the mean
SOC	System organ class
SOP	Standard operating procedure
SPA-M	Mobile smoking puff analyzer
S-PMA	S-phenylmercapturic acid
Tmax	Time of the maximum measured plasma concentration
Tneq	total nicotine equivalents
UB	Usual brand
UDS	Urine drug screen
ULOQ	Upper limit of quantitation
USA	United States of America
VLN	Very low nicotine
WHO	World Health Organization

5. ETHICS

5.1 Institutional Review Board

All pertinent study documents were reviewed by an independent Institutional Review Board (IRB), Advarra, Inc., prior to study initiation. The committee is constituted and operates in accordance with the principles and requirements described in the International Council for Harmonisation (ICH) Harmonised Tripartite Guideline regarding Good Clinical Practice (GCP) (E6 Consolidated Guidance, April 1996, and Integrated Addendum to ICH E6, Nov 2016).

A copy of the final protocol, protocol amendments, and protocol clarification letter (PCL) is included in [Appendix 16.1.1](#), and IRB roster information is included in [Appendix 16.1.3](#).

5.2 Ethical Conduct of the Study

The Investigators understood that by signing the Protocol Investigator Signature Page, they provided their commitment to comply with applicable GCP regulations and guidances and to conduct the study in accordance with the protocol, the ethical requirements referred to in the European Union (EU) directive 2001/20/EC, and the ethical principles set forth in the Declaration of Helsinki. This trial was conducted in conformance with GCP standards and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

5.3 Subject Information and Consent

Prior to initiation of any study-specific procedures, subjects received a copy of the Informed Consent Form (ICF) that summarized, in non-technical terms, the purpose of the study, the procedures to be carried out, and the potential hazards. The Principal Investigator (PI) or his representative explained the nature of the study to the subjects, in non-technical terms, and answered all questions regarding the study. Subjects reviewed, signed, and dated the ICF. Subjects received a copy of the fully signed ICF. A sample ICF is located in [Appendix 16.1.3](#).

6. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

This study was performed under the direction of the PIs:

Allen Hunt, MD
(Previously Dr. Philip Mathew, MD)
Celerion
621 Rose Street
Lincoln, Nebraska 68502, USA

and

Melanie Fein, MD
High Point Clinical Trials Center
4160 Mendenhall Oaks Parkway, Suite 105
High Point, North Carolina 27265, USA

Clinical laboratory tests required by this protocol were performed by the following certified clinical laboratory facility:

Celerion
621 Rose Street
Lincoln, Nebraska 68502, USA

and

Laboratory Corporation of America (Labcorp)
1447 York Court
Burlington, North Carolina 27215

Sample analysis for nicotine in plasma and urine biomarkers was performed at the following laboratories:

Celerion
621 Rose Street
Lincoln, Nebraska 68502, USA

and

Celerion Switzerland AG
Allmendstrasse 32, 8320
Fehraltorf, Switzerland

Pharmacokinetic (PK), pharmacodynamic (PD), safety, and statistical analyses were performed and a report was prepared at Celerion, Data Management and Biometrics department, under the direction of:

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Curricula vitae of the PIs are included in [Appendix 16.1.4](#).

The signature pages for the PIs and Data Management and Biometrics Director from Celerion, and 22nd Century Group, Inc. are located in [Appendix 16.1.5](#).

7. INTRODUCTION

7.1 Background

A gradual reduction of nicotine levels in cigarettes was first proposed by Benowitz and Henningfield in 1994. In this paper, the authors proposed a long-term (over many years) reduction in cigarette nicotine levels as a measure to reduce smoking addiction and to aid cessation for smokers. The underlying assumption of this proposal was that there is a nicotine exposure threshold, below which reinforcing effects of nicotine are insufficient to cause or sustain addiction. The absolute level of such a threshold has not yet been determined. Hatsukami et al. (2018) published results of a study where subjects were immediately or gradually switched to very low nicotine (VLN) cigarettes for 20 weeks. Significantly lower levels of carbon monoxide (CO) and urine biomarkers of exposure (BoE) were observed in the immediate versus gradual reduction group and no significant differences were observed between the gradual reduction and control groups.

In March 2018, the Food and Drug Administration (FDA) announced through an Advanced Notice of Proposed Rule Making that a tobacco standard for lowering nicotine in cigarettes is being considered (2018). As new cigarettes with reduced amounts of nicotine in the tobacco blend are developed, clinical studies are required to assess whether they lead to reductions in cigarette consumption and whether this is associated with reductions in biomarkers of exposure to cigarette smoke toxicants and changes in cigarette dependence. Furthermore, subjective assessments of urges to smoke, withdrawal symptoms and perceived health risks are also useful indicators of whether low nicotine cigarettes will give rise to reduced addiction to cigarette smoking.

7.2 Study Purpose

The purpose of this study is to examine whether measures of cigarette consumption behavior (cigarettes per day and smoking topography) are changed when smokers switch from smoking conventional cigarettes to smoking cigarettes with a VLN content (0.4 mg nicotine per gram of tobacco). A secondary purpose is to examine changes in BoE, nicotine PK, and subjective measures of dependence, smoking urges, withdrawal symptoms and perceived health risks, when subjects switch to smoking VLN cigarettes.

7.3 Hypothesis

It is anticipated that when adult smokers switch to smoking VLN cigarettes, after habitually consuming their usual quantity and brand of cigarettes, their daily cigarette consumption will be reduced. It is further anticipated that puffing topography parameters will be unchanged following smoking VLN cigarettes for 6 weeks (i.e., no smoking compensation will occur).

8. STUDY OBJECTIVES AND ENDPOINTS

8.1 Objectives

Primary Objective

1. To characterize cigarette consumption behavior (cigarettes per day and puffing topography) before, during, and after a switch from usual brand (UB) to VLN cigarettes for 6 weeks.

Secondary Objectives

1. To evaluate changes in tobacco-related BoE before, during and after a 6-week switch from UB to VLN cigarettes.
2. To evaluate nicotine PK before, during and after a 6-week switch from UB to VLN cigarettes.
3. To evaluate changes in subjective effects before, during and after a 6-week switch from UB cigarettes to VLN cigarettes.

8.2 Endpoints

Product use endpoints (Primary Objective 1)

- Cigarettes smoked per day (CPD). Both compliant and non-compliant smoking was captured in the e-diaries.
- Number of collected used cigarette butts (apparent compliant, apparent non-compliant, and total).
- Puffing topography parameters (puff duration, puff volume, peak puff flow rate, average flow rate and inter-puff interval).

Nicotine PK endpoints (Secondary Objective 2)

- C_{max}
- T_{max}
- AUC

BoE endpoints (Secondary Objective 1)

- In urine
 - Total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) (4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone [NNK] biomarker)
 - Total N-Nitrosonornicotine (NNN)
 - 3-hydroxypropylmercapturic acid (3-HPMA, acrolein biomarker)
 - S-phenylmercapturic acid (S-PMA, benzene biomarker)
 - 1-hydroxypyrene (1-OHP, hydroxypyrene biomarker)
 - Total nicotine equivalents (T_{neq})
 - Creatinine concentration (for normalization of urinary BoE endpoints)
- Carboxyhemoglobin (COHb) in blood
- Cotinine in plasma

Subjective effects endpoints are (Secondary Objective 3)

- Fagerström Test for Cigarette Dependence (FTCD)
- Brief Questionnaire of Smoking Urges (QSU-Brief)
- Minnesota Nicotine Withdrawal Scale-Revised (MNWS-R)
- Perceived Health Risk Scale

Safety endpoints include

- Adverse events (AEs)

9. INVESTIGATIONAL PLAN

9.1 Overall Study Design and Plan

This was an open-label, randomized, forced-switching study conducted at 2 study sites. Seventy-two (72) self-affirmed exclusive filtered non-mentholated cigarette smokers and 70 self-affirmed exclusive filtered mentholated cigarette smokers with no intention to quit during the study period were enrolled and began the study at Week -1.

All potential subjects provided informed consent and successfully completed the Screening procedures prior to participation in the study. Subjects also engaged in a brief product trial with the VLN cigarettes. Subjects who reacted negatively (i.e., unwilling to use and/or couldn't tolerate the product [experienced AEs that would prevent them from continuing to use the product as judged by the Investigators]) to the VLN cigarettes during the product trial period did not continue in the study.

At the start of Week -1, all subjects were asked to smoke their UB cigarettes as per their usual daily consumption for the following week. Subjects received an e-diary to record cigarettes smoked per day (CPD). Training in completion of the e-diary was provided at the visit at the start of Week -1. Subjects continued recording their CPD in their e-diaries through the end of Week 6.

Subjects returned at the end of Week -1 for collection of blood and 24-hour urine samples for baseline BoE assessments. Subjective questionnaires for dependence, withdrawal symptoms, urges to smoke, and perceived health risk were also completed at scheduled times. A subset of 18 non-menthol and 18 menthol smoker subjects completed an assessment of puffing topography with their UB cigarettes during this visit. A further subset of 12 of the non-menthol and 12 of the menthol smoker subjects who completed the topography assessment also completed a nicotine PK assessment at the end of this visit. Subjects who underwent topography and PK assessments were assigned to switch to smoking VLN cigarettes.

On Day -1 of Week 1, subjects were randomly selected to either remain smoking their non-menthol (22 subjects) or menthol (20 subjects) UB cigarettes, or to switch to smoking non-menthol (50 subjects) or menthol (50 subjects) VLN cigarettes as per their UB cigarette flavor. Subjects returned at the end of Weeks 2 and 6 for collection of blood and 24-hour

urine samples for BoE assessments. Subjective effects questionnaires were also completed at scheduled times. The same subset of subjects who completed the topography and PK assessments at Week -1 also were to complete these events at the Week 2 and Week 6 visits.

Additionally, all subjects were to visit the clinic at the end of Week 4 to receive further supplies of cigarettes (if assigned to the VLN groups) and to complete subjective effects questionnaires.

Subjects randomized to the VLN groups were provided with a supply of VLN cigarettes at each visit, which was 150% of their usual daily consumption as reported during Week 1. If a subject ran out of cigarettes between clinic visits, they may have visited the clinic to receive additional test cigarettes. All subjects were asked to smoke their cigarettes *ad libitum*, recording their actual daily consumption in their e-diaries. Non-compliant nicotine product consumption was also recorded. Used cigarette butts were also collected during ambulatory periods to verify product use and/or assess compliance. During Week 1 (all subjects) and all subsequent weeks (subjects randomized to continue smoking UB cigarettes) subjects were asked not to change their UB cigarette brand or flavor.

The clinical research unit (CRU) attempted to contact all subjects who participated in the study (including subjects who terminated the study early) using their standard procedures approximately 7 days after the last contact to determine if any AEs had occurred since the last study visit.

9.2 Discussion of Study Design and Choice of Control Groups

This study was designed to meet the objectives outlined in [Section 8.1](#).

9.2.1 Hypothesis

It was anticipated that when adult smokers switch to smoking VLN cigarettes, after habitually consuming their usual quantity and brand of cigarettes, their daily cigarette consumption would be reduced. It was further anticipated that puffing topography parameters would be unchanged following smoking VLN cigarettes for 6 weeks, i.e., no smoking compensation would occur.

9.2.2 Sample Size Estimation

9.2.2.1 Cigarette Consumption

The intended sample size was 50 subjects in each of the two groups who switched from smoking UB to VLN cigarettes. This was based on powering the primary objective of a within-group comparison of cigarette consumption at baseline and end-of-study. The calculation was based on the number of pairs required to perform a two-tailed paired t-test with 80% power and an alpha level of 0.05 for a decrease in cigarette consumption of three CPD compared to available historical consumption data ([Benowitz & Henningfield, 1994](#); [Hatsukami et al., 2018](#)). The sample size was determined to be adequate based on potential non-compliance with the use of VLN cigarettes ([Benowitz & Henningfield, 1994](#)). A lower number (20) of smokers was randomized to the continue-to-smoke UB groups, given the

lower variability in consumption data and lower non-compliance anticipated in these groups. This provided sufficient power for the secondary objective of between-group comparisons in cigarette consumption.

9.2.2.2 Puffing Topography

The intended sample size was 12 subjects in each of the two groups who switched from smoking UB to VLN cigarettes. This was based on powering the primary objective of a within-group comparison of puffing topography parameters at baseline and end-of-study. The calculation was based on the number of pairs required to perform a two-tailed paired t-test with 80% power and an alpha level of 0.05 to detect significant differences between UB and VLN cigarettes and was based on available puffing topography data ([FDA, 2018](#)). This sample size also provided sufficient power to detect differences in nicotine PK between UB and VLN cigarettes.

9.3 Selection of Study Population

9.3.1 Inclusion Criteria

Potential subjects must have fulfilled all of the following inclusion criteria to be eligible for participation in the study.

1. Was a healthy adult male or female adult smoker, 26 to 65 years of age, inclusive, at Screening.
2. Had been a smoker for at least 5 years prior to Screening. Brief periods of non-smoking (*e.g.*, up to 7 consecutive days due to illness, trying to quit, participation in a study where smoking was prohibited) during the last year was permitted at the discretion of the Investigator.
3. Reports smoking an average of 10 or more manufactured combustible cigarettes per day at Screening.
4. UB of cigarette was a filtered king size (with an approximate length of 84 mm \pm 3 mm) or 100's (with an approximate length of 100 mm \pm 3 mm) cigarette
5. Must have been willing, if their UB cigarette was a 100's cigarette, to switch to a king size cigarette of the same or similar brand for two weeks prior to the Start of Week -1 visit (all subjects), for the whole of Week -1 (subjects randomised to switch to VLN cigarettes), or for the duration of the study (subjects randomised to continue smoking UB cigarettes).
6. Had a positive urine cotinine (\geq 500 ng/ml) at Screening.
7. Had an exhaled CO $>$ 10 ppm at Screening.
8. If female, had a negative serum pregnancy test at Screening.
9. A female subject of childbearing potential must have been using one of the following forms of contraception and agreed to continue using it through completion of the study:
 - hormonal (*e.g.*, oral, vaginal ring, transdermal patch, implant, or injection) consistently for at least 3 months prior to Screening;
 - double barrier method (*e.g.*, condom with spermicide, diaphragm with spermicide) consistently for at least 14 days prior to Screening;
 - intrauterine device for at least 3 months prior to Screening;

- Essure® or similar nonsurgical sterilization procedure at least 6 months prior to Screening
 - a partner who had been vasectomized for at least 6 months prior to Screening;
 - abstinence beginning at least 14 days prior to Screening and through the End of Study.
10. A female subject of non-childbearing potential must have undergone one of the following sterilization procedures at least 6 months prior to Screening:
- hysteroscopic sterilization;
 - bilateral tubal ligation or bilateral salpingectomy;
 - hysterectomy;
 - bilateral oophorectomy;
- Or was postmenopausal with amenorrhea for at least 1 year prior to Day 1 and follicle-stimulating hormone (FSH) levels were consistent with postmenopausal status.
11. Willing to comply with the requirements of the study, including a willingness to use the test products.
12. Voluntary consent to participate in this study documented on the signed ICF.
13. Subject was not planning to leave the area during the course of the study.

9.3.2 Exclusion Criteria

Subjects may have been excluded from the study if there was evidence of any of the following criteria at Screening, start of Week -1 (first clinic visit), or during the study as noted, in the opinion of the Investigator.

1. History or presence of clinically significant gastrointestinal, renal, hepatic, neurologic, hematologic, endocrine, oncologic, urologic, pulmonary (especially bronchospastic diseases and asthma), immunologic, psychiatric, or cardiovascular disease, or any other condition that, in the opinion of the Investigator, would jeopardize the safety of the subject or impact the validity of the study results.
2. Clinically significant abnormal findings on the physical examination, medical history, ECG, or clinical laboratory results, in the opinion of the Investigator.
3. Positive test for human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), or hepatitis C virus (HCV).
4. An acute illness (e.g., upper respiratory infection, viral infection) requiring treatment with prescription medication(s) within 14 days prior to Screening or first clinic visit.
5. Fever ($>100.5^{\circ}\text{F}$) at Screening or first clinic visit.
6. Body mass index (BMI) greater than 40.0 kg/m^2 or less than 18.0 kg/m^2 at Screening.
7. History of drug or alcohol abuse or has used medical/recreational marijuana within 12 months of Screening.
8. Diabetes mellitus that was not controlled by diet/exercise alone, in the opinion of the Investigator.
9. Seated heart rate was lower than 40 bpm or higher than 99 bpm at Screening, unless deemed not clinically significant by the PI.

10. Seated systolic blood pressure < 90 mmHg or > 150 mmHg, diastolic blood pressure < 40 mmHg or > 95 mmHg at Screening, unless deemed not clinically significant by the PI.
11. Positive urine screen for drugs of abuse or urine/breath alcohol at Screening or at the first clinic visit.
12. Female subjects who were pregnant, lactating, or intended to become pregnant from Screening through the End of Study.
13. Use of medications known to interact with cytochrome p450 2A6 (including, but not limited to, amiodarone, desipramine, isoniazid, ketoconazole, miconazole, phenobarbital, rifampin, tranlycypromine, methoxsalen) within 3 months prior to Screening and throughout the study.
14. Use of inhalers to treat any medical condition within 3 months prior to Screening and throughout the study.
15. Use of nicotine-containing products other than factory manufactured cigarettes [e.g., roll-your-own cigarettes, e-vapor products, bidis, snuff, nicotine inhaler, pipe, cigar, chewing tobacco, nicotine patch, nicotine spray, nicotine lozenge, or nicotine gum] within 28 days prior to Screening.
16. Use of any prescription smoking cessation treatments, including, but not limited to, varenicline (Chantix[®]) or bupropion (Zyban[®]) within 3 months prior to Screening.
17. Self-reported puffer/non-inhaler (i.e., a smoker who draws smoke from the cigarette into the mouth and throat but does not inhale).
18. Planning to quit smoking during the study period or postponing a quit attempt in order to participate in the study.
19. Plasma donation within 7 days prior to Screening or at any time during the study.
20. Donation of blood or blood products (with the exception of plasma as noted above), had significant blood loss, or received whole blood or a blood product transfusion within 56 days prior to Screening.
21. Participation in a previous clinical study for an investigational drug, device, biologic, or tobacco product within 30 days prior to Screening.
22. Subject or a first-degree relative (i.e., parent, sibling, child) was a current or former employee of the tobacco industry or a named party or class representative in litigation with the tobacco industry.
23. Subject or a first-degree relative (i.e., parent, sibling, child) was a current employee of the clinic sites.

9.3.3 Removal of Subjects from Assessment

Subjects were advised that they were free to withdraw from the study at any time. In addition, subject participation in this trial may have been discontinued for any of the following reasons.

- AE
- Lost to follow-up
- Non-compliance with study procedures
- Protocol violation
- Pregnancy for female subjects

- Study terminated by Sponsor, US FDA, or other regulatory authorities
- Withdrawal of consent
- Investigator's discretion, including a severe laboratory abnormality or other medical condition that indicated to the Investigator that continued participation was not in the best interest of the subject

Subject's e-diary completion rates were checked at each study visit. If the percentage of days on which the e-diary was completed was below 70%, subjects may have been withdrawn from the study.

Other protocol deviations/violations did not lead to subject withdrawal unless they indicated a significant risk to the subject's safety or jeopardized the scientific integrity of the study.

If premature withdrawal from the study occurred for any reason, the Investigator determined the primary reason and recorded this information in the case report form (CRF). Additionally, subjects withdrawing after study product use underwent all end-of-study safety procedures as feasible and as deemed necessary by the Investigator.

A subject withdrawn from the study due to an AE or clinically significant abnormal laboratory test value was evaluated by the Investigator or other monitoring physician and was treated and/or followed up until the symptoms or values returned to normal or acceptable levels or until lost to follow-up, as appropriate in the opinion of the Investigator.

Subjects withdrawing or removed from this study could not re-enter.

9.4 Study Products

PARE Regular King Box (Part (b) (4))
Manufactured by 22nd Century Group, Inc.
Lot No.: (b) (4)
Expiration date: N/A
Date received: 26 April 2018
Received from: (b) (4)

PARE Menthol King Box (Part (b) (4))
Manufactured by 22nd Century Group, Inc.
Lot No.: (b) (4)
Expiration date: N/A
Date received: 26 April 018
Received from: (b) (4)

PARE was the previous name for VLN.

Subject's usual mentholated combustible cigarette brand
Manufactured by various
Lot No.: various
Expiration date: various
Date received: various
Received from: Study participant supplied

Subject's usual non-mentholated combustible cigarette brand
Manufactured by various
Lot No.: various
Expiration date: various
Date received: various

9.4.1 Study Product Characteristics

The following investigational products were used during the course of the study:

Product	Short Description	Long Description	Sponsor Supplied Product
VLN™ Kings	VLN non-mentholated	Non-mentholated VLN cigarettes	PARE Regular King Box (Part (b) (4))
VLN™ Menthol Kings	VLN mentholated	Mentholated VLN cigarettes	PARE Menthol King Box (Part (b) (4))
Usual Brand non-mentholated cigarette	UB non-mentholated	Subjects' UB non-mentholated filtered cigarettes	None
Usual Brand mentholated cigarette	UB mentholated	Subjects' UB mentholated filtered cigarettes	None

VLN cigarettes contained a target of 0.4 mg nicotine per gram of tobacco (wet weight). Subjects were provided with a supply of VLN cigarettes, up to 150% of their usual daily consumption as reported during Week -1.

9.4.2 Handling of Study Products

UB cigarettes were provided by the study subjects. All VLN study products were provided by the Sponsor. The pharmacy staff at the site coordinated receipt of products from the subjects and the Sponsor. The pharmacy documented the date on which products were received and recorded this in the inventory records. The site pharmacy documented and

reconciled the total number of products received at the site, the total number of products dispensed during the study, and the total number of products remaining at the end of clinical conduct.

Subjects were instructed to not bring any tobacco- or nicotine-containing products into the clinic, other than UB cigarettes at the end of Week -1 visit or VLN cigarettes at the end of Weeks 2 and 6 visits. After their Week -1 visit, subjects assigned to the VLN groups were requested only to smoke VLN cigarettes during all the clinic visits and the ambulatory periods.

All investigational products were stored in locked, limited-access areas in the clinic site's pharmacies at controlled room temperature (defined as 20°-25°C [68°-77°F], with excursions permitted to 15° - 30°C [59°-86°F]).

Individual study product dispensing records were maintained by the site pharmacy for each subject. During clinic visits, used cigarette butts were returned to the staff following each product use for accountability purposes and were disposed of following accountability by the pharmacy staff. During ambulatory periods, used cigarette butts were collected by subjects for the purposes of assessing cigarette consumption, checking compliance and study product accountability, and were disposed of following accountability checking.

Unused VLN cigarettes were disposed of as directed by the Sponsor. Unused UB cigarettes may have been returned to the study subjects at the end of the study, according to site policy. All returned products were documented. Subjects did not return unused UB.

Upon receipt at the clinical facilities, Celerion (Lincoln, Nebraska) and High Point Clinical Trials Center (High Point, North Carolina), the study products were transferred to the pharmacy. All study products were kept in a locked pharmacy storage room which had access limited to authorized associates.

While at the sites, products used during the study were kept in their packages until use and stored under temperature controlled conditions. All VLN products were securely stored at the clinical sites, in areas which were locked and with restricted access. No special procedures were required for the safe handling of the UB products.

During ambulatory periods, subjects were asked to keep the study products at room temperature.

The VLN cigarettes in this study did not have a specified shelf life. They were manufactured in March 2018.

9.4.3 Method of Assigning Subjects to Study Product Use Groups

A randomization scheme was provided by Celerion for the clinical sites. A suitably qualified person monitored the randomization to ensure the study groups were balanced in terms of age and gender, as far as practicable. Each study group included no fewer than 10 subjects of

either gender and no fewer than 10 subjects from each age group (≤ 40 years old and > 40 years old).

Each subject was assigned a unique identification number upon screening. Subjects who had given their informed consent, completed all pre-study evaluations, and met all eligibility criteria were randomized to receive study product.

The randomization schedule is presented in [Appendix 16.1.7](#).

9.4.4 Study Product Use

Subjects were provided with e-diaries to record their daily cigarette consumption, both when in clinical confinement during study visits and during ambulatory periods.

Subjects were instructed to record both compliant and non-compliant (if any) daily numbers of cigarettes smoked. Non-compliant consumption in the subjects randomized to smoke VLN cigarettes was defined as nicotine product consumption other than their UB cigarettes during the baseline period (Week -1) and any nicotine product consumption other than VLN cigarettes following switching (Weeks 1 to 6). Non-compliant consumption in the subjects randomized to continue to smoke their UB cigarettes was defined as nicotine product consumption other than their UB cigarettes between Week -1 and Week 6.

For the purposes of data analysis, the e-diary record of cigarette consumption was used as the primary variable.

9.4.5 Blinding

This was an open-label study. The randomization scheme was not available to bioanalytical laboratory personnel.

9.4.6 Study Product Usage Compliance

Subjects were provided with metal canisters in which to store their used cigarette butts during the ambulatory study periods. This was for the purposes of assessing both compliance with the study requirements and the accuracy of their self-reported (electronic diary) cigarette consumption. Subjects were requested to collect butts of all cigarettes smoked, both compliant and non-compliant.

At the end of each collection period, the total number of butts in the canisters for the whole of that period was counted and recorded. The number of each type of cigarette (study cigarette and non-study cigarette) was also recorded. The cigarette butt count was reconciled against that subject's e-diary record of cigarette consumption.

Except as required by the protocol, consumption of tobacco- or nicotine-containing products was not permitted during the entire duration of the study from the start of Week -1 through discharge from the study. During the baseline period, subjects were asked to confine their smoking to one brand, which was deemed their UB. While in the CRU during 24-hour confinement periods, cigarette consumption was tracked by the number of products dispensed.

A listing of products dispensed including type of product and number of cigarettes dispensed is presented in [Appendix 16.2.5.2.2.1](#). A listing of products returned including number of cigarettes returned and number of cigarette butts returned is presented in [Appendix 16.2.5.2.2.2](#).

9.5 Endpoint Assessments

9.5.1 Endpoint Measurements Assessed and Flow Chart

The study design and schedule of assessments conducted during this trial are summarized in the following schematic ([Table 9–1](#)), and are described in detail in the sections that follow.

Table 9–1 Summary of Study Events

STUDY EVENTS/ASSESSMENTS	Screening ¹	Clinic Visits					Out-of-CRU Between Clinic Visits		
		Start of Week -1	End of Week -1 (baseline)	End of Week 2	End of Week 4	End of Week 6	Weeks -1 to 6	End of study ²	Follow-up Call ³
Informed Consent	X								
Demographics	X								
Smoking/Tobacco/Nicotine Product Use History	X								
Usual Brand Cigarette and Flavor Documentation ⁴	X	X	X	X ⁵	X ⁶	X ⁷			
Medical History	X								
Review of Inclusion / Exclusion Criteria	X								
Review of Concomitant Medications	X								

¹ Up to 28 days prior to first study visit (start of Week -1).

² At end of Week 6 clinic visit or upon early discontinuation.

³ Approximately 7 days after their last clinic visit, including subjects who discontinue from the study early.

⁴ Including taking a color photocopy of the front and back of the subject's UB cigarette pack along with a ruler.

⁵ For subjects randomized to continue smoking UB cigarettes only.

⁶ For subjects randomized to continue smoking UB cigarettes only.

⁷ For subjects randomized to continue smoking UB cigarettes only.

STUDY EVENTS/ASSESSMENTS	Screening ¹	Clinic Visits					Out-of-CRU Between Clinic Visits		
		Start of Week -1	End of Week -1 (baseline)	End of Week 2	End of Week 4	End of Week 6	Weeks -1 to 6	End of study ²	Follow-up Call ³
Physical Examination ⁸	X	X ⁹						X ¹⁰	X ¹¹
Height, Body Weight, BMI	X	X ¹²						X ¹³	
Vital Signs	X	X	X	X	X	X		X	
12-Lead ECG	X							X	
Clinical Chemistry ¹⁴ , Hematology, Urinalysis	X							X	
Urine Drug and Urine/Breath Alcohol Screen	X	X	X	X	X	X		X	
HIV, HBsAg, and HCV Serology	X								
Serum FSH Test ¹⁵	X								
Urine Cotinine Screen	X	X							
Exhaled CO Measurement	X	X							

⁸ Standard physical examination including oral cavity and oropharynx. A symptom driven examination can be performed at other time, at Investigator or designee's discretion.

⁹ Symptom driven and if deemed necessary.

¹⁰ Symptom driven and if deemed necessary.

¹¹ Symptom driven and if deemed necessary based on the follow-up call. Subjects will visit the clinic for this to take place.

¹² Body weight only at Start of Week -1

¹³ Body weight only at end of study

¹⁴ Clinical chemistry tests will be performed after at least an 8 hour fast; however, in case of dropouts or rechecks, subjects may not have fasted for 8 hours prior to the clinical chemistry sample being taken.

¹⁵ Postmenopausal females only

STUDY EVENTS/ASSESSMENTS	Screening ¹	Clinic Visits					Out-of-CRU Between Clinic Visits		
		Start of Week -1	End of Week -1 (baseline)	End of Week 2	End of Week 4	End of Week 6	Weeks -1 to 6		
Test Product (VLN cigarette) Trial	X								
Provide Smoking Cessation Information ¹⁶	X							X	X
Review of AEs	X ¹⁷	X	X	X	X	X		X	X
Pregnancy Test (females)	X	X	X	X	X	X			
Review Restrictions on Smoking and Nicotine Product Use	X	X	X	X	X	X			
Reminder Contacts to return to the CRU ¹⁸		X ¹⁹					X ²⁰		
Test Product Dispensing			X	X	X				
Dispense Canisters for Used Cigarette Butt Collection		X	X	X	X				
Used Cigarette Butt Collection							X		
Used Cigarette Butt Canister Return			X	X	X	X			
24-hour Urine Collection for BoE analysis			X	X		X			

¹⁶ Subjects will be referred to the Quit Assist® website

¹⁷ AE recording to begin immediately after the product trial at Screening.

¹⁸ Phone calls or texts or instant messages (as per site preference) reminding subjects of clinic visits.

¹⁹ The day prior to clinic visit at start of Week -1 subjects will be contacted.

²⁰ The day prior to clinic visits at end of Weeks -1, 2, 4 and 6 subjects will be contacted.

STUDY EVENTS/ASSESSMENTS	Screening ¹	Clinic Visits					Out-of-CRU Between Clinic Visits		
		Start of Week -1	End of Week -1 (baseline)	End of Week 2	End of Week 4	End of Week 6	Weeks -1 to 6		
Plasma Sample for Cotinine Analysis			X	X		X			
Blood Sample for COHb Analysis ²¹			X	X		X			
Puffing Topography ²²			X	X		X			
Blood Samples for Nicotine PK Analysis ²³			X	X		X			
Training on e-diary use		X							
Daily e-diary use to record cigarette consumption		X	X	X	X	X	X		
Fagerström Test for Cigarette Dependence (FTCD)			X	X	X	X			
Brief Questionnaire of Smoking Urges (QSU-brief)			X	X	X	X			
Minnesota Nicotine Withdrawal Scale - Revised (MNWS-R)			X	X	X	X			
Perceived health risk scale			X	X	X	X			
Confinement to CRU for 24 hours			X	X		X			

²¹ Samples will be collected at approximately 13:00, following the subject's lunchtime meal, and will be preceded by at least a 30-minute abstention from study product use

²² In a randomly-selected subset of 18 non-menthol and 18 menthol cigarette smokers at a single site (Lincoln). These subjects will be/have been assigned to switch to smoking VLN cigarettes. To be performed during the clinic confinement period.

²³ In a randomly-selected subset of 12 non-menthol and 12 menthol cigarette smokers at a single site (Lincoln). These subjects will be/have been assigned to switch to smoking VLN cigarettes and will be randomly selected from the subjects selected to undergo topography assessments. To be performed on the day following 24-hour confined urine collection and after an overnight abstinence from cigarette smoking/nicotine product use.

		Clinic Visits					Out-of-CRU Between Clinic Visits		
STUDY EVENTS/ASSESSMENTS	Screening ¹	Start of Week -1	End of Week -1 (baseline)	End of Week 2	End of Week 4	End of Week 6	Weeks -1 to 6	End of study ²	Follow-up Call ³
Ambulatory Visits to CRU	X	X			X		X		

9.5.2 Appropriateness of Measurements

The safety assessments conducted in this study are standard and were judged appropriate by the PI.

The selection and timing of blood and urine samples for PK and BoE analysis were judged appropriate, given the product and nicotine yield.

9.5.3 Product Use Assessment

9.5.3.1 Product use History

Subjects were required to report previous tobacco- and nicotine-product use histories to satisfy the study inclusion and exclusion criteria. In addition, the subject was asked if he/she was planning to quit smoking within the next 3 months. Those planning to quit were excluded from participating in the study.

The subjects' tobacco use and smoking history (including a color photocopy of their UB cigarette package along with a ruler) were recorded at Screening. Verification of the subject's UB cigarette brand was made at the end of Week -1 clinic visit.

9.5.3.2 Product Use Recording

Subjects were provided with e-diaries to record their daily cigarette consumption, both when in clinical confinement during study visits and during ambulatory periods.

Subjects were instructed to record both compliant and non-compliant (if any) daily numbers of cigarettes smoked. Non-compliant consumption in the subjects randomized to smoke VLN cigarettes was defined as nicotine product consumption other than their UB cigarettes during the baseline period (Week -1) and any nicotine product consumption other than VLN cigarettes following switching (Weeks 1 to 6). Non-compliant consumption in the subjects randomized to continue to smoke their UB cigarettes was defined as nicotine product consumption other than their UB cigarettes between Week -1 and Week 6.

For the purposes of data analysis, the e-diary record of cigarette consumption was used as the primary variable.

Subjects were provided with metal canisters in which to store their used cigarette butts during the ambulatory study periods. This was for the purposes of assessing both compliance with the study requirements and the accuracy of their self-reported (electronic diary) cigarette consumption. Subjects were requested to collect butts of all cigarettes smoked, both compliant and non-compliant.

At the end of each collection period, the total number of butts in the canisters for the whole of that period were counted and recorded. The number of each type of cigarette (study cigarette and non-study cigarette) was also recorded. The cigarette butt count was reconciled against that subject's e-diary record of cigarette consumption.

9.5.3.3 Puffing Topography

At clinic visits at the end of Weeks -1, 2, and 6, a subset of 18 non-menthol and 18 menthol smoker subjects completed a puffing topography evaluation session with either their UB (Week -1) or the VLN (Weeks 2 and 6) cigarettes. These subjects had been assigned to switch to smoking VLN cigarettes. These assessments were only performed at a single clinical site (Lincoln) and took place during the 24-hour confinement periods.

During the puffing topography assessment, subjects engaged in a 1-hour *ad libitum* smoking session with their UB (Week -1) or the VLN (Weeks 2 and 6) cigarettes. In these sessions, subjects smoked cigarettes with the mobile smoking puff analyzer (SPA-M; Sodim). The topography device was monitored to ensure the device was actively recording during each session.

Topography assessments were started at least one hour following either the subject's breakfast or lunch. The puffing topography session for each subject at Weeks 2 and 6 was within ± 2 hours of the time of their Week -1 session.

Additional details and instructions for puffing topography procedures were provided separately.

The following topography parameters were assessed:

- Puff duration
- Puff volume
- Peak puff flow rate
- Average flow rate
- Inter-puff interval

9.5.3.4 Statistical Analysis of Primary Endpoints

Paired t-tests were used to compare cigarette consumption (CPD) and puffing topography parameters at the Week 2 and Week 6 time points with the baseline (Week -1) values. This analysis was conducted on the evaluable subjects in the per protocol (PP) and intent-to-treat (ITT) populations. If data were unexpectedly found not to be normally distributed, an appropriate non-parametric test was to be performed; however, this was not done because the sample sizes were too small to evaluate the distribution. A normal distribution was assumed. Differences were considered statistically significant at an alpha level of 0.05. Means, difference of means, 95% confidence interval (CI) for difference, and p-value were presented.

9.5.4 Biomarkers of Exposure Assessment

9.5.4.1 Urine Biomarkers

9.5.4.1.1. Urine Biomarkers Measurements and Collection Schedule

Urine was collected over 24-hour periods for urine BoE measurements, during the clinic visits at the end of Weeks -1, 2, and 6. The urine samples collected during a single 24-hour

period were pooled together and weighed. The total weight of all urine collected over each 24-hour period was documented. Concentrations of the following biomarkers were measured: total NNAL, total NNN, 3-HPMA, S-PMA, 1-OHP, and Tneq. Creatinine in urine was also measured and used to report BoE as amount per unit of creatinine.

9.5.4.1.2. Bioanalytical Method

Urine concentrations were determined using validated analytical methods at Celerion Bioanalytical Services, Lincoln, NE and Celerion, Switzerland.

Urine nicotine, cotinine, *trans*-3'-hydroxycotinine, nicotine-*N*-glucuronide, cotinine-*N*-glucuronide, *trans*-3'-hydroxycotinine-*O*-glucuronide, total NNN, total NNAL, total 1-OHP, and creatinine concentrations were analyzed by liquid chromatography-tandem mass spectrometry (LC-MS/MS) methods at Celerion, Lincoln, NE using validated analytical methods with appropriate quality controls according to applicable portions of Celerion Standard Operating Procedures (SOPs) which were written based on the FDA Guidance for Industry: Bioanalytical Method Validation (May, 2001) and the FDA Good Laboratory Practice regulations (Title 21 CFR Part 58).

Approximate lower limit of quantitation (LLOQ) values for each analyte are shown in the table below. LLOQs are reported out to the most current validation data and included in the bioanalytical report.

Analyte	LLOQ
Nicotine	50.0 ng/mL
Cotinine	50.0 ng/mL
<i>trans</i> -3'-hydroxycotinine	50.0 ng/mL
Nicotine- <i>N</i> -glucuronide	50.0 ng/mL
Cotinine- <i>N</i> -glucuronide	200 ng/mL
<i>trans</i> -3'-hydroxycotinine- <i>O</i> -glucuronide	200 ng/mL
NNN	0.200 pg/mL
NNAL	5.00 pg/mL
1-OHP	10.0 pg/mL
Creatinine	120 µg/mL (effective LLOQ)

Urine nicotine, cotinine, *trans*-3'-hydroxycotinine, nicotine-*N*-glucuronide, cotinine-*N*-glucuronide, *trans*-3'-hydroxycotinine-*O*-glucuronide, NNN, NNAL, 1-OHP, and creatinine concentrations were determined using validated analytical methods at Celerion, Lincoln, NE and Celerion, Switzerland.

Urine 3-HPMA and S-PMA concentrations were analyzed by LC-MS/MS methods at Celerion, Switzerland. The analysis was performed according to the standards described in the Swiss Ordinance relating to Good Laboratory Practice, adopted 18 May 2005 [RS 813.112.1]. This Ordinance is based on the Organisation for Economic Cooperation and Development (OECD) Principles of Good Laboratory Practice, as revised in 1997 and

adopted 26 November 1997 by decision of the OECD Council [C(97)186/Final]. The OECD Principles of Good Laboratory Practice are accepted by Regulatory Authorities throughout the EU, the United States of America (USA), and Japan. In addition, the analysis of clinical trial samples was conducted in accordance with the relevant standards of GCP and SOPs based on the recommendations of the EMA ‘Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples’ (EMA/INS/GCP/532137/2010), the EMA ‘Guideline on bioanalytical method validation’ (EMA/CHMP/EWP/192217/2009) and the FDA ‘Guidance for Industry, Bioanalytical Method Validation’, (U.S. Department of Health and Human Services, Food and Drug Administration, CDER, CVM, May 2018).

Approximate LLOQ values for each analyte are shown in the table below. LLOQs are reported out to the most current validation data and included in the bioanalytical report.

Analyte	LLOQ
3-HPMA	20 ng/mL
S-PMA	0.025 ng/mL

9.5.4.1.3. Urine Biomarkers Analysis

The following variables were determined for each urine biomarker at the end of each collection week (Weeks -1, 2, and 6):

- Measured concentration
- Total biomarker mass excreted per 24 hours (primary analysis variable)
- Total mass excreted per 24 hours absolute change from Baseline
- Total mass excreted per 24 hours percent change from Baseline
- Creatinine-normalized excretion level
- Creatinine-normalized change from baseline
- Creatinine-normalized percent change from baseline

The concentration of Tneq was calculated as the molar sum of nicotine, cotinine, trans 3’hydroxycotinine, and their glucuronides excreted in urine over 24 hours.

The concentration of each metabolite was first multiplied by the 24-hour urine volume to obtain the total amount excreted in 24 hours, then divided by the molecular weight of the metabolite to obtain the total amount of each in moles. The sum in moles was then converted to Tneq by multiplying by the molecular weight of nicotine.

$$\begin{aligned} \text{Nicotine (mg/24h)} &= \text{nicotine concentration [ng/mL]} \times 24\text{h urine volume [mL]} \div 1000\ 000 \\ \text{Nicotine-glucuronide (mg/24h)} &= \text{nicotine glucuronide concentration [ng/mL]} \times 24\text{h urine volume [mL]} \div 1000\ 000 \end{aligned}$$

Cotinine (mg/24 hours)	=	cotinine concentration [ng/mL] × 24h urine volume [mL] ÷ 1000 000
Cotinine-glucuronide (mg/24h)	=	cotinine glucuronide concentration [ng/mL] × 24h urine volume [mL] ÷ 1000 000
Trans-3'-hydroxycotinine (mg/24h)	=	trans-3'-hydroxycotinine concentration [ng/mL] × 24h urine volume [mL] ÷ 1000 000
Trans-3'-hydroxycotinine-glucuronide (mg/24h)	=	trans-3'-hydroxycotinine glucuronide concentration [ng/mL] × 24h urine volume [mL] ÷ 1000 000
Nicotine equivalents (mg/24 hours)	=	(nicotine [mg/24h]/162.23 [mg/mmol] + nicotine-gluc [mg/24h]/338.36 [mg/mmol] + cotinine [mg/24h]/176.22 [mg/mmol] + cotinine-gluc [mg/24h]/352.34 [mg/mmol] + trans-3'- hydroxycotinine [mg/24h]/192.22 [mg/mmol] + trans-3'- hydroxycotinine-gluc [mg/24h]/368.34 [mg/mmol]) x 162.23 (mg/mmol)

Urine biomarker concentration values reported as below the limit of quantitation (BLQ) were set to one-half of the limit of quantitation prior to calculating the 24-hour mass excreted or Tneq. Total urine weight (g) was collected during the study and converted to urine volume using the assumed density of 1 gram (g) equals 1 milliliter (mL).

Creatinine-adjusted concentrations were calculated as shown in [Section 9.5.4.1.4](#). Absolute and percent change from baseline was calculated as shown in [Section 9.5.4.1.5](#).

9.5.4.1.4. Creatinine Adjusted Urine Biomarker Concentrations

Creatinine concentrations were used to adjust the concentration values of all urine biomarkers (Total NNAL, total NNN, 3-HPMA, S-PMA, 1-OHP, and Tneq) as follows:

$$\text{Urine biomarker (unit2/g creatinine)} = \frac{\text{urine biomarker (unit1/mL)} \times 1000}{\text{creatinine (}\mu\text{g/mL)}}$$

Where: if unit1 = pg, then unit2 = ng and if unit1 = ng, then unit2 = μg

9.5.4.1.5. Change from Baseline Urine Biomarker Concentration

Urine biomarker change from baseline on Weeks 2 and 6 was calculated as follows, where Baseline = Week -1:

Absolute change from baseline = Post Product Use Value – Baseline Value

Percent change from baseline (%) = (Post Product Use Value – Baseline Value) / Baseline Value x 100 %

9.5.4.2 Blood Biomarkers

9.5.4.2.1. Blood Biomarkers Measurements and Collection Schedule

Blood samples for COHb in whole blood and cotinine in plasma were collected on Weeks -1, 2, and 6. Samples were collected at approximately 13:00, following the subject's lunchtime meal, and were preceded by at least a 30-minute abstention from study product use.

9.5.4.2.2. Bioanalytical Method

Whole blood COHb and plasma cotinine were analyzed by spectrophotometric measurement and LC-MS/MS, respectively, at Celerion Bioanalytical Services, Lincoln, NE, using validated analytical methods with appropriate quality controls according to applicable portions of Celerion SOPs which were written based on the FDA Guidance for Industry: Bioanalytical Method Validation (May, 2001) and the FDA Good Laboratory Practice regulations (Title 21 CFR Part 58). The LLOQ for COHb was 0.2%. The LLOQ for plasma cotinine was 1.00 ng/mL.

9.5.4.2.3. Blood Biomarkers Analysis

Absolute and percent change from baseline in blood biomarkers were calculated as described for urine in [Section 9.5.4.1.5](#).

9.5.4.2.4. Statistical Analysis of Biomarkers of Exposure

Paired t-tests were used to compare urinary NNAL, NNN, 3-HPMA, S-PMA, 1-OHP, Tneq mass excreted, and blood COHb measures at the Week 2 and 6 time points with the baseline (Week -1) values. This analysis was conducted on the evaluable subjects in the PP and ITT populations. If data were unexpectedly found not to be normally distributed, an appropriate non-parametric test was to be performed. Due to the small sample size, the distribution of the data could not be evaluated and a normal distribution was assumed. Differences were considered statistically significant at an alpha level of 0.05.

In addition, a linear mixed model analysis of variance (ANOVA) was used to compare the between product group differences in the absolute change from baseline values of each of the urinary and blood BoEs. The same statistical model in [Section 9.5.3.4](#) for product group comparisons was used for the analysis.

9.5.5 Pharmacokinetic Assessments

9.5.5.1 Nicotine Concentration Measurements

PK blood sampling occurred in a subset of 12 non-menthol and 12 menthol smoker subjects following the completion of the 24-hour urine collection period on clinic visits at Weeks -1, 2, and 6. The selected subjects remained in the clinic for an additional night, during which

they abstained from smoking any cigarettes or using any nicotine-containing products for at least 12 hours prior to the PK assessment session. During the PK session, subjects smoked a single cigarette (either their UB on Week -1 or the VLN on Weeks 2 and 6) *ad libitum* during a 5-minute period. Serial venous blood samples were collected for plasma nicotine analysis at 5 minutes prior to and at 2, 5, 7, 10, 12, 15, 20, 30, 45, 60, 90, 120, 150, and 180 minutes relative to the start of cigarette smoking.

All concentration data were included in the calculation of the individual PK parameters, the individual concentration-time plots (based on actual sample times), and in the mean concentration-time plots (based on nominal sample times).

9.5.5.2 Bioanalytical Method

Plasma concentrations of nicotine were determined using a liquid chromatography-tandem mass spectrometry method at Celerion Bioanalytical Services, Lincoln, NE. This was a validated analytical method with appropriate quality controls according to applicable portions of Celerion SOPs which were written based on the FDA Guidance for Industry: Bioanalytical Method Validation (May, 2001) and the FDA Good Laboratory Practice regulations (Title 21 Code of Federal Regulations Part 58). The analytical range (LLOQ – upper limit of quantitation [ULOQ]) for nicotine was 0.200 – 25.0 ng/mL.

9.5.5.3 Primary Pharmacokinetic Parameters

Noncompartmental PK parameters were calculated from the plasma nicotine concentration-time data using Phoenix[®] WinNonlin[®] Version 7.0. Actual sample times were used in the calculations of the PK parameters. Concentration data were presented as the measured, unadjusted values and as baseline-adjusted values. The baseline was the plasma nicotine concentration value obtained before the start of cigarette smoking (-5 minutes) and the adjustment was subject-specific. For the baseline adjustment, plasma nicotine concentrations BLQ were set to one-half (½) the LLOQ.

Baseline Adjustment

PK parameters were calculated using the baseline-adjusted concentrations. Adjustment was performed using a nicotine half-life of 120 minutes (elimination rate constant, $\lambda_z = 0.0058 \text{ min}^{-1}$) with the following equation:

$$C_{t(\text{adj})} = C_t - C_0 \times e^{-\lambda_z \times t_1}$$

where $C_{t(\text{adj})}$ was the adjusted concentration, C_t was the observed concentration, C_0 was the concentration at the pre-product use time point, t was the actual sampling time since product administration, and t_1 was the actual sampling time since pre-product administration sample time.

After correction for baseline values, all values obtained were reported as they were even if these values were BLQ or negative. Negative values were assigned a value of zero in summary statistics and for PK parameter calculations.

All PK parameters included in the protocol are listed in [Table 9–2](#) below, and are defined as appropriate for study design.

Table 9–2 Noncompartmental Pharmacokinetic Parameters Calculated

Parameter	Definition	Method of Determination
AUC0-180	Area under the concentration-time curve from time 0 to 180 minutes	Calculated using the Linear Trapezoidal with Linear Interpolation Method
Cmax	The maximum observed concentration	Taken from the baseline-adjusted concentration-time data
Tmax	The time to reach Cmax	Taken from the baseline-adjusted concentration versus time data as the actual time corresponding to the maximum observed concentration

For the calculation of PK parameters, subjects must have had at least 3 post product use data points. Subjects for whom there were insufficient data to calculate the PK parameters were included in the concentration tables only.

9.5.6 Subjective Effect Assessments

9.5.6.1 Measurements and Collection Schedule

The FTCD, QSU-Brief, MNWS-R, and Perceived Health Risk Scale were completed at the end of each clinic visit, at the end of Weeks -1 (Baseline), 2, 4, and 6.

9.5.6.2 Analysis variables

Total score for FTCD was calculated for each subject at each time point and used as the analysis variable for FTCD questionnaire.

The factor scores for QSU-Brief responses were used for the QSU-Brief questionnaire. There were two factor scores: Factor 1 (‘anticipation of pleasure from smoking’ calculated as the average of the response scores from Questions 1, 3, 6, 7, and 10) and Factor 2 (‘relief of nicotine withdrawal’ calculated as the average of the response scores from Questions 2, 4, 5, 8, and 9).

Total score for MNWS-R (calculated as the sum of the responses for each question) was used as the analysis variable for MNWS-R questionnaire.

Response for Perceived Health Risk Scale was used as the analysis variable.

Questionnaire answers were listed by subjects for each questionnaire. Change from baseline values were calculated for each post-baseline time point for the analysis variables. All data

were listed by subject and summarized by time point using descriptive statistics. The descriptive statistics were presented for both PP and ITT populations.

9.5.7 Other Clinical Considerations

Except for those medications noted in the exclusion criteria (See [Section 9.3.2](#)), stable doses (i.e., no dosage adjustments within approximately 30 days prior to Check-in) of prescription or over-the-counter medications required to treat an Investigator-approved disease or condition (e.g., hypertension) were permitted at the discretion of the Investigator. Hormonal contraceptives (e.g., oral, vaginal ring, transdermal patch, implant, injection) and hormonal replacement therapy were permitted. Occasional use of over-the-counter analgesics (e.g., acetaminophen, ibuprofen), antihistamines, nasal decongestants, and dietary supplements were permitted. Exceptions may have been permitted at the discretion of the Investigator in consultation with the Sponsor, providing the medication in question would have had no impact on the study. Any exceptions were documented.

All concomitant medications (and reasons for their use) taken by subjects during the study were recorded and listed.

9.5.7.1 Foods and Beverages

Consumption of foods and beverages containing the following substances should not have been consumed as indicated below.

- Xanthines/caffeine: throughout each clinic visit, apart from one approximately 250 mL caffeinated beverage with each meal.
- Alcohol: 48 hours prior to and throughout each clinic visit.
- Exceptions may have been permitted at the discretion of the Investigator.

9.5.7.2 Activity

Subjects were instructed to refrain from strenuous physical activity outside of their usual routine for the whole study period between Screening and the end of Week 6.

9.6 Data Quality Assurance

This trial was performed in accordance with the “ICH E6 Guideline: Good Clinical Practice: Consolidated Guidance” and applicable regulatory requirements. Data were handled and processed according to the principles of GCP.

Documentation of clinical laboratory reference ranges is included in [Appendix 16.1.10.1](#).

Each CRF was reviewed and signed by the PI. A sample CRF is presented in [Appendix 16.1.2](#).

The Clinical Study Report prepared by Celerion was audited by the Quality Assurance (QA) department of Celerion, with a final issuance of a QA audit certificate with the final report. The QA audit certificate is presented in [Appendix 16.1.8](#).

Final bioanalytical data were received from Celerion (Lincoln, NE) in Excel format.

The study monitor, Virginia Kotait, visited Celerion on 25 July 2018 to monitor the study.

The study monitor, Tamara Stier, visited Celerion on the following dates to monitor the study:

- 10 and 20 – 22 August 2018;
- 04, 05, 10 – 13, and 24 – 28 September 2018;
- 12, 15, 16, and 31 October 2018;
- 02, 05 – 09, 19 – 21, and 26 – 30 November 2018;
- 03 – 07, 20, and 21 December 2018;
- 02 – 04, 07, 08, 10, 14 – 16, 23 – 25, 28, and 29 January 2019;
- 01, 04 – 07, and 13 February 2019;
- 25 April 2019

The study monitor, Virginia Kotait, visited High Point Clinical Trials Center on the following dates to monitor the study:

- 07, 24 – 28 September 2018;
- 15 – 26 October 2018;
- 07 – 15 November 2018;
- 05 – 14 December 2018;
- 07 – 09 and 29 – 31 January 2019

9.7 Statistical Methods Planned in the Protocol and Determination of Sample Size

9.7.1 Statistical and Analytical Plans

Full details of the statistical analyses performed on the study data can be found in the final statistical analysis plan (SAP), presented in [Appendix 16.1.9.1](#).

9.7.1.1 Analysis Populations

The statistical analysis was based on separate, hierarchically organized, analysis populations defined as the following:

Intent-to-treat (ITT) population: All subjects who had at least one valid recording of cigarette consumption (a period of 1 week of > 70% completion of their e-diary).

Per-protocol (PP) population: All subjects who had valid recording of cigarette consumption and completed the study according to the protocol. Data were excluded from this population:

- If a subject self-reported smoking a significant number of cigarettes other than those which they had been assigned according to the protocol, or if this was apparent following checking of their collected used cigarette butts.
- If there was a significant discrepancy between the self-reported number of CPD and the number of used cigarette butts collected.

- If a subject was non-compliant based on a published method of assessing compliance (Benowitz & Henningfield, 1994). After switching, subjects were deemed non-compliant if their ratio of [plasma cotinine/CPD VLN]/[plasma cotinine/CPD baseline] exceeded 0.2.
- If it was determined that a subject was pregnant during the study, the pregnant subject's data were to be listed but excluded from all PK parameter summaries.

PK Population: Subjects in the PP or ITT population who had at least one PK blood draw resulting in at least one quantifiable plasma nicotine concentration. This population was used for PK analysis (secondary endpoint analysis) and all available data were included in the concentration and PK parameter tables to the extent possible.

9.7.2 Determination of Sample Size

Please refer to [Section 9.2.2](#).

9.7.3 Data Summarization and Presentation

All descriptive statistics were generated using SAS®.

9.7.3.1 Primary Endpoints

Study product use (study product, CPD and cigarette butts) and topography parameters (puff duration, puff volume, peak puff flow rate, average flow rate, and inter-puff interval) were listed by subject and summarized by population (ITT and PP), study product group and time point (Week -1, 2, or 6) using descriptive statistics (number of observations [n], arithmetic mean [Mean], standard deviation [SD], coefficient of variation [CV%], standard error of the mean [SEM], minimum, median, and maximum).

9.7.3.2 Biomarkers of Exposure

Blood biomarker concentrations, urine biomarker concentrations, urine creatinine concentrations, and the creatinine-adjusted urine biomarker concentrations were listed by study product group, subject and week for all biomarkers. All BLQ values were presented as "BLQ" in the listings.

Blood biomarker concentrations, blood biomarker absolute change from baseline and blood biomarker percent change from baseline as well as urine biomarker mass excreted per 24 hours, absolute change from baseline, percent change from baseline of total mass excreted per 24 hours, creatinine-normalized excretion level, creatinine-normalized excretion absolute change from baseline, and creatinine-normalized excretion percent change from baseline were summarized by population (ITT and PP), study product group and time point (Week -1, 2, or 6) for all biomarkers using descriptive statistics (n, Mean, SD, CV%, SEM, minimum, median, and maximum).

9.7.3.3 Pharmacokinetics

Plasma concentrations of nicotine and plasma nicotine PK parameters were listed by subject and summarized by population (ITT or PP), study product group, time point, and sex for all

subjects in the PK population. Summary statistics, including n, Mean, SD, CV%, SEM, minimum, median, and maximum, were calculated for all nominal concentration time points and for the plasma nicotine PK parameters AUC0-180, Cmax, and Tmax. In addition, geometric mean (Geom Mean) and geometric CV% (Geom CV%) were calculated for AUC0-180 and Cmax. Excluded subjects were included in the concentration listings or in the PK parameter tables, but were excluded from the summary statistics and noted as such in the tables. All BLQ values were presented as “BLQ” in the concentration listings and footnoted accordingly.

Mean and individual concentration-time profiles were presented on a linear scale and semi-log scale. Linear profiles were presented with and without SD.

9.7.3.4 Subjective Effects

All questionnaire data were listed by subject and summarized by time point using descriptive statistics for both PP and ITT populations.

9.7.4 Statistical Analyses

Product Use

Paired t-tests were used to compare CPD and puffing topography parameters at the Week 2 and Week 6 time points with the baseline (Week -1) values for each VLN product group. Product groups were VLN mentholated, VLN non-mentholated, and VLN combined (the pooled non-mentholated and mentholated groups). The primary analysis was based on the VLN combined product group. This analysis was conducted on the evaluable subjects in the ITT and PP populations. Differences were considered statistically significant at an alpha level of 0.05. The Means of the differences and their associated 95% CI and p-values were presented.

In addition, a linear mixed model ANOVA with the factors product group, week, and product group by week interaction was used to compare the between product group differences in the absolute change from baseline values of the consumption and puffing topography parameters. The least-squares mean (LSM) difference, 95% CI, and p-value were provided for the product group difference.

BoE

As for product use comparisons, paired t-tests were used to compare urinary NNAL, NNN, 3-HPMA, S-PMA, 1 OHP, Tneq mass excreted, and blood COHb measures at the Week 2 and 6 time points with the baseline (Week -1) values. This analysis was conducted on the evaluable subjects in the ITT and PP populations.

In addition, the same linear mixed model ANOVA used for product use group comparisons was used to compare the between product group differences in the absolute change from baseline values of each of the urinary and blood BoEs.

PK

Paired t-tests were also used to compare baseline-adjusted nicotine PK parameters (AUC₀₋₁₈₀ and C_{max}) at the Weeks 2 and 6 time points with the baseline (Week -1) values. This analysis was conducted on subjects in the PK population (from the ITT and PP populations). Differences were considered statistically significant at an alpha level of 0.05. geometric mean ratio (GMR), 95% CI for GMR, and p-value were presented. The analysis was based on the log-transformed data

Subjective Effects

Paired t-tests were used to compare subjective effects measures at the Weeks 2 and 6 time points with the baseline (Week -1) values. This analysis was conducted on subjects in the PK population (from the ITT and PP populations). Differences were considered statistically significant at an alpha level of 0.05.

In addition, a linear mixed model ANOVA was used to compare the between product group differences in the absolute change from baseline values of each of the subjective effect measures.

9.7.5 Safety

All CRF data were listed by subject and chronologically by assessment time points. This included rechecks, unscheduled assessments, and early termination.

Applicable continuous variables were summarized using n, arithmetic mean, SD, minimum, median, and maximum.

The level of precision was presented as follows: minimum/maximum in the same precision as in the database, mean/median in one more precision level than minimum/maximum, SD in one more precision level than mean/median, and n was presented as an integer.

Where individual data points were missing because of dropouts or other reasons, the data were summarized based on reduced denominators.

9.7.5.1 Subject Discontinuation

Subjects were summarized by number of subjects enrolled, completed, and discontinued the study with discontinuation reasons by product group and overall.

9.7.5.2 Demographics

Descriptive statistics were calculated for continuous variables (age, weight, height, and body mass index) by product group and overall. Age was derived from date of birth to date of informed consent.

Frequency counts were provided for categorical variables (race, ethnicity, and gender) by product group and overall.

9.7.5.3 Tobacco Product Use History

Descriptive statistics were calculated for number of cigarettes smoked per day and number of years used tobacco product based on the self-reported tobacco product use history by product group and overall.

Frequency counts were provided for categorical variables (cigarette brand, brand style, flavor, and size) by product group and overall.

9.7.5.4 Adverse Events

All AEs occurring during this clinical trial were coded using the Medical Dictionary for Regulatory Activities (MedDRA®) Version 21.0.

All AEs captured in the database were listed in by-subject data listings including verbatim term, coded term, product, severity, relationship to study medication, and action; however, only product-use-emergent AEs (PUEAEs) were summarized.

A PUEAE was defined as an AE that started or worsened at the time of or after study product administration. Each PUEAE was attributed to a product based on the onset date and time of the AE. If an AE increased in severity, that AE was given a resolution date and time and a new record was initiated with the new severity. If the severity of an AE remained the same or decreased, the AE was kept open through to resolution.

If the onset time of an AE was missing and the onset date was the same as the product administration date, then the AE was considered product use emergent in the prior product. If onset time of an AE was missing and the onset date did not fall on an administration date, then the AE was considered product use emergent for the last product administered. If the onset date of an AE was missing, then the AE was considered product use emergent and attributed to the product on the study.

PUEAEs were tabulated by System Organ Class (SOC) and Preferred Term. Summary tables included number of subjects reporting the AE and as percent of number of subjects used study product. The number of AEs was tabulated in a similar manner. Tables which tabulated the number of PUEAEs by severity and relationship to study product were also included.

Serious adverse events (SAEs), if present, were also listed. Applicable narratives were included in the clinical study report.

9.7.5.5 Clinical Laboratory Tests (Serum Chemistry, Hematology, Urinalysis)

Clinical laboratory tests were performed at Screening and end-of-study.

Clinical laboratory test results were summarized overall by time point and listed by subject.

Out-of-range values and corresponding recheck results were listed.

9.7.5.6 Vital Signs

Vital signs (respiratory rate, pulse rate, blood pressure, and oral temperature) were measured in the sitting position at Screening, at each study visit (Weeks -1, 2, 4) and at the end-of-study (Week 6).

Vital signs were listed by subject and time point of collection and were summarized by product group and time point.

9.7.5.7 Electrocardiogram

Electrocardiograms (ECGs) were performed at Screening and listed by subject.

9.7.5.8 Concomitant Medications

All concomitant medications recorded during the study were coded with the World Health Organization (WHO) Dictionary Version 01SEP2018 and listed.

9.7.5.9 Physical Examination

Physical examinations were performed at Screening. Symptom-driven physical examination may have been performed at Week -1, end-of-study (Week 6), and follow-up. All data found in the CRF were listed. Changes in physical examinations (if any) were described in the text of the final report.

9.8 Changes in the Conduct of the Study or Planned Analyses

As per the SAP, statistical comparisons were to be performed on subjects from the PP population only. However, most subjects were excluded from the PP population for non-compliance as determined by the criteria discussed in [Section 9.7.1.1](#). Therefore, statistical comparisons were also performed using the ITT population.

10. STUDY SUBJECTS

10.1 Disposition of Subjects

A total of 392 subjects were screened for this study and 250 subjects failed screening procedures or were not needed for product randomization. Reasons for screening failure are presented in [Table 10–1](#) below.

Table 10–1 Summary of Subject Screening, Enrollment, and Randomization

Categories	Number of Subjects
Screened	392
Enrolled into the Product Trial Period	142
Not Needed for Study Participation (Study full)	6
Screen Failure	244
Failed More Than One Inclusion/Exclusion Criteria	7
Smokes 10 or more cigarettes per day	1
Usual brand cigarette is filtered king size	1
Positive cotinine	29
Exhaled CO > 10 ppm	19
Childbearing female with proper contraception	1
Willing to comply with study, test products	35
Voluntary consent to participate in the study	1
Clinically significant disease or condition	21
Clinically significant abnormal examination finding	32
Abnormal virology	2
Acute illness	3
BMI	10
Drug or alcohol abuse	3
Blood pressure	19
Positive drug, alcohol screen	48
Cytochrome P450 2A6 interacting drug	8
Use of nicotine products other than manufactured cigarettes	2
Plasma donation	1
Previous clinical trial	1
Source: Appendix 16.2.5.1 , Section 9.3 , and on file at the clinical sites.	

A total of 142 (82 males, 60 females) subjects were enrolled in the Baseline Period (Week -1) and were randomized to product group on Day -1 of Week 1. Of these, 124 subjects completed the study per protocol and 18 subjects did not, including 11 subjects who were non-compliant, four who were lost to follow-up, two who withdrew from the study, and one subject who was discontinued due to an AE.

A summary of disposition is presented in [Table 14.1.1](#) and in [Table 10–2](#) below. Disposition listings for randomized subjects and for screen failure subjects are presented [Appendices 16.2.1.1](#) and [16.2.1.2](#), respectively.

Table 10–2 Disposition Summary (Safety, ITT, and PP Populations)

Population	Disposition	VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	Overall
Safety	Enrolled	50 (100%)	50 (100%)	22 (100%)	20 (100%)	142 (100%)
	Completed	43 (86%)	42 (84%)	19 (86%)	20 (100%)	124 (87%)
	Discontinued Early	7 (14%)	8 (16%)	3 (14%)	0 (0%)	18 (13%)
	Adverse Event	0 (0%)	1 (2%)	0 (0%)	0 (0%)	1 (1%)
	Lost To Follow-Up	0 (0%)	1 (2%)	3 (14%)	0 (0%)	4 (3%)
	Non-Compliance With Study	6 (12%)	5 (10%)	0 (0%)	0 (0%)	11 (8%)
	Withdrawal By Subject	1 (2%)	1 (2%)	0 (0%)	0 (0%)	2 (1%)
ITT	Enrolled	50 (100%)	50 (100%)	22 (100%)	20 (100%)	142 (100%)
	Completed	43 (86%)	42 (84%)	19 (86%)	20 (100%)	124 (87%)
	Discontinued Early	7 (14%)	8 (16%)	3 (14%)	0 (0%)	18 (13%)
	Adverse Event	0 (0%)	1 (2%)	0 (0%)	0 (0%)	1 (1%)
	Lost To Follow-Up	0 (0%)	1 (2%)	3 (14%)	0 (0%)	4 (3%)
	Non-Compliance With Study	6 (12%)	5 (10%)	0 (0%)	0 (0%)	11 (8%)
	Withdrawal By Subject	1 (2%)	1 (2%)	0 (0%)	0 (0%)	2 (1%)
PP	Enrolled	12 (100%)	17 (100%)	22 (100%)	20 (100%)	71 (100%)
	Completed	10 (83%)	9 (53%)	19 (86%)	20 (100%)	58 (82%)
	Discontinued Early	2 (17%)	8 (47%)	3 (14%)	0 (0%)	13 (18%)
	Adverse Event	0 (0%)	1 (6%)	0 (0%)	0 (0%)	1 (1%)
	Lost To Follow-Up	0 (0%)	1 (6%)	3 (14%)	0 (0%)	4 (6%)
	Non-Compliance With Study	1 (8%)	5 (29%)	0 (0%)	0 (0%)	6 (8%)
	Withdrawal By Subject	1 (8%)	1 (6%)	0 (0%)	0 (0%)	2 (3%)
VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population Source: Table 14.1.1 Program: /CA24914/sas_prg/stsas/intext/t_disp.sas 18JUN2019 11:18						

10.2 Protocol Deviations

All protocol deviations and deviations from site SOPs are listed in [Appendix 16.2.2](#).

The following deviations were considered important:

Noncompliance to study procedures

Subject 2058 was randomized with eCO results of 8 ppm at the start of Week -1 visit (should have been greater than 10 ppm to meet inclusion criteria, per protocol). Sponsor was notified and subject was allowed to continue.

The following subjects did not comply to study procedures and were dropped:

Subject 1084 was dropped on Week 4 (Day 28) due to a positive urine drug screen (UDS).
Subjects 2009 and 2016 were dropped on Weeks 4 and 3, respectively, due to a positive UDS.

Subject 2075 was dropped on Week 2 (Day 14) due to lack of compliance with study product.

Subject 2086 was dropped on Week 4 due to a positive UDS.

Subject 2115 was dropped on Week 2 (Day 14) due to a positive UDS and non-compliance to study procedures.

Subject 2136 was dropped on Week 6 due to a positive UDS.

Subject 2142 was dropped on Week 2 because they allowed their roommate to smoke the product.

Subject 2247 was dropped after Week 4 as they did not complete their diary, stopped the product, and were smoking their UB.

Missing urine data

Urine pooling jugs for Subjects 1008, 1010, and 1011 were discarded in error at Week 6.

Subject 1013's urine was pooled into Subject 1014's 24-hour pooling container in error.

Subject 1021's urine was spilled in error on Week -1.

Subject 1099 voided urine into the toilet on Week -1.

Subject 1095 spilled urine collection container at Week 2.

Subject 2170 had a 24-hour urine void placed in the collection container for Subject 2168 at Week 6.

All urine data for these subjects at those time points were excluded from the analysis.

Other deviations included missing plasma samples, non-completed questionnaires, administrative errors, unreturned cigarettes packs, and sample processing errors. None of these errors were judged to have a significant impact on study conclusions.

10.3 Demographic and Other Baseline Characteristics

Demographic descriptions by overall characteristics are summarized in [Table 14.1.2](#) and [Table 10–3](#). Individual demographic information, including informed consent dates, is presented in [Appendices 16.2.4.1.1](#) and [16.2.4.1.2](#).

Table 10–3 Demographic Summary (Safety Population)

Population	Trait	Category/Statistic	VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	Overall
Safety	Sex	Female	19 (38%)	22 (44%)	9 (41%)	10 (50%)	60 (42%)
		Male	31 (62%)	28 (56%)	13 (59%)	10 (50%)	82 (58%)
	Race	American Indian or Alaska Native	1 (2%)	1 (2%)	0 (0%)	0 (0%)	2 (1%)
		Asian	0 (0%)	1 (2%)	0 (0%)	0 (0%)	1 (1%)
		Black or African American	3 (6%)	29 (58%)	2 (9%)	12 (60%)	46 (32%)
		Multiple	1 (2%)	2 (4%)	1 (5%)	0 (0%)	4 (3%)
		Other	1 (2%)	0 (0%)	1 (5%)	0 (0%)	2 (1%)
		White	44 (88%)	17 (34%)	18 (82%)	8 (40%)	87 (61%)
		Ethnicity	Hispanic or Latino	1 (2%)	1 (2%)	1 (5%)	1 (5%)
	Not Hispanic or Latino		49 (98%)	49 (98%)	21 (96%)	19 (95%)	138 (97%)
	Age* (yrs)	n	50	50	22	20	142
		Mean	45.9	40.5	45.8	42.7	43.5
		SD	10.85	9.34	12.39	10.82	10.76
		Minimum	29	26	26	26	26
		Median	45.0	39.0	50.0	41.0	42.0
		Maximum	65	60	60	59	65
		Weight (kg)	n	50	50	22	20
	Mean		86.76	83.53	84.37	89.33	85.61
	SD		17.579	14.118	18.462	17.657	16.542
	Minimum		54.3	54.8	54.7	56.7	54.3
	Median		85.30	81.95	83.10	86.50	84.30
	Maximum		118.7	114.2	125.1	122.8	125.1
	Height (cm)	n	50	50	22	20	142
		Mean	172.20	172.63	172.13	170.41	172.09
		SD	9.549	7.836	9.077	11.670	9.174
		Minimum	154.4	154.0	151.0	149.7	149.7
		Median	173.00	172.20	175.00	168.00	172.65
		Maximum	188.5	191.2	186.0	196.8	196.8
	BMI (kg/m ²)	n	50	50	22	20	142
		Mean	29.24	27.95	28.35	30.78	28.87
		SD	5.442	3.939	5.075	5.459	4.944
		Minimum	19.2	20.6	19.3	21.9	19.2
		Median	29.15	27.70	27.50	30.15	28.05
		Maximum	39.8	37.7	39.0	40.0	40.0
VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes BMI = Body mass index *Age is calculated at the date of the informed consent.							
Source: Table 14.1.2 Program: /CA24914/sas prg/stsas/intext/t dem.sas 18JUN2019 11:18							

Individual information related to inclusion/exclusion criteria for all subjects is presented in [Appendix 16.2.5.1](#).

All subjects who were randomized to the study satisfied all inclusion and none of the exclusion criteria. Information obtained at Screening may be found in the following locations:

Physical Examinations	Appendix 16.2.4.2
Medical History	Appendix 16.2.4.3
Prior and Concomitant Medications	Appendix 16.2.5.4
Clinical Laboratory Information	Appendices 16.2.8.1.1.1 through 16.2.8.1.10
Vital Signs	Appendix 16.2.8.2
12-Lead ECGs	Appendix 16.2.8.3

10.4 Tobacco/Nicotine Product Use History

Tobacco/nicotine product use history is summarized in [Table 14.1.3](#) and [Table 10–4](#). Individual tobacco/nicotine product use history for enrolled subjects is presented in [Appendix 16.2.4.4](#).

All 142 randomized subjects were current combustible cigarette smokers at Screening, with an average of 17.6 CPD and 22.8 years of cigarette use. Approximately half of subjects each were menthol and non-menthol cigarette users. A total of 47 distinct cigarette brand styles were reported by subjects at Screening. Overall, the most common brand style was Newport Green, reported by 27.5% of subjects; all remaining brand styles were reported by < 8.0% of subjects.

Table 10–4 Smoking History Summary (Safety, ITT, and PP Population)

Population	Trait	Category/Statistic	VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	Overall
Safety, ITT	Duration (years)	n	50	50	22	20	142
		Mean	26.8	17.2	28.9	19.9	22.8
		SD	12.20	8.04	12.66	10.92	11.74
		Minimum	5	5	8	5	5
		Median	25.5	16.0	29.0	17.5	20.0
		Maximum	50	42	50	41	50
	CPD	n	50	50	22	20	142
		Mean	19.8	15.4	18.2	17.1	17.6
		SD	6.92	6.19	3.85	6.16	6.39
		Minimum	10	10	10	10	10
		Median	20.0	15.0	19.5	16.0	16.5
		Maximum	40	40	25	30	40
	Brand-Style	CAMEL-BLUE	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		CAMEL-CRUSH (POPPED)	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		CAMEL-CRUSH SILVER (POPPED)	0 (0%)	3 (6.0%)	0 (0%)	1 (5.0%)	4 (2.8%)
		CAMEL-FILTERS	1 (2.0%)	0 (0%)	2 (9.1%)	0 (0%)	3 (2.1%)

Population	Trait	Category/Statistic	VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	Overall
		CROWNS-GOLD	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		DORAL-SILVER	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (0.7%)
		EAGLE 20S-RED	5 (10.0%)	0 (0%)	2 (9.1%)	0 (0%)	7 (4.9%)
		EDGEFIELD-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		KAMEL RED-GENUINE ORIGINAL	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (0.7%)
		KOOL-BLUE	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		L&M-GREEN	0 (0%)	1 (2.0%)	0 (0%)	1 (5.0%)	2 (1.4%)
		L&M-RED	2 (4.0%)	0 (0%)	0 (0%)	0 (0%)	2 (1.4%)
		LD-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		MARLBORO-BLACK	3 (6.0%)	1 (2.0%)	3 (13.6%)	0 (0%)	7 (4.9%)
		MARLBORO-EIGHTY-THREES	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		MARLBORO-GOLD	9 (18.0%)	0 (0%)	1 (4.5%)	1 (5.0%)	11 (7.7%)
		MARLBORO-GREEN	0 (0%)	2 (4.0%)	0 (0%)	0 (0%)	2 (1.4%)
		MARLBORO-ICE	0 (0%)	2 (4.0%)	0 (0%)	0 (0%)	2 (1.4%)
		MARLBORO-RED	5 (10.0%)	0 (0%)	3 (13.6%)	0 (0%)	8 (5.6%)
		MARLBORO-SILVER	0 (0%)	1 (2.0%)	1 (4.5%)	0 (0%)	2 (1.4%)
		MARLBORO-SMOOTH	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (0.7%)
		MARLBORO-SPECIAL BLEND GOLD	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		MARLBORO-SPECIAL BLEND RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		MARLBORO-SPECIAL SELECT	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (0.7%)
		MARLBORO-SPECIAL SELECT RED	1 (2.0%)	0 (0%)	3 (13.6%)	0 (0%)	4 (2.8%)
		MAVERICK-FULL FLAVOR	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		NATURAL AMERICAN SPIRIT-GREEN	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		NATURAL AMERICAN SPIRIT-TURQUIOSE	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		NEWPORT-GREEN	0 (0%)	26 (52.0%)	0 (0%)	13 (65.0%)	39 (27.5%)
		NEWPORT-RED	3 (6.0%)	0 (0%)	1 (4.5%)	0 (0%)	4 (2.8%)
		OLD GOLD-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		PALL MALL-BLACK	0 (0%)	2 (4.0%)	0 (0%)	0 (0%)	2 (1.4%)
		PALL MALL-GREEN	0 (0%)	6 (12.0%)	0 (0%)	1 (5.0%)	7 (4.9%)
		PALL MALL-ORANGE	2 (4.0%)	0 (0%)	1 (4.5%)	0 (0%)	3 (2.1%)
		PALL MALL-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		PALL MALL-SILVER	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (0.7%)
		PARLIAMENT-BLUE	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		PYRAMID-BLUE	2 (4.0%)	0 (0%)	0 (0%)	0 (0%)	2 (1.4%)
		PYRAMID-GOLD	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		SALEM-GOLD	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		SALEM-GREEN	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (0.7%)
		TIMELESS-SILVER	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		USA GOLD-GOLD	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (0.7%)
		USA GOLD-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)

Population	Trait	Category/Statistic	VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	Overall
PP		WAVE-BLUE	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		WILDHORSE-GOLD	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		WILDHORSE-RED	2 (4.0%)	0 (0%)	1 (4.5%)	0 (0%)	3 (2.1%)
	Duration (years)	n	12	17	22	20	71
		Mean	32.1	16.8	28.9	19.9	24.0
		SD	14.33	9.02	12.66	10.92	12.95
		Minimum	8	6	8	5	5
		Median	35.5	15.0	29.0	17.5	21.0
		Maximum	50	40	50	41	50
	CPD	n	12	17	22	20	71
		Mean	17.8	15.2	18.2	17.1	17.1
		SD	6.73	5.87	3.85	6.16	5.57
		Minimum	10	10	10	10	10
		Median	16.0	14.0	19.5	16.0	15.0
		Maximum	30	36	25	30	36
	Brand-Style	CAMEL-CRUSH SILVER (POPPED)	0 (0%)	2 (11.8%)	0 (0%)	1 (5.0%)	3 (4.2%)
		CAMEL-FILTERS	0 (0%)	0 (0%)	2 (9.1%)	0 (0%)	2 (2.8%)
		CROWNS-GOLD	1 (8.3%)	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)
		DORAL-SILVER	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (1.4%)
		EAGLE 20S-RED	2 (16.7%)	0 (0%)	2 (9.1%)	0 (0%)	4 (5.6%)
		EDGEFIELD-RED	1 (8.3%)	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)
		KAMEL RED-GENUINE ORIGINAL	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (1.4%)
		L&M-GREEN	0 (0%)	1 (5.9%)	0 (0%)	1 (5.0%)	2 (2.8%)
		MARLBORO-BLACK	1 (8.3%)	0 (0%)	3 (13.6%)	0 (0%)	4 (5.6%)
		MARLBORO-GOLD	1 (8.3%)	0 (0%)	1 (4.5%)	1 (5.0%)	3 (4.2%)
		MARLBORO-ICE	0 (0%)	1 (5.9%)	0 (0%)	0 (0%)	1 (1.4%)
		MARLBORO-RED	1 (8.3%)	0 (0%)	3 (13.6%)	0 (0%)	4 (5.6%)
		MARLBORO-SILVER	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (1.4%)
		MARLBORO-SMOOTH	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (1.4%)
		MARLBORO-SPECIAL BLEND GOLD	1 (8.3%)	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)
		MARLBORO-SPECIAL SELECT	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (1.4%)
		MARLBORO-SPECIAL SELECT RED	0 (0%)	0 (0%)	3 (13.6%)	0 (0%)	3 (4.2%)
		MAVERICK-FULL FLAVOR	0 (0%)	1 (5.9%)	0 (0%)	0 (0%)	1 (1.4%)
		NATURAL AMERICAN SPIRIT-GREEN	0 (0%)	1 (5.9%)	0 (0%)	0 (0%)	1 (1.4%)
		NEWPORT-GREEN	0 (0%)	6 (35.3%)	0 (0%)	13 (65.0%)	19 (26.8%)
		NEWPORT-RED	1 (8.3%)	0 (0%)	1 (4.5%)	0 (0%)	2 (2.8%)
		PALL MALL-BLACK	0 (0%)	1 (5.9%)	0 (0%)	0 (0%)	1 (1.4%)
		PALL MALL-GREEN	0 (0%)	4 (23.5%)	0 (0%)	1 (5.0%)	5 (7.0%)
		PALL MALL-ORANGE	1 (8.3%)	0 (0%)	1 (4.5%)	0 (0%)	2 (2.8%)
		PALL MALL-SILVER	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (1.4%)
		SALEM-GREEN	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (1.4%)
		TIMELESS-SILVER	1 (8.3%)	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)

Population	Trait	Category/Statistic	VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	Overall
		USA GOLD-GOLD	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (1.4%)
		WILDHORSE-GOLD	1 (8.3%)	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)
		WILDHORSE-RED	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (1.4%)
VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population Note: Safety and ITT populations are the same Source: Table 14.1.3 Program: /CA24914/sas_prg/stsas/intext/t_dem2.sas 02JUL2019 8:50							

11. STUDY PRODUCT USE, TOPOGRAPHY, BIOMARKERS OF EXPOSURE, PHARMACOKINETIC, AND SUBJECTIVE EFFECTS EVALUATION

11.1 Data Sets Analyzed

All 142 randomized subjects were included in the ITT population based on product use. Out of these, 71 subjects were included in the PP Population and 71 were excluded. All excluded subjects had a ratio of [plasma cotinine/CPD VLN]/[plasma cotinine/CPD baseline] > 0.2. Additionally, Subject 1034 reported smoking $\geq 50\%$ non-assigned cigarettes on $\geq 50\%$ of post baseline days. The complete listing of subjects included and excluded from the ITT and PP is presented in [Appendix 16.2.3](#). The following are subsets of the ITT and PP populations used in data analyses.

Topography

The following subset of 36 subjects (18 non-mentholated and 18 mentholated cigarette smokers) participated in the puffing topography evaluation:

Non-Mentholated Cigarettes	Mentholated Cigarettes
1001, 1002, 1007, 1013, 1019, 1020, 1023, 1034, 1035, 1038, 1042, 1050, 1056, 1058, 1066, 1070, 1071, 1078	1003, 1008, 1014, 1015, 1018, 1029, 1032, 1052, 1053, 1055, 1060, 1063, 1072, 1079, 1088, 1092, 1094, 1097

All 36 subjects were included in the ITT population. Out of these, 9 subjects (3 smokers of non-mentholated cigarettes and 6 smokers of mentholated cigarettes) were included in the PP population: Subjects 1007, 1015, 1018, 1032, 1063, 1066, 1070, 1072, and 1079. The complete listing of subjects included and excluded from the topography ITT and PP populations is presented in [Appendix 16.2.6.2](#).

Urine BoE

All 142 subjects in the ITT population were included in the urine BoE analyses. Additionally, 2 subjects were partially excluded at baseline:

- Subject 1021's urine was spilled in error on Week -1 (subject was excluded from all descriptive statistics for Week -1 and all change-from-baseline calculations in subsequent weeks).
- Subject 1099 voided urine into the toilet on Week -1 (subject was excluded from all descriptive statistics for Week -1 and from all change-from-baseline calculations in subsequent weeks).

Available data from the other 140 subjects were included in the descriptive statistics and statistical comparisons for the ITT population. Out of these, 69 subjects were included in the PP population. The complete listing of subjects included and excluded from the urine ITT and PP populations is presented in [Appendix 16.2.6.7](#). Subjects with unavailable data on Weeks 2 and/or 6 are listed in [Appendix 16.2.3](#).

Blood BoE

All 142 subjects in the ITT population and 71 subjects in the PP population were included in the Blood COHb analyses.

Pharmacokinetics

Among the subjects who completed the puffing topography evaluation, the following subset of 24 subjects (12 non-mentholated and 12 mentholated cigarette smokers) participated in the PK evaluation:

Non-Mentholated Cigarettes	Mentholated Cigarettes
1001, 1002, 1007, 1013, 1019, 1020, 1023, 1035, 1038, 1042, 1056, 1058	1003, 1008, 1014, 1015, 1018, 1029, 1032, 1052, 1053, 1055, 1063, 1072

All 24 subjects were included in the ITT population. Out of these, 6 subjects (1 smoker of non-mentholated cigarettes and 5 smokers of mentholated cigarettes) were included in the PP population: Subjects 1007, 1015, 1018, 1032, 1063, and 1072. The complete listing of subjects included and excluded from the PK ITT and PP populations is presented in [Appendix 16.2.6.2](#).

Subjective effects

All 142 subjects the ITT population and 71 subjects in the PP population were included in the subjective effect analyses.

11.2 Study Product Use Summary

The locations of individual study product use and descriptive statistics are presented below:

Description	Number
Individual VLN Product Trial (Safety Population)	Appendix 16.2.5.2.1
Individual Product Dispensed (Safety Population)	Appendix 16.2.5.2.2.1

Description	Number
Individual Product Returned (Safety Population)	Appendices 16.2.5.2.2.2.1 and 16.2.5.2.2.2.2
Individual Number of Cigarettes Smoked and Cigarette Butts Collected per Week (Safety Population)	Appendix 16.2.6.1
Summary of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (PP Population)	Table 14.2.1.1.1.1
Summary of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (ITT Population)	Table 14.2.1.1.1.2
Summary of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (PP Population)	Table 14.2.1.2.1.1
Summary of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (ITT Population)	Table 14.2.1.2.1.2
Mean (\pm SD) of Number of Cigarettes Smoked Per Day by Study Product Group and Study Week (Mentholated Flavor) (PP Population)	Figures 14.2.2.1.1 and 14.2.2.1.2
Mean (\pm SD) of Number of Cigarettes Smoked Per Day by Study Product Group and Study Week (Mentholated Flavor) (ITT Population)	Figures 14.2.2.1.3 and 14.2.2.1.4
Mean (\pm SD) of Number of Cigarettes Smoked Per Day by Study Product Group and Study Week (Non-Mentholated Flavor) (PP Population)	Figures 14.2.2.2.1 and 14.2.2.2.2
Mean (\pm SD) of Number of Cigarettes Smoked Per Day by Study Product Group and Study Week (Non-Mentholated Flavor) (ITT Population)	Figures 14.2.2.2.3 and 14.2.2.2.4
Mean (\pm SD) of Number of Cigarettes Smoked Per Day by Study Product Group and Study Week (Combined) (PP Population)	Figures 14.2.2.2.5 and 14.2.2.2.6
Mean (\pm SD) of Number of Cigarettes Smoked Per Day by Study Product Group and Study Week (Combined) (ITT Population)	Figures 14.2.2.2.7 and 14.2.2.2.8
Mean (\pm SD) of Number of Cigarette Butts Collected Per Week by Study Product Group and Study Week (Mentholated Flavor) (PP Population)	Figures 14.2.2.3.1 and 14.2.2.3.2
Mean (\pm SD) of Number of Cigarette Butts Collected Per Week by Study Product Group and Study Week (Mentholated Flavor) (ITT Population)	Figures 14.2.2.3.3 and 14.2.2.3.4
Mean (\pm SD) of Number of Cigarette Butts Collected Per Week by Study Product Group and Study Week (Non-Mentholated Flavor) (PP Population)	Figures 14.2.2.4.1 and 14.2.2.4.2
Mean (\pm SD) of Number of Cigarette Butts Collected Per Week by Study Product Group and Study Week (Non-Mentholated Flavor) (ITT Population)	Figures 14.2.2.4.3 and 14.2.2.4.4

Description	Number
Mean (\pm SD) of Number of Cigarette Butts Collected Per Week by Study Product Group and Study Week (Combined) (PP Population)	Figures 14.2.2.4.5 and 14.2.2.4.6
Mean (\pm SD) of Number of Cigarette Butts Collected Per Week by Study Product Group and Study Week (Combined) (ITT Population)	Figures 14.2.2.4.7 and 14.2.2.4.8

Subjects were randomized to one of four study product groups, with menthol cigarette smokers randomized to either their usual brand menthol cigarettes or VLN mentholated cigarettes, and non-menthol cigarette smokers randomized to their usual brand non-menthol cigarettes or VLN non-mentholated cigarettes.

11.2.1.1 Analysis of Number of Cigarettes

Number of Cigarettes

Summary of number of cigarettes smoked per week in the PP population is shown in [Table 11–1](#).

Table 11–1 Summary of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (PP Population)

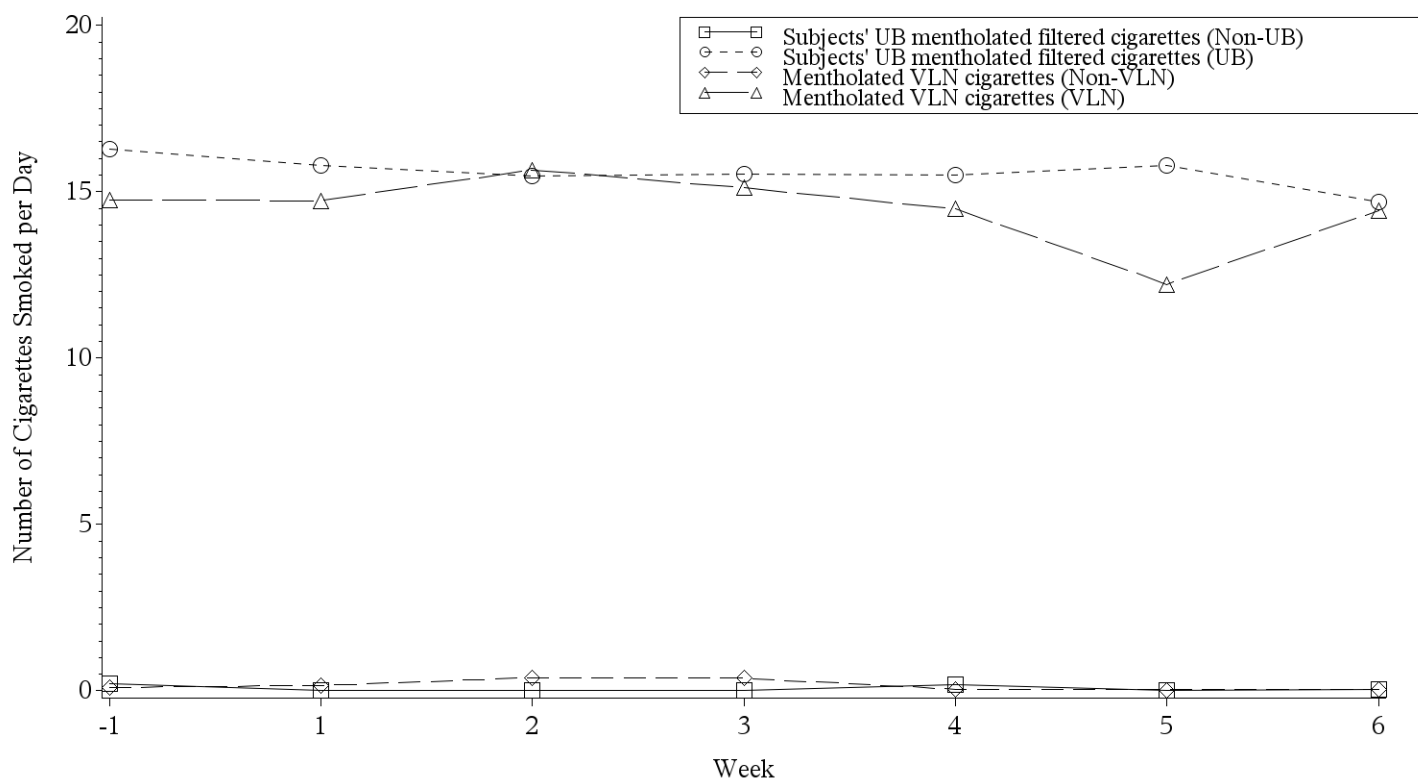
		VLN Mentholated		VLN Non-Mentholated		VLN Combined		UB Mentholated		UB Non-Mentholated		UB Combined	
Study Week	Statistics	Non-VLN	VLN	Non-VLN	VLN	Non-VLN	VLN	Non-UB	UB	Non-UB	UB	Non-UB	UB
Week -1 *	n	17	17	12	12	29	29	20	20	22	22	42	42
	Mean (SD)	0.11 (0.366)	14.75 (6.198)	0.18 (0.625)	17.19 (4.727)	0.14 (0.481)	15.76 (5.676)	0.21 (0.705)	16.29 (5.809)	0.29 (0.678)	16.80 (4.015)	0.25 (0.684)	16.55 (4.895)
	Median	0.00	13.83	0.00	16.33	0.00	15.14	0.00	14.64	0.00	16.14	0.00	15.29
	Range	0.0, 2.0	7.0, 29.0	0.0, 2.0	10.0, 26.0	0.0, 2.0	7.0, 29.0	0.0, 3.0	10.0, 33.0	0.0, 2.0	10.0, 24.0	0.0, 3.0	10.0, 33.0
Week 1	n	17	17	12	12	29	29	20	20	22	22	42	42
	Mean (SD)	0.16 (0.464)	14.73 (7.724)	0.48 (0.829)	24.08 (8.863)	0.29 (0.647)	18.60 (9.322)	0.02 (0.052)	15.79 (4.638)	0.10 (0.327)	17.33 (4.528)	0.06 (0.240)	16.60 (4.591)
	Median	0.00	12.71	0.07	26.54	0.00	15.29	0.00	16.43	0.00	17.07	0.00	16.43
	Range	0.0, 2.0	3.0, 34.0	0.0, 3.0	14.0, 43.0	0.0, 3.0	3.0, 43.0	0.0, 0.0	9.0, 25.0	0.0, 2.0	10.0, 26.0	0.0, 2.0	9.0, 26.0
Week 2	n	15	15	11	11	26	26	20	20	22	22	42	42
	Mean (SD)	0.39 (1.387)	15.66 (7.860)	0.35 (0.891)	23.32 (9.717)	0.38 (1.181)	18.90 (9.341)	0.03 (0.088)	15.47 (4.425)	0.36 (1.404)	16.17 (4.475)	0.20 (1.020)	15.84 (4.411)
	Median	0.00	14.00	0.00	23.14	0.00	17.36	0.00	15.36	0.00	16.29	0.00	15.86
	Range	0.0, 5.0	6.0, 33.0	0.0, 3.0	9.0, 38.0	0.0, 5.0	6.0, 38.0	0.0, 0.0	9.0, 25.0	0.0, 7.0	9.0, 25.0	0.0, 7.0	9.0, 25.0
Week 3	n	12	12	11	11	23	23	20	20	20	20	40	40
	Mean (SD)	0.38 (1.147)	15.12 (8.229)	0.62 (1.515)	21.60 (10.100)	0.50 (1.310)	18.22 (9.550)	0.02 (0.052)	15.52 (5.469)	0.30 (0.846)	16.95 (4.600)	0.16 (0.608)	16.24 (5.040)
	Median	0.00	13.07	0.00	20.14	0.00	15.57	0.00	14.64	0.00	16.79	0.00	16.21
	Range	0.0, 4.0	0.0, 30.0	0.0, 5.0	4.0, 41.0	0.0, 5.0	0.0, 41.0	0.0, 0.0	9.0, 28.0	0.0, 4.0	10.0, 27.0	0.0, 4.0	9.0, 28.0
Week 4	n	11	11	11	11	22	22	20	20	20	20	40	40
	Mean (SD)	0.05 (0.116)	14.48 (5.801)	0.68 (1.284)	21.66 (9.807)	0.36 (0.945)	18.07 (8.678)	0.19 (0.708)	15.49 (5.429)	0.55 (1.171)	16.84 (4.874)	0.37 (0.973)	16.16 (5.137)
	Median	0.00	13.29	0.00	19.14	0.00	17.50	0.00	15.00	0.00	17.14	0.00	15.64
	Range	0.0, 0.0	8.0, 28.0	0.0, 4.0	8.0, 42.0	0.0, 4.0	8.0, 42.0	0.0, 3.0	8.0, 27.0	0.0, 3.0	7.0, 26.0	0.0, 3.0	7.0, 27.0
Week 5	n	10	10	11	11	21	21	20	20	20	20	40	40
	Mean (SD)	0.03 (0.090)	12.22 (4.093)	0.35 (0.724)	21.34 (9.091)	0.20 (0.541)	17.00 (8.403)	0.01 (0.032)	15.80 (6.214)	1.29 (5.675)	17.85 (5.464)	0.65 (4.014)	16.83 (5.868)
	Median	0.00	11.14	0.00	18.71	0.00	16.00	0.00	15.14	0.00	17.43	0.00	16.14

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		VLN Mentholated		VLN Non- Mentholated		VLN Combined		UB Mentholated		UB Non- Mentholated		UB Combined	
Study Week	Statistics	Non-VLN	VLN	Non-VLN	VLN	Non-VLN	VLN	Non-UB	UB	Non-UB	UB	Non-UB	UB
	Range	0.0, 0.0	7.0, 19.0	0.0, 2.0	4.0, 37.0	0.0, 2.0	4.0, 37.0	0.0, 0.0	8.0, 32.0	0.0, 25.0	8.0, 34.0	0.0, 25.0	8.0, 34.0
Week 6	n	10	10	11	11	21	21	20	20	20	20	40	40
	Mean (SD)	0.04 (0.136)	14.43 (9.435)	0.37 (0.762)	21.20 (8.219)	0.21 (0.571)	17.98 (9.265)	0.04 (0.160)	14.69 (4.877)	0.04 (0.133)	15.89 (5.356)	0.04 (0.145)	15.29 (5.092)
	Median	0.00	10.56	0.00	21.14	0.00	17.71	0.00	14.71	0.00	16.85	0.00	15.43
	Range	0.0, 0.0	7.0, 39.0	0.0, 2.0	9.0, 35.0	0.0, 2.0	7.0, 39.0	0.0, 1.0	7.0, 24.0	0.0, 1.0	0.0, 24.0	0.0, 1.0	0.0, 24.0
Cigarettes per Day were calculated as the average cigarettes smoked per day in each week. * Subjects used their own usual brand cigarettes at Week -1. UB and Non-UB cigarettes were reported for all subjects on Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes Source: Tables 14.2.1.1.1.1 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_cigparam.sas 13JUN2019 5:06													

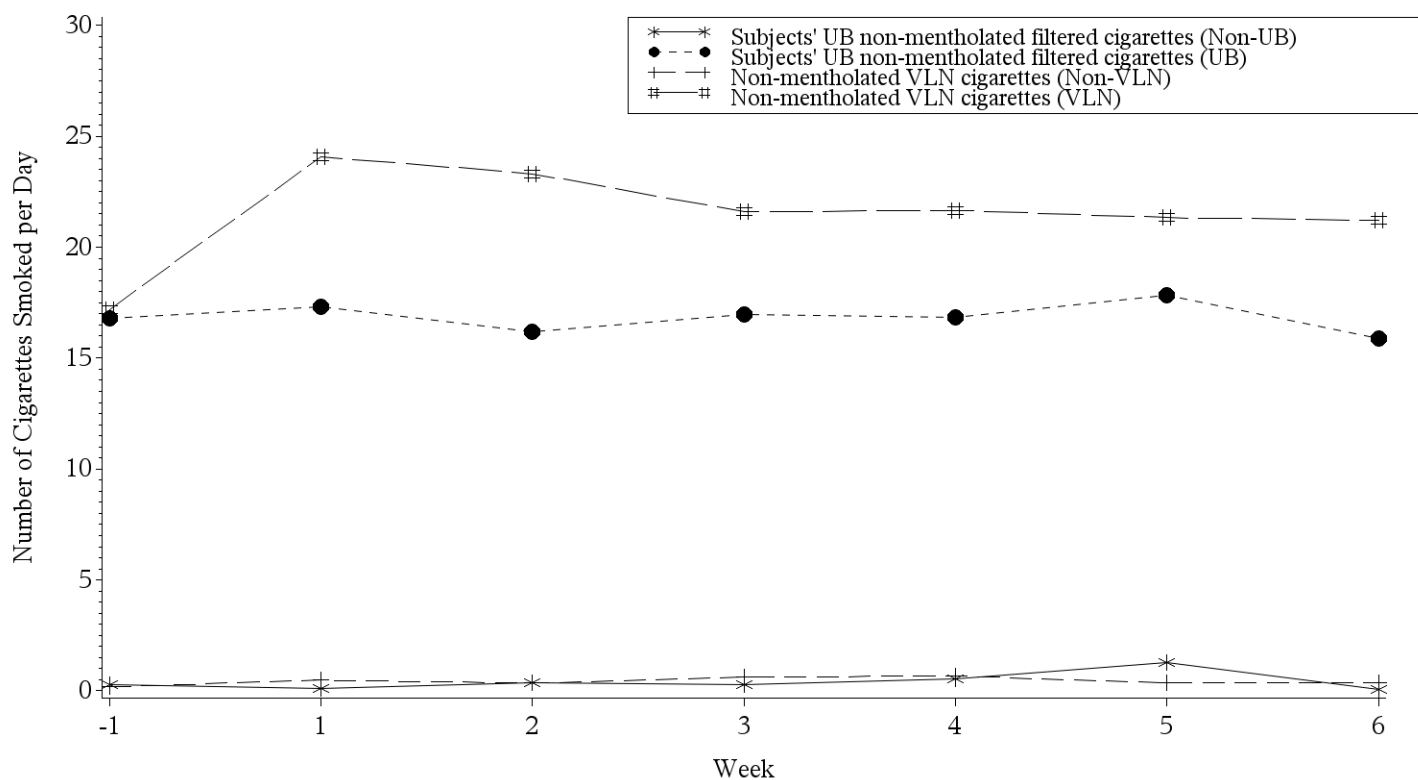
In the PP population at baseline, smokers of non-mentholated cigarettes smoked approximately 17 CPD of their UB cigarette. After switching to VLN non-mentholated cigarettes, the mean number of CPD increased to 24.08 CPD at Week 1 and remained above baseline, but decreased slightly from Week 2 through Week 6 (from 23.22 to 21.20 CPD). Smokers of mentholated cigarettes smoked approximately 15 to 16 CPD of their UB cigarette at baseline. After switching to VLN mentholated cigarettes, mean CPD in the PP population remained near baseline at all study weeks (ranging from 14.43 to 15.66), with the exception of a decrease at Week 5 (12.22 CPD). For VLN combined (mentholated and non-mentholated) in the PP population, the mean CPD was above baseline (15.76 CPD) at all study weeks (ranging from 17.00 to 18.90) ([Table 14.2.1.1.1.1](#)). Mean mentholated, non-mentholated, and combined CPD over time for the PP population are presented in [Figures 11-1, 11-2, and 11-3](#) below.

Figure 11–1 Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Mentholated Flavor) (PP Population)



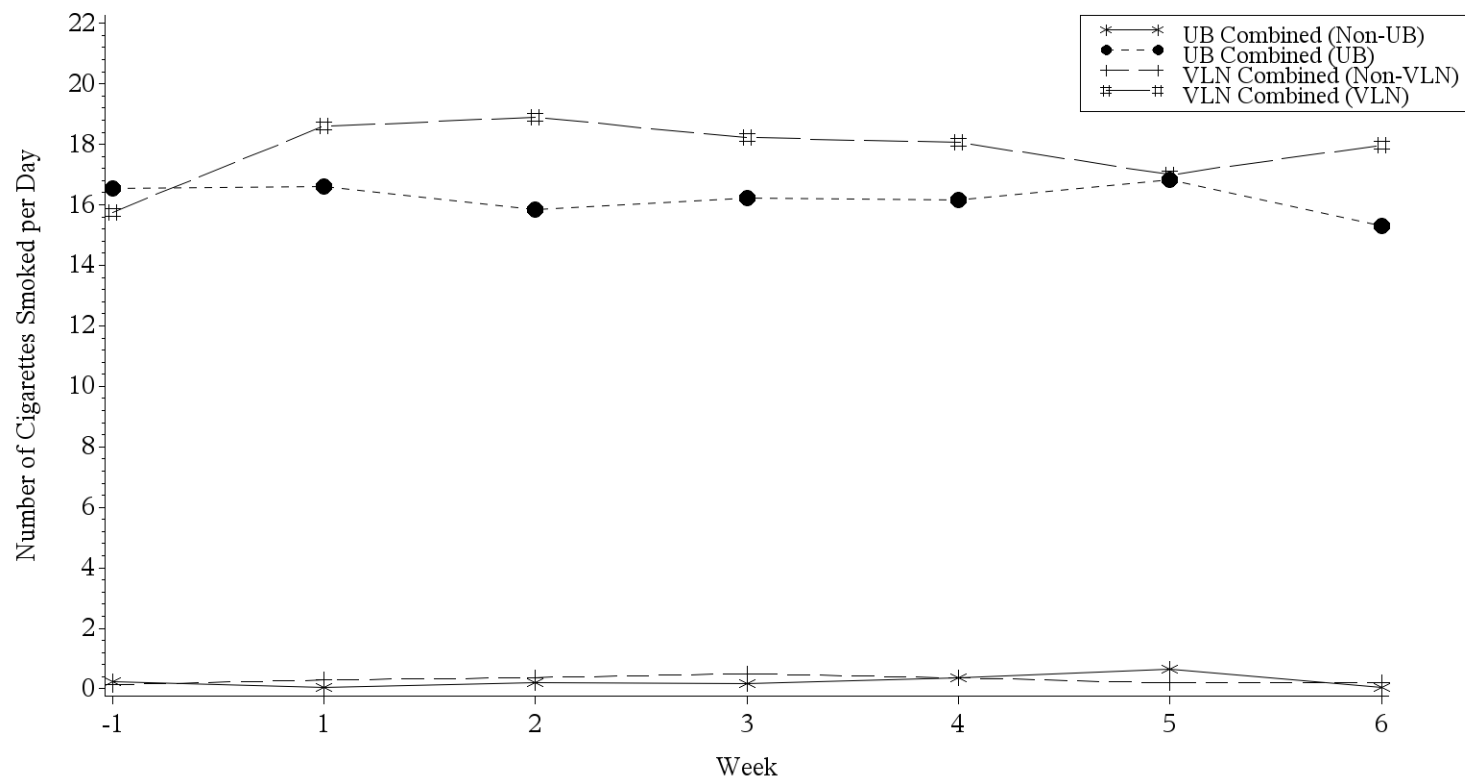
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_meangraph_cig1M.sas 28JUN2019 5:06

**Figure 11–2 Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week
 (Non-Mentholated Flavor) (PP Population)**



Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_meangraph_cig1NM.sas 28JUN2019 5:08

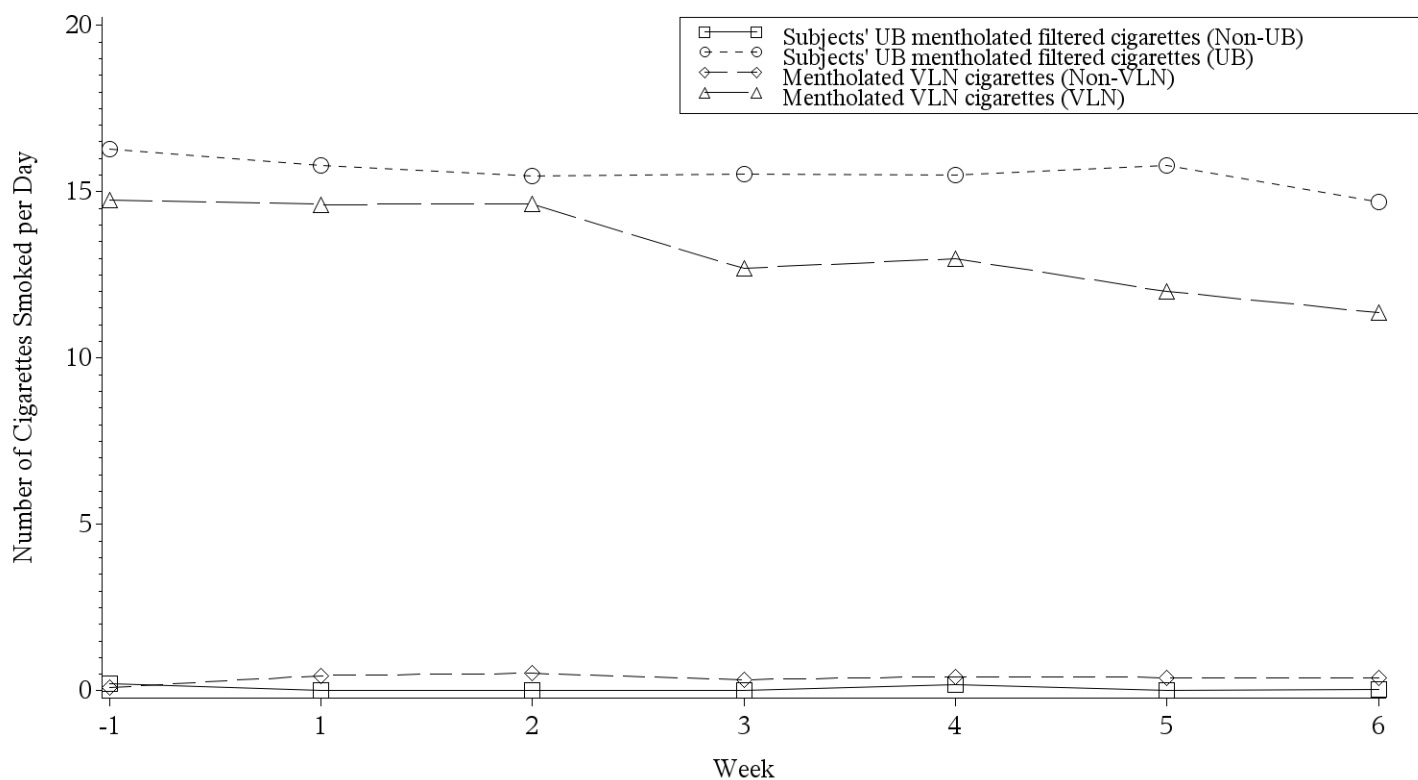
**Figure 11–3 Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week
 (Combined) (PP Population)**



Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_meangraph_cig1C.sas 13JUN2019 5:11

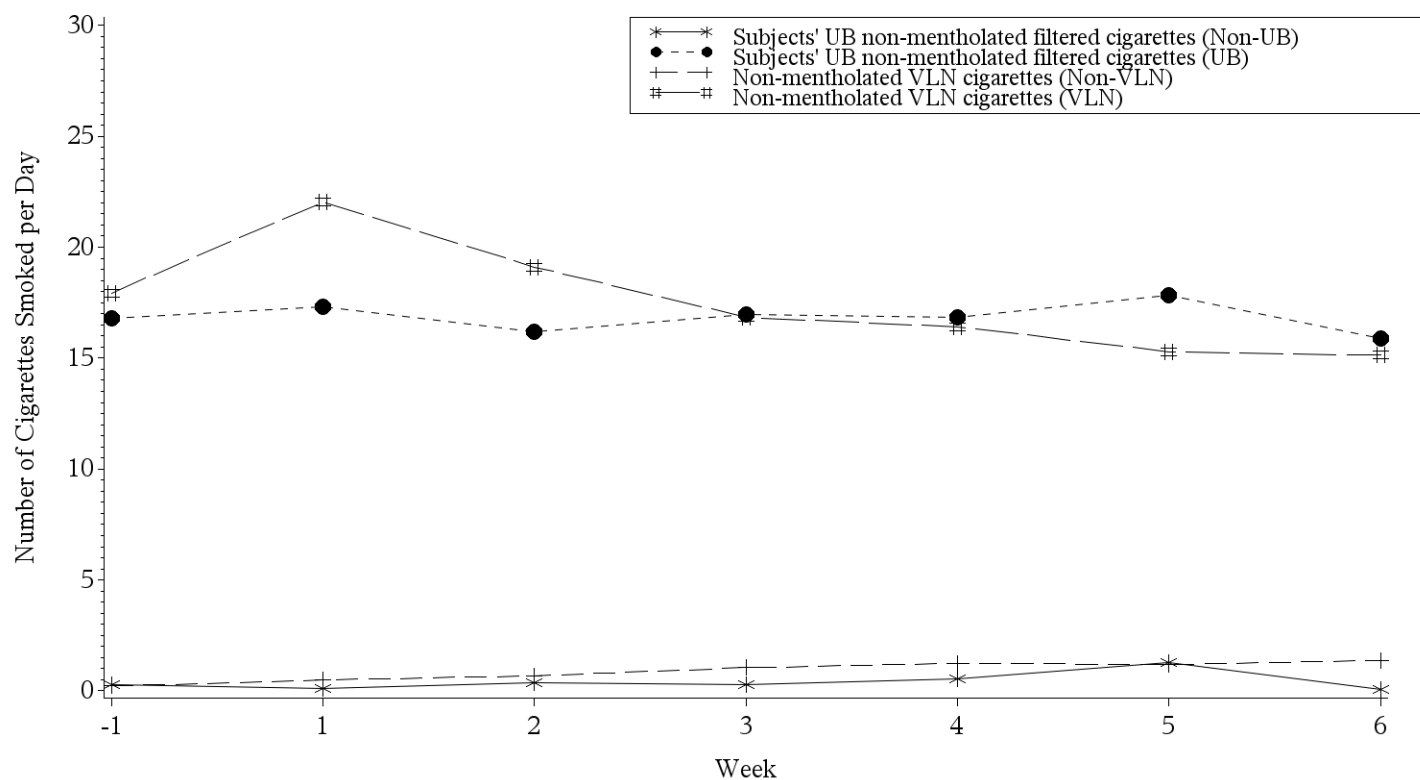
As with the PP population, the mean number of CPD in the ITT population increased from baseline on Week 1 for smokers of VLN non-mentholated cigarettes (from 17.94 to 22.02 CPD), with a small decrease at Week 2 (19.11 CPD). However, mean CPD was then below baseline and continually decreased from Week 3 through Week 6 (16.84 to 15.13 CPD). This finding was different from the PP population, where CPD remained above baseline throughout the six-week period. Mean CPD for VLN mentholated generally decreased from baseline (14.75 CPD) at Week 1 through Week 6 (from 14.62 to 11.37 CPD). This was also different than the PP population, where CPD remained similar to baseline throughout the six-week period. In the ITT population, VLN combined was above baseline (16.35 CPD) at Weeks 1 (18.32 CPD) and 2 (16.89 CPD), then continually decreased below baseline for the remainder of the study (from 14.86 to 13.25 CPD) ([Table 14.2.1.1.1.2](#)). Mean mentholated, non-mentholated, and combined CPD over time for the ITT population are presented in [Figures 11-4](#), [11-5](#), and [11-6](#) below.

Figure 11–4 Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Mentholated Flavor) (ITT Population)



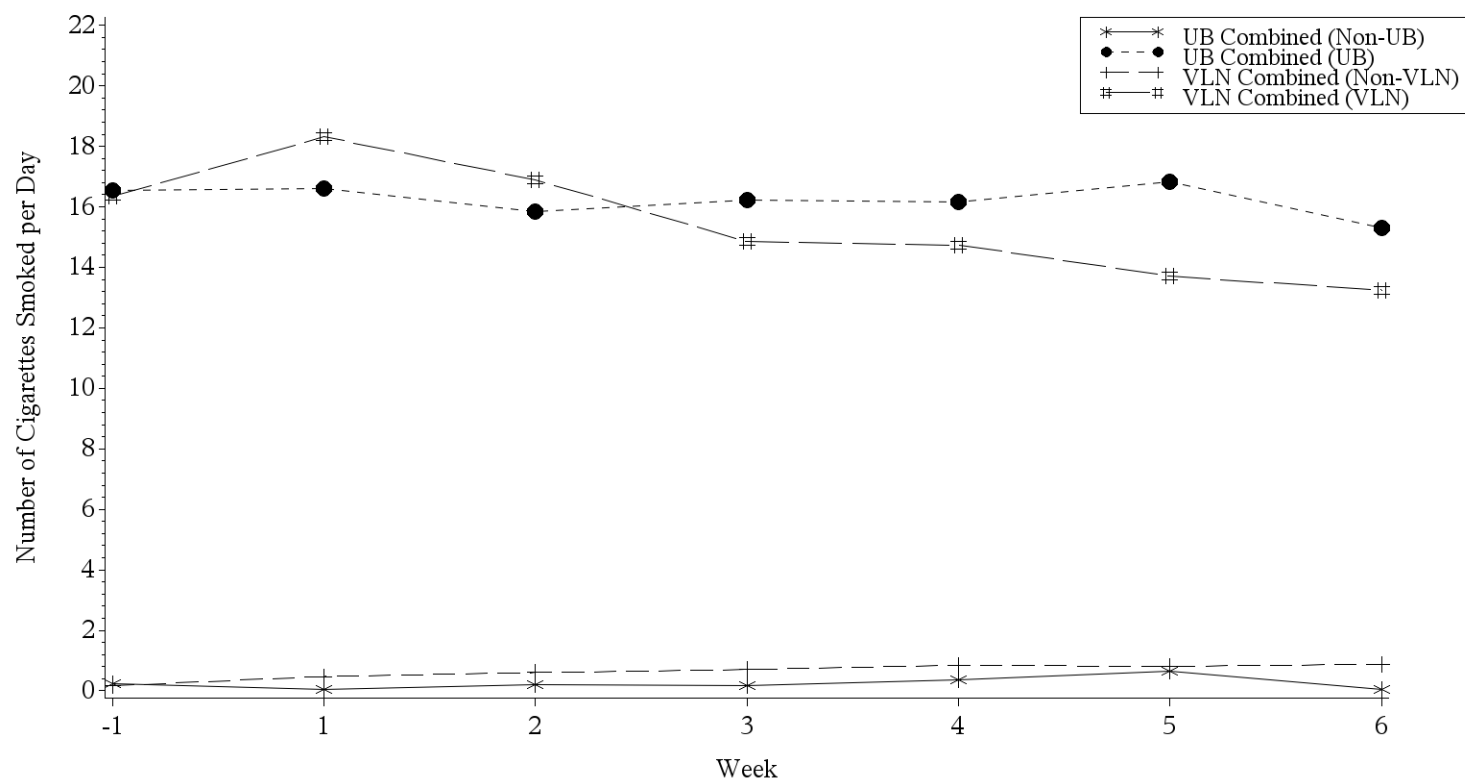
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_meangraph_cig1M.sas 28JUN2019 5:06

Figure 11–5 Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Non-Mentholated Flavor) (ITT Population)



Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_meangraph_cig1NM.sas 28JUN2019 5:08

**Figure 11–6 Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week
 (Combined) (ITT Population)**



Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_meangraph_cig1C.sas 13JUN2019 5:11

The ITT and PP populations were the same for the UB cigarette groups. At baseline, smokers of non-mentholated cigarettes smoked a mean of approximately 17 CPD and smokers of mentholated cigarettes smoked a mean approximately 16 CPD. There were no trends in CPD throughout the six-week study period in either group, with CPD ranging from approximately 16 to 18 in the non-mentholated group and 15 to 16 in the mentholated group (Tables 14.2.1.1.1.1 and 14.2.1.1.1.2).

Overall, subjects reported smoking very few non-compliant cigarettes across study product groups, with mean non-compliant cigarettes generally remaining less than 1.0 CPD (Tables 14.2.1.1.1.1 and 14.2.1.1.1.2).

Number of Cigarette Butts Collected

The collection of cigarette butts was for the purposes of assessing both compliance with the study requirements and the accuracy of the subjects' self-reported (electronic diary) cigarette consumption (Tables 14.2.1.2.1.1 and 14.2.1.2.1.2). The number of cigarette butts collected was reported per week, thus a day-by-day comparison with CPD was not possible. Nevertheless, the number of butts collected followed the same trend as CPD with bigger increases from baseline seen in subjects who switched to non-mentholated VLN cigarettes compared to those who switched to mentholated VLN cigarettes and those who remained on UB. The numbers also correlated with plasma cotinine data (See Section 11.3.2.2 for location) for which sharp decreases in plasma cotinine concentrations (up to 94% decrease in some subjects) were observed for subjects who switched to VLN mentholated and non-mentholated cigarettes, whereas for subjects who remained on UB, plasma cotinine levels remained within approximately 20% of baseline values.

11.2.1.2 Statistical Analysis of Number of Cigarettes

The locations of statistical summary and comparisons of numbers of CPD are listed below.

Statistical Comparison of Number of Cigarettes Smoked per Day at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)	Table 14.2.1.1.2
Statistical Comparison of Number of Cigarettes Smoked per Day Among Study Product Groups at Weeks 2 and 6 (PP Population)	Table 14.2.1.1.3
Statistical Comparison of Number of Cigarettes Smoked per Day at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)	Table 14.2.1.1.4
Statistical Comparison of Number of Cigarettes Smoked per Day Among Study Product Groups at Weeks 2 and 6 (ITT Population)	Table 14.2.1.1.5

Statistical comparison of number of cigarettes smoked per day at Weeks 2 and 6 versus Week -1 for the PP population is shown in Table 11-2.

Table 11–2 Statistical Comparison of Number of Cigarettes Smoked per Day at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Study Week	Product Group	Means		Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
		Test Week	Baseline			
Week 2	VLN Non-Mentholated	23.67	16.57	7.10	2.05 - 12.15	0.0106
	VLN Mentholated	16.05	15.35	0.70	-1.20 - 2.59	0.4419
	VLN Combined	19.27	15.87	3.41	0.87 - 5.95	0.0106
	UB Non-Mentholated	16.53	17.09	-0.56	-1.84 - 0.72	0.3733
	UB Mentholated	15.50	16.49	-0.99	-3.62 - 1.64	0.4393
	UB Combined	16.04	16.80	-0.77	-2.12 - 0.59	0.2609
Week 6	VLN Non-Mentholated	21.57	16.57	5.00	1.01 - 8.99	0.0190
	VLN Mentholated	14.47	16.55	-2.07	-8.32 - 4.17	0.4718
	VLN Combined	18.19	16.56	1.63	-2.04 - 5.30	0.3648
	UB Non-Mentholated	15.94	16.86	-0.92	-2.68 - 0.84	0.2871
	UB Mentholated	14.72	16.49	-1.77	-4.50 - 0.96	0.1912
	UB Combined	15.33	16.67	-1.34	-2.90 - 0.21	0.0883
<p>Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes Paired t-test method is used to perform analysis.</p> <p>Source: Table 14.2.1.1.2 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_cigstatsttest.sas 13JUN2019 5:07</p>						

In the PP population, there were statistically significant increases from baseline in CPD for VLN non-mentholated (7.1 CPD increase) and VLN combined (3.4 CPD increase) at Week 2, and for VLN non-mentholated (5 CPD increase) at Week 6. There were no significant changes noted in VLN mentholated or any of the UB groups. Regarding product comparisons, significantly greater CPD were noted in VLN non-mentholated and VLN combined compared to UB non-mentholated and UB combined, respectively, at Week 2, and for VLN non-mentholated compared to UB non-mentholated at Week 6.

Statistical comparison of number of cigarettes smoked per day at Weeks 2 and 6 versus Week -1 for the ITT population is shown in [Table 11–3](#).

Table 11–3 Statistical Comparison of Number of Cigarettes Smoked per Day at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

		Means				
Study Week	Product Group	Test Week	Baseline	Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
Week 2	VLN Non-Mentholated	19.79	18.00	1.79	-0.22 - 3.81	0.0798
	VLN Mentholated	15.16	15.01	0.15	-1.15 - 1.45	0.8190
	VLN Combined	17.50	16.52	0.98	-0.21 - 2.17	0.1068
	UB Non-Mentholated	16.53	17.09	-0.56	-1.84 - 0.72	0.3733
	UB Mentholated	15.50	16.49	-0.99	-3.62 - 1.64	0.4393
	UB Combined	16.04	16.80	-0.77	-2.12 - 0.59	0.2609
Week 6	VLN Non-Mentholated	16.51	17.97	-1.46	-3.64 - 0.72	0.1841
	VLN Mentholated	11.77	15.25	-3.48	-5.21 - -1.75	0.0002
	VLN Combined	14.14	16.61	-2.47	-3.85 - -1.09	0.0006
	UB Non-Mentholated	15.94	16.86	-0.92	-2.68 - 0.84	0.2871
	UB Mentholated	14.72	16.49	-1.77	-4.50 - 0.96	0.1912
	UB Combined	15.33	16.67	-1.34	-2.90 - 0.21	0.0883
<p>Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes Paired t-test method is used to perform analysis.</p> <p>Source: Table 14.2.1.1.4 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_cigstatsttest.sas 13JUN2019 5:07</p>						

In the ITT population, there were statistically significant decreases from baseline in CPD for VLN mentholated and VLN combined at Week 6, with no significant changes for VLN non-mentholated or any of the UB groups. There were no statistically significant changes for any of the groups at Week 2. There were no statistically significant comparisons between VLN and UB mentholated or non-mentholated at Weeks 2 or 6 in the ITT population.

11.3 Topography, Biomarker, Pharmacokinetic, and Subjective Effect Results and Tabulations of Individual Subject Data

11.3.1 Topography Analysis

Puffing topography parameters (average puff duration, average total puff duration, average puff volume, average total puff volume, average inter-puff interval, average peak puff flow rate, average flow rate, number of cigarettes, and average number of puffs) are summarized in [Table 14.2.3.1.1](#) for the PP population and [Table 14.2.3.1.2](#) for the ITT population. The statistical comparisons of puffing topography parameters (Weeks 2 and 6 versus baseline) are presented in [Table 14.2.3.2](#) for the PP population and [Table 14.2.3.3](#) for the ITT population. Individual topography data for the UB and VLN products are presented in [Appendix 16.2.5.2.2.3](#). The averages of the topography parameters for each subject by topography session are in [Appendix 16.2.6.2](#).

A summary of the topography parameters and the statistical comparisons of topography parameters are presented in [Tables 11–4](#) through [11–6](#).

Table 11–4 Summary of Puffing Topography Parameters by Study Product Group and Study Week (PP Population)

Parameter	Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	VLN Combined
Average Puff Duration (sec)	Week -1*	n	3	6	9
		Mean (SD)	1.923 (1.0295)	2.128 (0.4811)	2.059 (0.6482)
		Median	2.103	2.126	2.123
		Range	0.81, 2.85	1.62, 2.88	0.81, 2.88
	Week 2	n	3	5	8
		Mean (SD)	2.690 (1.9743)	2.255 (0.6036)	2.418 (1.1715)
		Median	2.295	1.950	2.123
		Range	0.94, 4.83	1.85, 3.28	0.94, 4.83
	Week 6	n	3	4	7
		Mean (SD)	2.065 (1.1200)	1.979 (0.4463)	2.016 (0.7210)
		Median	2.254	2.074	2.238
		Range	0.86, 3.08	1.38, 2.39	0.86, 3.08
Average Total Puff Duration (sec)	Week -1*	n	3	6	9
		Mean (SD)	21.233 (7.7511)	27.263 (7.7962)	25.253 (7.8801)
		Median	22.125	28.763	25.575
		Range	13.08, 28.50	17.15, 35.95	13.08, 35.95
	Week 2	n	3	5	8
		Mean (SD)	26.267 (7.8233)	24.480 (4.8143)	25.150 (5.6202)
		Median	27.500	25.850	26.013
		Range	17.90, 33.40	16.98, 30.00	16.98, 33.40
	Week 6	n	3	4	7
		Mean (SD)	23.275 (3.6127)	22.500 (8.0078)	22.832 (6.0485)
		Median	22.925	23.525	22.925
		Range	19.85, 27.05	12.40, 30.55	12.40, 30.55
Average Puff Volume (mL)	Week -1*	n	3	6	9
		Mean (SD)	46.7230 (21.20597)	68.8826 (27.54051)	61.4961 (26.63148)
		Median	53.2497	59.9617	59.3299
		Range	23.021, 63.898	46.523, 123.468	23.021, 123.468
	Week 2	n	3	5	8
		Mean (SD)	38.9233 (19.33072)	49.9217 (14.75558)	45.7973 (16.23519)
		Median	32.8058	45.3591	44.0304

Parameter	Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	VLN Combined
	Week 6	Range	23.391, 60.573	33.113, 71.522	23.391, 71.522
		n	3	4	7
		Mean (SD)	37.3258 (18.52739)	46.0518 (11.33347)	42.3121 (14.15629)
		Median	31.0672	47.4028	42.4244
		Range	22.738, 58.172	31.885, 57.516	22.738, 58.172
Average Total Puff Volume (mL)	Week -1 *	n	3	6	9
		Mean (SD)	519.9912 (135.50854)	850.5382 (293.19134)	740.3559 (292.62895)
		Median	557.9150	775.4165	697.8500
		Range	369.561, 632.498	621.414, 1433.167	369.561, 1433.167
	Week 2	n	3	5	8
		Mean (SD)	475.7597 (230.89090)	552.8127 (213.98975)	523.9178 (207.33681)
		Median	444.4380	463.5850	456.8133
		Range	262.129, 720.712	408.232, 929.785	262.129, 929.785
	Week 6	n	3	4	7
		Mean (SD)	500.0915 (210.35119)	500.9646 (105.52044)	500.5904 (142.53669)
		Median	522.9790	490.7632	510.1640
		Range	279.233, 698.063	384.212, 638.120	279.233, 698.063
Average Inter Puff Interval (sec)	Week -1 *	n	3	6	9
		Mean (SD)	32.432 (6.0510)	35.890 (5.7467)	34.737 (5.7257)
		Median	29.853	35.067	34.850
		Range	28.10, 39.35	29.34, 45.86	28.10, 45.86
	Week 2	n	3	5	8
		Mean (SD)	19.421 (8.6665)	30.716 (11.7516)	26.480 (11.5995)
		Median	17.098	26.631	25.013
		Range	12.15, 29.01	20.33, 49.88	12.15, 49.88
	Week 6	n	3	4	7
		Mean (SD)	19.988 (7.7493)	27.839 (10.5463)	24.474 (9.6562)
		Median	23.482	26.520	23.482
		Range	11.11, 25.38	17.35, 40.97	11.11, 40.97
Average Peak Puff Flow Rate (mL/sec)	Week -1 *	n	3	6	9
		Mean (SD)	43.4564 (5.79524)	55.2651 (26.52127)	51.3289 (21.97428)

Parameter	Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	VLN Combined
		Median	42.3331	49.1643	42.3331
		Range	38.305, 49.731	28.807, 91.406	28.807, 91.406
	Week 2	n	3	5	8
		Mean (SD)	43.6665 (27.16781)	36.2484 (11.86805)	39.0302 (17.49596)
		Median	43.7192	34.7233	38.2527
		Range	16.472, 70.808	24.727, 53.597	16.472, 70.808
	Week 6	n	3	4	7
		Mean (SD)	37.5340 (12.98328)	38.1122 (12.09966)	37.8644 (11.37914)
		Median	43.9681	35.7617	37.7579
		Range	22.590, 46.044	26.160, 54.765	22.590, 54.765
Average Flow Rate (mL/sec)	Week -1*	n	3	6	9
		Mean (SD)	27.0359 (3.82638)	35.7519 (15.87046)	32.8466 (13.41910)
		Median	26.5615	32.3133	26.5615
		Range	23.469, 31.077	21.156, 62.105	21.156, 62.105
	Week 2	n	3	5	8
		Mean (SD)	21.1808 (11.52364)	24.1156 (6.74146)	23.0151 (8.13746)
		Median	26.3697	22.4444	24.4071
		Range	7.975, 29.198	17.471, 32.055	7.975, 32.055
	Week 6	n	3	4	7
		Mean (SD)	22.3820 (9.48241)	24.0936 (5.90744)	23.3601 (6.94679)
		Median	27.4870	24.4472	24.6008
		Range	11.441, 28.218	16.524, 30.956	11.441, 30.956
Number of Cigarettes	Week -1*	n	3	6	9
		Mean (SD)	2.0 (0.00)	1.8 (0.75)	1.9 (0.60)
		Median	2.0	2.0	2.0
		Range	2, 2	1, 3	1, 3
	Week 2	n	3	5	8
		Mean (SD)	1.7 (0.58)	1.6 (0.55)	1.6 (0.52)
		Median	2.0	2.0	2.0
		Range	1, 2	1, 2	1, 2
	Week 6	n	3	4	7
		Mean (SD)	1.3 (0.58)	1.8 (0.50)	1.6 (0.53)
		Median	1.0	2.0	2.0

Parameter	Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	VLN Combined
		Range	1, 2	1, 2	1, 2
Average Number of Puffs	Week -1 *	n	3	6	9
		Mean (SD)	12.2 (3.33)	12.7 (1.56)	12.5 (2.09)
		Median	10.5	12.3	12.0
		Range	10, 16	11, 15	10, 16
	Week 2	n	3	5	8
		Mean (SD)	12.7 (6.03)	11.2 (2.59)	11.8 (3.85)
		Median	12.0	12.0	12.0
		Range	7, 19	8, 14	7, 19
	Week 6	n	3	4	7
		Mean (SD)	14.2 (7.97)	11.4 (3.30)	12.6 (5.37)
		Median	12.0	10.3	11.5
		Range	8, 23	9, 16	8, 23

* Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

Source: [Table 14.2.3.1.1](#)
Program: /CA24914/sas_prg/pksas/pd_top/adam_intext_topparam.sas 13JUN2019 5:30

Table 11–5 Statistical Comparisons of Puffing Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Parameter	Study Week	Product Group	Means				Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
			Test Week	n	Baseline	n			
Average Puff Duration (sec)	Week 2	VLN Non-Mentholated	2.690	3	1.923	3	0.77	-1.85 - 3.38	0.3339
		VLN Mentholated	2.255	5	2.230	5	0.02	-0.34 - 0.39	0.8611
		VLN Combined	2.418	8	2.115	8	0.30	-0.30 - 0.90	0.2706
	Week 6	VLN Non-Mentholated	2.065	3	1.923	3	0.14	-0.08 - 0.37	0.1123
		VLN Mentholated	1.979	4	2.068	4	-0.09	-0.47 - 0.29	0.5101
		VLN Combined	2.016	7	2.005	7	0.01	-0.19 - 0.21	0.9018
Average Total Puff Duration (sec)	Week 2	VLN Non-Mentholated	26.27	3	21.23	3	5.03	4.29 - 5.77	0.0012
		VLN Mentholated	24.48	5	28.84	5	-4.36	-8.97 - 0.26	0.0589
		VLN Combined	25.15	8	25.98	8	-0.83	-5.53 - 3.86	0.6869
	Week 6	VLN Non-Mentholated	23.28	3	21.23	3	2.04	-14.50 - 18.59	0.6485
		VLN Mentholated	22.50	4	27.06	4	-4.56	-14.80 - 5.69	0.2518
		VLN Combined	22.83	7	24.56	7	-1.73	-8.13 - 4.67	0.5334
Average Puff Volume (mL)	Week 2	VLN Non-Mentholated	38.92	3	46.72	3	-7.80	-58.65 - 43.05	0.5771
		VLN Mentholated	49.92	5	69.33	5	-19.40	-64.38 - 25.57	0.2971
		VLN Combined	45.80	8	60.85	8	-15.05	-40.21 - 10.10	0.2000
	Week 6	VLN Non-Mentholated	37.33	3	46.72	3	-9.40	-60.22 - 41.43	0.5097
		VLN Mentholated	46.05	4	71.51	4	-25.46	-69.29 - 18.37	0.1617
		VLN Combined	42.31	7	60.89	7	-18.57	-41.09 - 3.94	0.0901
Average Total Puff Volume (mL)	Week 2	VLN Non-Mentholated	475.8	3	520.0	3	-44.23	-754.31 - 665.84	0.8138
		VLN Mentholated	552.8	5	860.7	5	-307.84	-783.41 - 167.73	0.1467
		VLN Combined	523.9	8	732.9	8	-208.99	-505.49 - 87.52	0.1395
	Week 6	VLN Non-Mentholated	500.1	3	520.0	3	-19.90	-737.27 - 697.47	0.9159
		VLN Mentholated	501.0	4	886.6	4	-385.65	-828.92 - 57.61	0.0696
		VLN Combined	500.6	7	729.5	7	-228.90	-528.33 - 70.52	0.1106
Average Inter-Puff Interval (sec)	Week 2	VLN Non-Mentholated	19.42	3	32.43	3	-13.01	-20.00 - -6.02	0.0152
		VLN Mentholated	30.72	5	36.10	5	-5.38	-15.30 - 4.54	0.2064
		VLN Combined	26.48	8	34.72	8	-8.24	-14.40 - -2.08	0.0159
	Week 6	VLN Non-Mentholated	19.99	3	32.43	3	-12.44	-26.04 - 1.15	0.0588
		VLN Mentholated	27.84	4	36.30	4	-8.46	-23.80 - 6.88	0.1775

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			Means						
Parameter	Study Week	Product Group	Test Week	n	Baseline	n	Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
		VLN Combined	24.47	7	34.64	7	-10.17	-17.39 - -2.95	0.0137
Average Peak Puff Flow Rate (mL/sec)	Week 2	VLN Non-Mentholated	43.67	3	43.46	3	0.21	-63.69 - 64.11	0.9900
		VLN Mentholated	36.25	5	50.51	5	-14.26	-44.81 - 16.29	0.2647
		VLN Combined	39.03	8	47.86	8	-8.83	-29.16 - 11.49	0.3383
	Week 6	VLN Non-Mentholated	37.53	3	43.46	3	-5.92	-28.00 - 16.16	0.3677
		VLN Mentholated	38.11	4	55.93	4	-17.82	-56.24 - 20.59	0.2363
		VLN Combined	37.86	7	50.59	7	-12.72	-30.23 - 4.78	0.1257
Average Flow Rate (mL/sec)	Week 2	VLN Non-Mentholated	21.18	3	27.04	3	-5.86	-28.51 - 16.80	0.3819
		VLN Mentholated	24.12	5	34.06	5	-9.95	-31.18 - 11.29	0.2633
		VLN Combined	23.02	8	31.43	8	-8.41	-20.10 - 3.27	0.1325
	Week 6	VLN Non-Mentholated	22.38	3	27.04	3	-4.65	-21.20 - 11.89	0.3498
		VLN Mentholated	24.09	4	37.29	4	-13.19	-39.28 - 12.89	0.2059
		VLN Combined	23.36	7	32.89	7	-9.53	-21.59 - 2.53	0.1012
Average Number of Puffs (N)	Week 2	VLN Non-Mentholated	12.67	3	12.17	3	0.50	-7.26 - 8.26	0.8075
		VLN Mentholated	11.20	5	12.83	5	-1.63	-3.76 - 0.49	0.0995
		VLN Combined	11.75	8	12.58	8	-0.83	-2.82 - 1.16	0.3554
	Week 6	VLN Non-Mentholated	14.17	3	12.17	3	2.00	-9.85 - 13.85	0.5432
		VLN Mentholated	11.38	4	12.92	4	-1.54	-5.60 - 2.52	0.3133
		VLN Combined	12.57	7	12.60	7	-0.02	-3.54 - 3.49	0.9873
Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes Paired t-test method is used to perform analysis.									
Source: Table 14.2.3.2 Program: /CA24914/sas_prg/pksas/pd_top/adam_intext_statsttest.sas 13JUN2019 5:32									

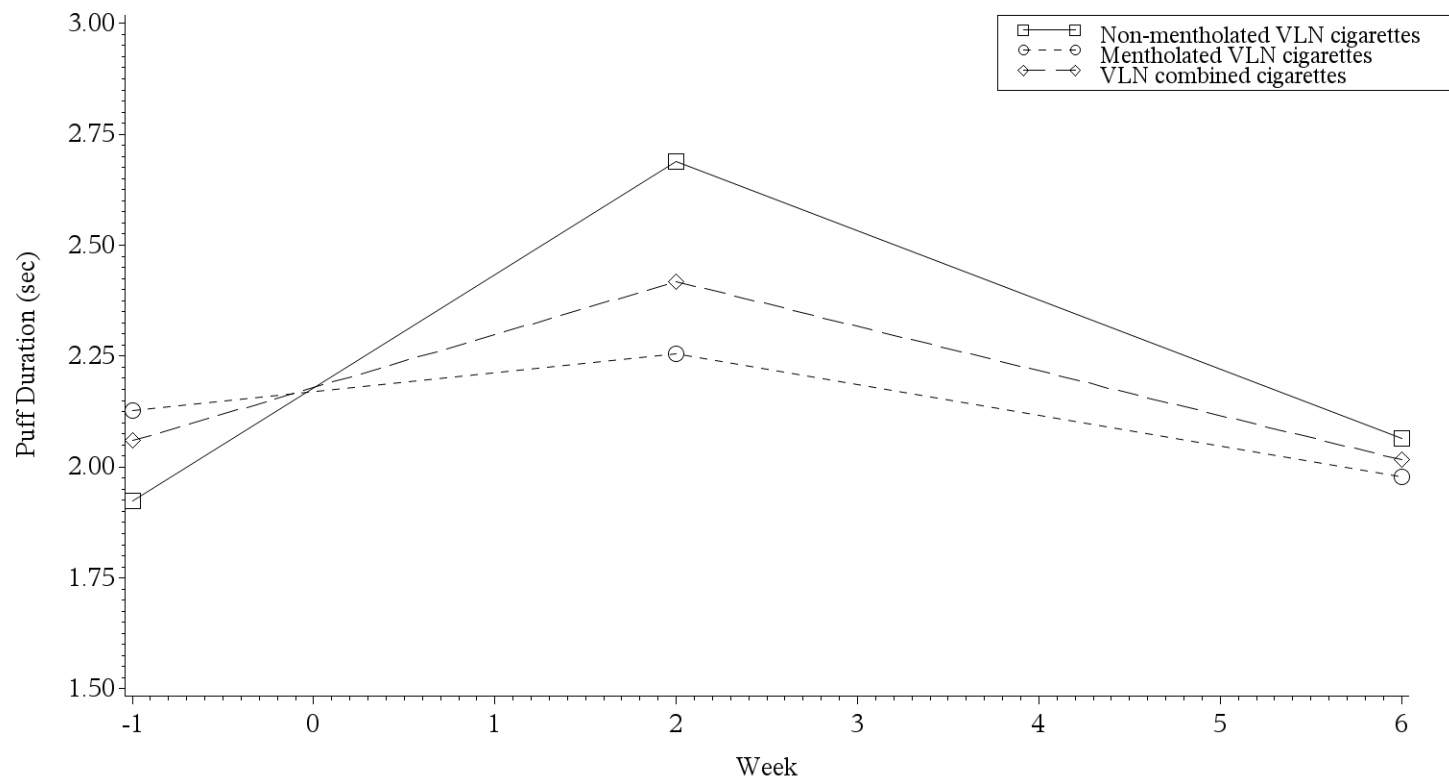
Table 11–6 Statistical Comparisons of Puffing Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Parameter	Study Week	Product Group	Means				Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
			Test Week	n	Baseline	n			
Average Puff Duration (sec)	Week 2	VLN Non-Mentholated	2.212	16	2.125	16	0.09	-0.24 - 0.41	0.5745
		VLN Mentholated	2.169	17	2.293	17	-0.12	-0.37 - 0.12	0.2937
		VLN Combined	2.190	33	2.212	33	-0.02	-0.21 - 0.17	0.8207
	Week 6	VLN Non-Mentholated	2.072	17	2.069	17	0.00	-0.19 - 0.19	0.9817
		VLN Mentholated	2.067	15	2.255	15	-0.19	-0.51 - 0.14	0.2327
		VLN Combined	2.069	32	2.156	32	-0.09	-0.26 - 0.09	0.3163
Average Total Puff Duration (sec)	Week 2	VLN Non-Mentholated	23.28	16	24.57	16	-1.29	-4.39 - 1.82	0.3917
		VLN Mentholated	24.56	17	28.28	17	-3.72	-6.33 - -1.11	0.0082
		VLN Combined	23.94	33	26.48	33	-2.54	-4.49 - -0.58	0.0125
	Week 6	VLN Non-Mentholated	21.97	17	24.03	17	-2.06	-4.90 - 0.77	0.1429
		VLN Mentholated	22.12	15	27.68	15	-5.56	-9.09 - -2.03	0.0045
		VLN Combined	22.04	32	25.74	32	-3.70	-5.90 - -1.50	0.0017
Average Puff Volume (mL)	Week 2	VLN Non-Mentholated	44.66	16	51.03	16	-6.38	-14.00 - 1.25	0.0951
		VLN Mentholated	49.74	17	57.38	17	-7.64	-20.28 - 5.00	0.2183
		VLN Combined	47.28	33	54.30	33	-7.03	-14.11 - 0.05	0.0516
	Week 6	VLN Non-Mentholated	47.97	17	50.27	17	-2.30	-8.22 - 3.63	0.4232
		VLN Mentholated	46.75	15	56.24	15	-9.49	-21.39 - 2.41	0.1092
		VLN Combined	47.40	32	53.07	32	-5.67	-11.81 - 0.47	0.0692
Average Total Puff Volume (mL)	Week 2	VLN Non-Mentholated	473.4	16	580.9	16	-107.47	-197.50 - -17.43	0.0225
		VLN Mentholated	576.2	17	708.5	17	-132.33	-277.07 - 12.41	0.0705
		VLN Combined	526.4	33	646.6	33	-120.27	-202.03 - -38.51	0.0052
	Week 6	VLN Non-Mentholated	508.9	17	576.8	17	-67.88	-159.34 - 23.58	0.1352
		VLN Mentholated	491.5	15	690.8	15	-199.38	-337.94 - -60.83	0.0080
		VLN Combined	500.7	32	630.3	32	-129.52	-209.37 - -49.67	0.0024
Average Inter-Puff Interval (sec)	Week 2	VLN Non-Mentholated	24.28	16	29.50	16	-5.22	-9.95 - -0.50	0.0325
		VLN Mentholated	26.62	17	28.89	17	-2.27	-7.62 - 3.08	0.3824
		VLN Combined	25.49	33	29.19	33	-3.70	-7.13 - -0.28	0.0351
	Week 6	VLN Non-Mentholated	21.04	17	29.46	17	-8.41	-12.62 - -4.21	0.0006
		VLN Mentholated	27.22	15	29.31	15	-2.09	-7.90 - 3.71	0.4516

			Means						
Parameter	Study Week	Product Group	Test Week	n	Baseline	n	Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
		VLN Combined	23.94	32	29.39	32	-5.45	-8.95 - -1.95	0.0034
Average Peak Puff Flow Rate (mL/sec)	Week 2	VLN Non-Mentholated	39.70	16	42.89	16	-3.19	-10.03 - 3.66	0.3370
		VLN Mentholated	41.44	17	44.02	17	-2.58	-13.49 - 8.33	0.6235
		VLN Combined	40.60	33	43.47	33	-2.87	-9.04 - 3.30	0.3500
	Week 6	VLN Non-Mentholated	43.43	17	43.73	17	-0.30	-5.32 - 4.71	0.8992
		VLN Mentholated	40.02	15	43.95	15	-3.93	-14.74 - 6.88	0.4484
		VLN Combined	41.83	32	43.83	32	-2.00	-7.41 - 3.40	0.4549
Average Flow Rate (mL/sec)	Week 2	VLN Non-Mentholated	23.63	16	26.65	16	-3.02	-6.60 - 0.56	0.0919
		VLN Mentholated	25.45	17	27.62	17	-2.17	-9.11 - 4.77	0.5171
		VLN Combined	24.57	33	27.15	33	-2.58	-6.34 - 1.18	0.1714
	Week 6	VLN Non-Mentholated	26.72	17	27.08	17	-0.37	-3.58 - 2.85	0.8117
		VLN Mentholated	24.12	15	27.62	15	-3.49	-10.39 - 3.40	0.2958
		VLN Combined	25.50	32	27.33	32	-1.83	-5.31 - 1.64	0.2901
Average Number of Puffs (N)	Week 2	VLN Non-Mentholated	11.08	16	11.70	16	-0.62	-1.91 - 0.67	0.3232
		VLN Mentholated	11.85	17	12.60	17	-0.75	-2.15 - 0.66	0.2772
		VLN Combined	11.48	33	12.16	33	-0.68	-1.59 - 0.22	0.1328
	Week 6	VLN Non-Mentholated	11.06	17	11.77	17	-0.72	-2.32 - 0.89	0.3594
		VLN Mentholated	10.90	15	12.58	15	-1.68	-2.79 - -0.57	0.0059
		VLN Combined	10.98	32	12.15	32	-1.17	-2.13 - -0.21	0.0189
Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes Paired t-test method is used to perform analysis.									
Source: Table 14.2.3.3 Program: /CA24914/sas_prg/pksas/pd_top/adam_intext_statsttest.sas 13JUN2019 5:32									

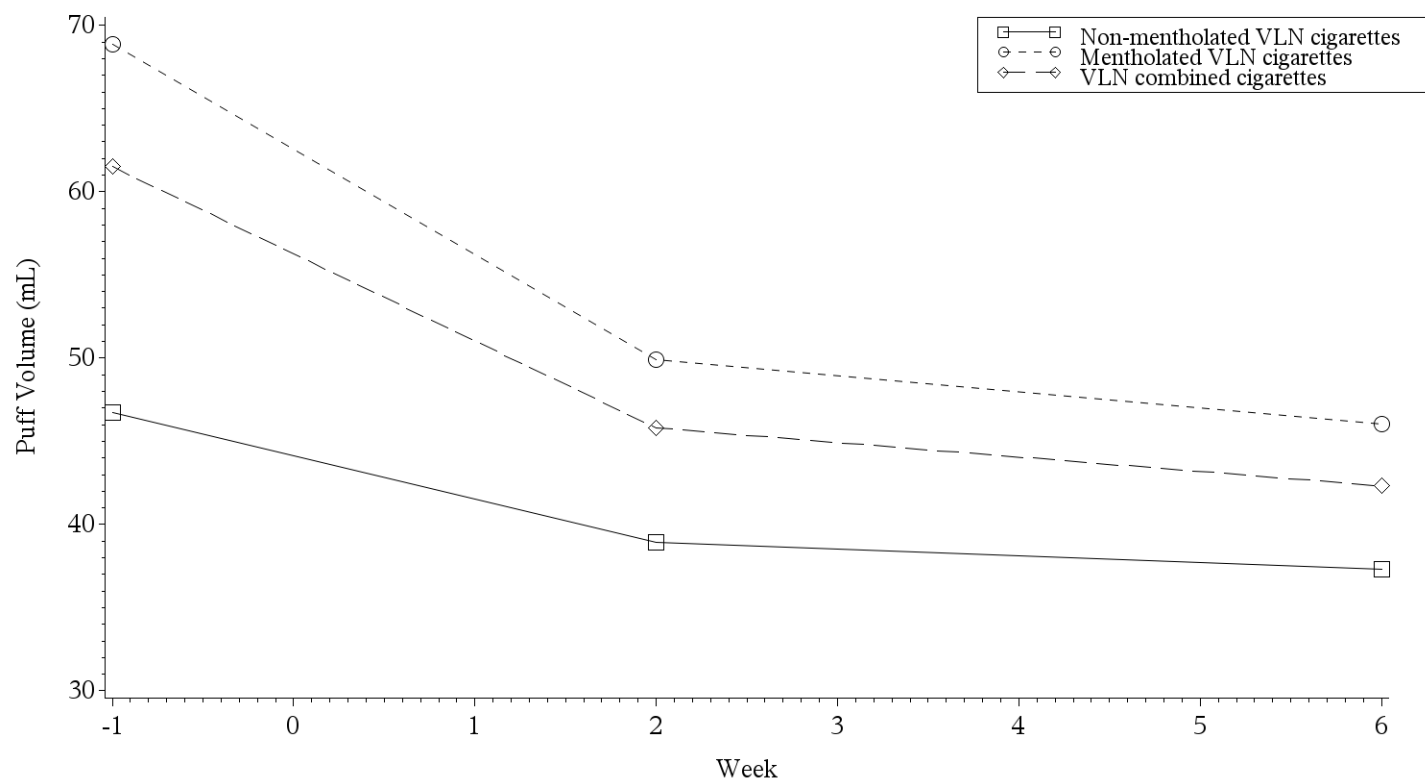
Mean puffing topography parameters by study product group and week for the PP population are presented in [Figures 11–7](#) through [11–16](#) below.

Figure 11–7 Mean Puffing Topography Parameter (Puff Duration) by Study Product Group and Study Week (PP Population)



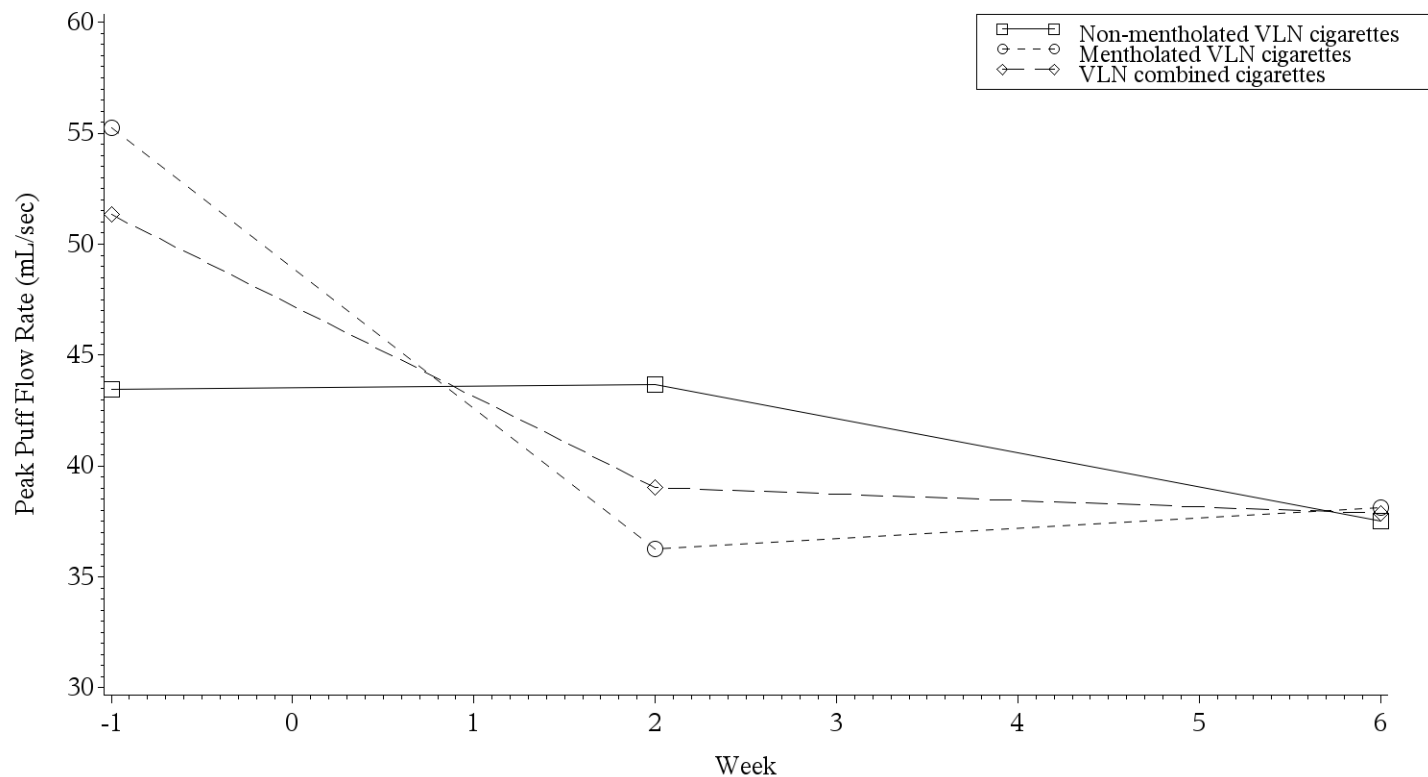
Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
Program: /CA24914/sas_prg/pksas/pd_top/adam_intext_meangraph_top.sas 01JUL2019 5:13

Figure 11–8 Mean Puffing Topography Parameter (Puff Volume) by Study Product Group and Study Week (PP Population)



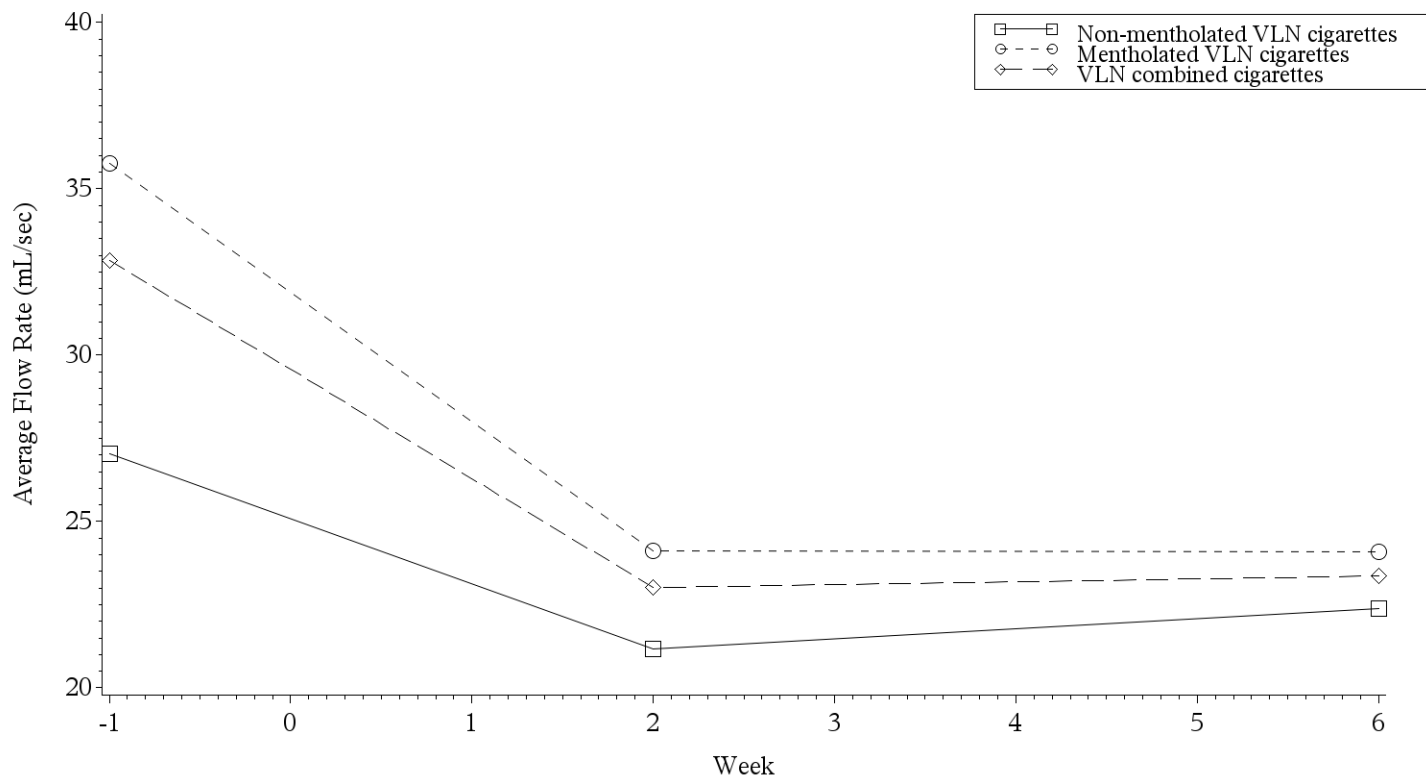
Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
Program: /CA24914/sas_prg/pksas/pd_top/adam_intext_meangraph_top.sas 01JUL2019 5:13

Figure 11–9 Mean Puffing Topography Parameter (Peak Puff Flow Rate) by Study Product Group and Study Week (PP Population)



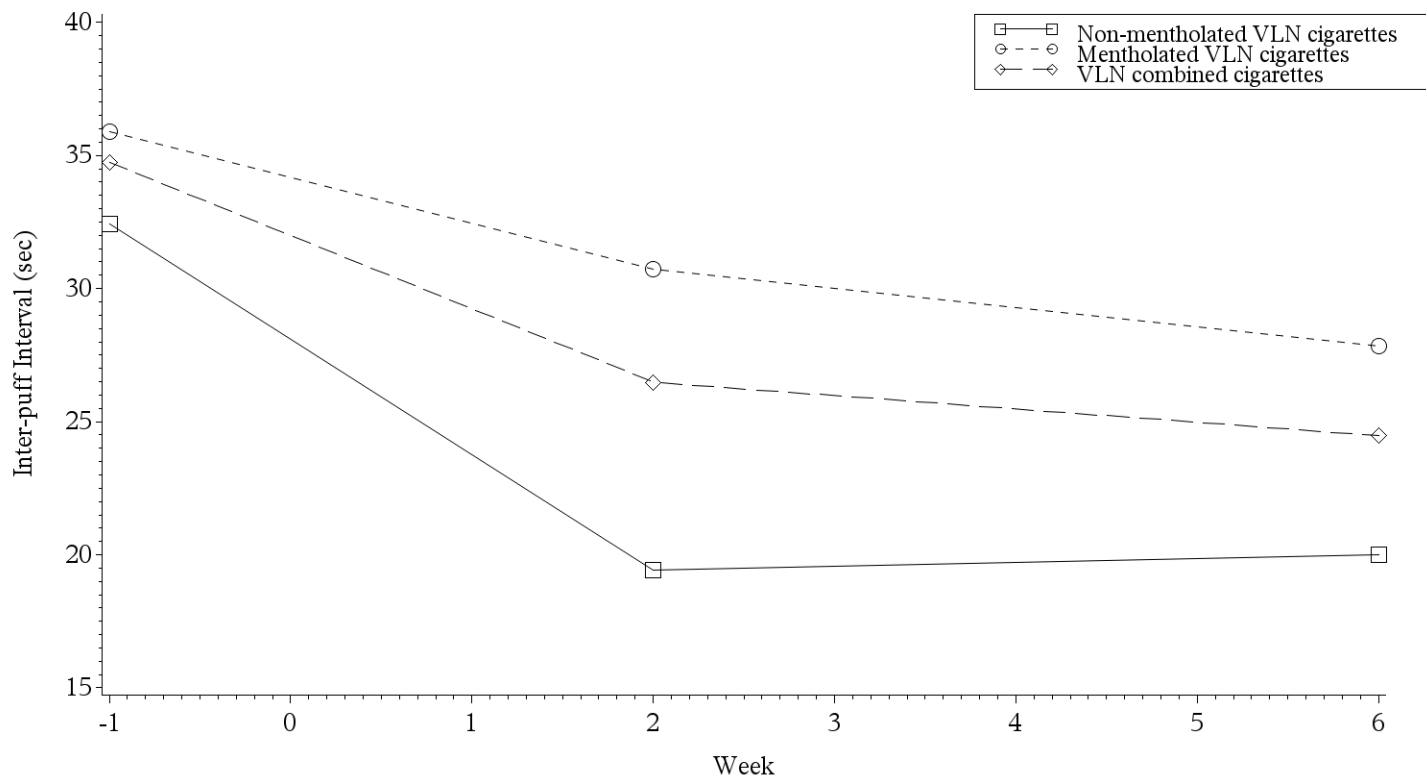
Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
Program: /CA24914/sas_prg/pksas/pd_top/adam_intext_meangraph_top.sas 01JUL2019 5:13

Figure 11–10 Mean Puffing Topography Parameter (Average Flow Rate) by Study Product Group and Study Week (PP Population)



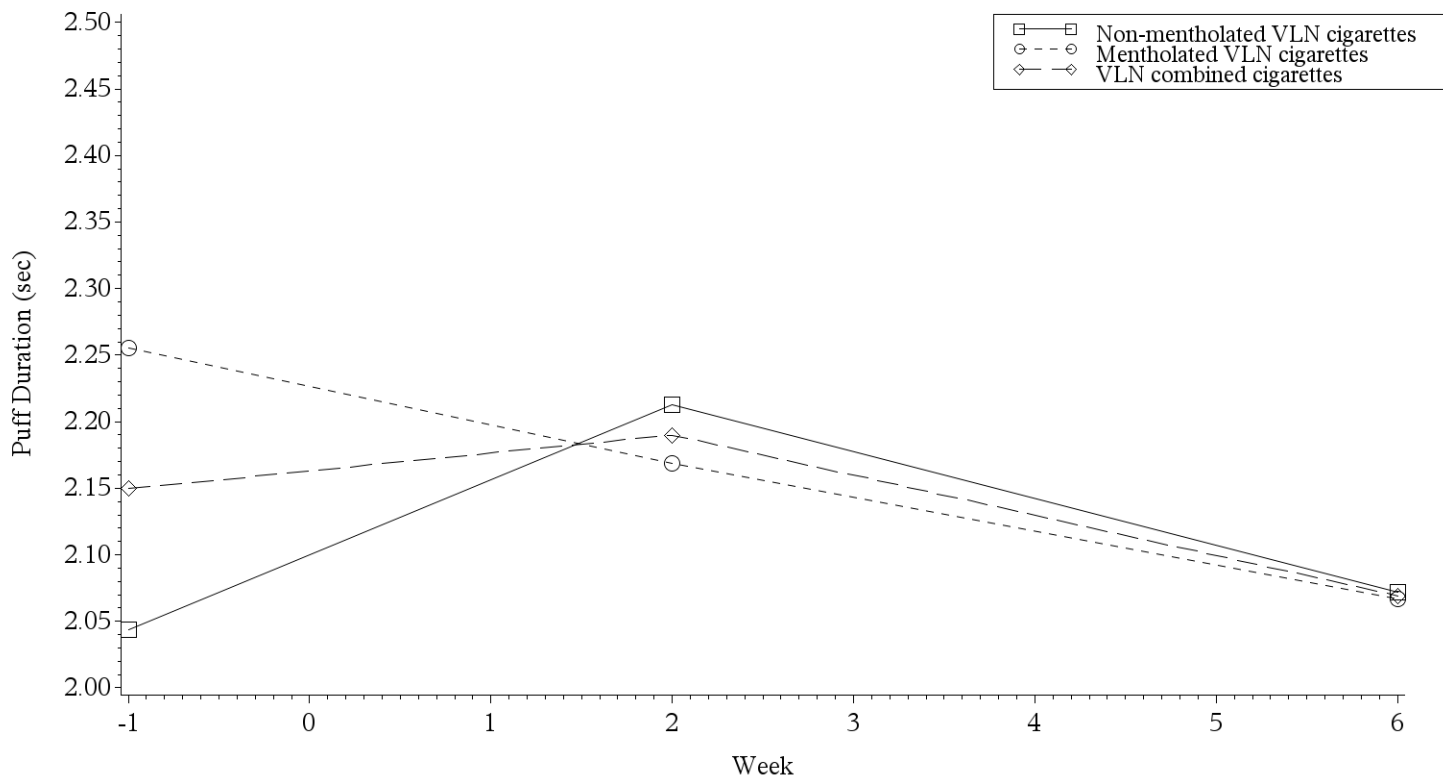
Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
Program: /CA24914/sas_prg/pksas/pd_top/adam_intext_meangraph_top.sas 01JUL2019 5:13

Figure 11–11 Mean Puffing Topography Parameter (Inter-puff Interval) by Study Product Group and Study Week (PP Population)



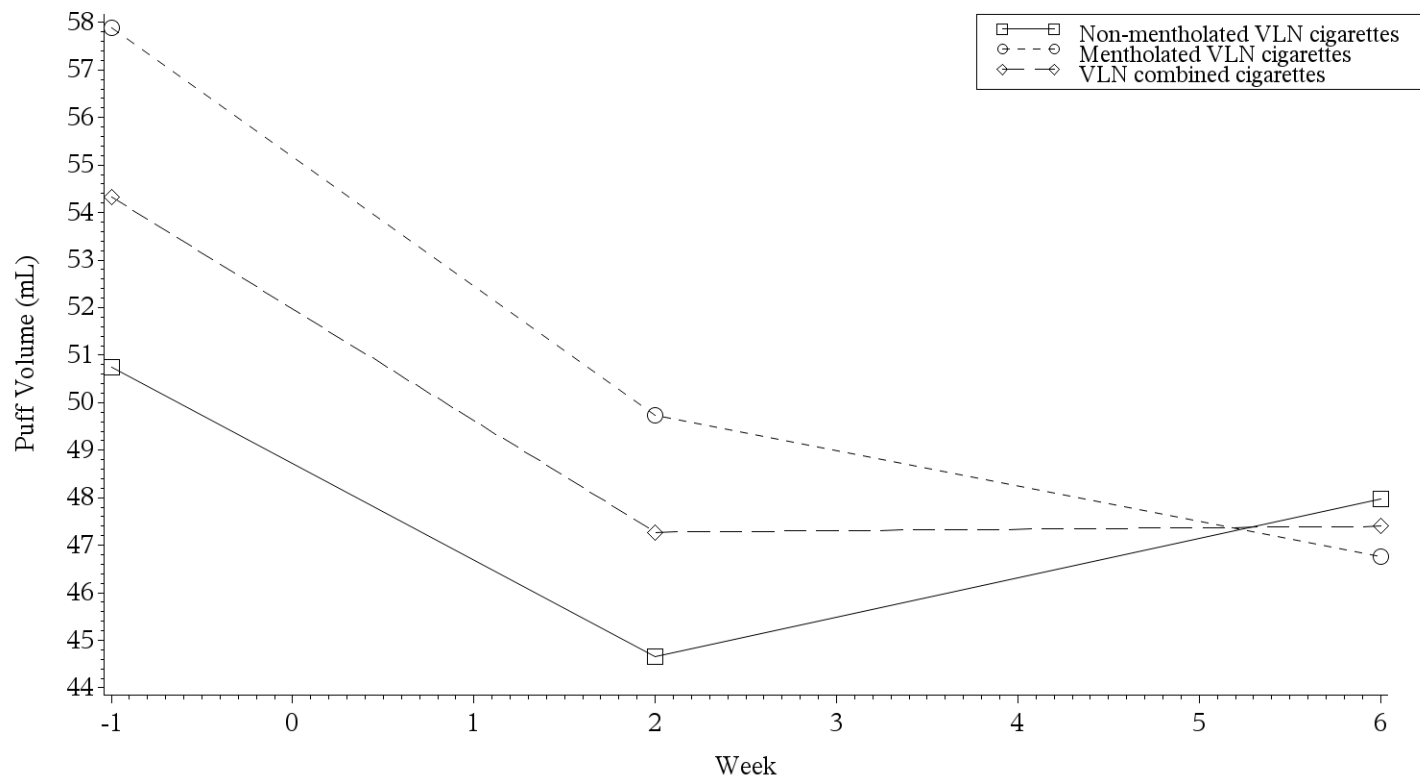
Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
Program: /CA24914/sas_prg/pksas/pd_top/adam_intext_meangraph_top.sas 01JUL2019 5:13

Figure 11–12 Mean Puffing Topography Parameter (Puff Duration) by Study Product Group and Study Week (ITT Population)



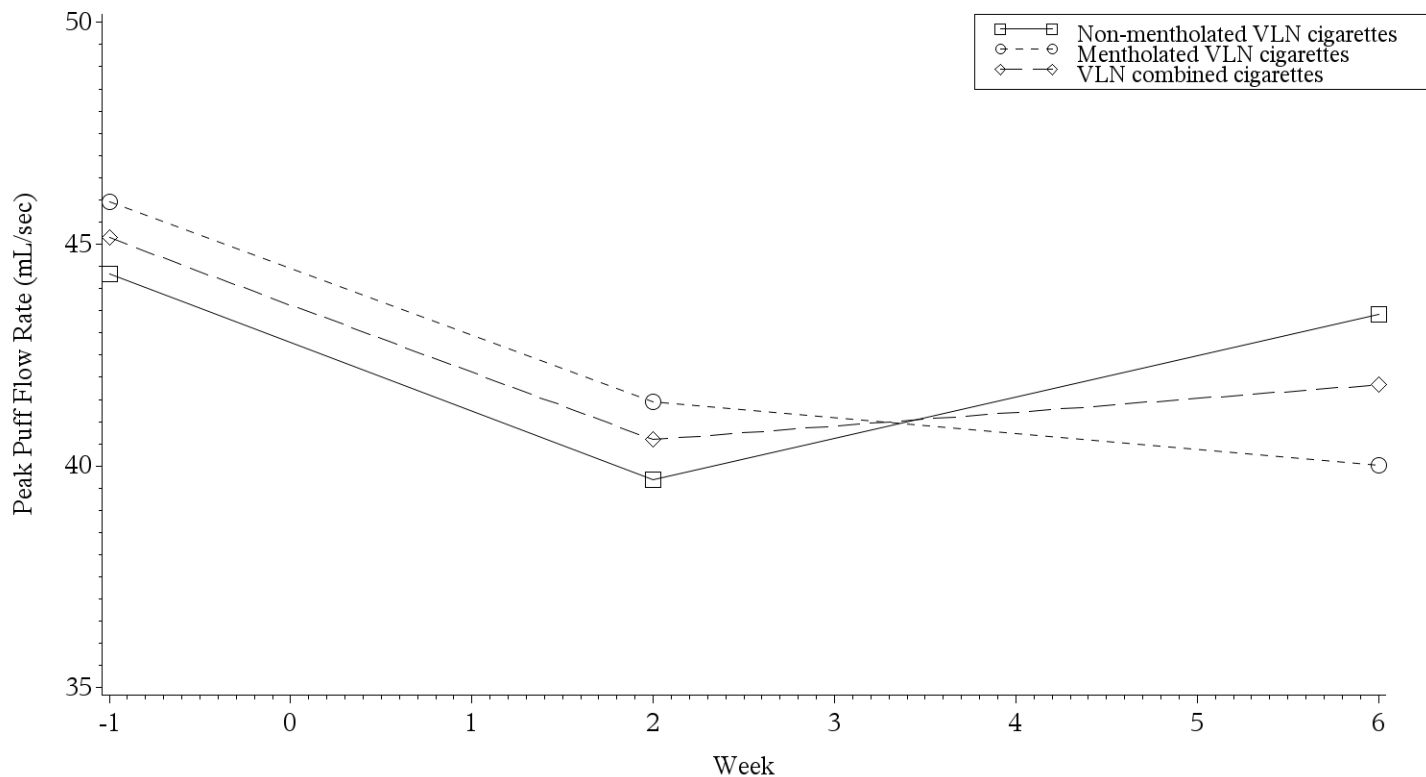
Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
Program: /CA24914/sas_prg/pksas/pd_top/adam_intext_meangraph_top.sas 01JUL2019 5:13

Figure 11–13 Mean Puffing Topography Parameter (Puff Volume) by Study Product Group and Study Week (ITT Population)



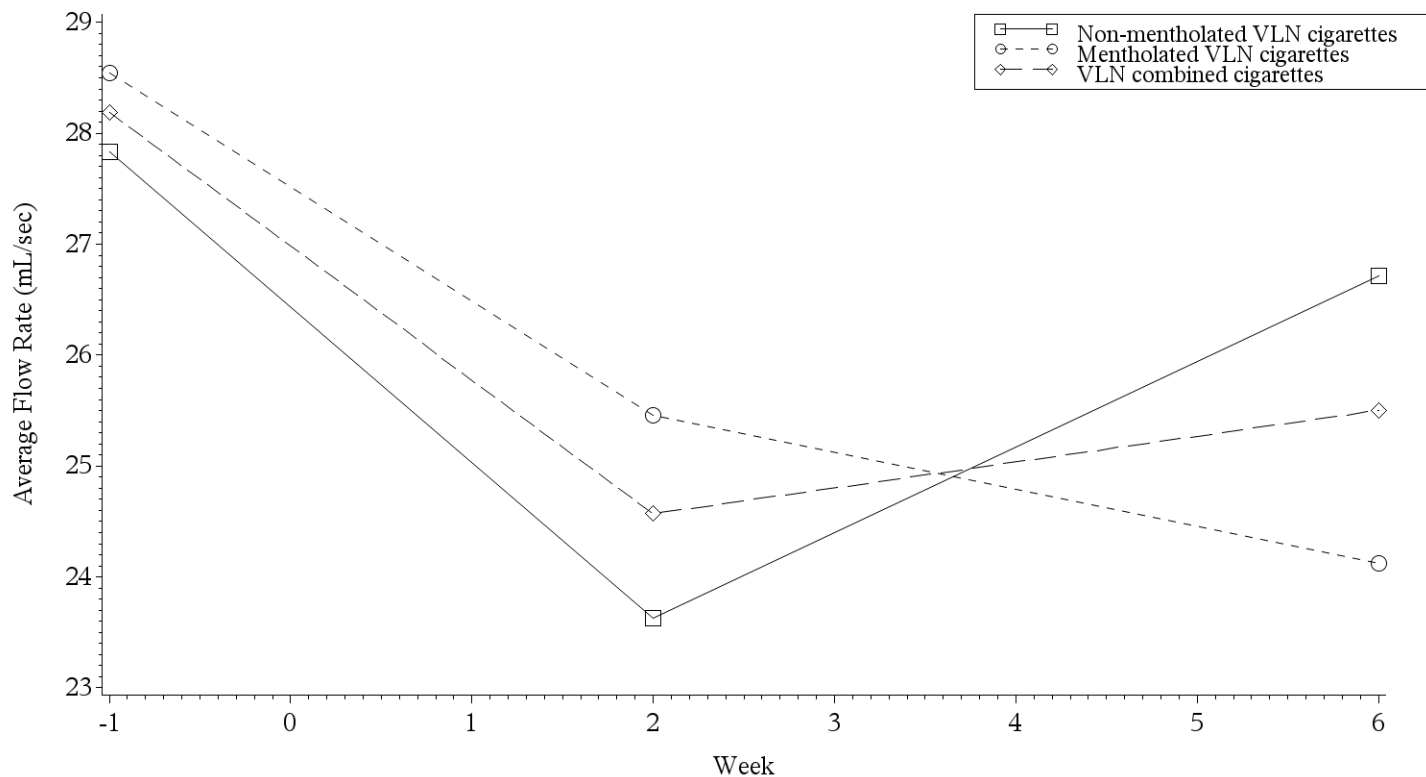
Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
Program: /CA24914/sas_prg/pksas/pd_top/adam_intext_meangraph_top.sas 01JUL2019 5:13

Figure 11–14 Mean Puffing Topography Parameter (Peak Puff Flow Rate) by Study Product Group and Study Week (ITT Population)



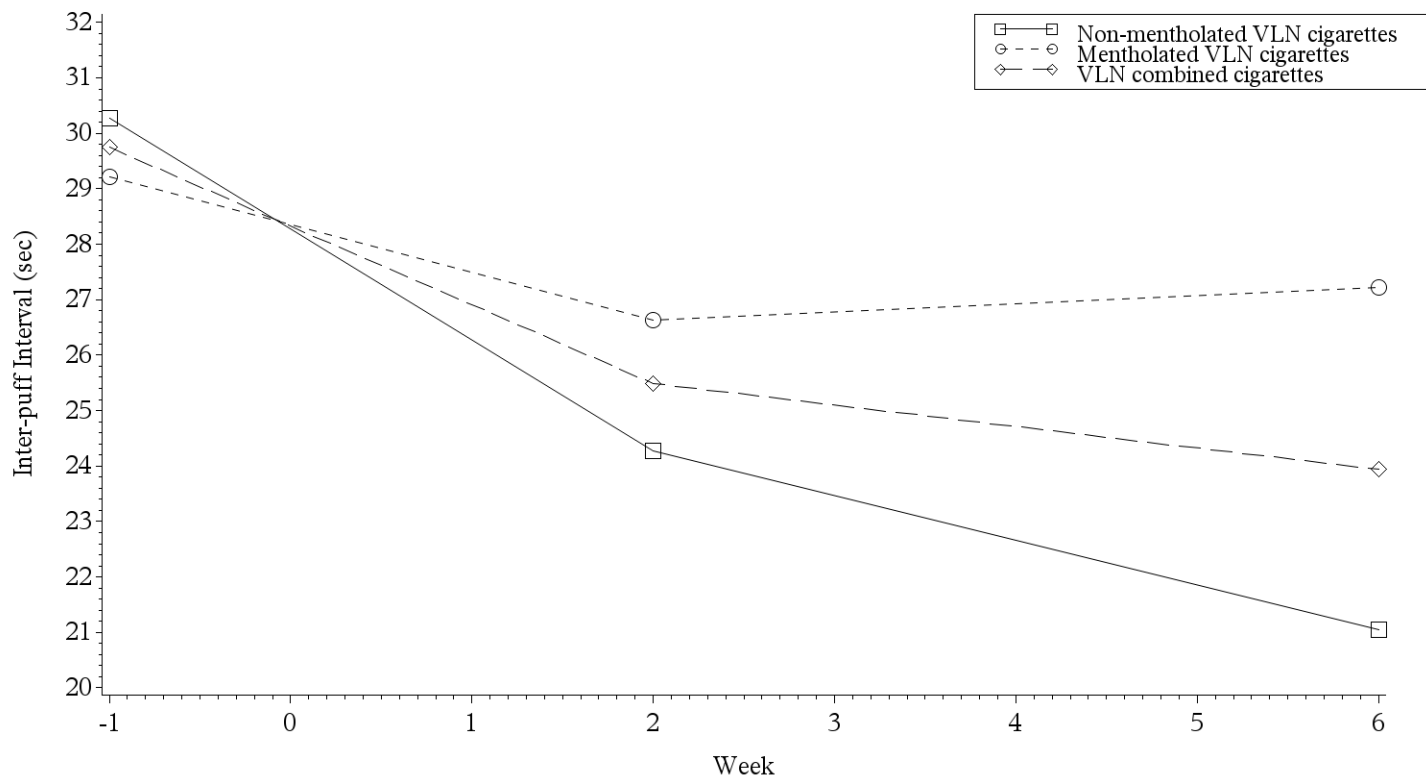
Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
Program: /CA24914/sas_prg/pksas/pd_top/adam_intext_meangraph_top.sas 01JUL2019 5:13

Figure 11–15 Mean Puffing Topography Parameter (Average Flow Rate) by Study Product Group and Study Week (ITT Population)



Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
Program: /CA24914/sas_prg/pksas/pd_top/adam_intext_meangraph_top.sas 01JUL2019 5:13

Figure 11–16 Mean Puffing Topography Parameter (Inter-puff Interval) by Study Product Group and Study Week (ITT Population)



Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
Program: /CA24914/sas_prg/pksas/pd_top/adam_intext_meangraph_top.sas 01JUL2019 5:13

For subjects in the PP population (smokers of either non-mentholated and mentholated filtered cigarettes combined), puff duration and volume (average and total) and average peak puff flow rate, average flow rate, and average number of puffs did not change significantly from baseline following the switch from UB to VLN cigarettes. There was a trend towards lower puff flow rates and lower puff volumes but the decreases were not significant. Significantly shorter inter-puff intervals were observed in Week 2 following the switch to VLN cigarettes and were still observed in Week 6. The sample size for the PP population was small (N = 3 to 8 for each cohort) making it difficult to robustly establish statistical significance.

The trends were more statistically evident in the ITT population, which had a larger sample size than the PP population, with significantly shorter total puff durations, significantly smaller total puff volumes, and significantly shorter inter-puff intervals observed at Weeks 2 and 6 following the switch from UB to VLN cigarettes. Average puff duration, average puff volume, and average peak puff flow rate and average flow rate were not significantly changed though were typically lower at Weeks 2 and 6 compared to baseline. A small but significant decrease in the average number of puffs taken was observed on Week 6 but not on Week 2 when compared to baseline.

Taken together, these data indicate that the subjects did not compensate for the much smaller nicotine content of the VLN cigarettes by changing their puffing behavior in a compensatory manner with the exception of a slightly shorter inter-puff interval.

11.3.2 Biomarker Analysis

11.3.2.1 Urine Biomarker Analysis

The locations of individual and mean estimates of urine BoE are tabulated below:

Biomarker	Number
NNAL urinary mass excreted	Tables 14.2.5.1.1.1.1 and 14.2.5.1.1.1.2
NNAL urinary mass excreted change from baseline	Tables 14.2.5.1.1.2.1 and 14.2.5.1.1.2.2
NNAL urinary mass excreted percent change from baseline	Tables 14.2.5.1.1.3.1 and 14.2.5.1.1.3.2
NNAL urinary mass excreted (creatinine-normalized)	Tables 14.2.5.1.1.4.1 and 14.2.5.1.1.4.2
NNAL urinary mass excreted (creatinine-normalized) change from baseline	Tables 14.2.5.1.1.5.1 and 14.2.5.1.1.5.2
NNAL urinary mass excreted (creatinine-normalized) percent change from baseline	Tables 14.2.5.1.1.6.1 and 14.2.5.1.1.6.2

Statistical comparisons of NNAL urinary mass excreted (Weeks 2 and 6 versus Week -1)	Tables 14.2.5.1.2.1 and 14.2.5.1.2.2
Statistical comparisons of NNAL between study products (VLN versus UB) at weeks 2 and 6	Tables 14.2.5.1.3.1 and 14.2.5.1.3.2
NNAL Urinary mass excreted versus time profiles	Figures 14.2.6.1.1 through 14.2.6.1.4
Individual listing for NNAL urinary mass excreted	Appendix 16.2.6.3
NNN urinary mass excreted	Tables 14.2.5.2.1.1.1 and 14.2.5.2.1.1.2
NNN urinary mass excreted change from baseline	Tables 14.2.5.2.1.2.1 and 14.2.5.2.1.2.2
NNN urinary mass excreted percent change from baseline	Tables 14.2.5.2.1.3.1 and 14.2.5.2.1.3.2
NNN urinary mass excreted (creatinine-normalized)	Tables 14.2.5.2.1.4.1 and 14.2.5.2.1.4.2
NNN urinary mass excreted (creatinine-normalized) change from baseline	Tables 14.2.5.2.1.5.1 and 14.2.5.2.1.5.2
NNN urinary mass excreted (creatinine-normalized) percent change from baseline	Tables 14.2.5.2.1.6.1 and 14.2.5.2.1.6.2
Statistical comparisons of NNN urinary mass excreted (Weeks 2 and 6 versus Week -1)	Tables 14.2.5.2.2.1 and 14.2.5.2.2.2
Statistical comparisons of NNN between study products (VLN versus UB) at weeks 2 and 6	Tables 14.2.5.2.3.1 and 14.2.5.2.3.2
NNN Urinary mass excreted versus time profiles	Figures 14.2.6.2.1 through 14.2.6.2.4
Individual listing for NNN urinary mass excreted	Appendix 16.2.6.4
3-HPMA urinary mass excreted	Tables 14.2.5.3.1.1.1 and 14.2.5.3.1.1.2
3-HPMA urinary mass excreted change from baseline	Tables 14.2.5.3.1.2.1 and 14.2.5.3.1.2.2
3-HPMA urinary mass excreted percent change from baseline	Tables 14.2.5.3.1.3.1 and 14.2.5.3.1.3.2
3-HPMA urinary mass excreted (creatinine-normalized)	Tables 14.2.5.3.1.4.1 and 14.2.5.3.1.4.2
3-HPMA urinary mass excreted (creatinine-normalized) change from baseline	Tables 14.2.5.3.1.5.1 and 14.2.5.3.1.5.2

3-HPMA urinary mass excreted (creatinine-normalized) percent change from baseline	Tables 14.2.5.3.1.6.1 and 14.2.5.3.1.6.2
Statistical comparisons of 3-HPMA urinary mass excreted (Weeks 2 and 6 versus Week -1)	Tables 14.2.5.3.2.1 and 14.2.5.3.2.2
Statistical comparisons of 3-HPMA between study products (VLN versus UB) at weeks 2 and 6	Tables 14.2.5.3.3.1 and 14.2.5.3.3.2
3-HPMA Urinary mass excreted versus time profiles	Figures 14.2.6.3.1 through 14.2.6.3.4
Individual listing for 3-HPMA urinary mass excreted	Appendix 16.2.6.5
S-PMA urinary mass excreted	Tables 14.2.5.4.1.1.1 and 14.2.5.4.1.1.2
S-PMA urinary mass excreted change from baseline	Tables 14.2.5.4.1.2.1 and 14.2.5.4.1.2.2
S-PMA urinary mass excreted percent change from baseline	Tables 14.2.5.4.1.3.1 and 14.2.5.4.1.3.2
S-PMA urinary mass excreted (creatinine-normalized)	Tables 14.2.5.4.1.4.1 and 14.2.5.4.1.4.2
S-PMA urinary mass excreted (creatinine-normalized) change from baseline	Tables 14.2.5.4.1.5.1 and 14.2.5.4.1.5.2
S-PMA urinary mass excreted (creatinine-normalized) percent change from baseline	Tables 14.2.5.4.1.6.1 and 14.2.5.4.1.6.2
Statistical comparisons of S-PMA urinary mass excreted (Weeks 2 and 6 versus Week -1)	Tables 14.2.5.4.2.1 and 14.2.5.4.2.2
Statistical comparisons of S-PMA between study products (VLN versus UB) at weeks 2 and 6	Tables 14.2.5.4.3.1 and 14.2.5.4.3.2
S-PMA Urinary mass excreted versus time profiles	Figures 14.2.6.4.1 through 14.2.6.4.4
Individual listing for S-PMA urinary mass excreted	Appendix 16.2.6.6
1-OHP urinary mass excreted	Tables 14.2.5.5.1.1.1 and 14.2.5.5.1.1.2
1-OHP urinary mass excreted change from baseline	Tables 14.2.5.5.1.2.1 and 14.2.5.5.1.2.2
1-OHP urinary mass excreted percent change from baseline	Tables 14.2.5.5.1.3.1 and 14.2.5.5.1.3.2
1-OHP urinary mass excreted (creatinine-normalized)	Tables 14.2.5.5.1.4.1 and 14.2.5.5.1.4.2

1-OHP urinary mass excreted (creatinine-normalized) change from baseline	Tables 14.2.5.5.1.5.1 and 14.2.5.5.1.5.2
1-OHP urinary mass excreted (creatinine-normalized) percent change from baseline	Tables 14.2.5.5.1.6.1 and 14.2.5.5.1.6.2
Statistical comparisons of 1-OHP urinary mass excreted (Weeks 2 and 6 versus Week -1)	Tables 14.2.5.5.2.1 and 14.2.5.5.2.2
Statistical comparisons of 1-OHP between study products (VLN versus UB) at weeks 2 and 6	Tables 14.2.5.5.3.1 and 14.2.5.5.3.2
1-OHP Urinary mass excreted versus time profiles	Figures 14.2.6.5.1 through 14.2.6.5.4
Individual listing for 1-OHP urinary mass excreted	Appendix 16.2.6.7
Tneq urinary mass excreted	Tables 14.2.5.6.1.1.1 and 14.2.5.6.1.1.2
Tneq urinary mass excreted change from baseline	Tables 14.2.5.6.1.2.1 and 14.2.5.6.1.2.2
Tneq urinary mass excreted percent change from baseline	Tables 14.2.5.6.1.3.1 and 14.2.5.6.1.3.2
Tneq urinary mass excreted (creatinine-normalized)	Tables 14.2.5.6.1.4.1 and 14.2.5.6.1.4.2
Tneq urinary mass excreted (creatinine-normalized) change from baseline	Tables 14.2.5.6.1.5.1 and 14.2.5.6.1.5.2
Tneq urinary mass excreted (creatinine-normalized) percent change from baseline	Tables 14.2.5.6.1.6.1 and 14.2.5.6.1.6.2
Statistical comparisons of Tneq urinary mass excreted (Weeks 2 and 6 versus Week -1)	Tables 14.2.5.6.2.1 and 14.2.5.6.2.2
Statistical comparisons of Tneq between study products (VLN versus UB) at weeks 2 and 6	Tables 14.2.5.6.3.1 and 14.2.5.6.3.2
Tneq Urinary mass excreted versus time profiles	Figures 14.2.6.6.1 through 14.2.6.6.4
Individual listing for Tneq urinary mass excreted	Appendix 16.2.6.8.1

A summary of the statistical comparisons of BoE at Weeks 2 and 6 versus Week -1 by Study Product Group is presented in [Table 11–7](#) below.

Table 11–7 Summary of Comparisons of BoE at Weeks 2 and 6 Versus Week -1 by Study Product Group

		ITT Population				PP Population			
		Baseline Mean (n)		Percent Change (p-Value)		Baseline Mean (n)		Percent Change (p-Value)	
Biomarker	Comparison	Week 2	Week 6	Week 2	Week 6	Week 2	Week 6	Week 2	Week 6
Urine NNAL (ng/24 hour)	VLN Non-Mentholated	588.208 (47)	603.830 (41)	-46.6 (<.0001)	-37.6 (<.0001)	519.023 (11)	536.996 (10)	-62.5 (0.0026)	-70.3 (0.0034)
	VLN Mentholated	422.377 (43)	438.907 (41)	-49.3 (<.0001)	-45.1 (<.0001)	354.460 (12)	355.164 (9)	-56.4 (<.0001)	-65.3 (<.0001)
	VLN Combined	508.977 (90)	521.368 (82)	-47.7 (<.0001)	-40.8 (<.0001)	433.164 (23)	450.865 (19)	-59.9 (<.0001)	-68.4 (<.0001)
	UB Non-Mentholated	614.089 (21)	633.464 (17)	-5.4 (0.1858)	-3.0 (0.4399)	614.089 (21)	633.464 (17)	-5.4 (0.1858)	-3.0 (0.4399)
	UB Mentholated	479.979 (20)	463.038 (19)	-4.6 (0.2278)	-6.8 (0.1538)	479.979 (20)	463.038 (19)	-4.6 (0.2278)	-6.8 (0.1538)
	UB Combined	548.670 (41)	543.517 (36)	-5.0 (0.0708)	-4.7 (0.1114)	548.670 (41)	543.517 (36)	-5.0 (0.0708)	-4.7 (0.1114)
Urine NNN (ng/24 hour)	VLN Non-Mentholated	20.398 (47)	21.861 (41)	-29.4 (0.0002)	-31.4 (0.0012)	27.153 (11)	28.786 (10)	-42.6 (0.0399)	-56.0 (0.0209)
	VLN Mentholated	12.230 (43)	13.476 (41)	-26.0 (0.0586)	-52.6 (<.0001)	9.983 (12)	11.102 (9)	17.3 (0.7530)	-52.1 (0.0149)
	VLN Combined	16.496 (90)	17.668 (82)	-28.2 (<.0001)	-39.5 (<.0001)	18.195 (23)	20.410 (19)	-25.4 (0.2402)	-55.0 (0.0033)
	UB Non-Mentholated	22.085 (21)	23.322 (17)	-5.8 (0.3573)	-5.3 (0.3863)	22.085 (21)	23.322 (17)	-5.8 (0.3573)	-5.3 (0.3863)
	UB Mentholated	13.641 (20)	13.108 (19)	-11.9 (0.0591)	-28.6 (0.0152)	13.641 (20)	13.108 (19)	-11.9 (0.0591)	-28.6 (0.0152)
	UB Combined	17.966 (41)	17.932 (36)	-8.0 (0.0746)	-14.3 (0.0143)	17.966 (41)	17.932 (36)	-8.0 (0.0746)	-14.3 (0.0143)
Urine 3- HPMA (µg/24 hour)	VLN Non-Mentholated	1787.779 (47)	1806.472 (41)	-4.7 (0.2961)	-17.5 (0.0002)	1551.988 (11)	1439.332 (10)	-2.1 (0.7906)	-17.0 (0.1268)
	VLN Mentholated	1634.959 (43)	1645.755 (41)	-26.3 (<.0001)	-37.1 (<.0001)	1598.680 (12)	1641.094 (9)	-22.0 (0.0007)	-35.4 (0.0022)
	VLN Combined	1714.765 (90)	1726.113 (82)	-14.5 (<.0001)	-26.9 (<.0001)	1576.349 (23)	1534.903 (19)	-12.6 (0.0151)	-26.3 (0.0011)
	UB Non-Mentholated	1888.019 (21)	1914.526 (17)	-9.4 (0.0127)	-5.2 (0.4519)	1888.019 (21)	1914.526 (17)	-9.4 (0.0127)	-5.2 (0.4519)
	UB Mentholated	1520.921 (20)	1469.554 (19)	-12.6 (0.0364)	-9.1 (0.1896)	1520.921 (20)	1469.554 (19)	-12.6 (0.0364)	-9.1 (0.1896)
	UB Combined	1708.947 (41)	1679.680 (36)	-10.8 (0.0011)	-7.0 (0.1447)	1708.947 (41)	1679.680 (36)	-10.8 (0.0011)	-7.0 (0.1447)
Urine S-PMA (µg/24 hour)	VLN Non-Mentholated	7.061 (47)	7.485 (41)	17.2 (0.0065)	-1.3 (0.8170)	6.399 (11)	6.473 (10)	37.0 (0.0139)	12.3 (0.4873)
	VLN Mentholated	6.914 (43)	7.006 (41)	-2.6 (0.7139)	-20.2 (0.0028)	6.341 (12)	7.354 (9)	-0.7 (0.9394)	-21.0 (0.1271)
	VLN Combined	6.991 (90)	7.245 (82)	7.8 (0.0996)	-10.4 (0.0170)	6.369 (23)	6.890 (19)	17.4 (0.0503)	-4.5 (0.6833)
	UB Non-Mentholated	7.906 (21)	7.812 (17)	-4.4 (0.2024)	-7.1 (0.1267)	7.906 (21)	7.812 (17)	-4.4 (0.2024)	-7.1 (0.1267)
	UB Mentholated	8.239 (20)	7.070 (19)	-6.2 (0.4121)	-3.2 (0.6276)	8.239 (20)	7.070 (19)	-6.2 (0.4121)	-3.2 (0.6276)
	UB Combined	8.068 (41)	7.420 (36)	-5.3 (0.1929)	-5.1 (0.1950)	8.068 (41)	7.420 (36)	-5.3 (0.1929)	-5.1 (0.1950)
Urine 1-OHP (ng/24 hour)	VLN Non-Mentholated	329.528 (47)	340.295 (41)	-20.6 (<.0001)	-18.6 (<.0001)	331.777 (11)	327.990 (10)	-27.3 (<.0001)	-30.4 (0.0010)
	VLN Mentholated	303.474 (43)	303.422 (41)	-29.5 (<.0001)	-33.0 (<.0001)	300.374 (12)	284.383 (9)	-25.5 (0.0104)	-38.6 (0.0005)
	VLN Combined	317.080 (90)	321.859 (82)	-24.7 (<.0001)	-25.4 (<.0001)	315.393 (23)	307.334 (19)	-26.4 (<.0001)	-34.0 (<.0001)
	UB Non-Mentholated	309.586 (21)	304.642 (17)	-6.6 (0.1063)	-1.7 (0.7898)	309.586 (21)	304.642 (17)	-6.6 (0.1063)	-1.7 (0.7898)
	UB Mentholated	316.566 (20)	309.295 (19)	-16.8 (0.0255)	-11.4 (0.1112)	316.566 (20)	309.295 (19)	-16.8 (0.0255)	-11.4 (0.1112)
	UB Combined	312.991 (41)	307.098 (36)	-11.7 (0.0057)	-6.9 (0.1543)	312.991 (41)	307.098 (36)	-11.7 (0.0057)	-6.9 (0.1543)

		ITT Population				PP Population			
		Baseline Mean (n)		Percent Change (p-Value)		Baseline Mean (n)		Percent Change (p-Value)	
Biomarker	Comparison	Week 2	Week 6	Week 2	Week 6	Week 2	Week 6	Week 2	Week 6
Urine Tneq (mg/24 hour)	VLN Non-Mentholated	17.234 (47)	17.559 (41)	-68.5 (<.0001)	-47.8 (<.0001)	16.144 (11)	15.463 (10)	-93.0 (<.0001)	-93.7 (<.0001)
	VLN Mentholated	16.020 (43)	16.138 (41)	-77.4 (<.0001)	-57.9 (<.0001)	15.600 (12)	16.806 (9)	-93.4 (<.0001)	-92.1 (<.0001)
	VLN Combined	16.654 (90)	16.848 (82)	-72.6 (<.0001)	-52.6 (<.0001)	15.860 (23)	16.099 (19)	-93.2 (<.0001)	-92.9 (<.0001)
	UB Non-Mentholated	17.500 (21)	17.178 (17)	-3.1 (0.2989)	2.0 (0.6626)	17.500 (21)	17.178 (17)	-3.1 (0.2989)	2.0 (0.6626)
	UB Mentholated	15.928 (20)	15.327 (19)	-4.1 (0.4487)	-5.9 (0.3069)	15.928 (20)	15.327 (19)	-4.1 (0.4487)	-5.9 (0.3069)
	UB Combined	16.733 (41)	16.201 (36)	-3.5 (0.2225)	-1.9 (0.5990)	16.733 (41)	16.201 (36)	-3.5 (0.2225)	-1.9 (0.5990)
Blood COHb (% Saturation)	VLN Non-Mentholated	6.159 (49)	6.423 (43)	15.2 (0.0002)	-7.0 (0.0520)	6.218 (11)	6.380 (10)	12.4 (0.0524)	-8.9 (0.0882)
	VLN Mentholated	5.722 (45)	5.764 (42)	-3.0 (0.4794)	-19.6 (<.0001)	5.633 (12)	5.800 (9)	-3.3 (0.7162)	-12.8 (0.2191)
	VLN Combined	5.950 (94)	6.098 (85)	6.8 (0.0251)	-12.9 (<.0001)	5.913 (23)	6.105 (19)	4.6 (0.3961)	-10.7 (0.0426)
	UB Non-Mentholated	5.338 (21)	5.316 (19)	1.2 (0.7694)	4.6 (0.2968)	5.338 (21)	5.316 (19)	1.2 (0.7694)	4.6 (0.2968)
	UB Mentholated	5.410 (20)	5.410 (20)	3.2 (0.6652)	-14.8 (0.0032)	5.410 (20)	5.410 (20)	3.2 (0.6652)	-14.8 (0.0032)
	UB Combined	5.373 (41)	5.364 (39)	2.2 (0.5949)	-5.4 (0.1176)	5.373 (41)	5.364 (39)	2.2 (0.5949)	-5.4 (0.1176)
<p>Baseline = Week -1 Percent change = mean difference (from t-test)/reference (baseline)*100 Subjects used their own usual brand cigarettes at Week -1 p-value is from the paired t-test comparing Week 2 and Week 6 to Week -1 VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes Source: Tables 14.2.5.1.2.1, 14.2.5.1.2.2, 14.2.5.2.2.1, 14.2.5.2.2.2, 14.2.5.3.2.1, 14.2.5.3.2.2, 14.2.5.4.2.1, 14.2.5.4.2.2, 14.2.5.5.2.1, 14.2.5.5.2.2, 14.2.5.6.2.1, 14.2.5.6.2.2, 14.2.5.7.2, 14.2.5.7.4 Program: /CA24914/sas_prg/pksas/pdurine/adam_intext_urinestatstest_pchg_land.sas 03JUL2019 8:13</p>									

NNAL

At Weeks 2 and 6, in both PP and ITT populations, significant decreases in urinary NNAL (56% to 70% in the PP population and 38% to 49% in the ITT population) were observed for subjects who switched to smoking mentholated or non-mentholated VLN cigarettes and in the combined data from smokers of mentholated and non-mentholated cigarettes. Decreases were greater at Week 6 in the PP population and less at Week 6 in the ITT population. No significant changes were observed for subjects who remained on UB.

NNN

For subjects in the PP population, at Week 2 significant decreases in urinary NNN were observed in subjects who switched to VLN non-mentholated cigarettes (43%). At Week 6, significant decreases in urinary NNN (> 52%) were observed for all subject groups who switched to VLN (smokers of mentholated and non-mentholated cigarettes and combined smokers). Significant decreases of lesser magnitude were also observed for smokers who remained on UB (smokers of mentholated cigarettes and combined smokers).

The same trends were observed for subjects in the ITT population: the decreases in urinary NNN observed at Week 2 (approximately 29%) were significant for some subject groups who switched to VLN (smokers of non-mentholated cigarettes and combined). At Week 6, significant decreases (31% to 53%) were observed in all subject groups who switched to VLN (smokers of mentholated and non-mentholated cigarettes and combined smokers) and for some who remained on UB (smokers of mentholated cigarettes and combined smokers showing 29% and 14% decreases, respectively) with greater changes observed in subjects who switched (VLN non-mentholated and VLN combined).

3-HPMA

For subjects in the PP and ITT populations, at Week 2 significant decreases (9% to 26%) in urinary 3-HPMA were observed in all product use groups except in subjects who switched to non-mentholated VLN cigarettes. Of note, significant decreases in 3-HPMA (9% to 13%) were also observed in the UB groups at Week 2. At Week 6, decreases in urinary 3-HPMA were only significant in subject groups who switched to VLN cigarettes (smokers of mentholated cigarettes and combined smokers in PP population showing 35% and 26% decrease, respectively; smokers of mentholated, non-mentholated cigarettes and combined smokers in ITT population showing 18% to 37% decrease).

S-PMA

For subjects in the PP and ITT populations, no significant changes from baseline in urinary S-PMA were observed except in subjects who switched to non-mentholated VLN cigarettes at Week 2 (PP and ITT populations) and saw a significant increase in urine S-PMA (37% and 17% in the PP and ITT populations, respectively). At Week 6, a significant decrease was observed in subjects who switched to VLN cigarettes (smokers of mentholated cigarettes and combined smokers showing 20% and 10% decrease, respectively) in the ITT population only.

1-OHP

For subjects in the PP and ITT population, at Week 2 significant decreases in urinary 1-OHP were observed in subjects who switched to VLN cigarettes (smokers of mentholated and

non-mentholated cigarettes and combined smokers showing approximately 21% to 30% decreases) as well as in subjects who remained on UB (smokers of mentholated cigarettes and combined smokers showing 12% and 17% decreases, respectively). At Week 6, the only significant decreases in urinary 1-OHP were seen in subjects who switched to VLN cigarettes (smokers of mentholated and non-mentholated cigarettes and combined smokers), with 30% to 39% decreases in the PP population and 19% to 33% decreases in the ITT population.

Tneq

Significant decreases in urinary Tneq were observed in subjects who switched to VLN cigarettes (smokers of mentholated and non-mentholated cigarettes and combined smokers) in the PP population (approximately 93% decrease at Weeks 2 and 6) and in the ITT population (69% to 73% at Week 2 and 48% to 58% and Week 6). No significant changes were noted in subjects who remained on UB.

[Table 11–8](#) summarizes the mean biomarker changes from baseline for the test (VLN) minus the reference (UB) groups. A negative number means that the test product resulted in a more substantial decrease in the biomarker as compared to the UB product. In the UB groups, subjects continued their usual smoking habits and minimal change from baseline was expected. Consequently, biomarkers that are affected by changing to the VLN product have values that are larger in magnitude.

Table 11–8 Summary of Comparisons of Biomarker Changes From Baseline Between VLN and UB Cigarette Groups

		ITT Population		PP Population	
		LS Mean Difference (p-Value)		LS Mean Difference (p-Value)	
Biomarker	Comparison	Week 2	Week 6	Week 2	Week 6
Urine NNAL (ng/24 hour)	Non-Mentholated	-233.388 (<.0001)	-203.034 (<.0001)	-286.350 (<.0001)	-352.687 (<.0001)
	Mentholated	-182.927 (<.0001)	-152.537 (0.0008)	-177.963 (0.0008)	-189.781 (0.0014)
	Combined	-208.157 (<.0001)	-177.785 (<.0001)	-232.157 (<.0001)	-271.234 (<.0001)
Urine NNN (ng/24 hour)	Non-Mentholated	-4.519 (0.0690)	-4.714 (0.0992)	-10.076 (0.0199)	-13.736 (0.0030)
	Mentholated	-1.827 (0.4645)	-1.497 (0.5926)	3.345 (0.4174)	3.322 (0.4434)
	Combined	-3.173 (0.0724)	-3.106 (0.1213)	-3.366 (0.2565)	-5.207 (0.0964)
Urine 3-HPMA (µg/24 hour)	Non-Mentholated	115.922 (0.3193)	-235.818 (0.0811)	162.276 (0.2032)	-154.535 (0.3891)
	Mentholated	-233.965 (0.0484)	-455.443 (0.0006)	-159.848 (0.1977)	-444.949 (0.0141)
	Combined	-59.022 (0.4756)	-345.631 (0.0003)	1.214 (0.9890)	-299.742 (0.0199)
Urine S-PMA (µg/24 hour)	Non-Mentholated	1.579 (0.0365)	0.367 (0.6093)	2.756 (0.0013)	1.244 (0.1976)
	Mentholated	0.356 (0.6386)	-0.992 (0.1509)	0.464 (0.5614)	-1.150 (0.2302)
	Combined	0.967 (0.0711)	-0.312 (0.5302)	1.610 (0.0064)	0.047 (0.9448)
Urine 1-OHP (ng/24 hour)	Non-Mentholated	-46.405 (0.0337)	-65.665 (0.0131)	-69.511 (0.0188)	-103.050 (0.0016)
	Mentholated	-32.365 (0.1415)	-62.452 (0.0145)	-23.356 (0.4073)	-82.147 (0.0099)
	Combined	-39.385 (0.0116)	-64.058 (0.0006)	-46.434 (0.0242)	-92.599 (<.0001)
Urine Tneq (mg/24 hour)	Non-Mentholated	-11.251 (<.0001)	-8.446 (<.0001)	-14.398 (<.0001)	-15.394 (<.0001)
	Mentholated	-11.704 (<.0001)	-8.078 (<.0001)	-13.920 (<.0001)	-12.963 (<.0001)
	Combined	-11.478 (<.0001)	-8.262 (<.0001)	-14.159 (<.0001)	-14.178 (<.0001)
Blood COHb (% Saturation)	Non-Mentholated	0.870 (0.0373)	-0.745 (0.0515)	0.706 (0.1969)	-0.797 (0.0703)
	Mentholated	-0.348 (0.4152)	-0.335 (0.3771)	-0.358 (0.5023)	0.040 (0.9271)
	Combined	0.261 (0.3813)	-0.540 (0.0457)	0.174 (0.6481)	-0.379 (0.2247)
Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. LS mean difference = LS mean VLN cigarette group - LS mean UB cigarette group Non-Mentholated = VLN Non-mentholated vs UB Non-mentholated Mentholated = VLN Mentholated vs UB Mentholated Combined = VLN Combined vs UB Combined Source: Tables 14.2.5.1.3.1, 14.2.5.1.3.2, 14.2.5.2.3.1, 14.2.5.2.3.2, 14.2.5.3.3.1, 14.2.5.3.3.2, 14.2.5.4.3.1, 14.2.5.4.3.2, 14.2.5.5.3.1, 14.2.5.5.3.2, 14.2.5.6.3.1, 14.2.5.6.3.2, 14.2.5.7.3, 14.2.5.7.5 Program: /CA24914/sas_prg/pksas/pdurine/adam_intext_urinestatsmixed.sas 12JUN2019 10:42					

Mean NNAL decreases from baseline were significantly greater in the VLN cigarette groups compared to the UB cigarette groups in the ITT and PP populations. Differences were greatest in the non-mentholated groups. Differences between VLN and UB groups were greater in the PP population than in the ITT population, and within the PP population the differences in NNAL were greater at Week 6 than at Week 2.

When comparing the NNN change from baseline between product use groups at Weeks 2 and 6, the decrease from baseline was more significant in subjects who switched to VLN non-mentholated cigarettes compared to subjects who remained on the corresponding UB product. For all other VLN smokers (VLN mentholated or VLN combined), there were no significant differences in change from baseline when compared to subjects who remained on the corresponding UB.

Mean 3-HPMA decreases from baseline were significantly greater in the mentholated VLN group compared to the mentholated UB group in the ITT population (Week 2 and Week 6) and the PP population (Week 6) and in the combined metholated VLN versus UB group at Week 6 in the ITT and PP populations.

Mean changes from baseline in S-PMA were generally not different between the VLN and UB groups, except at Week 2, where the change from baseline was significantly greater in the non-mentholated (PP and ITT populations) and combined VLN groups (PP only) compared to the non-mentholated UB and combined UB group.

Mean 1-OHP decreases from baseline were significantly greater in the VLN cigarette groups compared to the UB cigarette groups in the ITT and PP populations, with the exception of the comparisons of mentholated VLN group to mentholated UB group at Week 2. Differences were greatest in the non-mentholated groups and were also greatest at Week 6.

Mean decreases from baseline in urinary Tneq were significantly greater in the VLN cigarette groups compared to the UB cigarette groups in the ITT and PP populations. Differences between VLN and UB groups were greater in the PP population than in the ITT population. Within the ITT population, the differences in Tneq were greater at Week 2 than at Week 6 whereas in the PP population the differences remained stable over time.

11.3.2.2 Blood Biomarker Analysis

The location of individual and mean estimate of blood COHb (% saturation) data are tabulated below:

Biomarker	Number
Blood COHb	Tables 14.2.5.7.1.1.1 and 14.2.5.7.1.1.2
Blood COHb change from baseline	Tables 14.2.5.7.1.2.1 and 14.2.5.7.1.2.2
Blood COHb percent change from baseline	Tables 14.2.7.1.3.1 and 14.2.5.7.1.3.2
Statistical comparisons of blood COHb (Weeks 2 and 6 versus Week -1)	Tables 14.2.5.7.2 and 14.2.5.7.4
Statistical comparisons of blood COHb between study products (VLN versus UB) at Weeks 2 and 6	Tables 14.2.5.7.3 and 14.2.5.7.5
Blood COHb versus time profiles	Figures 14.2.6.7.1 through 14.2.6.7.4
Individual listing for blood COHb	Appendix 16.2.6.9
Individual listing for plasma cotinine	Appendix 16.2.6.10

A summary of the statistical comparisons of blood BoE at Weeks 2 and 6 versus Week -1 by study product group is presented in [Table 11–7](#) above while the comparisons in blood COHb changes from baseline are presented in [Table 11–8](#) above.

For subjects in the PP population, a non-significant increase in blood COHb was observed at Week 2 in smokers of non-mentholated cigarettes who switched to VLN. There were no major changes observed for smokers of mentholated cigarettes who switched to VLN or for those who remained on UB. No major changes were observed when looking at overall data (combined data from smokers of mentholated and non-mentholated cigarettes) at Week 2. At Week 6, a decrease in blood COHb was observed in all subject groups except smokers who remained on non-mentholated UB. The decrease in COHb was significant for smokers who switched to VLN (combined smokers of mentholated and non-mentholated cigarettes) and for those who remained on mentholated UB cigarettes.

Subjects in the ITT population followed the same trend as those in the PP Population. At Week 2, there was a significant increase in blood COHb for smokers who switched to VLN (smokers of non-mentholated cigarettes and combined) while no major changes were observed for other groups. At Week 6, there was a significant decrease in blood COHb for smokers who switched to VLN (smokers of mentholated cigarettes and combined) and for those who remained on mentholated UB cigarettes.

When comparing the COHb change from baseline between product use groups at Week 6, there was a trend for bigger COHb decreases from baseline for subjects who switched to VLN when compared to those who remained on UB but the differences were not significant. This trend was observed in both PP and ITT populations.

Plasma cotinine was measured to assess compliance and data were not summarized. Non-compliant subjects were removed from the analysis populations as discussed in [Sections 9.7.1.1](#) and [11.1](#).

11.3.3 Pharmacokinetic Analysis

The location of individual and mean estimates of plasma nicotine concentrations and PK parameters are tabulated below:

Biomarker	Number
Unadjusted plasma nicotine concentrations (non-mentholated)	Tables 14.2.7.1.1 and 14.2.7.1.2
Unadjusted plasma nicotine concentrations (mentholated)	Tables 14.2.7.2.1 and 14.2.7.2.2
Baseline-adjusted plasma nicotine concentrations (non-mentholated)	Tables 14.2.7.3.1 and 14.2.7.3.2
Baseline-adjusted plasma nicotine concentrations (mentholated)	Tables 14.2.7.4.1 and 14.2.7.4.2
Unadjusted plasma nicotine versus time profiles	Figures 14.2.8.1 through 14.2.8.3 and Figures 14.2.8.7 through 14.2.8.9
Baseline-adjusted plasma nicotine versus time profiles	Figures 14.2.8.4 through 14.2.8.6 and Figures 14.2.8.10 through 14.2.8.12
Individual listing for plasma nicotine	Appendices 16.2.6.11.1 and 16.2.6.11.2
Baseline-adjusted plasma nicotine PK parameters (non-mentholated)	Tables 14.2.7.5.1 and 14.2.7.5.2 Tables 14.2.7.6.1 and 14.2.7.6.2 Tables 14.2.7.7.1 and 14.2.7.7.2
Baseline-adjusted plasma nicotine PK parameters (mentholated)	Tables 14.2.7.8.1 and 14.2.7.8.2 Tables 14.2.7.9.1 and 14.2.7.9.2 Tables 14.2.7.10.1 and 14.2.7.10.2
Statistical comparisons of Baseline-adjusted plasma nicotine PK parameters (Weeks 2 and 6 versus Week -1)	Tables 14.2.7.11 and 14.2.7.12

At the baseline (Week -1) PK assessment, for subjects in the PP population and the ITT population (smokers of non-mentholated and mentholated cigarettes), nicotine concentrations were measurable prior to product use, peaked between 7 and 10 minutes following start of product use for the majority of subjects, and all subjects had measureable concentrations at the end of the sampling interval. Following use of VLN cigarettes, concentrations throughout the sampling interval were lower compared to baseline, peaked at approximately the same time as the baseline assessment, and more than 1/3 of subjects had concentrations BLQ by the end of the sampling interval. The PP population was much smaller than the ITT population, but both populations followed the same trends in nicotine exposure.

The baseline-adjusted nicotine PK parameters and the statistical comparisons of nicotine parameters are presented in [Tables 11–9](#) through [11–12](#) below. For subjects in the PP population (smokers of non-mentholated and mentholated cigarettes combined), nicotine peak and overall exposures (as measured by geometric mean C_{max} and geometric mean

AUC₀₋₁₈₀) were significantly lower following the switch to VLN cigarettes. The decrease was over 99% for AUC₀₋₁₈₀ on Weeks 2 and 6. Median T_{max} values following use of VLN cigarettes were within the same range as those observed following UB cigarettes.

For subjects in the ITT population, with a larger sample size, a similar significant decrease in nicotine exposure (> 98% decrease for AUC₀₋₁₈₀ and > 97% decrease for C_{max}) was observed.

Table 11–9 Summary of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Prior to and Following Use of VLN Cigarettes (Pharmacokinetic Population from PP)

Study Week	Pharmacokinetic Parameters	Sex	Non-Mentholated	Mentholated
Week -1 *	AUC0-180 (ng*hr/mL)	F		11.82 (22.0) [n=3]
		M	10.58 (.) [n=1]	9.862 (11.6) [n=2]
		T	10.58 (.) [n=1]	10.99 (19.4) [n=5]
	Cmax (ng/mL)	F		13.64 (37.2) [n=3]
		M	8.352 (.) [n=1]	7.031 (1.6) [n=2]
		T	8.352 (.) [n=1]	10.46 (46.6) [n=5]
	Tmax (hr)	F		0.1350 (0.115, 0.167) [n=3]
		M	0.1170 (0.117, 0.117) [n=1]	0.1575 (0.116, 0.199) [n=2]
		T	0.1170 (0.117, 0.117) [n=1]	0.1350 (0.115, 0.199) [n=5]
Week 2	AUC0-180 (ng*hr/mL)	F		0.07037 (.) [n=1]
		M	0.3006 (.) [n=1]	0.04687 (22.7) [n=2]
		T	0.3006 (.) [n=1]	0.05367 (28.9) [n=3]
	Cmax (ng/mL)	F		0.2371 (.) [n=1]
		M	0.5451 (.) [n=1]	0.2516 (117.5) [n=2]
		T	0.5451 (.) [n=1]	0.2467 (73.8) [n=3]
	Tmax (hr)	F		0.1610 (0.161, 0.161) [n=1]
		M	0.08500 (0.0850, 0.0850) [n=1]	0.1670 (0.0830, 0.251) [n=2]
		T	0.08500 (0.0850, 0.0850) [n=1]	0.1610 (0.0830, 0.251) [n=3]
Week 6	AUC0-180 (ng*hr/mL)	F		0.07368 (40.7) [n=2]
		M	0.4357 (.) [n=1]	0.05815 (.) [n=1]
		T	0.4357 (.) [n=1]	0.06809 (31.6) [n=3]
	Cmax (ng/mL)	F		0.2080 (15.0) [n=2]
		M	0.6131 (.) [n=1]	0.3641 (.) [n=1]
		T	0.6131 (.) [n=1]	0.2507 (35.0) [n=3]
	Tmax (hr)	F		0.1995 (0.199, 0.200) [n=2]
		M	0.05600 (0.0560, 0.0560) [n=1]	0.08300 (0.0830, 0.0830) [n=1]
		T	0.05600 (0.0560, 0.0560) [n=1]	0.1990 (0.0830, 0.200) [n=3]

*Subjects used their own usual brand cigarettes at Week -1.
non-mentholated = Non-mentholated VLN cigarettes for Week 2 and 6.
VLN mentholated = Mentholated VLN cigarettes for Week 2 and 6.
AUCs and Cmax are presented as geometric mean and geometric CV%
Tmax are presented as Median (Minimum, Maximum)
. = Value missing or not reportable
F = Female; M = Male; T = Total
Source: [Tables 14.2.7.5.1, 14.2.7.6.1, 14.2.7.7.1, 14.2.7.8.1, 14.2.7.9.1, and 14.2.7.10.1](#)
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Table 11–10 Summary of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Prior to and Following Use of VLN Cigarettes (Pharmacokinetic Population from ITT)

Study Week	Pharmacokinetic Parameters	Sex	Non-Mentholated	Mentholated
Week -1 *	AUC0-180 (ng*hr/mL)	F	14.48 (31.0) [n=5]	11.94 (23.5) [n=6]
		M	11.34 (35.2) [n=7]	13.84 (44.7) [n=6]
		T	12.56 (34.6) [n=12]	12.85 (34.6) [n=12]
	Cmax (ng/mL)	F	14.27 (56.2) [n=5]	11.79 (28.6) [n=6]
		M	10.87 (36.3) [n=7]	12.40 (52.9) [n=6]
		T	12.18 (45.4) [n=12]	12.09 (40.0) [n=12]
	Tmax (hr)	F	0.1160 (0.0860, 0.253) [n=5]	0.1510 (0.115, 0.205) [n=6]
		M	0.1170 (0.0830, 0.166) [n=7]	0.1160 (0.0840, 0.199) [n=6]
		T	0.1165 (0.0830, 0.253) [n=12]	0.1170 (0.0840, 0.205) [n=12]
Week 2	AUC0-180 (ng*hr/mL)	F	0.1223 (115.6) [n=5]	0.1285 (62.9) [n=4]
		M	0.1206 (212.0) [n=7]	0.1822 (158.2) [n=6]
		T	0.1213 (156.5) [n=12]	0.1584 (114.7) [n=10]
	Cmax (ng/mL)	F	0.2530 (35.1) [n=5]	0.1881 (19.9) [n=4]
		M	0.3339 (53.1) [n=7]	0.4161 (65.3) [n=6]
		T	0.2974 (46.8) [n=12]	0.3029 (67.8) [n=10]
	Tmax (hr)	F	0.1170 (0.116, 0.167) [n=5]	0.1395 (0.115, 0.168) [n=4]
		M	0.08400 (0.0830, 0.199) [n=7]	0.1010 (0.0830, 0.251) [n=6]
		T	0.1005 (0.0830, 0.199) [n=12]	0.1175 (0.0830, 0.251) [n=10]
Week 6	AUC0-180 (ng*hr/mL)	F	0.3579 (31.3) [n=5]	0.08695 (103.9) [n=5]
		M	0.1270 (145.8) [n=7]	0.2744 (117.1) [n=5]
		T	0.1956 (124.9) [n=12]	0.1545 (139.1) [n=10]
	Cmax (ng/mL)	F	0.3626 (36.4) [n=5]	0.2067 (21.7) [n=5]
		M	0.3876 (44.0) [n=7]	0.4202 (35.8) [n=5]
		T	0.3770 (39.2) [n=12]	0.2947 (48.9) [n=10]
	Tmax (hr)	F	0.1940 (0.119, 0.334) [n=5]	0.1990 (0.0840, 0.250) [n=5]
		M	0.08400 (0.0560, 0.203) [n=7]	0.1230 (0.0830, 1.50) [n=5]
		T	0.1180 (0.0560, 0.334) [n=12]	0.1610 (0.0830, 1.50) [n=10]

*Subjects used their own usual brand cigarettes at Week -1.

non-mentholated = Non-mentholated VLN cigarettes for Week 2 and 6.

VLN mentholated = Mentholated VLN cigarettes for Week 2 and 6.

AUCs and Cmax are presented as geometric mean and geometric CV%

Tmax are presented as Median (Minimum, Maximum)

F = Female; M = Male; T = Total

Source: [Tables 14.2.7.5.2, 14.2.7.6.2, 14.2.7.7.2, 14.2.7.8.2, 14.2.7.9.2, and 14.2.7.10.2](#)

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Table 11–11 Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters at Weeks 2 and 6 Versus Week -1 (Pharmacokinetic Population from PP)

			Geometric Means							
Parameter (Unit)	Study Week	Product Groups	Test Week (VLN)	(n)	Baseline (UB)	(n)	GMR (Test Week /Baseline)	% Reduction	95% Confidence Interval	p-Value
Cmax (ng/mL)	Week 2	Non-mentholated	0.5451	(1)	8.352	(1)	0.065	93.5	. - .	.
		Mentholated	0.2467	(3)	9.971	(3)	0.025	97.5	0.002 - 0.247	0.0202
		Combined	0.3007	(4)	9.539	(4)	0.032	96.8	0.008 - 0.132	0.0046
	Week 6	Non-mentholated	0.6131	(1)	8.352	(1)	0.073	92.7	. - .	.
		Mentholated	0.2507	(3)	11.11	(3)	0.023	97.7	0.003 - 0.153	0.0135
		Combined	0.3135	(4)	10.34	(4)	0.030	97.0	0.008 - 0.120	0.0039
AUC0-180 (hr*ng/mL)	Week 2	Non-mentholated	0.3006	(1)	10.58	(1)	0.028	97.2	. - .	.
		Mentholated	0.05367	(3)	11.06	(3)	0.005	99.5	0.003 - 0.009	0.0007
		Combined	0.08256	(4)	10.94	(4)	0.008	99.2	0.002 - 0.032	0.0017
	Week 6	Non-mentholated	0.4357	(1)	10.58	(1)	0.041	95.9	. - .	.
		Mentholated	0.06809	(3)	11.75	(3)	0.006	99.4	0.003 - 0.011	0.0008
		Combined	0.1083	(4)	11.45	(4)	0.009	99.1	0.002 - 0.047	0.0026
. = Value missing or not reportable										
Baseline = Week -1										
Subjects used their own usual brand cigarettes at Week -1.										
VLN non-mentholated = Non-mentholated VLN cigarettes										
VLN mentholated = Mentholated VLN cigarettes										
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes										
UB mentholated = Subjects' UB mentholated filtered cigarettes										
Analysis is based on the log-transformed data.										
Paired t-test method is used to perform the analysis.										
Geometric means are calculated by exponentiating the means.										
Geometric Mean Ratios (GMR) are calculated by exponentiating the mean of difference from paired t-test.										
95% Confidence Intervals are calculated by exponentiating the 95% Confidence Intervals of the mean difference from paired t-test.										
Source: Table 14.2.7.11										
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Table 11–12 Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters at Weeks 2 and 6 Versus Week -1 (Pharmacokinetic Population from ITT)

			Geometric Means							
Parameter (Unit)	Study Week	Product Groups	Test Week (VLN)	(n)	Baseline (UB)	(n)	GMR (Test Week /Baseline)	% Reduction	95% Confidence Interval	p-Value
Cmax (ng/mL)	Week 2	Non-mentholated	0.2974	(12)	12.18	(12)	0.024	97.6	0.017 - 0.035	<.0001
		Mentholated	0.3029	(10)	12.27	(10)	0.025	97.5	0.017 - 0.037	<.0001
		Combined	0.2999	(22)	12.22	(22)	0.025	97.5	0.019 - 0.031	<.0001
	Week 6	Non-mentholated	0.3770	(12)	12.18	(12)	0.031	96.9	0.023 - 0.041	<.0001
		Mentholated	0.2947	(10)	12.67	(10)	0.023	97.7	0.017 - 0.032	<.0001
		Combined	0.3371	(22)	12.40	(22)	0.027	97.3	0.022 - 0.033	<.0001
AUC0-180 (hr*ng/mL)	Week 2	Non-mentholated	0.1213	(12)	12.56	(12)	0.010	99.0	0.005 - 0.018	<.0001
		Mentholated	0.1584	(10)	13.29	(10)	0.012	98.8	0.007 - 0.020	<.0001
		Combined	0.1370	(22)	12.88	(22)	0.011	98.9	0.007 - 0.016	<.0001
	Week 6	Non-mentholated	0.1956	(12)	12.56	(12)	0.016	98.4	0.009 - 0.026	<.0001
		Mentholated	0.1545	(10)	13.53	(10)	0.011	98.9	0.006 - 0.021	<.0001
		Combined	0.1757	(22)	12.99	(22)	0.014	98.6	0.009 - 0.020	<.0001

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Analysis is based on the log-transformed data.
Paired t-test method is used to perform the analysis.
Geometric means are calculated by exponentiating the means.
Geometric Mean Ratios (GMR) are calculated by exponentiating the mean of difference from paired t-test.
95% Confidence Intervals are calculated by exponentiating the 95% Confidence Intervals of the mean difference from paired t-test.
Source: [Table 14.2.7.12](#)
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11.3.4 Analysis of Subjective Effect Questionnaires

11.3.4.1 Fagerström Test for Cigarette Dependence (FTCD)

The locations of individual FTCD Questionnaire responses and descriptive statistics are listed below:

Description	Number
Individual FTCD Response and Score (Safety Population)	Appendix 16.2.6.12
Summary of FTCD Score by Study Product Group and Week (PP Population)	Table 14.2.9.1.1.1
Summary of FTCD Score by Study Product Group and Week (ITT Population)	Table 14.2.9.1.1.2
Mean FTCD Score by Study Product Group and Study Week (PP Population)	Figures 14.2.10.1.1 and 14.2.10.1.2
Mean FTCD Score by Study Product Group and Study Week (ITT Population)	Figure 14.2.10.1.3 and 14.2.10.1.4

The FTCD questionnaire was administered at Weeks -1, 2, 4, and 6 to all subjects and consisted of six questions that were used to provide a score for cigarette dependence. The yes/no questions are scored from 0 to 1, and the multiple choice questions are scored from 0 to 3 to yield a total score of 0-10; with a higher score indicating a more intense dependence on cigarettes.

11.3.4.1.1. Analysis of FTCD

A summary of FTCD scores is presented in [Table 11–13](#).

Table 11–13 Summary of FTCD Score by Study Product Group and Study Week (PP Population)

Study Week	Statistics	VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week -1*	n	17	12	29	20	22	42
	Mean (SD)	4.6 (1.80)	5.9 (1.62)	5.1 (1.83)	5.2 (1.46)	5.4 (1.73)	5.3 (1.59)
	Median	4.0	6.0	5.0	5.0	5.0	5.0
	Range	2, 8	4, 10	2, 10	2, 7	1, 8	1, 8
Week 2	n	13	10	23	19	21	40
	Mean (SD)	4.2 (2.01)	6.5 (1.90)	5.2 (2.24)	5.2 (1.87)	4.9 (1.92)	5.1 (1.88)
	Median	4.0	6.5	4.0	6.0	5.0	5.0
	Range	1, 8	4, 10	1, 10	1, 8	1, 8	1, 8
Week 4	n	10	10	20	20	19	39
	Mean (SD)	4.1 (0.99)	6.7 (1.89)	5.4 (1.98)	5.3 (2.02)	5.3 (1.85)	5.3 (1.92)
	Median	4.0	6.5	5.0	6.0	5.0	6.0
	Range	3, 6	4, 10	3, 10	0, 8	1, 8	0, 8
Week 6	n	9	10	19	20	19	39
	Mean (SD)	3.8 (1.20)	5.9 (2.08)	4.9 (2.00)	5.4 (1.98)	5.2 (2.04)	5.3 (1.99)
	Median	4.0	6.0	4.0	6.0	5.0	5.0
	Range	2, 6	3, 10	2, 10	1, 8	1, 8	1, 8

* Subjects used their own usual brand cigarettes at Week -1.
VLN mentholated = Mentholated VLN cigarettes
VLN non-mentholated = Non-mentholated VLN cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

Source: [Tables 14.2.9.1.1.1](#)

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11.3.4.1.2. Statistical Analysis of FTCD

The locations of statistical summary and comparisons of FTCD scores are listed below.

Statistical Comparison of FTCD Score at Weeks 2 and 6 Versus Week - 1 by Study Product Group (PP Population)	Table 14.2.9.1.2
Statistical Comparison of FTCD Score Among Study Product Groups at Weeks 2 and 6 (PP Population)	Table 14.2.9.1.3
Statistical Comparison of FTCD Score at Weeks 2 and 6 Versus Week - 1 by Study Product Group (ITT Population)	Table 14.2.9.1.4
Statistical Comparison of FTCD Score Among Study Product Groups at Weeks 2 and 6 (ITT Population)	Table 14.2.9.1.5

Summaries of the comparison FTCD scores at Weeks 2 and 6 versus baseline are presented in [Tables 11–14](#) and [11–5](#).

Table 11–14 Statistical Comparison of FTCD Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

		Means				
Study Week	Product Group	Test Week	Baseline	Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
Week 2	VLN Non-Mentholated	6.50	5.80	0.70	-0.20 - 1.60	0.1108
	VLN Mentholated	4.23	4.31	-0.08	-0.87 - 0.72	0.8372
	VLN Combined	5.22	4.96	0.26	-0.31 - 0.83	0.3542
	UB Non-Mentholated	4.90	5.33	-0.43	-0.90 - 0.04	0.0706
	UB Mentholated	5.21	5.05	0.16	-0.36 - 0.67	0.5274
	UB Combined	5.05	5.20	-0.15	-0.49 - 0.19	0.3831
Week 6	VLN Non-Mentholated	5.90	5.90	0.00	-0.67 - 0.67	1.0000
	VLN Mentholated	3.78	4.11	-0.33	-1.77 - 1.10	0.6075
	VLN Combined	4.89	5.05	-0.16	-0.84 - 0.53	0.6348
	UB Non-Mentholated	5.21	5.21	0.00	-0.36 - 0.36	1.0000
	UB Mentholated	5.40	5.15	0.25	-0.34 - 0.84	0.3828
	UB Combined	5.31	5.18	0.13	-0.21 - 0.46	0.4420
<p>Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes Paired t-test method is used to perform analysis.</p> <p>Source: Table 14.2.9.1.2 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_qsstatsttest.sas 13JUN2019 5:08</p>						

In the PP population, there were no statistically significant differences from baseline in mean FTCD score for any study product group at Weeks 2 or 6 ([Table 14.2.9.1.2](#)).

Regarding product comparisons, mean FTCD score was significantly greater in VLN non-mentholated compared to UB non-mentholated at Week 2, and was significantly lower in VLN mentholated compared to UB mentholated at Week 6. All other comparisons were not statistically significant ([Table 14.2.9.1.3](#)). These results suggest that degree of addiction, as measured by FTCD, was not affected by use of VLN over 6 weeks.

Table 11–15 Statistical Comparison of FTCD Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

		Means				
Study Week	Product Group	Test Week	Baseline	Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
Week 2	VLN Non-Mentholated	6.30	5.96	0.34	0.04 - 0.64	0.0278
	VLN Mentholated	5.00	5.16	-0.13	-0.46 - 0.20	0.4204
	VLN Combined	5.66	5.57	0.11	-0.12 - 0.33	0.3387
	UB Non-Mentholated	4.90	5.33	-0.43	-0.90 - 0.04	0.0706
	UB Mentholated	5.21	5.05	0.16	-0.36 - 0.67	0.5274
	UB Combined	5.05	5.20	-0.15	-0.49 - 0.19	0.3831
Week 6	VLN Non-Mentholated	6.05	6.07	-0.02	-0.37 - 0.32	0.8926
	VLN Mentholated	4.74	5.20	-0.46	-0.90 - -0.03	0.0377
	VLN Combined	5.40	5.64	-0.24	-0.51 - 0.04	0.0887
	UB Non-Mentholated	5.21	5.21	0.00	-0.36 - 0.36	1.0000
	UB Mentholated	5.40	5.15	0.25	-0.34 - 0.84	0.3828
	UB Combined	5.31	5.18	0.13	-0.21 - 0.46	0.4420
<p>Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes Paired t-test method is used to perform analysis.</p> <p>Source: Table 14.2.9.1.4 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_qsstatsttest.sas 13JUN2019 5:08</p>						

In the ITT population, there was a statistically significant increase from baseline in mean FTCD score for VLN non-mentholated at Week 2, and a significant decrease from baseline in mean FTCD score for VLN mentholated at Week 6. There were no significant changes for UB cigarette ([Table 14.2.9.1.4](#)).

Regarding product comparisons, mean FTCD score was significantly higher in VLN non-mentholated compared to UB non-mentholated at Week 2. There were no significant comparisons for mentholated products ([Table 14.2.9.1.5](#)). These results suggest that degree of addiction, as measured by FTCD, was not affected by use of VLN over 6 weeks.

11.3.4.2 Questionnaire of Smoking Urges-Brief (QSU-brief)

The locations of individual QSU-Brief Questionnaire responses and descriptive statistics are listed below:

Description	Number
Individual QSU-Brief Response and Factor Score (Safety Population)	Appendix 16.2.6.13
Summary of QSU-Brief Factor Score by Study Product Group and Study Week (PP Population)	Table 14.2.9.2.1.1
Summary of QSU-Brief Factor Score by Study Product Group and Study Week (ITT Population)	Table 14.2.9.2.1.2
Mean QSU-Brief Factor Score (Factor 1) by Study Product Group and Study Week (PP Population)	Figures 14.2.10.2.1.1 and 14.2.10.2.1.2
Mean QSU-Brief Factor Score (Factor 1) by Study Product Group and Study Week (ITT Population)	Figures 14.2.10.2.1.3 and 14.2.10.2.1.4
Mean QSU-Brief Factor Score (Factor 2) by Study Product Group and Study Week (PP Population)	Figures 14.2.10.2.2.1 and 14.2.10.2.2.2
Mean QSU-Brief Factor Score (Factor 2) by Study Product Group and Study Week (ITT Population)	Figures 14.2.10.2.2.3 and 14.2.10.2.2.4

The QSU-Brief was administered at Weeks -1, 2, 4, and 6 to all subjects and consisted of ten questions that were used to derive factor scores for ‘anticipation of pleasure from smoking’ (Factor 1) and ‘relief of nicotine withdrawal’ (Factor 2). The maximum score for each question was 7 (ranging from 1=strongly disagree to 7=strongly agree) and the factor score for each subject was calculated as the mean of responses for five questions each used to derive the factor score of 0-7; with higher scores indicating more intense anticipation of pleasure and lower scores indicating relief of withdrawal .

11.3.4.2.1. Analysis of QSU-Brief

A summary of QSU-Brief factor scores is presented in [Table 11–16](#).

Table 11–16 Summary of QSU-Brief Factor Score by Study Product Group and Study Week (PP Population)

Factor	Study Week	Statistics	VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Factor 1	Week -1 *	n	17	12	29	20	22	42
		Mean (SD)	4.5 (1.86)	4.4 (2.29)	4.4 (2.01)	4.5 (1.50)	3.8 (1.26)	4.1 (1.41)
		Median	4.4	4.9	4.4	4.6	3.9	4.0
		Range	2, 7	1, 7	1, 7	1, 7	2, 6	1, 7
	Week 2	n	13	10	23	19	21	40
		Mean (SD)	3.5 (2.00)	5.2 (1.21)	4.2 (1.87)	4.3 (1.74)	3.7 (1.48)	4.0 (1.61)
		Median	3.0	5.4	4.8	4.2	3.8	4.0
		Range	1, 7	3, 7	1, 7	1, 7	1, 7	1, 7
	Week 4	n	10	10	20	20	19	39
		Mean (SD)	3.2 (1.47)	4.0 (1.94)	3.6 (1.73)	3.8 (1.47)	3.7 (1.42)	3.7 (1.43)
		Median	3.0	3.8	3.5	3.6	3.8	3.8
		Range	1, 5	2, 7	1, 7	1, 6	1, 7	1, 7
	Week 6	n	9	10	19	20	19	39
		Mean (SD)	2.0 (1.07)	3.6 (2.01)	2.8 (1.78)	4.1 (1.57)	3.5 (1.57)	3.8 (1.57)
		Median	1.8	3.1	2.2	4.0	3.2	3.6
		Range	1, 5	1, 7	1, 7	1, 7	1, 7	1, 7
Factor 2	Week -1 *	n	17	12	29	20	22	42
		Mean (SD)	3.3 (1.89)	3.2 (1.85)	3.2 (1.84)	3.7 (1.49)	2.9 (1.00)	3.3 (1.30)
		Median	2.6	3.1	2.6	3.7	2.8	3.3
		Range	1, 7	1, 7	1, 7	1, 6	1, 5	1, 6
	Week 2	n	13	10	23	19	21	40
		Mean (SD)	2.6 (1.71)	3.2 (1.62)	2.9 (1.66)	3.3 (1.35)	2.7 (1.00)	3.0 (1.21)
		Median	2.4	3.8	2.6	3.4	2.6	2.9
		Range	1, 7	1, 5	1, 7	1, 6	1, 5	1, 6
	Week 4	n	10	10	20	20	19	39
		Mean (SD)	2.5 (1.42)	2.9 (1.74)	2.7 (1.56)	3.0 (1.22)	2.8 (1.30)	2.9 (1.24)
		Median	2.0	2.5	2.3	3.1	2.6	3.0
		Range	1, 5	1, 6	1, 6	1, 6	1, 6	1, 6
	Week 6	n	9	10	19	20	19	39
		Mean (SD)	1.6 (1.09)	2.4 (1.23)	2.0 (1.21)	3.3 (1.33)	2.7 (1.00)	3.0 (1.20)
		Median	1.2	2.2	1.2	3.4	2.6	3.0

Factor	Study Week	Statistics	VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
		Range	1, 4	1, 4	1, 4	1, 6	1, 5	1, 6
* Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes Source: Tables 14.2.9.2.1.1 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_qsparm.sas 13JUN2019 5:07								

11.3.4.2.2. Statistical Analysis of QSU-Brief

The locations of statistical summary and comparisons of QSU-Brief factor scores are listed below.

Statistical Comparison of QSU-Brief Factor Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)	Table 14.2.9.2.2
Statistical Comparison of QSU-Brief Factor Score Among Study Product Groups at Weeks 2 and 6 (PP Population)	Table 14.2.9.2.3
Statistical Comparison of QSU-Brief Factor Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)	Table 14.2.9.2.4
Statistical Comparison of QSU-Brief Factor Score Among Study Product Groups at Weeks 2 and 6 (ITT Population)	Table 14.2.9.2.5

Summaries of the comparison of QSU-Brief factor scores at Weeks 2 and 6 versus baseline are presented in [Tables 11–17](#) and [11–8](#).

Table 11–17 Statistical Comparison of QSU-Brief Factor Scores at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Factor	Study Week	Product Group	Means		Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
			Test Week	Baseline			
Factor 1	Week 2	VLN Non-Mentholated	5.18	4.42	0.76	-0.28 - 1.80	0.1327
		VLN Mentholated	3.49	3.97	-0.48	-1.39 - 0.43	0.2760
		VLN Combined	4.23	4.17	0.06	-0.62 - 0.74	0.8551
		UB Non-Mentholated	3.70	3.69	0.01	-0.58 - 0.60	0.9736
		UB Mentholated	4.28	4.45	-0.17	-0.68 - 0.34	0.4961
		UB Combined	3.97	4.05	-0.07	-0.45 - 0.30	0.6899
	Week 6	VLN Non-Mentholated	3.56	4.46	-0.90	-2.95 - 1.15	0.3474
		VLN Mentholated	1.98	3.89	-1.91	-2.88 - -0.94	0.0019
		VLN Combined	2.81	4.19	-1.38	-2.47 - -0.29	0.0159
		UB Non-Mentholated	3.54	3.65	-0.12	-0.71 - 0.48	0.6859
		UB Mentholated	4.06	4.47	-0.41	-0.81 - -0.01	0.0434
		UB Combined	3.81	4.07	-0.27	-0.61 - 0.07	0.1199
Factor 2	Week 2	VLN Non-Mentholated	3.18	3.18	0.00	-0.80 - 0.80	1.0000
		VLN Mentholated	2.62	2.91	-0.29	-0.89 - 0.31	0.3105
		VLN Combined	2.86	3.03	-0.17	-0.61 - 0.28	0.4536
		UB Non-Mentholated	2.70	2.96	-0.27	-0.63 - 0.09	0.1391
		UB Mentholated	3.35	3.72	-0.37	-0.71 - -0.03	0.0362
		UB Combined	3.01	3.32	-0.32	-0.55 - -0.08	0.0111
	Week 6	VLN Non-Mentholated	2.38	3.22	-0.84	-2.41 - 0.73	0.2557
		VLN Mentholated	1.56	2.58	-1.02	-1.79 - -0.26	0.0152
		VLN Combined	1.99	2.92	-0.93	-1.74 - -0.11	0.0278
		UB Non-Mentholated	2.67	2.97	-0.29	-0.79 - 0.20	0.2261
		UB Mentholated	3.28	3.70	-0.42	-0.75 - -0.09	0.0145
		UB Combined	2.98	3.34	-0.36	-0.64 - -0.08	0.0133

			Means				
Factor	Study Week	Product Group	Test Week	Baseline	Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes Paired t-test method is used to perform analysis. Factor 1: 'anticipation of pleasure from smoking' Factor 2: 'relief of nicotine withdrawal' Source: Table 14.2.9.2.2 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_qsstatsttest.sas 13JUN2019 5:08							

In the PP population, decreases from baseline in the QSU-Brief factor score ‘anticipation of pleasure from smoking’ (Factor 1) were statistically significant for VLN mentholated and VLN combined, and for UB mentholated at Week 6. There were no statistically significant changes from baseline at Week 2 ([Table 14.2.9.2.2](#)).

Regarding product comparisons, mean ‘anticipation of pleasure from smoking’ was significantly greater for VLN non-mentholated compared to UB non-mentholated at Week 2, and was significantly lower in VLN mentholated and VLN combined compared to UB mentholated and UB combined, respectively, at Week 6 ([Table 14.2.9.2.3](#)).

‘Relief of nicotine withdrawal’ (Factor 2) values were significantly lower than baseline for VLN mentholated and VLN combined at Week 6, and for UB mentholated and UB combined at Weeks 2 and 6, indicating greater relief of withdrawal compared to baseline. There were no statistically significant changes for VLN or UB non-mentholated ([Table 14.2.9.2.2](#)).

Regarding product comparisons, mean ‘relief of nicotine withdrawal’ was significantly lower for VLN mentholated and VLN combined, compared to UB mentholated and UB combined, respectively, at Week 6. There were no significant comparisons for non-mentholated products ([Table 14.2.9.2.3](#)).

A summary of the comparison of QSU-Brief factor scores at Weeks 2 and 6 versus baseline in the ITT population is presented in [Table 11–18](#).

Table 11–18 Statistical Comparison of QSU-Brief Factor Scores at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Factor	Study Week	Product Group	Means		Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
			Test Week	Baseline			
Factor 1	Week 2	VLN Non-Mentholated	5.35	4.32	1.03	0.56 - 1.50	<.0001
		VLN Mentholated	3.69	3.99	-0.31	-0.75 - 0.13	0.1631
		VLN Combined	4.53	4.16	0.37	0.03 - 0.72	0.0354
		UB Non-Mentholated	3.70	3.69	0.01	-0.58 - 0.60	0.9736
		UB Mentholated	4.28	4.45	-0.17	-0.68 - 0.34	0.4961
		UB Combined	3.97	4.05	-0.07	-0.45 - 0.30	0.6899
	Week 6	VLN Non-Mentholated	4.39	4.39	-0.00	-0.63 - 0.62	0.9882
		VLN Mentholated	3.40	3.98	-0.57	-1.16 - 0.02	0.0577
		VLN Combined	3.90	4.19	-0.28	-0.71 - 0.15	0.1945
		UB Non-Mentholated	3.54	3.65	-0.12	-0.71 - 0.48	0.6859
		UB Mentholated	4.06	4.47	-0.41	-0.81 - -0.01	0.0434
		UB Combined	3.81	4.07	-0.27	-0.61 - 0.07	0.1199
Factor 2	Week 2	VLN Non-Mentholated	3.86	3.14	0.71	0.33 - 1.09	0.0005
		VLN Mentholated	2.63	2.88	-0.28	-0.60 - 0.03	0.0758
		VLN Combined	3.25	3.02	0.22	-0.04 - 0.49	0.0962
		UB Non-Mentholated	2.70	2.96	-0.27	-0.63 - 0.09	0.1391
		UB Mentholated	3.35	3.72	-0.37	-0.71 - -0.03	0.0362
		UB Combined	3.01	3.32	-0.32	-0.55 - -0.08	0.0111
	Week 6	VLN Non-Mentholated	3.23	3.21	0.02	-0.57 - 0.60	0.9492
		VLN Mentholated	2.35	2.81	-0.45	-0.87 - -0.03	0.0369
		VLN Combined	2.80	3.01	-0.21	-0.57 - 0.15	0.2498
		UB Non-Mentholated	2.67	2.97	-0.29	-0.79 - 0.20	0.2261
		UB Mentholated	3.28	3.70	-0.42	-0.75 - -0.09	0.0145
		UB Combined	2.98	3.34	-0.36	-0.64 - -0.08	0.0133

			Means				
Factor	Study Week	Product Group	Test Week	Baseline	Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes Paired t-test method is used to perform analysis. Factor 1: 'anticipation of pleasure from smoking' Factor 2: 'relief of nicotine withdrawal' Source: Table 14.2.9.2.4 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_qsstatsttest.sas 13JUN2019 5:08							

In the ITT population, increases from baseline in the QSU-Brief factor score ‘anticipation of pleasure from smoking’ (Factor 1) were statistically significant for VLN non-mentholated and VLN combined at Week 2, with a significant decrease from baseline for UB mentholated at Week 6 ([Table 14.2.9.2.4](#)).

Regarding product comparisons, mean ‘anticipation of pleasure from smoking’ was significantly greater for VLN non-mentholated compared to UB non-mentholated at Week 2. There were no significant comparisons for mentholated products ([Table 14.2.9.2.5](#)).

The increase from baseline for ‘relief of nicotine withdrawal’ (Factor 2) was statistically significant for VLN non-mentholated at Week 2. Decreases from baseline were significant for VLN mentholated at Week 6, and for UB mentholated and UB combined at Weeks 2 and 6 ([Table 14.2.9.2.4](#)).

Regarding product comparisons, mean ‘relief of nicotine withdrawal’ was statistically significantly greater for VLN non-mentholated compared to UB non-mentholated at Week 2, and was significantly lower for VLN mentholated compared to UB mentholated at Week 6 ([Table 14.2.9.2.5](#)).

11.3.4.3 Minnesota Nicotine Withdrawal (MNWS-R)

The locations of individual MNWS-R Questionnaire responses and descriptive statistics are listed below:

Description	Number
Individual MNWS-R Response and Total Score (Safety Population)	Appendix 16.2.6.14
Summary of MNWS-R Total Score by Study Product Group and Study Week (PP Population)	Table 14.2.9.3.1.1
Summary of MNWS-R Total Score by Study Product Group and Study Week (ITT Population)	Table 14.2.9.3.1.2
Mean MNWS-R Total Score by Study Product Group and Study Week (PP Population)	Figures 14.2.10.3.1 and 14.2.10.3.2
Mean MNWS-R Total Score by Study Product Group and Study Week (ITT Population)	Figures 14.2.10.3.3 and 14.2.10.3.4

The MNWS-R was administered at Weeks -1, 2, 4, and 6 to all subjects and consisted of 15 questions that were used to calculate a nicotine withdrawal total score. The maximum score for each question was 4 (ranging from 0=none to 4=severe) to yield a total score of 0-60; with a higher score indicating a more intense level of withdrawal.

11.3.4.3.1. Analysis of MNWS-R

Summary of MNWS-R total score is presented in [Table 11–19](#).

Table 11–19 Summary of MNWS-R Total Score by Study Product Group and Study Week (PP Population)

Study Week	Statistics	VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week -1*	n	17	12	29	20	22	42
	Mean (SD)	10.9 (10.36)	10.8 (7.69)	10.9 (9.19)	10.6 (9.68)	9.2 (7.49)	9.9 (8.52)
	Median	8.0	10.0	8.0	7.5	8.0	8.0
	Range	1, 33	2, 23	1, 33	0, 36	0, 26	0, 36
Week 2	n	13	10	23	19	21	40
	Mean (SD)	14.0 (11.91)	12.2 (9.67)	13.2 (10.79)	8.1 (9.02)	9.0 (6.94)	8.6 (7.90)
	Median	9.0	9.5	9.0	4.0	8.0	6.5
	Range	0, 33	3, 29	0, 33	0, 34	0, 25	0, 34
Week 4	n	10	10	20	20	19	39
	Mean (SD)	10.8 (10.03)	10.1 (9.00)	10.5 (9.28)	8.4 (8.76)	7.8 (7.10)	8.1 (7.89)
	Median	9.5	8.5	9.5	6.5	6.0	6.0
	Range	0, 26	0, 23	0, 26	0, 30	0, 25	0, 30
Week 6	n	9	10	19	20	19	39
	Mean (SD)	6.8 (7.36)	6.2 (5.90)	6.5 (6.45)	7.5 (7.32)	8.3 (7.53)	7.9 (7.33)
	Median	5.0	4.0	5.0	5.5	7.0	6.0
	Range	0, 20	0, 15	0, 20	0, 27	0, 25	0, 27
<p>* Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes</p> <p>Source: Tables 14.2.9.3.1.1 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_qsparm.sas 13JUN2019 5:07</p>							

11.3.4.3.2. Statistical Analysis of MNWS-R

The locations of statistical summary and comparisons of MNWS-R total scores are listed below.

Statistical Comparison of MNWS-R Total Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)	Table 14.2.9.3.2
Statistical Comparison of MNWS-R Total Score Among Study Product Groups at Weeks 2 and 6 (PP Population)	Table 14.2.9.3.3
Statistical Comparison of MNWS-R Total Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)	Table 14.2.9.3.4
Statistical Comparison of MNWS-R Total Score Among Study Product Groups at Weeks 2 and 6 (ITT Population)	Table 14.2.9.3.5

Summaries of the comparison of MNWS-R total scores at Weeks 2 and 6 versus baseline are presented in [Tables 11–20](#) and [11–21](#).

Table 11–20 Statistical Comparison of MNWS-R Total Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

		Means				
Study Week	Product Group	Test Week	Baseline	Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
Week 2	VLN Non-Mentholated	12.20	11.00	1.20	-4.11 - 6.51	0.6214
	VLN Mentholated	14.00	10.08	3.92	-3.60 - 11.44	0.2779
	VLN Combined	13.22	10.48	2.74	-1.77 - 7.25	0.2213
	UB Non-Mentholated	9.00	9.29	-0.29	-3.11 - 2.54	0.8353
	UB Mentholated	8.05	10.00	-1.95	-4.88 - 0.98	0.1795
	UB Combined	8.55	9.63	-1.07	-3.03 - 0.88	0.2741
Week 6	VLN Non-Mentholated	6.20	11.10	-4.90	-9.44 - -0.36	0.0374
	VLN Mentholated	6.78	10.22	-3.44	-10.09 - 3.20	0.2663
	VLN Combined	6.47	10.68	-4.21	-7.75 - -0.67	0.0224
	UB Non-Mentholated	8.26	8.84	-0.58	-4.15 - 3.00	0.7377
	UB Mentholated	7.50	10.60	-3.10	-5.14 - -1.06	0.0050
	UB Combined	7.87	9.74	-1.87	-3.85 - 0.11	0.0629
<p>Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes Paired t-test method is used to perform analysis.</p> <p>Source: Table 14.2.9.3.2 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_qsstatsttest.sas 13JUN2019 5:08</p>						

In the PP population, decreases from baseline in the MNWS-R total scores were statistically significant for VLN non-mentholated and VLN combined, and for UB mentholated at Week 6. There were no statistically significant changes at Week 2 ([Table 14.2.9.3.2](#)).

There were no significant comparisons in MNWS-R total score for any products ([Table 14.2.9.3.3](#)).

Table 11–21 Statistical Comparison of MNWS-R Total Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

		Means				
Study Week	Product Group	Test Week	Baseline	Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
Week 2	VLN Non-Mentholated	16.02	12.57	3.45	0.69 - 6.21	0.0155
	VLN Mentholated	8.43	7.58	0.87	-1.48 - 3.22	0.4615
	VLN Combined	12.27	10.13	2.18	0.38 - 3.99	0.0182
	UB Non-Mentholated	9.00	9.29	-0.29	-3.11 - 2.54	0.8353
	UB Mentholated	8.05	10.00	-1.95	-4.88 - 0.98	0.1795
	UB Combined	8.55	9.63	-1.07	-3.03 - 0.88	0.2741
Week 6	VLN Non-Mentholated	13.44	12.81	0.63	-2.42 - 3.68	0.6800
	VLN Mentholated	5.40	7.37	-1.95	-3.90 - -0.00	0.0497
	VLN Combined	9.47	10.15	-0.63	-2.44 - 1.18	0.4907
	UB Non-Mentholated	8.26	8.84	-0.58	-4.15 - 3.00	0.7377
	UB Mentholated	7.50	10.60	-3.10	-5.14 - -1.06	0.0050
	UB Combined	7.87	9.74	-1.87	-3.85 - 0.11	0.0629
<p>Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes Paired t-test method is used to perform analysis.</p> <p>Source: Table 14.2.9.3.4 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_qsstatsttest.sas 13JUN2019 5:08</p>						

In the ITT population, increases from baseline in the MNWS-R total score were statistically significant for VLN non-mentholated and VLN combined at Week 2, and decreases from baseline in the MNWS-R total score were significant for VLN mentholated and UB mentholated at Week 6 ([Table 14.2.9.3.4](#)).

Regarding product comparisons, mean MNWS-R total score was statistically significantly greater for VLN non-mentholated and VLN combined compared to UB non-mentholated and UB combined, respectively, at Week 2, and for VLN non-mentholated compared to UB non-mentholated at Week 6 ([Table 14.2.9.3.5](#)).

11.3.4.4 Perceived Health Risk Scale

The locations of individual Perceived Health Risk Scale responses and descriptive statistics are listed below:

Description	Number
Individual Perceived Health Risk Scale (Safety Population)	Appendix 16.2.6.15
Summary of Perceived Health Risk Scale by Study Product Group and Study Week (PP Population)	Table 14.2.9.4.1.1
Summary of Perceived Health Risk Scale by Study Product Group and Study Week (ITT Population)	Table 14.2.9.4.1.2
Mean Perceived Health Risk Scale by Study Product Group and Study Week (PP Population)	Figures 14.2.10.4.1 and 14.2.10.4.2
Mean Perceived Health Risk Scale by Study Product Group and Study Week (ITT Population)	Figures 14.2.10.4.3 and 14.2.10.4.4

The Perceived Health Risk Scale was administered at Weeks -1, 2, 4, and 6 to all subjects and consisted of one question, to indicate perception of risk of becoming addicted to the cigarette you are currently using. The maximum score for each question was ten (ranging from 1=very low risk to 10=very high risk) with a higher score indicating a greater perception of health risk.

11.3.4.4.1. Analysis of Perceived Health Risk Scale

Summary of Perceived Health Risk Scale is presented in [Table 11–22](#).

Table 11–22 Summary of Perceived Health Risk Scale by Study Product Group and Study Week (PP Population)

Study Week	Statistics	VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week -1*	n	17	12	29	20	22	42
	Mean (SD)	6.6 (1.93)	7.7 (2.19)	7.1 (2.07)	6.6 (2.09)	7.7 (2.25)	7.1 (2.23)
	Median	7.0	8.0	8.0	7.0	8.0	7.0
	Range	3, 10	4, 10	3, 10	2, 10	3, 10	2, 10
Week 2	n	13	10	23	19	21	40
	Mean (SD)	4.1 (2.72)	5.3 (2.83)	4.6 (2.78)	6.8 (2.07)	7.0 (2.68)	6.9 (2.38)
	Median	5.0	5.5	5.0	7.0	8.0	7.0
	Range	1, 9	1, 10	1, 10	3, 10	1, 10	1, 10
Week 4	n	10	10	20	20	19	39
	Mean (SD)	2.7 (2.91)	3.8 (2.94)	3.3 (2.90)	6.7 (2.37)	7.4 (2.55)	7.0 (2.45)
	Median	1.0	3.0	2.0	7.0	8.0	7.0
	Range	1, 9	1, 10	1, 10	1, 10	2, 10	1, 10
Week 6	n	9	10	19	20	19	39
	Mean (SD)	2.6 (2.65)	4.0 (3.56)	3.3 (3.16)	6.6 (1.70)	6.9 (2.54)	6.7 (2.12)
	Median	1.0	2.5	2.0	7.0	7.0	7.0
	Range	1, 9	1, 10	1, 10	3, 10	2, 10	2, 10
<p>* Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes</p> <p>Source: Tables 14.2.9.4.1.1 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_qsparm.sas 13JUN2019 5:07</p>							

11.3.4.4.2. Statistical Analysis of Perceived Health Risk Scale

The locations of statistical summary and comparisons of Perceived Health Risk Scale are listed below.

Statistical Comparison of Perceived Health Risk Scale at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)	Table 14.2.9.4.2
Statistical Comparison of Perceived Health Risk Scale Among Study Product Groups at Weeks 2 and 6 (PP Population)	Table 14.2.9.4.3
Statistical Comparison of Perceived Health Risk Scale at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)	Table 14.2.9.4.4
Statistical Comparison of Perceived Health Risk Scale Among Study Product Groups at Weeks 2 and 6 (ITT Population)	Table 14.2.9.4.5

Summaries of the comparison of Perceived Health Risk scores at Weeks 2 and 6 versus baseline are presented in [Tables 11–23](#) and [11–24](#).

Table 11–23 Statistical Comparison of Perceived Health Risk Scale at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

		Means				
Study Week	Product Group	Test Week	Baseline	Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
Week 2	VLN Non-Mentholated	5.30	7.40	-2.10	-4.81 - 0.61	0.1132
	VLN Mentholated	4.08	6.38	-2.31	-4.02 - -0.59	0.0126
	VLN Combined	4.61	6.83	-2.22	-3.60 - -0.83	0.0031
	UB Non-Mentholated	7.00	7.57	-0.57	-1.33 - 0.18	0.1305
	UB Mentholated	6.79	6.53	0.26	-0.70 - 1.23	0.5725
	UB Combined	6.90	7.08	-0.18	-0.77 - 0.42	0.5536
Week 6	VLN Non-Mentholated	4.00	7.70	-3.70	-7.32 - -0.08	0.0459
	VLN Mentholated	2.56	6.78	-4.22	-5.97 - -2.47	0.0005
	VLN Combined	3.32	7.26	-3.95	-5.82 - -2.07	0.0003
	UB Non-Mentholated	6.89	7.58	-0.68	-1.61 - 0.24	0.1371
	UB Mentholated	6.60	6.55	0.05	-0.94 - 1.04	0.9169
	UB Combined	6.74	7.05	-0.31	-0.97 - 0.35	0.3494
Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes Paired t-test method is used to perform analysis. Source: Table 14.2.9.4.2 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_qsstatsttest.sas 13JUN2019 5:08						

In the PP population, decreases from baseline for perceived health risk were statistically significant for VLN mentholated and VLN combined at Week 2, and for VLN mentholated, VLN non-mentholated, and VLN combined at Week 6. There were no statistically significant changes for UB mentholated or non-mentholated ([Table 14.2.9.4.2](#)).

Regarding product comparisons, with the exception of a non-significant lower value for VLN non-mentholated compared to UB non-mentholated at Week 2, mean perceived health risk was significantly lower for VLN non-mentholated, VLN mentholated, and VLN combined, compared to UB non-mentholated, UB mentholated, and UB combined, respectively, at Weeks 2 and 6 ([Table 14.2.9.4.3](#)).

Table 11–24 Statistical Comparison of Perceived Health Risk Scale at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

		Means				
Study Week	Product Group	Test Week	Baseline	Difference (Test Week - Baseline)	95% Confidence Interval	p-Value
Week 2	VLN Non-Mentholated	4.04	7.57	-3.53	-4.63 - -2.43	<.0001
	VLN Mentholated	3.43	6.98	-3.62	-4.56 - -2.68	<.0001
	VLN Combined	3.74	7.28	-3.58	-4.29 - -2.86	<.0001
	UB Non-Mentholated	7.00	7.57	-0.57	-1.33 - 0.18	0.1305
	UB Mentholated	6.79	6.53	0.26	-0.70 - 1.23	0.5725
	UB Combined	6.90	7.08	-0.18	-0.77 - 0.42	0.5536
Week 6	VLN Non-Mentholated	3.56	7.81	-4.26	-5.37 - -3.14	<.0001
	VLN Mentholated	3.21	7.12	-3.88	-4.93 - -2.83	<.0001
	VLN Combined	3.39	7.48	-4.07	-4.82 - -3.32	<.0001
	UB Non-Mentholated	6.89	7.58	-0.68	-1.61 - 0.24	0.1371
	UB Mentholated	6.60	6.55	0.05	-0.94 - 1.04	0.9169
	UB Combined	6.74	7.05	-0.31	-0.97 - 0.35	0.3494
<p>Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN mentholated = Mentholated VLN cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes Paired t-test method is used to perform analysis.</p> <p>Source: Table 14.2.9.4.4 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_intext_qsstatsttest.sas 13JUN2019 5:08</p>						

In the ITT population, decreases from baseline for perceived health risk were statistically significant for VLN non-mentholated, VLN mentholated, and VLN combined at Weeks 2 and 6. There were no statistically significant changes for UB mentholated or non-mentholated ([Table 14.2.9.4.4](#)).

Regarding product comparisons, mean perceived health risk was significantly lower for VLN non-mentholated, VLN mentholated and VLN combined, compared to UB non-mentholated, UB mentholated, and UB combined, respectively, at Weeks 2 and 6 ([Table 14.2.9.4.5](#)).

11.3.5 Statistical/Analytical Issues

The statistical analyses described in the protocol ([Appendix 16.1.1](#)), SAP ([Appendix 16.1.9.1](#)), and [Sections 9.7](#) and [9.8](#) were performed and all statistical outputs are presented in [Appendix 16.1.9.2](#). Most subjects were excluded from the PP population for non-compliance as determined by the criteria discussed in [Section 9.7.1.1](#). Therefore, statistical comparisons were also performed using the ITT population. Nevertheless, the same directional trends were observed in the ITT and PP populations.

11.3.5.1 Adjustments for Covariates

There were no adjustments for covariates in this analyses.

11.3.5.2 Handling of Dropouts or Missing Data

Where individual data points were missing (e.g., subject discontinued, missing samples or parameter could not be calculated), the data were analyzed based on available non missing data.

11.3.5.3 Multicenter Studies

This study was conducted in 2 sites. Product use, BoE, and subjective effect assessments were conducted in both sites. No notable differences in trends were observed between sites. Topography and PK assessments were conducted at the Celerion site only.

11.3.5.4 Multiple Comparisons/Multiplicity

Multiplicity adjustments were not performed for any of the analyses.

11.3.6 By-Subject Displays

The individual results are presented in [Appendix 16.2.6](#).

12. SAFETY EVALUATION

12.1 Adverse Events

12.1.1 Brief Summary of Adverse Events

There were no deaths reported in this study. One subject experienced a SAE (subarachnoid hemorrhage) after study completion that was not product related and is discussed in

[Section 12.2.2](#), and one subject was discontinued by the PI due to experiencing several AEs and is discussed in [Section 12.2.3](#).

During the Baseline period (Week -1), in which subjects smoked their usual brand cigarettes, 19 (13.4%) subjects experienced a total of 30 AEs; with headache being the most frequent event, reported by 12 (8.5%) subjects. The majority (16) of subjects experienced events that were mild in severity and three subjects experienced moderate events (migraine, presyncope, and vomiting). The PI considered two events (dyspepsia and headache) in the same subject to be possibly related to study product and the events in the remaining subjects unlikely/not related.

After study product group randomization, 45 of 142 (31.7%) subjects across study groups experienced a total of 83 AEs. Headache was the most frequently reported AE, experienced 24 times by a total of 22 (15.5%) subjects; all remaining AEs were experienced by seven or fewer (< 5%) subjects each. Regarding maximum severity, one subject experienced a severe AE (subarachnoid hemorrhage), nine subjects experienced moderate AEs (including five subjects with headache), and the remaining 35 subjects experienced only mild AEs. The PI considered an AE in one subject (nausea [VLN non-mentholated]) to be likely related to study product, AEs in 12 subjects to be possibly related to study product, and the remaining 32 subjects only experienced events considered unlikely/not related to study product.

Incidence of AEs by study product is presented below in [Table 12–1](#).

Table 12–1 AE Incidence by Study Product and Group

Study Product	Number (%) of Subjects Reporting AEs	Number of AEs Reported
Baseline Period* (n = 142)	19 (13.4%)	30
Randomized Study Product Groups		
UB non-mentholated (n = 22)	9 (40.9%)	13
VLN non-mentholated (n = 50)	16 (32.0%)	22
UB mentholated (n = 20)	5 (25.0%)	6
VLN mentholated (n = 50)	15 (30.0%)	42
Overall (n = 142) [#]	45 (31.7%)	83
n = Number of Subjects *Subjects used their usual brand cigarette at Baseline (Week -1). [#] Overall includes AEs after the start of Week 1 product use. VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes Source: Tables 14.3.1.1 and 14.3.1.2		

Table 12–2 presents AEs reported in this study by study product.

Table 12–2 Adverse Event Frequency - Number of Subjects Reporting the Event (% of Subjects Used Product) (Safety Population)

Adverse Events*	Baseline	Treatment				Overall#
		UB Non-Mentholated	VLN Non-Mentholated	UB Mentholated	VLN Mentholated	
Number of Subjects Use Study Product	142 (100%)	22 (100%)	50 (100%)	20 (100%)	50 (100%)	142 (100%)
Number of Subjects With Adverse Events	19 (13%)	9 (41%)	16 (32%)	5 (25%)	15 (30%)	45 (32%)
Number of Subjects Without Adverse Events	123 (87%)	13 (59%)	34 (68%)	15 (75%)	35 (70%)	97 (68%)
Eye disorders	2 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Erythema of eyelid	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Eye pruritus	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lacrimation increased	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ocular hyperaemia	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Gastrointestinal disorders	5 (4%)	2 (9%)	2 (4%)	0 (0%)	4 (8%)	8 (6%)
Abdominal discomfort	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Constipation	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)
Diarrhoea	0 (0%)	0 (0%)	1 (2%)	0 (0%)	1 (2%)	2 (1%)
Dyspepsia	2 (1%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Gastroesophageal reflux disease	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Nausea	0 (0%)	1 (5%)	1 (2%)	0 (0%)	1 (2%)	3 (2%)
Oral discomfort	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)
Toothache	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)
Vomiting	1 (1%)	2 (9%)	0 (0%)	0 (0%)	0 (0%)	2 (1%)
General disorders and administration site conditions	1 (1%)	0 (0%)	2 (4%)	0 (0%)	4 (8%)	6 (4%)
Chest discomfort	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)
Fatigue	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (4%)	2 (1%)
Pain	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)
Vessel puncture site pain	1 (1%)	0 (0%)	2 (4%)	0 (0%)	2 (4%)	4 (3%)
Infections and infestations	0 (0%)	1 (5%)	2 (4%)	1 (5%)	0 (0%)	4 (3%)
Nasal abscess	0 (0%)	0 (0%)	0 (0%)	1 (5%)	0 (0%)	1 (1%)
Tooth infection	0 (0%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)	1 (1%)
Upper respiratory tract infection	0 (0%)	1 (5%)	1 (2%)	0 (0%)	0 (0%)	2 (1%)
Injury, poisoning and procedural complications	1 (1%)	1 (5%)	1 (2%)	1 (5%)	2 (4%)	5 (4%)
Arthropod bite	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (4%)	2 (1%)
Contusion	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Laceration	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Meniscus injury	0 (0%)	0 (0%)	0 (0%)	1 (5%)	0 (0%)	1 (1%)
Subarachnoid haemorrhage	0 (0%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)	1 (1%)
Metabolism and nutrition disorders	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)
Increased appetite	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)
Musculoskeletal and connective tissue disorders	0 (0%)	1 (5%)	0 (0%)	0 (0%)	2 (4%)	3 (2%)
Back pain	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)

Adverse Events*	Baseline	Treatment				Overall#
		UB Non-Mentholated	VLN Non-Mentholated	UB Mentholated	VLN Mentholated	
Neck pain	0 (0%)	1 (5%)	0 (0%)	0 (0%)	1 (2%)	2 (1%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Skin papilloma	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Nervous system disorders	13 (9%)	5 (23%)	10 (20%)	3 (15%)	6 (12%)	24 (17%)
Dizziness	0 (0%)	0 (0%)	1 (2%)	0 (0%)	1 (2%)	2 (1%)
Headache	12 (8%)	5 (23%)	8 (16%)	3 (15%)	6 (12%)	22 (15%)
Lethargy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)
Migraine	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Presyncope	0 (0%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)	1 (1%)
Tremor	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)
Psychiatric disorders	0 (0%)	0 (0%)	3 (6%)	1 (5%)	5 (10%)	9 (6%)
Anxiety	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)
Depressed mood	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)
Insomnia	0 (0%)	0 (0%)	1 (2%)	0 (0%)	1 (2%)	2 (1%)
Irritability	0 (0%)	0 (0%)	3 (6%)	0 (0%)	4 (8%)	7 (5%)
Nightmare	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)
Stress	0 (0%)	0 (0%)	0 (0%)	1 (5%)	0 (0%)	1 (1%)
Respiratory, thoracic and mediastinal disorders	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (4%)	2 (1%)
Oropharyngeal pain	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)
Throat irritation	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (1%)
Skin and subcutaneous tissue disorders	1 (1%)	0 (0%)	0 (0%)	0 (0%)	2 (4%)	2 (1%)
Erythema	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Palmar erythema	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pruritus	1 (1%)	0 (0%)	0 (0%)	0 (0%)	2 (4%)	2 (1%)
Vascular disorders	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Presyncope	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes *Adverse events are classified according to MedDRA® Version 21.0 Subjects used their own usual brand cigarettes at Week -1. Although a subject may have had 2 or more clinical adverse experiences, the subject is counted only once within a category. The same subject may appear in different categories. # Overall includes AEs after the start of Week1 product use. Source: Table 14.3.1.1 Program: /CA24914/sas_prg/stsas/intext/t_ae.sas 02JUL2019 6:09						

12.1.2 Display of Adverse Events

The locations of AE summary tables and listings are presented below:

Product-Use-Emergent Adverse Event Frequency - Number of Subjects Reporting the Event (% of Subjects Used Study Product)	Table 14.3.1.1
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Product-Use-Emergent Adverse Event Frequency - Number of Adverse Events (% of Total Adverse Events)	Table 14.3.1.2
Product-Use-Emergent Adverse Event Frequency by Severity and Relationship to Study Product - Number of Subjects Reporting Adverse Events	Table 14.3.1.3
Serious Adverse Events	Table 14.3.2.1
Individual Adverse Events	Appendix 16.2.7.1

12.1.3 Analysis of Adverse Events

Headache was the most frequently experienced AE in this study, reported 24 times by 22 (15.5%) subjects across study product groups. Seventeen (17) subjects experienced mild headache AEs and five subjects (two each in VLN mentholated and VLN non-mentholated, and one in UB non-mentholated) experienced moderate events. The majority (16) of subjects received acetaminophen for product use-emergent headache AEs, with one subject receiving ibuprofen, and one receiving both medications. The PI considered headache AEs in five subjects (VLN mentholated [two subjects] and VLN non-mentholated [three subjects]) to be possibly related to study product and events in the remaining 17 subjects unlikely/not related.

All remaining events were experienced by seven or fewer (< 5%) subjects. Regarding maximum severity, the PI considered nausea (VLN non-mentholated) in one subject to be likely related to study product; while 12 subjects experienced AEs considered possibly related to study product and 32 subjects only experienced AEs considered unlikely/not related. All AEs are presented by relationship and severity in [Table 14.3.1.3](#).

All AEs resolved by the end of the study, with the exception of unresolved headache in Subject 2113, ongoing meniscus injury in Subject 2125, and several events in Subject 1018 as discussed in [Section 12.2.3](#). Concomitant medications administered for AE resolution are presented in [Appendix 16.2.5.4](#).

12.1.4 Listing of Adverse Events by Subject

[Appendix 16.2.7.1](#) presents the AEs by subject number, study product, product use-emergent status, and AE system organ class, preferred term, and verbatim term, and includes time from start of product use, onset/resolution dates and times, frequency, severity, seriousness, outcome, relationship to study product, and action taken.

12.2 Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

There were no deaths in this study. One subject experienced the SAE of subarachnoid hemorrhage after study completion ([Section 12.2.2](#)) and one subject was discontinued from the study due to an AE ([Section 12.2.3](#)).

12.2.1 Deaths

Not applicable.

12.2.2 Other Serious Adverse Events

Subject 1023 (a 50-year-old White female; VLN non-mentholated) experienced the SAE of subarachnoid hemorrhage after study completion.

The subject's reported medical history was notable only for carpal tunnel surgery, hysterectomy for abnormal menstrual bleeding, and thumb joint repair; she did not report any prior medications. During the study the subject experienced two headaches, one mild and one moderate, with durations of approximately one day and two weeks, respectively. Both headaches were considered possibly related to study product and she received acetaminophen for the moderate event. Physical examinations performed during the study were negative and vital signs were within normal limits.

On 15 September 2018, one day after completion of end of study procedures, the subject presented to a hospital emergency room due to experiencing severe headaches, nausea and vomiting, and a syncopal episode. A CT scan showed a large subarachnoid hemorrhage and subsequent angiogram revealed a right internal carotid artery aneurysm. The subject underwent a coil embolization of the aneurysm and placement of an external ventricular drain. The subject received several medications while hospitalized, including intravenous fentanyl and oral gabapentin, nimodipine, clopidogrel bisulfate, ondansetron, oxycodone, pantoprazole, aspirin, and docusate sodium.

Subject 1023's symptoms improved and the ventricular drain was removed. She was discharged from the hospital on 02 October 2018 and remained symptom free. The event was resolved at the time of hospital discharge (17 days after onset) and the PI considered it not related to study product (source data on file with Celerion).

12.2.3 Other Significant Adverse Events

Subject 1018 (a 41-year-old White female; VLN mentholated) was discontinued from the study after experiencing several mild AEs during Weeks 2 and 3, including anxiety (two events), nightmares, chest discomfort (two events), depressed mood, tremor, and headache. The events generally lasted between 30 minutes and two hours, with the exception of nightmares which lasted nearly two weeks. During the study, the subject also experienced the mild events of constipation, nausea, and pain, which had both unknown onset and resolution dates/times. She received concomitant medications for these events, including oral acetaminophen (pain), docusate sodium and magnesium hydroxide (constipation), and intravenous ondansetron (nausea). The subject was discontinued by the PI during Week 3. The mild AEs that occurred during Weeks 2 and 3 all resolved, with the exception of the headache event, which occurred on the day of study discontinuation and remained unresolved at the end of study. These events were all considered to be possibly related to study product by the PI.

12.3 Clinical Laboratory Evaluation

12.3.1 Listing of Individual Laboratory Measurements by Subject and Each Abnormal Laboratory Value

Clinical laboratory serum chemistry, hematology, and urinalysis were performed at Screening and at the end-of-study; urine cotinine test was performed at Screening and at the start of Week -1; urine drug screens and serum/urine pregnancy tests (females only) were performed at Screening and at several study time points, and serum FSH was performed at Screening (females only).

The listings of individual clinical laboratory results can be found in [Appendices 16.2.8.1.1.1 through 16.2.8.1.10](#). Mean serum chemistry, hematology, and urinalysis results are presented in [Table 14.3.5.1](#), [Table 14.3.5.2](#), and [Table 14.3.5.3](#), respectively. Out-of-range serum chemistry, hematology, and urinalysis results are presented in [Tables 14.3.4.1.1 through 14.3.4.3.6](#). Mean serum chemistry, hematology, and urinalysis results remained within normal limits at the End of Study time point, with minimal changes from baseline noted.

There were no individual clinically significant laboratory findings in this study, with the exception of positive urine occult blood in Subject 2211 at the end of study that was not considered an AE.

12.4 Vital Signs, Physical Findings, and Other Observations Related to Safety

12.4.1 Vital Signs

Vital sign summary statistics (blood pressure, pulse rate, respiration rate, and oral temperature) are presented in [Table 14.3.5.4](#) and are listed by individual subject in [Appendix 16.2.8.2](#). Mean vital sign values remained within normal limits at all study time points. There were no individual clinically significant vital sign findings in this study.

12.4.2 Electrocardiograms

Twelve (12)-lead ECGs were obtained at Screening and End of study and are listed by individual subject in [Appendix 16.2.8.3](#). There were no individual clinically significant ECG findings in this study.

12.4.3 Physical Examinations

Physical examination descriptions are presented by individual subject in [Appendix 16.2.4.2](#). Abnormal post-product administration physical examination findings were entered as AEs.

13. DISCUSSION AND OVERALL CONCLUSIONS

13.1 Discussion

The study objectives were to characterize cigarette consumption behavior (cigarettes per day and puffing topography) before, during, and after a switch from UB to VLN cigarettes for

6 weeks and to evaluate changes in tobacco-related BoE, nicotine PK, and in subjective effects before, during, and after a 6-week switch from UB to VLN cigarettes.

The sample size of 70 subjects (50 who switched and 20 who remained on UB) was based on powering the primary objective of a within-group comparison of cigarette consumption at baseline and end-of-study and to account for potential non-compliance. However, the final sample size in the PP population was much lower for all analyses due to a restrictive compliance criterion (having a ratio of [plasma cotinine/CPD VLN]/[plasma cotinine/CPD baseline] > 0.2). As a result, the power to detect significant differences in the PP population was reduced. Statistical comparisons performed in the ITT population were more likely to show statistical significance.

Nonetheless, the same directional trends were observed in the ITT and PP populations. They consisted of an increase in CPD observed at Week 2 for subjects who switched to VLN which was more pronounced in the non-mentholated VLN group. The increase in CPD was associated with a modest increase in blood COHb at Week 2 in the non-mentholated VLN group that was also not apparent by Week 6 suggesting that any compensation that might have occurred immediately following the switch to VLN cigarettes was not sustained through Week 6. Trends also consisted in decreases in average total puff duration, average puff volume, average total puff volume, and inter-puff interval observed at Weeks 2 and 6. The decrease in inter-puff interval observed in Weeks 2 and 6 was not associated with an increase in the average number of puffs taken. On the contrary, the number of puffs taken significantly decreased on Week 6. Subjects' average puff duration, average peak puff flow rate and average flow rate were not significantly changed. Together, these data indicate that the subjects did not compensate for the lower nicotine content of the VLN cigarettes by taking longer or deeper inhalations, by increasing the number of puffs taken during smoking episodes, or by increasing the number of cigarettes smoked, and may have inhaled less smoke compared to subjects who continued to smoke their usual brand cigarettes. As a result, significant decreases in plasma nicotine and in all urine BoE, with the exception of S-PMA, were observed in both populations by Week 6.

There were differences in behavior between smokers of mentholated and non-mentholated cigarettes that appear to have an effect on study results. For instance, the increase in CPD at Week 2 was driven by smokers of non-mentholated cigarettes with no significant increase in CPD by Week 6. On the contrary, smokers of mentholated cigarettes showed no significant change in CPD at Week 2 and a decrease at Week 6. In line with that, the observed increase in COHb at Week 2 was also driven by non-mentholated smokers with no change from baseline observed at Week 6 while for smokers of mentholated cigarettes, no changes from baseline were observed at Week 2 and decreases were seen at Week 6. S-PMA was the only other biomarker that followed the trend with a significant increase in urine S-PMA seen in non-mentholated smokers at Week 2 but not at Week 6 and a significant decrease at Week 6 seen in mentholated smokers. For all other urine biomarkers of exposure (with the exception of 3-HPMA at Week 2 who did not show clear trends), significant decreases of similar magnitude were observed following the switch. Nicotine exposure also decreased significantly by > 96% in all VLN groups. The increase in CPD for smokers of non-mentholated cigarettes was not due to outliers as it could be observed in over half the

subjects who switched to non-mentholated VLN. Rather it could be attributed to differences in subjective effects between smokers of mentholated and non-mentholated cigarettes. Non-mentholated smokers started out with a higher FTCD score at baseline compared with mentholated smokers indicating higher nicotine dependence (5.2 versus 6 in the ITT population and 4.1-4.3 versus 5.8-5.9 in the PP population). At Week 2, the FTCD score increased for non-mentholated smokers with no changes observed for mentholated smokers. By Week 6, it had decreased for mentholated smokers but not for non-mentholated smokers. Similarly at Week 2, non-mentholated smokers experienced more anticipated pleasure from smoking (factor 1), less relief from nicotine withdrawal (factor 2), and more nicotine withdrawal symptoms (based on NWS scores). By Week 6, there were no mean changes from baseline in the questionnaires for smokers of non-mentholated cigarettes but a decrease in nicotine withdrawal and anticipated pleasure could be seen in smokers of mentholated cigarettes. These observations are consistent with reports of a ‘menthol effect’ (Wailoo, 2019) in addition to a nicotine effect whereby subjects smoking mentholated cigarettes still get some ‘relief’ from menthol exposure and therefore experience less urge to smoke. This would explain why subjects in mentholated and non-mentholated groups had different nicotine withdrawal scores even though they all experienced >96% reduction in nicotine exposure. Nonetheless, these effects appeared to be temporary as for most subjects in the non-mentholated group, CPD returned near baseline levels by Week 6 or at least the increase from baseline was not as pronounced. Changes observed at Week 2 were not always sustained at Week 6 therefore Week 2 results should be viewed as an indication of the trend whereas Week 6 results should be viewed as the final determination of effects.

It is important to note that while some subjects were excluded from the PP population due to non-compliance based on their e-diary reports, PK, urine, and blood BoE, topography, and subjective effects assessments took place in the CRU where smoking conditions were monitored. As such, these assessments were conducted under compliant smoking conditions.

There were no deaths reported in this study. One subject experienced an SAE (subarachnoid hemorrhage) after study completion that was not product related. AEs were reported by 31.7% of subjects during the study, with headache being the most frequent event. The majority of subjects experienced AEs that were mild in severity and considered unlikely/not related to study product.

13.2 Conclusions

Exposure to nicotine and other BoEs was significantly reduced following the switch to VLN cigarettes and subjects did not exhibit behavior that was typical of compensation (increased number of cigarettes, puff duration, puff volume, or flow rate). An observed decrease in inter-puff interval may have suggested compensation but it was not associated with a higher number of puffs taken indicating that compensation did not take place following the switch to VLN cigarettes. Similarly, an increase in CPD was observed in Week 2 but it was not sustained in Week 6.

Overall, the use of the VLN products under the study conditions appeared to be well tolerated by the healthy adult smokers in this study.

14. TABLES, FIGURES AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT

14.1 Demographic and Tobacco/Nicotine Product Use History Data

Table 14.1.1	Summary of Disposition (Safety, ITT, and PP Population)
Table 14.1.2	Demographic Summary (Safety, ITT, and PP Populations)
Table 14.1.3	Tobacco/Nicotine Product Use History Summary (Safety, ITT, and PP Populations)

Table 14.1.1 Summary of Disposition (Safety, ITT, and PP Population)

Population	Category	Study Product Group				Overall
		VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	
Safety	Enrolled	50(100 %)	50(100 %)	22(100 %)	20(100 %)	142(100 %)
	Completed	43(86 %)	42(84 %)	19(86 %)	20(100 %)	124(87 %)
	Discontinued Early	7(14 %)	8(16 %)	3(14 %)	0(0 %)	18(13 %)
	Adverse Event	0(0 %)	1(2 %)	0(0 %)	0(0 %)	1(1 %)
	Lost To Follow-Up	0(0 %)	1(2 %)	3(14 %)	0(0 %)	4(3 %)
	Non-Compliance With Study	6(12 %)	5(10 %)	0(0 %)	0(0 %)	11(8 %)
	Withdrawal By Subject	1(2 %)	1(2 %)	0(0 %)	0(0 %)	2(1 %)
ITT	Enrolled	50(100 %)	50(100 %)	22(100 %)	20(100 %)	142(100 %)
	Completed	43(86 %)	42(84 %)	19(86 %)	20(100 %)	124(87 %)
	Discontinued Early	7(14 %)	8(16 %)	3(14 %)	0(0 %)	18(13 %)
	Adverse Event	0(0 %)	1(2 %)	0(0 %)	0(0 %)	1(1 %)
	Lost To Follow-Up	0(0 %)	1(2 %)	3(14 %)	0(0 %)	4(3 %)
	Non-Compliance With Study	6(12 %)	5(10 %)	0(0 %)	0(0 %)	11(8 %)
	Withdrawal By Subject	1(2 %)	1(2 %)	0(0 %)	0(0 %)	2(1 %)
PP	Enrolled	12(100 %)	17(100 %)	22(100 %)	20(100 %)	71(100 %)
	Completed	10(83 %)	9(53 %)	19(86 %)	20(100 %)	58(82 %)
	Discontinued Early	2(17 %)	8(47 %)	3(14 %)	0(0 %)	13(18 %)
	Adverse Event	0(0 %)	1(6 %)	0(0 %)	0(0 %)	1(1 %)
	Lost To Follow-Up	0(0 %)	1(6 %)	3(14 %)	0(0 %)	4(6 %)
	Non-Compliance With Study	1(8 %)	5(29 %)	0(0 %)	0(0 %)	6(8 %)
	Withdrawal By Subject	1(8 %)	1(6 %)	0(0 %)	0(0 %)	2(3 %)

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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Table 14.1.2 Demographic Summary (Safety, ITT, and PP Populations)

		Study Product Group					
Population	Trait		VLN	VLN	UB	UB	Overall
			Non-Mentholated	Mentholated	Non-Mentholated	Mentholated	
Safety	Sex	Female	19 (38.0%)	22 (44.0%)	9 (40.9%)	10 (50.0%)	60 (42.3%)
		Male	31 (62.0%)	28 (56.0%)	13 (59.1%)	10 (50.0%)	82 (57.7%)
	Race	American Indian or Alaska Native	1 (2.0%)	1 (2.0%)	0 (0%)	0 (0%)	2 (1.4%)
		Asian	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		Black or African American	3 (6.0%)	29 (58.0%)	2 (9.1%)	12 (60.0%)	46 (32.4%)
		Multiple	1 (2.0%)	2 (4.0%)	1 (4.5%)	0 (0%)	4 (2.8%)
		Other	1 (2.0%)	0 (0%)	1 (4.5%)	0 (0%)	2 (1.4%)
		White	44 (88.0%)	17 (34.0%)	18 (81.8%)	8 (40.0%)	87 (61.3%)
	Ethnicity	Hispanic or Latino	1 (2.0%)	1 (2.0%)	1 (4.5%)	1 (5.0%)	4 (2.8%)
		Not Hispanic or Latino	49 (98.0%)	49 (98.0%)	21 (95.5%)	19 (95.0%)	138 (97.2%)
	Age* (yrs)	n	50	50	22	20	142
		Mean	45.9	40.5	45.8	42.7	43.5
		SD	10.85	9.34	12.39	10.82	10.76
		Minimum	29	26	26	26	26
		Median	45.0	39.0	50.0	41.0	42.0
		Maximum	65	60	60	59	65
	Weight (kg)	n	50	50	22	20	142
		Mean	86.76	83.53	84.37	89.33	85.61
		SD	17.579	14.118	18.462	17.657	16.542
		Minimum	54.3	54.8	54.7	56.7	54.3
		Median	85.30	81.95	83.10	86.50	84.30
		Maximum	118.7	114.2	125.1	122.8	125.1

Note: * Age is derived from birth date to date of informed consent, BMI = Body Mass Index
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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Table 14.1.2 Demographic Summary (Safety, ITT, and PP Populations)

		Study Product Group					
		-----		-----			
Population	Trait	VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	Overall	
Safety	Height (cm)	n	50	50	22	20	142
		Mean	172.20	172.63	172.13	170.41	172.09
		SD	9.549	7.836	9.077	11.670	9.174
		Minimum	154.4	154.0	151.0	149.7	149.7
		Median	173.00	172.20	175.00	168.00	172.65
		Maximum	188.5	191.2	186.0	196.8	196.8
	BMI (kg/m²)	n	50	50	22	20	142
		Mean	29.24	27.95	28.35	30.78	28.87
		SD	5.442	3.939	5.075	5.459	4.944
		Minimum	19.2	20.6	19.3	21.9	19.2
		Median	29.15	27.70	27.50	30.15	28.05
		Maximum	39.8	37.7	39.0	40.0	40.0

Note: * Age is derived from birth date to date of informed consent, BMI = Body Mass Index
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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Table 14.1.2 Demographic Summary (Safety, ITT, and PP Populations)

		Study Product Group					
Population	Trait		VLN	VLN	UB	UB	Overall
			Non-Mentholated	Mentholated	Non-Mentholated	Mentholated	
ITT	Sex	Female	19 (38.0%)	22 (44.0%)	9 (40.9%)	10 (50.0%)	60 (42.3%)
		Male	31 (62.0%)	28 (56.0%)	13 (59.1%)	10 (50.0%)	82 (57.7%)
	Race	American Indian or Alaska Native	1 (2.0%)	1 (2.0%)	0 (0%)	0 (0%)	2 (1.4%)
		Asian	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		Black or African American	3 (6.0%)	29 (58.0%)	2 (9.1%)	12 (60.0%)	46 (32.4%)
		Multiple	1 (2.0%)	2 (4.0%)	1 (4.5%)	0 (0%)	4 (2.8%)
		Other	1 (2.0%)	0 (0%)	1 (4.5%)	0 (0%)	2 (1.4%)
		White	44 (88.0%)	17 (34.0%)	18 (81.8%)	8 (40.0%)	87 (61.3%)
	Ethnicity	Hispanic or Latino	1 (2.0%)	1 (2.0%)	1 (4.5%)	1 (5.0%)	4 (2.8%)
		Not Hispanic or Latino	49 (98.0%)	49 (98.0%)	21 (95.5%)	19 (95.0%)	138 (97.2%)
	Age* (yrs)	n	50	50	22	20	142
		Mean	45.9	40.5	45.8	42.7	43.5
		SD	10.85	9.34	12.39	10.82	10.76
		Minimum	29	26	26	26	26
		Median	45.0	39.0	50.0	41.0	42.0
		Maximum	65	60	60	59	65
	Weight (kg)	n	50	50	22	20	142
		Mean	86.76	83.53	84.37	89.33	85.61
		SD	17.579	14.118	18.462	17.657	16.542
		Minimum	54.3	54.8	54.7	56.7	54.3
		Median	85.30	81.95	83.10	86.50	84.30
		Maximum	118.7	114.2	125.1	122.8	125.1

Note: * Age is derived from birth date to date of informed consent, BMI = Body Mass Index
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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Table 14.1.2 Demographic Summary (Safety, ITT, and PP Populations)

		Study Product Group					
Population	Trait	VLN		UB		Overall	
		Non-Mentholated	Mentholated	Non-Mentholated	Mentholated		
ITT	Height (cm)	n	50	50	22	20	142
		Mean	172.20	172.63	172.13	170.41	172.09
		SD	9.549	7.836	9.077	11.670	9.174
		Minimum	154.4	154.0	151.0	149.7	149.7
		Median	173.00	172.20	175.00	168.00	172.65
		Maximum	188.5	191.2	186.0	196.8	196.8
	BMI (kg/m²)	n	50	50	22	20	142
		Mean	29.24	27.95	28.35	30.78	28.87
		SD	5.442	3.939	5.075	5.459	4.944
		Minimum	19.2	20.6	19.3	21.9	19.2
		Median	29.15	27.70	27.50	30.15	28.05
		Maximum	39.8	37.7	39.0	40.0	40.0

Note: * Age is derived from birth date to date of informed consent, BMI = Body Mass Index
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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Table 14.1.2 Demographic Summary (Safety, ITT, and PP Populations)

		Study Product Group					
Population	Trait		VLN	VLN	UB	UB	Overall
			Non-Mentholated	Mentholated	Non-Mentholated	Mentholated	
PP	Sex	Female	5 (41.7%)	6 (35.3%)	9 (40.9%)	10 (50.0%)	30 (42.3%)
		Male	7 (58.3%)	11 (64.7%)	13 (59.1%)	10 (50.0%)	41 (57.7%)
	Race	Black or African American	2 (16.7%)	9 (52.9%)	2 (9.1%)	12 (60.0%)	25 (35.2%)
		Multiple	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (1.4%)
		Other	1 (8.3%)	0 (0%)	1 (4.5%)	0 (0%)	2 (2.8%)
		White	9 (75.0%)	8 (47.1%)	18 (81.8%)	8 (40.0%)	43 (60.6%)
	Ethnicity	Hispanic or Latino	1 (8.3%)	0 (0%)	1 (4.5%)	1 (5.0%)	3 (4.2%)
		Not Hispanic or Latino	11 (91.7%)	17 (100%)	21 (95.5%)	19 (95.0%)	68 (95.8%)
	Age* (yrs)	n	12	17	22	20	71
		Mean	50.5	41.6	45.8	42.7	44.7
		SD	13.86	9.91	12.39	10.82	11.83
		Minimum	29	28	26	26	26
		Median	55.0	42.0	50.0	41.0	45.0
		Maximum	65	59	60	59	65
	Weight (kg)	n	12	17	22	20	71
		Mean	84.44	83.52	84.37	89.33	85.58
		SD	15.766	16.302	18.462	17.657	17.100
		Minimum	57.0	62.3	54.7	56.7	54.7
		Median	83.80	80.00	83.10	86.50	84.20
		Maximum	118.6	114.2	125.1	122.8	125.1

Note: * Age is derived from birth date to date of informed consent, BMI = Body Mass Index
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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Table 14.1.2 Demographic Summary (Safety, ITT, and PP Populations)

		Study Product Group					
		-----		-----			
Population	Trait	VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	Overall	

PP	Height (cm)	n	12	17	22	20	71
		Mean	170.57	174.43	172.13	170.41	171.93
		SD	9.728	8.387	9.077	11.670	9.754
		Minimum	155.7	162.4	151.0	149.7	149.7
		Median	172.00	174.80	175.00	168.00	172.50
		Maximum	182.0	191.2	186.0	196.8	196.8
	BMI (kg/m²)	n	12	17	22	20	71
		Mean	29.18	27.28	28.35	30.78	28.92
		SD	5.844	3.825	5.075	5.459	5.127
		Minimum	22.2	21.8	19.3	21.9	19.3
		Median	27.30	26.90	27.50	30.15	27.80
		Maximum	39.6	33.0	39.0	40.0	40.0

Note: * Age is derived from birth date to date of informed consent, BMI = Body Mass Index
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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Table 14.1.3 Tobacco/Nicotine Product Use History Summary (Safety, ITT, and PP Populations)

Population	Trait		Study Product Group				Overall
			VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	
Safety	Brand-Style	CAMEL-BLUE	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		CAMEL-CRUSH (POPPED)	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		CAMEL-CRUSH SILVER (POPPED)	0 (0%)	3 (6.0%)	0 (0%)	1 (5.0%)	4 (2.8%)
		CAMEL-FILTERS	1 (2.0%)	0 (0%)	2 (9.1%)	0 (0%)	3 (2.1%)
		CROWNS-GOLD	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		DORAL-SILVER	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (0.7%)
		EAGLE 20S-RED	5 (10.0%)	0 (0%)	2 (9.1%)	0 (0%)	7 (4.9%)
		EDGEFIELD-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		KAMEL RED-GENUINE ORIGINAL	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (0.7%)
		KOOL-BLUE	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		L&M-GREEN	0 (0%)	1 (2.0%)	0 (0%)	1 (5.0%)	2 (1.4%)
		L&M-RED	2 (4.0%)	0 (0%)	0 (0%)	0 (0%)	2 (1.4%)
		LD-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		MARLBORO-BLACK	3 (6.0%)	1 (2.0%)	3 (13.6%)	0 (0%)	7 (4.9%)
		MARLBORO-EIGHTY-THREES	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		MARLBORO-GOLD	9 (18.0%)	0 (0%)	1 (4.5%)	1 (5.0%)	11 (7.7%)
		MARLBORO-GREEN	0 (0%)	2 (4.0%)	0 (0%)	0 (0%)	2 (1.4%)
		MARLBORO-ICE	0 (0%)	2 (4.0%)	0 (0%)	0 (0%)	2 (1.4%)
		MARLBORO-RED	5 (10.0%)	0 (0%)	3 (13.6%)	0 (0%)	8 (5.6%)
		MARLBORO-SILVER	0 (0%)	1 (2.0%)	1 (4.5%)	0 (0%)	2 (1.4%)
		MARLBORO-SMOOTH	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (0.7%)
		MARLBORO-SPECIAL BLEND GOLD	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		MARLBORO-SPECIAL BLEND RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		MARLBORO-SPECIAL SELECT	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (0.7%)

Note: CPD = Cigarettes per day
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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Table 14.1.3 Tobacco/Nicotine Product Use History Summary (Safety, ITT, and PP Populations)

Population	Trait		Study Product Group				Overall
			VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	
Safety	Brand-Style	MARLBORO-SPECIAL SELECT RED	1 (2.0%)	0 (0%)	3 (13.6%)	0 (0%)	4 (2.8%)
		MAVERICK-FULL FLAVOR	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		NATURAL AMERICAN	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		SPIRIT-GREEN					
		NATURAL AMERICAN	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		SPIRIT-TURQUIOSE					
		NEWPORT-GREEN	0 (0%)	26 (52.0%)	0 (0%)	13 (65.0%)	39 (27.5%)
		NEWPORT-RED	3 (6.0%)	0 (0%)	1 (4.5%)	0 (0%)	4 (2.8%)
		OLD GOLD-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		PALL MALL-BLACK	0 (0%)	2 (4.0%)	0 (0%)	0 (0%)	2 (1.4%)
		PALL MALL-GREEN	0 (0%)	6 (12.0%)	0 (0%)	1 (5.0%)	7 (4.9%)
		PALL MALL-ORANGE	2 (4.0%)	0 (0%)	1 (4.5%)	0 (0%)	3 (2.1%)
		PALL MALL-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		PALL MALL-SILVER	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (0.7%)
		PARLIAMENT-BLUE	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		PYRAMID-BLUE	2 (4.0%)	0 (0%)	0 (0%)	0 (0%)	2 (1.4%)
		PYRAMID-GOLD	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		SALEM-GOLD	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		SALEM-GREEN	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (0.7%)
		TIMELESS-SILVER	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		USA GOLD-GOLD	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (0.7%)
		USA GOLD-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		WAVE-BLUE	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		WILDHORSE-GOLD	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		WILDHORSE-RED	2 (4.0%)	0 (0%)	1 (4.5%)	0 (0%)	3 (2.1%)
	Flavor	MENTHOL	0 (0%)	50 (100%)	0 (0%)	20 (100%)	70 (49.3%)

Note: CPD = Cigarettes per day
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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Table 14.1.3 Tobacco/Nicotine Product Use History Summary (Safety, ITT, and PP Populations)

Population	Trait		Study Product Group				Overall
			VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	
Safety	Flavor	NON-MENTHOL	50 (100%)	0 (0%)	22 (100%)	0 (0%)	72 (50.7%)
	Size	KING	50 (100%)	50 (100%)	22 (100%)	20 (100%)	142 (100%)
	Duration (yrs)	n	50	50	22	20	142
		Mean	26.8	17.2	28.9	19.9	22.8
		SD	12.20	8.04	12.66	10.92	11.74
		Minimum	5	5	8	5	5
		Median	25.5	16.0	29.0	17.5	20.0
		Maximum	50	42	50	41	50
	CPD	n	50	50	22	20	142
		Mean	19.8	15.4	18.2	17.1	17.6
		SD	6.92	6.19	3.85	6.16	6.39
		Minimum	10	10	10	10	10
		Median	20.0	15.0	19.5	16.0	16.5
		Maximum	40	40	25	30	40

Note: CPD = Cigarettes per day
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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Table 14.1.3 Tobacco/Nicotine Product Use History Summary (Safety, ITT, and PP Populations)

Population	Trait		Study Product Group				Overall
			VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	
ITT	Brand-Style	CAMEL-BLUE	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		CAMEL-CRUSH (POPPED)	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		CAMEL-CRUSH SILVER (POPPED)	0 (0%)	3 (6.0%)	0 (0%)	1 (5.0%)	4 (2.8%)
		CAMEL-FILTERS	1 (2.0%)	0 (0%)	2 (9.1%)	0 (0%)	3 (2.1%)
		CROWNS-GOLD	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		DORAL-SILVER	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (0.7%)
		EAGLE 20S-RED	5 (10.0%)	0 (0%)	2 (9.1%)	0 (0%)	7 (4.9%)
		EDGEFIELD-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		KAMEL RED-GENUINE ORIGINAL	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (0.7%)
		KOOL-BLUE	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)
		L&M-GREEN	0 (0%)	1 (2.0%)	0 (0%)	1 (5.0%)	2 (1.4%)
		L&M-RED	2 (4.0%)	0 (0%)	0 (0%)	0 (0%)	2 (1.4%)
		LD-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		MARLBORO-BLACK	3 (6.0%)	1 (2.0%)	3 (13.6%)	0 (0%)	7 (4.9%)
		MARLBORO-EIGHTY-THREES	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		MARLBORO-GOLD	9 (18.0%)	0 (0%)	1 (4.5%)	1 (5.0%)	11 (7.7%)
		MARLBORO-GREEN	0 (0%)	2 (4.0%)	0 (0%)	0 (0%)	2 (1.4%)
		MARLBORO-ICE	0 (0%)	2 (4.0%)	0 (0%)	0 (0%)	2 (1.4%)
		MARLBORO-RED	5 (10.0%)	0 (0%)	3 (13.6%)	0 (0%)	8 (5.6%)
		MARLBORO-SILVER	0 (0%)	1 (2.0%)	1 (4.5%)	0 (0%)	2 (1.4%)
		MARLBORO-SMOOTH	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (0.7%)
		MARLBORO-SPECIAL BLEND GOLD	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		MARLBORO-SPECIAL BLEND RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
		MARLBORO-SPECIAL SELECT	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (0.7%)

Note: CPD = Cigarettes per day
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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Table 14.1.3 Tobacco/Nicotine Product Use History Summary (Safety, ITT, and PP Populations)

Population	Trait		Study Product Group				Overall		
			VLN		UB				
			Non-Mentholated	Mentholated	Non-Mentholated	Mentholated			
ITT	Brand-Style	MARLBORO-SPECIAL SELECT RED	1 (2.0%)	0 (0%)	3 (13.6%)	0 (0%)	4 (2.8%)		
		MAVERICK-FULL FLAVOR	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)		
		NATURAL AMERICAN SPIRIT-GREEN	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)		
		NATURAL AMERICAN SPIRIT-TURQUIOSE	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)		
		NEWPORT-GREEN	0 (0%)	26 (52.0%)	0 (0%)	13 (65.0%)	39 (27.5%)		
		NEWPORT-RED	3 (6.0%)	0 (0%)	1 (4.5%)	0 (0%)	4 (2.8%)		
		OLD GOLD-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)		
		PALL MALL-BLACK	0 (0%)	2 (4.0%)	0 (0%)	0 (0%)	2 (1.4%)		
		PALL MALL-GREEN	0 (0%)	6 (12.0%)	0 (0%)	1 (5.0%)	7 (4.9%)		
		PALL MALL-ORANGE	2 (4.0%)	0 (0%)	1 (4.5%)	0 (0%)	3 (2.1%)		
		PALL MALL-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)		
		PALL MALL-SILVER	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (0.7%)		
		PARLIAMENT-BLUE	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)		
		PYRAMID-BLUE	2 (4.0%)	0 (0%)	0 (0%)	0 (0%)	2 (1.4%)		
		PYRAMID-GOLD	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)		
		SALEM-GOLD	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)	1 (0.7%)		
		SALEM-GREEN	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (0.7%)		
		TIMELESS-SILVER	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)		
		USA GOLD-GOLD	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (0.7%)		
		USA GOLD-RED	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)		
		WAVE-BLUE	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)		
		WILDHORSE-GOLD	1 (2.0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)		
		WILDHORSE-RED	2 (4.0%)	0 (0%)	1 (4.5%)	0 (0%)	3 (2.1%)		
			Flavor	MENTHOL	0 (0%)	50 (100%)	0 (0%)	20 (100%)	70 (49.3%)

Note: CPD = Cigarettes per day
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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Table 14.1.3 Tobacco/Nicotine Product Use History Summary (Safety, ITT, and PP Populations)

Population	Trait		Study Product Group				Overall
			VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	
ITT	Flavor	NON-MENTHOL	50 (100%)	0 (0%)	22 (100%)	0 (0%)	72 (50.7%)
	Size	KING	50 (100%)	50 (100%)	22 (100%)	20 (100%)	142 (100%)
	Duration (yrs)	n	50	50	22	20	142
		Mean	26.8	17.2	28.9	19.9	22.8
		SD	12.20	8.04	12.66	10.92	11.74
		Minimum	5	5	8	5	5
		Median	25.5	16.0	29.0	17.5	20.0
		Maximum	50	42	50	41	50
	CPD	n	50	50	22	20	142
		Mean	19.8	15.4	18.2	17.1	17.6
		SD	6.92	6.19	3.85	6.16	6.39
		Minimum	10	10	10	10	10
		Median	20.0	15.0	19.5	16.0	16.5
		Maximum	40	40	25	30	40

Note: CPD = Cigarettes per day
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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Table 14.1.3 Tobacco/Nicotine Product Use History Summary (Safety, ITT, and PP Populations)

Population	Trait		Study Product Group				Overall
			VLN		UB		
			Non-Mentholated	Mentholated	Non-Mentholated	Mentholated	
PP	Brand-Style	CAMEL-CRUSH SILVER (POPPED)	0 (0%)	2 (11.8%)	0 (0%)	1 (5.0%)	3 (4.2%)
		CAMEL-FILTERS	0 (0%)	0 (0%)	2 (9.1%)	0 (0%)	2 (2.8%)
		CROWNS-GOLD	1 (8.3%)	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)
		DORAL-SILVER	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (1.4%)
		EAGLE 20S-RED	2 (16.7%)	0 (0%)	2 (9.1%)	0 (0%)	4 (5.6%)
		EDGEFIELD-RED	1 (8.3%)	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)
		KAMEL RED-GENUINE ORIGINAL	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (1.4%)
		L&M-GREEN	0 (0%)	1 (5.9%)	0 (0%)	1 (5.0%)	2 (2.8%)
		MARLBORO-BLACK	1 (8.3%)	0 (0%)	3 (13.6%)	0 (0%)	4 (5.6%)
		MARLBORO-GOLD	1 (8.3%)	0 (0%)	1 (4.5%)	1 (5.0%)	3 (4.2%)
		MARLBORO-ICE	0 (0%)	1 (5.9%)	0 (0%)	0 (0%)	1 (1.4%)
		MARLBORO-RED	1 (8.3%)	0 (0%)	3 (13.6%)	0 (0%)	4 (5.6%)
		MARLBORO-SILVER	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (1.4%)
		MARLBORO-SMOOTH	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (1.4%)
		MARLBORO-SPECIAL BLEND GOLD	1 (8.3%)	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)
		MARLBORO-SPECIAL SELECT	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (1.4%)
		MARLBORO-SPECIAL SELECT RED	0 (0%)	0 (0%)	3 (13.6%)	0 (0%)	3 (4.2%)
		MAVERICK-FULL FLAVOR	0 (0%)	1 (5.9%)	0 (0%)	0 (0%)	1 (1.4%)
		NATURAL AMERICAN	0 (0%)	1 (5.9%)	0 (0%)	0 (0%)	1 (1.4%)
		SPIRIT-GREEN	0 (0%)	6 (35.3%)	0 (0%)	13 (65.0%)	19 (26.8%)
		NEWPORT-GREEN	1 (8.3%)	0 (0%)	1 (4.5%)	0 (0%)	2 (2.8%)
		NEWPORT-RED	0 (0%)	1 (5.9%)	0 (0%)	0 (0%)	1 (1.4%)
		PALL MALL-BLACK	0 (0%)	4 (23.5%)	0 (0%)	1 (5.0%)	5 (7.0%)
		PALL MALL-GREEN					

Note: CPD = Cigarettes per day
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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Table 14.1.3 Tobacco/Nicotine Product Use History Summary (Safety, ITT, and PP Populations)

Population	Trait		Study Product Group				Overall
			VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	
PP	Brand-Style	PALL MALL-ORANGE	1 (8.3%)	0 (0%)	1 (4.5%)	0 (0%)	2 (2.8%)
		PALL MALL-SILVER	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (1.4%)
		SALEM-GREEN	0 (0%)	0 (0%)	0 (0%)	1 (5.0%)	1 (1.4%)
		TIMELESS-SILVER	1 (8.3%)	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)
		USA GOLD-GOLD	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (1.4%)
		WILDHORSE-GOLD	1 (8.3%)	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)
		WILDHORSE-RED	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	1 (1.4%)
	Flavor	MENTHOL	0 (0%)	17 (100%)	0 (0%)	20 (100%)	37 (52.1%)
		NON-MENTHOL	12 (100%)	0 (0%)	22 (100%)	0 (0%)	34 (47.9%)
	Size	KING	12 (100%)	17 (100%)	22 (100%)	20 (100%)	71 (100%)
	Duration (yrs)	n	12	17	22	20	71
		Mean	32.1	16.8	28.9	19.9	24.0
		SD	14.33	9.02	12.66	10.92	12.95
		Minimum	8	6	8	5	5
		Median	35.5	15.0	29.0	17.5	21.0
		Maximum	50	40	50	41	50
	CPD	n	12	17	22	20	71
		Mean	17.8	15.2	18.2	17.1	17.1
		SD	6.73	5.87	3.85	6.16	5.57
		Minimum	10	10	10	10	10
		Median	16.0	14.0	19.5	16.0	15.0
		Maximum	30	36	25	30	36

Note: CPD = Cigarettes per day
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 ITT = Intent-to-treat (ITT) population, PP = Per-protocol (PP) population

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14.2 Pharmacokinetic and Pharmacodynamic Data Summary Tables and Figures

14.2.1 Product Use Tables

- Table 14.2.1.1.1.1 Summary of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (PP Population)
- Table 14.2.1.1.1.2 Summary of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (ITT Population)
- Table 14.2.1.1.2 Statistical Comparison of Number of Cigarettes Smoked per Day at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
- Table 14.2.1.1.3 Statistical Comparison of Number of Cigarettes Smoked per Day Among Study Product Groups at Weeks 2 and 6 (PP Population)
- Table 14.2.1.1.4 Statistical Comparison of Number of Cigarettes Smoked per Day at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)
- Table 14.2.1.1.5 Statistical Comparison of Number of Cigarettes Smoked per Day Among Study Product Groups at Weeks 2 and 6 (ITT Population)
- Table 14.2.1.2.1.1 Summary of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (PP Population)
- Table 14.2.1.2.1.2 Summary of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (ITT Population)

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Table 14.2.1.1.1.1 Summary of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (PP Population)

Study Week	Statistics	Study Product Group											
		VLN Mentholated		VLN Non-Mentholated		VLN Combined		UB Mentholated		UB Non-Mentholated		UB Combined	
		Non-VLN	VLN	Non-VLN	VLN	Non-VLN	VLN	Non-UB	UB	Non-UB	UB	Non-UB	UB
Week -1*	n	17	17	12	12	29	29	20	20	22	22	42	42
	Mean	0.11	14.75	0.18	17.19	0.14	15.76	0.21	16.29	0.29	16.80	0.25	16.55
	SD	0.366	6.198	0.625	4.727	0.481	5.676	0.705	5.809	0.678	4.015	0.684	4.895
	CV (%)	348.5	42.0	346.4	27.5	353.2	36.0	340.4	35.7	233.0	23.9	272.4	29.6
	SEM	0.089	1.503	0.181	1.365	0.089	1.054	0.158	1.299	0.145	0.856	0.106	0.755
	Minimum	0.0	7.0	0.0	10.0	0.0	7.0	0.0	10.0	0.0	10.0	0.0	10.0
	Median	0.00	13.83	0.00	16.33	0.00	15.14	0.00	14.64	0.00	16.14	0.00	15.29
	Maximum	2.0	29.0	2.0	26.0	2.0	29.0	3.0	33.0	2.0	24.0	3.0	33.0
Week 1	n	17	17	12	12	29	29	20	20	22	22	42	42
	Mean	0.16	14.73	0.48	24.08	0.29	18.60	0.02	15.79	0.10	17.33	0.06	16.60
	SD	0.464	7.724	0.829	8.863	0.647	9.322	0.052	4.638	0.327	4.528	0.240	4.591
	CV (%)	285.3	52.4	172.7	36.8	220.0	50.1	244.2	29.4	325.3	26.1	382.0	27.7
	SEM	0.112	1.873	0.239	2.558	0.120	1.731	0.012	1.037	0.070	0.965	0.037	0.708
	Minimum	0.0	3.0	0.0	14.0	0.0	3.0	0.0	9.0	0.0	10.0	0.0	9.0
	Median	0.00	12.71	0.07	26.54	0.00	15.29	0.00	16.43	0.00	17.07	0.00	16.43
	Maximum	2.0	34.0	3.0	43.0	3.0	43.0	0.0	25.0	2.0	26.0	2.0	26.0

Note: Cigarettes per Day were calculated as the average cigarettes smoked per day in each week.

* Subjects used their own usual brand cigarettes at Week -1. UB and Non-UB cigarettes were reported for all subjects on Week -1.

VLN non-mentholated = Non-mentholated VLN cigarettes

VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.1.1.1 Summary of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (PP Population)

Study Week	Statistics	Study Product Group											
		VLN Mentholated		VLN Non-Mentholated		VLN Combined		UB Mentholated		UB Non-Mentholated		UB Combined	
		Non-VLN	VLN	Non-VLN	VLN	Non-VLN	VLN	Non-UB	UB	Non-UB	UB	Non-UB	UB
Week 2	n	15	15	11	11	26	26	20	20	22	22	42	42
	Mean	0.39	15.66	0.35	23.32	0.38	18.90	0.03	15.47	0.36	16.17	0.20	15.84
	SD	1.387	7.860	0.891	9.717	1.181	9.341	0.088	4.425	1.404	4.475	1.020	4.411
	CV (%)	352.6	50.2	254.0	41.7	314.7	49.4	307.8	28.6	391.7	27.7	506.8	27.9
	SEM	0.358	2.029	0.269	2.930	0.232	1.832	0.020	0.990	0.299	0.954	0.157	0.681
	Minimum	0.0	6.0	0.0	9.0	0.0	6.0	0.0	9.0	0.0	9.0	0.0	9.0
	Median	0.00	14.00	0.00	23.14	0.00	17.36	0.00	15.36	0.00	16.29	0.00	15.86
	Maximum	5.0	33.0	3.0	38.0	5.0	38.0	0.0	25.0	7.0	25.0	7.0	25.0
Week 3	n	12	12	11	11	23	23	20	20	20	20	40	40
	Mean	0.38	15.12	0.62	21.60	0.50	18.22	0.02	15.52	0.30	16.95	0.16	16.24
	SD	1.147	8.229	1.515	10.100	1.310	9.550	0.052	5.469	0.846	4.600	0.608	5.040
	CV (%)	301.0	54.4	243.0	46.8	263.6	52.4	244.2	35.2	281.9	27.1	378.3	31.0
	SEM	0.331	2.375	0.457	3.045	0.273	1.991	0.012	1.223	0.189	1.029	0.096	0.797
	Minimum	0.0	0.0	0.0	4.0	0.0	0.0	0.0	9.0	0.0	10.0	0.0	9.0
	Median	0.00	13.07	0.00	20.14	0.00	15.57	0.00	14.64	0.00	16.79	0.00	16.21
	Maximum	4.0	30.0	5.0	41.0	5.0	41.0	0.0	28.0	4.0	27.0	4.0	28.0

Note: Cigarettes per Day were calculated as the average cigarettes smoked per day in each week.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.1.1.1 Summary of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (PP Population)

Study Week	Statistics	Study Product Group											
		VLN Mentholated		VLN Non-Mentholated		VLN Combined		UB Mentholated		UB Non-Mentholated		UB Combined	
		Non-VLN	VLN	Non-VLN	VLN	Non-VLN	VLN	Non-UB	UB	Non-UB	UB	Non-UB	UB
Week 4	n	11	11	11	11	22	22	20	20	20	20	40	40
	Mean	0.05	14.48	0.68	21.66	0.36	18.07	0.19	15.49	0.55	16.84	0.37	16.16
	SD	0.116	5.801	1.284	9.807	0.945	8.678	0.708	5.429	1.171	4.874	0.973	5.137
	CV (%)	222.5	40.0	190.2	45.3	260.0	48.0	381.0	35.0	212.9	28.9	264.4	31.8
	SEM	0.035	1.749	0.387	2.957	0.202	1.850	0.158	1.214	0.262	1.090	0.154	0.812
	Minimum	0.0	8.0	0.0	8.0	0.0	8.0	0.0	8.0	0.0	7.0	0.0	7.0
	Median	0.00	13.29	0.00	19.14	0.00	17.50	0.00	15.00	0.00	17.14	0.00	15.64
	Maximum	0.0	28.0	4.0	42.0	4.0	42.0	3.0	27.0	3.0	26.0	3.0	27.0
Week 5	n	10	10	11	11	21	21	20	20	20	20	40	40
	Mean	0.03	12.22	0.35	21.34	0.20	17.00	0.01	15.80	1.29	17.85	0.65	16.83
	SD	0.090	4.093	0.724	9.091	0.541	8.403	0.032	6.214	5.675	5.464	4.014	5.868
	CV (%)	316.2	33.5	207.9	42.6	275.9	49.4	447.2	39.3	439.5	30.6	618.3	34.9
	SEM	0.029	1.294	0.218	2.741	0.118	1.834	0.007	1.389	1.269	1.222	0.635	0.928
	Minimum	0.0	7.0	0.0	4.0	0.0	4.0	0.0	8.0	0.0	8.0	0.0	8.0
	Median	0.00	11.14	0.00	18.71	0.00	16.00	0.00	15.14	0.00	17.43	0.00	16.14
	Maximum	0.0	19.0	2.0	37.0	2.0	37.0	0.0	32.0	25.0	34.0	25.0	34.0

Note: Cigarettes per Day were calculated as the average cigarettes smoked per day in each week.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.1.1.1 Summary of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (PP Population)

Study Week	Statistics	Study Product Group											
		VLN Mentholated		VLN Non-Mentholated		VLN Combined		UB Mentholated		UB Non-Mentholated		UB Combined	
		Non-VLN	VLN	Non-VLN	VLN	Non-VLN	VLN	Non-UB	UB	Non-UB	UB	Non-UB	UB
Week 6	n	10	10	11	11	21	21	20	20	20	20	40	40
	Mean	0.04	14.43	0.37	21.20	0.21	17.98	0.04	14.69	0.04	15.89	0.04	15.29
	SD	0.136	9.435	0.762	8.219	0.571	9.265	0.160	4.877	0.133	5.356	0.145	5.092
	CV (%)	316.2	65.4	206.8	38.8	267.6	51.5	447.2	33.2	301.9	33.7	363.9	33.3
	SEM	0.043	2.984	0.230	2.478	0.125	2.022	0.036	1.091	0.030	1.198	0.023	0.805
	Minimum	0.0	7.0	0.0	9.0	0.0	7.0	0.0	7.0	0.0	0.0	0.0	0.0
	Median	0.00	10.56	0.00	21.14	0.00	17.71	0.00	14.71	0.00	16.85	0.00	15.43
	Maximum	0.0	39.0	2.0	35.0	2.0	39.0	1.0	24.0	1.0	24.0	1.0	24.0

Note: Cigarettes per Day were calculated as the average cigarettes smoked per day in each week.
 VLN non-mentholated = Non-mentholated VLN cigarettes
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 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.1.1.2 Summary of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	Study Product Group											
		VLN Mentholated		VLN Non-Mentholated		VLN Combined		UB Mentholated		UB Non-Mentholated		UB Combined	
		Non-VLN	VLN	Non-VLN	VLN	Non-VLN	VLN	Non-UB	UB	Non-UB	UB	Non-UB	UB
Week -1*	n	50	50	50	50	100	100	20	20	22	22	42	42
	Mean	0.10	14.75	0.22	17.94	0.16	16.35	0.21	16.29	0.29	16.80	0.25	16.55
	SD	0.345	5.605	0.698	5.472	0.551	5.739	0.705	5.809	0.678	4.015	0.684	4.895
	CV (%)	335.4	38.0	317.5	30.5	341.5	35.1	340.4	35.7	233.0	23.9	272.4	29.6
	SEM	0.049	0.793	0.099	0.774	0.055	0.574	0.158	1.299	0.145	0.856	0.106	0.755
	Minimum	0.0	7.0	0.0	8.0	0.0	7.0	0.0	10.0	0.0	10.0	0.0	10.0
	Median	0.00	14.00	0.00	17.43	0.00	15.29	0.00	14.64	0.00	16.14	0.00	15.29
	Maximum	2.0	33.0	3.0	39.0	3.0	39.0	3.0	33.0	2.0	24.0	3.0	33.0
Week 1	n	50	50	50	50	100	100	20	20	22	22	42	42
	Mean	0.46	14.62	0.49	22.02	0.48	18.32	0.02	15.79	0.10	17.33	0.06	16.60
	SD	0.815	7.942	0.911	9.531	0.860	9.488	0.052	4.638	0.327	4.528	0.240	4.591
	CV (%)	177.9	54.3	185.0	43.3	181.0	51.8	244.2	29.4	325.3	26.1	382.0	27.7
	SEM	0.115	1.123	0.129	1.348	0.086	0.949	0.012	1.037	0.070	0.965	0.037	0.708
	Minimum	0.0	1.0	0.0	6.0	0.0	1.0	0.0	9.0	0.0	10.0	0.0	9.0
	Median	0.00	12.69	0.00	22.43	0.00	15.64	0.00	16.43	0.00	17.07	0.00	16.43
	Maximum	3.0	46.0	4.0	60.0	4.0	60.0	0.0	25.0	2.0	26.0	2.0	26.0

Note: Cigarettes per Day were calculated as the average cigarettes smoked per day in each week.

* Subjects used their own usual brand cigarettes at Week -1. UB and Non-UB cigarettes were reported for all subjects on Week -1.

VLN non-mentholated = Non-mentholated VLN cigarettes

VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.1.1.2 Summary of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	Study Product Group											
		VLN Mentholated		VLN Non-Mentholated		VLN Combined		UB Mentholated		UB Non-Mentholated		UB Combined	
		Non-VLN	VLN	Non-VLN	VLN	Non-VLN	VLN	Non-UB	UB	Non-UB	UB	Non-UB	UB
Week 2	n	48	48	49	49	97	97	20	20	22	22	42	42
	Mean	0.53	14.63	0.68	19.11	0.61	16.89	0.03	15.47	0.36	16.17	0.20	15.84
	SD	1.098	6.687	1.346	8.250	1.225	7.810	0.088	4.425	1.404	4.475	1.020	4.411
	CV (%)	207.7	45.7	197.8	43.2	202.4	46.2	307.8	28.6	391.7	27.7	506.8	27.9
	SEM	0.158	0.965	0.192	1.179	0.124	0.793	0.020	0.990	0.299	0.954	0.157	0.681
	Minimum	0.0	2.0	0.0	4.0	0.0	2.0	0.0	9.0	0.0	9.0	0.0	9.0
	Median	0.00	14.00	0.00	18.29	0.00	16.14	0.00	15.36	0.00	16.29	0.00	15.86
	Maximum	5.0	33.0	7.0	47.0	7.0	47.0	0.0	25.0	7.0	25.0	7.0	25.0
Week 3	n	45	45	49	49	94	94	20	20	20	20	40	40
	Mean	0.34	12.70	1.04	16.84	0.71	14.86	0.02	15.52	0.30	16.95	0.16	16.24
	SD	0.842	5.613	2.875	8.048	2.174	7.257	0.052	5.469	0.846	4.600	0.608	5.040
	CV (%)	249.0	44.2	275.3	47.8	307.9	48.8	244.2	35.2	281.9	27.1	378.3	31.0
	SEM	0.126	0.837	0.411	1.150	0.224	0.749	0.012	1.223	0.189	1.029	0.096	0.797
	Minimum	0.0	0.0	0.0	1.0	0.0	0.0	0.0	9.0	0.0	10.0	0.0	9.0
	Median	0.00	11.17	0.00	15.33	0.00	13.64	0.00	14.64	0.00	16.79	0.00	16.21
	Maximum	4.0	30.0	19.0	43.0	19.0	43.0	0.0	28.0	4.0	27.0	4.0	28.0

Note: Cigarettes per Day were calculated as the average cigarettes smoked per day in each week.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.1.1.2 Summary of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	Study Product Group											
		VLN Mentholated		VLN Non-Mentholated		VLN Combined		UB Mentholated		UB Non-Mentholated		UB Combined	
		Non-VLN	VLN	Non-VLN	VLN	Non-VLN	VLN	Non-UB	UB	Non-UB	UB	Non-UB	UB
Week 4	n	44	44	46	46	90	90	20	20	20	20	40	40
	Mean	0.43	12.98	1.24	16.42	0.85	14.74	0.19	15.49	0.55	16.84	0.37	16.16
	SD	0.917	6.967	3.732	8.058	2.759	7.698	0.708	5.429	1.171	4.874	0.973	5.137
	CV (%)	212.3	53.7	300.5	49.1	326.2	52.2	381.0	35.0	212.9	28.9	264.4	31.8
	SEM	0.138	1.050	0.550	1.188	0.291	0.811	0.158	1.214	0.262	1.090	0.154	0.812
	Minimum	0.0	3.0	0.0	1.0	0.0	1.0	0.0	8.0	0.0	7.0	0.0	7.0
	Median	0.00	11.64	0.00	15.00	0.00	12.64	0.00	15.00	0.00	17.14	0.00	15.64
	Maximum	4.0	47.0	25.0	42.0	25.0	47.0	3.0	27.0	3.0	26.0	3.0	27.0
Week 5	n	42	42	45	45	87	87	20	20	20	20	40	40
	Mean	0.40	12.01	1.19	15.29	0.81	13.70	0.01	15.80	1.29	17.85	0.65	16.83
	SD	1.081	8.209	3.455	7.741	2.611	8.094	0.032	6.214	5.675	5.464	4.014	5.868
	CV (%)	269.7	68.4	291.0	50.6	323.4	59.1	447.2	39.3	439.5	30.6	618.3	34.9
	SEM	0.167	1.267	0.515	1.154	0.280	0.868	0.007	1.389	1.269	1.222	0.635	0.928
	Minimum	0.0	3.0	0.0	2.0	0.0	2.0	0.0	8.0	0.0	8.0	0.0	8.0
	Median	0.00	10.21	0.00	14.71	0.00	11.86	0.00	15.14	0.00	17.43	0.00	16.14
	Maximum	6.0	57.0	22.0	37.0	22.0	57.0	0.0	32.0	25.0	34.0	25.0	34.0

Note: Cigarettes per Day were calculated as the average cigarettes smoked per day in each week.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.1.1.2 Summary of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	Study Product Group											
		VLN Mentholated		VLN Non-Mentholated		VLN Combined		UB Mentholated		UB Non-Mentholated		UB Combined	
		Non-VLN	VLN	Non-VLN	VLN	Non-VLN	VLN	Non-UB	UB	Non-UB	UB	Non-UB	UB
Week 6	n	43	43	43	43	86	86	20	20	20	20	40	40
	Mean	0.39	11.37	1.38	15.13	0.89	13.25	0.04	14.69	0.04	15.89	0.04	15.29
	SD	0.835	7.295	4.007	7.261	2.919	7.478	0.160	4.877	0.133	5.356	0.145	5.092
	CV (%)	212.6	64.1	290.5	48.0	329.5	56.4	447.2	33.2	301.9	33.7	363.9	33.3
	SEM	0.127	1.112	0.611	1.107	0.315	0.806	0.036	1.091	0.030	1.198	0.023	0.805
	Minimum	0.0	2.0	0.0	5.0	0.0	2.0	0.0	7.0	0.0	0.0	0.0	0.0
	Median	0.00	9.83	0.00	12.86	0.00	11.14	0.00	14.71	0.00	16.85	0.00	15.43
	Maximum	3.0	39.0	25.0	35.0	25.0	39.0	1.0	24.0	1.0	24.0	1.0	24.0

Note: Cigarettes per Day were calculated as the average cigarettes smoked per day in each week.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.1.2 Statistical Comparison of Number of Cigarettes Smoked per Day at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	95% Confidence Intervals		p-Value
		Test Week	(n)	Baseline	(n)				
Week 2	VLN Non-Mentholated	23.67	(11)	16.57	(11)	7.10	2.05 - 12.15		0.0106
	VLN Mentholated	16.05	(15)	15.35	(15)	0.70	-1.20 - 2.59		0.4419
	VLN Combined	19.27	(26)	15.87	(26)	3.41	0.87 - 5.95		0.0106
	UB Non-Mentholated	16.53	(22)	17.09	(22)	-0.56	-1.84 - 0.72		0.3733
	UB Mentholated	15.50	(20)	16.49	(20)	-0.99	-3.62 - 1.64		0.4393
	UB Combined	16.04	(42)	16.80	(42)	-0.77	-2.12 - 0.59		0.2609
Week 6	VLN Non-Mentholated	21.57	(11)	16.57	(11)	5.00	1.01 - 8.99		0.0190
	VLN Mentholated	14.47	(10)	16.55	(10)	-2.07	-8.32 - 4.17		0.4718
	VLN Combined	18.19	(21)	16.56	(21)	1.63	-2.04 - 5.30		0.3648
	UB Non-Mentholated	15.94	(20)	16.86	(20)	-0.92	-2.68 - 0.84		0.2871
	UB Mentholated	14.72	(20)	16.49	(20)	-1.77	-4.50 - 0.96		0.1912
	UB Combined	15.33	(40)	16.67	(40)	-1.34	-2.90 - 0.21		0.0883

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 Paired t-test method is used to perform the analysis.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.1.3 Statistical Comparison of Number of Cigarettes Smoked per Day Among Study Product Groups at Weeks 2 and 6 (PP Population)

Study Week	Comparison	----- LSMeans -----		LSMean Difference (Test - Reference)	95%		p-value
		Test (n)	Reference (n)		Confidence Intervals		
Week 2	VLN Non-mentholated vs UB Non-mentholated	23.67(11)	16.53(22)	7.14	2.50	- 11.78	0.0031
	VLN Mentholated vs UB Mentholated	16.05(15)	15.50(20)	0.55	-3.74	- 4.84	0.7986
	VLN Combined vs UB Combined	19.86(26)	16.01(42)	3.84	0.69	- 7.00	0.0178
Week 6	VLN Non-mentholated vs UB Non-mentholated	21.57(11)	15.90(20)	5.67	0.79	- 10.55	0.0235
	VLN Mentholated vs UB Mentholated	12.48(10)	14.72(20)	-2.25	-6.94	- 2.45	0.3428
	VLN Combined vs UB Combined	17.02(21)	15.31(40)	1.71	-1.67	- 5.10	0.3165

Note: LSMeans, LMean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.1.4 Statistical Comparison of Number of Cigarettes Smoked per Day at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	95%		p-Value
		Test Week	(n)	Baseline	(n)		Confidence Intervals		
Week 2	VLN Non-Mentholated	19.79	(49)	18.00	(49)	1.79	-0.22 -	3.81	0.0798
	VLN Mentholated	15.16	(48)	15.01	(48)	0.15	-1.15 -	1.45	0.8190
	VLN Combined	17.50	(97)	16.52	(97)	0.98	-0.21 -	2.17	0.1068
	UB Non-Mentholated	16.53	(22)	17.09	(22)	-0.56	-1.84 -	0.72	0.3733
	UB Mentholated	15.50	(20)	16.49	(20)	-0.99	-3.62 -	1.64	0.4393
	UB Combined	16.04	(42)	16.80	(42)	-0.77	-2.12 -	0.59	0.2609
Week 6	VLN Non-Mentholated	16.51	(43)	17.97	(43)	-1.46	-3.64 -	0.72	0.1841
	VLN Mentholated	11.77	(43)	15.25	(43)	-3.48	-5.21 -	-1.75	0.0002
	VLN Combined	14.14	(86)	16.61	(86)	-2.47	-3.85 -	-1.09	0.0006
	UB Non-Mentholated	15.94	(20)	16.86	(20)	-0.92	-2.68 -	0.84	0.2871
	UB Mentholated	14.72	(20)	16.49	(20)	-1.77	-4.50 -	0.96	0.1912
	UB Combined	15.33	(40)	16.67	(40)	-1.34	-2.90 -	0.21	0.0883

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 Paired t-test method is used to perform the analysis.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.1.5 Statistical Comparison of Number of Cigarettes Smoked per Day Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Study Week	Comparison	----- LSMeans -----		LSMean Difference		95%		p-value
		Test	(n) Reference (n)	(Test - Reference)		Confidence Intervals		
Week 2	VLN Non-mentholated vs UB Non-mentholated	19.79(49)	16.53(22)	3.26		-0.22 - 6.75		0.0664
	VLN Mentholated vs UB Mentholated	15.16(48)	15.50(20)	-0.34		-3.96 - 3.27		0.8517
	VLN Combined vs UB Combined	17.47(97)	16.01(42)	1.46		-1.05 - 3.97		0.2522
Week 6	VLN Non-mentholated vs UB Non-mentholated	15.94(43)	15.90(20)	0.04		-3.45 - 3.52		0.9838
	VLN Mentholated vs UB Mentholated	11.43(43)	14.72(20)	-3.29		-6.85 - 0.27		0.0698
	VLN Combined vs UB Combined	13.69(86)	15.31(40)	-1.63		-4.12 - 0.86		0.1986

Note: LSMeans, LMean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.2.1.1 Summary of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (PP Population)

		Study Product Group								
Study Week	Statistics	VLN Mentholated		VLN Non-Mentholated		VLN Combined		UB Mentholated	UB Non-Mentholated	UB Combined
		Non-VLN	VLN	Non-VLN	VLN	Non-VLN	VLN			
Week -1*	n	.	17	.	12	.	29	20	22	42
	Mean	.	65.7	.	93.0	.	77.0	85.7	88.8	87.3
	SD	.	34.08	.	40.58	.	38.70	31.76	30.06	30.54
	CV (%)	.	51.9	.	43.6	.	50.3	37.1	33.8	35.0
	SEM	.	8.26	.	11.72	.	7.19	7.10	6.41	4.71
	Minimum	.	0	.	14	.	0	37	15	15
	Median	.	59.0	.	84.5	.	77.0	81.0	91.5	87.0
	Maximum	.	136	.	166	.	166	154	140	154
Week 2	n	13	13	11	11	24	24	20	21	41
	Mean	2.4	204.6	3.9	328.0	3.1	261.2	217.3	240.8	229.3
	SD	7.48	109.32	7.18	126.93	7.22	131.09	82.13	72.50	77.30
	CV (%)	313.6	53.4	183.6	38.7	234.2	50.2	37.8	30.1	33.7
	SEM	2.07	30.32	2.16	38.27	1.47	26.76	18.36	15.82	12.07
	Minimum	0	75	0	149	0	75	125	136	125
	Median	0.0	175.0	0.0	316.0	0.0	234.0	199.5	235.0	221.0
	Maximum	27	413	23	556	27	556	425	378	425

Note: * Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.2.1.1 Summary of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (PP Population)

		Study Product Group								
Study Week	Statistics	VLN Mentholated		VLN Non-Mentholated		VLN Combined		UB	UB Non-	UB
		Non-VLN	VLN	Non-VLN	VLN	Non-VLN	VLN	Mentholated	Mentholated	Combined
Week 4	n	10	10	11	11	21	21	20	20	40
	Mean	0.9	200.5	4.0	262.1	2.5	232.8	193.2	214.0	203.6
	SD	2.23	86.54	9.14	139.26	6.82	118.58	67.77	65.11	66.44
	CV (%)	248.2	43.2	228.6	53.1	270.4	50.9	35.1	30.4	32.6
	SEM	0.71	27.37	2.76	41.99	1.49	25.88	15.15	14.56	10.50
	Minimum	0	124	0	58	0	58	86	78	78
	Median	0.0	177.5	0.0	231.0	0.0	221.0	188.5	218.0	205.5
	Maximum	7	378	29	531	29	531	367	327	367
Week 6	n	9	9	10	10	19	19	20	19	39
	Mean	0.7	186.2	3.3	285.3	2.1	238.4	218.1	234.2	225.9
	SD	1.66	100.08	7.51	159.72	5.59	140.68	71.32	59.73	65.57
	CV (%)	248.7	53.7	227.7	56.0	272.4	59.0	32.7	25.5	29.0
	SEM	0.55	33.36	2.38	50.51	1.28	32.27	15.95	13.70	10.50
	Minimum	0	101	0	15	0	15	124	85	85
	Median	0.0	148.0	0.0	281.0	0.0	224.0	218.0	236.0	228.0
	Maximum	5	416	24	518	24	518	366	325	366

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.2.1.2 Summary of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (ITT Population)

		Study Product Group								
Study Week	Statistics	VLN Mentholated		VLN Non-Mentholated		VLN Combined		UB	UB Non-	UB
		Non-VLN	VLN	Non-VLN	VLN	Non-VLN	VLN	Mentholated	Mentholated	Combined
Week -1*	n	.	50	.	50	.	100	20	22	42
	Mean	.	73.7	.	99.9	.	86.8	85.7	88.8	87.3
	SD	.	33.06	.	35.73	.	36.68	31.76	30.06	30.54
	CV (%)	.	44.8	.	35.8	.	42.3	37.1	33.8	35.0
	SEM	.	4.68	.	5.05	.	3.67	7.10	6.41	4.71
	Minimum	.	0	.	14	.	0	37	15	15
	Median	.	69.0	.	92.5	.	85.0	81.0	91.5	87.0
	Maximum	.	187	.	206	.	206	154	140	154
Week 2	n	46	46	49	49	95	95	20	21	41
	Mean	11.5	190.8	14.3	275.3	12.9	234.4	217.3	240.8	229.3
	SD	18.95	97.74	19.55	126.34	19.21	120.52	82.13	72.50	77.30
	CV (%)	165.4	51.2	136.6	45.9	148.6	51.4	37.8	30.1	33.7
	SEM	2.79	14.41	2.79	18.05	1.97	12.37	18.36	15.82	12.07
	Minimum	0	17	0	76	0	17	125	136	125
	Median	0.0	167.0	3.0	271.0	3.0	210.0	199.5	235.0	221.0
	Maximum	98	515	72	719	98	719	425	378	425

Note: * Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.1.2.1.2 Summary of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (ITT Population)

		Study Product Group								
Study Week	Statistics	VLN Mentholated		VLN Non-Mentholated		VLN Combined		UB	UB Non-	UB
		Non-VLN	VLN	Non-VLN	VLN	Non-VLN	VLN	Mentholated	Mentholated	Combined
Week 4	n	43	43	46	46	89	89	20	20	40
	Mean	4.4	162.0	11.0	194.8	7.8	179.0	193.2	214.0	203.6
	SD	7.48	75.58	42.57	107.56	31.06	94.41	67.77	65.11	66.44
	CV (%)	171.2	46.6	387.0	55.2	398.3	52.8	35.1	30.4	32.6
	SEM	1.14	11.53	6.28	15.86	3.29	10.01	15.15	14.56	10.50
	Minimum	0	23	0	21	0	21	86	78	78
	Median	0.0	155.0	0.0	163.0	0.0	159.0	188.5	218.0	205.5
	Maximum	26	408	283	538	283	538	367	327	367
Week 6	n	42	42	43	43	85	85	20	19	39
	Mean	6.2	164.0	16.3	203.6	11.3	184.0	218.1	234.2	225.9
	SD	13.70	105.78	53.00	115.78	39.01	112.08	71.32	59.73	65.57
	CV (%)	222.2	64.5	325.1	56.9	345.4	60.9	32.7	25.5	29.0
	SEM	2.11	16.32	8.08	17.66	4.23	12.16	15.95	13.70	10.50
	Minimum	0	48	0	15	0	15	124	85	85
	Median	0.0	141.5	0.0	189.0	0.0	153.0	218.0	236.0	228.0
	Maximum	73	606	333	518	333	606	366	325	366

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

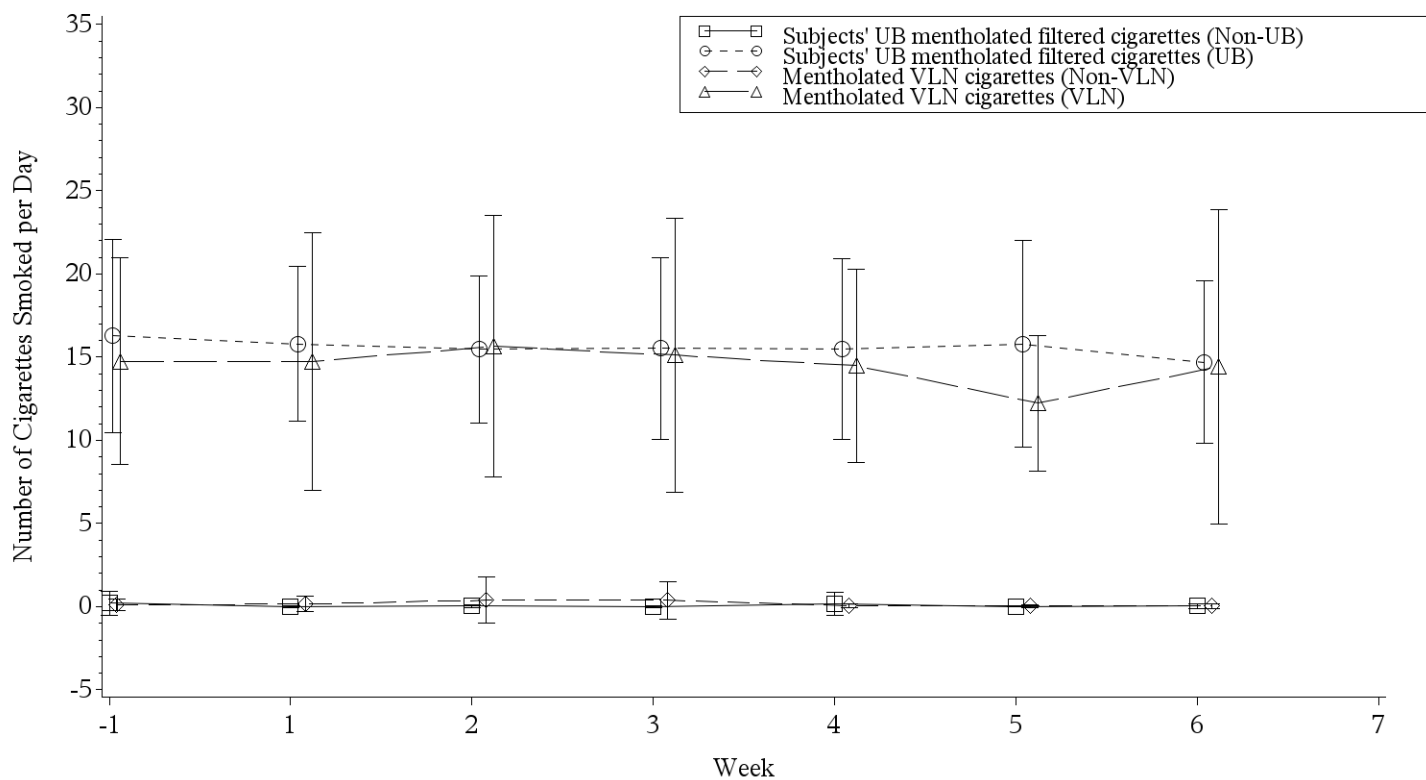
14.2.2 Product Use Figures

- Figure 14.2.2.1.1 Mean (\pm SD) of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Mentholated Flavor) (PP Population)
- Figure 14.2.2.1.2 Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Mentholated Flavor) (PP Population)
- Figure 14.2.2.1.3 Mean (\pm SD) of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Mentholated Flavor) (ITT Population)
- Figure 14.2.2.1.4 Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Mentholated Flavor) (ITT Population)
- Figure 14.2.2.2.1 Mean (\pm SD) of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Non-Mentholated flavor) (PP Population)
- Figure 14.2.2.2.2 Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Non-Mentholated flavor) (PP Population)
- Figure 14.2.2.2.3 Mean (\pm SD) of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Non-Mentholated flavor) (ITT Population)
- Figure 14.2.2.2.4 Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Non-Mentholated flavor) (ITT Population)
- Figure 14.2.2.2.5 Mean (\pm SD) of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Combined) (PP Population)
- Figure 14.2.2.2.6 Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Combined) (PP Population)
- Figure 14.2.2.2.7 Mean (\pm SD) of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Combined) (ITT Population)
- Figure 14.2.2.2.8 Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Combined) (ITT Population)
- Figure 14.2.2.3.1 Mean (\pm SD) of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Mentholated Flavor) (PP Population)
- Figure 14.2.2.3.2 Mean Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Mentholated Flavor) (PP Population)
- Figure 14.2.2.3.3 Mean (\pm SD) of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Mentholated Flavor) (ITT Population)
- Figure 14.2.2.3.4 Mean Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Mentholated Flavor) (ITT Population)

- Figure 14.2.2.4.1 Mean (\pm SD) of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Non-Mentholated Flavor) (PP Population)
- Figure 14.2.2.4.2 Mean Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Non-Mentholated Flavor) (PP Population)
- Figure 14.2.2.4.3 Mean (\pm SD) of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Non-Mentholated Flavor) (ITT Population)
- Figure 14.2.2.4.4 Mean Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Non-Mentholated Flavor) (ITT Population)
- Figure 14.2.2.4.5 Mean (\pm SD) of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Combined) (PP Population)
- Figure 14.2.2.4.6 Mean Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Combined) (PP Population)
- Figure 14.2.2.4.7 Mean (\pm SD) of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Combined) (ITT Population)
- Figure 14.2.2.4.8 Mean Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Combined) (ITT Population)

Figure 14.2.2.1.1

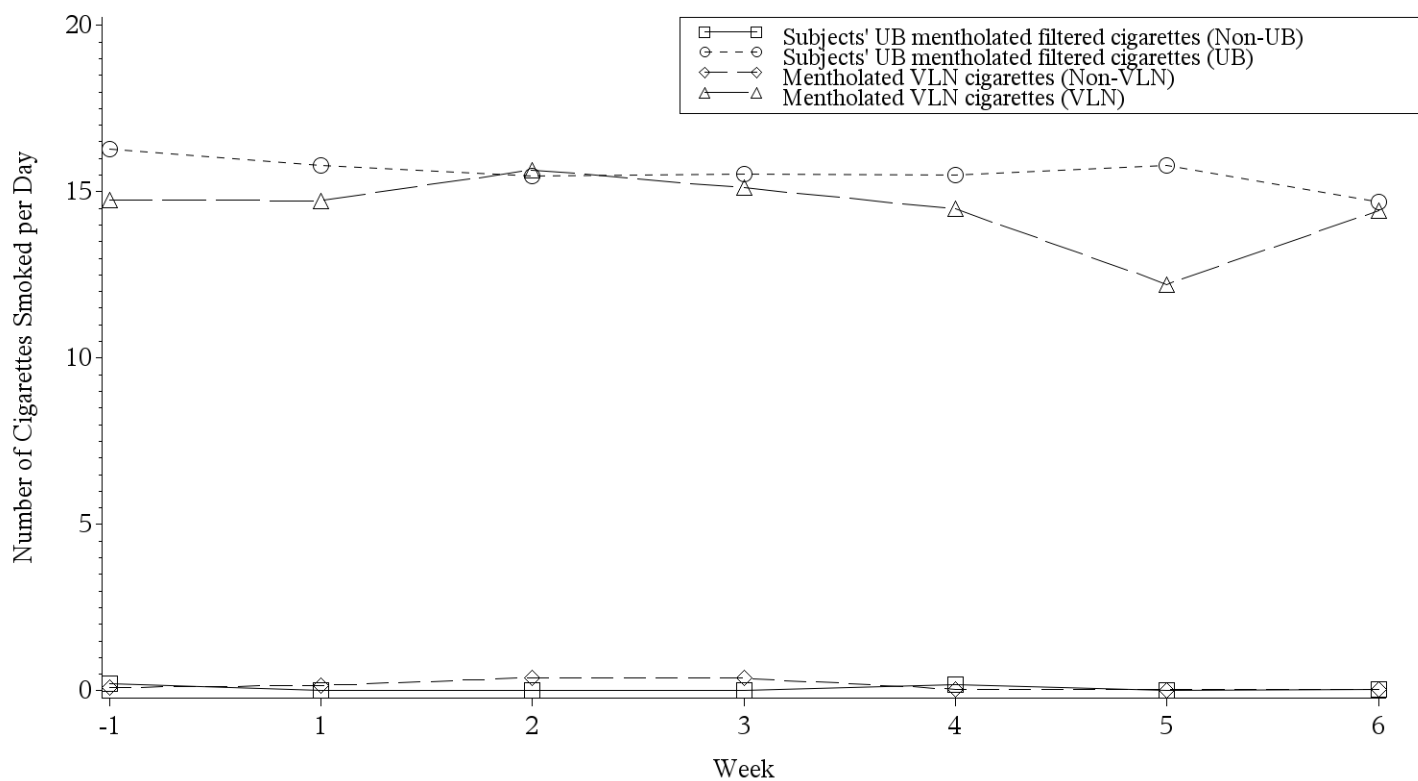
Mean (\pm SD) of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Mentholated Flavor)
 (PP Population)



All products except Subjects' UB mentholated filtered cigarettes (Non-UB) are shifted to the right for ease of reading.
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Figure 14.2.2.1.2

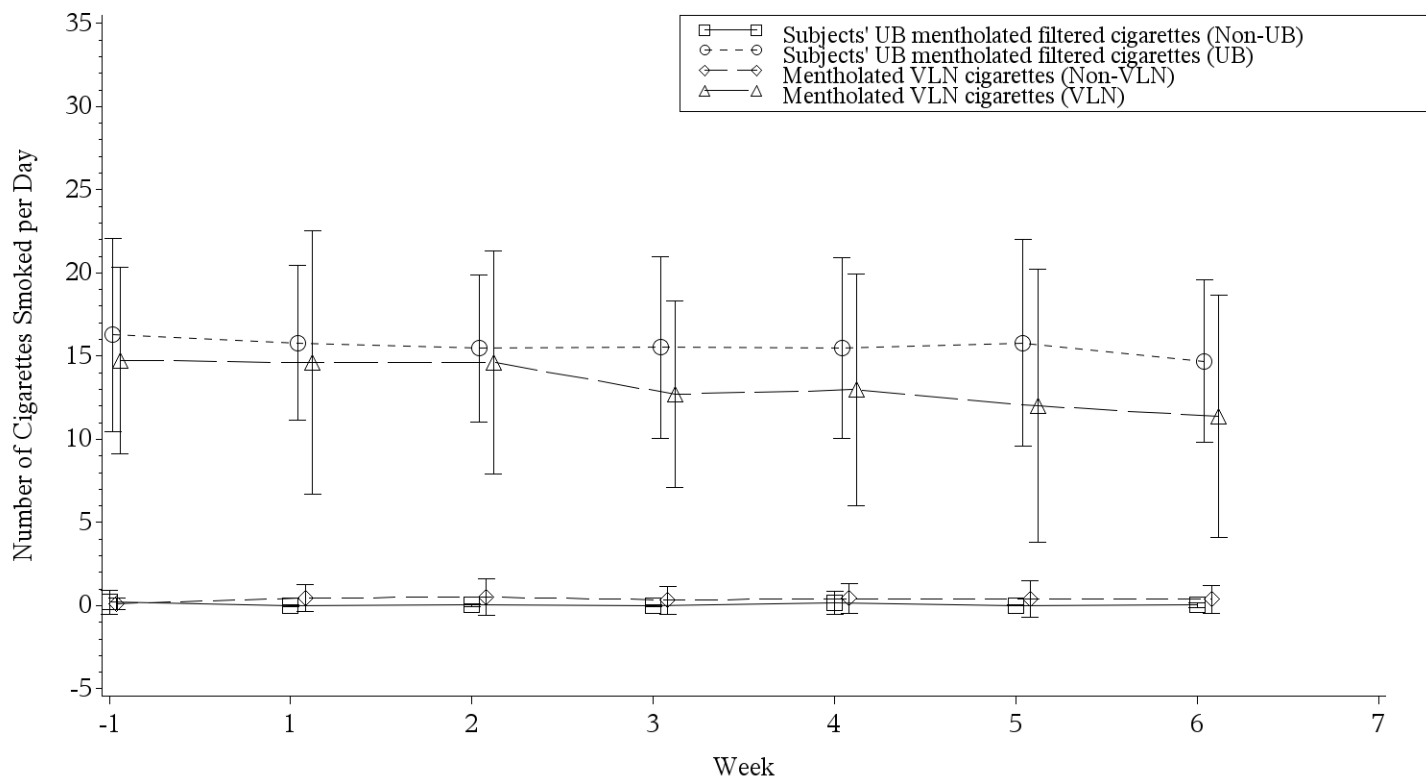
Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Mentholated Flavor)
 (PP Population)



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Figure 14.2.2.1.3

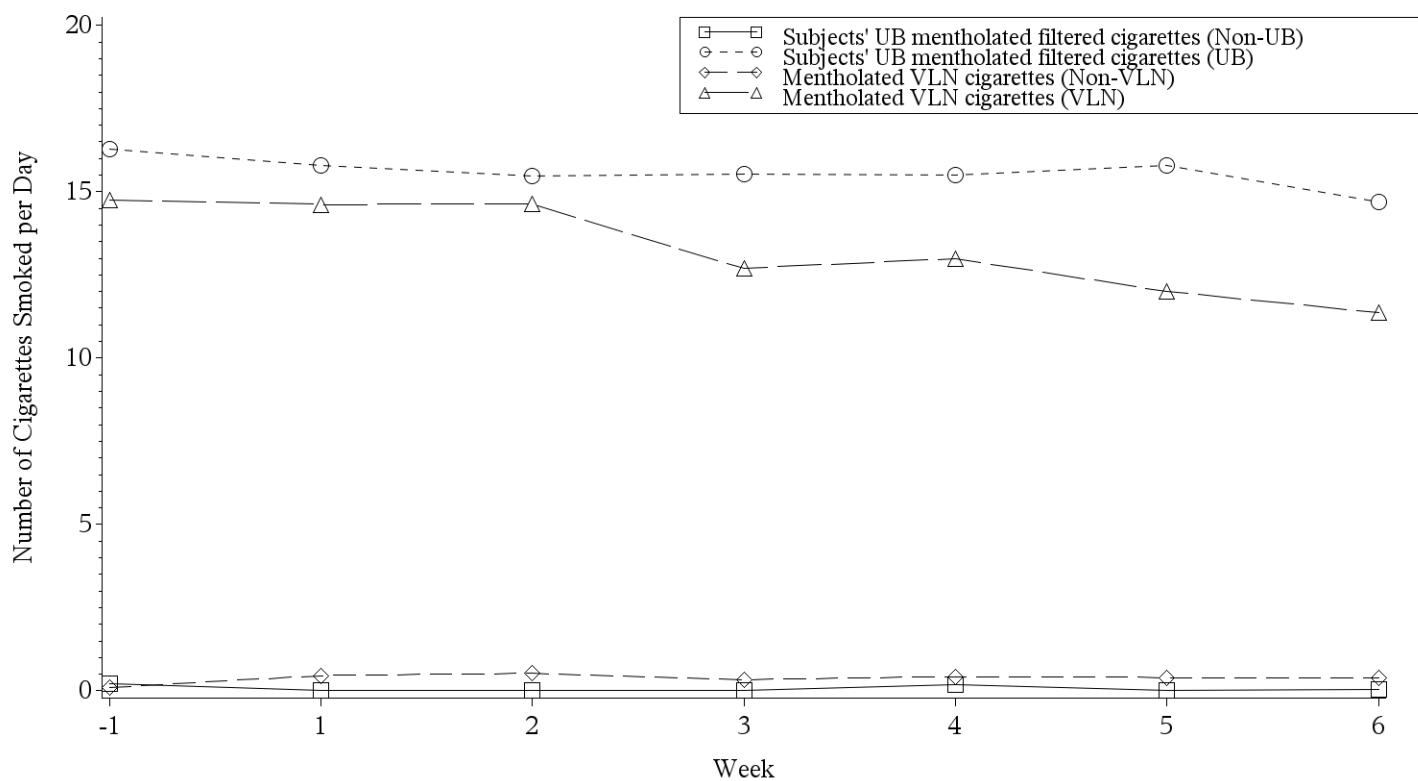
Mean (\pm SD) of Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Mentholated Flavor)
 (ITT Population)



All products except Subjects' UB mentholated filtered cigarettes (Non-UB) are shifted to the right for ease of reading.
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Figure 14.2.2.1.4

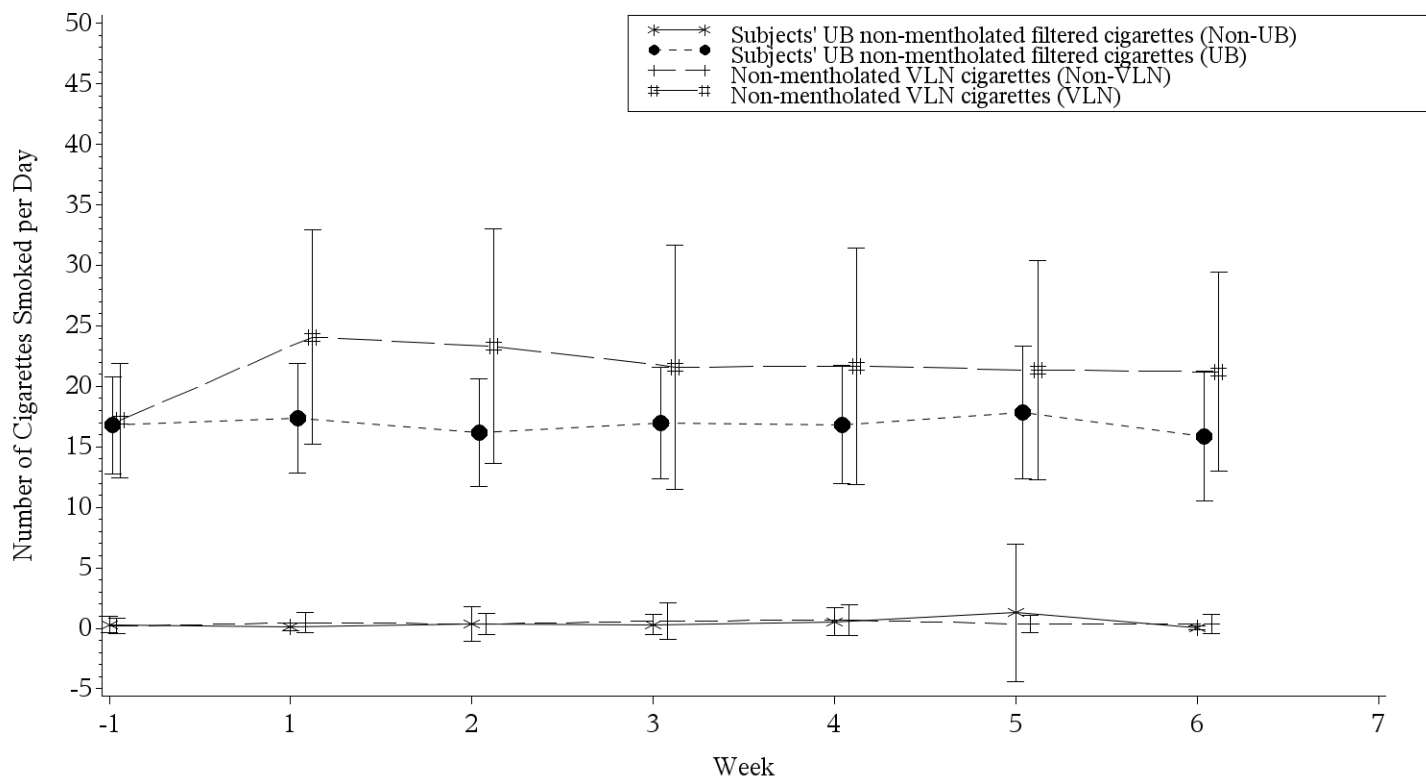
Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week (Mentholated Flavor)
(ITT Population)



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Figure 14.2.2.2.1

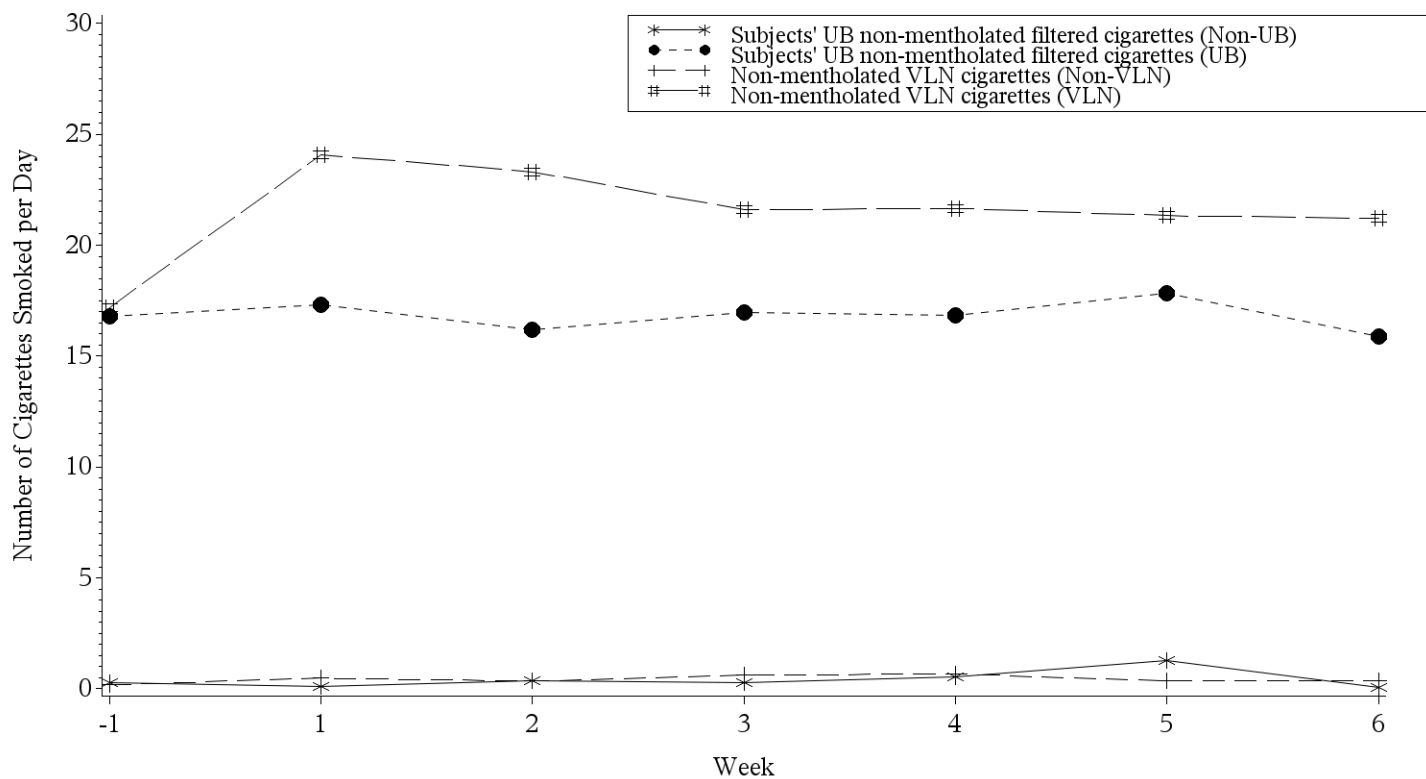
Mean (\pm SD) of Number of Cigarettes Smoked per Day by Study Product Group and Study Week
 (Non-Mentholated flavor) (PP Population)



All products except Subjects' UB non-mentholated filtered cigarettes (Non-UB) are shifted to the right for ease of reading.
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Figure 14.2.2.2.2

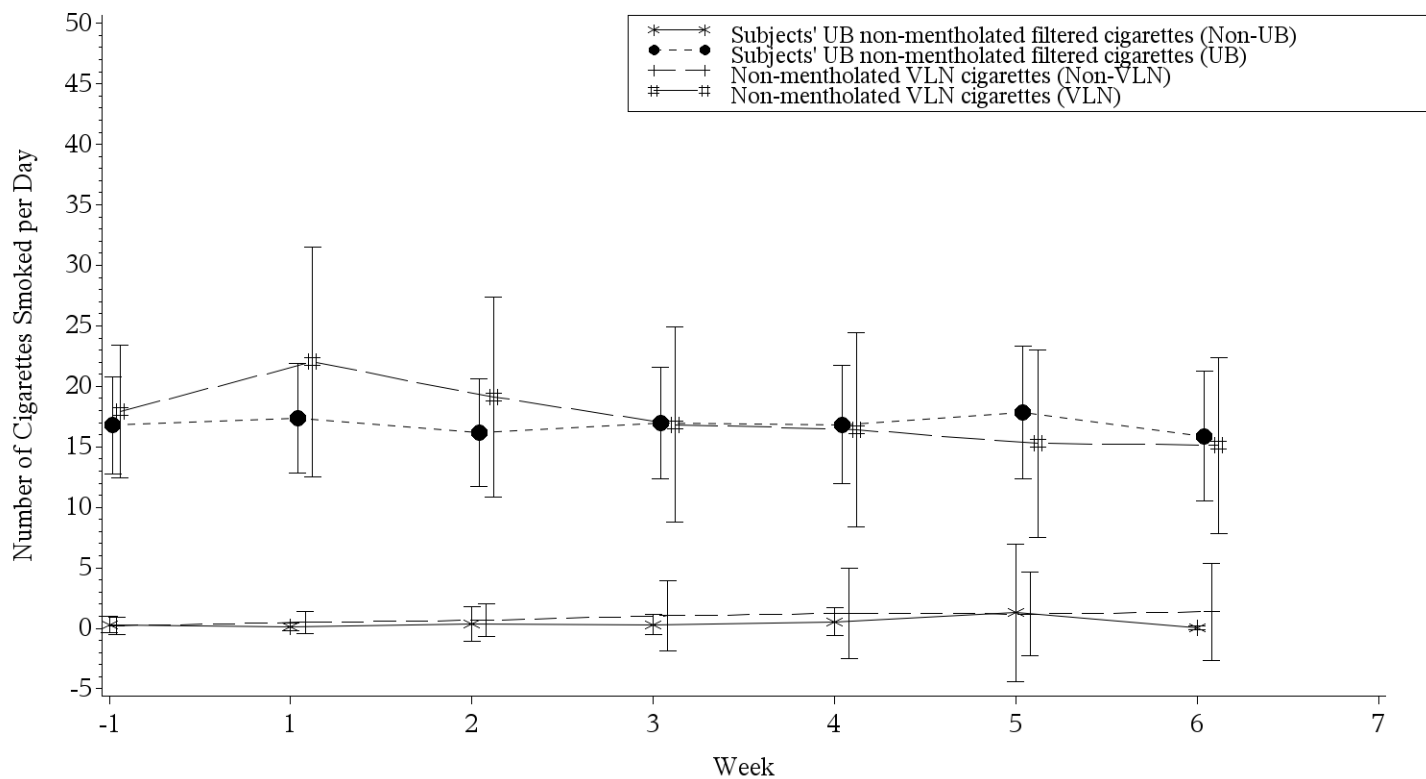
Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week
 (Non-Mentholated flavor) (PP Population)



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Figure 14.2.2.2.3

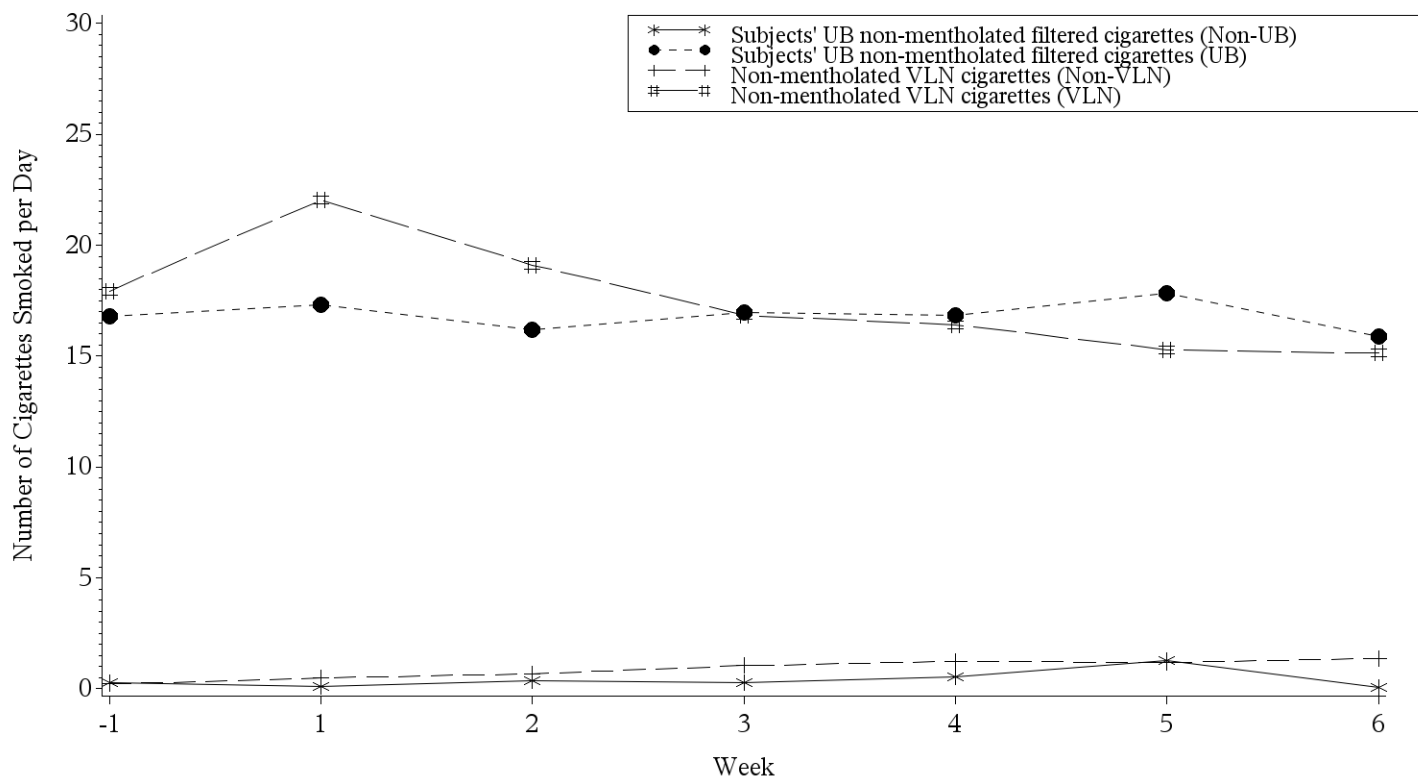
Mean (\pm SD) of Number of Cigarettes Smoked per Day by Study Product Group and Study Week
 (Non-Mentholated flavor) (ITT Population)



All products except Subjects' UB non-mentholated filtered cigarettes (Non-UB) are shifted to the right for ease of reading.
 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cig1NM.sas 28JUN2019 4:38

Figure 14.2.2.2.4

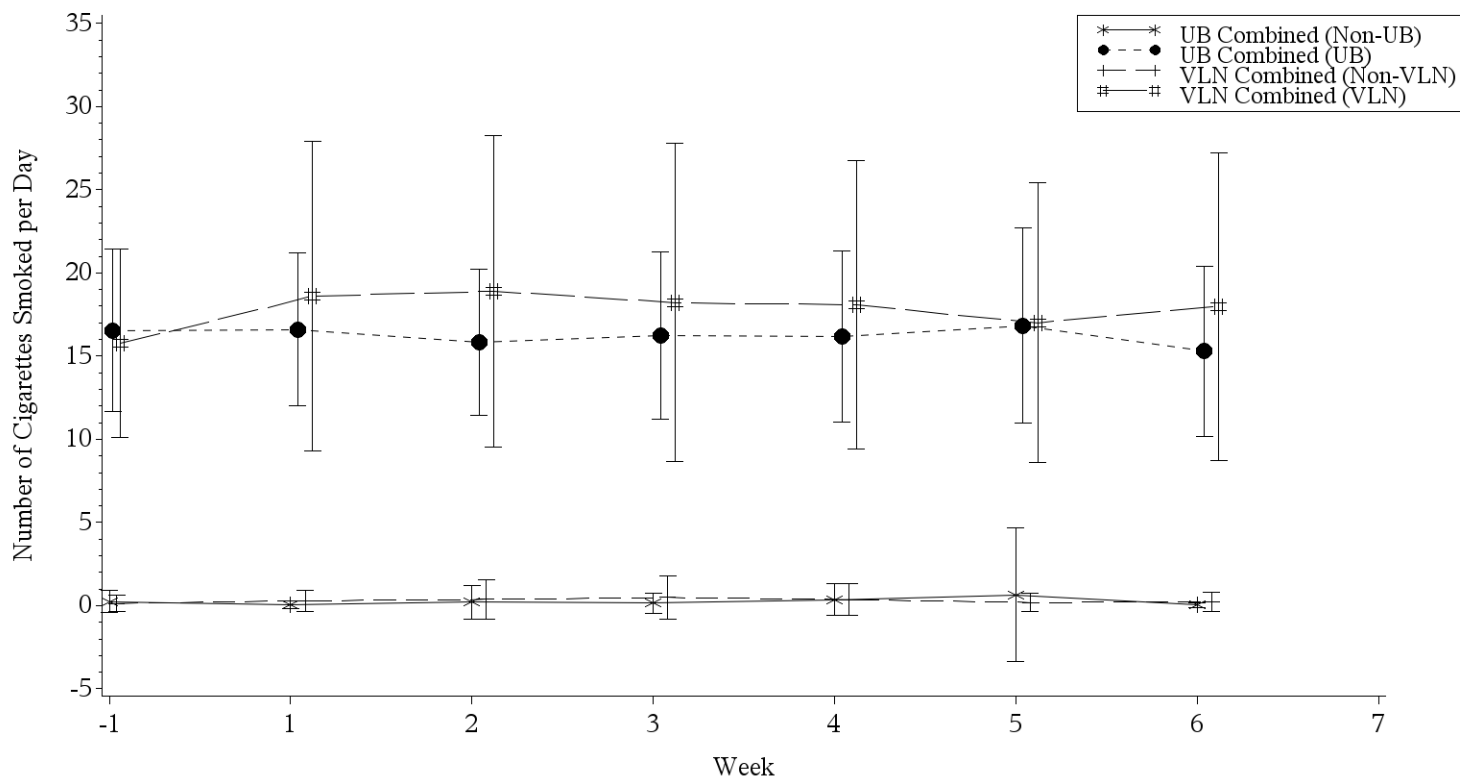
Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week
 (Non-Mentholated flavor) (ITT Population)



Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cig1NM.sas 28JUN2019 4:38

Figure 14.2.2.2.5

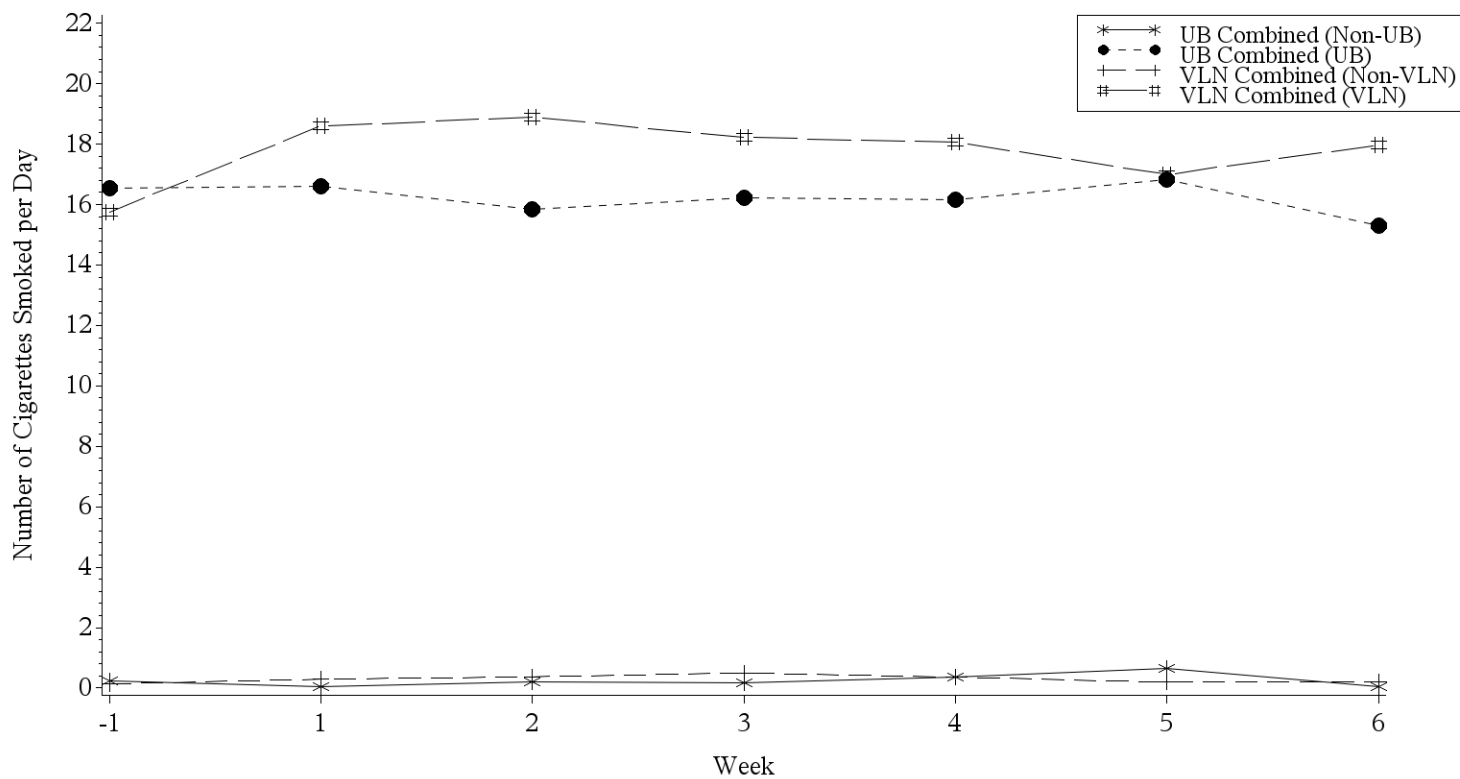
Mean (\pm SD) of Number of Cigarettes Smoked per Day by Study Product Group and Study Week
 (Combined) (PP Population)



All products except UB Combined (Non-UB) are shifted to the right for ease of reading.
 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cig1C.sas 13JUN2019 4:59

Figure 14.2.2.2.6

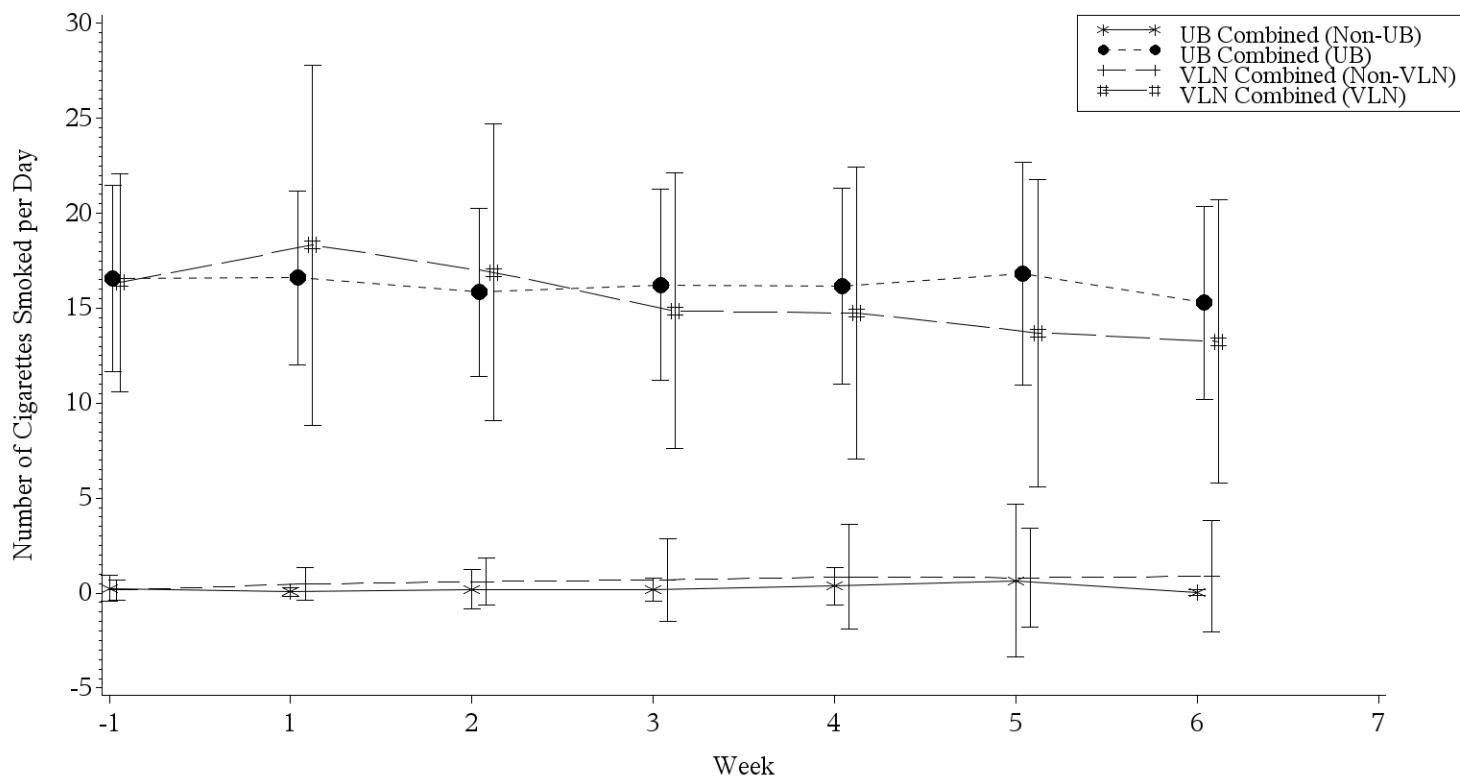
Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week
 (Combined) (PP Population)



Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cig1C.sas 13JUN2019 4:59

Figure 14.2.2.2.7

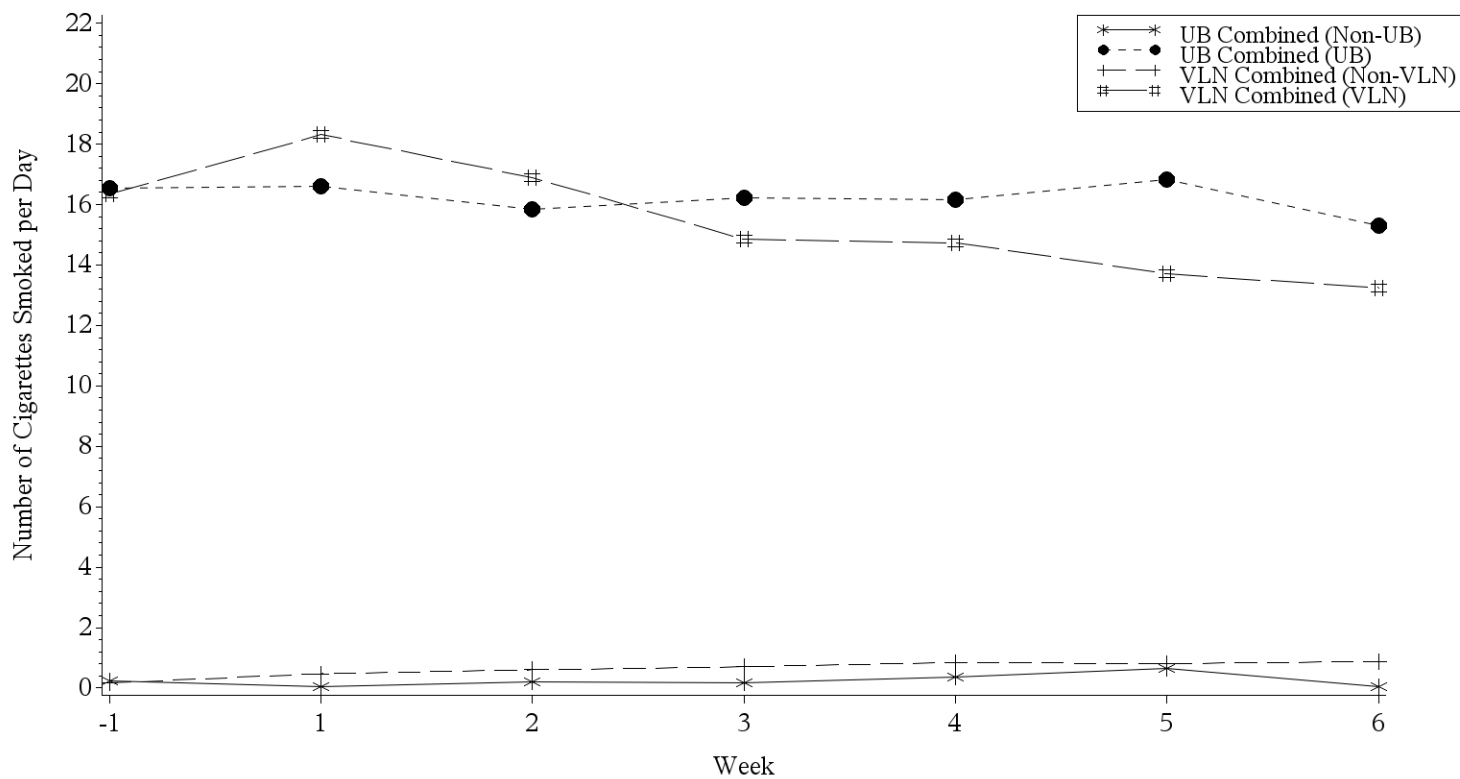
Mean (\pm SD) of Number of Cigarettes Smoked per Day by Study Product Group and Study Week
 (Combined) (ITT Population)



All products except UB Combined (Non-UB) are shifted to the right for ease of reading.
 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cig1C.sas 13JUN2019 4:59

Figure 14.2.2.2.8

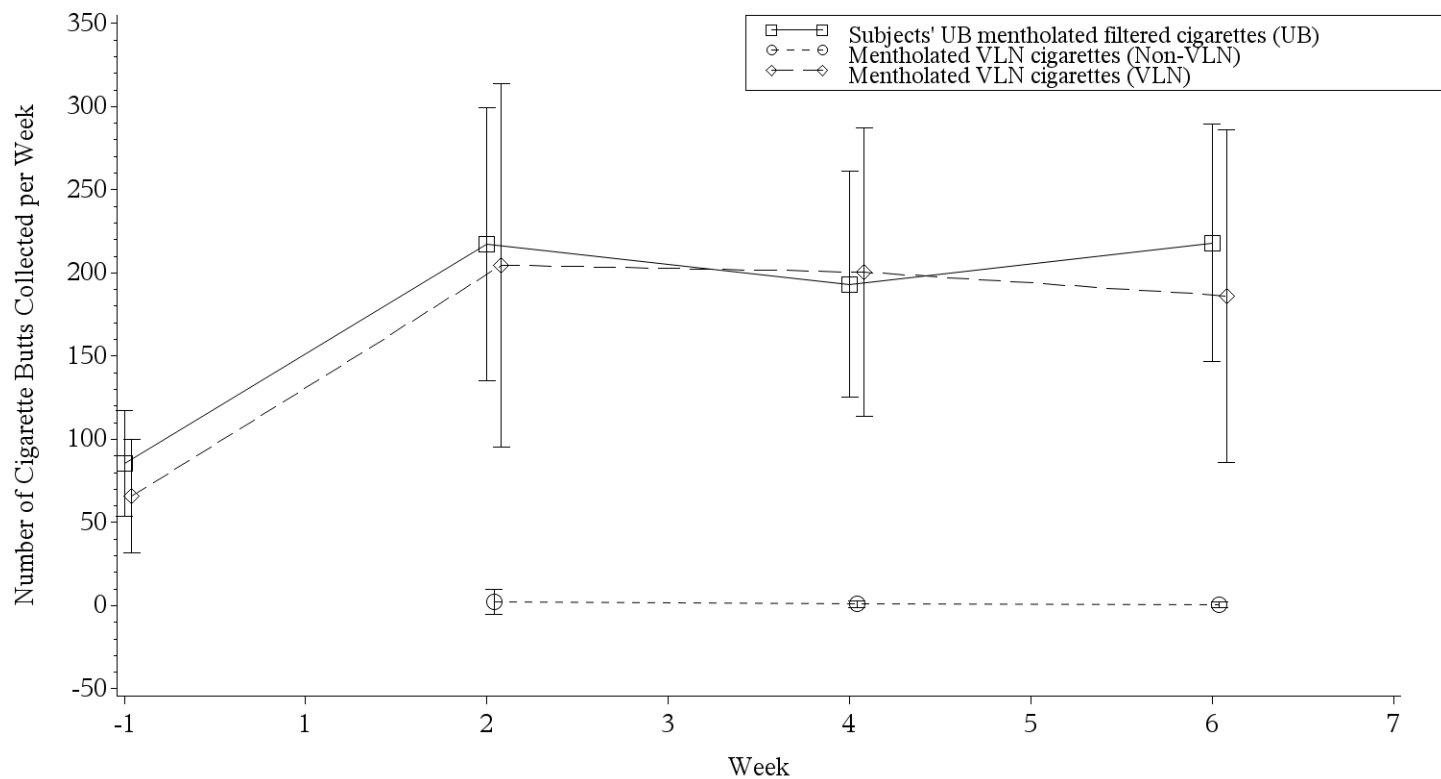
Mean Number of Cigarettes Smoked per Day by Study Product Group and Study Week
 (Combined) (ITT Population)



Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cig1C.sas 13JUN2019 4:59

Figure 14.2.2.3.1

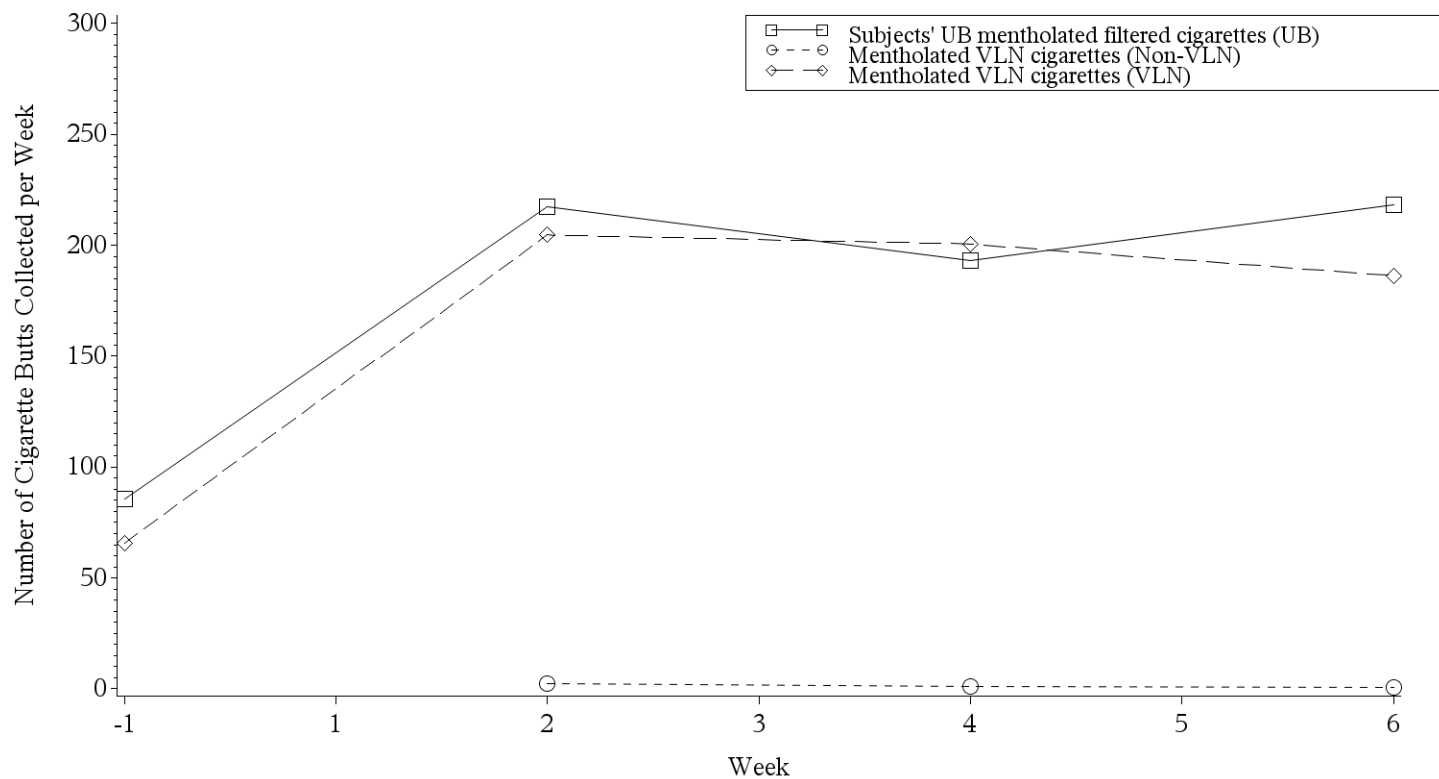
Mean (\pm SD) of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Mentholated Flavor)
 (PP Population)



All products except Subjects' UB mentholated filtered cigarettes (UB) are shifted to the right for ease of reading.
 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cigbutt1M.sas 28JUN2019 5:12

Figure 14.2.2.3.2

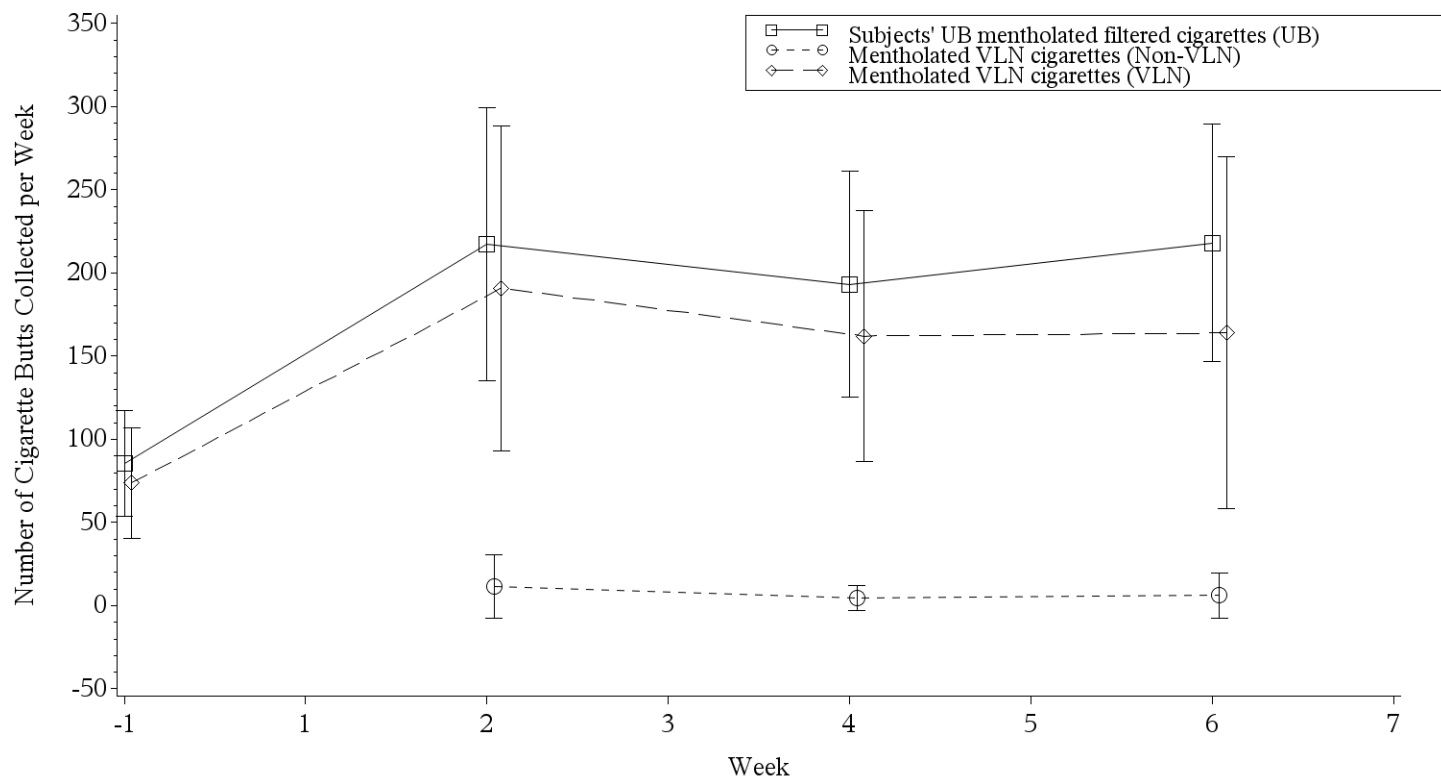
Mean Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Mentholated Flavor)
(PP Population)



Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cigbutt1M.sas 28JUN2019 5:13

Figure 14.2.2.3.3

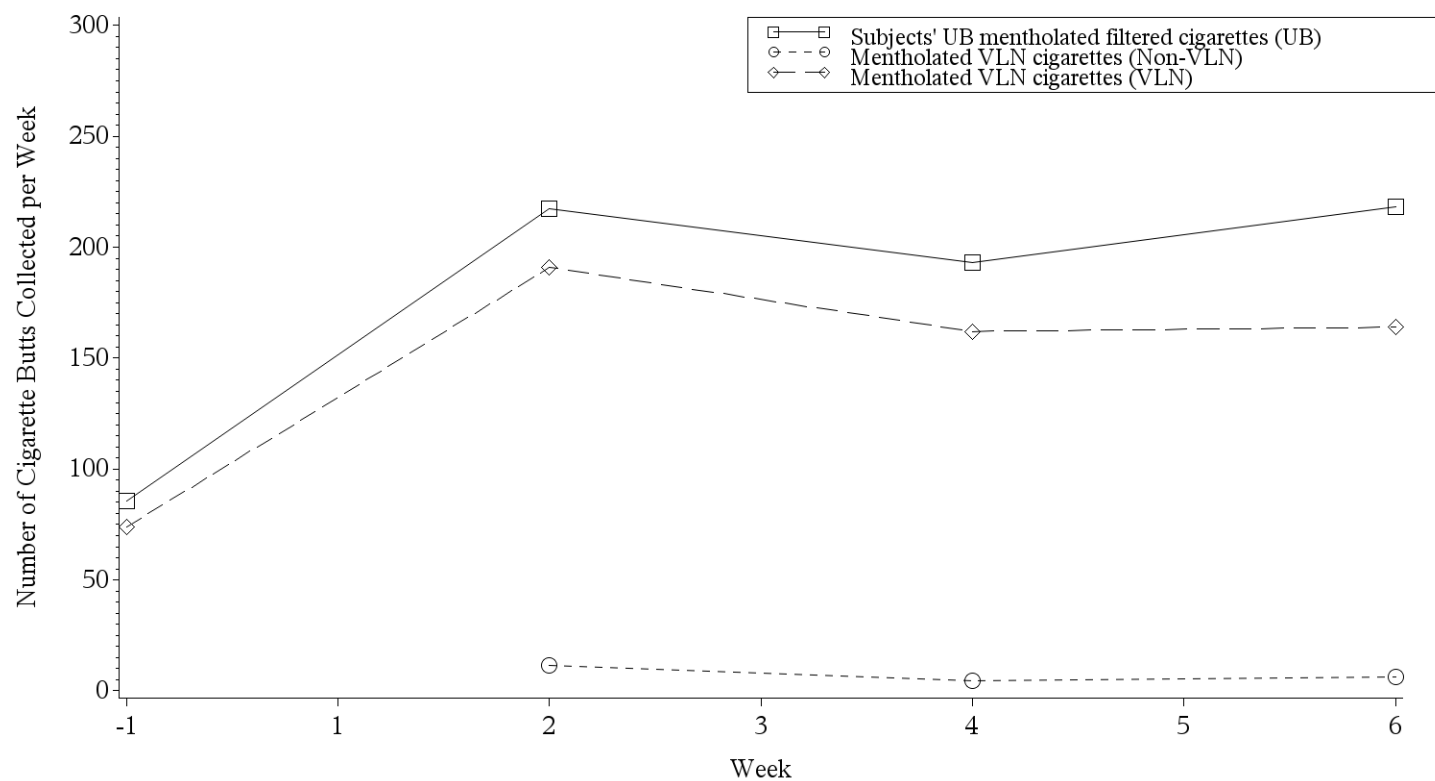
Mean (\pm SD) of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Mentholated Flavor)
 (ITT Population)



All products except Subjects' UB mentholated filtered cigarettes (UB) are shifted to the right for ease of reading.
 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cigbutt1M.sas 28JUN2019 5:13

Figure 14.2.2.3.4

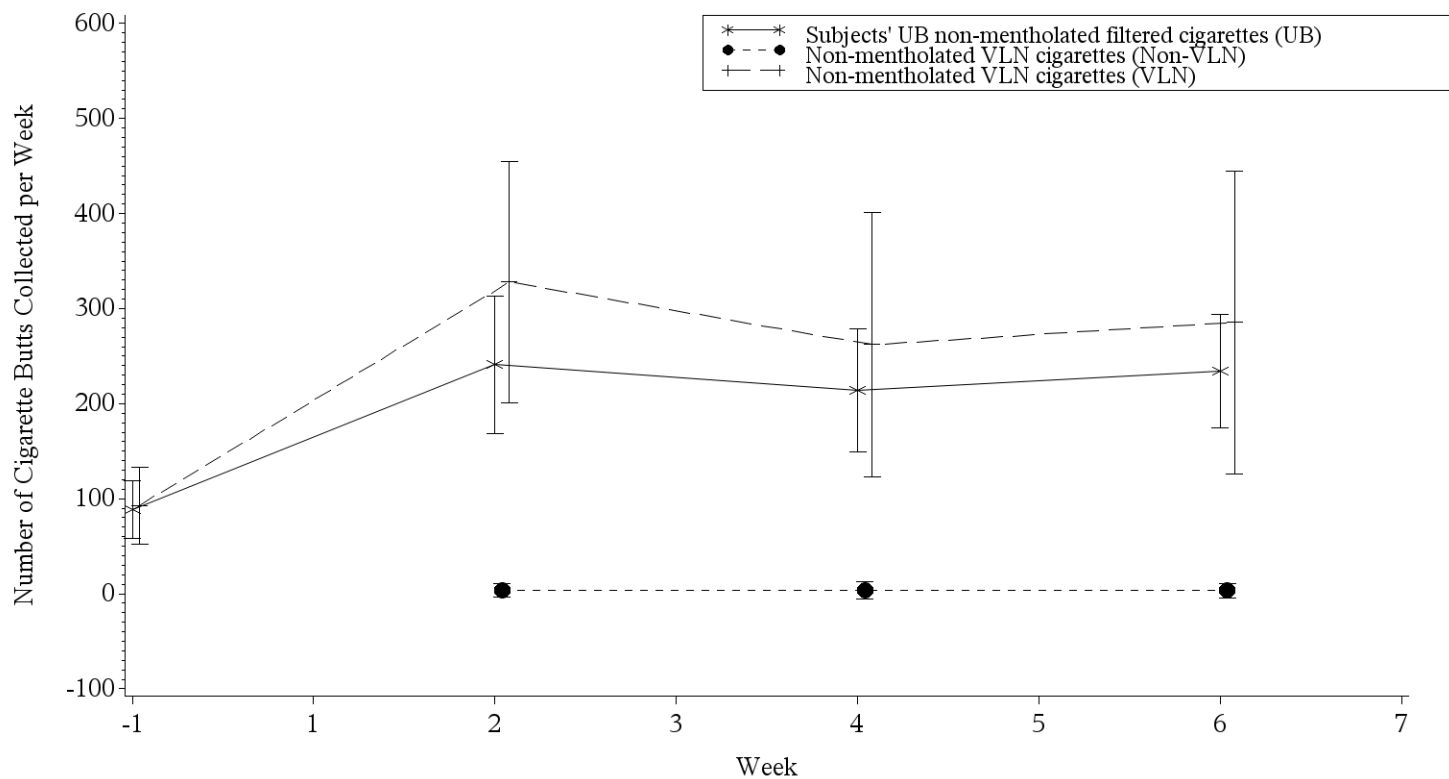
Mean Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (Mentholated Flavor)
(ITT Population)



Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cigbutt1M.sas 28JUN2019 5:13

Figure 14.2.2.4.1

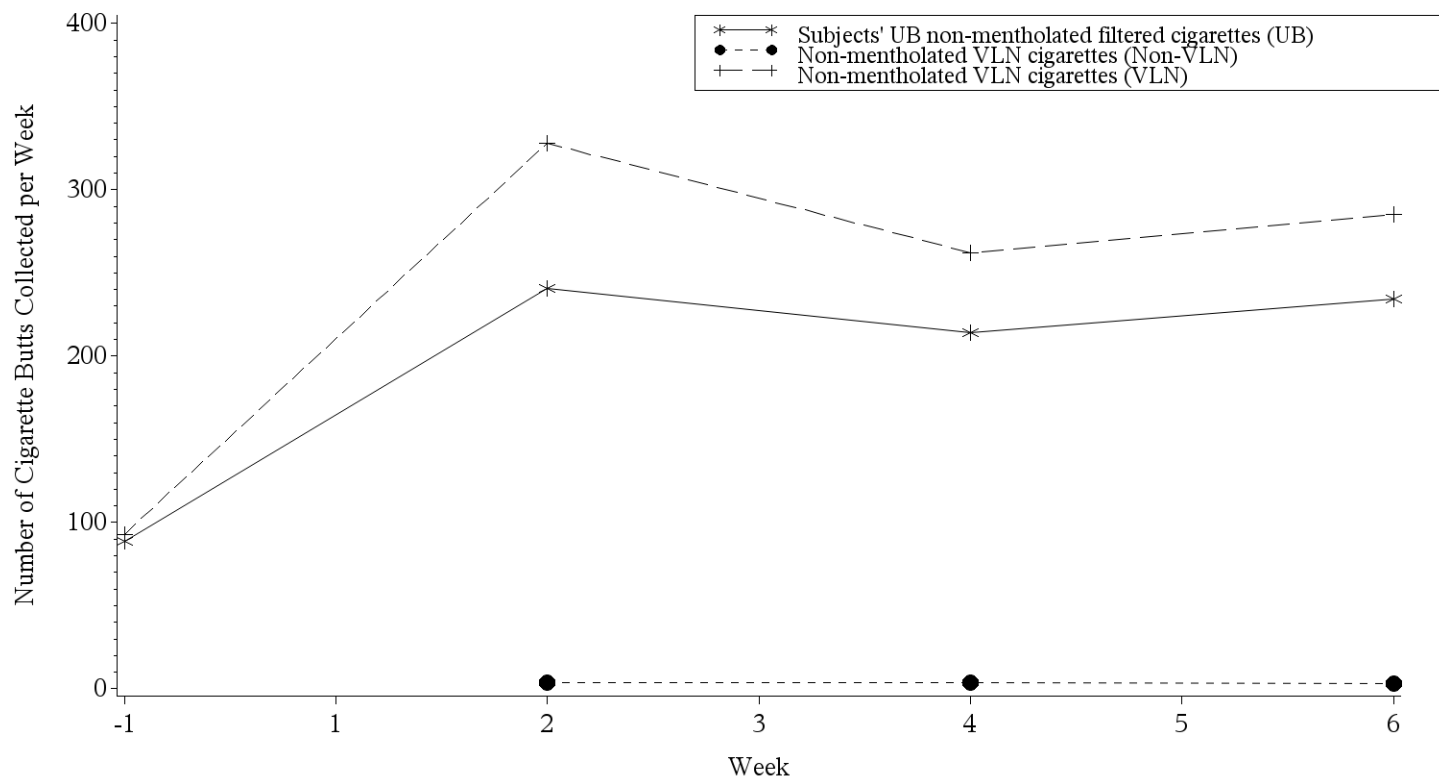
Mean (\pm SD) of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week
 (Non-Mentholated Flavor) (PP Population)



All products except Subjects' UB non-mentholated filtered cigarettes (UB) are shifted to the right for ease of reading.
 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cigbutt1NM.sas 28JUN2019 5:14

Figure 14.2.2.4.2

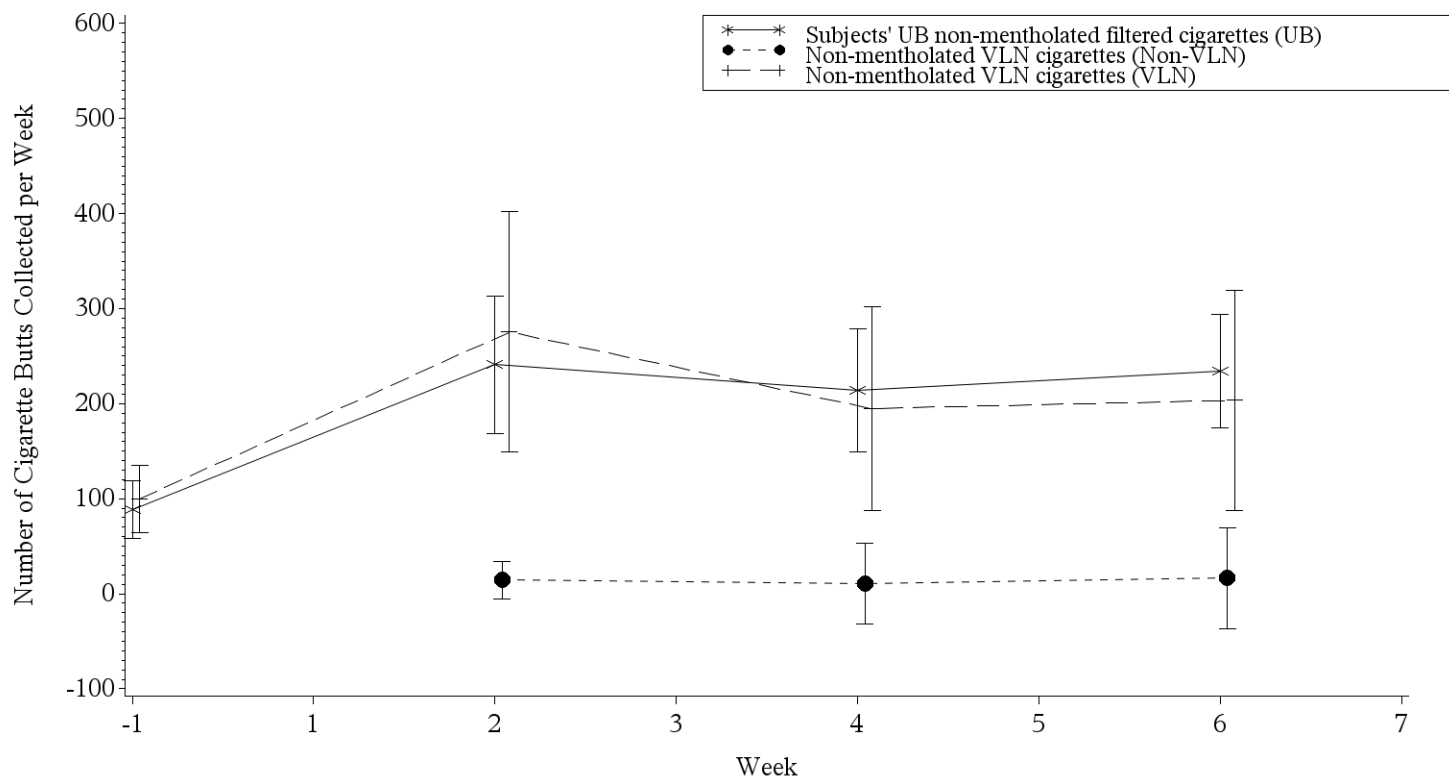
Mean Number of Cigarette Butts Collected per Week by Study Product Group and Study Week
(Non-Mentholated Flavor) (PP Population)



Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cigbutt1NM.sas 28JUN2019 5:14

Figure 14.2.2.4.3

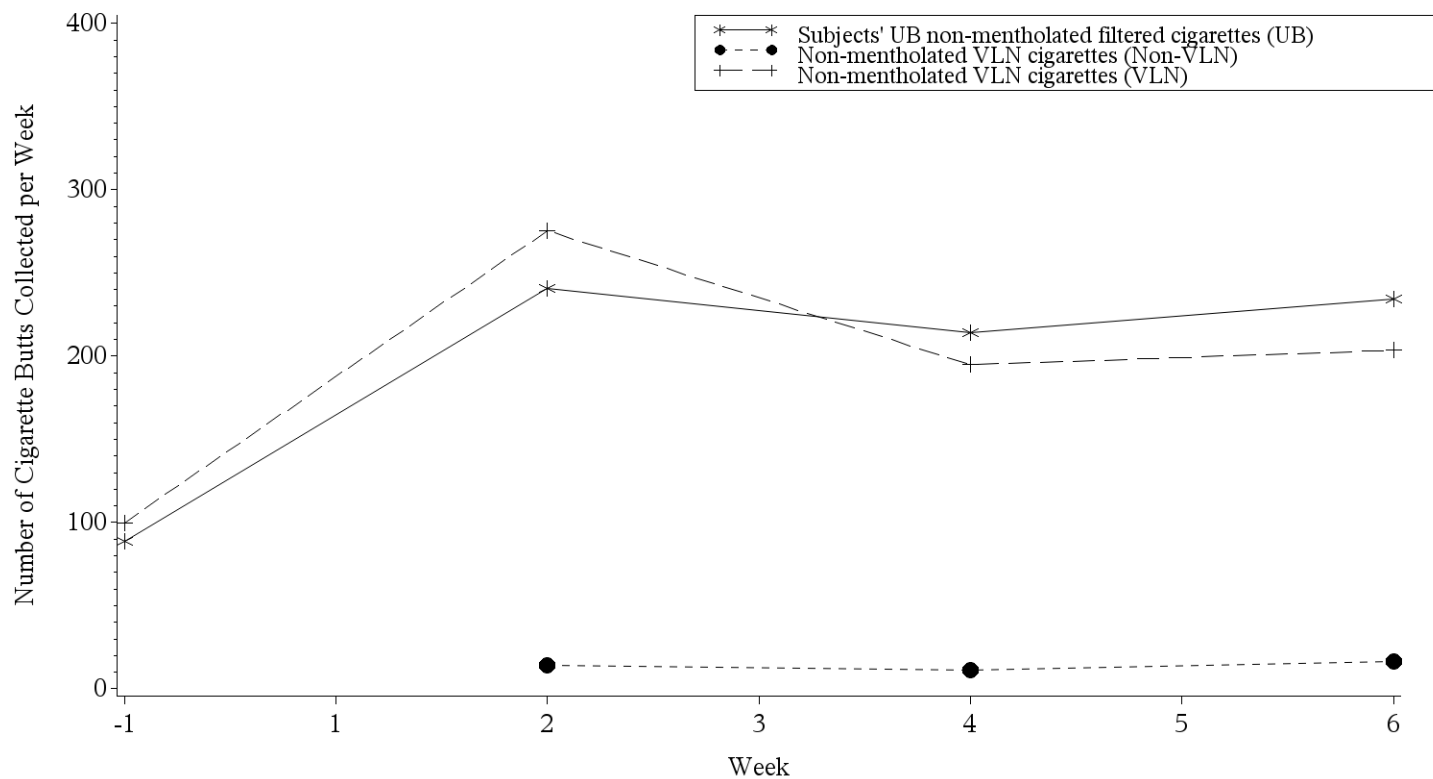
Mean (\pm SD) of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week
 (Non-Mentholated Flavor) (ITT Population)



All products except Subjects' UB non-mentholated filtered cigarettes (UB) are shifted to the right for ease of reading.
 Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cigbutt1NM.sas 28JUN2019 5:14

Figure 14.2.2.4.4

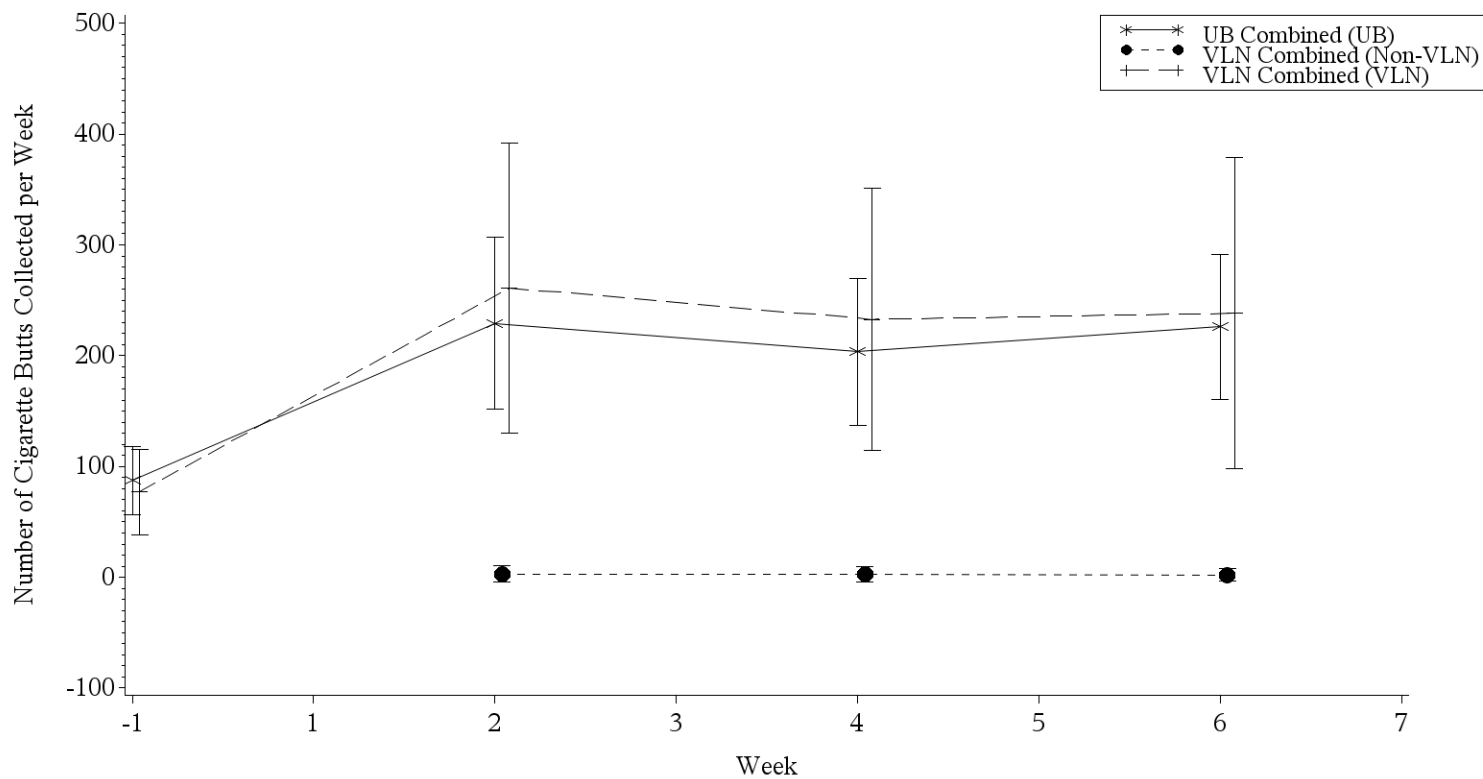
Mean Number of Cigarette Butts Collected per Week by Study Product Group and Study Week
(Non-Mentholated Flavor) (ITT Population)



Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cigbutt1NM.sas 28JUN2019 5:14

Figure 14.2.2.4.5

Mean (\pm SD) of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week
 (Combined) (PP Population)

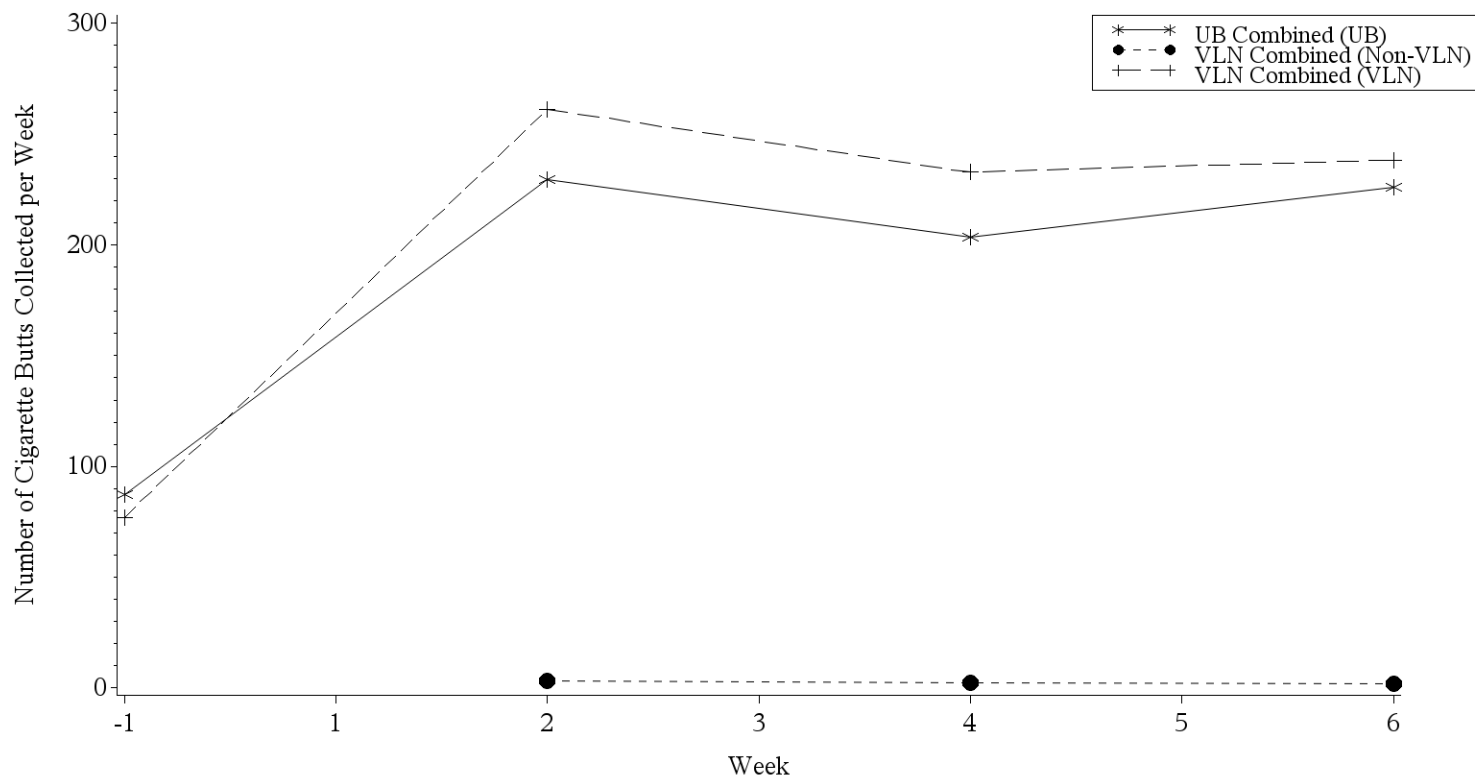


All products except UB Combined (UB) are shifted to the right for ease of reading.

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cigbutt1C.sas 13JUN2019 5:02

Figure 14.2.2.4.6

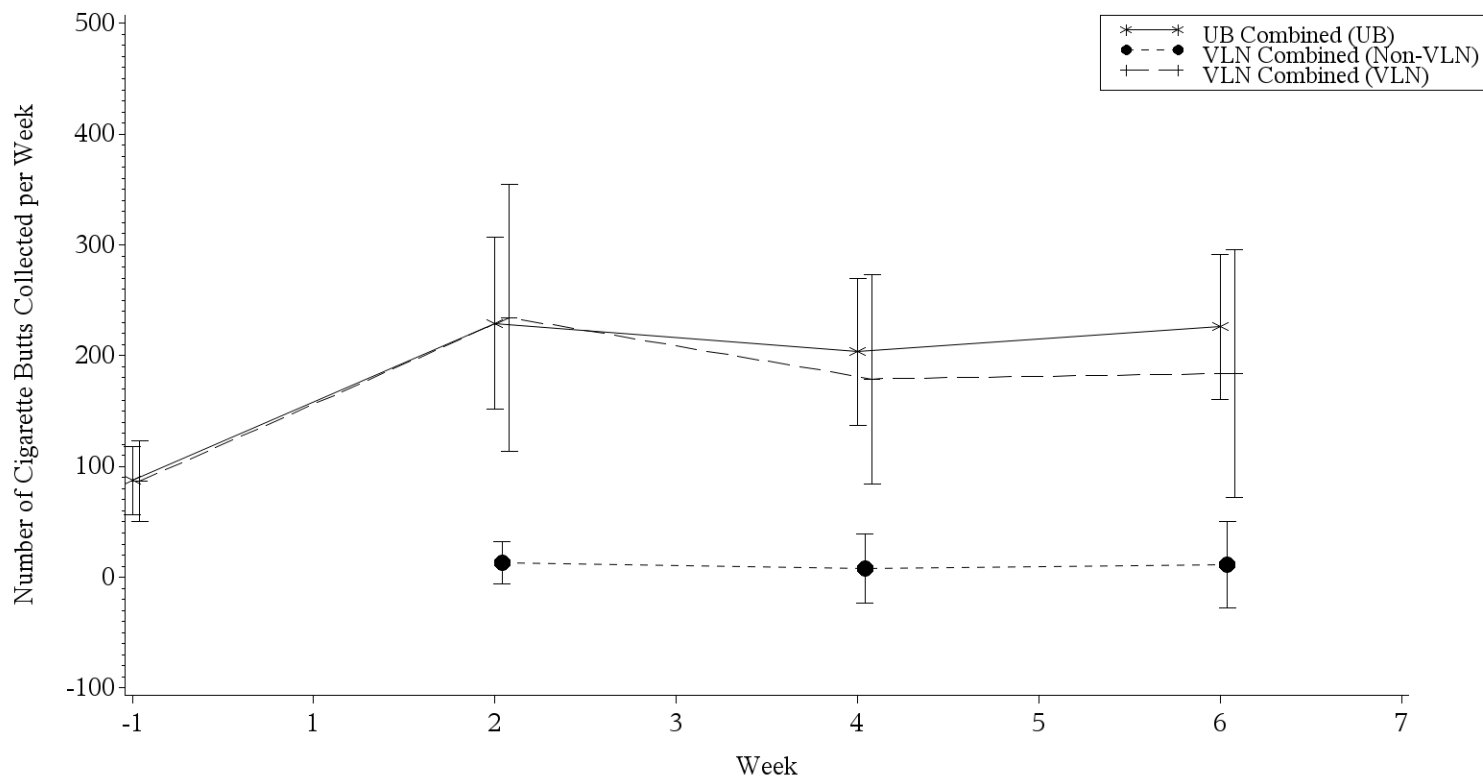
Mean Number of Cigarette Butts Collected per Week by Study Product Group and Study Week
(Combined) (PP Population)



Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cigbutt1C.sas 13JUN2019 5:02

Figure 14.2.2.4.7

Mean (\pm SD) of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week
 (Combined) (ITT Population)

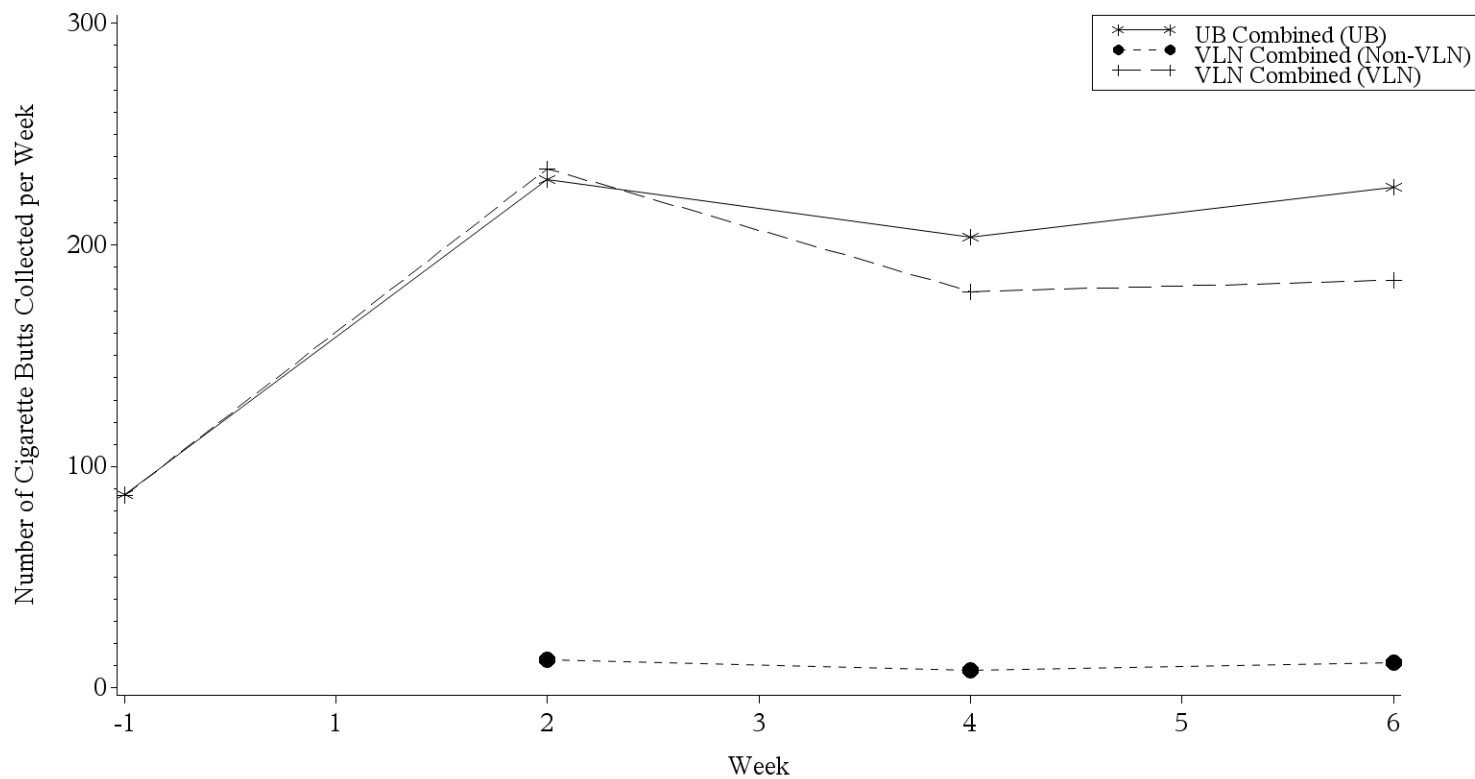


All products except UB Combined (UB) are shifted to the right for ease of reading.

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cigbutt1C.sas 13JUN2019 5:02

Figure 14.2.2.4.8

Mean Number of Cigarette Butts Collected per Week by Study Product Group and Study Week
(Combined) (ITT Population)



Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_meangraph_cigbutt1C.sas 13JUN2019 5:02

14.2.3 Puff Topography Parameter Tables

Table 14.2.3.1.1	Summary of Puffing Topography Parameters by Study Product Group and Study Week (PP Population)
Table 14.2.3.1.2	Summary of Puffing Topography Parameters by Study Product Group and Study Week (ITT Population)
Table 14.2.3.2	Statistical Summary of Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 14.2.3.3	Statistical Summary of Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Table 14.2.3.1.1 Summary of Puffing Topography Parameters by Study Product Group and Study Week (PP Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Puff Duration (sec)	Week -1*	n	3	6	9
		Mean	1.923	2.128	2.059
		SD	1.0295	0.4811	0.6482
		CV%	53.5	22.6	31.5
		SEM	0.5944	0.1964	0.2161
		Minimum	0.81	1.62	0.81
		Median	2.103	2.126	2.123
		Maximum	2.85	2.88	2.88
	Week 2	n	3	5	8
		Mean	2.690	2.255	2.418
		SD	1.9743	0.6036	1.1715
		CV%	73.4	26.8	48.5
		SEM	1.1399	0.2699	0.4142
		Minimum	0.94	1.85	0.94
		Median	2.295	1.950	2.123
		Maximum	4.83	3.28	4.83
	Week 6	n	3	4	7
		Mean	2.065	1.979	2.016
		SD	1.1200	0.4463	0.7210
		CV%	54.2	22.6	35.8
		SEM	0.6467	0.2231	0.2725
		Minimum	0.86	1.38	0.86
		Median	2.254	2.074	2.238
		Maximum	3.08	2.39	3.08

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.1 Summary of Puffing Topography Parameters by Study Product Group and Study Week (PP Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Total Puff Duration (sec)	Week -1*	n	3	6	9
		Mean	21.233	27.263	25.253
		SD	7.7511	7.7962	7.8801
		CV%	36.5	28.6	31.2
		SEM	4.4751	3.1828	2.6267
		Minimum	13.08	17.15	13.08
		Median	22.125	28.763	25.575
		Maximum	28.50	35.95	35.95
	Week 2	n	3	5	8
		Mean	26.267	24.480	25.150
		SD	7.8233	4.8143	5.6202
		CV%	29.8	19.7	22.3
		SEM	4.5168	2.1530	1.9870
		Minimum	17.90	16.98	16.98
		Median	27.500	25.850	26.013
		Maximum	33.40	30.00	33.40
	Week 6	n	3	4	7
		Mean	23.275	22.500	22.832
		SD	3.6127	8.0078	6.0485
		CV%	15.5	35.6	26.5
		SEM	2.0858	4.0039	2.2861
		Minimum	19.85	12.40	12.40
		Median	22.925	23.525	22.925
		Maximum	27.05	30.55	30.55

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.1 Summary of Puffing Topography Parameters by Study Product Group and Study Week (PP Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Puff Volume (mL)	Week -1*	n	3	6	9
		Mean	46.7230	68.8826	61.4961
		SD	21.20597	27.54051	26.63148
		CV%	45.4	40.0	43.3
		SEM	12.24327	11.24337	8.87716
		Minimum	23.021	46.523	23.021
		Median	53.2497	59.9617	59.3299
		Maximum	63.898	123.468	123.468
	Week 2	n	3	5	8
		Mean	38.9233	49.9217	45.7973
		SD	19.33072	14.75558	16.23519
		CV%	49.7	29.6	35.5
		SEM	11.16060	6.59889	5.74001
		Minimum	23.391	33.113	23.391
		Median	32.8058	45.3591	44.0304
		Maximum	60.573	71.522	71.522
	Week 6	n	3	4	7
		Mean	37.3258	46.0518	42.3121
		SD	18.52739	11.33347	14.15629
		CV%	49.6	24.6	33.5
		SEM	10.69680	5.66674	5.35057
		Minimum	22.738	31.885	22.738
		Median	31.0672	47.4028	42.4244
		Maximum	58.172	57.516	58.172

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.1 Summary of Puffing Topography Parameters by Study Product Group and Study Week (PP Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Total Puff Volume (mL)	Week -1*	n	3	6	9
		Mean	519.9912	850.5382	740.3559
		SD	135.50854	293.19134	292.62895
		CV%	26.1	34.5	39.5
		SEM	78.23589	119.69486	97.54298
		Minimum	369.561	621.414	369.561
		Median	557.9150	775.4165	697.8500
		Maximum	632.498	1433.167	1433.167
	Week 2	n	3	5	8
		Mean	475.7597	552.8127	523.9178
		SD	230.89090	213.98975	207.33681
		CV%	48.5	38.7	39.6
		SEM	133.30492	95.69913	73.30463
		Minimum	262.129	408.232	262.129
		Median	444.4380	463.5850	456.8133
		Maximum	720.712	929.785	929.785
	Week 6	n	3	4	7
		Mean	500.0915	500.9646	500.5904
		SD	210.35119	105.52044	142.53669
		CV%	42.1	21.1	28.5
		SEM	121.44632	52.76022	53.87380
		Minimum	279.233	384.212	279.233
		Median	522.9790	490.7632	510.1640
		Maximum	698.063	638.120	698.063

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.1 Summary of Puffing Topography Parameters by Study Product Group and Study Week (PP Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Inter Puff Interval (sec)	Week -1*	n	3	6	9
		Mean	32.432	35.890	34.737
		SD	6.0510	5.7467	5.7257
		CV%	18.7	16.0	16.5
		SEM	3.4935	2.3461	1.9086
		Minimum	28.10	29.34	28.10
		Median	29.853	35.067	34.850
		Maximum	39.35	45.86	45.86
	Week 2	n	3	5	8
		Mean	19.421	30.716	26.480
		SD	8.6665	11.7516	11.5995
		CV%	44.6	38.3	43.8
		SEM	5.0036	5.2555	4.1010
		Minimum	12.15	20.33	12.15
		Median	17.098	26.631	25.013
		Maximum	29.01	49.88	49.88
	Week 6	n	3	4	7
		Mean	19.988	27.839	24.474
		SD	7.7493	10.5463	9.6562
		CV%	38.8	37.9	39.5
		SEM	4.4740	5.2732	3.6497
		Minimum	11.11	17.35	11.11
		Median	23.482	26.520	23.482
		Maximum	25.38	40.97	40.97

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.1 Summary of Puffing Topography Parameters by Study Product Group and Study Week (PP Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Peak Puff Flow Rate (mL/sec)	Week -1*	n	3	6	9
		Mean	43.4564	55.2651	51.3289
		SD	5.79524	26.52127	21.97428
		CV%	13.3	48.0	42.8
		SEM	3.34588	10.82726	7.32476
		Minimum	38.305	28.807	28.807
		Median	42.3331	49.1643	42.3331
		Maximum	49.731	91.406	91.406
	Week 2	n	3	5	8
		Mean	43.6665	36.2484	39.0302
		SD	27.16781	11.86805	17.49596
		CV%	62.2	32.7	44.8
		SEM	15.68534	5.30755	6.18576
		Minimum	16.472	24.727	16.472
		Median	43.7192	34.7233	38.2527
		Maximum	70.808	53.597	70.808
	Week 6	n	3	4	7
		Mean	37.5340	38.1122	37.8644
		SD	12.98328	12.09966	11.37914
		CV%	34.6	31.7	30.1
		SEM	7.49590	6.04983	4.30091
		Minimum	22.590	26.160	22.590
		Median	43.9681	35.7617	37.7579
		Maximum	46.044	54.765	54.765

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.1 Summary of Puffing Topography Parameters by Study Product Group and Study Week (PP Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Flow Rate (mL/sec)	Week -1*	n	3	6	9
		Mean	27.0359	35.7519	32.8466
		SD	3.82638	15.87046	13.41910
		CV%	14.2	44.4	40.9
		SEM	2.20916	6.47909	4.47303
		Minimum	23.469	21.156	21.156
		Median	26.5615	32.3133	26.5615
		Maximum	31.077	62.105	62.105
	Week 2	n	3	5	8
		Mean	21.1808	24.1156	23.0151
		SD	11.52364	6.74146	8.13746
		CV%	54.4	28.0	35.4
		SEM	6.65318	3.01487	2.87703
		Minimum	7.975	17.471	7.975
		Median	26.3697	22.4444	24.4071
		Maximum	29.198	32.055	32.055
	Week 6	n	3	4	7
		Mean	22.3820	24.0936	23.3601
		SD	9.48241	5.90744	6.94679
		CV%	42.4	24.5	29.7
		SEM	5.47467	2.95372	2.62564
		Minimum	11.441	16.524	11.441
		Median	27.4870	24.4472	24.6008
		Maximum	28.218	30.956	30.956

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.1 Summary of Puffing Topography Parameters by Study Product Group and Study Week (PP Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Number of Cigarettes	Week -1*	n	3	6	9
		Mean	2.0	1.8	1.9
		SD	0.00	0.75	0.60
		CV%	0.0	41.1	31.8
		SEM	0.00	0.31	0.20
		Minimum	2	1	1
		Median	2.0	2.0	2.0
		Maximum	2	3	3
	Week 2	n	3	5	8
		Mean	1.7	1.6	1.6
		SD	0.58	0.55	0.52
		CV%	34.6	34.2	31.8
		SEM	0.33	0.24	0.18
		Minimum	1	1	1
		Median	2.0	2.0	2.0
		Maximum	2	2	2
	Week 6	n	3	4	7
		Mean	1.3	1.8	1.6
		SD	0.58	0.50	0.53
		CV%	43.3	28.6	34.0
		SEM	0.33	0.25	0.20
		Minimum	1	1	1
		Median	1.0	2.0	2.0
		Maximum	2	2	2

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.1 Summary of Puffing Topography Parameters by Study Product Group and Study Week (PP Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Number of Puffs	Week -1*	n	3	6	9
		Mean	12.2	12.7	12.5
		SD	3.33	1.56	2.09
		CV%	27.4	12.3	16.7
		SEM	1.92	0.64	0.70
		Minimum	10	11	10
		Median	10.5	12.3	12.0
		Maximum	16	15	16
	Week 2	n	3	5	8
		Mean	12.7	11.2	11.8
		SD	6.03	2.59	3.85
		CV%	47.6	23.1	32.7
		SEM	3.48	1.16	1.36
		Minimum	7	8	7
		Median	12.0	12.0	12.0
		Maximum	19	14	19
	Week 6	n	3	4	7
		Mean	14.2	11.4	12.6
		SD	7.97	3.30	5.37
		CV%	56.3	29.0	42.7
		SEM	4.60	1.65	2.03
		Minimum	8	9	8
		Median	12.0	10.3	11.5
		Maximum	23	16	23

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.2 Summary of Puffing Topography Parameters by Study Product Group and Study Week (ITT Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Puff Duration (sec)	Week -1*	n	18	18	36
		Mean	2.044	2.255	2.150
		SD	0.6057	0.7351	0.6725
		CV%	29.6	32.6	31.3
		SEM	0.1428	0.1733	0.1121
		Minimum	0.81	1.32	0.81
		Median	2.117	2.181	2.135
		Maximum	2.95	4.58	4.58
	Week 2	n	16	17	33
		Mean	2.212	2.169	2.190
		SD	0.8812	0.6937	0.7779
		CV%	39.8	32.0	35.5
		SEM	0.2203	0.1683	0.1354
		Minimum	0.94	1.15	0.94
		Median	2.099	1.950	2.000
		Maximum	4.83	3.66	4.83
	Week 6	n	17	15	32
		Mean	2.072	2.067	2.069
		SD	0.7092	0.5492	0.6291
		CV%	34.2	26.6	30.4
		SEM	0.1720	0.1418	0.1112
		Minimum	0.86	1.32	0.86
		Median	2.196	2.238	2.198
		Maximum	3.71	3.03	3.71

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.2 Summary of Puffing Topography Parameters by Study Product Group and Study Week (ITT Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Total Puff Duration (sec)	Week -1*	n	18	18	36
		Mean	23.494	27.783	25.639
		SD	7.9301	7.6979	8.0036
		CV%	33.8	27.7	31.2
		SEM	1.8692	1.8144	1.3339
		Minimum	12.85	16.92	12.85
		Median	24.488	27.238	26.175
		Maximum	35.60	45.85	45.85
	Week 2	n	16	17	33
		Mean	23.282	24.559	23.940
		SD	8.1071	6.9773	7.4545
		CV%	34.8	28.4	31.1
		SEM	2.0268	1.6922	1.2977
		Minimum	11.15	14.90	11.15
		Median	23.388	23.750	23.750
		Maximum	37.70	43.95	43.95
	Week 6	n	17	15	32
		Mean	21.966	22.122	22.039
		SD	7.0242	6.4746	6.6636
		CV%	32.0	29.3	30.2
		SEM	1.7036	1.6717	1.1780
		Minimum	7.25	12.10	7.25
		Median	25.000	21.625	23.563
		Maximum	33.40	33.95	33.95

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.2 Summary of Puffing Topography Parameters by Study Product Group and Study Week (ITT Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Puff Volume (mL)	Week -1*	n	18	18	36
		Mean	50.7496	57.8934	54.3215
		SD	12.88508	23.65244	19.11782
		CV%	25.4	40.9	35.2
		SEM	3.03704	5.57493	3.18630
		Minimum	21.475	0.643	0.643
		Median	53.2742	59.0605	54.3257
		Maximum	75.085	123.468	123.468
	Week 2	n	16	17	33
		Mean	44.6595	49.7368	47.2751
		SD	13.48557	13.17315	13.36612
		CV%	30.2	26.5	28.3
		SEM	3.37139	3.19496	2.32674
		Minimum	20.687	33.113	20.687
		Median	46.2450	47.8327	46.9855
		Maximum	73.097	82.073	82.073
	Week 6	n	17	15	32
		Mean	47.9733	46.7513	47.4005
		SD	13.25475	11.63150	12.33536
		CV%	27.6	24.9	26.0
		SEM	3.21475	3.00324	2.18060
		Minimum	22.738	26.800	22.738
		Median	46.3159	43.5155	45.7127
		Maximum	79.678	65.199	79.678

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.2 Summary of Puffing Topography Parameters by Study Product Group and Study Week (ITT Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Total Puff Volume (mL)	Week -1*	n	18	18	36
		Mean	574.2052	713.5905	643.8978
		SD	157.51025	269.03756	228.47920
		CV%	27.4	37.7	35.5
		SEM	37.12552	63.41276	38.07987
		Minimum	279.652	7.059	7.059
		Median	549.4070	712.0355	626.9559
		Maximum	938.671	1433.167	1433.167
	Week 2	n	16	17	33
		Mean	473.4290	576.1800	526.3613
		SD	145.98709	189.22450	174.96426
		CV%	30.8	32.8	33.2
		SEM	36.49677	45.89368	30.45737
		Minimum	249.115	373.151	249.115
		Median	470.6193	512.4210	491.8440
		Maximum	783.186	984.871	984.871
	Week 6	n	17	15	32
		Mean	508.9264	491.4643	500.7410
		SD	119.46079	106.43112	112.06998
		CV%	23.5	21.7	22.4
		SEM	28.97350	27.48040	19.81136
		Minimum	279.233	294.804	279.233
		Median	507.5250	507.4890	507.5070
		Maximum	717.102	651.991	717.102

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.2 Summary of Puffing Topography Parameters by Study Product Group and Study Week (ITT Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Inter Puff Interval (sec)	Week -1*	n	18	18	36
		Mean	30.269	29.222	29.746
		SD	10.2050	8.2654	9.1677
		CV%	33.7	28.3	30.8
		SEM	2.4053	1.9482	1.5280
		Minimum	16.69	14.70	14.70
		Median	29.252	29.905	29.863
		Maximum	52.30	45.86	52.30
	Week 2	n	16	17	33
		Mean	24.280	26.624	25.488
		SD	9.2227	12.1134	10.7076
		CV%	38.0	45.5	42.0
		SEM	2.3057	2.9379	1.8640
		Minimum	11.74	9.73	9.73
		Median	25.485	23.396	24.200
		Maximum	43.63	55.63	55.63
	Week 6	n	17	15	32
		Mean	21.044	27.215	23.937
		SD	7.1810	11.4332	9.7693
		CV%	34.1	42.0	40.8
		SEM	1.7417	2.9520	1.7270
		Minimum	9.44	9.53	9.44
		Median	21.144	26.215	21.923
		Maximum	38.21	46.08	46.08

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.2 Summary of Puffing Topography Parameters by Study Product Group and Study Week (ITT Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Peak Puff Flow Rate (mL/sec)	Week -1*	n	18	18	36
		Mean	44.3213	45.9639	45.1426
		SD	10.85319	20.10163	15.94278
		CV%	24.5	43.7	35.3
		SEM	2.55812	4.73800	2.65713
		Minimum	22.981	5.857	5.857
		Median	43.6273	43.3856	43.6273
		Maximum	64.067	91.406	91.406
	Week 2	n	16	17	33
		Mean	39.7010	41.4412	40.5975
		SD	13.72368	9.94555	11.76950
		CV%	34.6	24.0	29.0
		SEM	3.43092	2.41215	2.04881
		Minimum	16.472	24.727	16.472
		Median	41.5785	39.7534	41.4567
		Maximum	70.808	55.236	70.808
	Week 6	n	17	15	32
		Mean	43.4274	40.0195	41.8300
		SD	14.75467	9.05336	12.34352
		CV%	34.0	22.6	29.5
		SEM	3.57853	2.33757	2.18205
		Minimum	22.590	22.038	22.038
		Median	42.9566	41.2337	42.2946
		Maximum	81.162	54.765	81.162

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.2 Summary of Puffing Topography Parameters by Study Product Group and Study Week (ITT Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Flow Rate (mL/sec)	Week -1*	n	18	18	36
		Mean	27.8305	28.5428	28.1866
		SD	8.55885	12.99509	10.85056
		CV%	30.8	45.5	38.5
		SEM	2.01734	3.06297	1.80843
		Minimum	12.196	0.388	0.388
		Median	26.8053	28.2816	26.8053
		Maximum	45.389	62.105	62.105
	Week 2	n	16	17	33
		Mean	23.6309	25.4534	24.5698
		SD	7.84344	5.68677	6.77219
		CV%	33.2	22.3	27.6
		SEM	1.96086	1.37925	1.17889
		Minimum	7.975	17.471	7.975
		Median	26.3433	25.0306	26.3169
		Maximum	34.696	36.496	36.496
	Week 6	n	17	15	32
		Mean	26.7164	24.1247	25.5016
		SD	9.72496	5.15403	7.90798
		CV%	36.4	21.4	31.0
		SEM	2.35865	1.33076	1.39795
		Minimum	11.441	14.998	11.441
		Median	26.0233	25.4632	25.6752
		Maximum	47.828	33.121	47.828

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.2 Summary of Puffing Topography Parameters by Study Product Group and Study Week (ITT Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Number of Cigarettes	Week -1*	n	18	18	36
		Mean	1.9	1.6	1.8
		SD	0.47	0.61	0.55
		CV%	25.0	37.7	31.7
		SEM	0.11	0.14	0.09
		Minimum	1	1	1
		Median	2.0	2.0	2.0
		Maximum	3	3	3
	Week 2	n	16	17	33
		Mean	1.7	1.4	1.5
		SD	0.79	0.49	0.67
		CV%	47.0	36.4	44.0
		SEM	0.20	0.12	0.12
		Minimum	1	1	1
		Median	2.0	1.0	1.0
		Maximum	4	2	4
	Week 6	n	17	15	32
		Mean	1.2	1.5	1.3
		SD	0.44	0.52	0.48
		CV%	35.4	35.2	35.9
		SEM	0.11	0.13	0.09
		Minimum	1	1	1
		Median	1.0	1.0	1.0
		Maximum	2	2	2

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

Table 14.2.3.1.2 Summary of Puffing Topography Parameters by Study Product Group and Study Week (ITT Population)

Parameter (unit)	Study Week	Statistics	Study Product Group		
			Non-Mentholated	VLN Mentholated	VLN Combined
Average Number of Puffs	Week -1*	n	18	18	36
		Mean	11.6	12.6	12.1
		SD	2.45	2.21	2.35
		CV%	21.1	17.6	19.4
		SEM	0.58	0.52	0.39
		Minimum	7	10	7
		Median	11.3	12.0	12.0
		Maximum	16	19	19
	Week 2	n	16	17	33
		Mean	11.1	11.9	11.5
		SD	3.43	3.47	3.42
		CV%	30.9	29.3	29.8
		SEM	0.86	0.84	0.60
		Minimum	6	7	6
		Median	10.4	11.0	11.0
		Maximum	19	20	20
	Week 6	n	17	15	32
		Mean	11.1	10.9	11.0
		SD	3.68	2.67	3.20
		CV%	33.3	24.5	29.1
		SEM	0.89	0.69	0.57
		Minimum	7	8	7
		Median	11.0	10.0	11.0
		Maximum	23	16	23

Note: * Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.3.2 Statistical Summary of Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group
(PP Population)

Parameter (unit)	Study Week	Product Group	Means				Difference (Test Week - Baseline)	95% Confidence Intervals		p-Value
			Test Week	(n)	Baseline	(n)				
Average Puff Duration (sec)	Week 2	VLN Non-Mentholated	2.690	(3)	1.923	(3)	0.77	-1.85 -	3.38	0.3339
		VLN Mentholated	2.255	(5)	2.230	(5)	0.02	-0.34 -	0.39	0.8611
		VLN Combined	2.418	(8)	2.115	(8)	0.30	-0.30 -	0.90	0.2706
	Week 6	VLN Non-Mentholated	2.065	(3)	1.923	(3)	0.14	-0.08 -	0.37	0.1123
		VLN Mentholated	1.979	(4)	2.068	(4)	-0.09	-0.47 -	0.29	0.5101
		VLN Combined	2.016	(7)	2.005	(7)	0.01	-0.19 -	0.21	0.9018
Average Total Puff Duration (sec)	Week 2	VLN Non-Mentholated	26.27	(3)	21.23	(3)	5.03	4.29 -	5.77	0.0012
		VLN Mentholated	24.48	(5)	28.84	(5)	-4.36	-8.97 -	0.26	0.0589
		VLN Combined	25.15	(8)	25.98	(8)	-0.83	-5.53 -	3.86	0.6869
	Week 6	VLN Non-Mentholated	23.28	(3)	21.23	(3)	2.04	-14.50 -	18.59	0.6485
		VLN Mentholated	22.50	(4)	27.06	(4)	-4.56	-14.80 -	5.69	0.2518
		VLN Combined	22.83	(7)	24.56	(7)	-1.73	-8.13 -	4.67	0.5334

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
Paired t-test method is used to perform the analysis.

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Table 14.2.3.2 Statistical Summary of Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group
(PP Population)

Parameter (unit)	Study Week	Product Group	Means				Difference (Test Week - Baseline)	95% Confidence Intervals		p-Value
			Test Week	(n)	Baseline	(n)				
Average Puff Volume (mL)	Week 2	VLN Non-Mentholated	38.92	(3)	46.72	(3)	-7.80	-58.65 - 43.05		0.5771
		VLN Mentholated	49.92	(5)	69.33	(5)	-19.40	-64.38 - 25.57		0.2971
		VLN Combined	45.80	(8)	60.85	(8)	-15.05	-40.21 - 10.10		0.2000
	Week 6	VLN Non-Mentholated	37.33	(3)	46.72	(3)	-9.40	-60.22 - 41.43		0.5097
		VLN Mentholated	46.05	(4)	71.51	(4)	-25.46	-69.29 - 18.37		0.1617
		VLN Combined	42.31	(7)	60.89	(7)	-18.57	-41.09 - 3.94		0.0901
Average Total Puff Volume (mL)	Week 2	VLN Non-Mentholated	475.8	(3)	520.0	(3)	-44.23	-754.3 - 665.84		0.8138
		VLN Mentholated	552.8	(5)	860.7	(5)	-307.84	-783.4 - 167.73		0.1467
		VLN Combined	523.9	(8)	732.9	(8)	-208.99	-505.5 - 87.52		0.1395
	Week 6	VLN Non-Mentholated	500.1	(3)	520.0	(3)	-19.90	-737.3 - 697.47		0.9159
		VLN Mentholated	501.0	(4)	886.6	(4)	-385.65	-828.9 - 57.61		0.0696
		VLN Combined	500.6	(7)	729.5	(7)	-228.90	-528.3 - 70.52		0.1106

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
Paired t-test method is used to perform the analysis.

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Table 14.2.3.2 Statistical Summary of Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group
(PP Population)

Parameter (unit)	Study Week	Product Group	Means				Difference (Test Week - Baseline)	95%		p-Value
			Test Week	(n)	Baseline	(n)		Confidence Intervals		
Average Inter-Puff Interval (sec)	Week 2	VLN Non-Mentholated	19.42	(3)	32.43	(3)	-13.01	-20.00 -	-6.02	0.0152
		VLN Mentholated	30.72	(5)	36.10	(5)	-5.38	-15.30 -	4.54	0.2064
		VLN Combined	26.48	(8)	34.72	(8)	-8.24	-14.40 -	-2.08	0.0159
	Week 6	VLN Non-Mentholated	19.99	(3)	32.43	(3)	-12.44	-26.04 -	1.15	0.0588
		VLN Mentholated	27.84	(4)	36.30	(4)	-8.46	-23.80 -	6.88	0.1775
		VLN Combined	24.47	(7)	34.64	(7)	-10.17	-17.39 -	-2.95	0.0137
Average Peak Puff Flow Rate (mL/sec)	Week 2	VLN Non-Mentholated	43.67	(3)	43.46	(3)	0.21	-63.69 -	64.11	0.9900
		VLN Mentholated	36.25	(5)	50.51	(5)	-14.26	-44.81 -	16.29	0.2647
		VLN Combined	39.03	(8)	47.86	(8)	-8.83	-29.16 -	11.49	0.3383
	Week 6	VLN Non-Mentholated	37.53	(3)	43.46	(3)	-5.92	-28.00 -	16.16	0.3677
		VLN Mentholated	38.11	(4)	55.93	(4)	-17.82	-56.24 -	20.59	0.2363
		VLN Combined	37.86	(7)	50.59	(7)	-12.72	-30.23 -	4.78	0.1257

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
Paired t-test method is used to perform the analysis.

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Table 14.2.3.2 Statistical Summary of Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group
(PP Population)

Parameter (unit)	Study Week	Product Group	Means				Difference (Test Week - Baseline)	95% Confidence Intervals		p-Value
			Test Week	(n)	Baseline	(n)				
Average Flow Rate (mL/sec)	Week 2	VLN Non-Mentholated	21.18	(3)	27.04	(3)	-5.86	-28.51 - 16.80		0.3819
		VLN Mentholated	24.12	(5)	34.06	(5)	-9.95	-31.18 - 11.29		0.2633
		VLN Combined	23.02	(8)	31.43	(8)	-8.41	-20.10 - 3.27		0.1325
	Week 6	VLN Non-Mentholated	22.38	(3)	27.04	(3)	-4.65	-21.20 - 11.89		0.3498
		VLN Mentholated	24.09	(4)	37.29	(4)	-13.19	-39.28 - 12.89		0.2059
		VLN Combined	23.36	(7)	32.89	(7)	-9.53	-21.59 - 2.53		0.1012
Average Number of Puffs (N)	Week 2	VLN Non-Mentholated	12.67	(3)	12.17	(3)	0.50	-7.26 - 8.26		0.8075
		VLN Mentholated	11.20	(5)	12.83	(5)	-1.63	-3.76 - 0.49		0.0995
		VLN Combined	11.75	(8)	12.58	(8)	-0.83	-2.82 - 1.16		0.3554
	Week 6	VLN Non-Mentholated	14.17	(3)	12.17	(3)	2.00	-9.85 - 13.85		0.5432
		VLN Mentholated	11.38	(4)	12.92	(4)	-1.54	-5.60 - 2.52		0.3133
		VLN Combined	12.57	(7)	12.60	(7)	-0.02	-3.54 - 3.49		0.9873

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
Paired t-test method is used to perform the analysis.

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Table 14.2.3.3 Statistical Summary of Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Parameter (unit)	Study Week	Product Group	Means				Difference (Test Week - Baseline)	95% Confidence Intervals		p-Value
			Test Week	(n)	Baseline	(n)				
Average Puff Duration (sec)	Week 2	VLN Non-Mentholated	2.212	(16)	2.125	(16)	0.09	-0.24 - 0.41		0.5745
		VLN Mentholated	2.169	(17)	2.293	(17)	-0.12	-0.37 - 0.12		0.2937
		VLN Combined	2.190	(33)	2.212	(33)	-0.02	-0.21 - 0.17		0.8207
	Week 6	VLN Non-Mentholated	2.072	(17)	2.069	(17)	0.00	-0.19 - 0.19		0.9817
		VLN Mentholated	2.067	(15)	2.255	(15)	-0.19	-0.51 - 0.14		0.2327
		VLN Combined	2.069	(32)	2.156	(32)	-0.09	-0.26 - 0.09		0.3163
Average Total Puff Duration (sec)	Week 2	VLN Non-Mentholated	23.28	(16)	24.57	(16)	-1.29	-4.39 - 1.82		0.3917
		VLN Mentholated	24.56	(17)	28.28	(17)	-3.72	-6.33 - -1.11		0.0082
		VLN Combined	23.94	(33)	26.48	(33)	-2.54	-4.49 - -0.58		0.0125
	Week 6	VLN Non-Mentholated	21.97	(17)	24.03	(17)	-2.06	-4.90 - 0.77		0.1429
		VLN Mentholated	22.12	(15)	27.68	(15)	-5.56	-9.09 - -2.03		0.0045
		VLN Combined	22.04	(32)	25.74	(32)	-3.70	-5.90 - -1.50		0.0017

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
Paired t-test method is used to perform the analysis.

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Table 14.2.3.3 Statistical Summary of Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group
(ITT Population)

Parameter (unit)	Study Week	Product Group	Means				Difference (Test Week - Baseline)	95% Confidence Intervals		p-Value
			Test Week	(n)	Baseline	(n)				
Average Puff Volume (mL)	Week 2	VLN Non-Mentholated	44.66	(16)	51.03	(16)	-6.38	-14.00 - 1.25		0.0951
		VLN Mentholated	49.74	(17)	57.38	(17)	-7.64	-20.28 - 5.00		0.2183
		VLN Combined	47.28	(33)	54.30	(33)	-7.03	-14.11 - 0.05		0.0516
	Week 6	VLN Non-Mentholated	47.97	(17)	50.27	(17)	-2.30	-8.22 - 3.63		0.4232
		VLN Mentholated	46.75	(15)	56.24	(15)	-9.49	-21.39 - 2.41		0.1092
		VLN Combined	47.40	(32)	53.07	(32)	-5.67	-11.81 - 0.47		0.0692
Average Total Puff Volume (mL)	Week 2	VLN Non-Mentholated	473.4	(16)	580.9	(16)	-107.47	-197.5 - -17.43		0.0225
		VLN Mentholated	576.2	(17)	708.5	(17)	-132.33	-277.1 - 12.41		0.0705
		VLN Combined	526.4	(33)	646.6	(33)	-120.27	-202.0 - -38.51		0.0052
	Week 6	VLN Non-Mentholated	508.9	(17)	576.8	(17)	-67.88	-159.3 - 23.58		0.1352
		VLN Mentholated	491.5	(15)	690.8	(15)	-199.38	-337.9 - -60.83		0.0080
		VLN Combined	500.7	(32)	630.3	(32)	-129.52	-209.4 - -49.67		0.0024

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
Paired t-test method is used to perform the analysis.

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Table 14.2.3.3 Statistical Summary of Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group
(ITT Population)

Parameter (unit)	Study Week	Product Group	Means				Difference (Test Week - Baseline)	95% Confidence Intervals		p-Value
			Test Week	(n)	Baseline	(n)				
Average Inter-Puff Interval (sec)	Week 2	VLN Non-Mentholated	24.28	(16)	29.50	(16)	-5.22	-9.95 -	-0.50	0.0325
		VLN Mentholated	26.62	(17)	28.89	(17)	-2.27	-7.62 -	3.08	0.3824
		VLN Combined	25.49	(33)	29.19	(33)	-3.70	-7.13 -	-0.28	0.0351
	Week 6	VLN Non-Mentholated	21.04	(17)	29.46	(17)	-8.41	-12.62 -	-4.21	0.0006
		VLN Mentholated	27.22	(15)	29.31	(15)	-2.09	-7.90 -	3.71	0.4516
		VLN Combined	23.94	(32)	29.39	(32)	-5.45	-8.95 -	-1.95	0.0034
Average Peak Puff Flow Rate (mL/sec)	Week 2	VLN Non-Mentholated	39.70	(16)	42.89	(16)	-3.19	-10.03 -	3.66	0.3370
		VLN Mentholated	41.44	(17)	44.02	(17)	-2.58	-13.49 -	8.33	0.6235
		VLN Combined	40.60	(33)	43.47	(33)	-2.87	-9.04 -	3.30	0.3500
	Week 6	VLN Non-Mentholated	43.43	(17)	43.73	(17)	-0.30	-5.32 -	4.71	0.8992
		VLN Mentholated	40.02	(15)	43.95	(15)	-3.93	-14.74 -	6.88	0.4484
		VLN Combined	41.83	(32)	43.83	(32)	-2.00	-7.41 -	3.40	0.4549

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
Paired t-test method is used to perform the analysis.

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Table 14.2.3.3 Statistical Summary of Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group
(ITT Population)

Parameter (unit)	Study Week	Product Group	Means				Difference (Test Week - Baseline)	95%		
			Test Week	(n)	Baseline	(n)		Confidence Intervals	p-Value	
Average Flow Rate (mL/sec)	Week 2	VLN Non-Mentholated	23.63	(16)	26.65	(16)	-3.02	-6.60 -	0.56	0.0919
		VLN Mentholated	25.45	(17)	27.62	(17)	-2.17	-9.11 -	4.77	0.5171
		VLN Combined	24.57	(33)	27.15	(33)	-2.58	-6.34 -	1.18	0.1714
	Week 6	VLN Non-Mentholated	26.72	(17)	27.08	(17)	-0.37	-3.58 -	2.85	0.8117
		VLN Mentholated	24.12	(15)	27.62	(15)	-3.49	-10.39 -	3.40	0.2958
		VLN Combined	25.50	(32)	27.33	(32)	-1.83	-5.31 -	1.64	0.2901
Average Number of Puffs (N)	Week 2	VLN Non-Mentholated	11.08	(16)	11.70	(16)	-0.62	-1.91 -	0.67	0.3232
		VLN Mentholated	11.85	(17)	12.60	(17)	-0.75	-2.15 -	0.66	0.2772
		VLN Combined	11.48	(33)	12.16	(33)	-0.68	-1.59 -	0.22	0.1328
	Week 6	VLN Non-Mentholated	11.06	(17)	11.77	(17)	-0.72	-2.32 -	0.89	0.3594
		VLN Mentholated	10.90	(15)	12.58	(15)	-1.68	-2.79 -	-0.57	0.0059
		VLN Combined	10.98	(32)	12.15	(32)	-1.17	-2.13 -	-0.21	0.0189

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
Paired t-test method is used to perform the analysis.

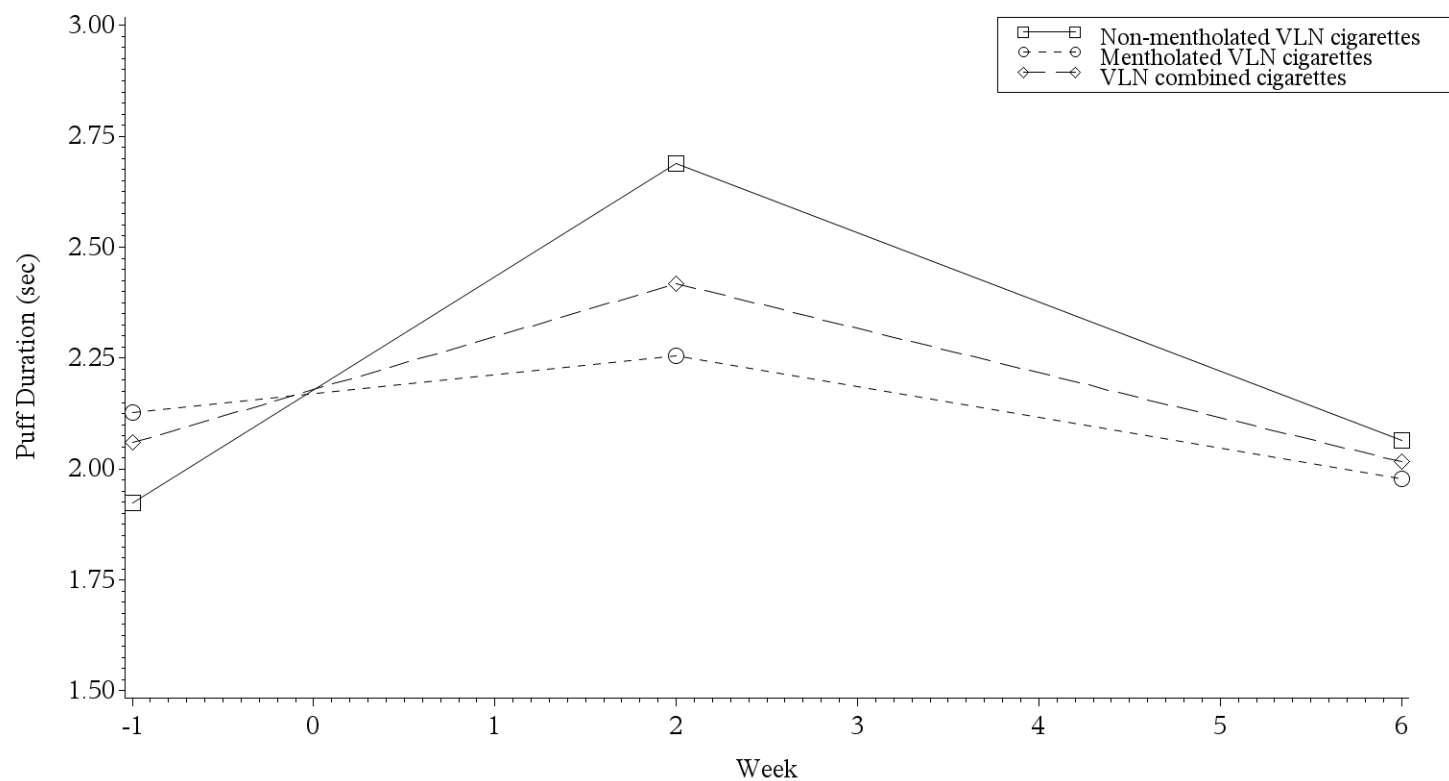
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14.2.4 Puff Topography Parameter Figures

- Figure 14.2.4.1 Mean Puffing Topography Parameter (Puff Duration) by Study Product Group and Study Week (PP Population)
- Figure 14.2.4.2 Mean Puffing Topography Parameter (Puff Volume) by Study Product Group and Study Week (PP Population)
- Figure 14.2.4.3 Mean Puffing Topography Parameter (Peak Puff Flow Rate) by Study Product Group and Study Week (PP Population)
- Figure 14.2.4.4 Mean Puffing Topography Parameter (Average Flow Rate) by Study Product Group and Study Week (PP Population)
- Figure 14.2.4.5 Mean Puffing Topography Parameter (Inter-puff Interval) by Study Product Group and Study Week (PP Population)
- Figure 14.2.4.6 Mean Puffing Topography Parameter (Puff Duration) by Study Product Group and Study Week (ITT Population)
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- Figure 14.2.4.9 Mean Puffing Topography Parameter (Average Flow Rate) by Study Product Group and Study Week (ITT Population)
- Figure 14.2.4.10 Mean Puffing Topography Parameter (Inter-puff Interval) by Study Product Group and Study Week (ITT Population)

Figure 14.2.4.1

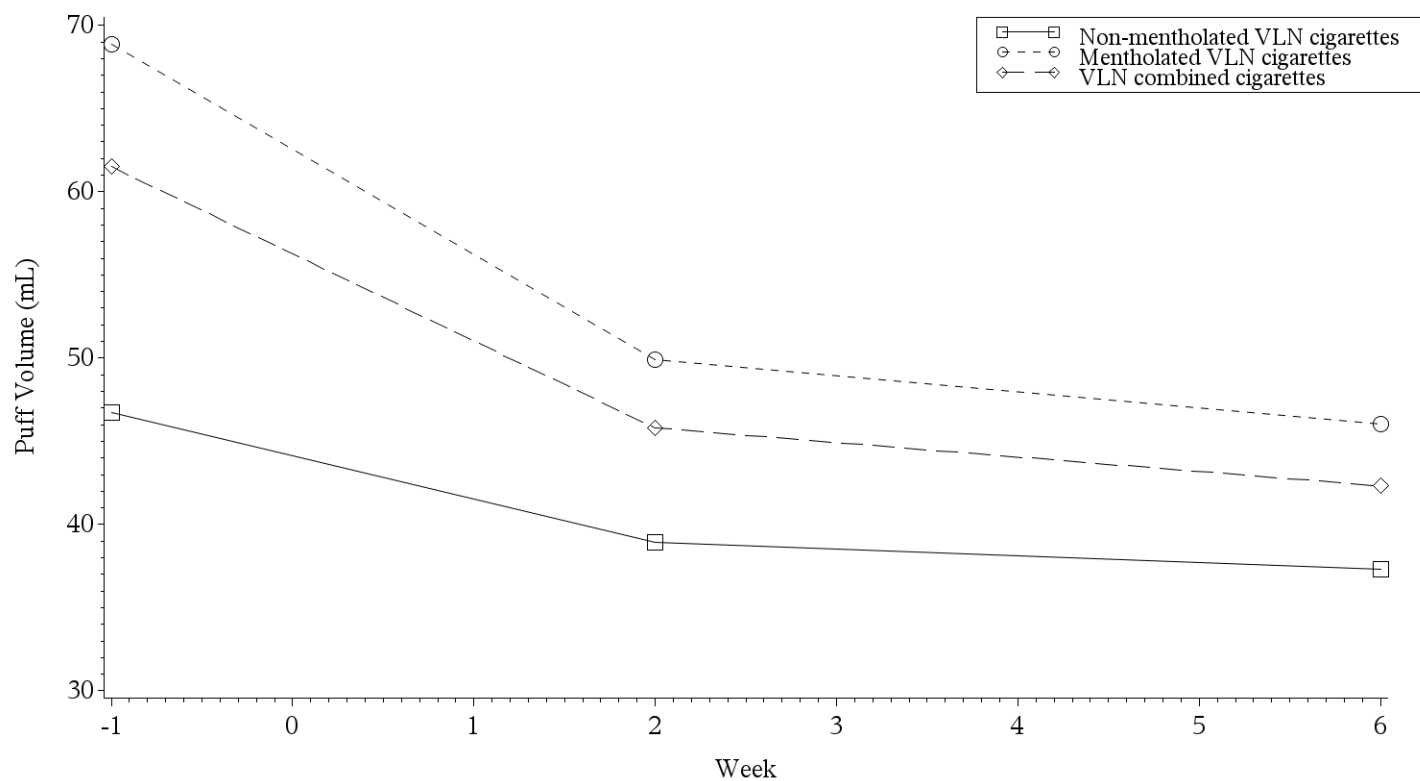
Mean Puffing Topography Parameter (Puff Duration) by Study Product Group and Study Week (PP Population)



Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
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Figure 14.2.4.2

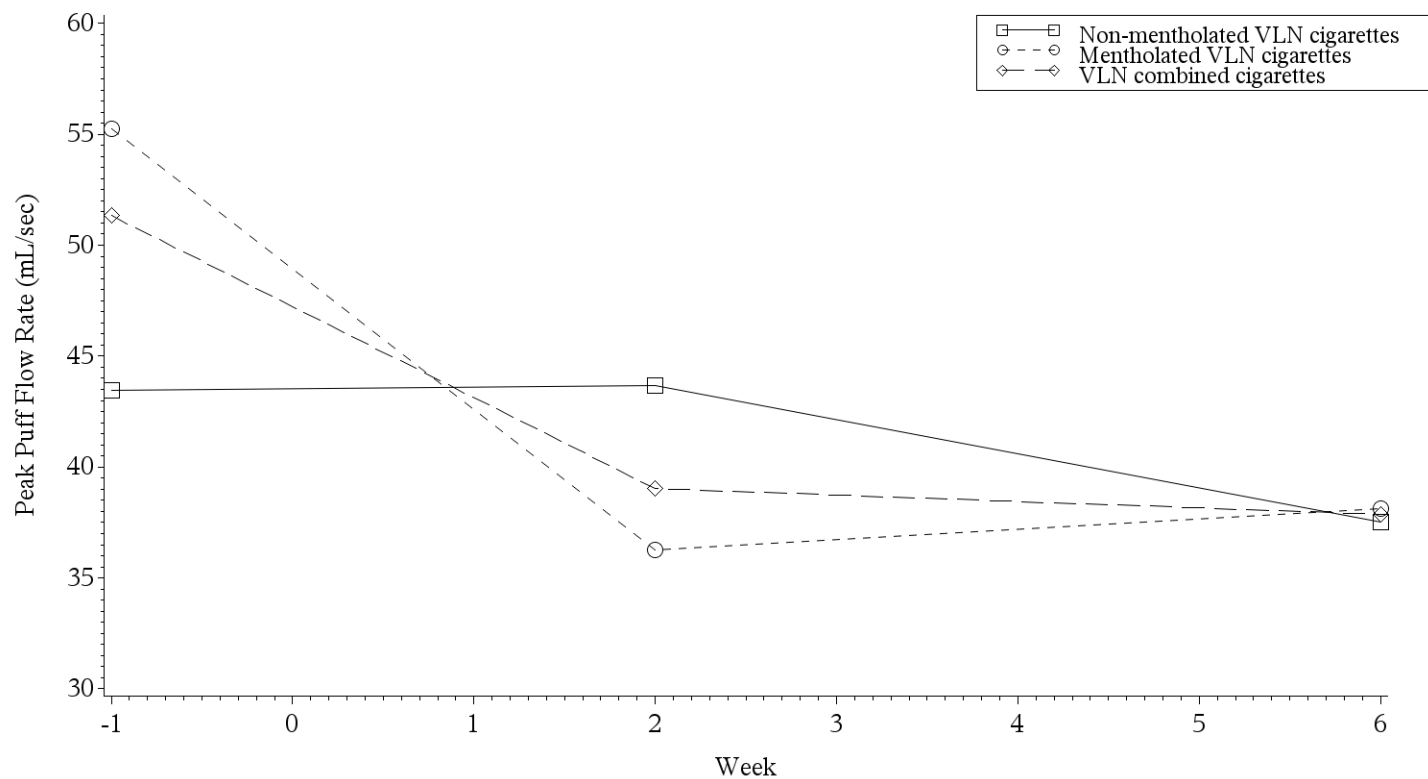
Mean Puffing Topography Parameter (Puff Volume) by Study Product Group and Study Week (PP Population)



Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
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Figure 14.2.4.3

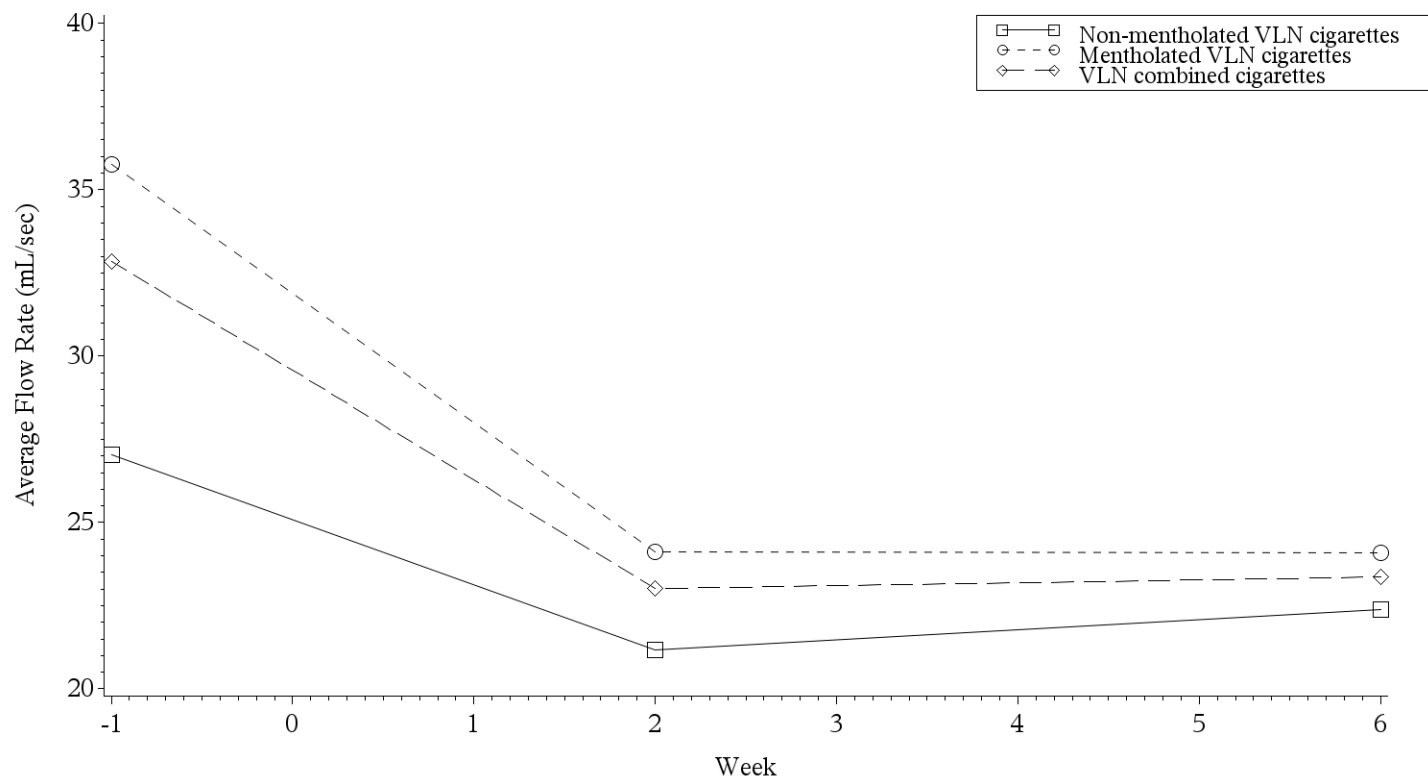
Mean Puffing Topography Parameter (Peak Puff Flow Rate) by Study Product Group and Study Week (PP Population)



Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
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Figure 14.2.4.4

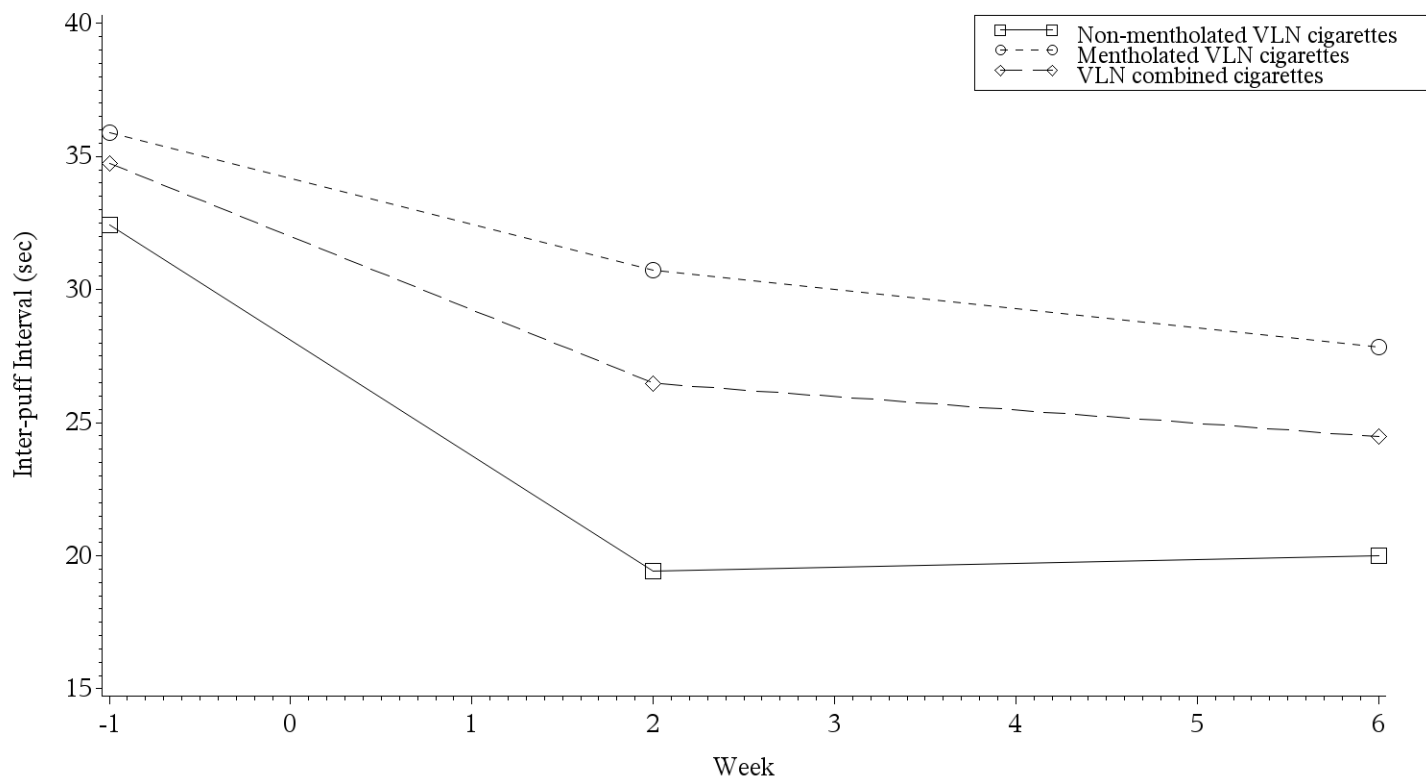
Mean Puffing Topography Parameter (Average Flow Rate) by Study Product Group and Study Week (PP Population)



Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
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Figure 14.2.4.5

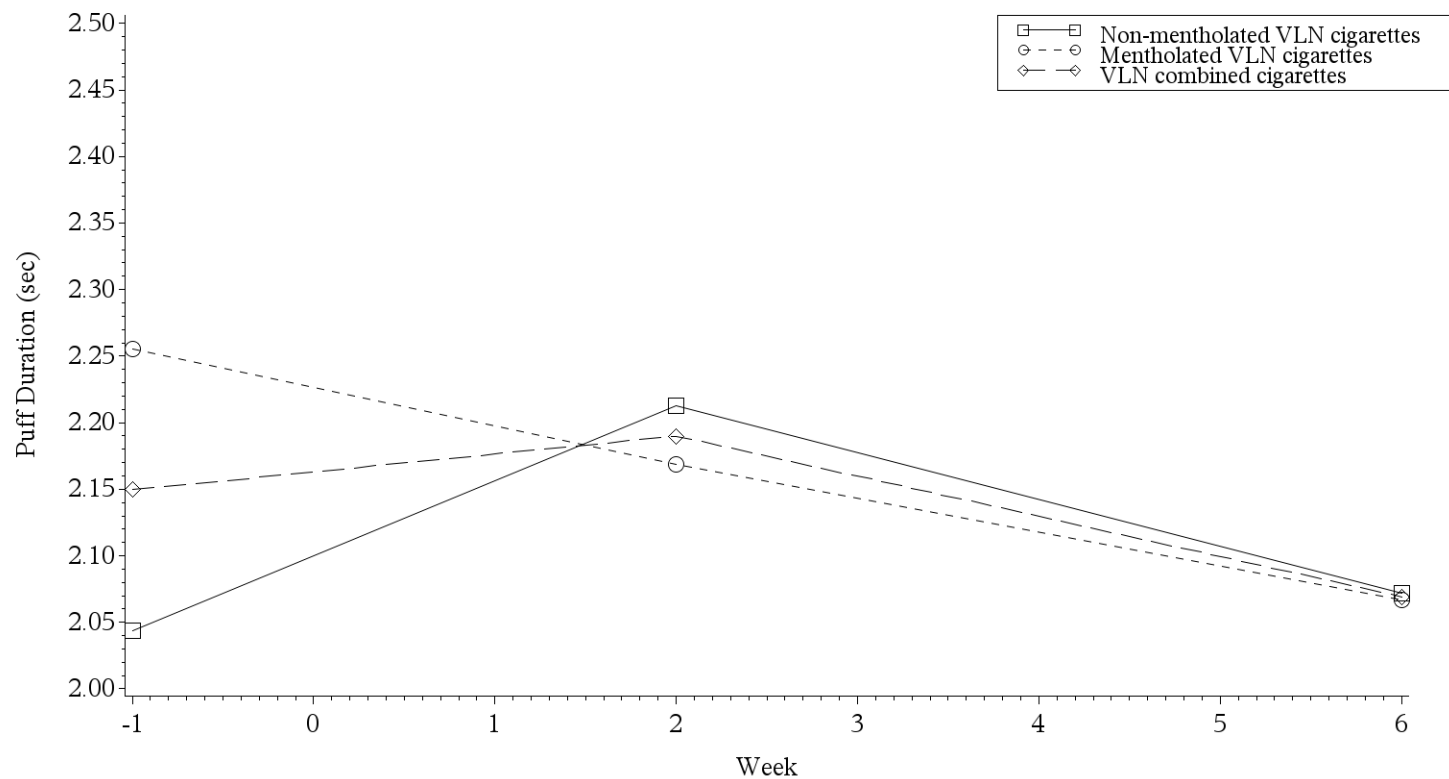
Mean Puffing Topography Parameter (Inter-puff Interval) by Study Product Group and Study Week (PP Population)



Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
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Figure 14.2.4.6

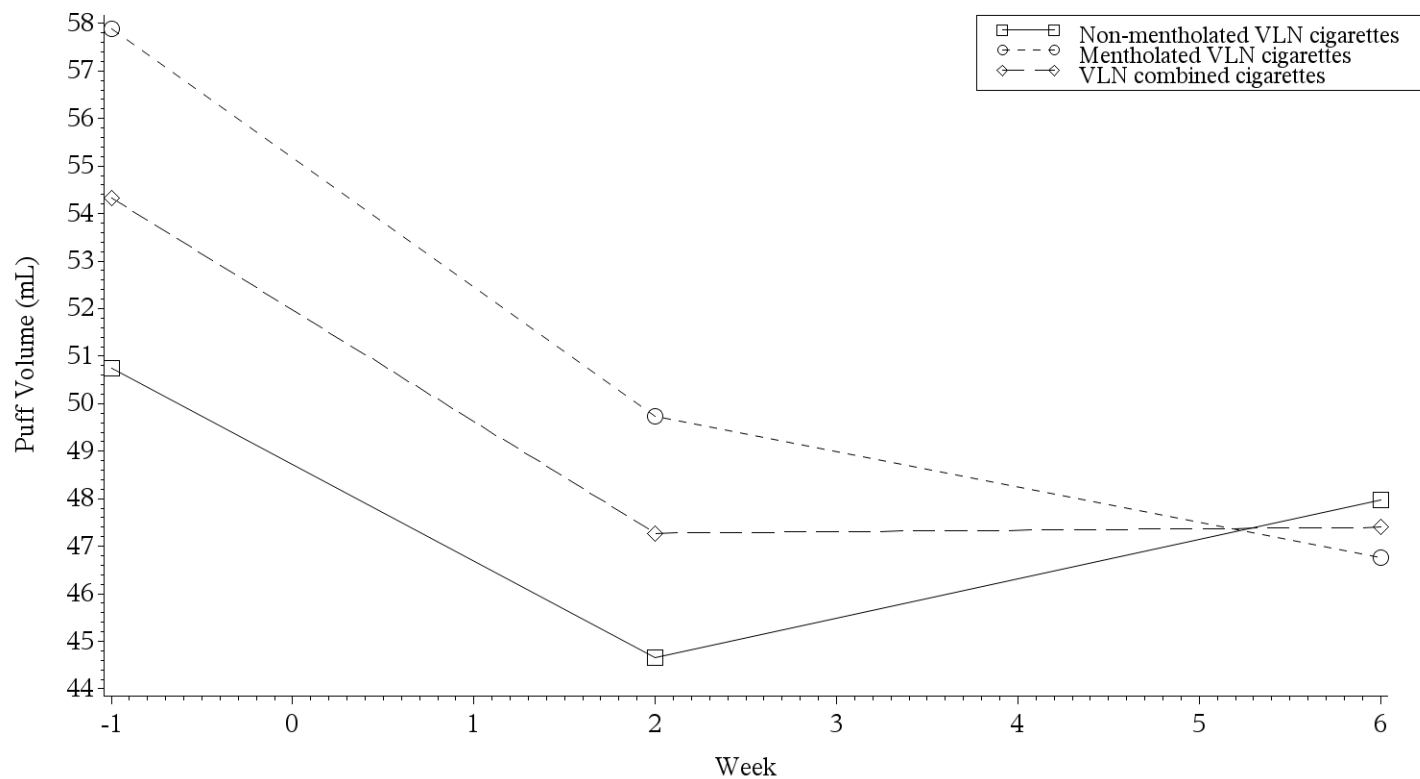
Mean Puffing Topography Parameter (Puff Duration) by Study Product Group and Study Week (ITT Population)



Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
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Figure 14.2.4.7

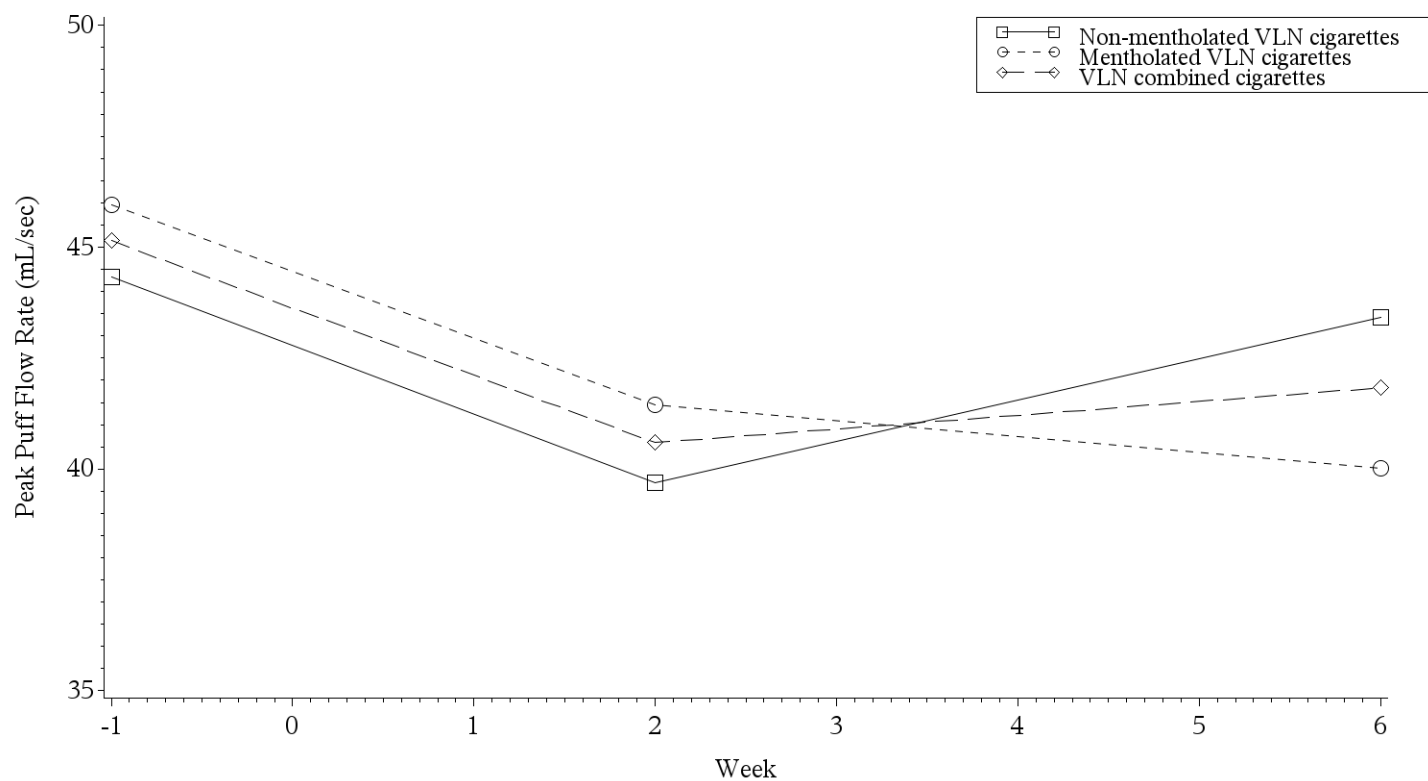
Mean Puffing Topography Parameter (Puff Volume) by Study Product Group and Study Week (ITT Population)



Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
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Figure 14.2.4.8

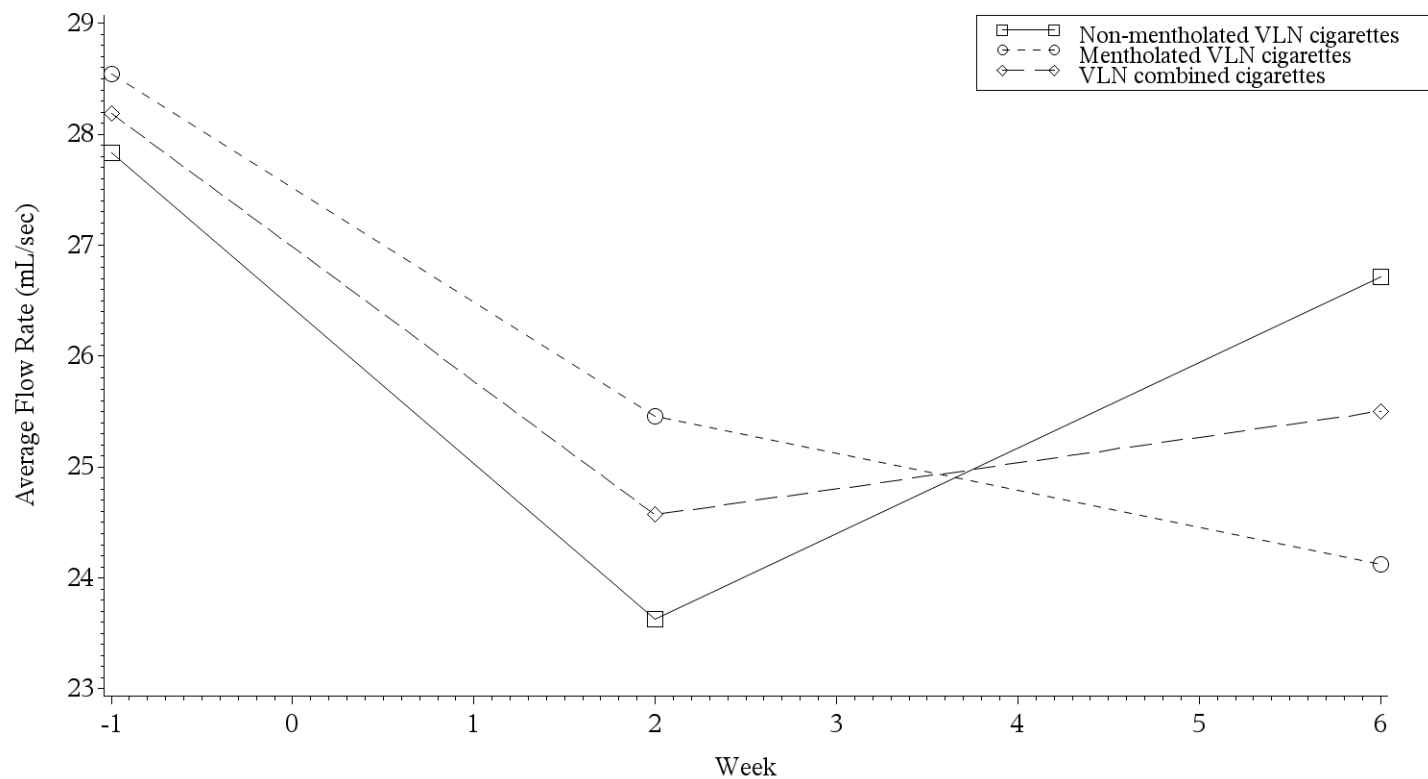
Mean Puffing Topography Parameter (Peak Puff Flow Rate) by Study Product Group and Study Week (ITT Population)



Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
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Figure 14.2.4.9

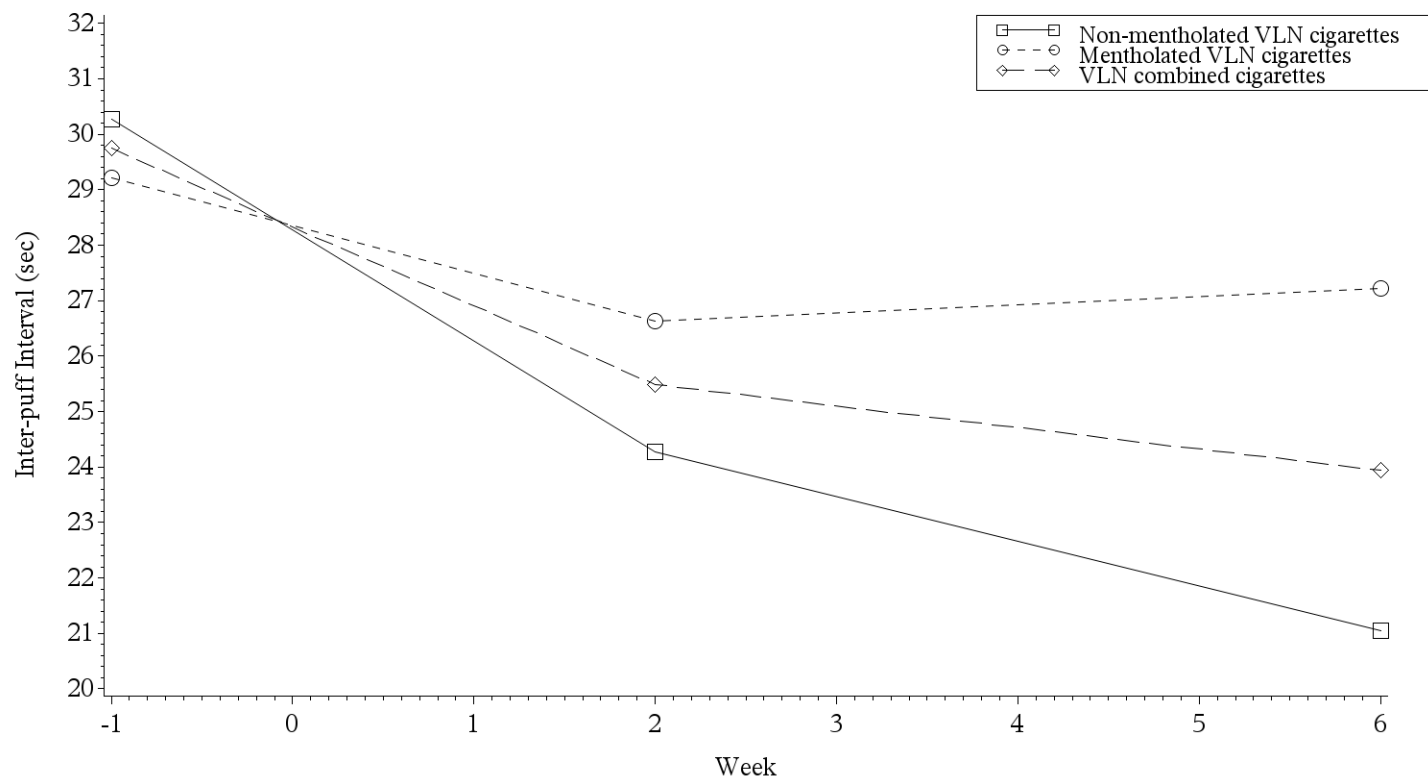
Mean Puffing Topography Parameter (Average Flow Rate) by Study Product Group and Study Week (ITT Population)



Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
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Figure 14.2.4.10

Mean Puffing Topography Parameter (Inter-puff Interval) by Study Product Group and Study Week (ITT Population)



Subjects used their own usual brand cigarettes at Week -1, and then switched to VLN products.
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14.2.5 Biomarker Tables

Urine NNAL

Table 14.2.5.1.1.1.1	Summary of Urinary NNAL Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.1.1.1.2	Summary of Urinary NNAL Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)
Table 14.2.5.1.1.2.1	Summary of Urinary NNAL Mass Excreted Change from Baseline (ng/24 hour) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.1.1.2.2	Summary of Urinary NNAL Mass Excreted Change from Baseline (ng/24 hour) by Study Product Group and Study Week (PP Population)
Table 14.2.5.1.1.3.1	Summary of Urinary NNAL Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.1.1.3.2	Summary of Urinary NNAL Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
Table 14.2.5.1.1.4.1	Summary of Urinary NNAL Creatinine-Normalized Excretion Level (ng/g creatinine) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.1.1.4.2	Summary of Urinary NNAL Creatinine-Normalized Excretion Level (ng/g creatinine) by Study Product Group and Study Week (PP Population)
Table 14.2.5.1.1.5.1	Summary of Urinary NNAL Creatinine-Normalized Excretion Level Change from Baseline (ng/g creatinine) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.1.1.5.2	Summary of Urinary NNAL Creatinine-Normalized Excretion Level Change from Baseline (ng/g creatinine) by Study Product Group and Study Week (PP Population)
Table 14.2.5.1.1.6.1	Summary of Urinary NNAL Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.1.1.6.2	Summary of Urinary NNAL Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
Table 14.2.5.1.2.1	Statistical Comparison of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 14.2.5.1.2.2	Statistical Comparison of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Table 14.2.5.1.3.1 Statistical Comparison of Absolute Change from Baseline in Urinary NNAL Mass Excreted (ng/24 hour) Among Study Product Groups at Weeks 2 and 6 (PP Population)

Table 14.2.5.1.3.2 Statistical Comparison of Absolute Change from Baseline in Urinary NNAL Mass Excreted (ng/24 hour) Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Urine NNN

Table 14.2.5.2.1.1.1 Summary of Urinary NNN Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)

Table 14.2.5.2.1.1.2 Summary of Urinary NNN Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)

Table 14.2.5.2.1.2.1 Summary of Urinary NNN Mass Excreted Change from Baseline (ng/24 hour) by Study Product Group and Study Week (ITT Population)

Table 14.2.5.2.1.2.2 Summary of Urinary NNN Mass Excreted Change from Baseline (ng/24 hour) by Study Product Group and Study Week (PP Population)

Table 14.2.5.2.1.3.1 Summary of Urinary NNN Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)

Table 14.2.5.2.1.3.2 Summary of Urinary NNN Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)

Table 14.2.5.2.1.4.1 Summary of Urinary NNN Creatinine-Normalized Excretion Level (ng/g creatinine) by Study Product Group and Study Week (ITT Population)

Table 14.2.5.2.1.4.2 Summary of Urinary NNN Creatinine-Normalized Excretion Level (ng/g creatinine) by Study Product Group and Study Week (PP Population)

Table 14.2.5.2.1.5.1 Summary of Urinary NNN Creatinine-Normalized Excretion Level Change from Baseline (ng/g creatinine) by Study Product Group and Study Week (ITT Population)

Table 14.2.5.2.1.5.2 Summary of Urinary NNN Creatinine-Normalized Excretion Level Change from Baseline (ng/g creatinine) by Study Product Group and Study Week (PP Population)

Table 14.2.5.2.1.6.1 Summary of Urinary NNN Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)

Table 14.2.5.2.1.6.2 Summary of Urinary NNN Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)

Table 14.2.5.2.2.1	Statistical Comparison of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 14.2.5.2.2.2	Statistical Comparison of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)
Table 14.2.5.2.3.1	Statistical Comparison of Absolute Change from Baseline in Urinary NNN Mass Excreted (ng/24 hour) Among Study Product Groups at Weeks 2 and 6 (PP Population)
Table 14.2.5.2.3.2	Statistical Comparison of Absolute Change from Baseline in Urinary NNN Mass Excreted (ng/24 hour) Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Urine 3-HPMA

Table 14.2.5.3.1.1.1	Summary of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.3.1.1.2	Summary of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (PP Population)
Table 14.2.5.3.1.2.1	Summary of Urinary 3-HPMA Mass Excreted Change from Baseline ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.3.1.2.2	Summary of Urinary 3-HPMA Mass Excreted Change from Baseline ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (PP Population)
Table 14.2.5.3.1.3.1	Summary of Urinary 3-HPMA Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.3.1.3.2	Summary of Urinary 3-HPMA Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
Table 14.2.5.3.1.4.1	Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level ($\mu\text{g}/\text{g}$ creatinine) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.3.1.4.2	Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level ($\mu\text{g}/\text{g}$ creatinine) by Study Product Group and Study Week (PP Population)
Table 14.2.5.3.1.5.1	Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level Change from Baseline ($\mu\text{g}/\text{g}$ creatinine) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.3.1.5.2	Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level Change from Baseline ($\mu\text{g}/\text{g}$ creatinine) by Study Product Group and Study Week (PP Population)

Table 14.2.5.3.1.6.1	Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.3.1.6.2	Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
Table 14.2.5.3.2.1	Statistical Comparison of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 14.2.5.3.2.2	Statistical Comparison of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)
Table 14.2.5.3.3.1	Statistical Comparison of Absolute Change from Baseline in Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) Among Study Product Groups at Weeks 2 and 6 (PP Population)
Table 14.2.5.3.3.2	Statistical Comparison of Absolute Change from Baseline in Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Urine S-PMA

Table 14.2.5.4.1.1.1	Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.4.1.1.2	Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (PP Population)
Table 14.2.5.4.1.2.1	Summary of Urinary S-PMA Mass Excreted Change from Baseline ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (ITT Population)
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Table 14.2.5.4.1.3.1	Summary of Urinary S-PMA Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
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Table 14.2.5.4.1.5.1	Summary of Urinary S-PMA Creatinine-Normalized Excretion Level Change from Baseline (µg/g creatinine) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.4.1.5.2	Summary of Urinary S-PMA Creatinine-Normalized Excretion Level Change from Baseline (µg/g creatinine) by Study Product Group and Study Week (PP Population)
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Table 14.2.5.4.3.1	Statistical Comparison of Absolute Change from Baseline in Urinary S-PMA Mass Excreted (µg/24 hour) Among Study Product Groups at Weeks 2 and 6 (PP Population)
Table 14.2.5.4.3.2	Statistical Comparison of Absolute Change from Baseline in Urinary S-PMA Mass Excreted (µg/24 hour) Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Urine 1-OHP

Table 14.2.5.5.1.1.1	Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.5.1.1.2	Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)
Table 14.2.5.5.1.2.1	Summary of Urinary 1-OHP Mass Excreted Change from Baseline (ng/24 hour) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.5.1.2.2	Summary of Urinary 1-OHP Mass Excreted Change from Baseline (ng/24 hour) by Study Product Group and Study Week (PP Population)
Table 14.2.5.5.1.3.1	Summary of Urinary 1-OHP Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.5.1.3.2	Summary of Urinary 1-OHP Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)

Table 14.2.5.5.1.4.1	Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level (ng/g creatinine) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.5.1.4.2	Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level (ng/g creatinine) by Study Product Group and Study Week (PP Population)
Table 14.2.5.5.1.5.1	Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level Change from Baseline (ng/g creatinine) by Study Product Group and Study Week (ITT Population)
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Table 14.2.5.5.1.6.1	Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
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Table 14.2.5.5.3.1	Statistical Comparison of Absolute Change from Baseline in Urinary 1-OHP Mass Excreted (ng/24 hour) Among Study Product Groups at Weeks 2 and 6 (PP Population)
Table 14.2.5.5.3.2	Statistical Comparison of Absolute Change from Baseline in Urinary 1-OHP Mass Excreted (ng/24 hour) Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Urine Tneq

Table 14.2.5.6.1.1.1	Summary of Urinary Tneq Mass Excreted (mg/24 hour) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.6.1.1.2	Summary of Urinary Tneq Mass Excreted (mg/24 hour) by Study Product Group and Study Week (PP Population)
Table 14.2.5.6.1.2.1	Summary of Urinary Tneq Mass Excreted Change from Baseline (mg/24 hour) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.6.1.2.2	Summary of Urinary Tneq Mass Excreted Change from Baseline (mg/24 hour) by Study Product Group and Study Week (PP Population)

Table 14.2.5.6.1.3.1	Summary of Urinary Tneq Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.6.1.3.2	Summary of Urinary Tneq Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
Table 14.2.5.6.1.4.1	Summary of Urinary Tneq Creatinine-Normalized Excretion Level (mg/g creatinine) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.6.1.4.2	Summary of Urinary Tneq Creatinine-Normalized Excretion Level (mg/g creatinine) by Study Product Group and Study Week (PP Population)
Table 14.2.5.6.1.5.1	Summary of Urinary Tneq Creatinine-Normalized Excretion Level Change from Baseline (mg/g creatinine) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.6.1.5.2	Summary of Urinary Tneq Creatinine-Normalized Excretion Level Change from Baseline (mg/g creatinine) by Study Product Group and Study Week (PP Population)
Table 14.2.5.6.1.6.1	Summary of Urinary Tneq Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.6.1.6.2	Summary of Urinary Tneq Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
Table 14.2.5.6.2.1	Statistical Comparison of Urinary Tneq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 14.2.5.6.2.2	Statistical Comparison of Urinary Tneq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)
Table 14.2.5.6.3.1	Statistical Comparison of Absolute Change from Baseline in Urinary Tneq Mass Excreted (mg/24 hour) Among Study Product Groups at Weeks 2 and 6 (PP Population)
Table 14.2.5.6.3.2	Statistical Comparison of Absolute Change from Baseline in Urinary Tneq Mass Excreted (mg/24 hour) Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Blood COHb

Table 14.2.5.7.1.1.1	Summary of Blood COHb (% Saturation) by Study Product Group and Study Week (PP Population)
Table 14.2.5.7.1.1.2	Summary of Blood COHb (% Saturation) by Study Product Group and Study Week (ITT Population)

Table 14.2.5.7.1.2.1	Summary of Blood COHb Change from Baseline (% Saturation) by Study Product Group and Study Week (PP Population)
Table 14.2.5.7.1.2.2	Summary of Blood COHb Change from Baseline (% Saturation) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.7.1.3.1	Summary of Blood COHb Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
Table 14.2.5.7.1.3.2	Summary of Blood COHb Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
Table 14.2.5.7.2	Statistical Comparison of Blood COHb (% Saturation) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 14.2.5.7.3	Statistical Comparison of Blood COHb Absolute Change From Baseline (% Saturation) Among Study Product Groups at Weeks 2 and 6 (PP Population)
Table 14.2.5.7.4	Statistical Comparison of Blood COHb (% Saturation) at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)
Table 14.2.5.7.5	Statistical Comparison of Blood COHb Absolute Change From Baseline (% Saturation) Among Study Product Groups at Weeks 2 and 6 (ITT Population)

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Table 14.2.5.1.1.1.1
 Summary of Urinary NNAL Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	49	50	99	21	20	41
	Mean	582.855	423.752	502.500	614.066	479.979	548.658
	SD	288.3650	185.6953	253.6974	353.9198	203.2470	294.7134
	CV%	49.5	43.8	50.5	57.6	42.3	53.7
	SEM	41.1950	26.2613	25.4976	77.2316	45.4474	46.0265
	Minimum	67.47	82.08	67.47	161.22	150.99	150.99
	Median	531.216	419.860	440.713	538.539	451.461	469.392
	Maximum	1264.49	898.66	1264.49	1663.44	996.00	1663.44
Week 2	n	48	43	91	21	20	41
	Mean	313.911	214.139	266.766	581.039	458.036	521.037
	SD	176.1390	131.4077	163.6124	312.7864	203.4045	269.1556
	CV%	56.1	61.4	61.3	53.8	44.4	51.7
	SEM	25.4235	20.0395	17.1512	68.2556	45.4826	42.0350
	Minimum	77.70	11.30	11.30	114.92	164.95	114.92
	Median	264.138	202.718	236.592	542.872	408.890	465.120
	Maximum	748.52	656.26	748.52	1344.94	1027.18	1344.94
Week 6	n	42	41	83	17	19	36
	Mean	377.057	240.970	309.833	614.717	431.458	517.997
	SD	217.6683	173.1282	207.3562	416.6105	173.9915	321.7481
	CV%	57.7	71.8	66.9	67.8	40.3	62.1
	SEM	33.5869	27.0381	22.7603	101.0429	39.9164	53.6247
	Minimum	89.32	5.66	5.66	120.58	185.85	120.58
	Median	324.130	206.634	259.597	459.025	416.010	416.733
	Maximum	878.56	691.85	878.56	1717.98	808.74	1717.98

* Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.1.1.1.2
 Summary of Urinary NNAL Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	12	17	29	21	20	41
	Mean	526.297	368.047	433.530	614.066	479.979	548.658
	SD	298.9409	122.8057	223.6456	353.9198	203.2470	294.7134
	CV%	56.8	33.4	51.6	57.6	42.3	53.7
	SEM	86.2968	29.7847	41.5299	77.2316	45.4474	46.0265
	Minimum	188.30	172.18	172.18	161.22	150.99	150.99
	Median	457.030	412.069	412.069	538.539	451.461	469.392
	Maximum	1184.16	602.85	1184.16	1663.44	996.00	1663.44
Week 2	n	11	12	23	21	20	41
	Mean	194.738	154.553	173.772	581.039	458.036	521.037
	SD	63.3151	86.2503	77.2205	312.7864	203.4045	269.1556
	CV%	32.5	55.8	44.4	53.8	44.4	51.7
	SEM	19.0902	24.8983	16.1016	68.2556	45.4826	42.0350
	Minimum	97.20	44.96	44.96	114.92	164.95	114.92
	Median	213.288	162.623	170.467	542.872	408.890	465.120
	Maximum	280.85	304.90	304.90	1344.94	1027.18	1344.94
Week 6	n	10	9	19	17	19	36
	Mean	159.446	123.174	142.265	614.717	431.458	517.997
	SD	45.6912	89.9799	70.6290	416.6105	173.9915	321.7481
	CV%	28.7	73.1	49.6	67.8	40.3	62.1
	SEM	14.4488	29.9933	16.2034	101.0429	39.9164	53.6247
	Minimum	89.32	31.00	31.00	120.58	185.85	120.58
	Median	156.196	130.186	142.362	459.025	416.010	416.733
	Maximum	235.43	294.52	294.52	1717.98	808.74	1717.98

* Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.1.1.2.1
 Summary of Urinary NNAL Mass Excreted Change from Baseline (ng/24 hour) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-274.059	-208.238	-242.611	-37.934	-21.943	-29.939
	SD	205.3464	106.4319	168.0269	111.0695	78.7366	95.3722
	CV%	-74.9	-51.1	-69.3	-292.8	-358.8	-318.6
	SEM	29.9529	16.2307	17.7116	24.8359	17.6060	15.0797
	Minimum	-916.52	-400.03	-916.52	-318.50	-193.44	-318.50
	Median	-254.230	-218.629	-240.524	-36.570	-12.063	-27.792
	Maximum	24.99	142.14	142.14	185.95	83.34	185.95
Week 6	n	41	41	82	16	19	35
	Mean	-227.235	-197.937	-212.586	-20.923	-31.580	-26.708
	SD	224.3245	120.8982	179.6812	100.3595	92.4514	94.8555
	CV%	-98.7	-61.1	-84.5	-479.7	-292.8	-355.2
	SEM	35.0336	18.8811	19.8425	25.0899	21.2098	16.0335
	Minimum	-993.34	-437.33	-993.34	-210.42	-187.26	-210.42
	Median	-167.948	-213.888	-192.737	-39.058	-34.380	-38.282
	Maximum	64.03	174.97	174.97	214.42	205.86	214.42

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.5.1.1.2.2
 Summary of Urinary NNAL Mass Excreted Change from Baseline (ng/24 hour) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-324.284	-199.906	-259.391	-37.934	-21.943	-29.939
	SD	269.6384	69.6152	198.7622	111.0695	78.7366	95.3722
	CV%	-83.1	-34.8	-76.6	-292.8	-358.8	-318.6
	SEM	81.2990	20.0962	41.4448	24.8359	17.6060	15.0797
	Minimum	-916.52	-297.95	-916.52	-318.50	-193.44	-318.50
	Median	-266.997	-210.384	-222.360	-36.570	-12.063	-27.792
	Maximum	24.99	-63.61	24.99	185.95	83.34	185.95
Week 6	n	10	9	19	16	19	35
	Mean	-377.551	-231.990	-308.601	-20.923	-31.580	-26.708
	SD	303.2654	90.1669	234.8916	100.3595	92.4514	94.8555
	CV%	-80.3	-38.9	-76.1	-479.7	-292.8	-355.2
	SEM	95.9009	30.0556	53.8878	25.0899	21.2098	16.0335
	Minimum	-993.34	-324.41	-993.34	-210.42	-187.26	-210.42
	Median	-316.840	-258.882	-277.877	-39.058	-34.380	-38.282
	Maximum	-45.94	-78.94	-45.94	214.42	205.86	214.42

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.5.1.1.3.1
 Summary of Urinary NNAL Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-43.020	-48.532	-45.653	-6.064	-2.894	-4.479
	SD	23.6989	28.5814	26.1429	15.8020	18.6453	17.1346
	CV%	-55.1	-58.9	-57.3	-260.6	-644.3	-382.5
	SEM	3.4568	4.3586	2.7557	3.5334	4.1692	2.7092
	Minimum	-79.04	-96.58	-96.58	-28.72	-35.11	-35.11
	Median	-48.855	-53.056	-49.817	-10.870	-3.292	-6.949
	Maximum	15.16	107.58	107.58	28.45	35.02	35.02
Week 6	n	41	41	82	16	19	35
	Mean	-35.294	-48.514	-41.904	-6.602	-4.637	-5.535
	SD	26.1519	27.2065	27.3404	15.1173	19.2802	17.2802
	CV%	-74.1	-56.1	-65.2	-229.0	-415.8	-312.2
	SEM	4.0842	4.2489	3.0192	3.7793	4.4232	2.9209
	Minimum	-87.29	-93.11	-93.11	-25.44	-30.74	-30.74
	Median	-36.792	-49.374	-42.891	-9.258	-5.921	-7.287
	Maximum	17.15	41.53	41.53	23.71	45.09	45.09

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.5.1.1.3.2
Summary of Urinary NNAL Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-53.392	-58.249	-55.926	-6.064	-2.894	-4.479
	SD	26.2809	15.0335	20.8112	15.8020	18.6453	17.1346
	CV%	-49.2	-25.8	-37.2	-260.6	-644.3	-382.5
	SEM	7.9240	4.3398	4.3394	3.5334	4.1692	2.7092
	Minimum	-77.40	-76.09	-77.40	-28.72	-35.11	-35.11
	Median	-61.681	-59.944	-61.681	-10.870	-3.292	-6.949
	Maximum	13.27	-27.33	13.27	28.45	35.02	35.02
Week 6	n	10	9	19	16	19	35
	Mean	-61.236	-66.721	-63.834	-6.602	-4.637	-5.535
	SD	20.4800	18.0033	19.0180	15.1173	19.2802	17.2802
	CV%	-33.4	-27.0	-29.8	-229.0	-415.8	-312.2
	SEM	6.4763	6.0011	4.3630	3.7793	4.4232	2.9209
	Minimum	-87.29	-91.28	-91.28	-25.44	-30.74	-30.74
	Median	-69.156	-67.755	-67.755	-9.258	-5.921	-7.287
	Maximum	-24.40	-33.92	-24.40	23.71	45.09	45.09

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.1.1.4.1 Summary of Urinary NNAL Creatinine-Normalized Excretion Level (ng/g creatinine)
by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	49	50	99	21	20	41
	Mean	406.804	259.585	332.451	341.683	299.523	321.117
	SD	270.1241	157.5777	231.5761	154.8874	164.5504	159.0967
	CV%	66.4	60.7	69.7	45.3	54.9	49.5
	SEM	38.5892	22.2849	23.2743	33.7992	36.7946	24.8467
	Minimum	34.45	58.57	34.45	140.14	104.60	104.60
	Median	371.296	228.019	263.473	309.524	264.819	292.285
	Maximum	1727.67	865.50	1727.67	756.52	788.95	788.95
Week 2	n	48	43	91	21	20	41
	Mean	216.799	127.788	174.739	335.992	300.430	318.645
	SD	149.0012	83.7787	129.8700	160.0269	159.9040	158.9767
	CV%	68.7	65.6	74.3	47.6	53.2	49.9
	SEM	21.5065	12.7761	13.6141	34.9207	35.7556	24.8280
	Minimum	34.29	25.66	25.66	98.01	112.99	98.01
	Median	164.873	117.544	145.192	311.611	266.369	288.973
	Maximum	803.03	451.15	803.03	727.27	748.58	748.58
Week 6	n	42	41	83	17	19	36
	Mean	254.451	152.452	204.066	330.583	271.392	299.343
	SD	174.1804	121.0649	157.9598	164.3405	151.7827	158.4066
	CV%	68.5	79.4	77.4	49.7	55.9	52.9
	SEM	26.8766	18.9072	17.3383	39.8584	34.8213	26.4011
	Minimum	65.25	6.39	6.39	95.01	101.28	95.01
	Median	218.552	126.772	156.757	301.413	225.385	262.520
	Maximum	918.60	575.94	918.60	651.43	628.26	651.43

* Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.1.1.4.2 Summary of Urinary NNAL Creatinine-Normalized Excretion Level (ng/g creatinine)
by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	12	17	29	21	20	41
	Mean	344.707	220.309	271.784	341.683	299.523	321.117
	SD	179.0381	95.6012	147.3204	154.8874	164.5504	159.0967
	CV%	51.9	43.4	54.2	45.3	54.9	49.5
	SEM	51.6838	23.1867	27.3567	33.7992	36.7946	24.8467
	Minimum	119.50	96.41	96.41	140.14	104.60	104.60
	Median	388.575	218.241	230.357	309.524	264.819	292.285
	Maximum	560.38	376.18	560.38	756.52	788.95	788.95
Week 2	n	11	12	23	21	20	41
	Mean	127.435	87.325	106.508	335.992	300.430	318.645
	SD	46.1368	49.0623	50.8999	160.0269	159.9040	158.9767
	CV%	36.2	56.2	47.8	47.6	53.2	49.9
	SEM	13.9108	14.1631	10.6134	34.9207	35.7556	24.8280
	Minimum	34.29	25.66	25.66	98.01	112.99	98.01
	Median	142.686	87.958	118.960	311.611	266.369	288.973
	Maximum	181.22	164.92	181.22	727.27	748.58	748.58
Week 6	n	10	9	19	17	19	36
	Mean	103.126	69.017	86.969	330.583	271.392	299.343
	SD	30.1563	52.0141	44.3092	164.3405	151.7827	158.4066
	CV%	29.2	75.4	50.9	49.7	55.9	52.9
	SEM	9.5363	17.3380	10.1652	39.8584	34.8213	26.4011
	Minimum	65.25	11.44	11.44	95.01	101.28	95.01
	Median	101.117	68.231	80.556	301.413	225.385	262.520
	Maximum	145.25	147.17	147.17	651.43	628.26	651.43

* Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.1.1.5.1 Summary of Urinary NNAL Creatinine-Normalized Excretion Level Change from Baseline (ng/g creatinine)
 by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-193.043	-119.906	-158.100	-13.038	0.907	-6.065
	SD	170.5729	83.5449	140.2902	64.4630	42.0968	54.2003
	CV%	-88.4	-69.7	-88.7	-494.4	4642.1	-893.6
	SEM	24.8806	12.7405	14.7879	14.4144	9.4131	8.5698
	Minimum	-924.64	-414.35	-924.64	-147.87	-85.41	-147.87
	Median	-168.502	-97.626	-128.720	-22.026	3.533	-17.013
	Maximum	4.92	64.65	64.65	168.28	70.43	168.28
Week 6	n	41	41	82	16	19	35
	Mean	-151.011	-113.419	-132.215	-26.771	-21.802	-24.074
	SD	154.1994	81.7187	124.0861	47.0566	54.5848	50.6023
	CV%	-102.1	-72.1	-93.9	-175.8	-250.4	-210.2
	SEM	24.0819	12.7623	13.7030	11.7642	12.5226	8.5534
	Minimum	-470.79	-374.88	-470.79	-105.09	-160.69	-160.69
	Median	-132.341	-99.373	-110.474	-20.707	-32.598	-29.026
	Maximum	375.68	14.21	375.68	89.69	65.00	89.69

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.1.1.5.2 Summary of Urinary NNAL Creatinine-Normalized Excretion Level Change from Baseline (ng/g creatinine)
 by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-202.791	-111.007	-154.903	-13.038	0.907	-6.065
	SD	148.7731	51.7676	116.6115	64.4630	42.0968	54.2003
	CV%	-73.4	-46.6	-75.3	-494.4	4642.1	-893.6
	SEM	44.8568	14.9440	24.3152	14.4144	9.4131	8.5698
	Minimum	-418.90	-239.19	-418.90	-147.87	-85.41	-147.87
	Median	-217.157	-96.483	-113.220	-22.026	3.533	-17.013
	Maximum	-4.16	-25.32	-4.16	168.28	70.43	168.28
Week 6	n	10	9	19	16	19	35
	Mean	-248.172	-122.685	-188.731	-26.771	-21.802	-24.074
	SD	157.6376	67.2373	136.3011	47.0566	54.5848	50.6023
	CV%	-63.5	-54.8	-72.2	-175.8	-250.4	-210.2
	SEM	49.8494	22.4124	31.2696	11.7642	12.5226	8.5534
	Minimum	-470.79	-272.19	-470.79	-105.09	-160.69	-160.69
	Median	-280.767	-108.996	-117.963	-20.707	-32.598	-29.026
	Maximum	-48.23	-28.88	-28.88	89.69	65.00	89.69

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.1.1.6.1 Summary of Urinary NNAL Creatinine-Normalized Excretion Level Percent Change from Baseline (%)
by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-44.090	-46.451	-45.218	-5.217	2.566	-1.326
	SD	22.8037	28.9123	25.7809	15.7987	15.1896	15.7966
	CV%	-51.7	-62.2	-57.0	-302.8	592.0	-1191.7
	SEM	3.3263	4.4091	2.7175	3.5327	3.3965	2.4977
	Minimum	-75.98	-80.44	-80.44	-30.93	-24.26	-30.93
	Median	-45.428	-50.118	-47.852	-8.116	2.543	-4.947
	Maximum	14.28	110.39	110.39	30.10	31.21	31.21
Week 6	n	41	41	82	16	19	35
	Mean	-36.816	-45.016	-40.916	-9.000	-5.933	-7.335
	SD	28.9225	23.6448	26.5744	12.0206	19.2765	16.2133
	CV%	-78.6	-52.5	-64.9	-133.6	-324.9	-221.0
	SEM	4.5169	3.6927	2.9346	3.0051	4.4223	2.7405
	Minimum	-85.39	-93.06	-93.06	-33.05	-32.37	-33.05
	Median	-38.626	-43.648	-40.687	-12.931	-9.779	-12.563
	Maximum	69.20	8.86	69.20	16.04	41.43	41.43

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.1.1.6.2 Summary of Urinary NNAL Creatinine-Normalized Excretion Level Percent Change from Baseline (%)
by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-54.126	-57.227	-55.744	-5.217	2.566	-1.326
	SD	23.0124	15.5212	19.0703	15.7987	15.1896	15.7966
	CV%	-42.5	-27.1	-34.2	-302.8	592.0	-1191.7
	SEM	6.9385	4.4806	3.9764	3.5327	3.3965	2.4977
	Minimum	-75.98	-75.88	-75.98	-30.93	-24.26	-30.93
	Median	-63.074	-60.235	-62.689	-8.116	2.543	-4.947
	Maximum	-3.38	-26.07	-3.38	30.10	31.21	31.21
Week 6	n	10	9	19	16	19	35
	Mean	-64.278	-65.807	-65.002	-9.000	-5.933	-7.335
	SD	15.6890	20.1220	17.4253	12.0206	19.2765	16.2133
	CV%	-24.4	-30.6	-26.8	-133.6	-324.9	-221.0
	SEM	4.9613	6.7073	3.9976	3.0051	4.4223	2.7405
	Minimum	-85.39	-90.50	-90.50	-33.05	-32.37	-33.05
	Median	-70.705	-67.412	-67.852	-12.931	-9.779	-12.563
	Maximum	-39.17	-29.74	-29.74	16.04	41.43	41.43

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.1.2.1 Statistical Comparison of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1
by Study Product Group (PP Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	Percent Change (%)	95%		p-Value
		Test Week	(n)	Baseline	(n)			Confidence Intervals		
Week 2	VLN Non-Mentholated	194.738	(11)	519.023	(11)	-324.284	-62.5	-505.430 ,	-143.139	0.0026
	VLN Mentholated	154.553	(12)	354.460	(12)	-199.906	-56.4	-244.138 ,	-155.675	<.0001
	VLN Combined	173.772	(23)	433.164	(23)	-259.391	-59.9	-345.343 ,	-173.440	<.0001
	UB Non-Mentholated	581.039	(21)	614.089	(21)	-33.051	-5.4	-83.370 ,	17.269	0.1858
	UB Mentholated	458.036	(20)	479.979	(20)	-21.943	-4.6	-58.793 ,	14.907	0.2278
	UB Combined	521.037	(41)	548.670	(41)	-27.632	-5.0	-57.720 ,	2.455	0.0708
Week 6	VLN Non-Mentholated	159.446	(10)	536.996	(10)	-377.551	-70.3	-594.494 ,	-160.608	0.0034
	VLN Mentholated	123.174	(9)	355.164	(9)	-231.990	-65.3	-301.298 ,	-162.682	<.0001
	VLN Combined	142.265	(19)	450.865	(19)	-308.601	-68.4	-421.815 ,	-195.387	<.0001
	UB Non-Mentholated	614.717	(17)	633.464	(17)	-18.747	-3.0	-68.921 ,	31.427	0.4399
	UB Mentholated	431.458	(19)	463.038	(19)	-31.580	-6.8	-76.140 ,	12.980	0.1538
	UB Combined	517.997	(36)	543.517	(36)	-25.520	-4.7	-57.245 ,	6.204	0.1114

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Paired t-test method is used to perform the analysis.
Percent change = mean of the differences/reference (baseline)*100

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Table 14.2.5.1.2.2 Statistical Comparison of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	Percent Change (%)	95% Confidence Intervals		p-Value
		Test Week	(n)	Baseline	(n)					
Week 2	VLN Non-Mentholated	313.911	(48)	588.208	(47)	-274.059	-46.6	-334.351 ,	-213.767	<.0001
	VLN Mentholated	214.139	(43)	422.377	(43)	-208.238	-49.3	-240.993 ,	-175.483	<.0001
	VLN Combined	266.766	(91)	508.977	(90)	-242.611	-47.7	-277.804 ,	-207.419	<.0001
	UB Non-Mentholated	581.039	(21)	614.089	(21)	-33.051	-5.4	-83.370 ,	17.269	0.1858
	UB Mentholated	458.036	(20)	479.979	(20)	-21.943	-4.6	-58.793 ,	14.907	0.2278
	UB Combined	521.037	(41)	548.670	(41)	-27.632	-5.0	-57.720 ,	2.455	0.0708
Week 6	VLN Non-Mentholated	377.057	(42)	603.830	(41)	-227.235	-37.6	-298.040 ,	-156.429	<.0001
	VLN Mentholated	240.970	(41)	438.907	(41)	-197.937	-45.1	-236.097 ,	-159.776	<.0001
	VLN Combined	309.833	(83)	521.368	(82)	-212.586	-40.8	-252.066 ,	-173.105	<.0001
	UB Non-Mentholated	614.717	(17)	633.464	(17)	-18.747	-3.0	-68.921 ,	31.427	0.4399
	UB Mentholated	431.458	(19)	463.038	(19)	-31.580	-6.8	-76.140 ,	12.980	0.1538
	UB Combined	517.997	(36)	543.517	(36)	-25.520	-4.7	-57.245 ,	6.204	0.1114

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Paired t-test method is used to perform the analysis.
Percent change = mean of the differences/reference (baseline)*100

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Table 14.2.5.1.3.1 Statistical Comparison of Absolute Change from Baseline in Urinary NNAL Mass Excreted (ng/24 hour)
 Among Study Product Groups at Weeks 2 and 6 (PP Population)

Study Week	Comparison	----- LSMeans -----		LSMean Difference		95%		p-value
		Test	(n)	Reference	(n)	(Test - Reference)	Confidence Intervals	
Week 2	VLN Non-mentholated vs UB Non-mentholated	-324.284	(11)	-37.934	(20)	-286.350	-390.418 , -182.283	<.0001
	VLN Mentholated vs UB Mentholated	-199.906	(12)	-21.943	(20)	-177.963	-279.195 , -76.732	0.0008
	VLN Combined vs UB Combined	-262.095	(23)	-29.939	(40)	-232.157	-304.748 , -159.566	<.0001
Week 6	VLN Non-mentholated vs UB Non-mentholated	-370.140	(10)	-17.453	(16)	-352.687	-467.834 , -237.539	<.0001
	VLN Mentholated vs UB Mentholated	-225.859	(9)	-36.078	(19)	-189.781	-302.986 , -76.577	0.0014
	VLN Combined vs UB Combined	-297.999	(19)	-26.765	(35)	-271.234	-351.971 , -190.497	<.0001

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN Non-Mentholated = Non-mentholated VLN cigarettes
 VLN Mentholated = Mentholated VLN cigarettes
 UB Non-Mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB Mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.5.1.3.2 Statistical Comparison of Absolute Change from Baseline in Urinary NNAL Mass Excreted (ng/24 hour)
 Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Study Week	Comparison	----- LSMeans -----		LSMean Difference		95%		p-value
		Test	(n)	Reference	(n)	(Test - Reference)	Confidence Intervals	
Week 2	VLN Non-mentholated vs UB Non-mentholated	-271.322	(47)	-37.934	(20)	-233.388	-311.345 , -155.431	<.0001
	VLN Mentholated vs UB Mentholated	-204.870	(43)	-21.943	(20)	-182.927	-261.750 , -104.104	<.0001
	VLN Combined vs UB Combined	-238.096	(90)	-29.939	(40)	-208.157	-263.588 , -152.727	<.0001
Week 6	VLN Non-mentholated vs UB Non-mentholated	-220.482	(41)	-17.449	(16)	-203.034	-292.577 , -113.490	<.0001
	VLN Mentholated vs UB Mentholated	-188.620	(41)	-36.084	(19)	-152.537	-240.678 , -64.396	0.0008
	VLN Combined vs UB Combined	-204.551	(82)	-26.766	(35)	-177.785	-240.607 , -114.963	<.0001

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN Non-Mentholated = Non-mentholated VLN cigarettes
 VLN Mentholated = Mentholated VLN cigarettes
 UB Non-Mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB Mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.2.1.1.1
Summary of Urinary NNN Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	49	50	99	21	20	41
	Mean	20.070	12.370	16.181	22.614	13.641	18.237
	SD	14.4934	7.9412	12.2224	24.4627	11.1026	19.4522
	CV%	72.2	64.2	75.5	108.2	81.4	106.7
	SEM	2.0705	1.1230	1.2284	5.3382	2.4826	3.0379
	Minimum	1.43	2.46	1.43	4.34	1.86	1.86
	Median	15.848	11.150	12.794	14.706	10.836	12.801
	Maximum	76.17	43.45	76.17	109.52	38.62	109.52
Week 2	n	48	43	91	21	20	41
	Mean	14.246	9.052	11.792	20.809	12.024	16.523
	SD	11.6548	10.2762	11.2701	21.2301	9.0103	16.8430
	CV%	81.8	113.5	95.6	102.0	74.9	101.9
	SEM	1.6822	1.5671	1.1814	4.6328	2.0148	2.6304
	Minimum	2.00	0.19	0.19	2.43	3.33	2.43
	Median	10.993	7.506	8.293	13.786	10.459	12.708
	Maximum	66.19	66.73	66.73	96.99	36.83	96.99
Week 6	n	42	41	83	17	19	36
	Mean	14.803	6.382	10.643	22.095	9.359	15.373
	SD	11.4754	4.5544	9.6904	25.7769	6.0602	19.0844
	CV%	77.5	71.4	91.0	116.7	64.8	124.1
	SEM	1.7707	0.7113	1.0637	6.2518	1.3903	3.1807
	Minimum	2.01	0.39	0.39	2.93	3.23	2.93
	Median	11.760	5.189	8.437	12.799	6.665	10.471
	Maximum	60.66	18.31	60.66	93.18	23.90	93.18

* Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.2.1.1.2
Summary of Urinary NNN Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	12	17	29	21	20	41
	Mean	25.610	9.409	16.113	22.614	13.641	18.237
	SD	21.9085	5.7121	16.5275	24.4627	11.1026	19.4522
	CV%	85.5	60.7	102.6	108.2	81.4	106.7
	SEM	6.3244	1.3854	3.0691	5.3382	2.4826	3.0379
	Minimum	7.76	2.70	2.70	4.34	1.86	1.86
	Median	17.216	8.130	10.821	14.706	10.836	12.801
	Maximum	76.17	22.88	76.17	109.52	38.62	109.52
Week 2	n	11	12	23	21	20	41
	Mean	15.590	11.711	13.566	20.809	12.024	16.523
	SD	11.9679	17.8387	15.1043	21.2301	9.0103	16.8430
	CV%	76.8	152.3	111.3	102.0	74.9	101.9
	SEM	3.6085	5.1496	3.1495	4.6328	2.0148	2.6304
	Minimum	3.10	1.12	1.12	2.43	3.33	2.43
	Median	10.250	6.736	8.293	13.786	10.459	12.708
	Maximum	38.73	66.73	66.73	96.99	36.83	96.99
Week 6	n	10	9	19	17	19	36
	Mean	12.672	5.318	9.188	22.095	9.359	15.373
	SD	7.3615	4.2139	7.0156	25.7769	6.0602	19.0844
	CV%	58.1	79.2	76.4	116.7	64.8	124.1
	SEM	2.3279	1.4046	1.6095	6.2518	1.3903	3.1807
	Minimum	2.01	0.67	0.67	2.93	3.23	2.93
	Median	11.558	3.529	9.943	12.799	6.665	10.471
	Maximum	23.91	11.28	23.91	93.18	23.90	93.18

* Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.2.1.2.1
 Summary of Urinary NNN Mass Excreted Change from Baseline (ng/24 hour) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-6.001	-3.178	-4.652	-1.487	-1.617	-1.552
	SD	10.2617	10.7189	10.5193	6.2890	3.6016	5.0589
	CV%	-171.0	-337.2	-226.1	-423.0	-222.7	-326.0
	SEM	1.4968	1.6346	1.1088	1.4063	0.8053	0.7999
	Minimum	-47.35	-14.56	-47.35	-14.84	-12.80	-14.84
	Median	-4.659	-4.319	-4.488	-0.644	-0.580	-0.580
	Maximum	11.79	59.75	59.75	9.77	2.55	9.77
Week 6	n	41	41	82	16	19	35
	Mean	-6.866	-7.094	-6.980	-1.584	-3.749	-2.759
	SD	12.6074	6.6443	10.0153	5.6694	6.0923	5.9185
	CV%	-183.6	-93.7	-143.5	-357.9	-162.5	-214.5
	SEM	1.9689	1.0377	1.1060	1.4174	1.3977	1.0004
	Minimum	-52.26	-27.10	-52.26	-16.34	-19.04	-19.04
	Median	-4.829	-5.455	-4.935	-1.216	-1.478	-1.406
	Maximum	16.86	1.86	16.86	9.89	3.87	9.89

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.5.2.1.2.2
 Summary of Urinary NNN Mass Excreted Change from Baseline (ng/24 hour) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-11.563	1.728	-4.629	-1.487	-1.617	-1.552
	SD	16.2454	18.5541	18.3894	6.2890	3.6016	5.0589
	CV%	-140.5	1073.8	-397.3	-423.0	-222.7	-326.0
	SEM	4.8982	5.3561	3.8345	1.4063	0.8053	0.7999
	Minimum	-47.35	-10.32	-47.35	-14.84	-12.80	-14.84
	Median	-5.041	-2.146	-4.659	-0.644	-0.580	-0.580
	Maximum	6.20	59.75	59.75	9.77	2.55	9.77
Week 6	n	10	9	19	16	19	35
	Mean	-16.115	-5.784	-11.221	-1.584	-3.749	-2.759
	SD	18.2281	5.6181	14.4306	5.6694	6.0923	5.9185
	CV%	-113.1	-97.1	-128.6	-357.9	-162.5	-214.5
	SEM	5.7642	1.8727	3.3106	1.4174	1.3977	1.0004
	Minimum	-52.26	-14.85	-52.26	-16.34	-19.04	-19.04
	Median	-10.060	-2.661	-4.026	-1.216	-1.478	-1.406
	Maximum	1.69	-1.08	1.69	9.89	3.87	9.89

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.5.2.1.3.1
Summary of Urinary NNN Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-22.756	-13.111	-18.148	-2.883	-0.270	-1.576
	SD	37.8324	139.7799	99.9181	25.9576	30.9051	28.2016
	CV%	-166.2	-1066.1	-550.6	-900.4	-11448.3	-1789.0
	SEM	5.5184	21.3162	10.5323	5.8043	6.9106	4.4591
	Minimum	-71.00	-98.10	-98.10	-50.04	-41.51	-50.04
	Median	-30.237	-34.141	-32.517	-4.724	-3.636	-3.636
	Maximum	80.16	855.98	855.98	43.48	79.29	79.29
Week 6	n	41	41	82	16	19	35
	Mean	-23.763	-48.585	-36.174	-8.412	-8.471	-8.444
	SD	42.5998	31.0452	39.0903	22.6645	57.7770	44.6530
	CV%	-179.3	-63.9	-108.1	-269.4	-682.1	-528.8
	SEM	6.6530	4.8484	4.3168	5.6661	13.2549	7.5477
	Minimum	-91.51	-96.75	-96.75	-36.33	-64.06	-64.06
	Median	-31.274	-56.537	-43.134	-8.487	-21.206	-14.918
	Maximum	81.83	36.55	81.83	41.26	206.75	206.75

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.2.1.3.2
 Summary of Urinary NNN Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-36.129	42.214	4.746	-2.883	-0.270	-1.576
	SD	31.6854	257.0649	187.3463	25.9576	30.9051	28.2016
	CV%	-87.7	609.0	3947.5	-900.4	-11448.3	-1789.0
	SEM	9.5535	74.2082	39.0644	5.8043	6.9106	4.4591
	Minimum	-68.22	-61.57	-68.22	-50.04	-41.51	-50.04
	Median	-46.581	-31.023	-33.380	-4.724	-3.636	-3.636
	Maximum	25.94	855.98	855.98	43.48	79.29	79.29
Week 6	n	10	9	19	16	19	35
	Mean	-43.311	-50.120	-46.536	-8.412	-8.471	-8.444
	SD	33.3010	27.7587	30.1520	22.6645	57.7770	44.6530
	CV%	-76.9	-55.4	-64.8	-269.4	-682.1	-528.8
	SEM	10.5307	9.2529	6.9174	5.6661	13.2549	7.5477
	Minimum	-84.31	-83.74	-84.31	-36.33	-64.06	-64.06
	Median	-46.397	-53.142	-49.655	-8.487	-21.206	-14.918
	Maximum	17.88	-10.12	17.88	41.26	206.75	206.75

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.2.1.4.1 Summary of Urinary NNN Creatinine-Normalized Excretion Level (ng/g creatinine)
 by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	49	50	99	21	20	41
	Mean	13.326	7.905	10.588	12.605	8.972	10.833
	SD	9.4745	7.1273	8.7628	12.5095	8.4373	10.7443
	CV%	71.1	90.2	82.8	99.2	94.0	99.2
	SEM	1.3535	1.0080	0.8807	2.7298	1.8866	1.6780
	Minimum	0.73	1.22	0.73	3.41	0.64	0.64
	Median	11.880	6.029	8.767	9.255	6.241	8.221
	Maximum	50.75	44.12	50.75	59.05	30.43	59.05
Week 2	n	48	43	91	21	20	41
	Mean	9.328	6.405	7.947	12.065	8.216	10.187
	SD	6.7186	12.4383	9.8956	12.5252	6.8967	10.2385
	CV%	72.0	194.2	124.5	103.8	83.9	100.5
	SEM	0.9697	1.8968	1.0373	2.7332	1.5421	1.5990
	Minimum	1.01	0.49	0.49	1.98	1.18	1.18
	Median	7.509	4.058	5.311	8.696	6.698	7.944
	Maximum	29.90	83.52	83.52	60.70	26.84	60.70
Week 6	n	42	41	83	17	19	36
	Mean	9.227	4.095	6.692	11.724	6.123	8.768
	SD	6.1926	3.2887	5.5780	12.5860	4.7990	9.6073
	CV%	67.1	80.3	83.4	107.4	78.4	109.6
	SEM	0.9555	0.5136	0.6123	3.0525	1.1010	1.6012
	Minimum	1.19	0.31	0.31	2.50	1.54	1.54
	Median	7.080	3.326	5.058	8.166	5.484	6.664
	Maximum	27.29	13.61	27.29	53.42	18.23	53.42

* Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.2.1.4.2 Summary of Urinary NNN Creatinine-Normalized Excretion Level (ng/g creatinine)
 by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	12	17	29	21	20	41
	Mean	15.914	5.864	10.022	12.605	8.972	10.833
	SD	13.1476	4.4965	10.2392	12.5095	8.4373	10.7443
	CV%	82.6	76.7	102.2	99.2	94.0	99.2
	SEM	3.7954	1.0906	1.9014	2.7298	1.8866	1.6780
	Minimum	3.81	1.22	1.22	3.41	0.64	0.64
	Median	12.165	4.739	6.634	9.255	6.241	8.221
	Maximum	50.75	18.90	50.75	59.05	30.43	59.05
Week 2	n	11	12	23	21	20	41
	Mean	9.494	10.502	10.020	12.065	8.216	10.187
	SD	6.6392	23.2105	17.0195	12.5252	6.8967	10.2385
	CV%	69.9	221.0	169.9	103.8	83.9	100.5
	SEM	2.0018	6.7003	3.5488	2.7332	1.5421	1.5990
	Minimum	2.04	0.54	0.54	1.98	1.18	1.18
	Median	7.903	3.924	4.263	8.696	6.698	7.944
	Maximum	21.14	83.52	83.52	60.70	26.84	60.70
Week 6	n	10	9	19	17	19	36
	Mean	7.640	3.206	5.540	11.724	6.123	8.768
	SD	3.7934	2.9731	4.0370	12.5860	4.7990	9.6073
	CV%	49.7	92.7	72.9	107.4	78.4	109.6
	SEM	1.1996	0.9910	0.9262	3.0525	1.1010	1.6012
	Minimum	1.83	0.31	0.31	2.50	1.54	1.54
	Median	7.893	1.398	5.050	8.166	5.484	6.664
	Maximum	14.75	7.86	14.75	53.42	18.23	53.42

* Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.2.1.5.1 Summary of Urinary NNN Creatinine-Normalized Excretion Level Change from Baseline (ng/g creatinine)
by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-4.133	-0.957	-2.616	-0.470	-0.756	-0.613
	SD	6.8424	12.4563	9.9983	3.6267	2.1404	2.9429
	CV%	-165.6	-1301.8	-382.3	-771.2	-283.1	-480.0
	SEM	0.9981	1.8996	1.0539	0.8109	0.4786	0.4653
	Minimum	-32.70	-13.06	-32.70	-9.04	-6.21	-9.04
	Median	-2.926	-1.910	-2.318	0.012	-0.325	-0.196
	Maximum	8.49	76.12	76.12	7.65	1.72	7.65
Week 6	n	41	41	82	16	19	35
	Mean	-4.767	-4.461	-4.614	-1.470	-2.667	-2.120
	SD	7.8997	5.9015	6.9311	1.9631	4.3427	3.4714
	CV%	-165.7	-132.3	-150.2	-133.6	-162.9	-163.8
	SEM	1.2337	0.9217	0.7654	0.4908	0.9963	0.5868
	Minimum	-36.01	-30.51	-36.01	-5.63	-15.37	-15.37
	Median	-4.221	-3.042	-3.560	-1.726	-1.151	-1.638
	Maximum	15.12	4.72	15.12	1.86	1.80	1.86

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.2.1.5.2 Summary of Urinary NNN Creatinine-Normalized Excretion Level Change from Baseline (ng/g creatinine)
 by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-7.214	4.504	-1.100	-0.470	-0.756	-0.613
	SD	10.0739	22.6422	18.3926	3.6267	2.1404	2.9429
	CV%	-139.6	502.7	-1671.6	-771.2	-283.1	-480.0
	SEM	3.0374	6.5362	3.8351	0.8109	0.4786	0.4653
	Minimum	-32.70	-6.42	-32.70	-9.04	-6.21	-9.04
	Median	-3.733	-1.294	-1.910	0.012	-0.325	-0.196
	Maximum	1.16	76.12	76.12	7.65	1.72	7.65
Week 6	n	10	9	19	16	19	35
	Mean	-10.358	-3.220	-6.977	-1.470	-2.667	-2.120
	SD	10.9384	3.9427	8.9522	1.9631	4.3427	3.4714
	CV%	-105.6	-122.4	-128.3	-133.6	-162.9	-163.8
	SEM	3.4590	1.3142	2.0538	0.4908	0.9963	0.5868
	Minimum	-36.01	-11.86	-36.01	-5.63	-15.37	-15.37
	Median	-5.806	-1.027	-3.838	-1.726	-1.151	-1.638
	Maximum	-0.56	-0.21	-0.21	1.86	1.80	1.86

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.2.1.6.1 Summary of Urinary NNN Creatinine-Normalized Excretion Level Percent Change from Baseline (%)
by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-24.385	-6.717	-15.944	-1.333	5.953	2.310
	SD	37.8210	165.7609	117.4079	29.0696	31.8275	30.3118
	CV%	-155.1	-2467.8	-736.4	-2180.9	534.7	1312.3
	SEM	5.5168	25.2783	12.3759	6.5002	7.1169	4.7927
	Minimum	-69.71	-89.11	-89.11	-49.51	-37.78	-49.51
	Median	-34.549	-33.969	-34.259	-0.529	-3.350	-2.593
	Maximum	83.46	1029.69	1029.69	53.44	84.50	84.50
Week 6	n	41	41	82	16	19	35
	Mean	-26.463	-44.715	-35.589	-10.310	-9.929	-10.103
	SD	46.5754	34.3226	41.6809	23.8813	56.4178	44.0085
	CV%	-176.0	-76.8	-117.1	-231.6	-568.2	-435.6
	SEM	7.2739	5.3603	4.6029	5.9703	12.9431	7.4388
	Minimum	-85.75	-87.40	-87.40	-39.37	-62.71	-62.71
	Median	-33.648	-53.081	-47.739	-14.815	-23.059	-19.901
	Maximum	166.05	68.76	166.05	54.67	199.02	199.02

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.2.1.6.2 Summary of Urinary NNN Creatinine-Normalized Excretion Level Percent Change from Baseline (%)
 by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-37.349	57.294	12.030	-1.333	5.953	2.310
	SD	28.1263	306.9127	223.1456	29.0696	31.8275	30.3118
	CV%	-75.3	535.7	1854.9	-2180.9	534.7	1312.3
	SEM	8.4804	88.5981	46.5291	6.5002	7.1169	4.7927
	Minimum	-66.22	-61.24	-66.22	-49.51	-37.78	-49.51
	Median	-47.272	-29.163	-33.969	-0.529	-3.350	-2.593
	Maximum	7.43	1029.69	1029.69	53.44	84.50	84.50
Week 6	n	10	9	19	16	19	35
	Mean	-48.575	-48.588	-48.581	-10.310	-9.929	-10.103
	SD	24.4407	30.8371	26.8572	23.8813	56.4178	44.0085
	CV%	-50.3	-63.5	-55.3	-231.6	-568.2	-435.6
	SEM	7.7288	10.2790	6.1615	5.9703	12.9431	7.4388
	Minimum	-80.02	-83.49	-83.49	-39.37	-62.71	-62.71
	Median	-48.442	-51.232	-49.339	-14.815	-23.059	-19.901
	Maximum	-10.23	-2.65	-2.65	54.67	199.02	199.02

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.2.2.1 Statistical Comparison of Urinary MNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1
by Study Product Group (PP Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	Percent Change (%)	95%		p-Value
		Test Week	(n)	Baseline	(n)			Confidence Intervals		
Week 2	VLN Non-Mentholated	15.590	(11)	27.153	(11)	-11.563	-42.6	-22.477 ,	-0.649	0.0399
	VLN Mentholated	11.711	(12)	9.983	(12)	1.728	17.3	-10.061 ,	13.517	0.7530
	VLN Combined	13.566	(23)	18.195	(23)	-4.629	-25.4	-12.581 ,	3.324	0.2402
	UB Non-Mentholated	20.809	(21)	22.085	(21)	-1.276	-5.8	-4.101 ,	1.549	0.3573
	UB Mentholated	12.024	(20)	13.641	(20)	-1.617	-11.9	-3.303 ,	0.069	0.0591
	UB Combined	16.523	(41)	17.966	(41)	-1.442	-8.0	-3.035 ,	0.150	0.0746
Week 6	VLN Non-Mentholated	12.672	(10)	28.786	(10)	-16.115	-56.0	-29.154 ,	-3.075	0.0209
	VLN Mentholated	5.318	(9)	11.102	(9)	-5.784	-52.1	-10.103 ,	-1.466	0.0149
	VLN Combined	9.188	(19)	20.410	(19)	-11.221	-55.0	-18.177 ,	-4.266	0.0033
	UB Non-Mentholated	22.095	(17)	23.322	(17)	-1.228	-5.3	-4.149 ,	1.694	0.3863
	UB Mentholated	9.359	(19)	13.108	(19)	-3.749	-28.6	-6.685 ,	-0.813	0.0152
	UB Combined	15.373	(36)	17.932	(36)	-2.558	-14.3	-4.574 ,	-0.543	0.0143

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Paired t-test method is used to perform the analysis.
Percent change = mean of the differences/reference (baseline)*100

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Table 14.2.5.2.2.2 Statistical Comparison of Urinary MNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1
 by Study Product Group (ITT Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	Percent Change (%)	95%		p-Value
		Test Week	(n)	Baseline	(n)			Confidence Intervals		
Week 2	VLN Non-Mentholated	14.246	(48)	20.398	(47)	-6.001	-29.4	-9.014 ,	-2.988	0.0002
	VLN Mentholated	9.052	(43)	12.230	(43)	-3.178	-26.0	-6.477 ,	0.120	0.0586
	VLN Combined	11.792	(91)	16.496	(90)	-4.652	-28.2	-6.856 ,	-2.449	<.0001
	UB Non-Mentholated	20.809	(21)	22.085	(21)	-1.276	-5.8	-4.101 ,	1.549	0.3573
	UB Mentholated	12.024	(20)	13.641	(20)	-1.617	-11.9	-3.303 ,	0.069	0.0591
	UB Combined	16.523	(41)	17.966	(41)	-1.442	-8.0	-3.035 ,	0.150	0.0746
Week 6	VLN Non-Mentholated	14.803	(42)	21.861	(41)	-6.866	-31.4	-10.846 ,	-2.887	0.0012
	VLN Mentholated	6.382	(41)	13.476	(41)	-7.094	-52.6	-9.191 ,	-4.997	<.0001
	VLN Combined	10.643	(83)	17.668	(82)	-6.980	-39.5	-9.181 ,	-4.779	<.0001
	UB Non-Mentholated	22.095	(17)	23.322	(17)	-1.228	-5.3	-4.149 ,	1.694	0.3863
	UB Mentholated	9.359	(19)	13.108	(19)	-3.749	-28.6	-6.685 ,	-0.813	0.0152
	UB Combined	15.373	(36)	17.932	(36)	-2.558	-14.3	-4.574 ,	-0.543	0.0143

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 Paired t-test method is used to perform the analysis.
 Percent change = mean of the differences/reference (baseline)*100

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Table 14.2.5.2.3.1 Statistical Comparison of Absolute Change from Baseline in Urinary NNN Mass Excreted (ng/24 hour)
 Among Study Product Groups at Weeks 2 and 6 (PP Population)

Study Week	Comparison	----- LSMeans -----				LSMean Difference (Test - Reference)	95%		
		Test	(n)	Reference	(n)		Confidence Intervals	p-value	
Week 2	VLN Non-mentholated vs UB Non-mentholated	-11.563	(11)	-1.487	(20)	-10.076	-18.502	, -1.651	0.0199
	VLN Mentholated vs UB Mentholated	1.728	(12)	-1.617	(20)	3.345	-4.851	, 11.541	0.4174
	VLN Combined vs UB Combined	-4.918	(23)	-1.552	(40)	-3.366	-9.243	, 2.512	0.2565
Week 6	VLN Non-mentholated vs UB Non-mentholated	-15.549	(10)	-1.813	(16)	-13.736	-22.550	, -4.922	0.0030
	VLN Mentholated vs UB Mentholated	-0.671	(9)	-3.993	(19)	3.322	-5.333	, 11.978	0.4434
	VLN Combined vs UB Combined	-8.110	(19)	-2.903	(35)	-5.207	-11.384	, 0.970	0.0964

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN Non-Mentholated = Non-mentholated VLN cigarettes
 VLN Mentholated = Mentholated VLN cigarettes
 UB Non-Mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB Mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.5.2.3.2 Statistical Comparison of Absolute Change from Baseline in Urinary NNN Mass Excreted (ng/24 hour)
 Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Study Week	Comparison	----- LSMeans -----		LSMean Difference		95%		p-value
		Test	(n)	Reference	(n)	(Test - Reference)	Confidence Intervals	
Week 2	VLN Non-mentholated vs UB Non-mentholated	-6.005	(47)	-1.487	(20)	-4.519	-9.393 , 0.356	0.0690
	VLN Mentholated vs UB Mentholated	-3.444	(43)	-1.617	(20)	-1.827	-6.756 , 3.101	0.4645
	VLN Combined vs UB Combined	-4.725	(90)	-1.552	(40)	-3.173	-6.639 , 0.293	0.0724
Week 6	VLN Non-mentholated vs UB Non-mentholated	-6.539	(41)	-1.825	(16)	-4.714	-10.332 , 0.904	0.0992
	VLN Mentholated vs UB Mentholated	-5.503	(41)	-4.006	(19)	-1.497	-7.031 , 4.036	0.5926
	VLN Combined vs UB Combined	-6.021	(82)	-2.915	(35)	-3.106	-7.048 , 0.837	0.1213

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN Non-Mentholated = Non-mentholated VLN cigarettes
 VLN Mentholated = Mentholated VLN cigarettes
 UB Non-Mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB Mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.3.1.1.1
Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	49	50	99	21	20	41
	Mean	1795.719	1644.113	1719.151	1910.675	1520.921	1720.551
	SD	708.6089	500.1249	613.8453	772.7715	605.2480	715.1892
	CV%	39.5	30.4	35.7	40.4	39.8	41.6
	SEM	101.2298	70.7283	61.6938	168.6326	135.3376	111.6938
	Minimum	570.35	658.66	570.35	857.31	851.29	851.29
	Median	1682.051	1639.139	1682.051	1658.740	1343.584	1584.315
	Maximum	4443.63	2592.74	4443.63	3933.29	3056.94	3933.29
Week 2	n	48	43	91	21	20	41
	Mean	1706.862	1204.530	1469.496	1710.747	1329.844	1524.940
	SD	901.3990	543.2655	790.9739	732.7759	319.7909	595.1580
	CV%	52.8	45.1	53.8	42.8	24.0	39.0
	SEM	130.1057	82.8472	82.9166	159.9048	71.5074	92.9481
	Minimum	461.09	71.31	71.31	388.37	775.98	388.37
	Median	1569.890	1052.636	1414.626	1730.995	1337.619	1419.840
	Maximum	5931.54	2230.04	5931.54	3886.81	1913.32	3886.81
Week 6	n	42	41	83	17	19	36
	Mean	1481.693	1035.064	1261.069	1815.382	1336.103	1562.429
	SD	694.6765	475.3512	634.0203	828.3606	397.2953	673.6060
	CV%	46.9	45.9	50.3	45.6	29.7	43.1
	SEM	107.1909	74.2374	69.5928	200.9070	91.1458	112.2677
	Minimum	555.02	132.17	132.17	555.89	690.17	555.89
	Median	1365.462	967.200	1180.452	1816.750	1309.680	1508.965
	Maximum	3870.45	1993.42	3870.45	3482.05	2185.87	3482.05

* Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.3.1.1.2
 Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	12	17	29	21	20	41
	Mean	1639.196	1614.429	1624.678	1910.675	1520.921	1720.551
	SD	711.8832	458.4133	565.0902	772.7715	605.2480	715.1892
	CV%	43.4	28.4	34.8	40.4	39.8	41.6
	SEM	205.5030	111.1815	104.9346	168.6326	135.3376	111.6938
	Minimum	710.71	782.25	710.71	857.31	851.29	851.29
	Median	1554.097	1590.228	1590.228	1658.740	1343.584	1584.315
	Maximum	2678.55	2226.96	2678.55	3933.29	3056.94	3933.29
Week 2	n	11	12	23	21	20	41
	Mean	1519.913	1247.755	1377.917	1710.747	1329.844	1524.940
	SD	722.7630	529.8595	630.1956	732.7759	319.7909	595.1580
	CV%	47.6	42.5	45.7	42.8	24.0	39.0
	SEM	217.9212	152.9572	131.4049	159.9048	71.5074	92.9481
	Minimum	461.09	575.09	461.09	388.37	775.98	388.37
	Median	1671.376	1399.056	1461.134	1730.995	1337.619	1419.840
	Maximum	2770.25	2230.04	2770.25	3886.81	1913.32	3886.81
Week 6	n	10	9	19	17	19	36
	Mean	1194.700	1060.717	1131.234	1815.382	1336.103	1562.429
	SD	462.4303	467.3088	456.8387	828.3606	397.2953	673.6060
	CV%	38.7	44.1	40.4	45.6	29.7	43.1
	SEM	146.2333	155.7696	104.8060	200.9070	91.1458	112.2677
	Minimum	555.02	512.20	512.20	555.89	690.17	555.89
	Median	1253.489	956.035	1093.928	1816.750	1309.680	1508.965
	Maximum	1861.20	1993.42	1993.42	3482.05	2185.87	3482.05

* Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.3.1.2.1
 Summary of Urinary 3-HPMA Mass Excreted Change from Baseline (µg/24 hour) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-83.578	-430.429	-249.296	-194.351	-191.077	-192.714
	SD	542.2161	371.0215	497.2626	293.6456	379.6416	335.0033
	CV%	-648.8	-86.2	-199.5	-151.1	-198.7	-173.8
	SEM	79.0903	56.5803	52.4161	65.6612	84.8904	52.9687
	Minimum	-1411.58	-1376.14	-1411.58	-749.11	-1190.14	-1190.14
	Median	-85.068	-455.520	-254.173	-172.148	-209.165	-202.451
	Maximum	1487.91	266.88	1487.91	300.85	332.44	332.44
Week 6	n	41	41	82	16	19	35
	Mean	-316.339	-610.691	-463.515	-112.598	-133.451	-123.918
	SD	502.8197	441.8125	493.1283	544.5190	426.6986	476.7717
	CV%	-158.9	-72.3	-106.4	-483.6	-319.7	-384.7
	SEM	78.5272	68.9995	54.4569	136.1298	97.8914	80.5891
	Minimum	-1512.19	-1674.41	-1674.41	-1094.92	-1553.58	-1553.58
	Median	-219.592	-529.445	-449.147	-207.548	-158.619	-167.964
	Maximum	1031.69	231.33	1031.69	998.73	663.28	998.73

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.3.1.2.2
Summary of Urinary 3-HPMA Mass Excreted Change from Baseline (µg/24 hour) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-32.075	-350.925	-198.432	-194.351	-191.077	-192.714
	SD	390.1290	263.0664	360.9785	293.6456	379.6416	335.0033
	CV%	-1216.3	-75.0	-181.9	-151.1	-198.7	-173.8
	SEM	117.6283	75.9407	75.2692	65.6612	84.8904	52.9687
	Minimum	-873.37	-647.26	-873.37	-749.11	-1190.14	-1190.14
	Median	91.699	-435.756	-171.220	-172.148	-209.165	-202.451
	Maximum	519.38	149.36	519.38	300.85	332.44	332.44
Week 6	n	10	9	19	16	19	35
	Mean	-244.632	-580.377	-403.669	-112.598	-133.451	-123.918
	SD	459.8291	391.8362	451.2470	544.5190	426.6986	476.7717
	CV%	-188.0	-67.5	-111.8	-483.6	-319.7	-384.7
	SEM	145.4107	130.6121	103.5232	136.1298	97.8914	80.5891
	Minimum	-1364.30	-1141.96	-1364.30	-1094.92	-1553.58	-1553.58
	Median	-72.330	-538.194	-305.902	-207.548	-158.619	-167.964
	Maximum	176.03	69.42	176.03	998.73	663.28	998.73

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.3.1.3.1
Summary of Urinary 3-HPMA Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-3.579	-26.695	-14.623	-10.057	-6.921	-8.489
	SD	27.2631	22.6970	27.6061	17.7515	21.1132	19.3186
	CV%	-761.8	-85.0	-188.8	-176.5	-305.1	-227.6
	SEM	3.9767	3.4613	2.9099	3.9694	4.7210	3.0545
	Minimum	-58.91	-95.07	-95.07	-58.86	-38.93	-58.86
	Median	-5.510	-27.950	-15.070	-8.315	-15.141	-13.380
	Maximum	52.42	26.11	52.42	18.99	39.05	39.05
Week 6	n	41	41	82	16	19	35
	Mean	-15.488	-36.552	-26.020	-4.538	-4.190	-4.349
	SD	25.2228	24.4861	26.8801	27.9969	26.1591	26.6104
	CV%	-162.9	-67.0	-103.3	-617.0	-624.4	-611.9
	SEM	3.9391	3.8241	2.9684	6.9992	6.0013	4.4980
	Minimum	-61.15	-89.14	-89.14	-41.11	-50.82	-50.82
	Median	-14.528	-40.040	-26.022	-11.198	-8.006	-9.041
	Maximum	48.32	20.59	48.32	63.04	77.91	77.91

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.3.1.3.2
Summary of Urinary 3-HPMA Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-2.264	-23.324	-13.252	-10.057	-6.921	-8.489
	SD	25.3456	19.1423	24.3087	17.7515	21.1132	19.3186
	CV%	-1119.6	-82.1	-183.4	-176.5	-305.1	-227.6
	SEM	7.6420	5.5259	5.0687	3.9694	4.7210	3.0545
	Minimum	-43.02	-52.95	-52.95	-58.86	-38.93	-58.86
	Median	3.423	-25.459	-14.716	-8.315	-15.141	-13.380
	Maximum	36.32	11.93	36.32	18.99	39.05	39.05
Week 6	n	10	9	19	16	19	35
	Mean	-13.158	-35.245	-23.620	-4.538	-4.190	-4.349
	SD	23.5945	17.2704	23.2226	27.9969	26.1591	26.6104
	CV%	-179.3	-49.0	-98.3	-617.0	-624.4	-611.9
	SEM	7.4613	5.7568	5.3276	6.9992	6.0013	4.4980
	Minimum	-53.61	-54.43	-54.43	-41.11	-50.82	-50.82
	Median	-6.581	-40.612	-24.429	-11.198	-8.006	-9.041
	Maximum	11.92	3.61	11.92	63.04	77.91	77.91

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.3.1.4.1 Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level (µg/g creatinine)
by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	49	50	99	21	20	41
	Mean	1218.135	993.375	1104.620	1073.343	932.381	1004.581
	SD	533.4871	431.1334	495.0707	268.8980	371.7845	326.9526
	CV%	43.8	43.4	44.8	25.1	39.9	32.5
	SEM	76.2124	60.9715	49.7565	58.6783	83.1335	51.0614
	Minimum	291.20	334.82	291.20	555.08	292.50	292.50
	Median	1110.577	916.919	977.143	1091.603	950.309	1009.390
	Maximum	2854.03	2497.08	2854.03	1524.06	1628.14	1628.14
Week 2	n	48	43	91	21	20	41
	Mean	1139.041	713.687	938.049	981.083	873.228	928.471
	SD	617.9144	322.2190	541.7026	294.4913	282.6115	290.3094
	CV%	54.2	45.1	57.7	30.0	32.4	31.3
	SEM	89.1883	49.1379	56.7859	64.2633	63.1938	45.3387
	Minimum	371.70	180.36	180.36	316.15	418.54	316.15
	Median	961.768	687.850	797.203	1000.000	890.318	952.830
	Maximum	3526.57	1559.61	3526.57	1497.85	1431.72	1497.85
Week 6	n	42	41	83	17	19	36
	Mean	974.346	648.662	813.466	1002.742	817.481	904.965
	SD	472.2828	329.8398	437.5304	317.9318	283.6210	310.4451
	CV%	48.5	50.8	53.8	31.7	34.7	34.3
	SEM	72.8748	51.5123	48.0252	77.1098	65.0671	51.7408
	Minimum	380.92	243.61	243.61	473.60	253.62	253.62
	Median	905.364	545.395	769.113	988.470	810.476	900.188
	Maximum	2701.55	1787.18	2701.55	1497.80	1238.10	1497.80

* Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.3.1.4.2 Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level (µg/g creatinine)
by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	12	17	29	21	20	41
	Mean	1045.921	985.480	1010.490	1073.343	932.381	1004.581
	SD	463.1309	445.6693	445.7349	268.8980	371.7845	326.9526
	CV%	44.3	45.2	44.1	25.1	39.9	32.5
	SEM	133.6944	108.0907	82.7709	58.6783	83.1335	51.0614
	Minimum	493.26	334.82	334.82	555.08	292.50	292.50
	Median	989.822	987.539	987.539	1091.603	950.309	1009.390
	Maximum	2160.00	1860.12	2160.00	1524.06	1628.14	1628.14
Week 2	n	11	12	23	21	20	41
	Mean	907.114	730.966	815.211	981.083	873.228	928.471
	SD	334.6140	394.5337	369.8872	294.4913	282.6115	290.3094
	CV%	36.9	54.0	45.4	30.0	32.4	31.3
	SEM	100.8899	113.8921	77.1268	64.2633	63.1938	45.3387
	Minimum	371.70	281.63	281.63	316.15	418.54	316.15
	Median	827.128	725.436	757.241	1000.000	890.318	952.830
	Maximum	1402.12	1559.61	1559.61	1497.85	1431.72	1497.85
Week 6	n	10	9	19	17	19	36
	Mean	766.771	609.615	692.328	1002.742	817.481	904.965
	SD	287.5422	406.9799	348.5028	317.9318	283.6210	310.4451
	CV%	37.5	66.8	50.3	31.7	34.7	34.3
	SEM	90.9288	135.6600	79.9520	77.1098	65.0671	51.7408
	Minimum	384.96	243.61	243.61	473.60	253.62	253.62
	Median	744.773	433.291	525.362	988.470	810.476	900.188
	Maximum	1149.52	1389.94	1389.94	1497.80	1238.10	1497.80

* Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.3.1.5.1 Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level Change from Baseline (µg/g creatinine)
 by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-73.162	-241.080	-153.390	-99.694	-59.153	-79.424
	SD	372.7744	271.4938	337.2249	195.7350	179.0845	186.3083
	CV%	-509.5	-112.6	-219.8	-196.3	-302.7	-234.6
	SEM	54.3747	41.4024	35.5466	43.7677	40.0445	29.4579
	Minimum	-974.27	-1206.85	-1206.85	-486.57	-524.54	-524.54
	Median	-84.001	-210.339	-145.046	-76.980	-80.306	-76.980
	Maximum	1120.91	245.06	1120.91	282.64	168.76	282.64
Week 6	n	41	41	82	16	19	35
	Mean	-232.565	-333.777	-283.171	-82.082	-95.177	-89.190
	SD	316.9126	335.1572	328.1176	261.6802	232.1763	242.4715
	CV%	-136.3	-100.4	-115.9	-318.8	-243.9	-271.9
	SEM	49.4934	52.3428	36.2345	65.4201	53.2649	40.9852
	Minimum	-1023.93	-1738.36	-1738.36	-440.82	-797.37	-797.37
	Median	-212.015	-282.329	-218.503	-70.150	-105.171	-93.509
	Maximum	633.84	151.44	633.84	518.42	231.59	518.42

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.3.1.5.2 Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level Change from Baseline (µg/g creatinine)
 by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-37.527	-202.400	-123.548	-99.694	-59.153	-79.424
	SD	209.0486	167.8667	202.5957	195.7350	179.0845	186.3083
	CV%	-557.1	-82.9	-164.0	-196.3	-302.7	-234.6
	SEM	63.0305	48.4589	42.2441	43.7677	40.0445	29.4579
	Minimum	-404.52	-574.86	-574.86	-486.57	-524.54	-524.54
	Median	8.839	-201.895	-115.197	-76.980	-80.306	-76.980
	Maximum	268.46	81.80	268.46	282.64	168.76	282.64
Week 6	n	10	9	19	16	19	35
	Mean	-177.995	-309.845	-240.450	-82.082	-95.177	-89.190
	SD	209.3754	290.6662	253.0683	261.6802	232.1763	242.4715
	CV%	-117.6	-93.8	-105.2	-318.8	-243.9	-271.9
	SEM	66.2103	96.8887	58.0578	65.4201	53.2649	40.9852
	Minimum	-686.50	-747.10	-747.10	-440.82	-797.37	-797.37
	Median	-115.095	-213.551	-139.868	-70.150	-105.171	-93.509
	Maximum	42.86	151.44	151.44	518.42	231.59	518.42

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.3.1.6.1 Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level Percent Change from Baseline (%)
 by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-4.942	-23.472	-13.795	-8.739	-1.425	-5.082
	SD	27.0948	23.9247	27.1327	20.5799	19.7736	20.2617
	CV%	-548.2	-101.9	-196.7	-235.5	-1387.2	-398.7
	SEM	3.9522	3.6485	2.8600	4.6018	4.4215	3.2037
	Minimum	-62.51	-71.83	-71.83	-60.62	-33.28	-60.62
	Median	-8.140	-25.901	-15.566	-6.692	-9.400	-8.042
	Maximum	51.28	36.59	51.28	28.41	43.09	43.09
Week 6	n	41	41	82	16	19	35
	Mean	-18.066	-31.972	-25.019	-7.099	-5.298	-6.121
	SD	22.6180	21.9442	23.2244	25.1434	26.9668	25.7824
	CV%	-125.2	-68.6	-92.8	-354.2	-509.0	-421.2
	SEM	3.5323	3.4271	2.5647	6.2858	6.1866	4.3580
	Minimum	-65.70	-69.62	-69.62	-41.00	-48.97	-48.97
	Median	-17.495	-37.892	-24.080	-7.792	-12.721	-12.293
	Maximum	30.65	12.61	30.65	52.93	73.43	73.43

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.3.1.6.2 Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level Percent Change from Baseline (%)
by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-2.923	-22.205	-12.983	-8.739	-1.425	-5.082
	SD	22.9965	16.7099	21.8400	20.5799	19.7736	20.2617
	CV%	-786.7	-75.3	-168.2	-235.5	-1387.2	-398.7
	SEM	6.9337	4.8237	4.5539	4.6018	4.4215	3.2037
	Minimum	-39.40	-44.40	-44.40	-60.62	-33.28	-60.62
	Median	0.634	-21.807	-15.244	-6.692	-9.400	-8.042
	Maximum	31.84	12.60	31.84	28.41	43.09	43.09
Week 6	n	10	9	19	16	19	35
	Mean	-17.425	-34.106	-25.326	-7.099	-5.298	-6.121
	SD	17.0524	20.6306	20.1937	25.1434	26.9668	25.7824
	CV%	-97.9	-60.5	-79.7	-354.2	-509.0	-421.2
	SEM	5.3924	6.8769	4.6327	6.2858	6.1866	4.3580
	Minimum	-57.94	-56.81	-57.94	-41.00	-48.97	-48.97
	Median	-16.621	-40.601	-21.955	-7.792	-12.721	-12.293
	Maximum	4.17	12.23	12.23	52.93	73.43	73.43

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.3.2.1 Statistical Comparison of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1
by Study Product Group (PP Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	Percent Change (%)	95%		p-Value
		Test Week	(n)	Baseline	(n)			Confidence Intervals		
Week 2	VLN Non-Mentholated	1519.913	(11)	1551.988	(11)	-32.075	-2.1	-294.167 ,	230.017	0.7906
	VLN Mentholated	1247.755	(12)	1598.680	(12)	-350.925	-22.0	-518.070 ,	-183.781	0.0007
	VLN Combined	1377.917	(23)	1576.349	(23)	-198.432	-12.6	-354.530 ,	-42.333	0.0151
	UB Non-Mentholated	1710.747	(21)	1888.019	(21)	-177.272	-9.4	-312.337 ,	-42.208	0.0127
	UB Mentholated	1329.844	(20)	1520.921	(20)	-191.077	-12.6	-368.755 ,	-13.399	0.0364
	UB Combined	1524.940	(41)	1708.947	(41)	-184.006	-10.8	-289.889 ,	-78.124	0.0011
Week 6	VLN Non-Mentholated	1194.700	(10)	1439.332	(10)	-244.632	-17.0	-573.574 ,	84.310	0.1268
	VLN Mentholated	1060.717	(9)	1641.094	(9)	-580.377	-35.4	-881.569 ,	-279.185	0.0022
	VLN Combined	1131.234	(19)	1534.903	(19)	-403.669	-26.3	-621.163 ,	-186.175	0.0011
	UB Non-Mentholated	1815.382	(17)	1914.526	(17)	-99.144	-5.2	-371.716 ,	173.427	0.4519
	UB Mentholated	1336.103	(19)	1469.554	(19)	-133.451	-9.1	-339.113 ,	72.212	0.1896
	UB Combined	1562.429	(36)	1679.680	(36)	-117.250	-7.0	-276.821 ,	42.320	0.1447

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Paired t-test method is used to perform the analysis.
Percent change = mean of the differences/reference (baseline)*100

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Table 14.2.5.3.2.2 Statistical Comparison of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1
by Study Product Group (ITT Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	Percent Change (%)	95%		p-Value
		Test Week	(n)	Baseline	(n)			Confidence Intervals		
Week 2	VLN Non-Mentholated	1706.862	(48)	1787.779	(47)	-83.578	-4.7	-242.779 ,	75.622	0.2961
	VLN Mentholated	1204.530	(43)	1634.959	(43)	-430.429	-26.3	-544.613 ,	-316.246	<.0001
	VLN Combined	1469.496	(91)	1714.765	(90)	-249.296	-14.5	-353.446 ,	-145.146	<.0001
	UB Non-Mentholated	1710.747	(21)	1888.019	(21)	-177.272	-9.4	-312.337 ,	-42.208	0.0127
	UB Mentholated	1329.844	(20)	1520.921	(20)	-191.077	-12.6	-368.755 ,	-13.399	0.0364
	UB Combined	1524.940	(41)	1708.947	(41)	-184.006	-10.8	-289.889 ,	-78.124	0.0011
Week 6	VLN Non-Mentholated	1481.693	(42)	1806.472	(41)	-316.339	-17.5	-475.048 ,	-157.629	0.0002
	VLN Mentholated	1035.064	(41)	1645.755	(41)	-610.691	-37.1	-750.144 ,	-471.238	<.0001
	VLN Combined	1261.069	(83)	1726.113	(82)	-463.515	-26.9	-571.867 ,	-355.163	<.0001
	UB Non-Mentholated	1815.382	(17)	1914.526	(17)	-99.144	-5.2	-371.716 ,	173.427	0.4519
	UB Mentholated	1336.103	(19)	1469.554	(19)	-133.451	-9.1	-339.113 ,	72.212	0.1896
	UB Combined	1562.429	(36)	1679.680	(36)	-117.250	-7.0	-276.821 ,	42.320	0.1447

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Paired t-test method is used to perform the analysis.
Percent change = mean of the differences/reference (baseline)*100

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Table 14.2.5.3.3.1 Statistical Comparison of Absolute Change from Baseline in Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour)
 Among Study Product Groups at Weeks 2 and 6 (PP Population)

Study Week	Comparison	----- LSMeans -----				LSMean Difference (Test - Reference)	95%		p-value
		Test	(n)	Reference	(n)		Confidence Intervals		
Week 2	VLN Non-mentholated vs UB Non-mentholated	-32.075	(11)	-194.351	(20)	162.276	-90.088	, 414.640	0.2032
	VLN Mentholated vs UB Mentholated	-350.925	(12)	-191.077	(20)	-159.848	-405.334	, 85.638	0.1977
	VLN Combined vs UB Combined	-191.500	(23)	-192.714	(40)	1.214	-174.819	, 177.247	0.9890
Week 6	VLN Non-mentholated vs UB Non-mentholated	-231.927	(10)	-77.392	(16)	-154.535	-511.048	, 201.979	0.3891
	VLN Mentholated vs UB Mentholated	-611.476	(9)	-166.527	(19)	-444.949	-796.986	, -92.912	0.0141
	VLN Combined vs UB Combined	-421.702	(19)	-121.960	(35)	-299.742	-550.256	, -49.228	0.0199

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN Non-Mentholated = Non-mentholated VLN cigarettes
 VLN Mentholated = Mentholated VLN cigarettes
 UB Non-Mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB Mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.5.3.3.2 Statistical Comparison of Absolute Change from Baseline in Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour)
 Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Study Week	Comparison	----- LSMeans -----		LSMean Difference		95%		p-value
		Test	(n)	Reference	(n)	(Test - Reference)	Confidence Intervals	
Week 2	VLN Non-mentholated vs UB Non-mentholated	-78.429	(47)	-194.351	(20)	115.922	-113.508 , 345.352	0.3193
	VLN Mentholated vs UB Mentholated	-425.042	(43)	-191.077	(20)	-233.965	-466.232 , -1.698	0.0484
	VLN Combined vs UB Combined	-251.736	(90)	-192.714	(40)	-59.022	-222.259 , 104.216	0.4756
Week 6	VLN Non-mentholated vs UB Non-mentholated	-326.189	(41)	-90.371	(16)	-235.818	-501.162 , 29.525	0.0811
	VLN Mentholated vs UB Mentholated	-609.776	(41)	-154.333	(19)	-455.443	-711.011 , -199.874	0.0006
	VLN Combined vs UB Combined	-467.983	(82)	-122.352	(35)	-345.631	-529.831 , -161.431	0.0003

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN Non-Mentholated = Non-mentholated VLN cigarettes
 VLN Mentholated = Mentholated VLN cigarettes
 UB Non-Mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB Mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.5.4.1.1.1
 Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	49	50	99	21	20	41
	Mean	7.144	6.561	6.850	7.935	8.239	8.083
	SD	5.9255	3.8833	4.9823	3.8120	7.3290	5.7274
	CV%	82.9	59.2	72.7	48.0	89.0	70.9
	SEM	0.8465	0.5492	0.5007	0.8319	1.6388	0.8945
	Minimum	0.73	0.71	0.71	1.23	1.26	1.23
	Median	5.977	6.092	5.977	8.112	6.543	7.680
	Maximum	34.50	17.22	34.50	15.60	30.45	30.45
Week 2	n	48	43	91	21	20	41
	Mean	8.160	6.734	7.486	7.561	7.731	7.644
	SD	7.8142	4.7617	6.5560	3.7582	5.9223	4.8713
	CV%	95.8	70.7	87.6	49.7	76.6	63.7
	SEM	1.1279	0.7261	0.6873	0.8201	1.3243	0.7608
	Minimum	0.60	0.11	0.11	1.25	1.19	1.19
	Median	6.647	5.954	6.315	7.933	5.853	7.366
	Maximum	47.53	21.03	47.53	15.46	21.25	21.25
Week 6	n	42	41	83	17	19	36
	Mean	7.282	5.589	6.446	7.261	6.845	7.042
	SD	6.4350	3.6334	5.2792	4.4329	5.2829	4.8353
	CV%	88.4	65.0	81.9	61.1	77.2	68.7
	SEM	0.9929	0.5674	0.5795	1.0751	1.2120	0.8059
	Minimum	0.46	0.48	0.46	1.11	1.22	1.11
	Median	6.046	5.896	5.896	6.453	4.825	6.420
	Maximum	38.59	12.44	38.59	18.34	22.32	22.32

* Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.4.1.1.2
Summary of Urinary S-PMA Mass Excreted (µg/24 hour) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	12	17	29	21	20	41
	Mean	6.770	5.769	6.183	7.935	8.239	8.083
	SD	5.1740	3.4965	4.2136	3.8120	7.3290	5.7274
	CV%	76.4	60.6	68.1	48.0	89.0	70.9
	SEM	1.4936	0.8480	0.7824	0.8319	1.6388	0.8945
	Minimum	1.28	0.71	0.71	1.23	1.26	1.23
	Median	6.015	5.387	5.465	8.112	6.543	7.680
	Maximum	18.15	13.81	18.15	15.60	30.45	30.45
Week 2	n	11	12	23	21	20	41
	Mean	8.767	6.297	7.478	7.561	7.731	7.644
	SD	7.0466	4.5797	5.8862	3.7582	5.9223	4.8713
	CV%	80.4	72.7	78.7	49.7	76.6	63.7
	SEM	2.1246	1.3220	1.2274	0.8201	1.3243	0.7608
	Minimum	0.84	0.78	0.78	1.25	1.19	1.19
	Median	7.494	6.134	6.854	7.933	5.853	7.366
	Maximum	20.91	15.73	20.91	15.46	21.25	21.25
Week 6	n	10	9	19	17	19	36
	Mean	7.271	5.806	6.577	7.261	6.845	7.042
	SD	5.6920	3.2888	4.6444	4.4329	5.2829	4.8353
	CV%	78.3	56.6	70.6	61.1	77.2	68.7
	SEM	1.8000	1.0963	1.0655	1.0751	1.2120	0.8059
	Minimum	0.46	1.31	0.46	1.11	1.22	1.11
	Median	6.715	6.400	6.400	6.453	4.825	6.420
	Maximum	17.77	11.21	17.77	18.34	22.32	22.32

* Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.4.1.2.1
 Summary of Urinary S-PMA Mass Excreted Change from Baseline ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	1.214	-0.180	0.548	-0.388	-0.508	-0.448
	SD	2.9212	3.2051	3.1223	1.2137	2.7101	2.0735
	CV%	240.6	-1776.4	570.1	-312.8	-533.3	-462.7
	SEM	0.4261	0.4888	0.3291	0.2714	0.6060	0.3279
	Minimum	-4.87	-9.02	-9.02	-3.40	-9.20	-9.20
	Median	1.098	-0.120	0.165	-0.315	0.032	-0.077
	Maximum	13.03	11.15	13.03	1.60	3.38	3.38
Week 6	n	41	41	82	16	19	35
	Mean	-0.096	-1.417	-0.757	-0.558	-0.224	-0.377
	SD	2.6479	2.8467	2.8117	1.4554	1.9809	1.7437
	CV%	-2748.4	-200.9	-371.6	-260.6	-883.1	-462.5
	SEM	0.4135	0.4446	0.3105	0.3638	0.4545	0.2947
	Minimum	-7.19	-11.33	-11.33	-2.87	-4.53	-4.53
	Median	0.434	-0.881	-0.294	-0.611	0.204	-0.227
	Maximum	5.62	4.74	5.62	2.74	4.00	4.00

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.5.4.1.2.2
 Summary of Urinary S-PMA Mass Excreted Change from Baseline ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	2.368	-0.044	1.110	-0.388	-0.508	-0.448
	SD	2.6370	1.9621	2.5697	1.2137	2.7101	2.0735
	CV%	111.4	-4454.6	231.6	-312.8	-533.3	-462.7
	SEM	0.7951	0.5664	0.5358	0.2714	0.6060	0.3279
	Minimum	-0.43	-2.21	-2.21	-3.40	-9.20	-9.20
	Median	1.833	-0.249	0.574	-0.315	0.032	-0.077
	Maximum	8.28	4.80	8.28	1.60	3.38	3.38
Week 6	n	10	9	19	16	19	35
	Mean	0.798	-1.547	-0.313	-0.558	-0.224	-0.377
	SD	3.4846	2.7267	3.2898	1.4554	1.9809	1.7437
	CV%	436.7	-176.2	-1051.4	-260.6	-883.1	-462.5
	SEM	1.1019	0.9089	0.7547	0.3638	0.4545	0.2947
	Minimum	-7.19	-6.46	-7.19	-2.87	-4.53	-4.53
	Median	0.813	-1.824	0.434	-0.611	0.204	-0.227
	Maximum	5.62	2.53	5.62	2.74	4.00	4.00

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.5.4.1.3.1
Summary of Urinary S-PMA Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	20.528	-3.061	9.257	-3.718	1.614	-1.052
	SD	42.8642	46.5536	45.9649	14.2374	24.0472	19.6917
	CV%	208.8	-1520.8	496.5	-383.0	1489.9	-1872.1
	SEM	6.2524	7.0994	4.8451	3.1836	5.3771	3.1135
	Minimum	-59.30	-97.76	-97.76	-32.04	-33.52	-33.52
	Median	15.327	-3.320	6.553	-3.184	0.510	-1.012
	Maximum	184.57	216.27	216.27	19.08	49.27	49.27
Week 6	n	41	41	82	16	19	35
	Mean	5.265	-20.544	-7.639	-7.848	2.956	-1.983
	SD	36.6238	36.2460	38.4672	14.4645	30.5407	24.8179
	CV%	695.6	-176.4	-503.5	-184.3	1033.0	-1251.7
	SEM	5.7197	5.6607	4.2480	3.6161	7.0065	4.1950
	Minimum	-69.63	-89.99	-89.99	-30.01	-35.36	-35.36
	Median	7.729	-22.332	-6.588	-9.718	4.543	-8.959
	Maximum	112.46	91.99	112.46	28.53	70.97	70.97

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

Table 14.2.5.4.1.3.2
 Summary of Urinary S-PMA Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	30.679	-5.802	11.645	-3.718	1.614	-1.052
	SD	31.3418	29.6208	35.1051	14.2374	24.0472	19.6917
	CV%	102.2	-510.6	301.4	-383.0	1489.9	-1872.1
	SEM	9.4499	8.5508	7.3199	3.1836	5.3771	3.1135
	Minimum	-33.87	-51.26	-51.26	-32.04	-33.52	-33.52
	Median	34.184	-3.477	10.655	-3.184	0.510	-1.012
	Maximum	72.11	43.92	72.11	19.08	49.27	49.27
Week 6	n	10	9	19	16	19	35
	Mean	16.120	-20.935	-1.433	-7.848	2.956	-1.983
	SD	39.1848	33.9039	40.4961	14.4645	30.5407	24.8179
	CV%	243.1	-161.9	-2826.8	-184.3	1033.0	-1251.7
	SEM	12.3913	11.3013	9.2904	3.6161	7.0065	4.1950
	Minimum	-63.76	-57.08	-63.76	-30.01	-35.36	-35.36
	Median	26.953	-30.045	11.504	-9.718	4.543	-8.959
	Maximum	67.07	40.35	67.07	28.53	70.97	70.97

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.4.1.4.1 Summary of Urinary S-PMA Creatinine-Normalized Excretion Level ($\mu\text{g/g}$ creatinine)
by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	49	50	99	21	20	41
	Mean	4.741	3.928	4.330	4.654	5.028	4.837
	SD	3.5588	2.4411	3.0577	2.2540	4.1809	3.2984
	CV%	75.1	62.1	70.6	48.4	83.1	68.2
	SEM	0.5084	0.3452	0.3073	0.4919	0.9349	0.5151
	Minimum	0.45	0.31	0.31	0.60	0.60	0.60
	Median	4.081	3.384	3.666	4.449	4.133	4.158
	Maximum	18.68	10.84	18.68	9.50	15.94	15.94
Week 2	n	48	43	91	21	20	41
	Mean	5.337	3.999	4.705	4.583	5.021	4.797
	SD	4.7306	2.8330	3.9853	2.3684	3.8610	3.1519
	CV%	88.6	70.8	84.7	51.7	76.9	65.7
	SEM	0.6828	0.4320	0.4178	0.5168	0.8634	0.4922
	Minimum	0.54	0.27	0.27	0.61	0.66	0.61
	Median	3.847	3.829	3.829	4.215	3.988	4.136
	Maximum	28.26	12.53	28.26	10.30	12.32	12.32
Week 6	n	42	41	83	17	19	36
	Mean	4.607	3.413	4.017	4.133	4.283	4.212
	SD	3.5369	2.1509	2.9787	2.0936	3.5511	2.9146
	CV%	76.8	63.0	74.1	50.7	82.9	69.2
	SEM	0.5458	0.3359	0.3270	0.5078	0.8147	0.4858
	Minimum	0.31	0.26	0.26	0.54	0.45	0.45
	Median	4.139	3.007	3.476	4.097	3.093	3.728
	Maximum	20.12	7.94	20.12	8.09	12.64	12.64

* Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.4.1.4.2 Summary of Urinary S-PMA Creatinine-Normalized Excretion Level ($\mu\text{g/g}$ creatinine)
by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	12	17	29	21	20	41
	Mean	4.339	3.389	3.782	4.654	5.028	4.837
	SD	3.1035	2.1868	2.5967	2.2540	4.1809	3.2984
	CV%	71.5	64.5	68.7	48.4	83.1	68.2
	SEM	0.8959	0.5304	0.4822	0.4919	0.9349	0.5151
	Minimum	0.65	0.31	0.31	0.60	0.60	0.60
	Median	3.479	3.134	3.134	4.449	4.133	4.158
	Maximum	9.02	9.03	9.03	9.50	15.94	15.94
Week 2	n	11	12	23	21	20	41
	Mean	5.293	3.663	4.443	4.583	5.021	4.797
	SD	3.9171	3.0257	3.4992	2.3684	3.8610	3.1519
	CV%	74.0	82.6	78.8	51.7	76.9	65.7
	SEM	1.1810	0.8735	0.7296	0.5168	0.8634	0.4922
	Minimum	0.54	0.38	0.38	0.61	0.66	0.61
	Median	4.353	3.023	3.152	4.215	3.988	4.136
	Maximum	11.66	11.00	11.66	10.30	12.32	12.32
Week 6	n	10	9	19	17	19	36
	Mean	4.351	3.392	3.897	4.133	4.283	4.212
	SD	2.9555	2.5384	2.7337	2.0936	3.5511	2.9146
	CV%	67.9	74.8	70.1	50.7	82.9	69.2
	SEM	0.9346	0.8461	0.6272	0.5078	0.8147	0.4858
	Minimum	0.42	0.60	0.42	0.54	0.45	0.45
	Median	4.090	2.712	3.524	4.097	3.093	3.728
	Maximum	9.35	7.94	9.35	8.09	12.64	12.64

* Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.4.1.5.1 Summary of Urinary S-PMA Creatinine-Normalized Excretion Level Change from Baseline ($\mu\text{g/g}$ creatinine)
 by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	0.745	-0.060	0.360	-0.156	-0.008	-0.082
	SD	2.1202	1.6424	1.9390	0.7805	1.3190	1.0723
	CV%	284.6	-2738.4	538.1	-499.4	-16831.8	-1306.7
	SEM	0.3093	0.2505	0.2044	0.1745	0.2949	0.1696
	Minimum	-4.00	-3.55	-4.00	-1.57	-3.62	-3.62
	Median	0.291	-0.168	0.087	0.097	0.151	0.124
	Maximum	9.58	5.94	9.58	0.86	2.24	2.24
Week 6	n	41	41	82	16	19	35
	Mean	-0.192	-0.767	-0.479	-0.513	-0.171	-0.328
	SD	1.6933	1.3885	1.5657	0.7304	1.4306	1.1614
	CV%	-883.1	-181.1	-326.8	-142.3	-835.2	-354.5
	SEM	0.2644	0.2168	0.1729	0.1826	0.3282	0.1963
	Minimum	-4.59	-4.39	-4.59	-1.73	-2.67	-2.67
	Median	0.061	-0.725	-0.252	-0.597	-0.083	-0.481
	Maximum	3.97	2.38	3.97	1.04	2.61	2.61

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.4.1.5.2 Summary of Urinary S-PMA Creatinine-Normalized Excretion Level Change from Baseline ($\mu\text{g/g}$ creatinine)
by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	1.380	0.001	0.660	-0.156	-0.008	-0.082
	SD	1.3871	1.0195	1.3748	0.7805	1.3190	1.0723
	CV%	100.5	119295.8	208.2	-499.4	-16831.8	-1306.7
	SEM	0.4182	0.2943	0.2867	0.1745	0.2949	0.1696
	Minimum	-0.11	-1.71	-1.71	-1.57	-3.62	-3.62
	Median	1.282	-0.085	0.232	0.097	0.151	0.124
	Maximum	3.92	1.97	3.92	0.86	2.24	2.24
Week 6	n	10	9	19	16	19	35
	Mean	0.246	-0.667	-0.186	-0.513	-0.171	-0.328
	SD	1.6396	1.3708	1.5488	0.7304	1.4306	1.1614
	CV%	665.7	-205.6	-832.0	-142.3	-835.2	-354.5
	SEM	0.5185	0.4569	0.3553	0.1826	0.3282	0.1963
	Minimum	-3.82	-2.26	-3.82	-1.73	-2.67	-2.67
	Median	0.542	-0.725	-0.021	-0.597	-0.083	-0.481
	Maximum	2.70	2.10	2.70	1.04	2.61	2.61

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.4.1.6.1 Summary of Urinary S-PMA Creatinine-Normalized Excretion Level Percent Change from Baseline (%)
 by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	18.674	0.086	9.793	-2.646	7.277	2.315
	SD	41.0458	48.8818	45.6678	15.5699	20.9805	18.9156
	CV%	219.8	56702.4	466.3	-588.3	288.3	817.0
	SEM	5.9871	7.4544	4.8138	3.4815	4.6914	2.9908
	Minimum	-62.87	-87.18	-87.18	-34.94	-30.23	-34.94
	Median	13.486	-6.889	3.303	3.274	8.583	4.446
	Maximum	146.03	242.55	242.55	23.42	45.06	45.06
Week 6	n	41	41	82	16	19	35
	Mean	1.314	-16.759	-7.722	-9.733	1.726	-3.512
	SD	32.2642	32.7957	33.5837	15.2416	31.0514	25.4261
	CV%	2455.5	-195.7	-434.9	-156.6	1798.7	-724.0
	SEM	5.0388	5.1218	3.7087	3.8104	7.1237	4.2978
	Minimum	-49.05	-63.19	-63.19	-29.68	-39.57	-39.57
	Median	6.923	-22.268	-11.898	-10.959	-4.227	-10.811
	Maximum	82.89	97.34	97.34	23.86	66.67	66.67

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.4.1.6.2 Summary of Urinary S-PMA Creatinine-Normalized Excretion Level Percent Change from Baseline (%)
by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	29.648	-4.524	11.819	-2.646	7.277	2.315
	SD	30.0135	27.0350	32.8561	15.5699	20.9805	18.9156
	CV%	101.2	-597.6	278.0	-588.3	288.3	817.0
	SEM	9.0494	7.8043	6.8510	3.4815	4.6914	2.9908
	Minimum	-17.44	-44.78	-44.78	-34.94	-30.23	-34.94
	Median	29.305	-2.415	15.171	3.274	8.583	4.446
	Maximum	98.95	38.89	98.95	23.42	45.06	45.06
Week 6	n	10	9	19	16	19	35
	Mean	8.636	-19.675	-4.775	-9.733	1.726	-3.512
	SD	32.1038	36.8019	36.4445	15.2416	31.0514	25.4261
	CV%	371.7	-187.0	-763.3	-156.6	1798.7	-724.0
	SEM	10.1521	12.2673	8.3609	3.8104	7.1237	4.2978
	Minimum	-45.25	-60.10	-60.10	-29.68	-39.57	-39.57
	Median	12.637	-24.964	-2.360	-10.959	-4.227	-10.811
	Maximum	68.12	52.03	68.12	23.86	66.67	66.67

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.4.2.1 Statistical Comparison of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1
by Study Product Group (PP Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	Percent Change (%)	95%		p-Value
		Test Week	(n)	Baseline	(n)			Confidence Intervals		
Week 2	VLN Non-Mentholated	8.767	(11)	6.399	(11)	2.368	37.0	0.596 ,	4.139	0.0139
	VLN Mentholated	6.297	(12)	6.341	(12)	-0.044	-0.7	-1.291 ,	1.203	0.9394
	VLN Combined	7.478	(23)	6.369	(23)	1.110	17.4	-0.002 ,	2.221	0.0503
	UB Non-Mentholated	7.561	(21)	7.906	(21)	-0.345	-4.4	-0.891 ,	0.201	0.2024
	UB Mentholated	7.731	(20)	8.239	(20)	-0.508	-6.2	-1.777 ,	0.760	0.4121
	UB Combined	7.644	(41)	8.068	(41)	-0.425	-5.3	-1.073 ,	0.223	0.1929
Week 6	VLN Non-Mentholated	7.271	(10)	6.473	(10)	0.798	12.3	-1.695 ,	3.291	0.4873
	VLN Mentholated	5.806	(9)	7.354	(9)	-1.547	-21.0	-3.643 ,	0.549	0.1271
	VLN Combined	6.577	(19)	6.890	(19)	-0.313	-4.5	-1.899 ,	1.273	0.6833
	UB Non-Mentholated	7.261	(17)	7.812	(17)	-0.551	-7.1	-1.275 ,	0.174	0.1267
	UB Mentholated	6.845	(19)	7.070	(19)	-0.224	-3.2	-1.179 ,	0.730	0.6276
	UB Combined	7.042	(36)	7.420	(36)	-0.378	-5.1	-0.960 ,	0.203	0.1950

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Paired t-test method is used to perform the analysis.
Percent change = mean of the differences/reference (baseline)*100

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Table 14.2.5.4.2.2 Statistical Comparison of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1
by Study Product Group (ITT Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	Percent Change (%)	95%		p-Value
		Test Week	(n)	Baseline	(n)			Confidence Intervals		
Week 2	VLN Non-Mentholated	8.160	(48)	7.061	(47)	1.214	17.2	0.356 ,	2.072	0.0065
	VLN Mentholated	6.734	(43)	6.914	(43)	-0.180	-2.6	-1.167 ,	0.806	0.7139
	VLN Combined	7.486	(91)	6.991	(90)	0.548	7.8	-0.106 ,	1.202	0.0996
	UB Non-Mentholated	7.561	(21)	7.906	(21)	-0.345	-4.4	-0.891 ,	0.201	0.2024
	UB Mentholated	7.731	(20)	8.239	(20)	-0.508	-6.2	-1.777 ,	0.760	0.4121
	UB Combined	7.644	(41)	8.068	(41)	-0.425	-5.3	-1.073 ,	0.223	0.1929
Week 6	VLN Non-Mentholated	7.282	(42)	7.485	(41)	-0.096	-1.3	-0.932 ,	0.739	0.8170
	VLN Mentholated	5.589	(41)	7.006	(41)	-1.417	-20.2	-2.316 ,	-0.518	0.0028
	VLN Combined	6.446	(83)	7.245	(82)	-0.757	-10.4	-1.374 ,	-0.139	0.0170
	UB Non-Mentholated	7.261	(17)	7.812	(17)	-0.551	-7.1	-1.275 ,	0.174	0.1267
	UB Mentholated	6.845	(19)	7.070	(19)	-0.224	-3.2	-1.179 ,	0.730	0.6276
	UB Combined	7.042	(36)	7.420	(36)	-0.378	-5.1	-0.960 ,	0.203	0.1950

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Paired t-test method is used to perform the analysis.
Percent change = mean of the differences/reference (baseline)*100

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Table 14.2.5.4.3.1 Statistical Comparison of Absolute Change from Baseline in Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour)
 Among Study Product Groups at Weeks 2 and 6 (PP Population)

Study Week	Comparison	----- LSMeans -----				LSMean Difference (Test - Reference)	95%		p-value
		Test	(n)	Reference	(n)		Confidence Intervals		
Week 2	VLN Non-mentholated vs UB Non-mentholated	2.368	(11)	-0.388	(20)	2.756	1.121	, 4.391	0.0013
	VLN Mentholated vs UB Mentholated	-0.044	(12)	-0.508	(20)	0.464	-1.126	, 2.054	0.5614
	VLN Combined vs UB Combined	1.162	(23)	-0.448	(40)	1.610	0.470	, 2.750	0.0064
Week 6	VLN Non-mentholated vs UB Non-mentholated	0.762	(10)	-0.481	(16)	1.244	-0.670	, 3.157	0.1976
	VLN Mentholated vs UB Mentholated	-1.679	(9)	-0.528	(19)	-1.150	-3.052	, 0.752	0.2302
	VLN Combined vs UB Combined	-0.458	(19)	-0.505	(35)	0.047	-1.302	, 1.396	0.9448

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN Non-Mentholated = Non-mentholated VLN cigarettes
 VLN Mentholated = Mentholated VLN cigarettes
 UB Non-Mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB Mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.5.4.3.2 Statistical Comparison of Absolute Change from Baseline in Urinary S-PMA Mass Excreted (µg/24 hour)
 Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Study Week	Comparison	----- LSMeans -----		LSMean Difference		95%		p-value
		Test	(n)	Reference	(n)	(Test - Reference)	Confidence Intervals	
Week 2	VLN Non-mentholated vs UB Non-mentholated	1.191	(47)	-0.388	(20)	1.579	0.101 , 3.056	0.0365
	VLN Mentholated vs UB Mentholated	-0.152	(43)	-0.508	(20)	0.356	-1.140 , 1.853	0.6386
	VLN Combined vs UB Combined	0.519	(90)	-0.448	(40)	0.967	-0.084 , 2.019	0.0711
Week 6	VLN Non-mentholated vs UB Non-mentholated	-0.137	(41)	-0.504	(16)	0.367	-1.052 , 1.787	0.6093
	VLN Mentholated vs UB Mentholated	-1.430	(41)	-0.438	(19)	-0.992	-2.352 , 0.367	0.1509
	VLN Combined vs UB Combined	-0.783	(82)	-0.471	(35)	-0.312	-1.295 , 0.670	0.5302

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN Non-Mentholated = Non-mentholated VLN cigarettes
 VLN Mentholated = Mentholated VLN cigarettes
 UB Non-Mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB Mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.5.1.1.1
 Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	49	50	99	21	20	41
	Mean	334.920	315.203	324.962	314.736	316.566	315.629
	SD	167.7463	160.6678	163.6689	90.9545	140.5579	116.2823
	CV%	50.1	51.0	50.4	28.9	44.4	36.8
	SEM	23.9638	22.7219	16.4493	19.8479	31.4297	18.1602
	Minimum	68.92	95.12	68.92	138.40	105.73	105.73
	Median	316.500	278.580	299.268	327.084	289.998	321.966
	Maximum	945.36	799.00	945.36	462.90	658.19	658.19
Week 2	n	48	43	91	21	20	41
	Mean	262.756	214.010	239.722	289.071	263.305	276.502
	SD	157.8692	117.0220	141.4377	97.7694	101.9363	99.4242
	CV%	60.1	54.7	59.0	33.8	38.7	36.0
	SEM	22.7865	17.8457	14.8267	21.3350	22.7936	15.5275
	Minimum	69.28	47.30	47.30	117.50	67.67	67.67
	Median	214.503	182.628	203.089	304.835	276.171	290.676
	Maximum	905.98	563.60	905.98	426.53	456.96	456.96
Week 6	n	42	41	83	17	19	36
	Mean	278.998	203.396	241.652	299.312	274.171	286.043
	SD	178.6065	122.0693	157.0509	118.7805	128.5495	122.9241
	CV%	64.0	60.0	65.0	39.7	46.9	43.0
	SEM	27.5596	19.0640	17.2386	28.8085	29.4913	20.4874
	Minimum	81.41	27.12	27.12	128.64	83.49	83.49
	Median	242.741	176.098	221.200	283.222	278.731	280.977
	Maximum	1077.05	593.40	1077.05	544.03	488.27	544.03

* Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.5.1.1.2
 Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	12	17	29	21	20	41
	Mean	358.464	335.771	345.161	314.736	316.566	315.629
	SD	148.2581	173.6450	161.2284	90.9545	140.5579	116.2823
	CV%	41.4	51.7	46.7	28.9	44.4	36.8
	SEM	42.7984	42.1151	29.9394	19.8479	31.4297	18.1602
	Minimum	105.03	95.32	95.32	138.40	105.73	105.73
	Median	356.840	270.603	322.973	327.084	289.998	321.966
	Maximum	652.03	799.00	799.00	462.90	658.19	658.19
Week 2	n	11	12	23	21	20	41
	Mean	241.056	223.757	232.030	289.071	263.305	276.502
	SD	91.3472	142.4304	118.3814	97.7694	101.9363	99.4242
	CV%	37.9	63.7	51.0	33.8	38.7	36.0
	SEM	27.5422	41.1161	24.6842	21.3350	22.7936	15.5275
	Minimum	69.28	53.34	53.34	117.50	67.67	67.67
	Median	230.748	174.349	212.386	304.835	276.171	290.676
	Maximum	395.08	563.60	563.60	426.53	456.96	456.96
Week 6	n	10	9	19	17	19	36
	Mean	228.439	174.502	202.890	299.312	274.171	286.043
	SD	76.7789	99.5309	90.0885	118.7805	128.5495	122.9241
	CV%	33.6	57.0	44.4	39.7	46.9	43.0
	SEM	24.2796	33.1770	20.6677	28.8085	29.4913	20.4874
	Minimum	85.19	59.34	59.34	128.64	83.49	83.49
	Median	228.360	156.497	182.135	283.222	278.731	280.977
	Maximum	338.39	397.09	397.09	544.03	488.27	544.03

* Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.5.1.2.1
 Summary of Urinary 1-OHP Mass Excreted Change from Baseline (ng/24 hour) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-67.868	-89.464	-78.186	-21.210	-53.261	-37.235
	SD	65.4207	93.6086	80.4045	56.9387	98.2858	80.9262
	CV%	-96.4	-104.6	-102.8	-268.5	-184.5	-217.3
	SEM	9.5426	14.2752	8.4754	12.7319	21.9774	12.7956
	Minimum	-238.14	-471.51	-471.51	-124.58	-382.04	-382.04
	Median	-75.009	-83.408	-75.723	-17.227	-28.590	-20.531
	Maximum	73.13	142.49	142.49	89.30	54.28	89.30
Week 6	n	41	41	82	16	19	35
	Mean	-63.342	-100.026	-81.684	-4.092	-35.124	-20.938
	SD	82.1715	106.1919	96.1443	83.5468	91.4078	88.0278
	CV%	-129.7	-106.2	-117.7	-2041.7	-260.2	-420.4
	SEM	12.8330	16.5844	10.6174	20.8867	20.9704	14.8794
	Minimum	-271.48	-475.34	-475.34	-124.36	-333.69	-333.69
	Median	-43.863	-73.842	-60.460	-9.355	-31.242	-22.242
	Maximum	131.68	179.60	179.60	119.51	121.31	121.31

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.5.5.1.2.2
Summary of Urinary 1-OHP Mass Excreted Change from Baseline (ng/24 hour) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-90.721	-76.617	-83.362	-21.210	-53.261	-37.235
	SD	44.7283	86.0051	68.2620	56.9387	98.2858	80.9262
	CV%	-49.3	-112.3	-81.9	-268.5	-184.5	-217.3
	SEM	13.4861	24.8275	14.2336	12.7319	21.9774	12.7956
	Minimum	-167.71	-181.02	-181.02	-124.58	-382.04	-382.04
	Median	-92.590	-93.896	-92.590	-17.227	-28.590	-20.531
	Maximum	-17.14	142.49	142.49	89.30	54.28	89.30
Week 6	n	10	9	19	16	19	35
	Mean	-99.551	-109.881	-104.444	-4.092	-35.124	-20.938
	SD	65.8860	58.7150	61.0800	83.5468	91.4078	88.0278
	CV%	-66.2	-53.4	-58.5	-2041.7	-260.2	-420.4
	SEM	20.8350	19.5717	14.0127	20.8867	20.9704	14.8794
	Minimum	-181.55	-226.70	-226.70	-124.36	-333.69	-333.69
	Median	-109.927	-105.334	-106.048	-9.355	-31.242	-22.242
	Maximum	6.84	-35.98	6.84	119.51	121.31	121.31

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

Table 14.2.5.5.1.3.1
Summary of Urinary 1-OHP Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-20.551	-27.325	-23.787	-6.582	-13.341	-9.961
	SD	19.6844	23.3774	21.6736	17.9894	22.5003	20.3965
	CV%	-95.8	-85.6	-91.1	-273.3	-168.7	-204.8
	SEM	2.8713	3.5650	2.2846	4.0226	5.0312	3.2250
	Minimum	-67.48	-83.04	-83.04	-48.93	-61.52	-61.52
	Median	-23.397	-28.988	-26.247	-6.056	-12.116	-9.314
	Maximum	25.62	48.81	48.81	29.25	18.50	29.25
Week 6	n	41	41	82	16	19	35
	Mean	-17.824	-32.497	-25.161	-0.367	-10.325	-5.773
	SD	22.8771	24.1825	24.5302	25.7354	22.2304	24.0657
	CV%	-128.4	-74.4	-97.5	-7014.7	-215.3	-416.9
	SEM	3.5728	3.7767	2.7089	6.4338	5.1000	4.0678
	Minimum	-76.93	-87.86	-87.86	-38.47	-55.69	-55.69
	Median	-19.350	-35.019	-24.594	-6.527	-13.536	-12.923
	Maximum	60.62	43.40	60.62	47.23	38.88	47.23

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

Table 14.2.5.5.1.3.2
Summary of Urinary 1-OHP Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-27.029	-27.956	-27.513	-6.582	-13.341	-9.961
	SD	9.1178	24.6686	18.5008	17.9894	22.5003	20.3965
	CV%	-33.7	-88.2	-67.2	-273.3	-168.7	-204.8
	SEM	2.7491	7.1212	3.8577	4.0226	5.0312	3.2250
	Minimum	-38.64	-64.96	-64.96	-48.93	-61.52	-61.52
	Median	-28.234	-33.893	-28.327	-6.056	-12.116	-9.314
	Maximum	-9.23	33.84	33.84	29.25	18.50	29.25
Week 6	n	10	9	19	16	19	35
	Mean	-27.608	-39.174	-33.087	-0.367	-10.325	-5.773
	SD	13.6531	10.2667	13.2383	25.7354	22.2304	24.0657
	CV%	-49.5	-26.2	-40.0	-7014.7	-215.3	-416.9
	SEM	4.3175	3.4222	3.0371	6.4338	5.1000	4.0678
	Minimum	-43.89	-56.28	-56.28	-38.47	-55.69	-55.69
	Median	-32.338	-38.955	-37.744	-6.527	-13.536	-12.923
	Maximum	2.87	-21.10	2.87	47.23	38.88	47.23

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.5.1.4.1 Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level (ng/g creatinine)
 by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	49	50	99	21	20	41
	Mean	229.539	192.704	210.935	183.698	198.656	190.995
	SD	126.1058	118.7445	123.2145	56.1734	97.7570	78.5769
	CV%	54.9	61.6	58.4	30.6	49.2	41.1
	SEM	18.0151	16.7930	12.3835	12.2580	21.8591	12.2717
	Minimum	38.65	43.11	38.65	100.87	38.30	38.30
	Median	193.509	156.596	177.054	180.392	204.457	188.489
	Maximum	542.00	514.62	542.00	305.04	455.98	455.98
Week 2	n	48	43	91	21	20	41
	Mean	173.707	129.457	152.798	171.961	174.383	173.142
	SD	101.8388	76.3470	92.8958	61.0888	77.5822	68.7491
	CV%	58.6	59.0	60.8	35.5	44.5	39.7
	SEM	14.6992	11.6428	9.7381	13.3307	17.3479	10.7368
	Minimum	37.48	25.82	25.82	88.92	37.77	37.77
	Median	146.095	113.043	125.877	168.868	184.757	173.239
	Maximum	538.65	394.16	538.65	354.13	305.00	354.13
Week 6	n	42	41	83	17	19	36
	Mean	183.830	128.413	156.455	168.544	169.719	169.164
	SD	114.1749	85.6779	104.2871	46.5390	81.4381	66.3423
	CV%	62.1	66.7	66.7	27.6	48.0	39.2
	SEM	17.6176	13.3806	11.4470	11.2874	18.6832	11.0570
	Minimum	49.80	27.25	27.25	107.77	30.68	30.68
	Median	163.640	117.323	130.435	165.105	187.395	167.424
	Maximum	581.40	493.98	581.40	276.43	277.78	277.78

* Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.5.1.4.2 Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level (ng/g creatinine)
by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	12	17	29	21	20	41
	Mean	232.857	204.788	216.403	183.698	198.656	190.995
	SD	123.7762	119.0055	119.6221	56.1734	97.7570	78.5769
	CV%	53.2	58.1	55.3	30.6	49.2	41.1
	SEM	35.7311	28.8631	22.2133	12.2580	21.8591	12.2717
	Minimum	130.19	43.11	43.11	100.87	38.30	38.30
	Median	192.030	175.497	190.551	180.392	204.457	188.489
	Maximum	542.00	419.64	542.00	305.04	455.98	455.98
Week 2	n	11	12	23	21	20	41
	Mean	150.530	129.467	139.540	171.961	174.383	173.142
	SD	65.5278	96.5928	82.0524	61.0888	77.5822	68.7491
	CV%	43.5	74.6	58.8	35.5	44.5	39.7
	SEM	19.7574	27.8839	17.1091	13.3307	17.3479	10.7368
	Minimum	91.13	25.82	25.82	88.92	37.77	37.77
	Median	147.482	108.383	118.456	168.868	184.757	173.239
	Maximum	301.72	394.16	394.16	354.13	305.00	354.13
Week 6	n	10	9	19	17	19	36
	Mean	146.510	94.895	122.060	168.544	169.719	169.164
	SD	53.9592	55.5458	59.3982	46.5390	81.4381	66.3423
	CV%	36.8	58.5	48.7	27.6	48.0	39.2
	SEM	17.0634	18.5153	13.6269	11.2874	18.6832	11.0570
	Minimum	89.44	27.25	27.25	107.77	30.68	30.68
	Median	134.890	84.187	114.796	165.105	187.395	167.424
	Maximum	258.80	177.74	258.80	276.43	277.78	277.78

* Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.5.1.5.1 Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level Change from Baseline (ng/g creatinine)
by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-52.058	-48.757	-50.481	-11.903	-24.273	-18.088
	SD	53.6475	53.6464	53.3705	40.7575	64.8683	53.8380
	CV%	-103.1	-110.0	-105.7	-342.4	-267.2	-297.6
	SEM	7.8253	8.1810	5.6257	9.1137	14.5050	8.5125
	Minimum	-246.06	-222.92	-246.06	-113.22	-266.82	-266.82
	Median	-47.072	-37.905	-42.847	-11.595	-12.642	-11.861
	Maximum	29.74	46.20	46.20	53.38	43.95	53.38
Week 6	n	41	41	82	16	19	35
	Mean	-50.237	-53.772	-52.005	-11.749	-26.864	-19.955
	SD	72.5426	63.2914	67.6762	44.7829	71.5676	60.4546
	CV%	-144.4	-117.7	-130.1	-381.2	-266.4	-303.0
	SEM	11.3293	9.8845	7.4736	11.1957	16.4187	10.2187
	Minimum	-262.07	-279.27	-279.27	-100.69	-257.78	-257.78
	Median	-42.796	-37.948	-40.799	-1.786	-16.938	-8.087
	Maximum	195.66	73.82	195.66	68.79	89.29	89.29

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.5.1.5.2 Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level Change from Baseline (ng/g creatinine)
 by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-54.222	-43.623	-48.693	-11.903	-24.273	-18.088
	SD	21.3238	49.8597	38.4575	40.7575	64.8683	53.8380
	CV%	-39.3	-114.3	-79.0	-342.4	-267.2	-297.6
	SEM	6.4294	14.3932	8.0190	9.1137	14.5050	8.5125
	Minimum	-88.66	-167.93	-167.93	-113.22	-266.82	-266.82
	Median	-51.483	-43.442	-47.072	-11.595	-12.642	-11.861
	Maximum	-17.99	46.20	46.20	53.38	43.95	53.38
Week 6	n	10	9	19	16	19	35
	Mean	-65.699	-59.738	-62.875	-11.749	-26.864	-19.955
	SD	41.2522	46.3530	42.6047	44.7829	71.5676	60.4546
	CV%	-62.8	-77.6	-67.8	-381.2	-266.4	-303.0
	SEM	13.0451	15.4510	9.7742	11.1957	16.4187	10.2187
	Minimum	-131.58	-170.22	-170.22	-100.69	-257.78	-257.78
	Median	-61.231	-46.081	-58.581	-1.786	-16.938	-8.087
	Maximum	-0.10	-15.86	-0.10	68.79	89.29	89.29

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.5.1.6.1 Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level Percent Change from Baseline (%)
by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-21.949	-23.945	-22.903	-5.494	-8.906	-7.200
	SD	18.1253	20.7556	19.3417	19.2423	19.5862	19.2422
	CV%	-82.6	-86.7	-84.5	-350.3	-219.9	-267.3
	SEM	2.6439	3.1652	2.0388	4.3027	4.3796	3.0425
	Minimum	-67.35	-58.59	-67.35	-50.51	-58.52	-58.52
	Median	-24.581	-29.783	-25.092	-6.140	-6.659	-6.140
	Maximum	19.70	64.56	64.56	35.26	21.21	35.26
Week 6	n	41	41	82	16	19	35
	Mean	-20.003	-27.934	-23.969	-3.014	-10.557	-7.109
	SD	22.3703	18.2452	20.6745	22.8943	26.4970	24.8490
	CV%	-111.8	-65.3	-86.3	-759.5	-251.0	-349.6
	SEM	3.4937	2.8494	2.2831	5.7236	6.0788	4.2002
	Minimum	-61.29	-61.74	-61.74	-44.92	-56.53	-56.53
	Median	-23.872	-32.769	-25.039	-1.853	-18.183	-7.077
	Maximum	50.73	17.57	50.73	45.45	47.37	47.37

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.5.1.6.2 Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level Percent Change from Baseline (%)
 by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-27.139	-27.615	-27.388	-5.494	-8.906	-7.200
	SD	7.9231	18.9347	14.4172	19.2423	19.5862	19.2422
	CV%	-29.2	-68.6	-52.6	-350.3	-219.9	-267.3
	SEM	2.3889	5.4660	3.0062	4.3027	4.3796	3.0425
	Minimum	-38.79	-58.59	-58.59	-50.51	-58.52	-58.52
	Median	-25.237	-28.993	-26.229	-6.140	-6.659	-6.140
	Maximum	-10.35	13.28	13.28	35.26	21.21	35.26
Week 6	n	10	9	19	16	19	35
	Mean	-29.866	-38.518	-33.965	-3.014	-10.557	-7.109
	SD	13.6490	12.0316	13.3111	22.8943	26.4970	24.8490
	CV%	-45.7	-31.2	-39.2	-759.5	-251.0	-349.6
	SEM	4.3162	4.0105	3.0538	5.7236	6.0788	4.2002
	Minimum	-50.49	-52.38	-52.38	-44.92	-56.53	-56.53
	Median	-30.786	-40.848	-36.792	-1.853	-18.183	-7.077
	Maximum	-0.05	-16.12	-0.05	45.45	47.37	47.37

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.5.2.1 Statistical Comparison of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1
 by Study Product Group (PP Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	Percent Change (%)	95%		p-Value
		Test Week	(n)	Baseline	(n)			Confidence Intervals		
Week 2	VLN Non-Mentholated	241.056	(11)	331.777	(11)	-90.721	-27.3	-120.769 ,	-60.672	<.0001
	VLN Mentholated	223.757	(12)	300.374	(12)	-76.617	-25.5	-131.262 ,	-21.972	0.0104
	VLN Combined	232.030	(23)	315.393	(23)	-83.362	-26.4	-112.881 ,	-53.844	<.0001
	UB Non-Mentholated	289.071	(21)	309.586	(21)	-20.515	-6.6	-45.818 ,	4.789	0.1063
	UB Mentholated	263.305	(20)	316.566	(20)	-53.261	-16.8	-99.260 ,	-7.262	0.0255
	UB Combined	276.502	(41)	312.991	(41)	-36.489	-11.7	-61.756 ,	-11.221	0.0057
Week 6	VLN Non-Mentholated	228.439	(10)	327.990	(10)	-99.551	-30.4	-146.683 ,	-52.419	0.0010
	VLN Mentholated	174.502	(9)	284.383	(9)	-109.881	-38.6	-155.014 ,	-64.749	0.0005
	VLN Combined	202.890	(19)	307.334	(19)	-104.444	-34.0	-133.884 ,	-75.005	<.0001
	UB Non-Mentholated	299.312	(17)	304.642	(17)	-5.330	-1.7	-47.004 ,	36.345	0.7898
	UB Mentholated	274.171	(19)	309.295	(19)	-35.124	-11.4	-79.181 ,	8.933	0.1112
	UB Combined	286.043	(36)	307.098	(36)	-21.055	-6.9	-50.411 ,	8.302	0.1543

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 Paired t-test method is used to perform the analysis.
 Percent change = mean of the differences/reference (baseline)*100

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Table 14.2.5.5.2.2 Statistical Comparison of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1
 by Study Product Group (ITT Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	Percent Change (%)	95%		p-Value
		Test Week	(n)	Baseline	(n)			Confidence Intervals		
Week 2	VLN Non-Mentholated	262.756	(48)	329.528	(47)	-67.868	-20.6	-87.076 ,	-48.660	<.0001
	VLN Mentholated	214.010	(43)	303.474	(43)	-89.464	-29.5	-118.273 ,	-60.656	<.0001
	VLN Combined	239.722	(91)	317.080	(90)	-78.186	-24.7	-95.027 ,	-61.346	<.0001
	UB Non-Mentholated	289.071	(21)	309.586	(21)	-20.515	-6.6	-45.818 ,	4.789	0.1063
	UB Mentholated	263.305	(20)	316.566	(20)	-53.261	-16.8	-99.260 ,	-7.262	0.0255
	UB Combined	276.502	(41)	312.991	(41)	-36.489	-11.7	-61.756 ,	-11.221	0.0057
Week 6	VLN Non-Mentholated	278.998	(42)	340.295	(41)	-63.342	-18.6	-89.278 ,	-37.405	<.0001
	VLN Mentholated	203.396	(41)	303.422	(41)	-100.026	-33.0	-133.544 ,	-66.508	<.0001
	VLN Combined	241.652	(83)	321.859	(82)	-81.684	-25.4	-102.809 ,	-60.559	<.0001
	UB Non-Mentholated	299.312	(17)	304.642	(17)	-5.330	-1.7	-47.004 ,	36.345	0.7898
	UB Mentholated	274.171	(19)	309.295	(19)	-35.124	-11.4	-79.181 ,	8.933	0.1112
	UB Combined	286.043	(36)	307.098	(36)	-21.055	-6.9	-50.411 ,	8.302	0.1543

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 Paired t-test method is used to perform the analysis.
 Percent change = mean of the differences/reference (baseline)*100

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Table 14.2.5.5.3.1 Statistical Comparison of Absolute Change from Baseline in Urinary 1-OHP Mass Excreted (ng/24 hour)
 Among Study Product Groups at Weeks 2 and 6 (PP Population)

Study Week	Comparison	----- LSMeans -----		LSMean Difference		95%		p-value
		Test	(n)	Reference	(n)	(Test - Reference)	Confidence Intervals	
Week 2	VLN Non-mentholated vs UB Non-mentholated	-90.721	(11)	-21.210	(20)	-69.511	-127.074 , -11.948	0.0188
	VLN Mentholated vs UB Mentholated	-76.617	(12)	-53.261	(20)	-23.356	-79.351 , 32.638	0.4073
	VLN Combined vs UB Combined	-83.669	(23)	-37.235	(40)	-46.434	-86.586 , -6.281	0.0242
Week 6	VLN Non-mentholated vs UB Non-mentholated	-99.457	(10)	3.593	(16)	-103.050	-165.311 , -40.790	0.0016
	VLN Mentholated vs UB Mentholated	-121.458	(9)	-39.311	(19)	-82.147	-143.795 , -20.499	0.0099
	VLN Combined vs UB Combined	-110.458	(19)	-17.859	(35)	-92.599	-136.407 , -48.790	<.0001

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN Non-Mentholated = Non-mentholated VLN cigarettes
 VLN Mentholated = Mentholated VLN cigarettes
 UB Non-Mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB Mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.5.5.3.2 Statistical Comparison of Absolute Change from Baseline in Urinary 1-OHP Mass Excreted (ng/24 hour)
 Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Study Week	Comparison	----- LSMeans -----		LSMean Difference		95%		p-value
		Test	(n)	Reference	(n)	(Test - Reference)	Confidence Intervals	
Week 2	VLN Non-mentholated vs UB Non-mentholated	-67.615	(47)	-21.210	(20)	-46.405	-89.169 , -3.641	0.0337
	VLN Mentholated vs UB Mentholated	-85.626	(43)	-53.261	(20)	-32.365	-75.653 , 10.924	0.1415
	VLN Combined vs UB Combined	-76.620	(90)	-37.235	(40)	-39.385	-69.810 , -8.960	0.0116
Week 6	VLN Non-mentholated vs UB Non-mentholated	-62.261	(41)	3.404	(16)	-65.665	-117.324 , -14.006	0.0131
	VLN Mentholated vs UB Mentholated	-101.660	(41)	-39.208	(19)	-62.452	-112.295 , -12.609	0.0145
	VLN Combined vs UB Combined	-81.961	(82)	-17.902	(35)	-64.058	-99.950 , -28.167	0.0006

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN Non-Mentholated = Non-mentholated VLN cigarettes
 VLN Mentholated = Mentholated VLN cigarettes
 UB Non-Mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB Mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.6.1.1.1
Summary of Urinary Theq Mass Excreted (mg/24 hour) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	49	50	99	21	20	41
	Mean	17.511	15.885	16.690	17.732	15.928	16.852
	SD	6.1103	5.3291	5.7580	6.3013	5.9611	6.1291
	CV%	34.9	33.5	34.5	35.5	37.4	36.4
	SEM	0.8729	0.7537	0.5787	1.3751	1.3329	0.9572
	Minimum	8.35	6.01	6.01	4.71	8.32	4.71
	Median	17.043	15.506	16.082	17.895	15.269	16.424
	Maximum	40.37	27.81	40.37	28.91	27.34	28.91
Week 2	n	48	43	91	21	20	41
	Mean	5.404	3.616	4.559	16.962	15.279	16.141
	SD	4.5528	3.5530	4.1858	6.2675	4.7106	5.5594
	CV%	84.3	98.2	91.8	36.9	30.8	34.4
	SEM	0.6571	0.5418	0.4388	1.3677	1.0533	0.8682
	Minimum	0.25	0.33	0.25	4.08	8.13	4.08
	Median	4.785	1.861	3.485	17.624	14.825	15.589
	Maximum	20.56	12.56	20.56	27.78	23.49	27.78
Week 6	n	42	41	83	17	19	36
	Mean	9.150	6.800	7.989	17.530	14.418	15.888
	SD	6.1240	5.2118	5.7792	7.3994	5.5176	6.5703
	CV%	66.9	76.6	72.3	42.2	38.3	41.4
	SEM	0.9450	0.8140	0.6343	1.7946	1.2658	1.0950
	Minimum	0.39	0.23	0.23	5.37	6.34	5.37
	Median	9.148	5.789	7.652	16.809	13.972	14.352
	Maximum	23.15	18.61	23.15	30.65	26.46	30.65

* Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.6.1.1.2
Summary of Urinary Theq Mass Excreted (mg/24 hour) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	12	17	29	21	20	41
	Mean	17.097	15.553	16.192	17.732	15.928	16.852
	SD	6.9722	5.6625	6.1659	6.3013	5.9611	6.1291
	CV%	40.8	36.4	38.1	35.5	37.4	36.4
	SEM	2.0127	1.3734	1.1450	1.3751	1.3329	0.9572
	Minimum	8.41	8.13	8.13	4.71	8.32	4.71
	Median	17.009	15.942	15.942	17.895	15.269	16.424
	Maximum	27.57	27.81	27.81	28.91	27.34	28.91
Week 2	n	11	12	23	21	20	41
	Mean	1.137	1.032	1.082	16.962	15.279	16.141
	SD	0.6372	0.5201	0.5680	6.2675	4.7106	5.5594
	CV%	56.0	50.4	52.5	36.9	30.8	34.4
	SEM	0.1921	0.1501	0.1184	1.3677	1.0533	0.8682
	Minimum	0.25	0.33	0.25	4.08	8.13	4.08
	Median	0.979	0.933	0.979	17.624	14.825	15.589
	Maximum	2.34	2.03	2.34	27.78	23.49	27.78
Week 6	n	10	9	19	17	19	36
	Mean	0.979	1.327	1.144	17.530	14.418	15.888
	SD	0.6589	1.1657	0.9235	7.3994	5.5176	6.5703
	CV%	67.3	87.8	80.7	42.2	38.3	41.4
	SEM	0.2084	0.3886	0.2119	1.7946	1.2658	1.0950
	Minimum	0.39	0.23	0.23	5.37	6.34	5.37
	Median	0.845	1.144	0.952	16.809	13.972	14.352
	Maximum	2.53	3.96	3.96	30.65	26.46	30.65

* Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.5.6.1.2.1
Summary of Urinary Theq Mass Excreted Change from Baseline (mg/24 hour) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-11.812	-12.404	-12.095	-0.609	-0.649	-0.629
	SD	6.0548	5.1803	5.6304	2.3450	3.7494	3.0868
	CV%	-51.3	-41.8	-46.6	-385.0	-578.1	-490.8
	SEM	0.8832	0.7900	0.5935	0.5244	0.8384	0.4881
	Minimum	-25.61	-27.06	-27.06	-6.03	-8.59	-8.59
	Median	-10.259	-12.098	-10.913	-0.733	-0.165	-0.468
	Maximum	-1.80	-3.30	-1.80	3.47	4.60	4.60
Week 6	n	41	41	82	16	19	35
	Mean	-8.394	-9.337	-8.866	0.290	-0.909	-0.361
	SD	6.5925	5.8568	6.2150	3.3581	3.7664	3.5850
	CV%	-78.5	-62.7	-70.1	1156.4	-414.5	-994.4
	SEM	1.0296	0.9147	0.6863	0.8395	0.8641	0.6060
	Minimum	-25.86	-27.26	-27.26	-6.01	-9.42	-9.42
	Median	-7.137	-8.855	-8.672	0.024	-0.515	-0.370
	Maximum	1.29	4.72	4.72	7.78	8.14	8.14

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

Table 14.2.5.6.1.2.2
 Summary of Urinary Theq Mass Excreted Change from Baseline (mg/24 hour) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-15.008	-14.568	-14.778	-0.609	-0.649	-0.629
	SD	6.3466	6.3774	6.2205	2.3450	3.7494	3.0868
	CV%	-42.3	-43.8	-42.1	-385.0	-578.1	-490.8
	SEM	1.9136	1.8410	1.2971	0.5244	0.8384	0.4881
	Minimum	-25.61	-27.06	-27.06	-6.03	-8.59	-8.59
	Median	-13.727	-14.945	-14.431	-0.733	-0.165	-0.468
	Maximum	-6.39	-6.93	-6.39	3.47	4.60	4.60
Week 6	n	10	9	19	16	19	35
	Mean	-14.484	-15.479	-14.955	0.290	-0.909	-0.361
	SD	6.1794	6.3990	6.1280	3.3581	3.7664	3.5850
	CV%	-42.7	-41.3	-41.0	1156.4	-414.5	-994.4
	SEM	1.9541	2.1330	1.4058	0.8395	0.8641	0.6060
	Minimum	-25.86	-27.26	-27.26	-6.01	-9.42	-9.42
	Median	-12.681	-16.534	-14.069	0.024	-0.515	-0.370
	Maximum	-7.25	-6.64	-6.64	7.78	8.14	8.14

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.5.6.1.3.1
 Summary of Urinary Theq Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-68.020	-78.154	-72.862	-3.157	0.313	-1.422
	SD	24.2398	17.9713	21.9547	12.8808	23.2558	18.6386
	CV%	-35.6	-23.0	-30.1	-408.1	7427.9	-1311.0
	SEM	3.5357	2.7406	2.3142	2.8802	5.2001	2.9470
	Minimum	-97.43	-97.30	-97.43	-25.27	-35.53	-35.53
	Median	-71.521	-85.229	-76.278	-3.833	-1.236	-2.753
	Maximum	-12.26	-38.42	-12.26	23.05	48.65	48.65
Week 6	n	41	41	82	16	19	35
	Mean	-47.335	-57.683	-52.509	1.533	-3.383	-1.135
	SD	33.0500	29.9744	31.7835	16.4885	29.2366	24.0551
	CV%	-69.8	-52.0	-60.5	1075.3	-864.2	-2118.5
	SEM	5.1616	4.6812	3.5099	4.1221	6.7073	4.0661
	Minimum	-97.23	-98.03	-98.03	-22.82	-42.44	-42.44
	Median	-45.309	-60.411	-49.688	0.138	-2.692	-2.107
	Maximum	7.45	35.97	35.97	36.88	86.04	86.04

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

Table 14.2.5.6.1.3.2
Summary of Urinary Theq Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-92.098	-92.298	-92.203	-3.157	0.313	-1.422
	SD	6.2012	5.1493	5.5451	12.8808	23.2558	18.6386
	CV%	-6.7	-5.6	-6.0	-408.1	7427.9	-1311.0
	SEM	1.8697	1.4865	1.1562	2.8802	5.2001	2.9470
	Minimum	-97.43	-97.30	-97.43	-25.27	-35.53	-35.53
	Median	-95.015	-95.282	-95.121	-3.833	-1.236	-2.753
	Maximum	-75.96	-82.56	-75.96	23.05	48.65	48.65
Week 6	n	10	9	19	16	19	35
	Mean	-93.221	-91.732	-92.516	1.533	-3.383	-1.135
	SD	4.1774	6.2353	5.1564	16.4885	29.2366	24.0551
	CV%	-4.5	-6.8	-5.6	1075.3	-864.2	-2118.5
	SEM	1.3210	2.0784	1.1830	4.1221	6.7073	4.0661
	Minimum	-97.23	-98.03	-98.03	-22.82	-42.44	-42.44
	Median	-94.745	-93.578	-93.659	0.138	-2.692	-2.107
	Maximum	-86.17	-81.68	-81.68	36.88	86.04	86.04

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.6.1.4.1 Summary of Urinary Theq Creatinine-Normalized Excretion Level (mg/g creatinine)
 by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	49	50	99	21	20	41
	Mean	12.035	9.466	10.738	9.961	9.930	9.946
	SD	5.1747	3.8360	4.7053	2.3422	4.1561	3.3088
	CV%	43.0	40.5	43.8	23.5	41.9	33.3
	SEM	0.7392	0.5425	0.4729	0.5111	0.9293	0.5167
	Minimum	3.87	3.48	3.48	4.00	3.25	3.25
	Median	11.614	9.211	9.866	9.788	9.967	9.821
	Maximum	24.32	20.40	24.32	14.51	17.53	17.53
Week 2	n	48	43	91	21	20	41
	Mean	3.540	2.201	2.907	9.848	10.050	9.946
	SD	3.0081	2.1939	2.7246	2.9474	3.9386	3.4238
	CV%	85.0	99.7	93.7	29.9	39.2	34.4
	SEM	0.4342	0.3346	0.2856	0.6432	0.8807	0.5347
	Minimum	0.23	0.16	0.16	3.32	4.55	3.32
	Median	2.874	1.165	1.981	9.435	9.944	9.872
	Maximum	12.22	8.78	12.22	15.37	18.28	18.28
Week 6	n	42	41	83	17	19	36
	Mean	5.932	4.307	5.130	9.710	8.932	9.299
	SD	3.8264	3.0134	3.5240	2.5729	4.1685	3.4811
	CV%	64.5	70.0	68.7	26.5	46.7	37.4
	SEM	0.5904	0.4706	0.3868	0.6240	0.9563	0.5802
	Minimum	0.18	0.10	0.10	4.57	2.97	2.97
	Median	6.465	3.850	5.517	9.526	8.155	8.416
	Maximum	13.84	12.53	13.84	14.35	17.86	17.86

* Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.6.1.4.2 Summary of Urinary Theq Creatinine-Normalized Excretion Level (mg/g creatinine)
by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	12	17	29	21	20	41
	Mean	11.278	9.370	10.159	9.961	9.930	9.946
	SD	5.4429	4.4892	4.9060	2.3422	4.1561	3.3088
	CV%	48.3	47.9	48.3	23.5	41.9	33.3
	SEM	1.5712	1.0888	0.9110	0.5111	0.9293	0.5167
	Minimum	5.09	3.48	3.48	4.00	3.25	3.25
	Median	9.969	9.069	9.127	9.788	9.967	9.821
	Maximum	22.92	20.40	22.92	14.51	17.53	17.53
Week 2	n	11	12	23	21	20	41
	Mean	0.724	0.631	0.675	9.848	10.050	9.946
	SD	0.4754	0.4097	0.4346	2.9474	3.9386	3.4238
	CV%	65.7	64.9	64.4	29.9	39.2	34.4
	SEM	0.1433	0.1183	0.0906	0.6432	0.8807	0.5347
	Minimum	0.23	0.16	0.16	3.32	4.55	3.32
	Median	0.632	0.522	0.537	9.435	9.944	9.872
	Maximum	1.87	1.42	1.87	15.37	18.28	18.28
Week 6	n	10	9	19	17	19	36
	Mean	0.610	0.782	0.692	9.710	8.932	9.299
	SD	0.3378	0.8260	0.6067	2.5729	4.1685	3.4811
	CV%	55.3	105.6	87.7	26.5	46.7	37.4
	SEM	0.1068	0.2753	0.1392	0.6240	0.9563	0.5802
	Minimum	0.18	0.10	0.10	4.57	2.97	2.97
	Median	0.487	0.708	0.487	9.526	8.155	8.416
	Maximum	1.14	2.80	2.80	14.35	17.86	17.86

* Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.6.1.5.1 Summary of Urinary Theq Creatinine-Normalized Excretion Level Change from Baseline (mg/g creatinine)
 by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-8.269	-7.030	-7.677	-0.131	0.120	-0.006
	SD	4.7922	3.6577	4.3094	1.2509	1.9635	1.6299
	CV%	-58.0	-52.0	-56.1	-952.8	1640.1	-28201.9
	SEM	0.6990	0.5578	0.4542	0.2797	0.4390	0.2577
	Minimum	-20.14	-19.64	-20.14	-1.37	-3.99	-3.99
	Median	-7.656	-6.098	-6.563	-0.528	0.084	-0.323
	Maximum	2.38	-2.45	2.38	3.07	3.53	3.53
Week 6	n	41	41	82	16	19	35
	Mean	-6.087	-5.209	-5.648	-0.138	-0.768	-0.480
	SD	4.5947	3.6520	4.1481	1.5976	2.3058	2.0105
	CV%	-75.5	-70.1	-73.4	-1158.7	-300.4	-419.1
	SEM	0.7176	0.5703	0.4581	0.3994	0.5290	0.3398
	Minimum	-17.35	-17.59	-17.59	-1.99	-4.72	-4.72
	Median	-5.473	-4.206	-4.973	-0.227	-0.716	-0.555
	Maximum	3.29	-0.30	3.29	3.34	3.11	3.34

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.6.1.5.2 Summary of Urinary Theq Creatinine-Normalized Excretion Level Change from Baseline (mg/g creatinine)
by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-9.496	-8.358	-8.902	-0.131	0.120	-0.006
	SD	4.2714	4.8564	4.5191	1.2509	1.9635	1.6299
	CV%	-45.0	-58.1	-50.8	-952.8	1640.1	-28201.9
	SEM	1.2879	1.4019	0.9423	0.2797	0.4390	0.2577
	Minimum	-17.17	-19.64	-19.64	-1.37	-3.99	-3.99
	Median	-8.772	-6.944	-7.645	-0.528	0.084	-0.323
	Maximum	-4.81	-2.97	-2.97	3.07	3.53	3.53
Week 6	n	10	9	19	16	19	35
	Mean	-9.822	-8.643	-9.264	-0.138	-0.768	-0.480
	SD	4.3312	5.0313	4.5822	1.5976	2.3058	2.0105
	CV%	-44.1	-58.2	-49.5	-1158.7	-300.4	-419.1
	SEM	1.3696	1.6771	1.0512	0.3994	0.5290	0.3398
	Minimum	-17.35	-17.59	-17.59	-1.99	-4.72	-4.72
	Median	-9.142	-5.999	-8.862	-0.227	-0.716	-0.555
	Maximum	-4.91	-2.77	-2.77	3.34	3.11	3.34

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.6.1.6.1 Summary of Urinary Theq Creatinine-Normalized Excretion Level Percent Change from Baseline (%)
by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	47	43	90	20	20	40
	Mean	-67.996	-76.719	-72.164	-2.481	5.907	1.713
	SD	27.5895	19.2987	24.2565	11.8574	20.7883	17.2357
	CV%	-40.6	-25.2	-33.6	-478.0	352.0	1006.2
	SEM	4.0243	2.9430	2.5569	2.6514	4.6484	2.7252
	Minimum	-97.26	-97.35	-97.35	-16.96	-23.84	-23.84
	Median	-71.655	-84.105	-77.743	-4.729	1.345	-3.123
	Maximum	41.72	-25.37	41.72	27.85	52.97	52.97
Week 6	n	41	41	82	16	19	35
	Mean	-48.616	-55.035	-51.826	-0.800	-4.160	-2.624
	SD	34.0415	26.4405	30.4619	15.5886	30.2982	24.4148
	CV%	-70.0	-48.0	-58.8	-1947.6	-728.3	-930.3
	SEM	5.3164	4.1293	3.3640	3.8972	6.9509	4.1269
	Minimum	-97.70	-98.30	-98.30	-18.67	-54.20	-54.20
	Median	-47.588	-54.011	-50.954	-2.129	-7.287	-3.996
	Maximum	31.13	-4.56	31.13	30.28	81.36	81.36

Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.6.1.6.2 Summary of Urinary Theq Creatinine-Normalized Excretion Level Percent Change from Baseline (%)
 by Study Product Group and Study Week (PP Population)

Study Week	Statistics	-----Study Product Group-----					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	20	20	40
	Mean	-91.899	-91.908	-91.904	-2.481	5.907	1.713
	SD	6.5192	5.7829	6.0032	11.8574	20.7883	17.2357
	CV%	-7.1	-6.3	-6.5	-478.0	352.0	1006.2
	SEM	1.9656	1.6694	1.2518	2.6514	4.6484	2.7252
	Minimum	-97.26	-97.35	-97.35	-16.96	-23.84	-23.84
	Median	-94.537	-95.226	-95.068	-4.729	1.345	-3.123
	Maximum	-76.26	-80.61	-76.26	27.85	52.97	52.97
Week 6	n	10	9	19	16	19	35
	Mean	-93.608	-91.584	-92.649	-0.800	-4.160	-2.624
	SD	3.5452	6.4718	5.0968	15.5886	30.2982	24.4148
	CV%	-3.8	-7.1	-5.5	-1947.6	-728.3	-930.3
	SEM	1.1211	2.1573	1.1693	3.8972	6.9509	4.1269
	Minimum	-97.70	-98.30	-98.30	-18.67	-54.20	-54.20
	Median	-94.109	-93.180	-93.957	-2.129	-7.287	-3.996
	Maximum	-87.13	-79.64	-79.64	30.28	81.36	81.36

 Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes

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Table 14.2.5.6.2.1 Statistical Comparison of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1
by Study Product Group (PP Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	Percent Change (%)	95%		p-Value
		Test Week	(n)	Baseline	(n)			Confidence Intervals		
Week 2	VLN Non-Mentholated	1.137	(11)	16.144	(11)	-15.008	-93.0	-19.271 ,	-10.744	<.0001
	VLN Mentholated	1.032	(12)	15.600	(12)	-14.568	-93.4	-18.620 ,	-10.516	<.0001
	VLN Combined	1.082	(23)	15.860	(23)	-14.778	-93.2	-17.468 ,	-12.088	<.0001
	UB Non-Mentholated	16.962	(21)	17.500	(21)	-0.537	-3.1	-1.589 ,	0.514	0.2989
	UB Mentholated	15.279	(20)	15.928	(20)	-0.649	-4.1	-2.403 ,	1.106	0.4487
	UB Combined	16.141	(41)	16.733	(41)	-0.592	-3.5	-1.557 ,	0.373	0.2225
Week 6	VLN Non-Mentholated	0.979	(10)	15.463	(10)	-14.484	-93.7	-18.904 ,	-10.063	<.0001
	VLN Mentholated	1.327	(9)	16.806	(9)	-15.479	-92.1	-20.398 ,	-10.560	<.0001
	VLN Combined	1.144	(19)	16.099	(19)	-14.955	-92.9	-17.909 ,	-12.002	<.0001
	UB Non-Mentholated	17.530	(17)	17.178	(17)	0.352	2.0	-1.325 ,	2.028	0.6626
	UB Mentholated	14.418	(19)	15.327	(19)	-0.909	-5.9	-2.724 ,	0.907	0.3069
	UB Combined	15.888	(36)	16.201	(36)	-0.314	-1.9	-1.513 ,	0.886	0.5990

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Paired t-test method is used to perform the analysis.
Percent change = mean of the differences/reference (baseline)*100

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Table 14.2.5.6.2.2 Statistical Comparison of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1
by Study Product Group (ITT Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	Percent Change (%)	95%		
		Test Week	(n)	Baseline	(n)			Confidence Intervals	p-Value	
Week 2	VLN Non-Mentholated	5.404	(48)	17.234	(47)	-11.812	-68.5	-13.589 ,	-10.034	<.0001
	VLN Mentholated	3.616	(43)	16.020	(43)	-12.404	-77.4	-13.998 ,	-10.810	<.0001
	VLN Combined	4.559	(91)	16.654	(90)	-12.095	-72.6	-13.274 ,	-10.915	<.0001
	UB Non-Mentholated	16.962	(21)	17.500	(21)	-0.537	-3.1	-1.589 ,	0.514	0.2989
	UB Mentholated	15.279	(20)	15.928	(20)	-0.649	-4.1	-2.403 ,	1.106	0.4487
	UB Combined	16.141	(41)	16.733	(41)	-0.592	-3.5	-1.557 ,	0.373	0.2225
Week 6	VLN Non-Mentholated	9.150	(42)	17.559	(41)	-8.394	-47.8	-10.475 ,	-6.314	<.0001
	VLN Mentholated	6.800	(41)	16.138	(41)	-9.337	-57.9	-11.186 ,	-7.489	<.0001
	VLN Combined	7.989	(83)	16.848	(82)	-8.866	-52.6	-10.231 ,	-7.500	<.0001
	UB Non-Mentholated	17.530	(17)	17.178	(17)	0.352	2.0	-1.325 ,	2.028	0.6626
	UB Mentholated	14.418	(19)	15.327	(19)	-0.909	-5.9	-2.724 ,	0.907	0.3069
	UB Combined	15.888	(36)	16.201	(36)	-0.314	-1.9	-1.513 ,	0.886	0.5990

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Paired t-test method is used to perform the analysis.
Percent change = mean of the differences/reference (baseline)*100

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Table 14.2.5.6.3.1 Statistical Comparison of Absolute Change from Baseline in Urinary Theq Mass Excreted (mg/24 hour)
 Among Study Product Groups at Weeks 2 and 6 (PP Population)

Study Week	Comparison	----- LSMeans -----		LSMean Difference		95%		p-value
		Test	(n)	Reference	(n)	(Test - Reference)	Confidence Intervals	
Week 2	VLN Non-mentholated vs UB Non-mentholated	-15.008	(11)	-0.609	(20)	-14.398	-17.816 , -10.980	<.0001
	VLN Mentholated vs UB Mentholated	-14.568	(12)	-0.649	(20)	-13.920	-17.244 , -10.595	<.0001
	VLN Combined vs UB Combined	-14.788	(23)	-0.629	(40)	-14.159	-16.543 , -11.775	<.0001
Week 6	VLN Non-mentholated vs UB Non-mentholated	-15.108	(10)	0.285	(16)	-15.394	-19.012 , -11.775	<.0001
	VLN Mentholated vs UB Mentholated	-14.191	(9)	-1.228	(19)	-12.963	-16.508 , -9.418	<.0001
	VLN Combined vs UB Combined	-14.650	(19)	-0.472	(35)	-14.178	-16.711 , -11.645	<.0001

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN Non-Mentholated = Non-mentholated VLN cigarettes
 VLN Mentholated = Mentholated VLN cigarettes
 UB Non-Mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB Mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.5.6.3.2 Statistical Comparison of Absolute Change from Baseline in Urinary Theq Mass Excreted (mg/24 hour)
 Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Study Week	Comparison	----- LSMeans -----		LSMean Difference		95%		p-value
		Test	(n)	Reference	(n)	(Test - Reference)	Confidence Intervals	
Week 2	VLN Non-mentholated vs UB Non-mentholated	-11.860	(47)	-0.609	(20)	-11.251	-13.888 , -8.614	<.0001
	VLN Mentholated vs UB Mentholated	-12.353	(43)	-0.649	(20)	-11.704	-14.372 , -9.037	<.0001
	VLN Combined vs UB Combined	-12.107	(90)	-0.629	(40)	-11.478	-13.353 , -9.602	<.0001
Week 6	VLN Non-mentholated vs UB Non-mentholated	-8.161	(41)	0.286	(16)	-8.446	-11.515 , -5.378	<.0001
	VLN Mentholated vs UB Mentholated	-9.275	(41)	-1.197	(19)	-8.078	-11.079 , -5.077	<.0001
	VLN Combined vs UB Combined	-8.718	(82)	-0.456	(35)	-8.262	-10.408 , -6.116	<.0001

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN Non-Mentholated = Non-mentholated VLN cigarettes
 VLN Mentholated = Mentholated VLN cigarettes
 UB Non-Mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB Mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.5.7.1.1.1
 Summary of Blood COHb (% Saturation) by Study Product Group and Study Week (PP Population)

		Study Product Group					
Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	12	17	29	22	20	42
	Mean	6.38	5.58	5.91	5.25	5.41	5.33
	SD	1.446	1.430	1.467	1.294	1.322	1.294
	CV%	22.7	25.6	24.8	24.7	24.4	24.3
	SEM	0.417	0.347	0.272	0.276	0.296	0.200
	Minimum	4.6	2.4	2.4	2.7	3.3	2.7
	Median	6.20	5.80	5.90	5.20	5.50	5.30
	Maximum	8.4	7.9	8.4	8.8	7.6	8.8
Week 2	n	11	12	23	21	20	41
	Mean	6.99	5.45	6.19	5.40	5.59	5.49
	SD	1.877	2.296	2.204	1.206	2.060	1.659
	CV%	26.8	42.1	35.6	22.3	36.9	30.2
	SEM	0.566	0.663	0.460	0.263	0.461	0.259
	Minimum	4.3	3.0	3.0	2.7	3.7	2.7
	Median	6.50	4.90	5.70	5.50	4.90	5.20
	Maximum	10.8	11.6	11.6	7.5	13.1	13.1
Week 6	n	10	9	19	19	20	39
	Mean	5.81	5.06	5.45	5.56	4.61	5.07
	SD	1.769	2.455	2.096	1.323	1.259	1.361
	CV%	30.4	48.6	38.4	23.8	27.3	26.8
	SEM	0.559	0.818	0.481	0.304	0.281	0.218
	Minimum	3.8	2.4	2.4	2.5	3.2	2.5
	Median	6.05	4.50	4.60	5.60	4.05	5.00
	Maximum	9.1	9.9	9.9	7.8	7.4	7.8

Note: * Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.5.7.1.1.2
 Summary of Blood COHb (% Saturation) by Study Product Group and Study Week (ITT Population)

		Study Product Group					
Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	50	50	100	22	20	42
	Mean	6.20	5.69	5.95	5.25	5.41	5.33
	SD	1.801	1.526	1.680	1.294	1.322	1.294
	CV%	29.1	26.8	28.2	24.7	24.4	24.3
	SEM	0.255	0.216	0.168	0.276	0.296	0.200
	Minimum	1.3	2.4	1.3	2.7	3.3	2.7
	Median	5.85	5.70	5.80	5.20	5.50	5.30
	Maximum	12.2	8.7	12.2	8.8	7.6	8.8
Week 2	n	49	45	94	21	20	41
	Mean	7.10	5.55	6.36	5.40	5.59	5.49
	SD	2.794	2.167	2.618	1.206	2.060	1.659
	CV%	39.4	39.1	41.2	22.3	36.9	30.2
	SEM	0.399	0.323	0.270	0.263	0.461	0.259
	Minimum	2.3	2.6	2.3	2.7	3.7	2.7
	Median	6.70	5.10	6.05	5.50	4.90	5.20
	Maximum	19.5	11.6	19.5	7.5	13.1	13.1
Week 6	n	43	42	85	19	20	39
	Mean	5.97	4.63	5.31	5.56	4.61	5.07
	SD	1.930	1.898	2.019	1.323	1.259	1.361
	CV%	32.3	41.0	38.0	23.8	27.3	26.8
	SEM	0.294	0.293	0.219	0.304	0.281	0.218
	Minimum	3.1	2.4	2.4	2.5	3.2	2.5
	Median	5.80	4.25	4.90	5.60	4.05	5.00
	Maximum	11.9	9.9	11.9	7.8	7.4	7.8

Note: * Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.5.7.1.2.1
 Summary of Blood COHb Change from Baseline (% Saturation) by Study Product Group and Study Week (PP Population)

		Study Product Group					
Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	21	20	41
	Mean	0.77	-0.18	0.27	0.07	0.18	0.12
	SD	1.165	1.702	1.518	1.028	1.781	1.427
	CV%	150.7	-928.5	554.1	1542.4	1017.5	1194.4
	SEM	0.351	0.491	0.316	0.224	0.398	0.223
	Minimum	-1.8	-2.8	-2.8	-1.7	-1.9	-1.9
	Median	0.90	-0.20	0.30	0.10	0.25	0.10
	Maximum	2.6	3.8	3.8	2.0	6.7	6.7
Week 6	n	10	9	19	19	20	39
	Mean	-0.57	-0.74	-0.65	0.24	-0.80	-0.29
	SD	0.943	1.675	1.304	0.982	1.062	1.140
	CV%	-165.4	-225.0	-199.7	405.7	-132.8	-390.0
	SEM	0.298	0.558	0.299	0.225	0.238	0.183
	Minimum	-1.8	-2.8	-2.8	-1.8	-3.8	-3.8
	Median	-0.75	-1.60	-0.80	0.30	-0.50	-0.40
	Maximum	0.7	2.1	2.1	2.2	1.0	2.2

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.5.7.1.2.2
Summary of Blood COHb Change from Baseline (% Saturation) by Study Product Group and Study Week (ITT Population)

		Study Product Group					
Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	49	45	94	21	20	41
	Mean	0.94	-0.17	0.41	0.07	0.18	0.12
	SD	1.653	1.630	1.726	1.028	1.781	1.427
	CV%	176.5	-940.3	425.8	1542.4	1017.5	1194.4
	SEM	0.236	0.243	0.178	0.224	0.398	0.223
	Minimum	-2.5	-3.1	-3.1	-1.7	-1.9	-1.9
	Median	0.90	-0.30	0.35	0.10	0.25	0.10
	Maximum	7.3	3.8	7.3	2.0	6.7	6.7
Week 6	n	43	42	85	19	20	39
	Mean	-0.45	-1.13	-0.79	0.24	-0.80	-0.29
	SD	1.472	1.614	1.572	0.982	1.062	1.140
	CV%	-327.9	-142.7	-200.1	405.7	-132.8	-390.0
	SEM	0.224	0.249	0.171	0.225	0.238	0.183
	Minimum	-3.2	-4.7	-4.7	-1.8	-3.8	-3.8
	Median	-0.50	-1.35	-0.90	0.30	-0.50	-0.40
	Maximum	3.7	2.1	3.7	2.2	1.0	2.2

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.5.7.1.3.1
 Summary of Blood COHb Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)

		Study Product Group					
Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	11	12	23	21	20	41
	Mean	12.968	-2.322	4.990	3.502	4.487	3.983
	SD	18.2173	27.9406	24.5393	23.8907	28.1175	25.7131
	CV%	140.5	-1203.1	491.7	682.2	626.6	645.6
	SEM	5.4927	8.0658	5.1168	5.2134	6.2873	4.0157
	Minimum	-29.51	-48.28	-48.28	-35.71	-28.79	-35.71
	Median	16.667	-3.125	4.615	1.667	6.012	2.500
	Maximum	32.61	48.72	48.72	74.07	104.69	104.69
Week 6	n	10	9	19	19	20	39
	Mean	-9.755	-13.423	-11.492	6.070	-13.406	-3.918
	SD	14.9598	26.3650	20.6004	20.8472	16.5741	20.9875
	CV%	-153.4	-196.4	-179.3	343.5	-123.6	-535.7
	SEM	4.7307	8.7883	4.7261	4.7827	3.7061	3.3607
	Minimum	-29.51	-48.28	-48.28	-34.21	-50.00	-50.00
	Median	-12.170	-26.230	-14.583	6.154	-11.081	-6.349
	Maximum	9.52	26.92	26.92	52.38	15.63	52.38

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.5.7.1.3.2
Summary of Blood COHb Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)

		Study Product Group					
Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	49	45	94	21	20	41
	Mean	15.718	-1.704	7.378	3.502	4.487	3.983
	SD	25.9767	32.1903	30.2505	23.8907	28.1175	25.7131
	CV%	165.3	-1888.9	410.0	682.2	626.6	645.6
	SEM	3.7110	4.7986	3.1201	5.2134	6.2873	4.0157
	Minimum	-43.64	-48.28	-48.28	-35.71	-28.79	-35.71
	Median	16.071	-5.714	6.465	1.667	6.012	2.500
	Maximum	83.33	127.59	127.59	74.07	104.69	104.69
Week 6	n	43	42	85	19	20	39
	Mean	-6.083	-18.178	-12.059	6.070	-13.406	-3.918
	SD	23.1754	27.1291	25.7834	20.8472	16.5741	20.9875
	CV%	-381.0	-149.2	-213.8	343.5	-123.6	-535.7
	SEM	3.5342	4.1861	2.7966	4.7827	3.7061	3.3607
	Minimum	-43.10	-55.93	-55.93	-34.21	-50.00	-50.00
	Median	-9.756	-26.230	-16.216	6.154	-11.081	-6.349
	Maximum	56.06	68.97	68.97	52.38	15.63	52.38

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.7.2 Statistical Comparison of Blood COHb (% Saturation) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Study Week	Product Groups	----- Means -----				Difference (Test Week - Baseline)	Percent Change (%)	95%		p-Value
		Test Week	(n)	Baseline	(n)			Confidence Intervals		
Week 2	VLN Non-Mentholated	6.991	(11)	6.218	(11)	0.773	12.4	-0.010 -	1.555	0.0524
	VLN Mentholated	5.450	(12)	5.633	(12)	-0.183	-3.3	-1.265 -	0.898	0.7162
	VLN Combined	6.187	(23)	5.913	(23)	0.274	4.6	-0.382 -	0.930	0.3961
	UB Non-Mentholated	5.405	(21)	5.338	(21)	0.067	1.2	-0.401 -	0.535	0.7694
	UB Mentholated	5.585	(20)	5.410	(20)	0.175	3.2	-0.658 -	1.008	0.6652
	UB Combined	5.493	(41)	5.373	(41)	0.120	2.2	-0.331 -	0.570	0.5949
Week 6	VLN Non-Mentholated	5.810	(10)	6.380	(10)	-0.570	-8.9	-1.244 -	0.104	0.0882
	VLN Mentholated	5.056	(9)	5.800	(9)	-0.744	-12.8	-2.032 -	0.543	0.2191
	VLN Combined	5.453	(19)	6.105	(19)	-0.653	-10.7	-1.281 -	-0.024	0.0426
	UB Non-Mentholated	5.558	(19)	5.316	(19)	0.242	4.6	-0.231 -	0.716	0.2968
	UB Mentholated	4.610	(20)	5.410	(20)	-0.800	-14.8	-1.297 -	-0.303	0.0032
	UB Combined	5.072	(39)	5.364	(39)	-0.292	-5.4	-0.662 -	0.077	0.1176

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes; VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Paired t-test method is used to perform the analysis.
Percent change = mean of the differences/reference (baseline)*100.

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Table 14.2.5.7.3 Statistical Comparison of Blood COHb Absolute Change From Baseline (% Saturation) Among Study Product Groups at Weeks 2 and 6 (PP Population)

Study Week	Comparison	----- LS Means -----		LS Mean Difference (Test - Reference)	95% Confidence Interval		p-value
		Test (n)	Reference (n)				
2	VLN Non-mentholated vs UB Non-mentholated	0.773 (11)	0.067 (21)	0.706	-0.376 - 1.788		0.1969
	VLN Mentholated vs UB Mentholated	-0.183 (12)	0.175 (20)	-0.358	-1.420 - 0.704		0.5023
	VLN Combined vs UB Combined	0.295 (23)	0.121 (41)	0.174	-0.584 - 0.932		0.6481
6	VLN Non-mentholated vs UB Non-mentholated	-0.542 (10)	0.256 (19)	-0.797	-1.663 - 0.068		0.0703
	VLN Mentholated vs UB Mentholated	-0.760 (9)	-0.800 (20)	0.040	-0.840 - 0.921		0.9271
	VLN Combined vs UB Combined	-0.651 (19)	-0.272 (39)	-0.379	-0.996 - 0.239		0.2247

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observations used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.5.7.4 Statistical Comparison of Blood COHb (% Saturation) at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Study Week	Product Groups	----- Means -----				Difference (Test Week - Baseline)	Percent Change (%)	95%		p-Value
		Test Week	(n)	Baseline	(n)			Confidence Intervals		
Week 2	VLN Non-Mentholated	7.096	(49)	6.159	(49)	0.937	15.2	0.462 -	1.412	0.0002
	VLN Mentholated	5.549	(45)	5.722	(45)	-0.173	-3.0	-0.663 -	0.316	0.4794
	VLN Combined	6.355	(94)	5.950	(94)	0.405	6.8	0.052 -	0.759	0.0251
	UB Non-Mentholated	5.405	(21)	5.338	(21)	0.067	1.2	-0.401 -	0.535	0.7694
	UB Mentholated	5.585	(20)	5.410	(20)	0.175	3.2	-0.658 -	1.008	0.6652
	UB Combined	5.493	(41)	5.373	(41)	0.120	2.2	-0.331 -	0.570	0.5949
Week 6	VLN Non-Mentholated	5.974	(43)	6.423	(43)	-0.449	-7.0	-0.902 -	0.004	0.0520
	VLN Mentholated	4.633	(42)	5.764	(42)	-1.131	-19.6	-1.634 -	-0.628	<.0001
	VLN Combined	5.312	(85)	6.098	(85)	-0.786	-12.9	-1.125 -	-0.447	<.0001
	UB Non-Mentholated	5.558	(19)	5.316	(19)	0.242	4.6	-0.231 -	0.716	0.2968
	UB Mentholated	4.610	(20)	5.410	(20)	-0.800	-14.8	-1.297 -	-0.303	0.0032
	UB Combined	5.072	(39)	5.364	(39)	-0.292	-5.4	-0.662 -	0.077	0.1176

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes; VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Paired t-test method is used to perform the analysis.
Percent change = mean of the differences/reference (baseline)*100.

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Table 14.2.5.7.5 Statistical Comparison of Blood COHb Absolute Change From Baseline (% Saturation) Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Study Week	Comparison	----- LS Means -----		LS Mean Difference (Test - Reference)	95% Confidence Interval		p-value
		Test (n)	Reference (n)				
2	VLN Non-mentholated vs UB Non-mentholated	0.937 (49)	0.067 (21)	0.870	0.052 - 1.688		0.0373
	VLN Mentholated vs UB Mentholated	-0.173 (45)	0.175 (20)	-0.348	-1.191 - 0.495		0.4152
	VLN Combined vs UB Combined	0.382 (94)	0.121 (41)	0.261	-0.327 - 0.848		0.3813
6	VLN Non-mentholated vs UB Non-mentholated	-0.487 (43)	0.258 (19)	-0.745	-1.496 - 0.005		0.0515
	VLN Mentholated vs UB Menthoholated	-1.135 (42)	-0.800 (20)	-0.335	-1.083 - 0.413		0.3771
	VLN Combined vs UB Combined	-0.811 (85)	-0.271 (39)	-0.540	-1.070 - -0.010		0.0457

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observations used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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14.2.6 Biomarker Figures

Urine NNAL

- Figure 14.2.6.1.1 Mean (\pm SD) of Urinary NNAL Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.1.2 Mean Urinary NNAL Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.1.3 Mean (\pm SD) of Urinary NNAL Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)
- Figure 14.2.6.1.4 Mean Urinary NNAL Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)

Urine NNN

- Figure 14.2.6.2.1 Mean (\pm SD) of Urinary NNN Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.2.2 Mean Urinary NNN Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.2.3 Mean (\pm SD) of Urinary NNN Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)
- Figure 14.2.6.2.4 Mean Urinary NNN Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)

Urine 3-HPMA

- Figure 14.2.6.3.1 Mean (\pm SD) of Urinary 3-HPMA Mass Excreted (μ g/24 hour) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.3.2 Mean Urinary 3-HPMA Mass Excreted (μ g/24 hour) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.3.3 Mean (\pm SD) of Urinary 3-HPMA Mass Excreted (μ g/24 hour) by Study Product Group and Study Week (ITT Population)
- Figure 14.2.6.3.4 Mean Urinary 3-HPMA Mass Excreted (μ g/24 hour) by Study Product Group and Study Week (ITT Population)

Urine S-PMA

- Figure 14.2.6.4.1 Mean (\pm SD) of Urinary S-PMA Mass Excreted (μ g/24 hour) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.4.2 Mean Urinary S-PMA Mass Excreted (μ g/24 hour) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.4.3 Mean (\pm SD) of Urinary S-PMA Mass Excreted (μ g/24 hour) by Study Product Group and Study Week (ITT Population)

Figure 14.2.6.4.4 Mean Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (ITT Population)

Urine 1-OHP

Figure 14.2.6.5.1 Mean ($\pm\text{SD}$) of Urinary 1-OHP Mass Excreted ($\text{ng}/24$ hour) by Study Product Group and Study Week (PP Population)

Figure 14.2.6.5.2 Mean Urinary 1-OHP Mass Excreted ($\text{ng}/24$ hour) by Study Product Group and Study Week (PP Population)

Figure 14.2.6.5.3 Mean ($\pm\text{SD}$) of Urinary 1-OHP Mass Excreted ($\text{ng}/24$ hour) by Study Product Group and Study Week (ITT Population)

Figure 14.2.6.5.4 Mean Urinary 1-OHP Mass Excreted ($\text{ng}/24$ hour) by Study Product Group and Study Week (ITT Population)

Urine Tneq

Figure 14.2.6.6.1 Mean ($\pm\text{SD}$) of Urinary Tneq Mass Excreted ($\text{mg}/24$ hour) by Study Product Group and Study Week (PP Population)

Figure 14.2.6.6.2 Mean Urinary Tneq Mass Excreted ($\text{mg}/24$ hour) by Study Product Group and Study Week (PP Population)

Figure 14.2.6.6.3 Mean ($\pm\text{SD}$) of Urinary Tneq Mass Excreted ($\text{mg}/24$ hour) by Study Product Group and Study Week (ITT Population)

Figure 14.2.6.6.4 Mean Urinary Tneq Mass Excreted ($\text{mg}/24$ hour) by Study Product Group and Study Week (ITT Population)

Blood COHb

Figure 14.2.6.7.1 Mean ($\pm\text{SD}$) of Blood COHb (% Saturation) by Study Product Group and Study Week (PP Population)

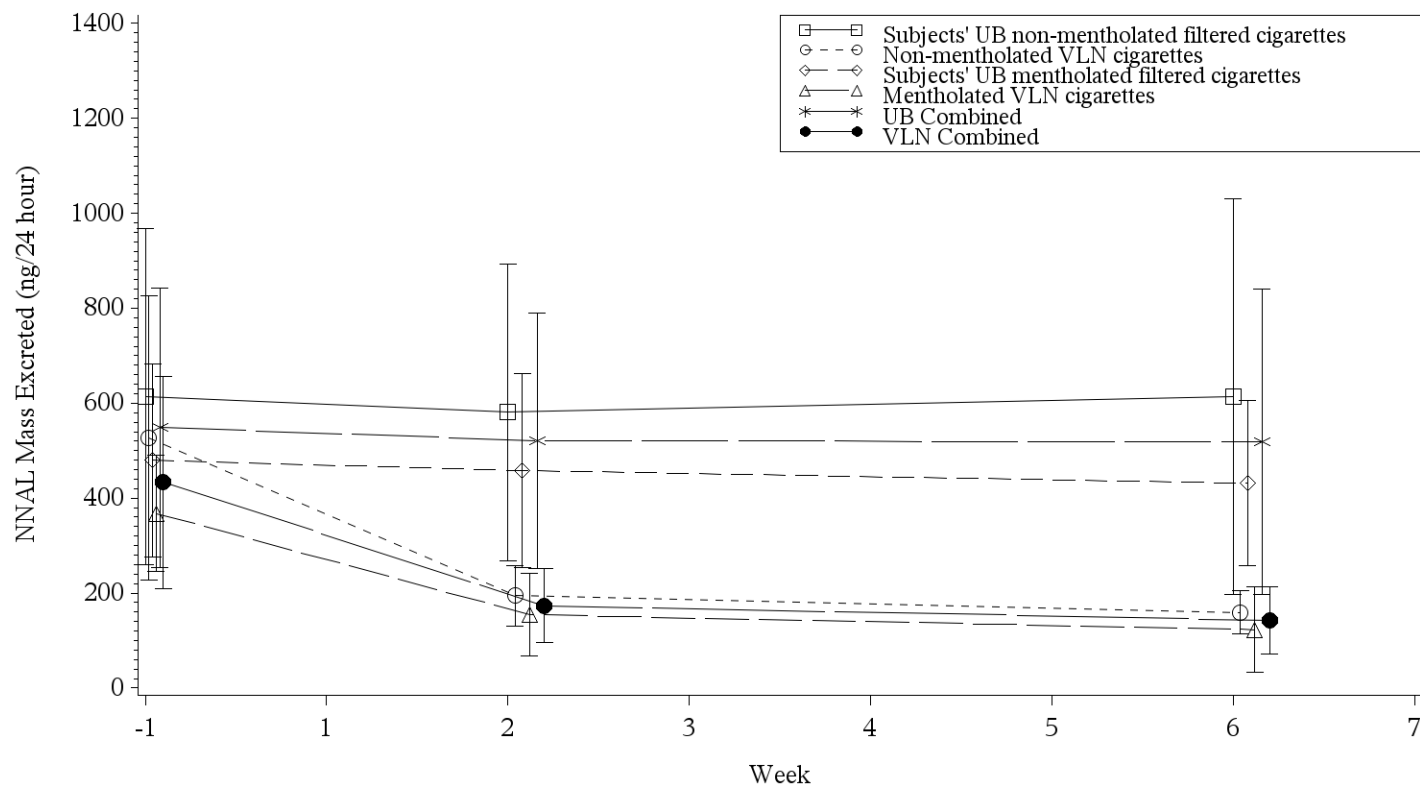
Figure 14.2.6.7.2 Mean Blood COHb (% Saturation) by Study Product Group and Study Week (PP Population)

Figure 14.2.6.7.3 Mean ($\pm\text{SD}$) of Blood COHb (% Saturation) by Study Product Group and Study Week (ITT Population)

Figure 14.2.6.7.4 Mean Blood COHb (% Saturation) by Study Product Group and Study Week (ITT Population)

Figure 14.2.6.1.1

Mean (\pm SD) of Urinary NNAL Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)



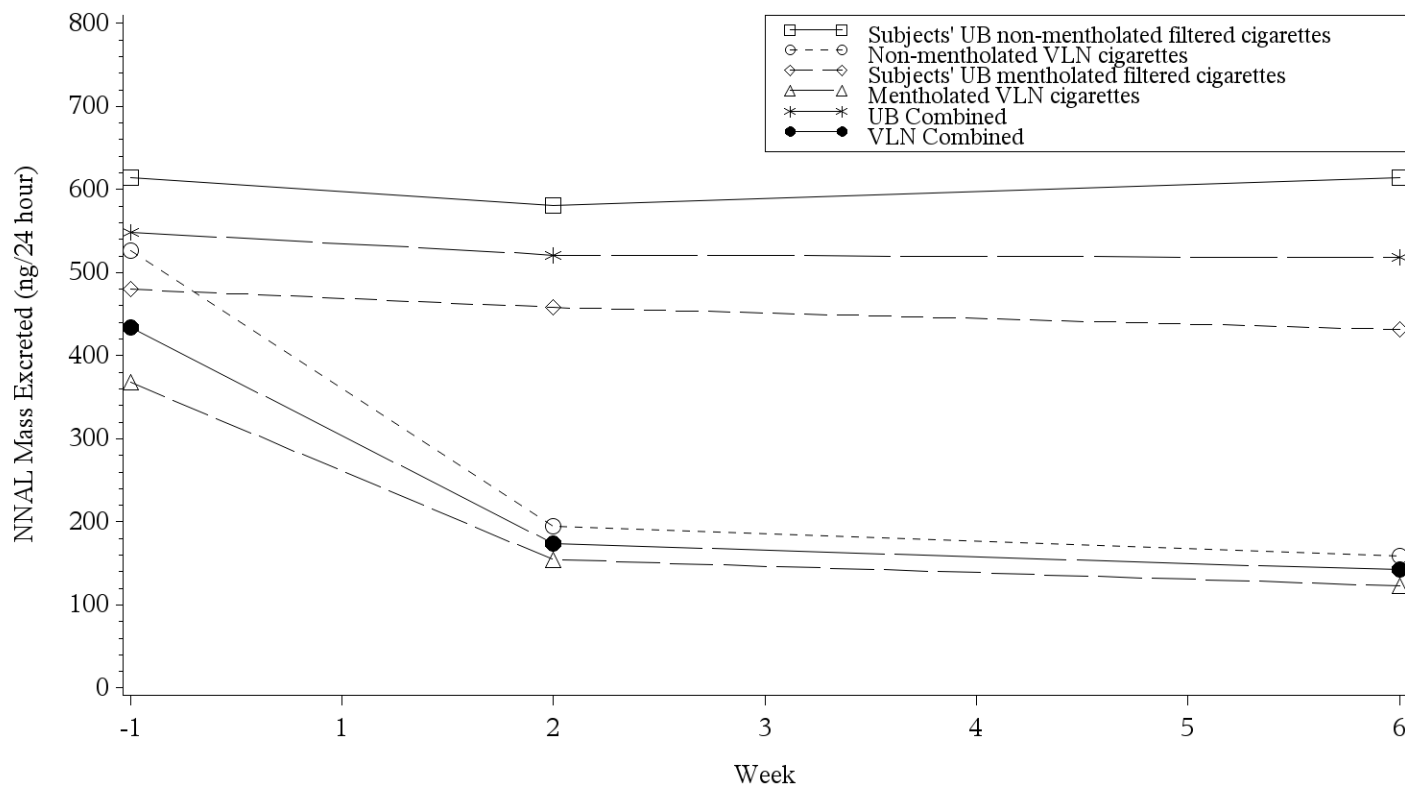
All products except UB Non-Mentholated are shifted to the right for ease of reading

Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.1.2

Mean Urinary NNAL Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)

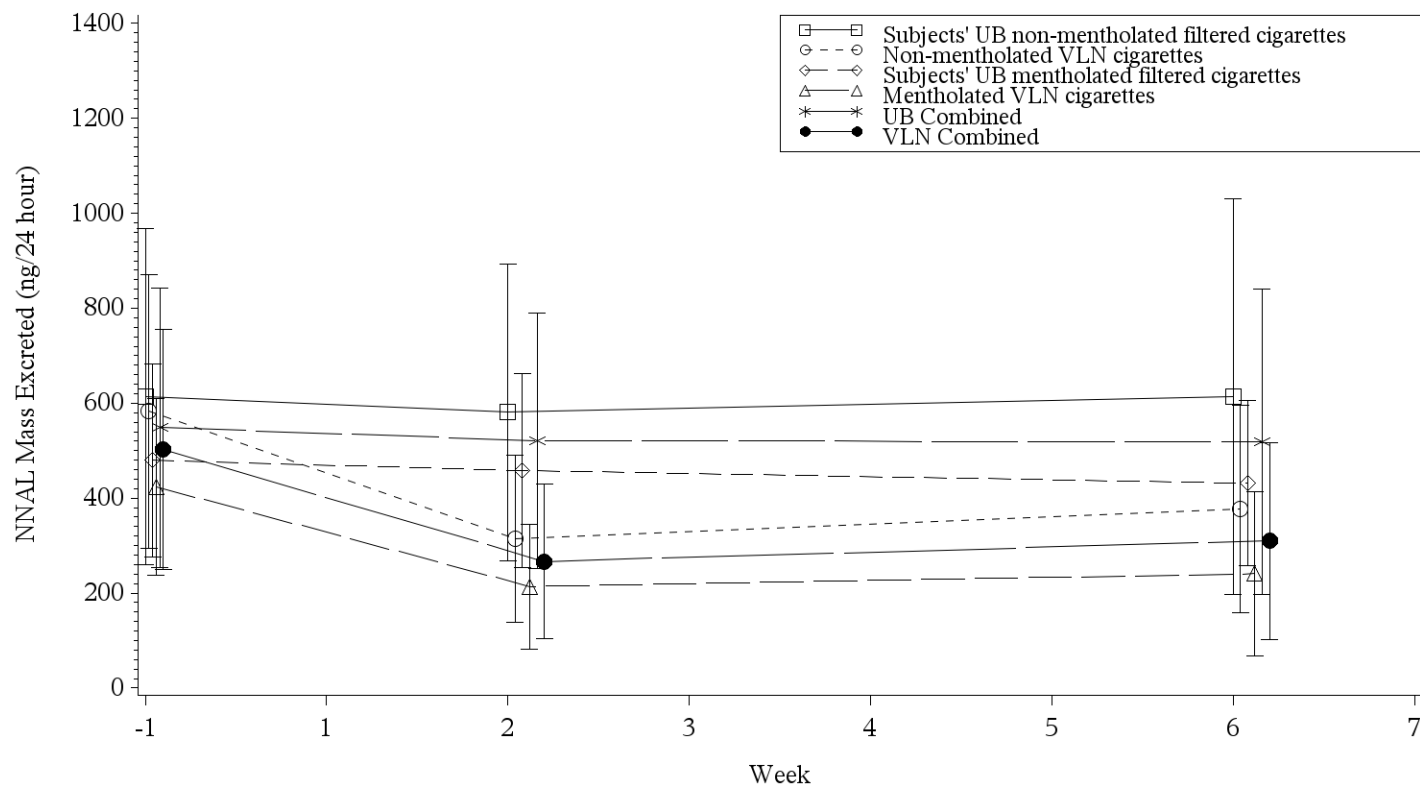


Subjects used their own usual brand cigarettes at Week -1

Program: /CA24914/sas_prg/pksas/pdurine/adam_urinemeangraph.sas 12JUN2019 10:37

Figure 14.2.6.1.3

Mean (\pm SD) of Urinary NNAL Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)



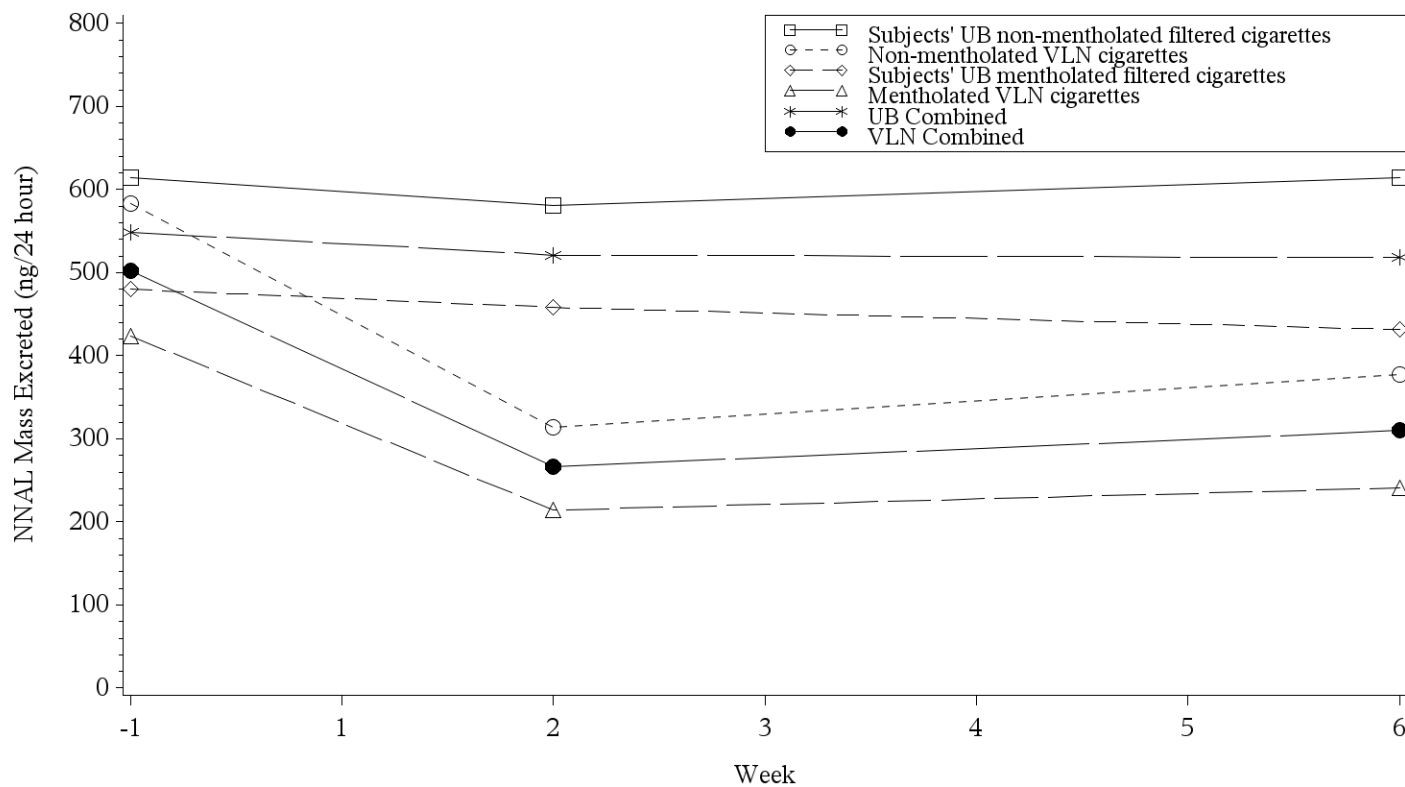
All products except UB Non-Mentholated are shifted to the right for ease of reading

Subjects used their own usual brand cigarettes at Week -1

Program: /CA24914/sas_prg/pksas/pdurine/adam_urinemeangraph.sas 12JUN2019 10:37

Figure 14.2.6.1.4

Mean Urinary NNAL Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)

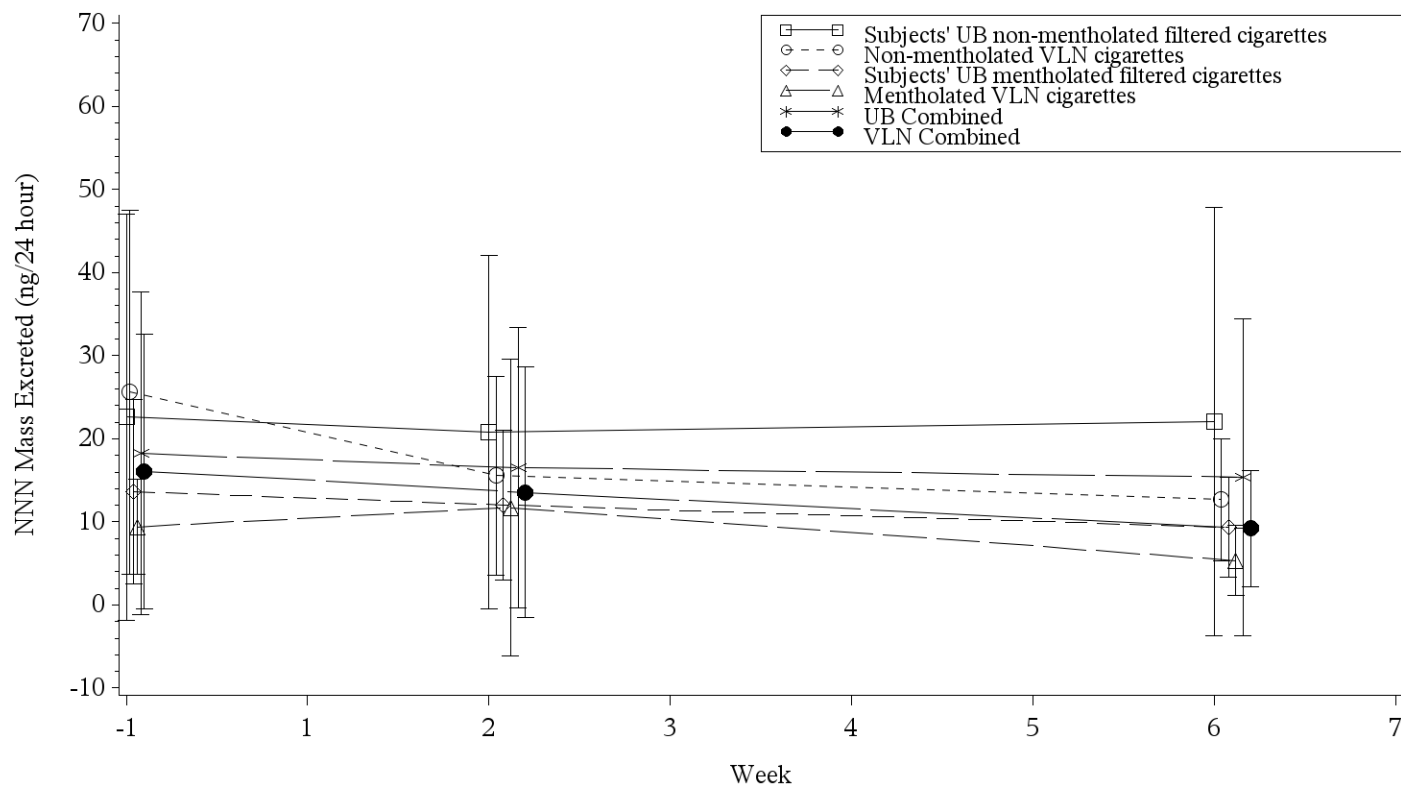


Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.2.1

Mean (\pm SD) of Urinary NNN Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)



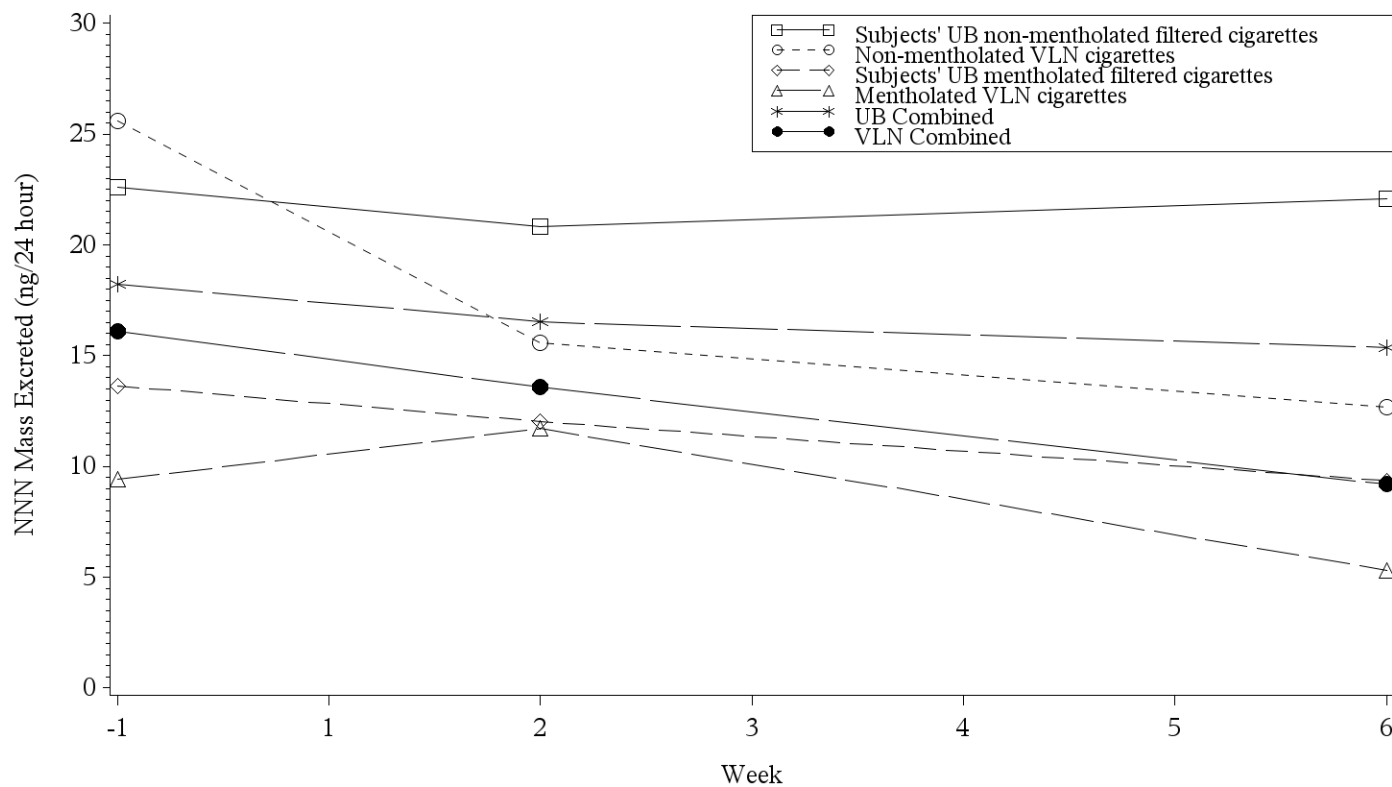
All products except UB Non-Mentholated are shifted to the right for ease of reading

Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.2.2

Mean Urinary NNN Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)

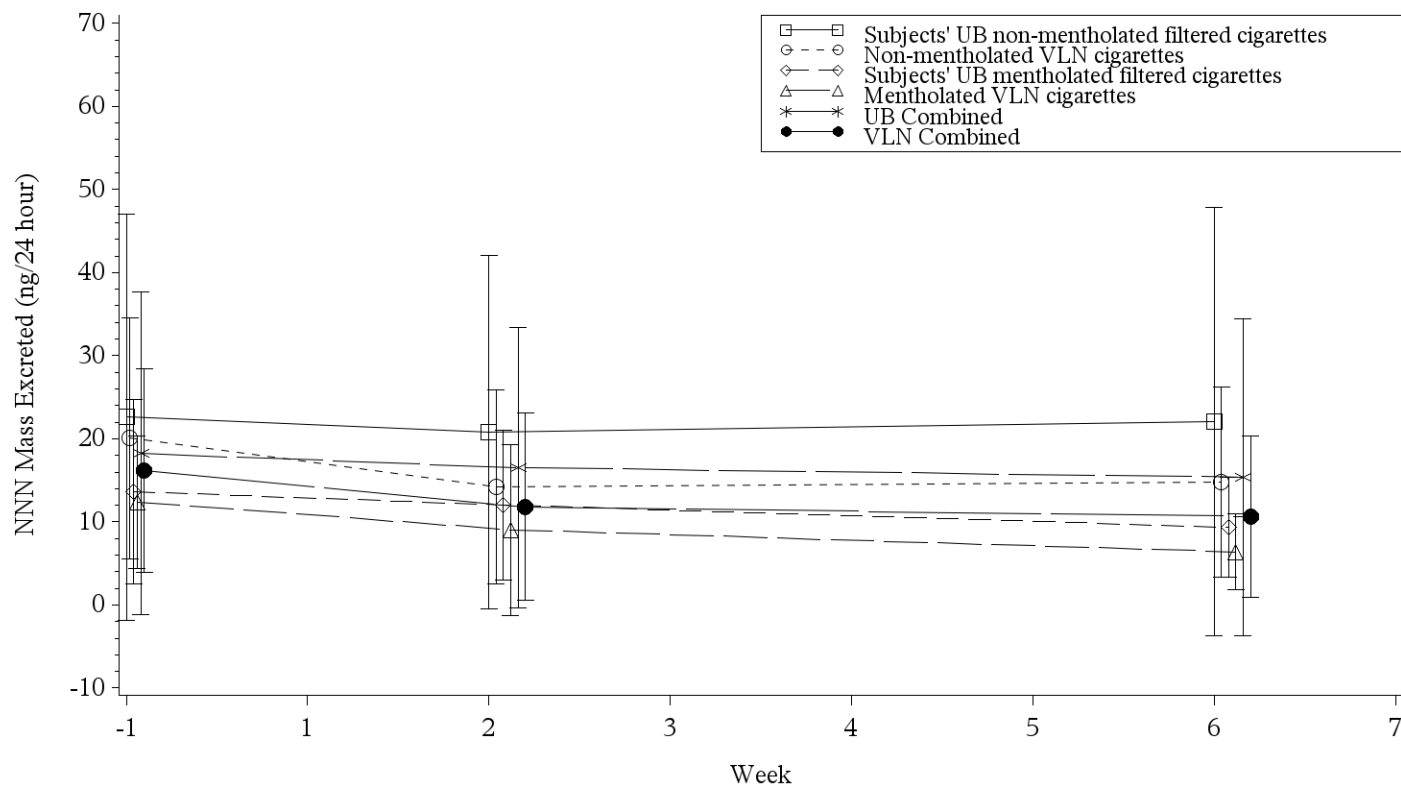


Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.2.3

Mean (\pm SD) of Urinary NNN Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)



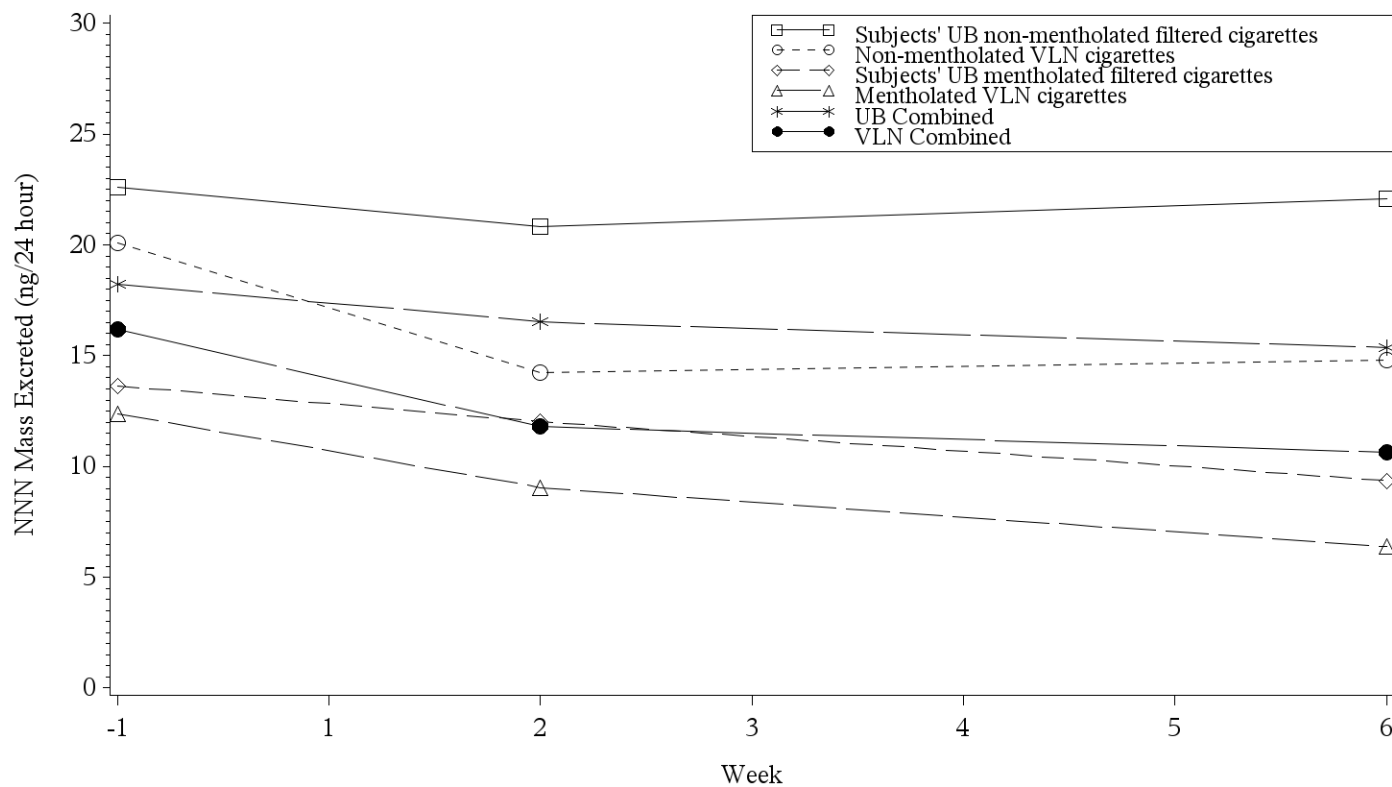
All products except UB Non-Mentholated are shifted to the right for ease of reading

Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.2.4

Mean Urinary NNN Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)

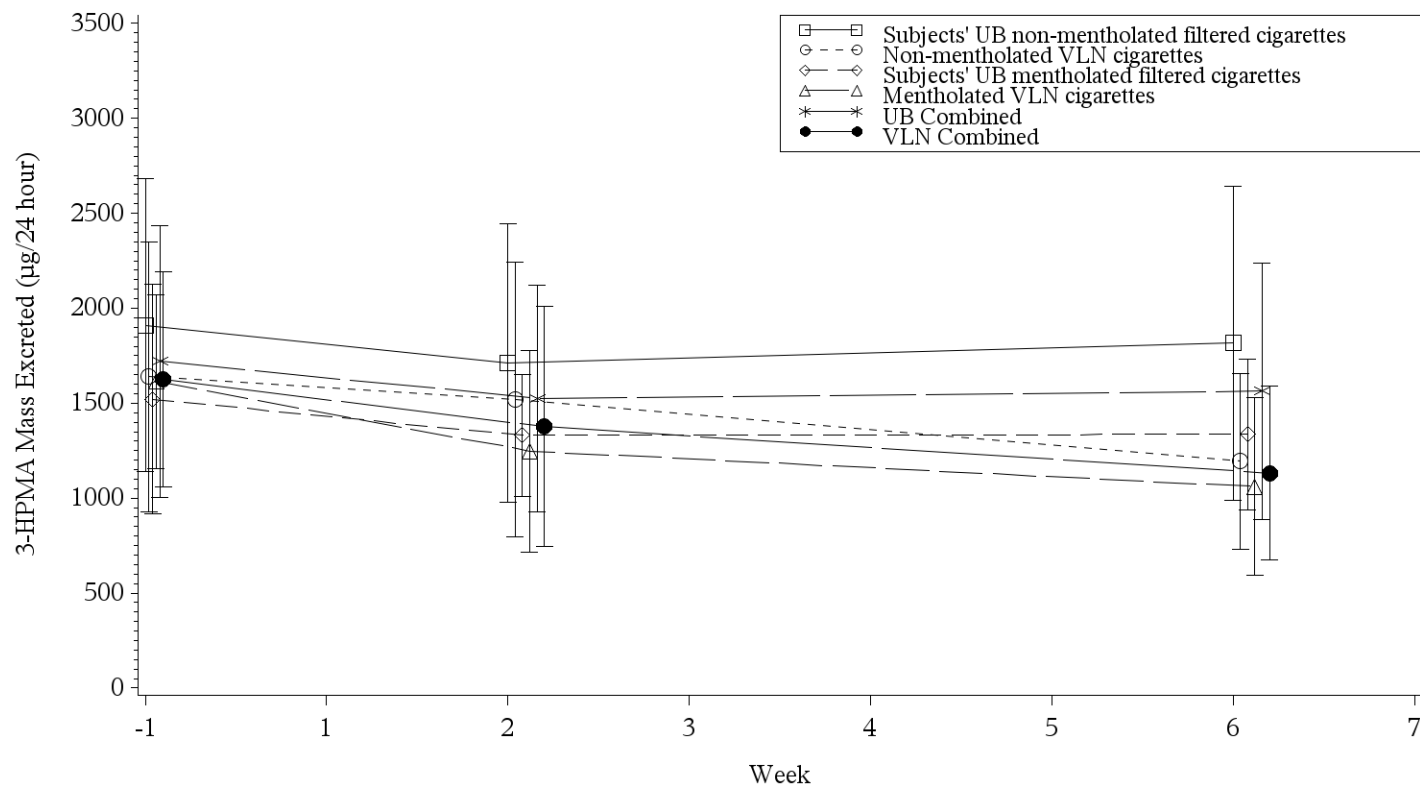


Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.3.1

Mean (\pm SD) of Urinary 3-HPMA Mass Excreted (μ g/24 hour) by Study Product Group and Study Week (PP Population)



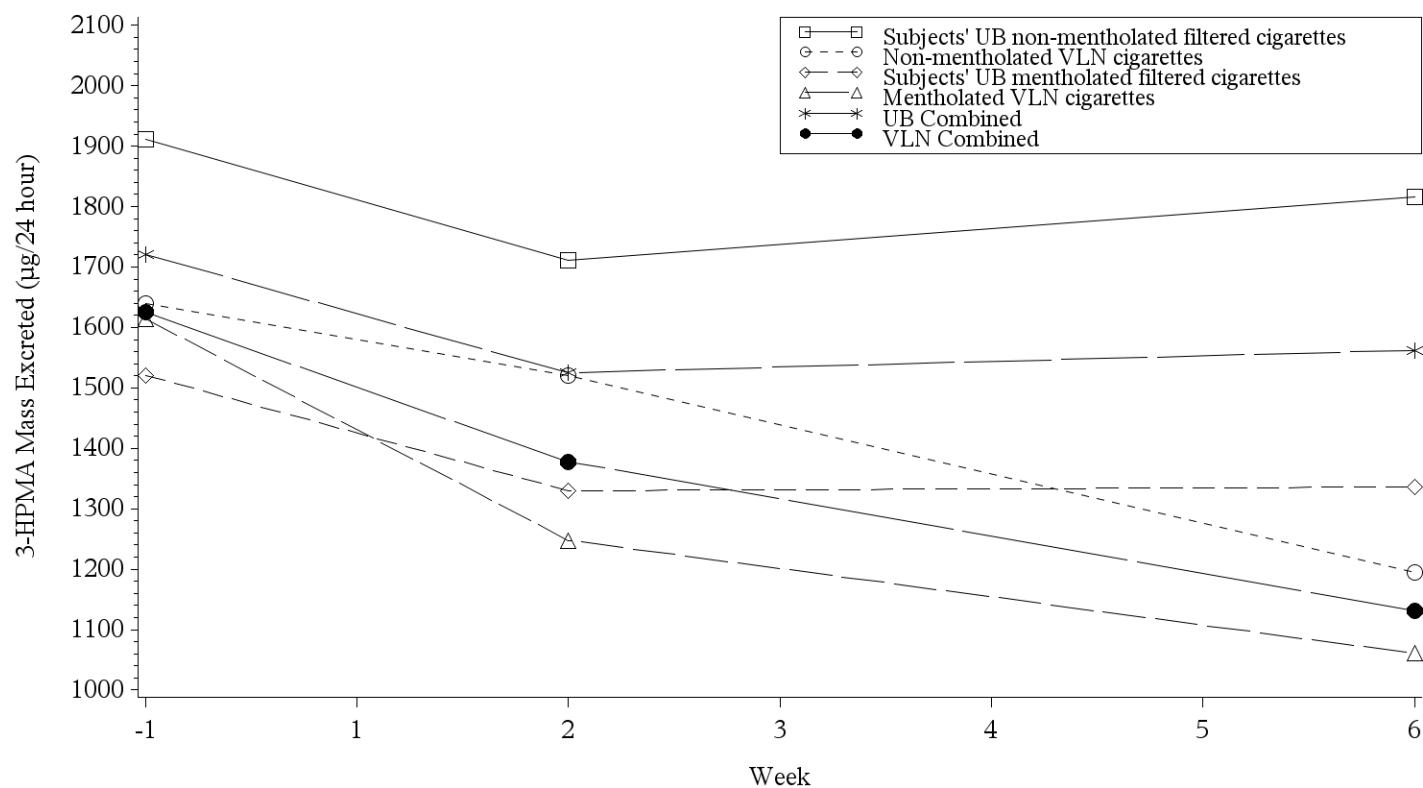
All products except UB Non-Mentholated are shifted to the right for ease of reading

Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.3.2

Mean Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (PP Population)

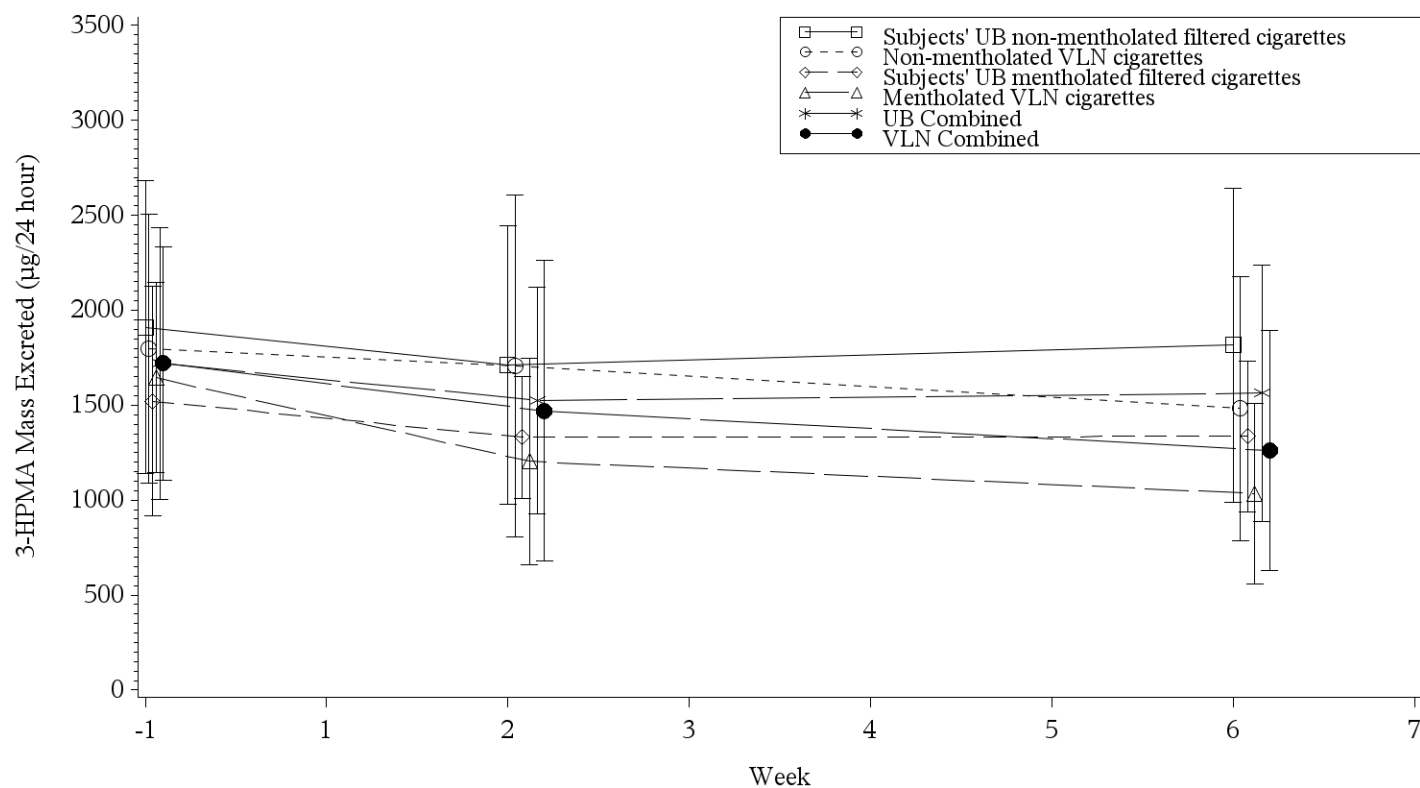


Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.3.3

Mean (\pm SD) of Urinary 3-HPMA Mass Excreted (μ g/24 hour) by Study Product Group and Study Week (ITT Population)



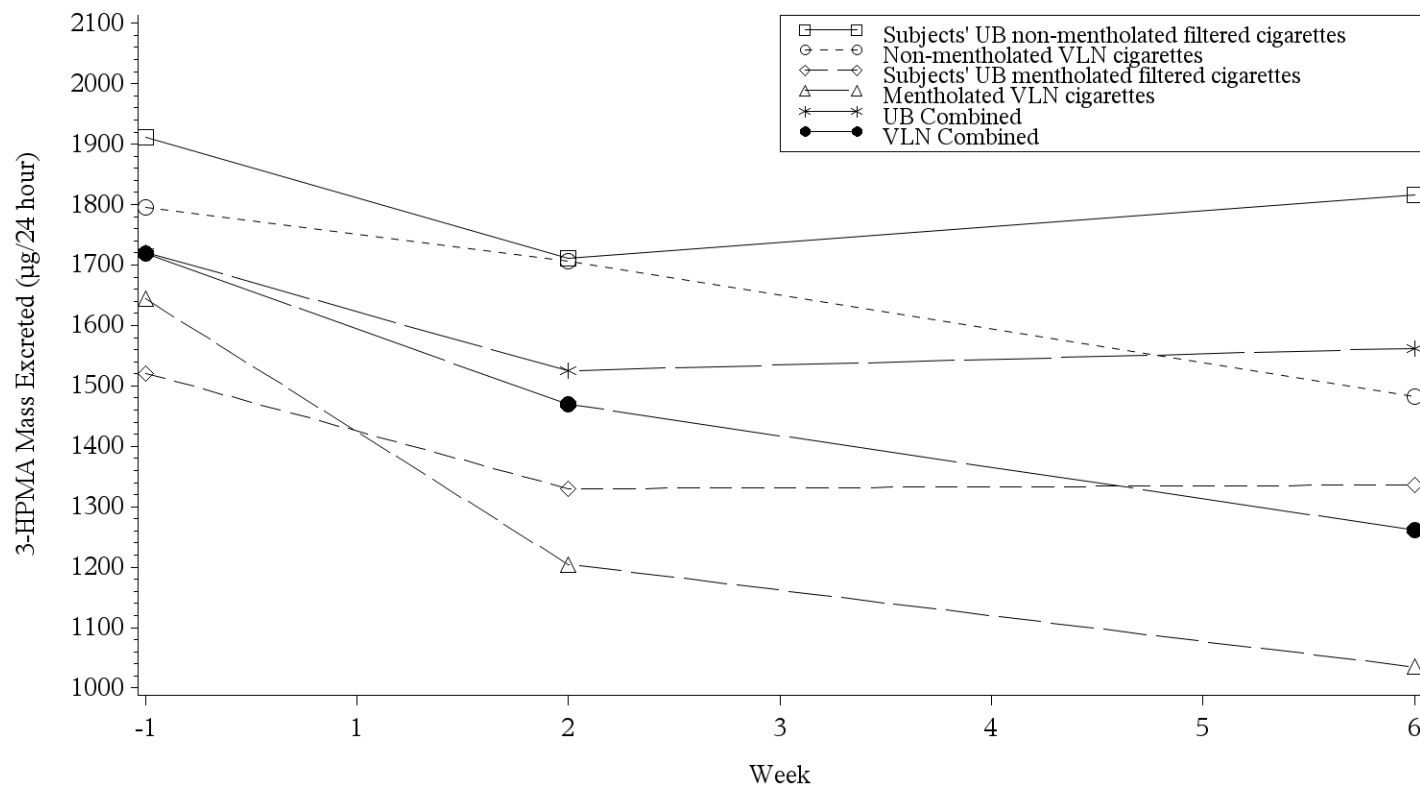
All products except UB Non-Mentholated are shifted to the right for ease of reading

Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.3.4

Mean Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (ITT Population)

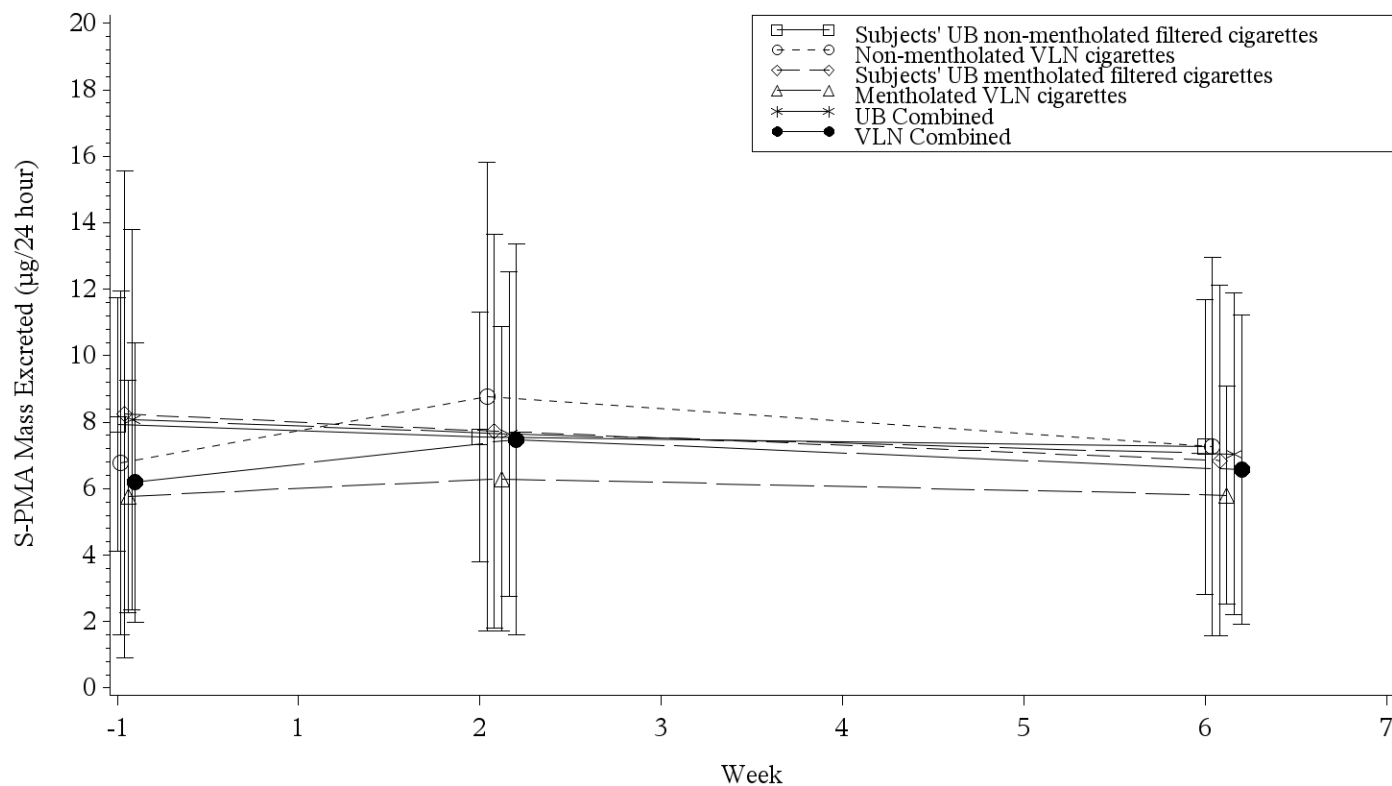


Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.4.1

Mean (\pm SD) of Urinary S-PMA Mass Excreted (μ g/24 hour) by Study Product Group and Study Week (PP Population)



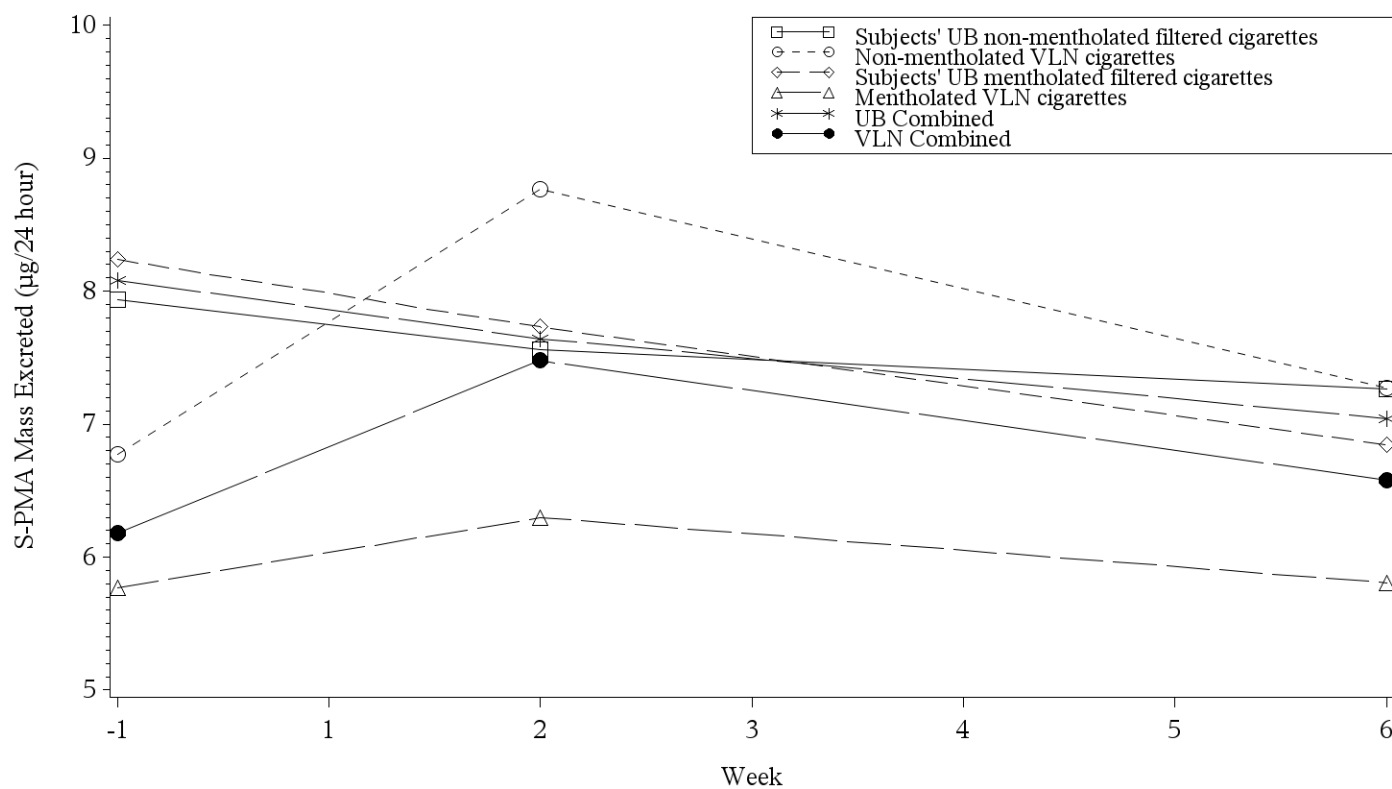
All products except UB Non-Mentholated are shifted to the right for ease of reading

Subjects used their own usual brand cigarettes at Week -1

Program: /CA24914/sas_prg/pksas/pdurine/adam_urinemeangraph.sas 12JUN2019 10:37

Figure 14.2.6.4.2

Mean Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (PP Population)

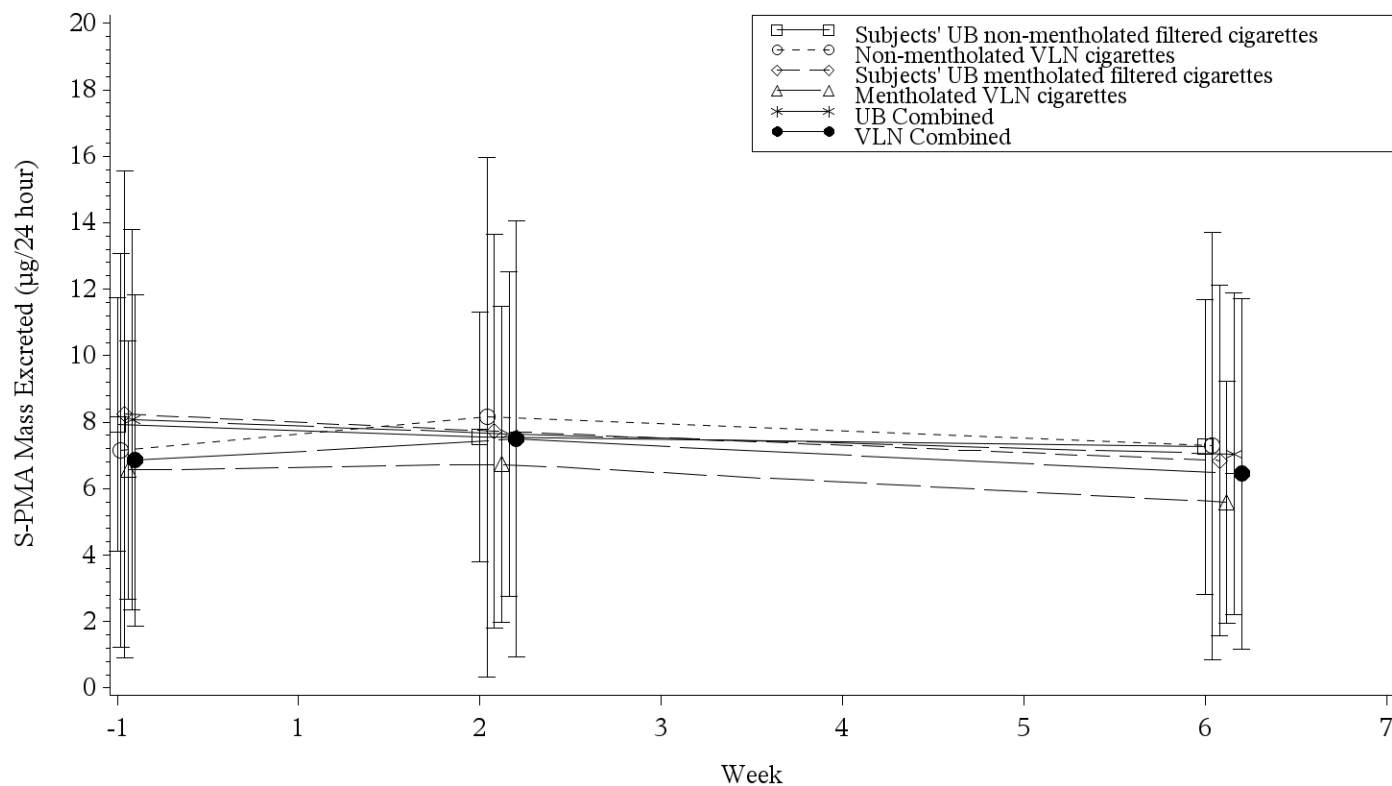


Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.4.3

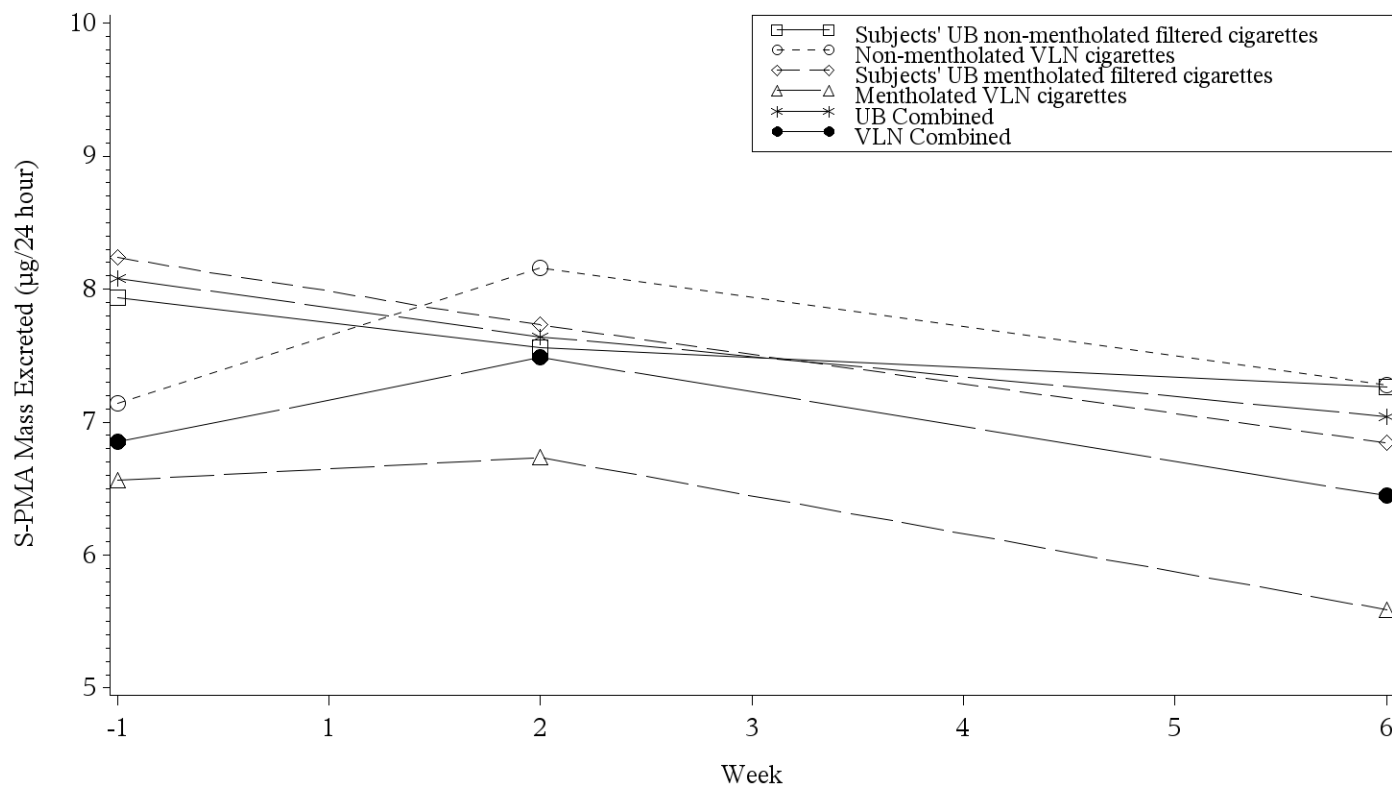
Mean (\pm SD) of Urinary S-PMA Mass Excreted (μ g/24 hour) by Study Product Group and Study Week (ITT Population)



All products except UB Non-Mentholated are shifted to the right for ease of reading
 Subjects used their own usual brand cigarettes at Week -1
 Program: /CA24914/sas_prg/pksas/pdurine/adam_urinemeangraph.sas 12JUN2019 10:37

Figure 14.2.6.4.4

Mean Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) by Study Product Group and Study Week (ITT Population)

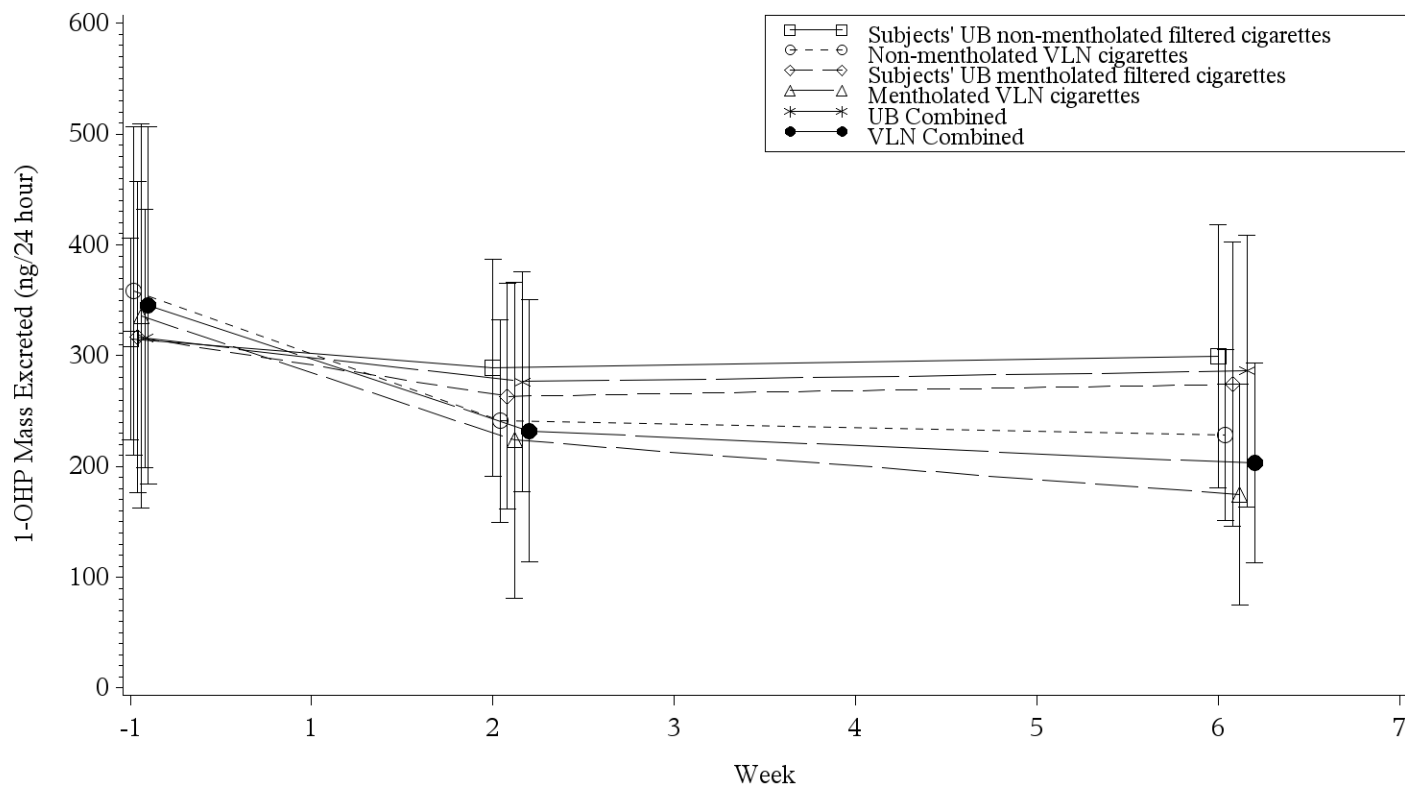


Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.5.1

Mean (\pm SD) of Urinary 1-OHP Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)



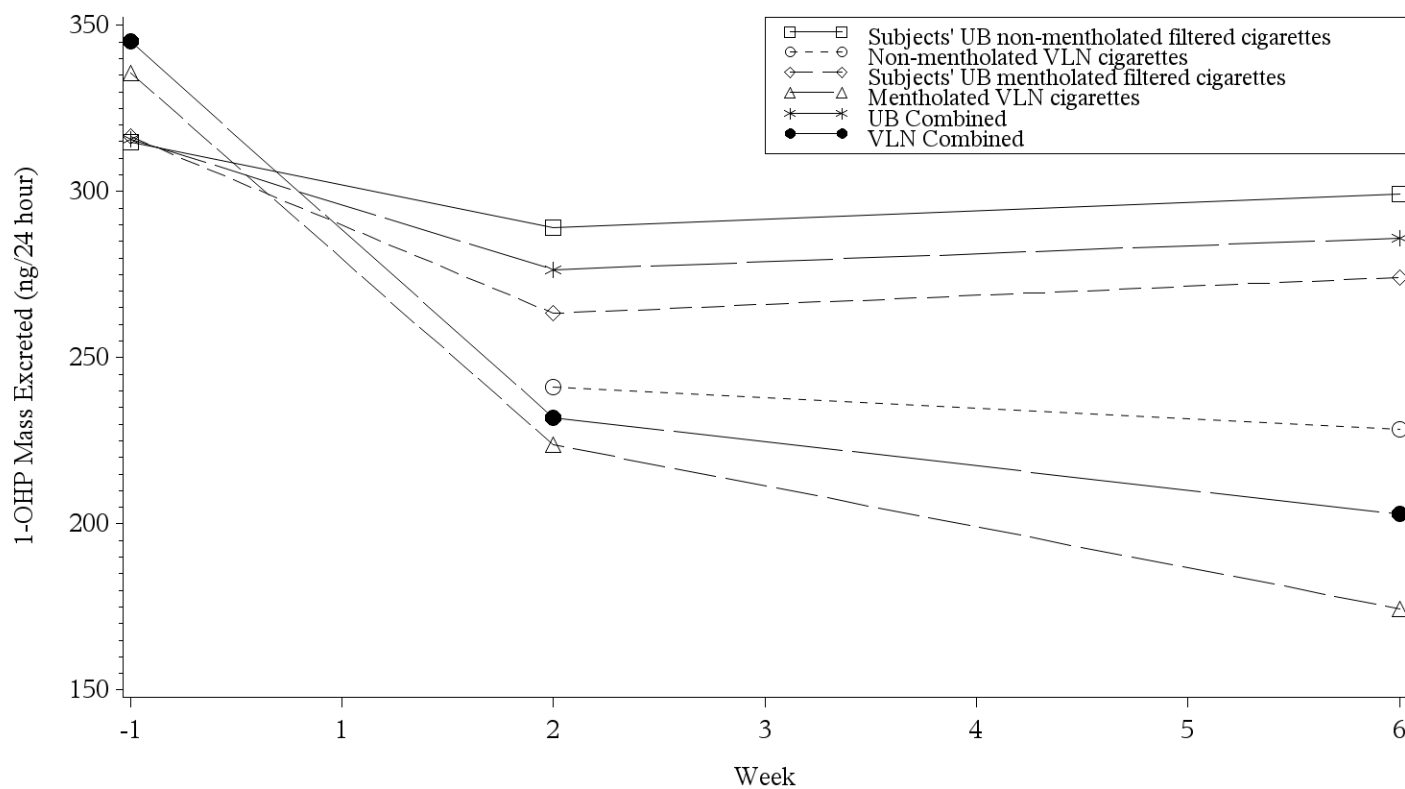
All products except UB Non-Mentholated are shifted to the right for ease of reading

Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.5.2

Mean Urinary 1-OHP Mass Excreted (ng/24 hour) by Study Product Group and Study Week (PP Population)

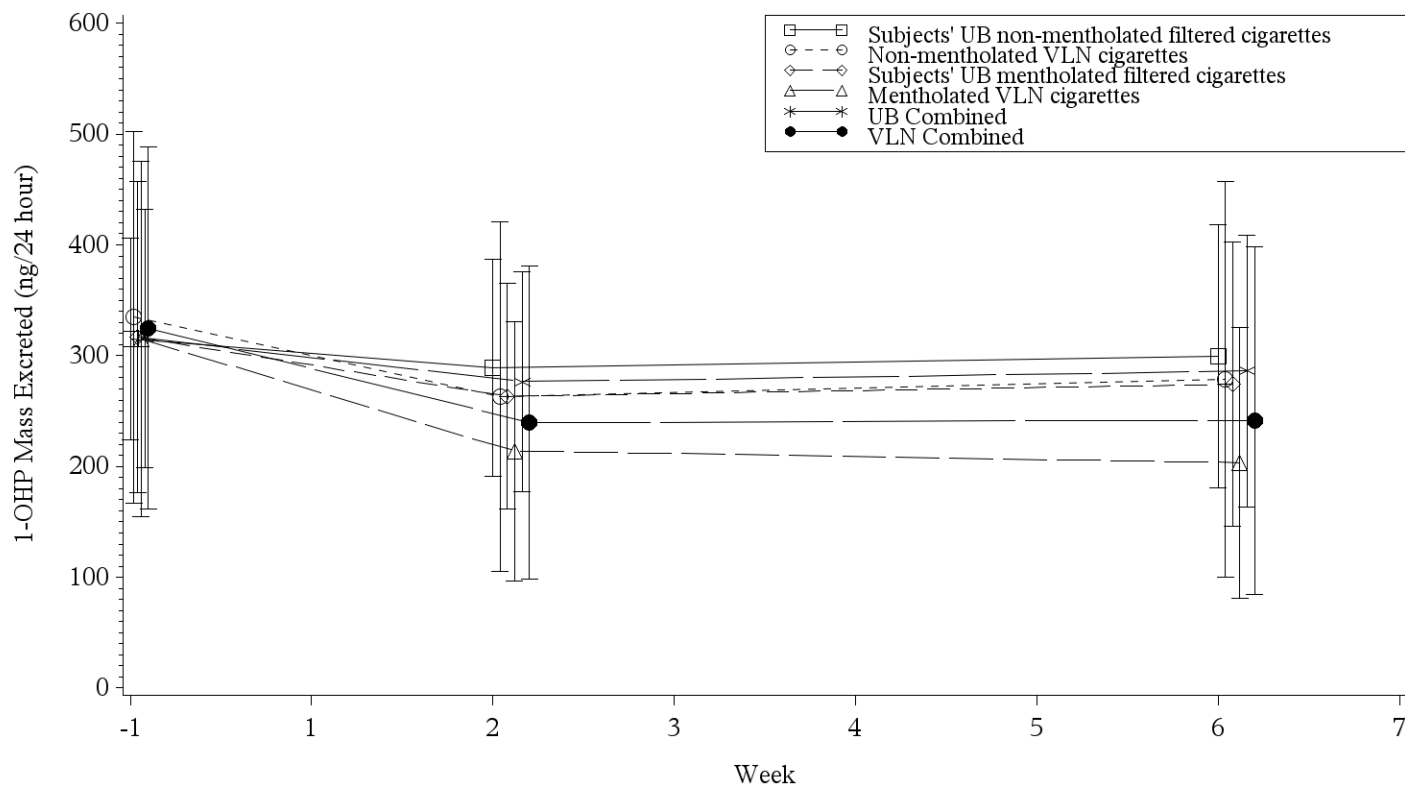


Subjects used their own usual brand cigarettes at Week -1

Program: /CA24914/sas_prg/pksas/pdurine/adam_urinemeangraph.sas 12JUN2019 10:37

Figure 14.2.6.5.3

Mean (\pm SD) of Urinary 1-OHP Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)



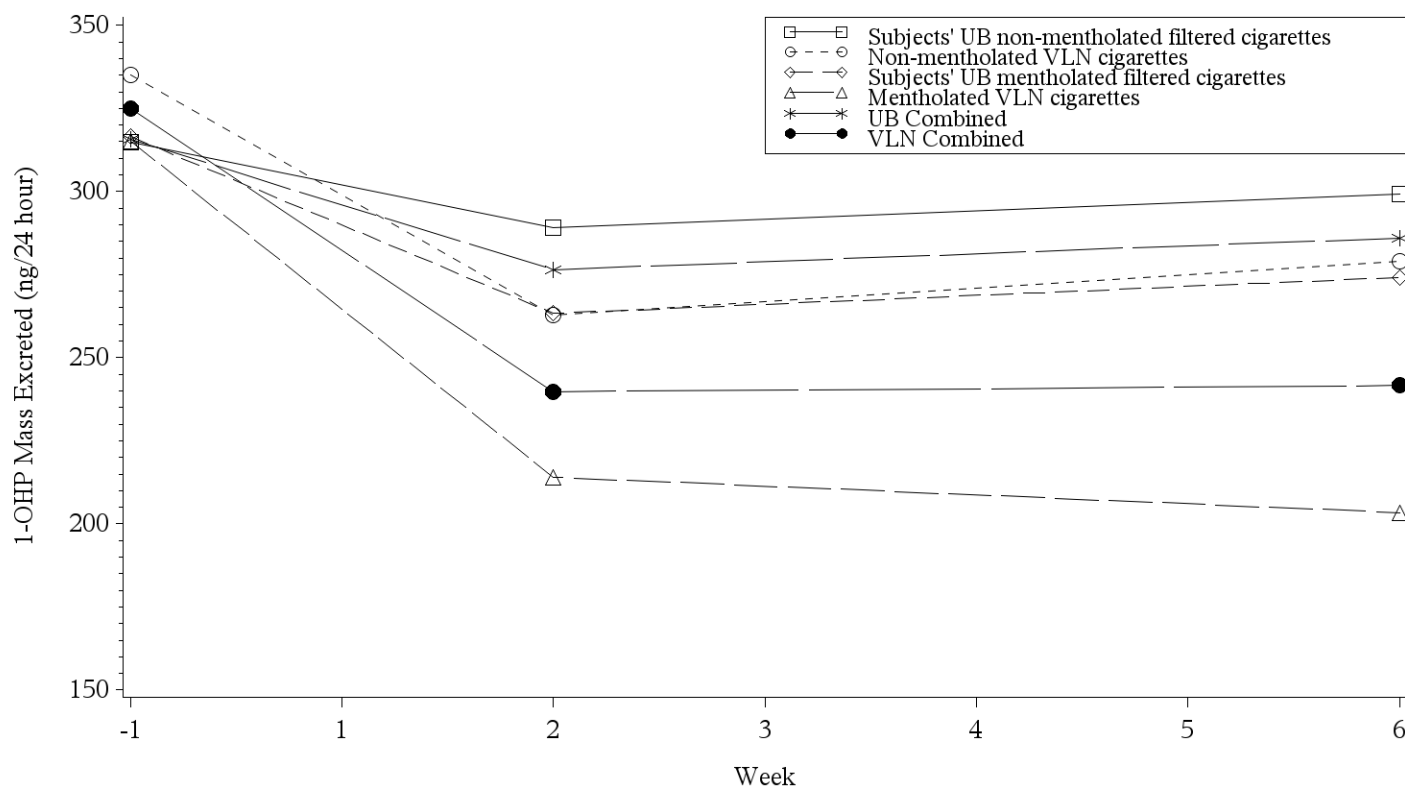
All products except UB Non-Mentholated are shifted to the right for ease of reading

Subjects used their own usual brand cigarettes at Week -1

Program: /CA24914/sas_prg/pksas/pdurine/adam_urinemeangraph.sas 12JUN2019 10:37

Figure 14.2.6.5.4

Mean Urinary 1-OHP Mass Excreted (ng/24 hour) by Study Product Group and Study Week (ITT Population)

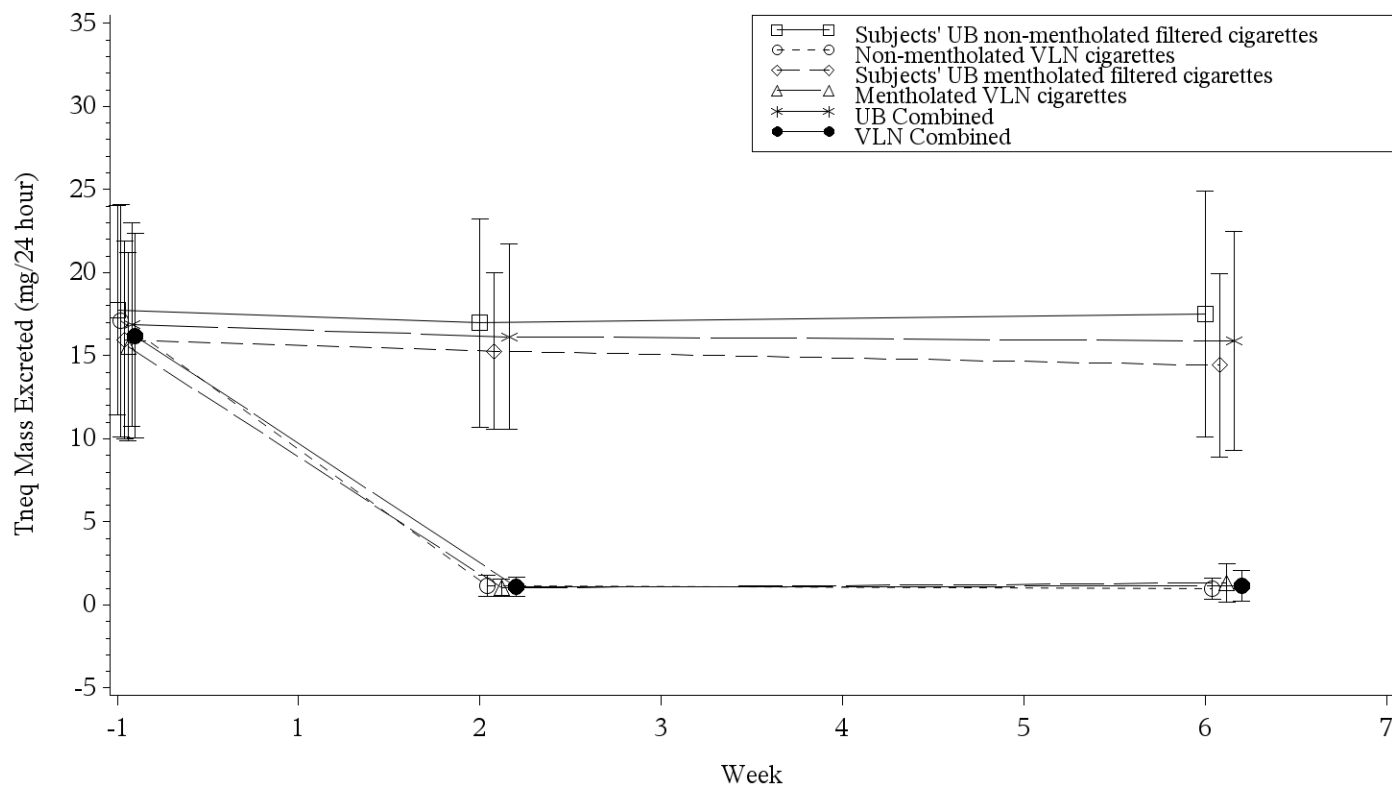


Subjects used their own usual brand cigarettes at Week -1

Program: /CA24914/sas_prg/pksas/pdurine/adam_urinemeangraph.sas 12JUN2019 10:37

Figure 14.2.6.6.1

Mean (\pm SD) of Urinary Tneq Mass Excreted (mg/24 hour) by Study Product Group and Study Week (PP Population)



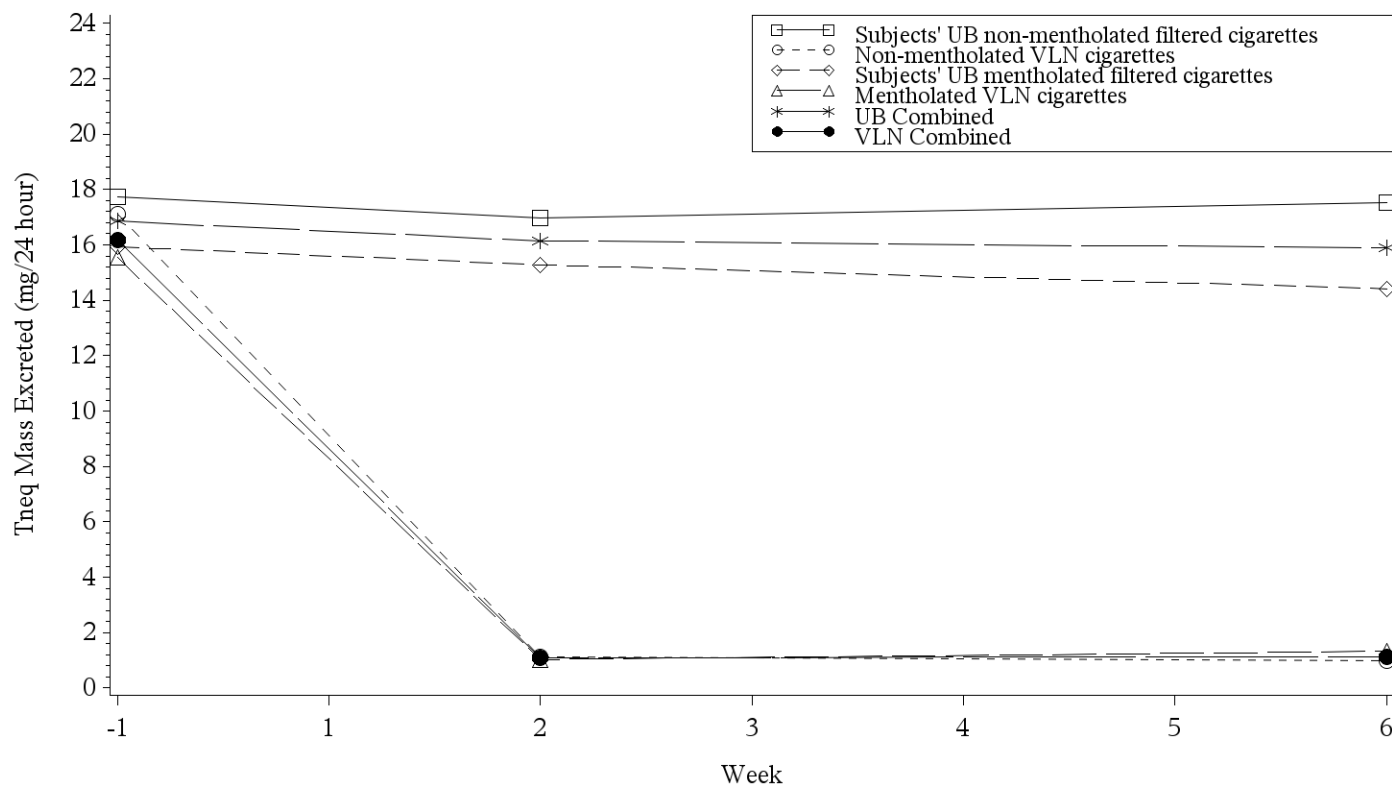
All products except UB Non-Mentholated are shifted to the right for ease of reading

Subjects used their own usual brand cigarettes at Week -1

Program: /CA24914/sas_prg/pksas/pdurine/adam_urinemeangraph.sas 12JUN2019 10:37

Figure 14.2.6.6.2

Mean Urinary Tneq Mass Excreted (mg/24 hour) by Study Product Group and Study Week (PP Population)

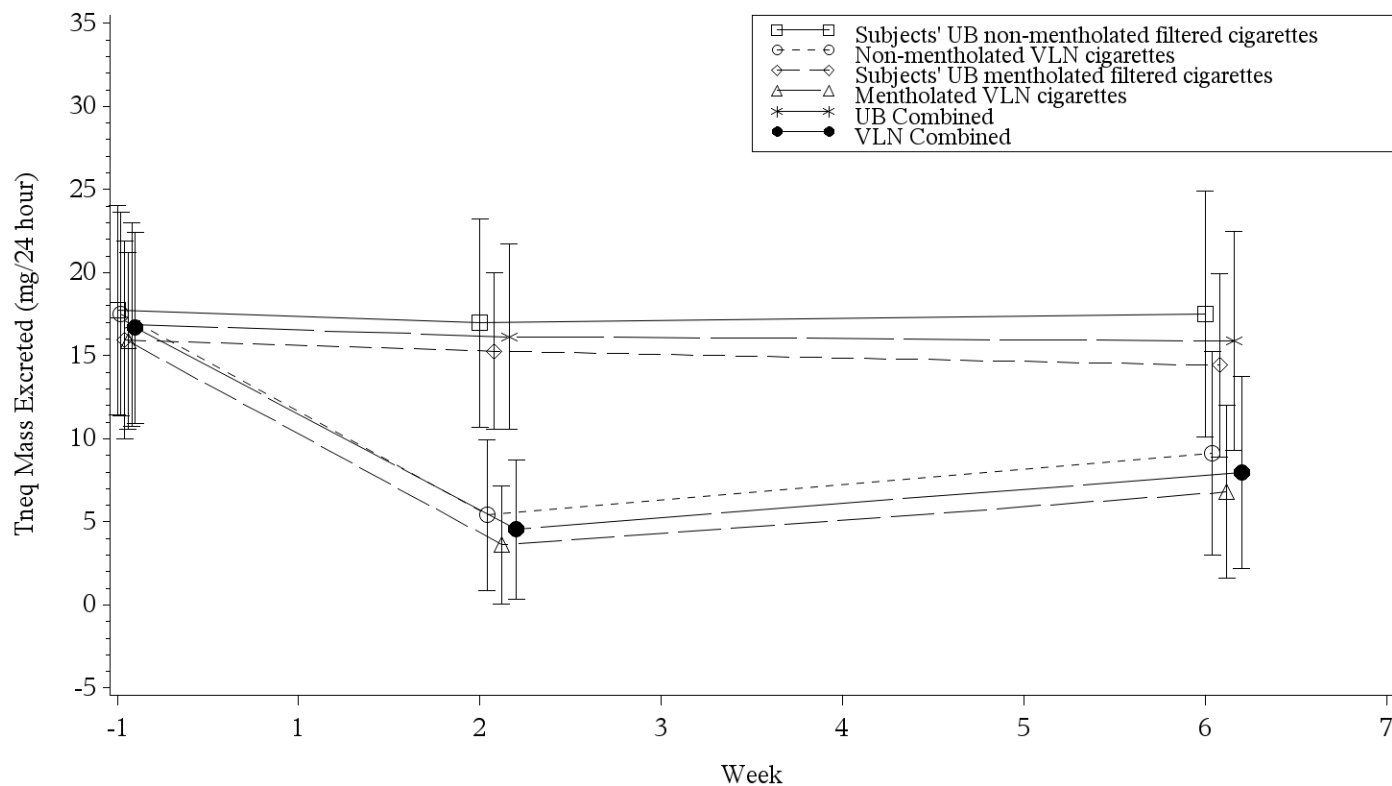


Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.6.3

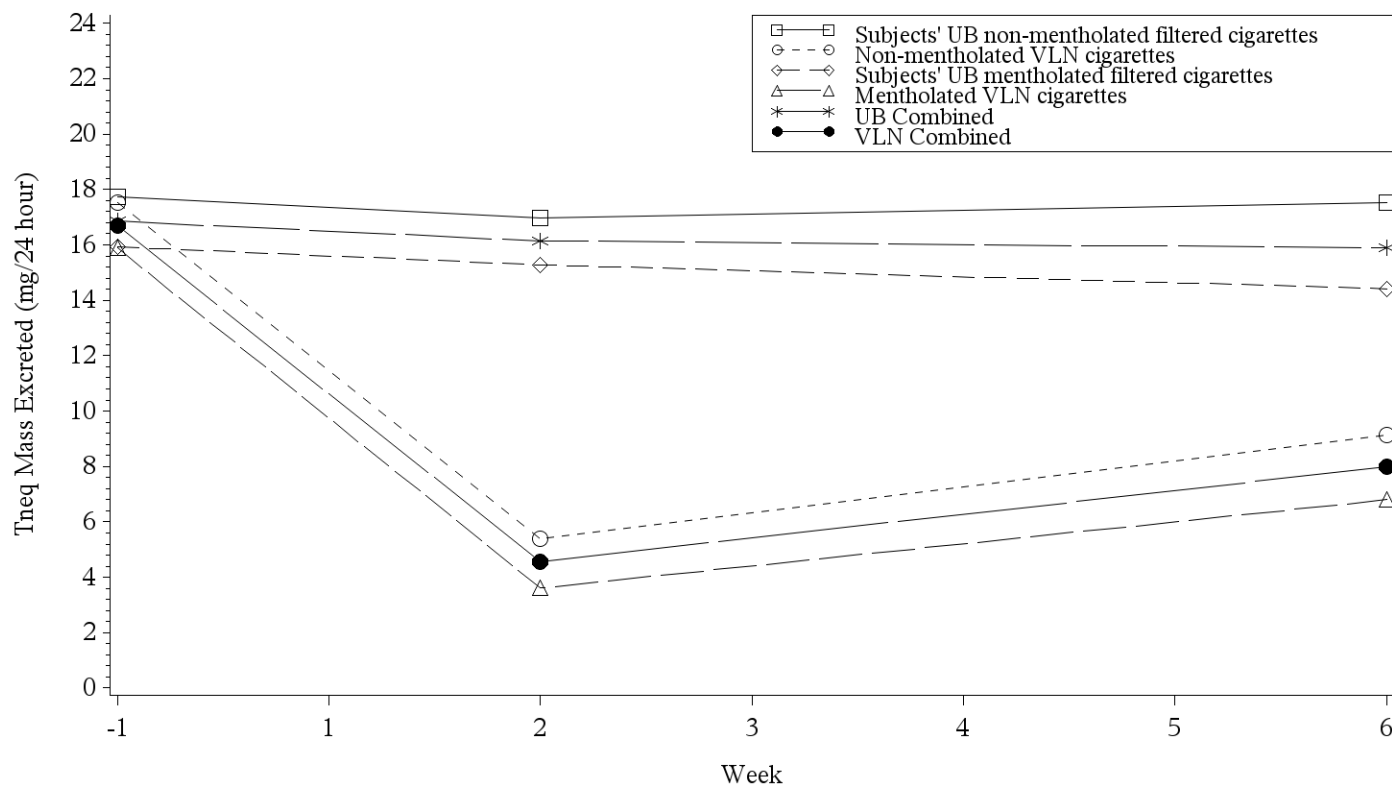
Mean (\pm SD) of Urinary Tneq Mass Excreted (mg/24 hour) by Study Product Group and Study Week (ITT Population)



All products except UB Non-Mentholated are shifted to the right for ease of reading
 Subjects used their own usual brand cigarettes at Week -1
 Program: /CA24914/sas_prg/pksas/pdurine/adam_urinemeangraph.sas 12JUN2019 10:37

Figure 14.2.6.6.4

Mean Urinary Tneq Mass Excreted (mg/24 hour) by Study Product Group and Study Week (ITT Population)

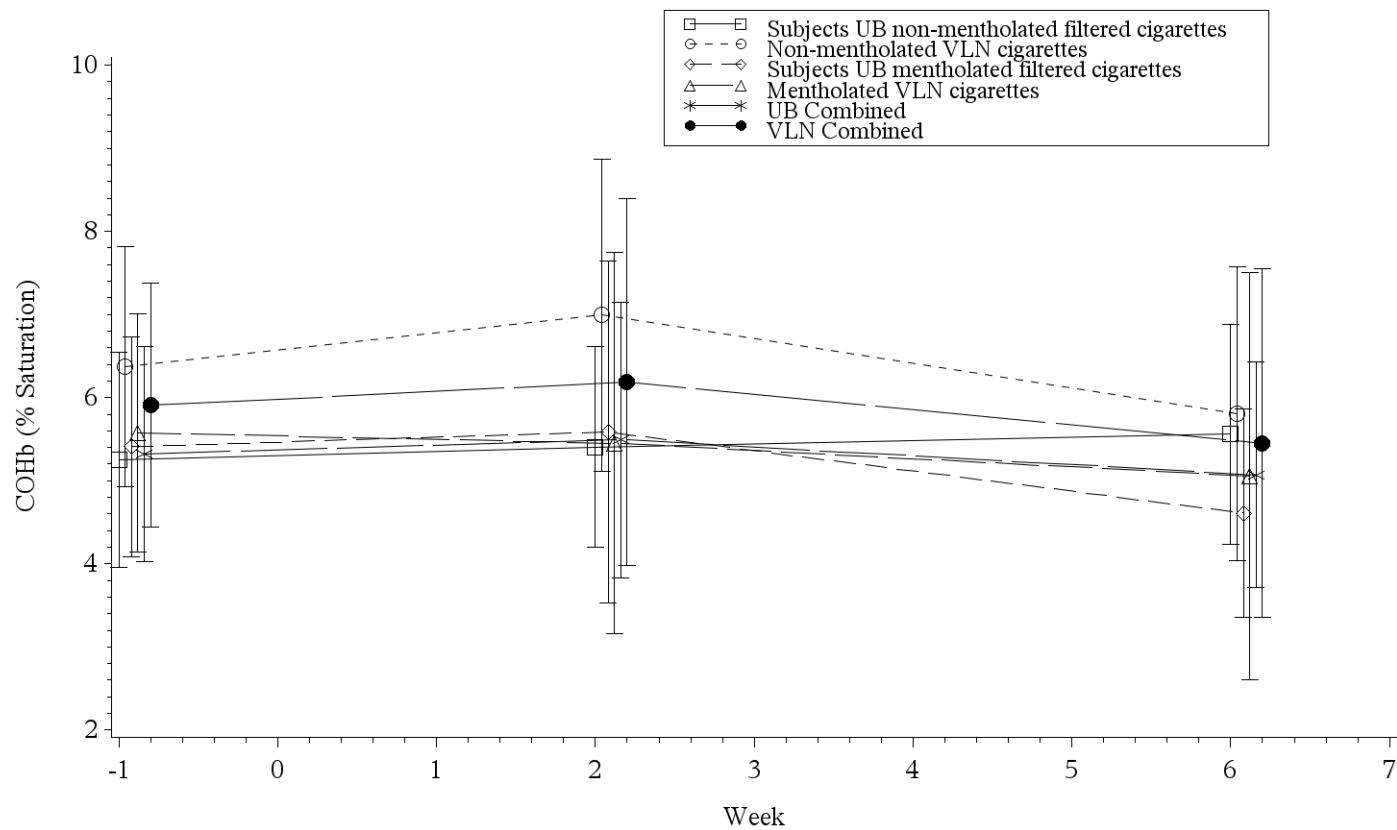


Subjects used their own usual brand cigarettes at Week -1

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Figure 14.2.6.7.1

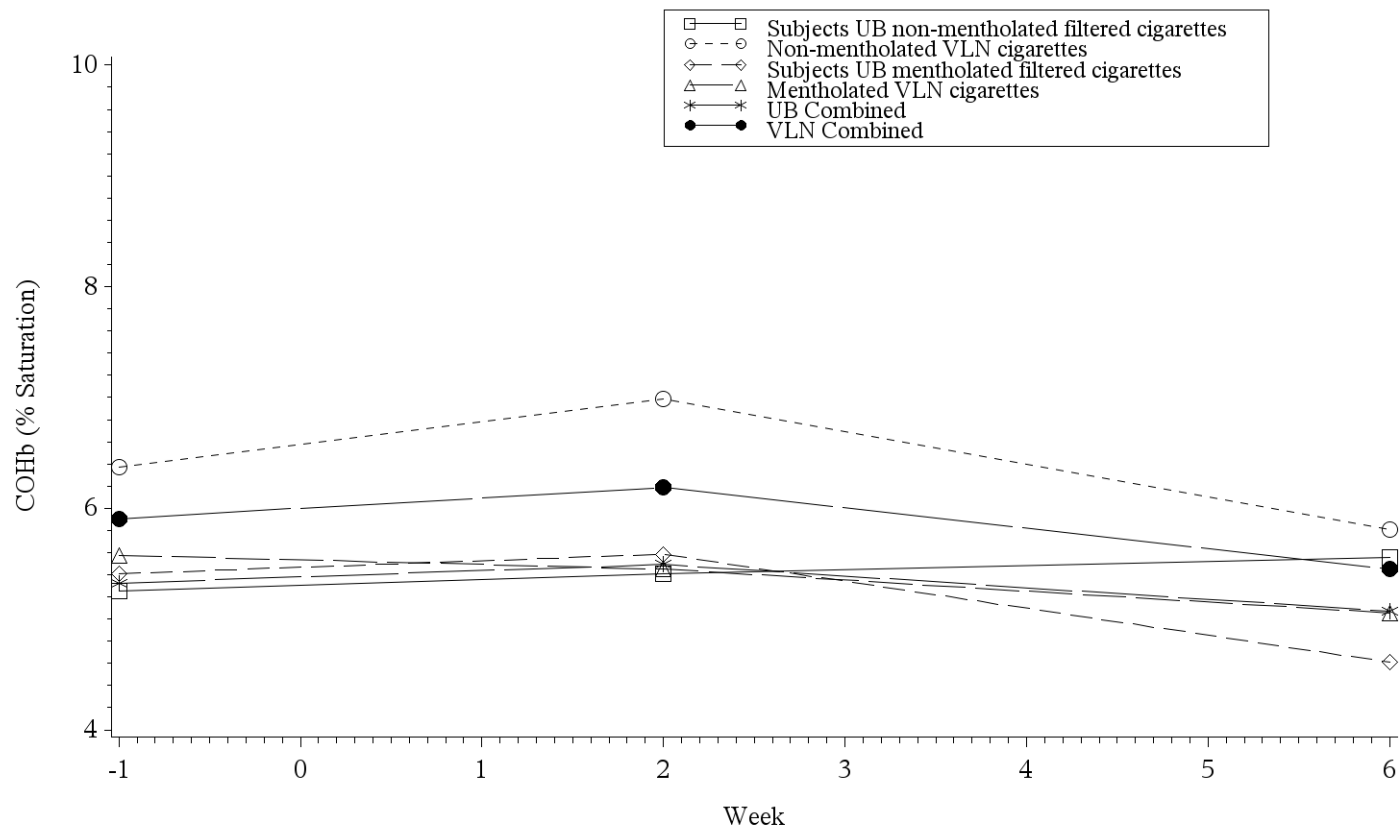
Mean (\pm SD) of Blood COHb (% Saturation) by Study Product Group and Study Week (PP Population)



All products except UB Non-Mentholated are shifted to the right for ease of reading
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Figure 14.2.6.7.2

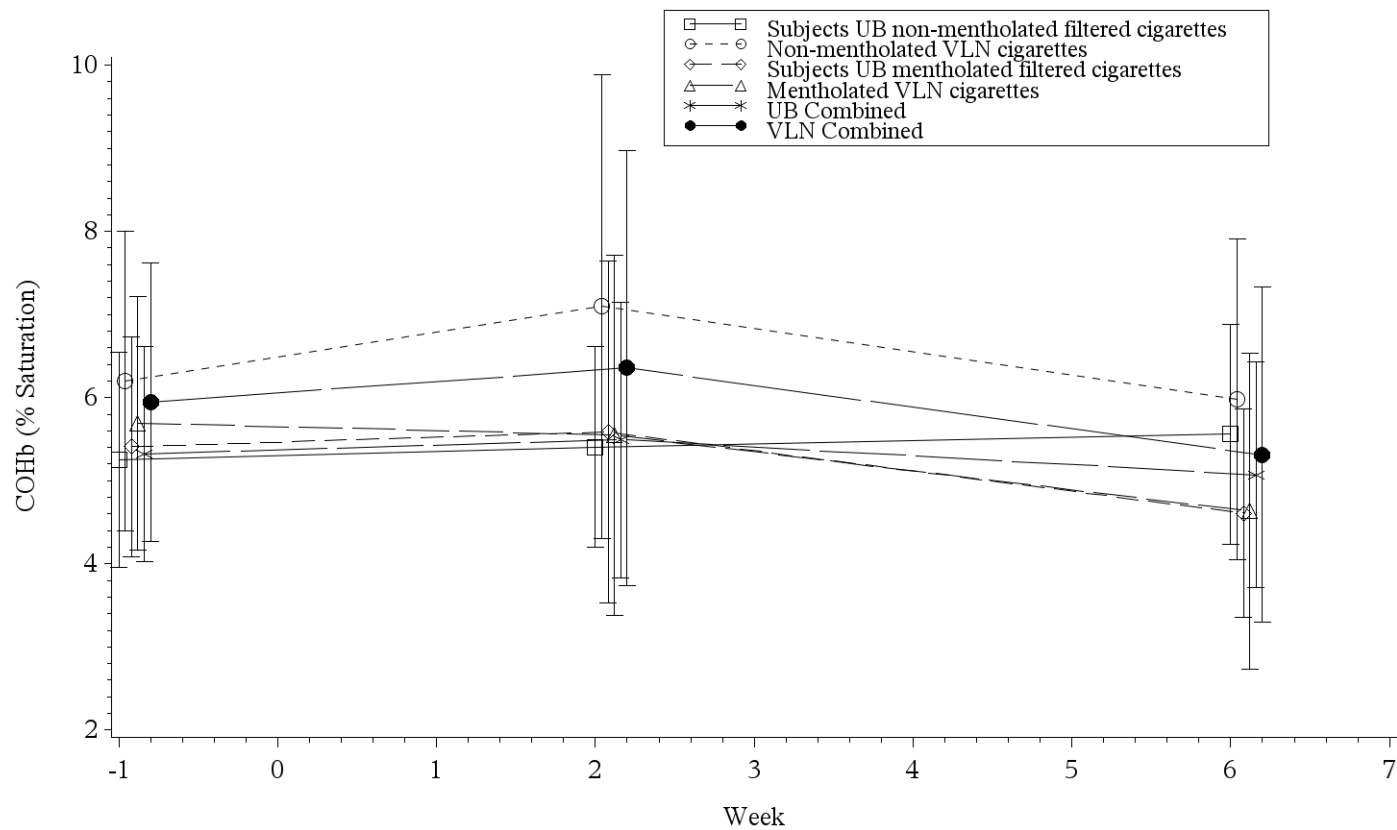
Mean Blood COHb (% Saturation) by Study Product Group and Study Week (PP Population)



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Figure 14.2.6.7.3

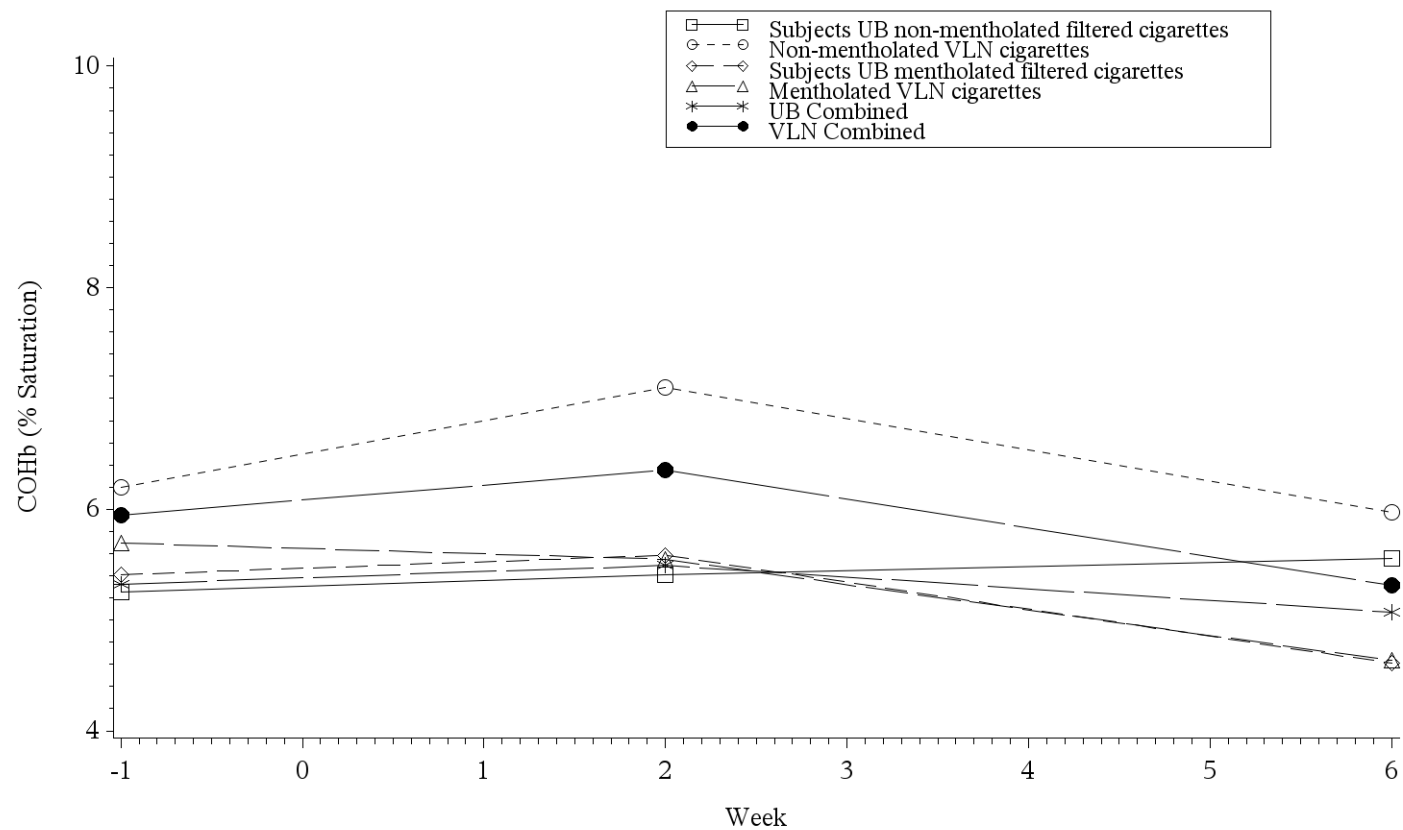
Mean (\pm SD) of Blood COHb (% Saturation) by Study Product Group and Study Week (ITT Population)



All products except UB Non-Mentholated are shifted to the right for ease of reading
 Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodmeangraph_comb.sas 12JUN2019 9:29

Figure 14.2.6.7.4

Mean Blood COHb (% Saturation) by Study Product Group and Study Week (ITT Population)



Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodmeangraph_comb.sas 12JUN2019 9:29

14.2.7 Plasma Nicotine Tables

Concentrations

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Pharmacokinetics

- Table 14.2.7.5.1 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of UB Non-Mentholated Filtered Cigarettes (Week -1) (Pharmacokinetic Population from PP)
- Table 14.2.7.5.2 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of UB Non-Mentholated Filtered Cigarettes (Week -1) (Pharmacokinetic Population from ITT)

Table 14.2.7.6.1	Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of Non-Mentholated VLN Cigarettes (Week 2) (Pharmacokinetic Population from PP)
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Table 14.2.7.1.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week -1 (minutes)						
	Pre-Use	2	5	7	10	12	15
1007	0.418	2.24	7.65	8.77	8.73	8.29	7.21

Table 14.2.7.1.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week -1 (minutes)							
	20	30	45	60	90	120	150	180
1007	7.12	6.06	4.95	4.70	3.45	2.28	2.68	1.97

Table 14.2.7.1.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 2 (minutes)						
	Pre-Use	2	5	7	10	12	15
1007	BLQ	0.404	0.645	0.436	0.385	0.325	0.300

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.1.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	----- Week 2 (minutes) -----							
	20	30	45	60	90	120	150	180
1007	0.295	0.274	0.210	BLQ	0.246	0.207	BLQ	BLQ

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.1.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 6 (minutes)						
	Pre-Use	2	5	7	10	12	15
1007	BLQ	0.713	0.623	0.429	0.419	0.378	0.378

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.1.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 6 (minutes)							
	20	30	45	60	90	120	150	180
1007	0.340	0.254	0.320	0.233	0.255	0.202	BLQ	0.256

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.1.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Pre-Use	2	5	7	10	12	15
1001	0.427	6.37	10.8	14.4	14.3	14.4	15.5
1002	1.20	1.80	5.52	7.57	9.44	8.08	8.77
1007	0.418	2.24	7.65	8.77	8.73	8.29	7.21
1013	0.602	8.30	15.9	19.0	10.5	10.2	8.01
1019	1.06	9.68	17.6
1020	1.20	7.68	29.0	24.1	19.6	15.4	14.0
1023	0.265	1.93	6.97	7.03	7.18	6.69	7.01
1035	1.87	2.62	8.35	8.09	7.74	7.63	7.36
1038	0.484	7.49	10.3	11.6	9.95	9.91	11.2
1042	0.457	2.59	12.1	14.5	10.2	7.88	7.07
1056	0.391	6.64	10.2	12.5	11.1	10.3	11.2
1058	0.989	7.36	15.1	15.3	12.5	12.3	11.9
Overall							
n	12	12	12	11	11	11	11
Mean	0.7803	5.392	12.46	12.99	11.02	10.10	9.930
SD	0.48231	2.9112	6.3945	5.2730	3.4915	2.8552	3.0073
CV%	61.8	54.0	51.3	40.6	31.7	28.3	30.3
SEM	0.13923	0.84039	1.8459	1.5899	1.0527	0.86087	0.90673
Minimum	0.265	1.80	5.52	7.03	7.18	6.69	7.01
Median	0.5430	6.505	10.55	12.50	10.20	9.910	8.770
Maximum	1.87	9.68	29.0	24.1	19.6	15.4	15.5

. = Value missing or not reportable.

Table 14.2.7.1.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week -1 (minutes)						
	Pre-Use	2	5	7	10	12	15
Female							
n	5	5	5	5	5	5	5
Mean	0.5956	6.354	14.59	15.23	12.31	11.32	11.14
SD	0.35900	2.5694	8.6631	6.5954	4.8028	3.5641	3.6758
CV%	60.3	40.4	59.4	43.3	39.0	31.5	33.0
SEM	0.16055	1.1491	3.8743	2.9495	2.1479	1.5939	1.6439
Minimum	0.265	1.93	6.97	7.03	7.18	6.69	7.01
Median	0.4840	7.490	10.80	14.40	10.50	10.20	11.20
Maximum	1.20	8.30	29.0	24.1	19.6	15.4	15.5
Male							
n	7	7	7	6	6	6	6
Mean	0.9121	4.704	10.93	11.12	9.952	9.080	8.918
SD	0.54022	3.1326	4.2907	3.4090	1.7041	1.8452	2.1392
CV%	59.2	66.6	39.3	30.7	17.1	20.3	24.0
SEM	0.20418	1.1840	1.6217	1.3917	0.69570	0.75329	0.87334
Minimum	0.391	1.80	5.52	7.57	7.74	7.63	7.07
Median	0.9890	2.620	10.20	10.64	9.820	8.185	8.065
Maximum	1.87	9.68	17.6	15.3	12.5	12.3	11.9

Table 14.2.7.1.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week -1 (minutes)							
	20	30	45	60	90	120	150	180
1001	14.3	12.0	9.07	7.32	5.91	4.07	3.08	2.67
1002	7.71	8.10	7.35	6.58	5.54	5.42	4.32	3.64
1007	7.12	6.06	4.95	4.70	3.45	2.28	2.68	1.97
1013	8.68	7.97	7.21	6.32	5.08	3.81	3.48	2.92
1019	9.40	8.11	7.04	5.68	5.28	3.94	3.02	2.35
1020	12.5	10.9	8.60	6.79	5.77	4.56	4.16	3.58
1023	6.34	4.99	4.38	4.02	2.82	2.01	1.49	1.11
1035	6.66	6.31	5.44	5.44	4.09	3.54	3.00	2.51
1038	10.1	8.09	6.38	5.88	4.35	3.39	2.58	2.30
1042	5.64	4.02	2.74	2.56	1.87	1.66	1.14	1.00
1056	7.84	7.56	5.09	4.75	3.51	2.61	2.19	1.86
1058	11.7	11.0	9.37	7.98	5.81	5.14	4.38	3.87
Overall								
n	12	12	12	12	12	12	12	12
Mean	8.999	7.926	6.468	5.668	4.457	3.536	2.960	2.482
SD	2.6881	2.4325	2.0208	1.5028	1.3257	1.2060	1.0394	0.92831
CV%	29.9	30.7	31.2	26.5	29.7	34.1	35.1	37.4
SEM	0.77600	0.70221	0.58335	0.43382	0.38271	0.34814	0.30006	0.26798
Minimum	5.64	4.02	2.74	2.56	1.87	1.66	1.14	1.00
Median	8.260	8.030	6.710	5.780	4.715	3.675	3.010	2.430
Maximum	14.3	12.0	9.37	7.98	5.91	5.42	4.38	3.87

Table 14.2.7.1.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week -1 (minutes)							
	20	30	45	60	90	120	150	180

Female								
n	5	5	5	5	5	5	5	5
Mean	10.38	8.790	7.128	6.066	4.786	3.568	2.958	2.516
SD	3.1285	2.7549	1.8746	1.2631	1.2623	0.96872	1.0038	0.91413
CV%	30.1	31.3	26.3	20.8	26.4	27.2	33.9	36.3
SEM	1.3991	1.2320	0.83833	0.56489	0.56451	0.43323	0.44889	0.40881
Minimum	6.34	4.99	4.38	4.02	2.82	2.01	1.49	1.11
Median	10.10	8.090	7.210	6.320	5.080	3.810	3.080	2.670
Maximum	14.3	12.0	9.07	7.32	5.91	4.56	4.16	3.58

Male								
n	7	7	7	7	7	7	7	7
Mean	8.010	7.309	5.997	5.384	4.221	3.513	2.961	2.457
SD	1.9958	2.1729	2.1265	1.6884	1.4160	1.4281	1.1442	1.0105
CV%	24.9	29.7	35.5	31.4	33.5	40.7	38.6	41.1
SEM	0.75433	0.82128	0.80375	0.63817	0.53520	0.53976	0.43246	0.38194
Minimum	5.64	4.02	2.74	2.56	1.87	1.66	1.14	1.00
Median	7.710	7.560	5.440	5.440	4.090	3.540	3.000	2.350
Maximum	11.7	11.0	9.37	7.98	5.81	5.42	4.38	3.87

Table 14.2.7.1.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)						
	Pre-Use	2	5	7	10	12	15
1001	BLQ	BLQ	0.307	0.341	0.332	0.300	0.322
1002	BLQ	0.210	0.299	0.388	0.355	0.401	0.336
1007	BLQ	0.404	0.645	0.436	0.385	0.325	0.300
1013	BLQ	0.228	0.437	0.472	0.491	0.402	0.425
1019	BLQ	0.344	0.773	0.505	0.484	0.366	0.367
1020	BLQ	BLQ	0.368	0.415	0.378	0.348	0.281
1023	BLQ	BLQ	0.205	0.262	0.238	0.242	0.201
1035	0.545	0.456	0.818	0.676	0.613	0.676	0.673
1038	BLQ	BLQ	0.214	0.292	0.315	0.213	BLQ
1042	BLQ	BLQ	0.249	0.225	0.200	BLQ	BLQ
1056	BLQ	BLQ	0.479	0.425	0.349	0.312	0.243
1058	0.599	0.613	0.869	0.791	0.688	0.680	0.734
Overall							
n	12	12	12	12	12	12	12
Mean	0.1787	0.2379	0.4719	0.4357	0.4023	0.3638	0.3402
SD	0.18409	0.17635	0.24396	0.16435	0.14366	0.16948	0.19620
CV%	103.0	74.1	51.7	37.7	35.7	46.6	57.7
SEM	0.053141	0.050908	0.070425	0.047443	0.041470	0.048926	0.056637
Minimum	0.100	0.100	0.205	0.225	0.200	0.100	0.100
Median	0.1000	0.1550	0.4025	0.4200	0.3665	0.3365	0.3110
Maximum	0.599	0.613	0.869	0.791	0.688	0.680	0.734

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.1.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)						
	Pre-Use	2	5	7	10	12	15
Female							
n	5	5	5	5	5	5	5
Mean	0.1000	0.1256	0.3062	0.3564	0.3508	0.3010	0.2658
SD	0.00	0.057243	0.099588	0.086737	0.093213	0.076870	0.12291
CV%	0.00	45.6	32.5	24.3	26.6	25.5	46.2
SEM	0.00	0.025600	0.044537	0.038790	0.041686	0.034377	0.054965
Minimum	0.100	0.100	0.205	0.262	0.238	0.213	0.100
Median	0.1000	0.1000	0.3070	0.3410	0.3320	0.3000	0.2810
Maximum	0.100	0.228	0.437	0.472	0.491	0.402	0.425
Male							
n	7	7	7	7	7	7	7
Mean	0.2349	0.3181	0.5903	0.4923	0.4391	0.4086	0.3933
SD	0.23084	0.19186	0.25154	0.18848	0.16807	0.20760	0.22935
CV%	98.3	60.3	42.6	38.3	38.3	50.8	58.3
SEM	0.087249	0.072515	0.095072	0.071240	0.063526	0.078466	0.086685
Minimum	0.100	0.100	0.249	0.225	0.200	0.100	0.100
Median	0.1000	0.3440	0.6450	0.4360	0.3850	0.3660	0.3360
Maximum	0.599	0.613	0.869	0.791	0.688	0.680	0.734

Table 14.2.7.1.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)							
	20	30	45	60	90	120	150	180
1001	0.239	0.235	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1002	0.338	0.368	0.341	0.282	0.355	0.226	0.255	0.214
1007	0.295	0.274	0.210	BLQ	0.246	0.207	BLQ	BLQ
1013	0.361	0.331	0.301	0.241	0.230	BLQ	0.252	BLQ
1019	0.344	0.344	0.262	0.272	0.200	BLQ	0.226	0.303
1020	0.285	0.334	0.242	0.263	BLQ	BLQ	BLQ	BLQ
1023	0.208	0.204	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1035	0.603	0.539	0.527	0.505	0.455	0.470	0.457	0.417
1038	0.204	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1042	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1056	0.249	0.206	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1058	0.687	0.603	0.639	0.601	0.473	0.453	0.426	0.370
Overall								
n	12	12	12	12	12	12	12	12
Mean	0.3261	0.3032	0.2518	0.2303	0.2133	0.1797	0.1930	0.1753
SD	0.16645	0.15387	0.17919	0.17065	0.14286	0.13905	0.13244	0.12041
CV%	51.0	50.8	71.2	74.1	67.0	77.4	68.6	68.7
SEM	0.048050	0.044419	0.051728	0.049263	0.041239	0.040139	0.038232	0.034760
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.2900	0.3025	0.2260	0.1705	0.1500	0.1000	0.1000	0.1000
Maximum	0.687	0.603	0.639	0.601	0.473	0.470	0.457	0.417

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.1.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	5	5	5	5	5	5	5	5
Mean	0.2594	0.2408	0.1686	0.1608	0.1260	0.1000	0.1304	0.1000
SD	0.065393	0.097513	0.096223	0.083616	0.058138	0.00	0.067976	0.00
CV%	25.2	40.5	57.1	52.0	46.1	0.00	52.1	0.00
SEM	0.029245	0.043609	0.043032	0.037394	0.026000	0.00	0.030400	0.00
Minimum	0.204	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.2390	0.2350	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
Maximum	0.361	0.334	0.301	0.263	0.230	0.100	0.252	0.100
Male								
n	7	7	7	7	7	7	7	7
Mean	0.3737	0.3477	0.3113	0.2800	0.2756	0.2366	0.2377	0.2291
SD	0.20394	0.17751	0.20687	0.20451	0.15584	0.16241	0.15323	0.13592
CV%	54.6	51.1	66.5	73.0	56.6	68.7	64.5	59.3
SEM	0.077082	0.067094	0.078191	0.077296	0.058902	0.061387	0.057914	0.051374
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.3380	0.3440	0.2620	0.2720	0.2460	0.2070	0.2260	0.2140
Maximum	0.687	0.603	0.639	0.601	0.473	0.470	0.457	0.417

Table 14.2.7.1.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)						
	Pre-Use	2	5	7	10	12	15
1001	BLQ	.	0.370	0.529	0.563	0.558	0.402
1002	0.241	0.277	0.331	0.353	0.363	0.530	0.364
1007	BLQ	0.713	0.623	0.429	0.419	0.378	0.378
1013	BLQ	0.234	0.340	0.399	0.348	0.387	0.353
1019	0.842	1.11	1.49	1.38	1.14	1.06	1.03
1020	0.200	0.658	0.759	0.763	0.581	0.541	0.483
1023	BLQ	BLQ	0.291	0.304	0.241	0.283	0.344
1035	0.532	0.647	0.835	0.791	0.536	0.677	0.676
1038	BLQ	0.201	0.394	0.387	0.412	0.361	0.341
1042	BLQ	0.270	0.318	BLQ	BLQ	BLQ	BLQ
1056	BLQ	BLQ	0.619	0.490	0.368	0.346	0.313
1058	1.84	1.83	2.16	2.17	1.97	1.99	1.98
Overall							
n	12	11	12	12	12	12	12
Mean	0.3629	0.5582	0.7108	0.6746	0.5868	0.6009	0.5637
SD	0.51919	0.52711	0.56969	0.57211	0.50387	0.49786	0.50119
CV%	143.1	94.4	80.1	84.8	85.9	82.9	88.9
SEM	0.14988	0.15893	0.16445	0.16515	0.14545	0.14372	0.14468
Minimum	0.100	0.100	0.291	0.100	0.100	0.100	0.100
Median	0.1000	0.2770	0.5065	0.4595	0.4155	0.4585	0.3710
Maximum	1.84	1.83	2.16	2.17	1.97	1.99	1.98

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.
. = Value missing or not reportable.

Table 14.2.7.1.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)						
	Pre-Use	2	5	7	10	12	15
Female							
n	5	4	5	5	5	5	5
Mean	0.1200	0.2983	0.4308	0.4764	0.4290	0.4260	0.3846
SD	0.044721	0.24651	0.18745	0.17931	0.14427	0.11921	0.060277
CV%	37.3	82.7	43.5	37.6	33.6	28.0	15.7
SEM	0.020000	0.12326	0.083832	0.080191	0.064519	0.053312	0.026957
Minimum	0.100	0.100	0.291	0.304	0.241	0.283	0.341
Median	0.1000	0.2175	0.3700	0.3990	0.4120	0.3870	0.3530
Maximum	0.200	0.658	0.759	0.763	0.581	0.558	0.483
Male							
n	7	7	7	7	7	7	7
Mean	0.5364	0.7067	0.9109	0.8161	0.6994	0.7259	0.6916
SD	0.63919	0.60159	0.67790	0.72285	0.64500	0.63344	0.64210
CV%	119.2	85.1	74.4	88.6	92.2	87.3	92.8
SEM	0.24159	0.22738	0.25622	0.27321	0.24379	0.23942	0.24269
Minimum	0.100	0.100	0.318	0.100	0.100	0.100	0.100
Median	0.2410	0.6470	0.6230	0.4900	0.4190	0.5300	0.3780
Maximum	1.84	1.83	2.16	2.17	1.97	1.99	1.98

Table 14.2.7.1.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)							
	20	30	45	60	90	120	150	180
1001	0.588	0.393	0.332	0.317	0.221	0.204	BLQ	BLQ
1002	0.336	0.300	0.410	0.303	0.306	0.284	0.232	0.275
1007	0.340	0.254	0.320	0.233	0.255	0.202	BLQ	0.256
1013	0.332	0.367	0.290	0.263	0.275	0.216	BLQ	0.224
1019	1.06	1.10	1.03	0.815	0.895	0.738	0.732	0.620
1020	0.409	0.367	0.331	0.309	0.322	0.213	0.338	0.214
1023	0.285	0.275	BLQ	0.230	0.208	BLQ	BLQ	BLQ
1035	0.637	0.550	0.563	0.507	0.553	0.479	0.472	0.422
1038	0.369	0.294	0.279	0.236	BLQ	0.288	BLQ	BLQ
1042	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1056	0.278	0.289	0.302	BLQ	BLQ	0.206	BLQ	BLQ
1058	1.98	1.75	1.76	1.60	1.49	1.36	1.12	1.04
Overall								
n	12	12	12	12	12	12	12	12
Mean	0.5595	0.5033	0.4848	0.4178	0.4021	0.3658	0.2995	0.2959
SD	0.50898	0.46415	0.46896	0.41854	0.40976	0.35906	0.32679	0.28291
CV%	91.0	92.2	96.7	100.2	101.9	98.1	109.1	95.6
SEM	0.14693	0.13399	0.13538	0.12082	0.11829	0.10365	0.094335	0.081669
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.3545	0.3335	0.3255	0.2830	0.2650	0.2145	0.1000	0.2190
Maximum	1.98	1.75	1.76	1.60	1.49	1.36	1.12	1.04

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.1.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	5	5	5	5	5	5	5	5
Mean	0.3966	0.3392	0.2664	0.2710	0.2252	0.2042	0.1476	0.1476
SD	0.11638	0.051490	0.096022	0.040404	0.083425	0.067262	0.10644	0.065275
CV%	29.3	15.2	36.0	14.9	37.0	32.9	72.1	44.2
SEM	0.052047	0.023027	0.042943	0.018069	0.037309	0.030081	0.047600	0.029192
Minimum	0.285	0.275	0.100	0.230	0.100	0.100	0.100	0.100
Median	0.3690	0.3670	0.2900	0.2630	0.2210	0.2130	0.1000	0.1000
Maximum	0.588	0.393	0.332	0.317	0.322	0.288	0.338	0.224
Male								
n	7	7	7	7	7	7	7	7
Mean	0.6759	0.6204	0.6407	0.5226	0.5284	0.4813	0.4080	0.4019
SD	0.65423	0.59561	0.57352	0.53787	0.50842	0.44274	0.39404	0.33537
CV%	96.8	96.0	89.5	102.9	96.2	92.0	96.6	83.5
SEM	0.24727	0.22512	0.21677	0.20329	0.19216	0.16734	0.14893	0.12676
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.3400	0.3000	0.4100	0.3030	0.3060	0.2840	0.2320	0.2750
Maximum	1.98	1.75	1.76	1.60	1.49	1.36	1.12	1.04

Table 14.2.7.2.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Pre-Use	2	5	7	10	12	15
1015	0.345	3.29	13.1	20.4	18.8	14.3	10.0
1018	0.634	9.86	12.5	13.5	10.9	9.71	8.55
1032	0.768	3.65	.	9.76	10.6	10.2	9.78
1063	0.848	1.83	5.59	7.80	6.72	7.53	6.85
1072	0.431	1.08	6.70	5.63	6.42	7.54	6.23
Overall							
n	5	5	4	5	5	5	5
Mean	0.6052	3.942	9.473	11.42	10.69	9.856	8.282
SD	0.21467	3.4708	3.8766	5.7955	4.9954	2.7687	1.6977
CV%	35.5	88.0	40.9	50.8	46.7	28.1	20.5
SEM	0.096004	1.5522	1.9383	2.5918	2.2340	1.2382	0.75923
Minimum	0.345	1.08	5.59	5.63	6.42	7.53	6.23
Median	0.6340	3.290	9.600	9.760	10.60	9.710	8.550
Maximum	0.848	9.86	13.1	20.4	18.8	14.3	10.0

. = Value missing or not reportable.

Table 14.2.7.2.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Pre-Use	2	Week -1 (minutes) 5	7	10	12	15

Female							
n	3	3	2	3	3	3	3
Mean	0.5823	5.600	12.80	14.55	13.43	11.40	9.443
SD	0.21618	3.6937	0.42426	5.3976	4.6501	2.5205	0.78143
CV%	37.1	66.0	3.3	37.1	34.6	22.1	8.3
SEM	0.12481	2.1325	0.30000	3.1163	2.6847	1.4552	0.45116
Minimum	0.345	3.29	12.5	9.76	10.6	9.71	8.55
Median	0.6340	3.650	12.80	13.50	10.90	10.20	9.780
Maximum	0.768	9.86	13.1	20.4	18.8	14.3	10.0

Male							
n	2	2	2	2	2	2	2
Mean	0.6395	1.455	6.145	6.715	6.570	7.535	6.540
SD	0.29486	0.53033	0.78489	1.5344	0.21213	0.0070711	0.43841
CV%	46.1	36.4	12.8	22.9	3.2	0.1	6.7
SEM	0.20850	0.37500	0.55500	1.0850	0.15000	0.0050000	0.31000
Minimum	0.431	1.08	5.59	5.63	6.42	7.53	6.23
Median	0.6395	1.455	6.145	6.715	6.570	7.535	6.540
Maximum	0.848	1.83	6.70	7.80	6.72	7.54	6.85

Table 14.2.7.2.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week -1 (minutes)							
	20	30	45	60	90	120	150	180
1015	10.0	8.54	5.80	5.34	3.81	2.80	2.15	1.74
1018	6.49	5.66	4.48	3.59	2.66	2.17	2.00	1.51
1032	9.78	8.28	6.92	5.66	4.49	3.47	2.62	2.33
1063	6.33	6.26	5.20	4.45	3.57	3.04	2.14	1.85
1072	5.99	6.11	5.55	5.09	3.91	2.98	2.42	1.79
Overall								
n	5	5	5	5	5	5	5	5
Mean	7.718	6.970	5.590	4.826	3.688	2.892	2.266	1.844
SD	1.9925	1.3361	0.89426	0.82136	0.66672	0.47262	0.24956	0.30063
CV%	25.8	19.2	16.0	17.0	18.1	16.3	11.0	16.3
SEM	0.89106	0.59753	0.39992	0.36732	0.29817	0.21136	0.11161	0.13445
Minimum	5.99	5.66	4.48	3.59	2.66	2.17	2.00	1.51
Median	6.490	6.260	5.550	5.090	3.810	2.980	2.150	1.790
Maximum	10.0	8.54	6.92	5.66	4.49	3.47	2.62	2.33

Table 14.2.7.2.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week -1 (minutes)							
	20	30	45	60	90	120	150	180

Female								
n	3	3	3	3	3	3	3	3
Mean	8.757	7.493	5.733	4.863	3.653	2.813	2.257	1.860
SD	1.9661	1.5930	1.2214	1.1143	0.92500	0.65010	0.32347	0.42297
CV%	22.5	21.3	21.3	22.9	25.3	23.1	14.3	22.7
SEM	1.1351	0.91973	0.70516	0.64333	0.53405	0.37534	0.18676	0.24420
Minimum	6.49	5.66	4.48	3.59	2.66	2.17	2.00	1.51
Median	9.780	8.280	5.800	5.340	3.810	2.800	2.150	1.740
Maximum	10.0	8.54	6.92	5.66	4.49	3.47	2.62	2.33

Male								
n	2	2	2	2	2	2	2	2
Mean	6.160	6.185	5.375	4.770	3.740	3.010	2.280	1.820
SD	0.24042	0.10607	0.24749	0.45255	0.24042	0.042426	0.19799	0.042426
CV%	3.9	1.7	4.6	9.5	6.4	1.4	8.7	2.3
SEM	0.17000	0.075000	0.17500	0.32000	0.17000	0.030000	0.14000	0.030000
Minimum	5.99	6.11	5.20	4.45	3.57	2.98	2.14	1.79
Median	6.160	6.185	5.375	4.770	3.740	3.010	2.280	1.820
Maximum	6.33	6.26	5.55	5.09	3.91	3.04	2.42	1.85

Table 14.2.7.2.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 2 (minutes)						
	Pre-Use	2	5	7	10	12	15
1015	BLQ	BLQ	0.248	0.327	0.337	0.318	0.304
1032	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1063	BLQ	0.205	0.586	0.316	0.225	0.232	0.218
1072	BLQ	BLQ	0.213	0.213	0.205	BLQ	0.230
Overall							
n	4	4	4	4	4	4	4
Mean	0.1000	0.1263	0.2868	0.2390	0.2168	0.1875	0.2130
SD	0.00	0.052500	0.20926	0.10594	0.097120	0.10696	0.084388
CV%	0.00	41.6	73.0	44.3	44.8	57.0	39.6
SEM	0.00	0.026250	0.10463	0.052970	0.048560	0.053481	0.042194
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.1000	0.1000	0.2305	0.2645	0.2150	0.1660	0.2240
Maximum	0.100	0.205	0.586	0.327	0.337	0.318	0.304

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.2.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 2 (minutes)						
	Pre-Use	2	5	7	10	12	15
Female							
n	2	2	2	2	2	2	2
Mean	0.1000	0.1000	0.1740	0.2135	0.2185	0.2090	0.2020
SD	0.00	0.00	0.10465	0.16051	0.16758	0.15415	0.14425
CV%	0.00	0.00	60.1	75.2	76.7	73.8	71.4
SEM	0.00	0.00	0.074000	0.11350	0.11850	0.10900	0.10200
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.1000	0.1000	0.1740	0.2135	0.2185	0.2090	0.2020
Maximum	0.100	0.100	0.248	0.327	0.337	0.318	0.304
Male							
n	2	2	2	2	2	2	2
Mean	0.1000	0.1525	0.3995	0.2645	0.2150	0.1660	0.2240
SD	0.00	0.074246	0.26375	0.072832	0.014142	0.093338	0.0084853
CV%	0.00	48.7	66.0	27.5	6.6	56.2	3.8
SEM	0.00	0.052500	0.18650	0.051500	0.010000	0.066000	0.0060000
Minimum	0.100	0.100	0.213	0.213	0.205	0.100	0.218
Median	0.1000	0.1525	0.3995	0.2645	0.2150	0.1660	0.2240
Maximum	0.100	0.205	0.586	0.316	0.225	0.232	0.230

Table 14.2.7.2.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 2 (minutes)							
	20	30	45	60	90	120	150	180
1015	0.239	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1032	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1063	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1072	0.218	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
Overall								
n	4	4	4	4	4	4	4	4
Mean	0.1643	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
SD	0.074683	0.00	0.00	0.00	0.00	0.00	0.00	0.00
CV%	45.5	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SEM	0.037342	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.1590	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
Maximum	0.239	0.100	0.100	0.100	0.100	0.100	0.100	0.100

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.2.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 2 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	2	2	2	2	2	2	2	2
Mean	0.1695	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
SD	0.098288	0.00	0.00	0.00	0.00	0.00	0.00	0.00
CV%	58.0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SEM	0.069500	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.1695	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
Maximum	0.239	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Male								
n	2	2	2	2	2	2	2	2
Mean	0.1590	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
SD	0.083439	0.00	0.00	0.00	0.00	0.00	0.00	0.00
CV%	52.5	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SEM	0.059000	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.1590	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
Maximum	0.218	0.100	0.100	0.100	0.100	0.100	0.100	0.100

Table 14.2.7.2.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 6 (minutes)						
	Pre-Use	2	5	7	10	12	15
1015	BLQ	BLQ	0.329	0.307	0.301	0.331	0.279
1032	BLQ	BLQ	0.223	0.274	0.233	0.287	0.263
1063	BLQ	BLQ	0.464	0.381	0.336	0.294	0.251
Overall							
n	3	3	3	3	3	3	3
Mean	0.1000	0.1000	0.3387	0.3207	0.2900	0.3040	0.2643
SD	0.00	0.00	0.12079	0.054794	0.052374	0.023643	0.014048
CV%	0.00	0.00	35.7	17.1	18.1	7.8	5.3
SEM	0.00	0.00	0.069738	0.031635	0.030238	0.013650	0.0081104
Minimum	0.100	0.100	0.223	0.274	0.233	0.287	0.251
Median	0.1000	0.1000	0.3290	0.3070	0.3010	0.2940	0.2630
Maximum	0.100	0.100	0.464	0.381	0.336	0.331	0.279

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.2.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 6 (minutes)						
	Pre-Use	2	5	7	10	12	15
Female							
n	2	2	2	2	2	2	2
Mean	0.1000	0.1000	0.2760	0.2905	0.2670	0.3090	0.2710
SD	0.00	0.00	0.074953	0.023335	0.048083	0.031113	0.011314
CV%	0.00	0.00	27.2	8.0	18.0	10.1	4.2
SEM	0.00	0.00	0.053000	0.016500	0.034000	0.022000	0.0080000
Minimum	0.100	0.100	0.223	0.274	0.233	0.287	0.263
Median	0.1000	0.1000	0.2760	0.2905	0.2670	0.3090	0.2710
Maximum	0.100	0.100	0.329	0.307	0.301	0.331	0.279
Male							
n	1	1	1	1	1	1	1
Mean	0.1000	0.1000	0.4640	0.3810	0.3360	0.2940	0.2510
SD
CV%
SEM
Minimum	0.100	0.100	0.464	0.381	0.336	0.294	0.251
Median	0.1000	0.1000	0.4640	0.3810	0.3360	0.2940	0.2510
Maximum	0.100	0.100	0.464	0.381	0.336	0.294	0.251

. = Value missing or not reportable.

Table 14.2.7.2.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 6 (minutes)							
	20	30	45	60	90	120	150	180
1015	0.240	0.238	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1032	0.232	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1063	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
Overall								
n	3	3	3	3	3	3	3	3
Mean	0.1907	0.1460	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
SD	0.078621	0.079674	0.00	0.00	0.00	0.00	0.00	0.00
CV%	41.2	54.6	0.00	0.00	0.00	0.00	0.00	0.00
SEM	0.045392	0.046000	0.00	0.00	0.00	0.00	0.00	0.00
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.2320	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
Maximum	0.240	0.238	0.100	0.100	0.100	0.100	0.100	0.100

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.2.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 6 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	2	2	2	2	2	2	2	2
Mean	0.2360	0.1690	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
SD	0.0056569	0.097581	0.00	0.00	0.00	0.00	0.00	0.00
CV%	2.4	57.7	0.00	0.00	0.00	0.00	0.00	0.00
SEM	0.0040000	0.069000	0.00	0.00	0.00	0.00	0.00	0.00
Minimum	0.232	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.2360	0.1690	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
Maximum	0.240	0.238	0.100	0.100	0.100	0.100	0.100	0.100
Male								
n	1	1	1	1	1	1	1	1
Mean	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
SD
CV%
SEM
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
Maximum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100

. = Value missing or not reportable.

Table 14.2.7.2.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week -1 (minutes)						
	Pre-Use	2	5	7	10	12	15
1003	1.13	3.00	11.2	14.7	11.9	13.4	12.0
1008	2.03	8.12	17.5	17.5	11.7	11.7	7.65
1014	2.69	6.30	10.3	11.7	11.8	12.2	10.8
1015	0.345	3.29	13.1	20.4	18.8	14.3	10.0
1018	0.634	9.86	12.5	13.5	10.9	9.71	8.55
1029	BLQ	2.36	9.95	10.7	9.43	7.92	7.28
1032	0.768	3.65	.	9.76	10.6	10.2	9.78
1052	2.34	10.0	15.8	27.9	18.2	20.1	20.4
1053	1.49	5.59	15.2	15.1	13.7	12.7	12.2
1055	0.689	2.11	6.14	9.26	11.2	11.2	11.1
1063	0.848	1.83	5.59	7.80	6.72	7.53	6.85
1072	0.431	1.08	6.70	5.63	6.42	7.54	6.23
Overall							
n	12	12	11	12	12	12	12
Mean	1.125	4.766	11.27	13.66	11.78	11.54	10.24
SD	0.83414	3.1510	4.0223	6.1209	3.7727	3.5240	3.7826
CV%	74.2	66.1	35.7	44.8	32.0	30.5	37.0
SEM	0.24080	0.90962	1.2128	1.7670	1.0891	1.0173	1.0919
Minimum	0.100	1.08	5.59	5.63	6.42	7.53	6.23
Median	0.8080	3.470	11.20	12.60	11.45	11.45	9.890
Maximum	2.69	10.0	17.5	27.9	18.8	20.1	20.4

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.
. = Value missing or not reportable.

Table 14.2.7.2.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Pre-Use	2	5	7	10	12	15
----- Week -1 (minutes) -----							

Female							
n	6	6	5	6	6	6	6
Mean	0.8710	4.595	10.40	12.55	12.12	10.92	9.585
SD	0.92518	2.9797	2.7414	4.1298	3.3647	2.1965	1.4399
CV%	106.2	64.8	26.4	32.9	27.8	20.1	15.0
SEM	0.37770	1.2165	1.2260	1.6860	1.3736	0.89673	0.58782
Minimum	0.100	2.11	6.14	9.26	9.43	7.92	7.28
Median	0.6615	3.470	10.30	11.20	11.05	10.70	9.890
Maximum	2.69	9.86	13.1	20.4	18.8	14.3	11.1

Male							
n	6	6	6	6	6	6	6
Mean	1.378	4.937	12.00	14.77	11.44	12.16	10.89
SD	0.72143	3.5909	4.9950	7.9004	4.4399	4.6447	5.3277
CV%	52.3	72.7	41.6	53.5	38.8	38.2	48.9
SEM	0.29452	1.4660	2.0392	3.2253	1.8126	1.8962	2.1750
Minimum	0.431	1.08	5.59	5.63	6.42	7.53	6.23
Median	1.310	4.295	13.20	14.90	11.80	12.20	9.825
Maximum	2.34	10.0	17.5	27.9	18.2	20.1	20.4

Table 14.2.7.2.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week -1 (minutes)							
	20	30	45	60	90	120	150	180
<hr/>								
1003	10.1	10.2	8.78	7.25	5.56	4.38	3.72	3.11
1008	8.35	6.67	5.94	4.95	4.57	3.81	3.27	2.77
1014	11.6	10.2	10.0	8.82	7.44	6.70	5.43	4.79
1015	10.0	8.54	5.80	5.34	3.81	2.80	2.15	1.74
1018	6.49	5.66	4.48	3.59	2.66	2.17	2.00	1.51
1029	6.03	5.06	3.76	3.83	2.03	1.59	1.16	0.891
1032	9.78	8.28	6.92	5.66	4.49	3.47	2.62	2.33
1052	17.7	16.0	13.6	12.4	9.80	9.64	8.64	6.63
1053	12.1	11.0	9.35	8.39	6.60	5.06	4.29	3.97
1055	8.82	7.81	6.48	5.58	4.67	3.68	3.18	2.64
1063	6.33	6.26	5.20	4.45	3.57	3.04	2.14	1.85
1072	5.99	6.11	5.55	5.09	3.91	2.98	2.42	1.79
<hr/>								
Overall								
n	12	12	12	12	12	12	12	12
Mean	9.441	8.483	7.155	6.279	4.926	4.110	3.418	2.835
SD	3.3617	3.0567	2.7960	2.5375	2.1596	2.1992	2.0052	1.6147
CV%	35.6	36.0	39.1	40.4	43.8	53.5	58.7	57.0
SEM	0.97044	0.88240	0.80713	0.73252	0.62341	0.63485	0.57886	0.46614
Minimum	5.99	5.06	3.76	3.59	2.03	1.59	1.16	0.891
Median	9.300	8.045	6.210	5.460	4.530	3.575	2.900	2.485
Maximum	17.7	16.0	13.6	12.4	9.80	9.64	8.64	6.63
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Table 14.2.7.2.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week -1 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	6	6	6	6	6	6	6	6
Mean	8.787	7.592	6.240	5.470	4.183	3.402	2.757	2.317
SD	2.1563	1.9165	2.1954	1.8714	1.8991	1.7957	1.4720	1.3593
CV%	24.5	25.2	35.2	34.2	45.4	52.8	53.4	58.7
SEM	0.88032	0.78241	0.89627	0.76402	0.77532	0.73308	0.60096	0.55491
Minimum	6.03	5.06	3.76	3.59	2.03	1.59	1.16	0.891
Median	9.300	8.045	6.140	5.460	4.150	3.135	2.385	2.035
Maximum	11.6	10.2	10.0	8.82	7.44	6.70	5.43	4.79
Male								
n	6	6	6	6	6	6	6	6
Mean	10.10	9.373	8.070	7.088	5.668	4.818	4.080	3.353
SD	4.3801	3.8702	3.2202	3.0153	2.3087	2.4923	2.3725	1.8011
CV%	43.4	41.3	39.9	42.5	40.7	51.7	58.1	53.7
SEM	1.7882	1.5800	1.3146	1.2310	0.94254	1.0175	0.96855	0.73531
Minimum	5.99	6.11	5.20	4.45	3.57	2.98	2.14	1.79
Median	9.225	8.435	7.360	6.170	5.065	4.095	3.495	2.940
Maximum	17.7	16.0	13.6	12.4	9.80	9.64	8.64	6.63

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Table 14.2.7.2.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)						
	Pre-Use	2	5	7	10	12	15
1003	0.453	0.500	0.903	1.04	0.908	0.964	1.13
1008	0.266	0.604	0.684	0.580	0.523	0.484	0.500
1014	0.216	0.260	0.407	0.422	0.390	0.363	0.391
1015	BLQ	BLQ	0.248	0.327	0.337	0.318	0.304
1029	BLQ	BLQ	0.227	0.265	0.214	0.213	0.204
1032	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1052	0.317	0.614	0.873	0.927	0.821	0.744	0.775
1053	BLQ	0.493	0.574	0.487	0.375	0.339	0.369
1055	BLQ	BLQ	BLQ	0.226	0.255	0.238	0.229
1063	BLQ	0.205	0.586	0.316	0.225	0.232	0.218
1072	BLQ	BLQ	0.213	0.213	0.205	BLQ	0.230
Overall							
n	11	11	11	11	11	11	11
Mean	0.1775	0.2887	0.4468	0.4457	0.3957	0.3723	0.4045
SD	0.12113	0.21852	0.29431	0.29844	0.25869	0.26763	0.30220
CV%	68.3	75.7	65.9	67.0	65.4	71.9	74.7
SEM	0.036521	0.065885	0.088739	0.089982	0.077998	0.080695	0.091116
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.1000	0.2050	0.4070	0.3270	0.3370	0.3180	0.3040
Maximum	0.453	0.614	0.903	1.04	0.908	0.964	1.13

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.2.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)						
	Pre-Use	2	5	7	10	12	15
Female							
n	5	5	5	5	5	5	5
Mean	0.1232	0.1320	0.2164	0.2680	0.2592	0.2464	0.2456
SD	0.051877	0.071554	0.12702	0.11958	0.11244	0.10166	0.10927
CV%	42.1	54.2	58.7	44.6	43.4	41.3	44.5
SEM	0.023200	0.032000	0.056805	0.053476	0.050283	0.045465	0.048866
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.1000	0.1000	0.2270	0.2650	0.2550	0.2380	0.2290
Maximum	0.216	0.260	0.407	0.422	0.390	0.363	0.391
Male							
n	6	6	6	6	6	6	6
Mean	0.2227	0.4193	0.6388	0.5938	0.5095	0.4772	0.5370
SD	0.14763	0.21533	0.25099	0.32982	0.29925	0.32549	0.35606
CV%	66.3	51.4	39.3	55.5	58.7	68.2	66.3
SEM	0.060269	0.087910	0.10247	0.13465	0.12217	0.13288	0.14536
Minimum	0.100	0.100	0.213	0.213	0.205	0.100	0.218
Median	0.1830	0.4965	0.6350	0.5335	0.4490	0.4115	0.4345
Maximum	0.453	0.614	0.903	1.04	0.908	0.964	1.13

Table 14.2.7.2.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)							
	20	30	45	60	90	120	150	180
1003	0.586	0.944	0.432	0.431	0.500	0.378	0.270	0.273
1008	0.424	0.428	0.405	0.396	0.333	0.299	0.310	0.276
1014	0.357	0.370	0.334	0.345	0.308	0.275	0.243	0.243
1015	0.239	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1029	BLQ	BLQ	BLQ	BLQ	BLQ	0.218	0.203	BLQ
1032	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1052	0.697	0.703	0.605	0.605	0.626	0.395	0.464	0.384
1053	0.355	0.313	0.226	0.275	BLQ	BLQ	BLQ	BLQ
1055	0.221	0.207	0.236	BLQ	BLQ	BLQ	BLQ	BLQ
1063	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1072	0.218	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
Overall								
n	11	11	11	11	11	11	11	11
Mean	0.3088	0.3150	0.2489	0.2411	0.2243	0.1968	0.1900	0.1705
SD	0.19922	0.28369	0.17421	0.17997	0.19088	0.12056	0.12143	0.10357
CV%	64.5	90.1	70.0	74.6	85.1	61.3	63.9	60.7
SEM	0.060067	0.085534	0.052526	0.054262	0.057552	0.036350	0.036613	0.031227
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.2390	0.2070	0.2260	0.1000	0.1000	0.1000	0.1000	0.1000
Maximum	0.697	0.944	0.605	0.605	0.626	0.395	0.464	0.384

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.2.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	5	5	5	5	5	5	5	5
Mean	0.2034	0.1754	0.1740	0.1490	0.1416	0.1586	0.1492	0.1286
SD	0.10788	0.11824	0.10709	0.10957	0.093020	0.082733	0.068838	0.063952
CV%	53.0	67.4	61.5	73.5	65.7	52.2	46.1	49.7
SEM	0.048246	0.052879	0.047892	0.049000	0.041600	0.036999	0.030785	0.028600
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.2210	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
Maximum	0.357	0.370	0.334	0.345	0.308	0.275	0.243	0.243
Male								
n	6	6	6	6	6	6	6	6
Mean	0.3967	0.4313	0.3113	0.3178	0.2932	0.2287	0.2240	0.2055
SD	0.22292	0.33770	0.20307	0.19906	0.23112	0.14462	0.15049	0.12229
CV%	56.2	78.3	65.2	62.6	78.8	63.2	67.2	59.5
SEM	0.091006	0.13787	0.082901	0.081265	0.094355	0.059042	0.061438	0.049926
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.3895	0.3705	0.3155	0.3355	0.2165	0.1995	0.1850	0.1865
Maximum	0.697	0.944	0.605	0.605	0.626	0.395	0.464	0.384

Table 14.2.7.2.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)						
	Pre-Use	2	5	7	10	12	15
1003	0.575	0.591	0.777	0.788	0.809	0.715	0.637
1008	0.650	0.979	1.30	1.31	0.924	0.945	1.05
1014	0.423	0.451	0.704	0.623	0.651	0.645	0.634
1015	BLQ	BLQ	0.329	0.307	0.301	0.331	0.279
1029	BLQ	BLQ	0.292	0.201	0.268	0.229	BLQ
1032	BLQ	BLQ	0.223	0.274	0.233	0.287	0.263
1052	0.930	1.17	1.42	1.46	1.31	1.32	1.47
1053	0.210	0.535	0.425	0.571	0.420	0.449	0.457
1055	BLQ	BLQ	BLQ	0.257	0.247	0.244	0.261
1063	BLQ	BLQ	0.464	0.381	0.336	0.294	0.251

Overall							
n	10	10	10	10	10	10	10
Mean	0.3288	0.4226	0.6034	0.6172	0.5499	0.5459	0.5402
SD	0.29999	0.39866	0.44895	0.44652	0.36382	0.36126	0.42817
CV%	91.2	94.3	74.4	72.3	66.2	66.2	79.3
SEM	0.094866	0.12607	0.14197	0.14120	0.11505	0.11424	0.13540
Minimum	0.100	0.100	0.100	0.201	0.233	0.229	0.100
Median	0.1550	0.2755	0.4445	0.4760	0.3780	0.3900	0.3680
Maximum	0.930	1.17	1.42	1.46	1.31	1.32	1.47

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.2.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)						
	Pre-Use	2	5	7	10	12	15
Female							
n	5	5	5	5	5	5	5
Mean	0.1646	0.1702	0.3296	0.3324	0.3400	0.3472	0.3074
SD	0.14445	0.15697	0.22675	0.16692	0.17573	0.17117	0.19660
CV%	87.8	92.2	68.8	50.2	51.7	49.3	64.0
SEM	0.064600	0.070200	0.10141	0.074651	0.078589	0.076548	0.087924
Minimum	0.100	0.100	0.100	0.201	0.233	0.229	0.100
Median	0.1000	0.1000	0.2920	0.2740	0.2680	0.2870	0.2630
Maximum	0.423	0.451	0.704	0.623	0.651	0.645	0.634
Male							
n	5	5	5	5	5	5	5
Mean	0.4930	0.6750	0.8772	0.9020	0.7598	0.7446	0.7730
SD	0.33796	0.41675	0.46332	0.46686	0.39597	0.40698	0.48820
CV%	68.6	61.7	52.8	51.8	52.1	54.7	63.2
SEM	0.15114	0.18638	0.20720	0.20879	0.17708	0.18201	0.21833
Minimum	0.100	0.100	0.425	0.381	0.336	0.294	0.251
Median	0.5750	0.5910	0.7770	0.7880	0.8090	0.7150	0.6370
Maximum	0.930	1.17	1.42	1.46	1.31	1.32	1.47

Table 14.2.7.2.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)							
	20	30	45	60	90	120	150	180
1003	0.744	0.661	0.649	0.660	0.848	0.665	0.583	0.554
1008	0.896	0.892	0.944	0.821	0.708	0.803	0.623	0.717
1014	0.571	0.580	0.570	0.555	0.498	0.477	0.446	0.444
1015	0.240	0.238	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1029	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1032	0.232	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
1052	1.25	1.18	1.22	1.30	1.22	0.966	0.969	0.944
1053	0.372	0.357	0.344	0.382	0.245	0.270	0.203	0.200
1055	0.255	0.255	0.218	BLQ	BLQ	BLQ	BLQ	BLQ
1063	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
Overall								
n	10	10	10	10	10	10	10	10
Mean	0.4760	0.4463	0.4345	0.4218	0.4019	0.3681	0.3324	0.3359
SD	0.38209	0.37248	0.40050	0.41156	0.40160	0.33593	0.30772	0.31109
CV%	80.3	83.5	92.2	97.6	99.9	91.3	92.6	92.6
SEM	0.12083	0.11779	0.12665	0.13015	0.12700	0.10623	0.097309	0.098375
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.3135	0.3060	0.2810	0.2410	0.1725	0.1850	0.1515	0.1500
Maximum	1.25	1.18	1.22	1.30	1.22	0.966	0.969	0.944

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of 0.200 ng/mL are treated as 1/2 limit of quantitation.

Table 14.2.7.2.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	5	5	5	5	5	5	5	5
Mean	0.2796	0.2546	0.2176	0.1910	0.1796	0.1754	0.1692	0.1688
SD	0.17436	0.19619	0.20352	0.20348	0.17799	0.16860	0.15474	0.15384
CV%	62.4	77.1	93.5	106.5	99.1	96.1	91.5	91.1
SEM	0.077977	0.087739	0.091015	0.091000	0.079600	0.075400	0.069200	0.068800
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.2400	0.2380	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
Maximum	0.571	0.580	0.570	0.555	0.498	0.477	0.446	0.444
Male								
n	5	5	5	5	5	5	5	5
Mean	0.6724	0.6380	0.6514	0.6526	0.6242	0.5608	0.4956	0.5030
SD	0.44906	0.42638	0.44929	0.45446	0.45570	0.36421	0.35003	0.35253
CV%	66.8	66.8	69.0	69.6	73.0	64.9	70.6	70.1
SEM	0.20083	0.19068	0.20093	0.20324	0.20380	0.16288	0.15654	0.15765
Minimum	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Median	0.7440	0.6610	0.6490	0.6600	0.7080	0.6650	0.5830	0.5540
Maximum	1.25	1.18	1.22	1.30	1.22	0.966	0.969	0.944

Table 14.2.7.3.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week -1 (minutes)						
	Pre-Use	2	5	7	10	12	15
1007	0.00	1.82	7.23	8.35	8.31	7.87	6.79

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.3.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week -1 (minutes)							
	20	30	45	60	90	120	150	180
1007	6.70	5.64	4.53	4.28	3.04	1.87	2.27	1.56

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.3.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 2 (minutes)						
	Pre-Use	2	5	7	10	12	15
1007	0.00	0.304	0.545	0.336	0.285	0.225	0.200

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.3.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 2 (minutes)							
	20	30	45	60	90	120	150	180
1007	0.195	0.174	0.110	0.000651	0.147	0.108	0.00149	0.00177

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.3.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 6 (minutes)						
	Pre-Use	2	5	7	10	12	15
1007	0.00	0.613	0.523	0.329	0.319	0.278	0.278

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.3.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 6 (minutes)							
	20	30	45	60	90	120	150	180
1007	0.240	0.154	0.220	0.134	0.156	0.103	0.00150	0.158

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.3.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Pre-Use	2	5	7	10	12	15
1001	0.00	5.94	10.4	14.0	13.9	14.0	15.1
1002	0.00	0.601	4.32	6.37	8.24	6.88	7.57
1007	0.00	1.82	7.23	8.35	8.31	7.87	6.79
1013	0.00	7.70	15.3	18.4	9.90	9.60	7.41
1019	0.00	8.62	16.5
1020	0.00	6.48	27.8	22.9	18.4	14.2	12.8
1023	0.00	1.67	6.71	6.77	6.92	6.43	6.75
1035	0.00	0.751	6.48	6.22	5.87	5.76	5.49
1038	0.00	7.01	9.82	11.1	9.47	9.43	10.7
1042	0.00	2.13	11.6	14.0	9.74	7.42	6.61
1056	0.00	6.25	9.81	12.1	10.7	9.91	10.8
1058	0.00	6.37	14.1	14.3	11.5	11.3	10.9
Overall							
n	12	12	12	11	11	11	11
Mean	0.00	4.612	11.68	12.23	10.27	9.345	9.177
SD	0.00	2.9538	6.3023	5.2836	3.4705	2.8733	3.0561
CV%	.	64.0	54.0	43.2	33.8	30.7	33.3
SEM	0.00	0.85270	1.8193	1.5931	1.0464	0.86632	0.92146
Minimum	0.00	0.601	4.32	6.22	5.87	5.76	5.49
Median	0.00	6.096	10.09	12.11	9.744	9.427	7.572
Maximum	0.00	8.62	27.8	22.9	18.4	14.2	15.1

For the calculation of summary statistics, negative values are assigned a value of zero
 . = Value missing or not reportable.

Table 14.2.7.3.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week -1 (minutes)						
	Pre-Use	2	5	7	10	12	15
Female							
n	5	5	5	5	5	5	5
Mean	0.00	5.759	14.00	14.63	11.71	10.73	10.55
SD	0.00	2.3786	8.3070	6.2699	4.4933	3.3197	3.5322
CV%	.	41.3	59.3	42.9	38.4	31.0	33.5
SEM	0.00	1.0638	3.7150	2.8040	2.0095	1.4846	1.5796
Minimum	0.00	1.67	6.71	6.77	6.92	6.43	6.75
Median	0.00	6.481	10.37	13.97	9.899	9.599	10.72
Maximum	0.00	7.70	27.8	22.9	18.4	14.2	15.1
Male							
n	7	7	7	6	6	6	6
Mean	0.00	3.793	10.02	10.24	9.065	8.194	8.033
SD	0.00	3.2164	4.3726	3.7206	2.0293	2.0492	2.2898
CV%	.	84.8	43.6	36.4	22.4	25.0	28.5
SEM	0.00	1.2157	1.6527	1.5189	0.82844	0.83659	0.93482
Minimum	0.00	0.601	4.32	6.22	5.87	5.76	5.49
Median	0.00	2.133	9.809	10.23	9.028	7.648	7.183
Maximum	0.00	8.62	16.5	14.3	11.5	11.3	10.9

For the calculation of summary statistics, negative values are assigned a value of zero
. = Value missing or not reportable.

Table 14.2.7.3.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week -1 (minutes)							
	20	30	45	60	90	120	150	180
1001	13.9	11.6	8.65	6.90	5.49	3.65	2.66	2.25
1002	6.51	6.90	6.16	5.39	4.35	4.23	3.14	2.46
1007	6.70	5.64	4.53	4.28	3.04	1.87	2.27	1.56
1013	8.08	7.37	6.61	5.72	4.48	3.22	2.89	2.33
1019	8.34	7.05	5.99	4.63	4.23	2.89	1.98	1.31
1020	11.3	9.70	7.41	5.60	4.58	3.37	2.98	2.40
1023	6.08	4.73	4.12	3.76	2.56	1.75	1.23	0.850
1035	4.79	4.45	3.58	3.58	2.24	1.69	1.16	0.673
1038	9.62	7.61	5.90	5.40	3.87	2.91	2.10	1.82
1042	5.18	3.56	2.29	2.11	1.42	1.21	0.690	0.551
1056	7.45	7.17	4.70	4.36	3.12	2.22	1.80	1.48
1058	10.7	10.0	8.39	7.00	4.83	4.16	3.41	2.90
Overall								
n	12	12	12	12	12	12	12	12
Mean	8.221	7.148	5.692	4.893	3.684	2.765	2.191	1.715
SD	2.7142	2.3921	1.9301	1.4021	1.2069	1.0096	0.86080	0.77102
CV%	33.0	33.5	33.9	28.7	32.8	36.5	39.3	45.0
SEM	0.78351	0.69054	0.55718	0.40475	0.34839	0.29144	0.24849	0.22258
Minimum	4.79	3.56	2.29	2.11	1.42	1.21	0.690	0.551
Median	7.765	7.112	5.942	5.007	4.050	2.902	2.186	1.692
Maximum	13.9	11.6	8.65	7.00	5.49	4.23	3.41	2.90

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.3.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week -1 (minutes)							
	20	30	45	60	90	120	150	180

Female								
n	5	5	5	5	5	5	5	5
Mean	9.790	8.196	6.535	5.474	4.196	2.980	2.371	1.931
SD	2.9883	2.5864	1.6935	1.1239	1.0826	0.73812	0.72347	0.64458
CV%	30.5	31.6	25.9	20.5	25.8	24.8	30.5	33.4
SEM	1.3364	1.1567	0.75736	0.50263	0.48416	0.33010	0.32355	0.28827
Minimum	6.08	4.73	4.12	3.76	2.56	1.75	1.23	0.850
Median	9.617	7.608	6.611	5.597	4.484	3.215	2.659	2.251
Maximum	13.9	11.6	8.65	6.90	5.49	3.65	2.98	2.40

Male								
n	7	7	7	7	7	7	7	7
Mean	7.100	6.400	5.089	4.478	3.318	2.612	2.063	1.561
SD	2.0088	2.1122	1.9753	1.5098	1.2305	1.1998	0.98147	0.86395
CV%	28.3	33.0	38.8	33.7	37.1	45.9	47.6	55.3
SEM	0.75925	0.79832	0.74658	0.57065	0.46507	0.45349	0.37096	0.32654
Minimum	4.79	3.56	2.29	2.11	1.42	1.21	0.690	0.551
Median	6.703	6.904	4.701	4.361	3.123	2.224	1.976	1.476
Maximum	10.7	10.0	8.39	7.00	4.83	4.23	3.41	2.90

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.3.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)						
	Pre-Use	2	5	7	10	12	15
1001	0.00	0.0000676	0.207	0.241	0.232	0.200	0.222
1002	0.00	0.110	0.199	0.288	0.255	0.301	0.236
1007	0.00	0.304	0.545	0.336	0.285	0.225	0.200
1013	0.00	0.128	0.337	0.372	0.391	0.302	0.325
1019	0.00	0.244	0.673	0.405	0.384	0.266	0.267
1020	0.00	0.0000858	0.268	0.315	0.278	0.248	0.181
1023	0.00	0.0000870	0.105	0.162	0.138	0.142	0.101
1035	0.00	0.00	0.274	0.132	0.0688	0.132	0.129
1038	0.00	0.0000694	0.114	0.192	0.215	0.113	0.000196
1042	0.00	0.0000673	0.149	0.125	0.100	0.000163	0.000194
1056	0.00	0.0000662	0.379	0.325	0.249	0.212	0.143
1058	0.00	0.0144	0.271	0.193	0.0899	0.0820	0.136
Overall							
n	12	12	12	12	12	12	12
Mean	0.00	0.06676	0.2934	0.2572	0.2239	0.1854	0.1619
SD	0.00	0.10757	0.17139	0.095893	0.10736	0.092921	0.098546
CV%	.	161.1	58.4	37.3	47.9	50.1	60.9
SEM	0.00	0.031051	0.049475	0.027682	0.030993	0.026824	0.028448
Minimum	0.00	0.00	0.105	0.125	0.0688	0.000163	0.000194
Median	0.00	0.0000864	0.2693	0.2646	0.2406	0.2062	0.1622
Maximum	0.00	0.304	0.673	0.405	0.391	0.302	0.325

For the calculation of summary statistics, negative values are assigned a value of zero
 . = Value missing or not reportable.

Table 14.2.7.3.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)						
	Pre-Use	2	5	7	10	12	15
Female							
n	5	5	5	5	5	5	5
Mean	0.00	0.02568	0.2063	0.2565	0.2510	0.2012	0.1660
SD	0.00	0.057245	0.099590	0.086740	0.093213	0.076875	0.12291
CV%	.	222.9	48.3	33.8	37.1	38.2	74.0
SEM	0.00	0.025601	0.044538	0.038791	0.041686	0.034379	0.054966
Minimum	0.00	0.0000676	0.105	0.162	0.138	0.113	0.000196
Median	0.00	0.0000858	0.2071	0.2411	0.2321	0.2002	0.1812
Maximum	0.00	0.128	0.337	0.372	0.391	0.302	0.325
Male							
n	7	7	7	7	7	7	7
Mean	0.00	0.09611	0.3557	0.2577	0.2046	0.1741	0.1589
SD	0.00	0.12890	0.19078	0.10882	0.11957	0.10739	0.087800
CV%	.	134.1	53.6	42.2	58.4	61.7	55.3
SEM	0.00	0.048721	0.072107	0.041130	0.045193	0.040591	0.033185
Minimum	0.00	0.00	0.149	0.125	0.0688	0.000163	0.000194
Median	0.00	0.01441	0.2735	0.2881	0.2491	0.2122	0.1432
Maximum	0.00	0.304	0.673	0.405	0.384	0.301	0.267

For the calculation of summary statistics, negative values are assigned a value of zero
 . = Value missing or not reportable.

Table 14.2.7.3.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)							
	20	30	45	60	90	120	150	180
1001	0.139	0.135	0.000491	0.000636	0.000914	0.00120	0.00149	0.00177
1002	0.238	0.268	0.241	0.183	0.256	0.127	0.156	0.116
1007	0.195	0.174	0.110	0.000651	0.147	0.108	0.00149	0.00177
1013	0.261	0.231	0.201	0.142	0.131	0.00122	0.154	0.00179
1019	0.244	0.244	0.163	0.173	0.101	0.00123	0.128	0.205
1020	0.185	0.234	0.142	0.164	0.000930	0.00122	0.00150	0.00179
1023	0.108	0.104	0.000501	0.000646	0.000933	0.00122	0.00151	0.00179
1035	0.0593	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1038	0.104	0.000342	0.000482	0.000629	0.000915	0.00120	0.00149	0.00177
1042	0.000242	0.000336	0.000482	0.000626	0.000913	0.00120	0.00149	0.00177
1056	0.149	0.106	0.000481	0.000625	0.000912	0.00120	0.00148	0.00177
1058	0.0894	0.00602	0.0429	0.00585	0.00	0.00	0.00	0.00
Overall								
n	12	12	12	12	12	12	12	12
Mean	0.1479	0.1255	0.07532	0.05585	0.05335	0.02042	0.03733	0.02790
SD	0.080087	0.10542	0.091257	0.081243	0.085416	0.045620	0.065784	0.064688
CV%	54.2	84.0	121.2	145.5	160.1	223.4	176.2	231.9
SEM	0.023119	0.030431	0.026344	0.023453	0.024657	0.013169	0.018990	0.018674
Minimum	0.000242	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Median	0.1442	0.1208	0.02169	0.0006481	0.0009226	0.001211	0.001487	0.001773
Maximum	0.261	0.268	0.241	0.183	0.256	0.127	0.156	0.205

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.3.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	5	5	5	5	5	5	5	5
Mean	0.1597	0.1411	0.06909	0.06144	0.02692	0.001214	0.03190	0.001783
SD	0.065398	0.097517	0.096225	0.083620	0.058140	0.0000105	0.067978	0.0000096
CV%	41.0	69.1	139.3	136.1	215.9	0.9	213.1	0.5
SEM	0.029247	0.043611	0.043033	0.037396	0.026001	0.0000047	0.030401	0.0000043
Minimum	0.104	0.000342	0.000482	0.000629	0.000914	0.00120	0.00149	0.00177
Median	0.1392	0.1353	0.0005009	0.0006457	0.0009301	0.001218	0.001503	0.001786
Maximum	0.261	0.234	0.201	0.164	0.131	0.00122	0.154	0.00179
Male								
n	7	7	7	7	7	7	7	7
Mean	0.1394	0.1142	0.07976	0.05186	0.07223	0.03415	0.04121	0.04656
SD	0.093322	0.11697	0.095076	0.085992	0.10062	0.057343	0.069362	0.081837
CV%	66.9	102.4	119.2	165.8	139.3	167.9	168.3	175.8
SEM	0.035272	0.044209	0.035935	0.032502	0.038031	0.021674	0.026216	0.030931
Minimum	0.000242	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Median	0.1492	0.1063	0.04289	0.0006505	0.0009133	0.001201	0.001486	0.001771
Maximum	0.244	0.268	0.241	0.183	0.256	0.127	0.156	0.205

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.3.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)						
	Pre-Use	2	5	7	10	12	15
<hr/>							
1001	0.00	.	0.270	0.429	0.463	0.458	0.302
1002	0.00	0.0362	0.0903	0.112	0.122	0.289	0.124
1007	0.00	0.613	0.523	0.329	0.319	0.278	0.278
1013	0.00	0.134	0.240	0.299	0.248	0.287	0.253
1019	0.00	0.269	0.649	0.539	0.299	0.219	0.190
1020	0.00	0.458	0.559	0.563	0.381	0.341	0.283
1023	0.00	0.0000675	0.191	0.204	0.141	0.183	0.244
1035	0.00	0.115	0.304	0.260	0.00479	0.146	0.145
1038	0.00	0.101	0.294	0.287	0.312	0.261	0.241
1042	0.00	0.170	0.218	0.000115	0.000145	0.000164	0.000193
1056	0.00	0.0000691	0.519	0.390	0.268	0.246	0.213
1058	0.00	0.00	0.322	0.332	0.133	0.153	0.144
<hr/>							
Overall							
n	12	11	12	12	12	12	12
Mean	0.00	0.1724	0.3483	0.3121	0.2244	0.2386	0.2015
SD	0.00	0.20064	0.17221	0.16166	0.14480	0.11363	0.086458
CV%	.	116.4	49.4	51.8	64.5	47.6	42.9
SEM	0.00	0.060496	0.049713	0.046666	0.041800	0.032803	0.024958
Minimum	0.00	0.00	0.0903	0.000115	0.000145	0.000164	0.000193
Median	0.00	0.1154	0.2988	0.3141	0.2581	0.2537	0.2272
Maximum	0.00	0.613	0.649	0.563	0.463	0.458	0.302

For the calculation of summary statistics, negative values are assigned a value of zero
 . = Value missing or not reportable.

Table 14.2.7.3.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Pre-Use	2	5	7	10	12	15
Female							
n	5	4	5	5	5	5	5
Mean	0.00	0.1733	0.3109	0.3565	0.3092	0.3062	0.2648
SD	0.00	0.19824	0.14402	0.14084	0.12336	0.10228	0.026733
CV%	.	114.4	46.3	39.5	39.9	33.4	10.1
SEM	0.00	0.099120	0.064405	0.062985	0.055168	0.045742	0.011955
Minimum	0.00	0.0000675	0.191	0.204	0.141	0.183	0.241
Median	0.00	0.1176	0.2701	0.2991	0.3122	0.2872	0.2532
Maximum	0.00	0.458	0.559	0.563	0.463	0.458	0.302
Male							
n	7	7	7	7	7	7	7
Mean	0.00	0.1719	0.3750	0.2803	0.1638	0.1903	0.1562
SD	0.00	0.21782	0.19634	0.17851	0.13423	0.10085	0.086546
CV%	.	126.7	52.4	63.7	82.0	53.0	55.4
SEM	0.00	0.082328	0.074210	0.067469	0.050735	0.038119	0.032711
Minimum	0.00	0.00	0.0903	0.000115	0.000145	0.000164	0.000193
Median	0.00	0.1154	0.3218	0.3291	0.1327	0.2194	0.1450
Maximum	0.00	0.613	0.649	0.539	0.319	0.289	0.278

For the calculation of summary statistics, negative values are assigned a value of zero
. = Value missing or not reportable.

Table 14.2.7.3.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)							
	20	30	45	60	90	120	150	180
1001	0.488	0.293	0.232	0.218	0.122	0.105	0.00148	0.00176
1002	0.0956	0.0599	0.170	0.0636	0.0672	0.0459	0.00	0.0383
1007	0.240	0.154	0.220	0.134	0.156	0.103	0.00150	0.158
1013	0.232	0.267	0.190	0.164	0.176	0.117	0.00149	0.126
1019	0.220	0.261	0.192	0.00	0.0607	0.00	0.00	0.00
1020	0.209	0.168	0.132	0.110	0.124	0.0154	0.141	0.0175
1023	0.185	0.175	0.000486	0.131	0.109	0.00122	0.00153	0.00177
1035	0.106	0.0198	0.0336	0.00	0.0259	0.00	0.00	0.00
1038	0.269	0.194	0.179	0.137	0.000913	0.189	0.00149	0.00177
1042	0.000251	0.000337	0.000482	0.000626	0.000913	0.00120	0.00149	0.00177
1056	0.178	0.189	0.202	0.000627	0.000913	0.107	0.00149	0.00177
1058	0.144	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Overall								
n	12	12	12	12	12	12	12	12
Mean	0.1975	0.1485	0.1295	0.07977	0.07025	0.05715	0.01262	0.02902
SD	0.11843	0.10490	0.093062	0.078371	0.065345	0.064601	0.040428	0.054270
CV%	60.0	70.6	71.9	98.3	93.0	113.0	320.4	187.0
SEM	0.034189	0.030281	0.026865	0.022624	0.018863	0.018649	0.011670	0.015666
Minimum	0.000251	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Median	0.1974	0.1715	0.1748	0.08690	0.06397	0.03067	0.001487	0.001773
Maximum	0.488	0.293	0.232	0.218	0.176	0.189	0.141	0.158

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.3.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	5	5	5	5	5	5	5	5
Mean	0.2769	0.2196	0.1470	0.1517	0.1063	0.08565	0.02939	0.02972
SD	0.12212	0.057016	0.089362	0.041460	0.064246	0.077724	0.062376	0.054126
CV%	44.1	26.0	60.8	27.3	60.4	90.7	212.2	182.1
SEM	0.054615	0.025498	0.039964	0.018541	0.028732	0.034759	0.027895	0.024206
Minimum	0.185	0.168	0.000486	0.110	0.000913	0.00122	0.00148	0.00176
Median	0.2322	0.1943	0.1795	0.1366	0.1219	0.1052	0.001489	0.001773
Maximum	0.488	0.293	0.232	0.218	0.176	0.189	0.141	0.126
Male								
n	7	7	7	7	7	7	7	7
Mean	0.1407	0.09779	0.1170	0.02835	0.04451	0.03679	0.0006390	0.02852
SD	0.082229	0.10388	0.10059	0.052078	0.056752	0.049632	0.0007969	0.058701
CV%	58.4	106.2	85.9	183.7	127.5	134.9	124.7	205.8
SEM	0.031080	0.039263	0.038019	0.019684	0.021450	0.018759	0.0003012	0.022187
Minimum	0.000251	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Median	0.1444	0.05986	0.1702	0.0006264	0.02586	0.001201	0.00	0.001773
Maximum	0.240	0.261	0.220	0.134	0.156	0.107	0.00150	0.158

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.4.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week -1 (minutes)						
	Pre-Use	2	5	7	10	12	15
1015	0.00	2.95	12.8	20.1	18.5	14.0	9.66
1018	0.00	9.23	11.9	12.9	10.3	9.08	7.92
1032	0.00	2.88	.	8.99	9.83	9.43	9.01
1063	0.00	0.983	4.74	6.95	5.87	6.68	6.00
1072	0.00	0.649	6.27	5.20	5.99	7.11	5.80
Overall							
n	5	5	4	5	5	5	5
Mean	0.00	3.337	8.909	10.81	10.08	9.252	7.678
SD	0.00	3.4574	3.9944	5.9026	5.1155	2.8885	1.7380
CV%	.	103.6	44.8	54.6	50.7	31.2	22.6
SEM	0.00	1.5462	1.9972	2.6397	2.2877	1.2918	0.77727
Minimum	0.00	0.649	4.74	5.20	5.87	6.68	5.80
Median	0.00	2.883	9.068	8.993	9.833	9.077	7.917
Maximum	0.00	9.23	12.8	20.1	18.5	14.0	9.66

For the calculation of summary statistics, negative values are assigned a value of zero
. = Value missing or not reportable.

Table 14.2.7.4.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week -1 (minutes)						
	Pre-Use	2	5	7	10	12	15
Female							
n	3	3	2	3	3	3	3
Mean	0.00	5.018	12.31	13.97	12.85	10.82	8.862
SD	0.00	3.6447	0.62843	5.6134	4.8578	2.7196	0.87905
CV%	.	72.6	5.1	40.2	37.8	25.1	9.9
SEM	0.00	2.1043	0.44437	3.2409	2.8046	1.5702	0.50752
Minimum	0.00	2.88	11.9	8.99	9.83	9.08	7.92
Median	0.00	2.945	12.31	12.87	10.27	9.433	9.013
Maximum	0.00	9.23	12.8	20.1	18.5	14.0	9.66
Male							
n	2	2	2	2	2	2	2
Mean	0.00	0.8159	5.506	6.076	5.931	6.897	5.902
SD	0.00	0.23564	1.0795	1.2399	0.082335	0.30148	0.14408
CV%	.	28.9	19.6	20.4	1.4	4.4	2.4
SEM	0.00	0.16662	0.76332	0.87671	0.058220	0.21318	0.10188
Minimum	0.00	0.649	4.74	5.20	5.87	6.68	5.80
Median	0.00	0.8159	5.506	6.076	5.931	6.897	5.902
Maximum	0.00	0.983	6.27	6.95	5.99	7.11	6.00

For the calculation of summary statistics, negative values are assigned a value of zero
 . = Value missing or not reportable.

Table 14.2.7.4.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week -1 (minutes)							
	20	30	45	60	90	120	150	180
1015	9.66	8.20	5.46	5.00	3.47	2.46	1.81	1.40
1018	5.86	5.03	3.85	2.96	2.03	1.54	1.38	0.887
1032	9.01	7.51	6.16	4.90	3.73	2.71	1.86	1.58
1063	5.48	5.41	4.36	3.61	2.73	2.20	1.30	1.02
1072	5.56	5.68	5.12	4.66	3.48	2.55	2.00	1.37
Overall								
n	5	5	5	5	5	5	5	5
Mean	7.114	6.367	4.988	4.225	3.088	2.294	1.670	1.250
SD	2.0446	1.3994	0.90794	0.89727	0.69916	0.45841	0.30956	0.28651
CV%	28.7	22.0	18.2	21.2	22.6	20.0	18.5	22.9
SEM	0.91435	0.62583	0.40604	0.40127	0.31267	0.20501	0.13844	0.12813
Minimum	5.48	5.03	3.85	2.96	2.03	1.54	1.30	0.887
Median	5.858	5.680	5.121	4.662	3.468	2.459	1.810	1.367
Maximum	9.66	8.20	6.16	5.00	3.73	2.71	2.00	1.58

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.4.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week -1 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	3	3	3	3	3	3	3	3
Mean	8.176	6.913	5.154	4.285	3.076	2.238	1.683	1.288
SD	2.0331	1.6675	1.1828	1.1483	0.91393	0.61442	0.26773	0.35785
CV%	24.9	24.1	22.9	26.8	29.7	27.5	15.9	27.8
SEM	1.1738	0.96273	0.68287	0.66299	0.52766	0.35473	0.15458	0.20661
Minimum	5.86	5.03	3.85	2.96	2.03	1.54	1.38	0.887
Median	9.014	7.515	5.457	4.897	3.468	2.459	1.810	1.401
Maximum	9.66	8.20	6.16	5.00	3.73	2.71	1.86	1.58
Male								
n	2	2	2	2	2	2	2	2
Mean	5.522	5.548	4.739	4.134	3.106	2.378	1.650	1.192
SD	0.053720	0.18784	0.54095	0.74560	0.53262	0.24893	0.48851	0.24725
CV%	1.0	3.4	11.4	18.0	17.1	10.5	29.6	20.7
SEM	0.037986	0.13282	0.38251	0.52722	0.37662	0.17602	0.34543	0.17483
Minimum	5.48	5.41	4.36	3.61	2.73	2.20	1.30	1.02
Median	5.522	5.548	4.739	4.134	3.106	2.378	1.650	1.192
Maximum	5.56	5.68	5.12	4.66	3.48	2.55	2.00	1.37

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.4.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 2 (minutes)						
	Pre-Use	2	5	7	10	12	15
1015	0.00	0.0000656	0.148	0.227	0.237	0.218	0.204
1063	0.00	0.105	0.486	0.216	0.125	0.132	0.118
1072	0.00	0.0000656	0.113	0.113	0.105	0.000162	0.130
Overall							
n	3	3	3	3	3	3	3
Mean	0.00	0.03507	0.2491	0.1855	0.1558	0.1168	0.1509
SD	0.00	0.060624	0.20599	0.062889	0.071140	0.10981	0.046574
CV%	.	172.9	82.7	33.9	45.7	94.0	30.9
SEM	0.00	0.035001	0.11893	0.036309	0.041073	0.063398	0.026890
Minimum	0.00	0.0000656	0.113	0.113	0.105	0.000162	0.118
Median	0.00	0.0000655	0.1481	0.2161	0.1251	0.1322	0.1302
Maximum	0.00	0.105	0.486	0.227	0.237	0.218	0.204

For the calculation of summary statistics, negative values are assigned a value of zero
 . = Value missing or not reportable.

Table 14.2.7.4.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 2 (minutes)						
	Pre-Use	2	5	7	10	12	15
Female							
n	1	1	1	1	1	1	1
Mean	0.00	0.0000655	0.1481	0.2271	0.2371	0.2182	0.2042
SD
CV%
SEM
Minimum	0.00	0.0000656	0.148	0.227	0.237	0.218	0.204
Median	0.00	0.0000655	0.1481	0.2271	0.2371	0.2182	0.2042
Maximum	0.00	0.0000656	0.148	0.227	0.237	0.218	0.204
Male							
n	2	2	2	2	2	2	2
Mean	0.00	0.05257	0.2996	0.1646	0.1151	0.06616	0.1242
SD	0.00	0.074248	0.26375	0.072834	0.014144	0.093341	0.0084840
CV%	.	141.2	88.0	44.2	12.3	141.1	6.8
SEM	0.00	0.052502	0.18650	0.051501	0.010001	0.066002	0.0059991
Minimum	0.00	0.0000656	0.113	0.113	0.105	0.000162	0.118
Median	0.00	0.05257	0.2996	0.1646	0.1151	0.06616	0.1242
Maximum	0.00	0.105	0.486	0.216	0.125	0.132	0.130

For the calculation of summary statistics, negative values are assigned a value of zero
. = Value missing or not reportable.

Table 14.2.7.4.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 2 (minutes)							
	20	30	45	60	90	120	150	180
1015	0.139	0.000337	0.000480	0.000627	0.000926	0.00120	0.00148	0.00177
1063	0.000243	0.000340	0.000483	0.000628	0.000914	0.00120	0.00149	0.00177
1072	0.118	0.000336	0.000480	0.000625	0.000912	0.00120	0.00149	0.00177
Overall								
n	3	3	3	3	3	3	3	3
Mean	0.08591	0.0003375	0.0004810	0.0006267	0.0009173	0.001200	0.001486	0.001771
SD	0.074933	0.0000020	0.0000018	0.0000015	0.0000076	0.0000011	0.0000020	0.0000017
CV%	87.2	0.6	0.4	0.3	0.8	0.1	0.1	0.1
SEM	0.043263	0.0000011	0.0000010	0.0000009	0.0000044	0.0000006	0.0000012	0.0000010
Minimum	0.000243	0.000336	0.000480	0.000625	0.000912	0.00120	0.00148	0.00177
Median	0.1182	0.0003366	0.0004802	0.0006275	0.0009143	0.001200	0.001486	0.001771
Maximum	0.139	0.000340	0.000483	0.000628	0.000926	0.00120	0.00149	0.00177

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.4.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 2 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	1	1	1	1	1	1	1	1
Mean	0.1393	0.0003366	0.0004798	0.0006275	0.0009259	0.001200	0.001484	0.001770
SD
CV%
SEM
Minimum	0.139	0.000337	0.000480	0.000627	0.000926	0.00120	0.00148	0.00177
Median	0.1393	0.0003366	0.0004798	0.0006275	0.0009259	0.001200	0.001484	0.001770
Maximum	0.139	0.000337	0.000480	0.000627	0.000926	0.00120	0.00148	0.00177
Male								
n	2	2	2	2	2	2	2	2
Mean	0.05924	0.0003379	0.0004817	0.0006264	0.0009129	0.001200	0.001487	0.001772
SD	0.083436	0.0000027	0.0000020	0.0000020	0.0000019	0.0000015	0.0000017	0.0000011
CV%	140.8	0.8	0.4	0.3	0.2	0.1	0.1	0.1
SEM	0.058998	0.0000019	0.0000014	0.0000014	0.0000013	0.0000011	0.0000012	0.0000007
Minimum	0.000243	0.000336	0.000480	0.000625	0.000912	0.00120	0.00149	0.00177
Median	0.05924	0.0003379	0.0004817	0.0006264	0.0009129	0.001200	0.001487	0.001772
Maximum	0.118	0.000340	0.000483	0.000628	0.000914	0.00120	0.00149	0.00177

For the calculation of summary statistics, negative values are assigned a value of zero
 . = Value missing or not reportable.

Table 14.2.7.4.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 6 (minutes)						
	Pre-Use	2	5	7	10	12	15
1015	0.00	0.0000680	0.229	0.207	0.201	0.231	0.179
1032	0.00	0.0000678	0.123	0.174	0.133	0.187	0.163
1063	0.00	0.0000662	0.364	0.281	0.236	0.194	0.151

Overall							
n	3	3	3	3	3	3	3
Mean	0.00	0.0000673	0.2388	0.2208	0.1901	0.2042	0.1645
SD	0.00	0.0000009	0.12079	0.054793	0.052373	0.023644	0.014047
CV%	.	1.5	50.6	24.8	27.5	11.6	8.5
SEM	0.00	0.0000005	0.069738	0.031635	0.030238	0.013651	0.0081102
Minimum	0.00	0.0000662	0.123	0.174	0.133	0.187	0.151
Median	0.00	0.0000678	0.2291	0.2071	0.2011	0.1942	0.1632
Maximum	0.00	0.0000680	0.364	0.281	0.236	0.231	0.179

For the calculation of summary statistics, negative values are assigned a value of zero
 . = Value missing or not reportable.

Table 14.2.7.4.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 6 (minutes)						
	Pre-Use	2	5	7	10	12	15
Female							
n	2	2	2	2	2	2	2
Mean	0.00	0.0000678	0.1761	0.1906	0.1671	0.2092	0.1712
SD	0.00	0.0000001	0.074954	0.023335	0.048084	0.031113	0.011314
CV%	.	0.2	42.6	12.2	28.8	14.9	6.6
SEM	0.00	0.0000000	0.053001	0.016500	0.034000	0.022000	0.0080005
Minimum	0.00	0.0000678	0.123	0.174	0.133	0.187	0.163
Median	0.00	0.0000678	0.1761	0.1906	0.1671	0.2092	0.1712
Maximum	0.00	0.0000680	0.229	0.207	0.201	0.231	0.179
Male							
n	1	1	1	1	1	1	1
Mean	0.00	0.0000661	0.3641	0.2811	0.2361	0.1942	0.1512
SD
CV%
SEM
Minimum	0.00	0.0000662	0.364	0.281	0.236	0.194	0.151
Median	0.00	0.0000661	0.3641	0.2811	0.2361	0.1942	0.1512
Maximum	0.00	0.0000662	0.364	0.281	0.236	0.194	0.151

For the calculation of summary statistics, negative values are assigned a value of zero
. = Value missing or not reportable.

Table 14.2.7.4.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 6 (minutes)							
	20	30	45	60	90	120	150	180
1015	0.140	0.138	0.000483	0.000627	0.000915	0.00120	0.00149	0.00177
1032	0.132	0.000337	0.000482	0.000627	0.000914	0.00120	0.00149	0.00177
1063	0.000242	0.000336	0.000481	0.000623	0.000913	0.00120	0.00149	0.00177
Overall								
n	3	3	3	3	3	3	3	3
Mean	0.09091	0.04634	0.0004821	0.0006255	0.0009141	0.001201	0.001488	0.001772
SD	0.078622	0.079675	0.0000008	0.0000023	0.0000005	0.0000013	0.0000015	0.0000008
CV%	86.5	171.9	0.2	0.4	0.1	0.1	0.1	0.0
SEM	0.045392	0.046001	0.0000004	0.0000013	0.0000003	0.0000007	0.0000008	0.0000004
Minimum	0.000242	0.000336	0.000481	0.000623	0.000913	0.00120	0.00149	0.00177
Median	0.1322	0.0003371	0.0004822	0.0006265	0.0009141	0.001202	0.001488	0.001773
Maximum	0.140	0.138	0.000483	0.000627	0.000915	0.00120	0.00149	0.00177

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.4.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject Number	Week 6 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	2	2	2	2	2	2	2	2
Mean	0.1362	0.06934	0.0004825	0.0006268	0.0009144	0.001202	0.001487	0.001773
SD	0.0056573	0.097582	0.0000004	0.0000004	0.0000003	0.0000004	0.0000004	0.0000002
CV%	4.2	140.7	0.1	0.1	0.0	0.0	0.0	0.0
SEM	0.0040003	0.069001	0.0000003	0.0000003	0.0000002	0.0000003	0.0000003	0.0000001
Minimum	0.132	0.000337	0.000482	0.000627	0.000914	0.00120	0.00149	0.00177
Median	0.1362	0.06934	0.0004825	0.0006268	0.0009144	0.001202	0.001487	0.001773
Maximum	0.140	0.138	0.000483	0.000627	0.000915	0.00120	0.00149	0.00177
Male								
n	1	1	1	1	1	1	1	1
Mean	0.0002417	0.0003357	0.0004812	0.0006228	0.0009135	0.001200	0.001490	0.001771
SD
CV%
SEM
Minimum	0.000242	0.000336	0.000481	0.000623	0.000913	0.00120	0.00149	0.00177
Median	0.0002417	0.0003357	0.0004812	0.0006228	0.0009135	0.001200	0.001490	0.001771
Maximum	0.000242	0.000336	0.000481	0.000623	0.000913	0.00120	0.00149	0.00177

For the calculation of summary statistics, negative values are assigned a value of zero
 . = Value missing or not reportable.

Table 14.2.7.4.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week -1 (minutes)						
	Pre-Use	2	5	7	10	12	15
1003	0.00	1.87	10.1	13.6	10.8	12.3	10.9
1008	0.00	6.09	15.5	15.5	9.67	9.67	5.62
1014	0.00	3.61	7.61	9.01	9.11	9.51	8.12
1015	0.00	2.95	12.8	20.1	18.5	14.0	9.66
1018	0.00	9.23	11.9	12.9	10.3	9.08	7.92
1029	0.00	2.26	9.85	10.6	9.33	7.82	7.18
1032	0.00	2.88	.	8.99	9.83	9.43	9.01
1052	0.00	7.66	13.5	25.6	15.9	17.8	18.1
1053	0.00	4.10	13.7	13.6	12.2	11.2	10.7
1055	0.00	1.42	5.45	8.57	10.5	10.5	10.4
1063	0.00	0.983	4.74	6.95	5.87	6.68	6.00
1072	0.00	0.649	6.27	5.20	5.99	7.11	5.80
Overall							
n	12	12	11	12	12	12	12
Mean	0.00	3.642	10.12	12.54	10.66	10.42	9.114
SD	0.00	2.7073	3.6689	5.7731	3.5801	3.1091	3.3946
CV%	.	74.3	36.3	46.0	33.6	29.8	37.2
SEM	0.00	0.78153	1.1062	1.6666	1.0335	0.89752	0.97992
Minimum	0.00	0.649	4.74	5.20	5.87	6.68	5.62
Median	0.00	2.914	10.07	11.73	10.05	9.594	8.564
Maximum	0.00	9.23	15.5	25.6	18.5	17.8	18.1

For the calculation of summary statistics, negative values are assigned a value of zero
 . = Value missing or not reportable.

Table 14.2.7.4.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Pre-Use	2	5	7	10	12	15
----- Week -1 (minutes) -----							

Female							
n	6	6	5	6	6	6	6
Mean	0.00	3.725	9.507	11.68	11.25	10.05	8.716
SD	0.00	2.7946	3.0113	4.3981	3.5690	2.1001	1.2006
CV%	.	75.0	31.7	37.6	31.7	20.9	13.8
SEM	0.00	1.1409	1.3467	1.7955	1.4570	0.85738	0.49013
Minimum	0.00	1.42	5.45	8.57	9.11	7.82	7.18
Median	0.00	2.914	9.850	9.807	10.05	9.474	8.564
Maximum	0.00	9.23	12.8	20.1	18.5	14.0	10.4

Male							
n	6	6	6	6	6	6	6
Mean	0.00	3.559	10.62	13.40	10.06	10.79	9.513
SD	0.00	2.8807	4.3577	7.2265	3.8227	4.0661	4.8506
CV%	.	80.9	41.0	53.9	38.0	37.7	51.0
SEM	0.00	1.1761	1.7790	2.9502	1.5606	1.6600	1.9802
Minimum	0.00	0.649	4.74	5.20	5.87	6.68	5.62
Median	0.00	2.986	11.77	13.59	10.22	10.44	8.358
Maximum	0.00	7.66	15.5	25.6	15.9	17.8	18.1

For the calculation of summary statistics, negative values are assigned a value of zero
. = Value missing or not reportable.

Table 14.2.7.4.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week -1 (minutes)							
	20	30	45	60	90	120	150	180
1003	8.97	9.07	7.66	6.13	4.44	3.26	2.61	2.00
1008	6.32	4.65	3.92	2.93	2.56	1.80	1.27	0.776
1014	8.92	7.52	7.32	6.15	4.77	4.04	2.78	2.15
1015	9.66	8.20	5.46	5.00	3.47	2.46	1.81	1.40
1018	5.86	5.03	3.85	2.96	2.03	1.54	1.38	0.887
1029	5.93	4.96	3.66	3.73	1.93	1.49	1.06	0.793
1032	9.01	7.51	6.16	4.90	3.73	2.71	1.86	1.58
1052	15.4	13.7	11.3	10.1	7.48	7.33	6.33	4.33
1053	10.6	9.52	7.87	6.91	5.12	3.59	2.82	2.51
1055	8.13	7.12	5.79	4.90	3.99	3.00	2.50	1.96
1063	5.48	5.41	4.36	3.61	2.73	2.20	1.30	1.02
1072	5.56	5.68	5.12	4.66	3.48	2.55	2.00	1.37
Overall								
n	12	12	12	12	12	12	12	12
Mean	8.319	7.362	6.036	5.162	3.812	2.999	2.310	1.730
SD	2.8508	2.5821	2.2159	1.9953	1.5439	1.5745	1.4104	0.99745
CV%	34.3	35.1	36.7	38.7	40.5	52.5	61.0	57.6
SEM	0.82296	0.74538	0.63967	0.57599	0.44569	0.45453	0.40714	0.28794
Minimum	5.48	4.65	3.66	2.93	1.93	1.49	1.06	0.776
Median	8.525	7.319	5.625	4.896	3.606	2.633	1.929	1.488
Maximum	15.4	13.7	11.3	10.1	7.48	7.33	6.33	4.33

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.4.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week -1 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	6	6	6	6	6	6	6	6
Mean	7.918	6.724	5.373	4.604	3.320	2.541	1.899	1.461
SD	1.6408	1.3835	1.4039	1.1110	1.1260	0.95880	0.65171	0.55068
CV%	20.7	20.6	26.1	24.1	33.9	37.7	34.3	37.7
SEM	0.66986	0.56481	0.57314	0.45355	0.45969	0.39143	0.26606	0.22481
Minimum	5.86	4.96	3.66	2.96	1.93	1.49	1.06	0.793
Median	8.525	7.319	5.625	4.896	3.599	2.585	1.837	1.488
Maximum	9.66	8.20	7.32	6.15	4.77	4.04	2.78	2.15
Male								
n	6	6	6	6	6	6	6	6
Mean	8.720	8.000	6.698	5.719	4.303	3.457	2.722	2.000
SD	3.8473	3.4316	2.7888	2.6037	1.8431	2.0080	1.8826	1.3083
CV%	44.1	42.9	41.6	45.5	42.8	58.1	69.2	65.4
SEM	1.5706	1.4010	1.1385	1.0630	0.75244	0.81975	0.76858	0.53412
Minimum	5.48	4.65	3.92	2.93	2.56	1.80	1.27	0.776
Median	7.649	7.377	6.388	5.394	3.962	2.909	2.301	1.683
Maximum	15.4	13.7	11.3	10.1	7.48	7.33	6.33	4.33

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.4.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)						
	Pre-Use	2	5	7	10	12	15
<hr/>							
1003	0.00	0.0473	0.450	0.588	0.456	0.512	0.678
1008	0.00	0.338	0.418	0.314	0.257	0.218	0.235
1014	0.00	0.0442	0.191	0.206	0.174	0.147	0.175
1015	0.00	0.0000656	0.148	0.227	0.237	0.218	0.204
1029	0.00	0.0000673	0.127	0.165	0.114	0.113	0.104
1052	0.00	0.297	0.556	0.610	0.504	0.428	0.459
1053	0.00	0.393	0.474	0.387	0.275	0.239	0.269
1055	0.00	0.0000684	0.0000969	0.126	0.155	0.138	0.129
1063	0.00	0.105	0.486	0.216	0.125	0.132	0.118
1072	0.00	0.0000656	0.113	0.113	0.105	0.000162	0.130
<hr/>							
Overall							
n	10	10	10	10	10	10	10
Mean	0.00	0.1225	0.2965	0.2953	0.2404	0.2146	0.2502
SD	0.00	0.15716	0.19911	0.17983	0.14013	0.15191	0.18332
CV%	.	128.3	67.2	60.9	58.3	70.8	73.3
SEM	0.00	0.049699	0.062964	0.056868	0.044312	0.048038	0.057969
Minimum	0.00	0.0000656	0.0000969	0.113	0.105	0.000162	0.104
Median	0.00	0.04574	0.3048	0.2216	0.2057	0.1828	0.1898
Maximum	0.00	0.393	0.556	0.610	0.504	0.512	0.678

For the calculation of summary statistics, negative values are assigned a value of zero
 . = Value missing or not reportable.

Table 14.2.7.4.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)						
	Pre-Use	2	5	7	10	12	15
Female							
n	4	4	4	4	4	4	4
Mean	0.00	0.01110	0.1166	0.1812	0.1702	0.1542	0.1533
SD	0.00	0.022058	0.082153	0.044840	0.051208	0.045015	0.044994
CV%	.	198.8	70.4	24.8	30.1	29.2	29.4
SEM	0.00	0.011029	0.041077	0.022420	0.025604	0.022507	0.022497
Minimum	0.00	0.0000656	0.0000969	0.126	0.114	0.113	0.104
Median	0.00	0.0000678	0.1376	0.1857	0.1647	0.1428	0.1523
Maximum	0.00	0.0442	0.191	0.227	0.237	0.218	0.204
Male							
n	6	6	6	6	6	6	6
Mean	0.00	0.1968	0.4164	0.3714	0.2872	0.2549	0.3148
SD	0.00	0.16617	0.15551	0.19907	0.16494	0.18831	0.21622
CV%	.	84.4	37.3	53.6	57.4	73.9	68.7
SEM	0.00	0.067838	0.063487	0.081270	0.067335	0.076876	0.088273
Minimum	0.00	0.0000656	0.113	0.113	0.105	0.000162	0.118
Median	0.00	0.2011	0.4623	0.3507	0.2663	0.2288	0.2519
Maximum	0.00	0.393	0.556	0.610	0.504	0.512	0.678

For the calculation of summary statistics, negative values are assigned a value of zero
. = Value missing or not reportable.

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Table 14.2.7.4.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)							
	20	30	45	60	90	120	150	180
1003	0.134	0.493	0.00	0.00	0.0512	0.00	0.00	0.00
1008	0.159	0.163	0.140	0.132	0.0695	0.0362	0.0480	0.0147
1014	0.142	0.155	0.119	0.130	0.0940	0.0616	0.0303	0.0309
1015	0.139	0.000337	0.000480	0.000627	0.000926	0.00120	0.00148	0.00177
1029	0.000241	0.000337	0.000482	0.000626	0.000914	0.119	0.104	0.00177
1052	0.381	0.387	0.290	0.290	0.312	0.0818	0.152	0.0726
1053	0.255	0.213	0.126	0.176	0.000920	0.00120	0.00149	0.00177
1055	0.121	0.107	0.136	0.000627	0.000914	0.00120	0.00149	0.00177
1063	0.000243	0.000340	0.000483	0.000628	0.000914	0.00120	0.00149	0.00177
1072	0.118	0.000336	0.000480	0.000625	0.000912	0.00120	0.00149	0.00177
Overall								
n	10	10	10	10	10	10	10	10
Mean	0.1450	0.1519	0.08138	0.07309	0.05321	0.03048	0.03418	0.01288
SD	0.11119	0.17292	0.097808	0.10321	0.097346	0.043108	0.053203	0.023098
CV%	76.7	113.8	120.2	141.2	183.0	141.4	155.6	179.3
SEM	0.035163	0.054682	0.030929	0.032639	0.030784	0.013632	0.016824	0.0073043
Minimum	0.000241	0.000336	0.00	0.00	0.000912	0.00	0.00	0.00
Median	0.1367	0.1311	0.05978	0.0006276	0.0009231	0.001201	0.001488	0.001773
Maximum	0.381	0.493	0.290	0.290	0.312	0.119	0.152	0.0726

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.4.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 2 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	4	4	4	4	4	4	4	4
Mean	0.1006	0.06569	0.06413	0.03307	0.02419	0.04581	0.03443	0.009045
SD	0.067499	0.077913	0.073839	0.064882	0.046547	0.056617	0.048635	0.014547
CV%	67.1	118.6	115.1	196.2	192.4	123.6	141.3	160.8
SEM	0.033749	0.038956	0.036920	0.032441	0.023274	0.028309	0.024318	0.0072734
Minimum	0.000241	0.000337	0.000480	0.000626	0.000914	0.00120	0.00148	0.00177
Median	0.1302	0.05384	0.05978	0.0006272	0.0009200	0.03142	0.01587	0.001773
Maximum	0.142	0.155	0.136	0.130	0.0940	0.119	0.104	0.0309
Male								
n	6	6	6	6	6	6	6	6
Mean	0.1746	0.2094	0.09289	0.09976	0.07255	0.02027	0.03402	0.01544
SD	0.12998	0.20066	0.11641	0.12047	0.12097	0.033293	0.060628	0.028526
CV%	74.5	95.8	125.3	120.8	166.7	164.3	178.2	184.7
SEM	0.053064	0.081919	0.047524	0.049183	0.049388	0.013592	0.024751	0.011646
Minimum	0.000243	0.000336	0.00	0.00	0.000912	0.00	0.00	0.00
Median	0.1464	0.1881	0.06348	0.06617	0.02604	0.001201	0.001488	0.001773
Maximum	0.381	0.493	0.290	0.290	0.312	0.0818	0.152	0.0726

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.4.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)						
	Pre-Use	2	5	7	10	12	15
<hr/>							
1003	0.00	0.0164	0.203	0.214	0.235	0.141	0.0631
1008	0.00	0.329	0.651	0.661	0.275	0.296	0.401
1014	0.00	0.0283	0.281	0.200	0.229	0.223	0.212
1015	0.00	0.0000680	0.229	0.207	0.201	0.231	0.179
1029	0.00	0.0000673	0.192	0.101	0.168	0.129	0.000194
1032	0.00	0.0000678	0.123	0.174	0.133	0.187	0.163
1052	0.00	0.241	0.491	0.531	0.381	0.392	0.542
1053	0.00	0.325	0.215	0.361	0.210	0.239	0.247
1055	0.00	0.0000676	0.0000968	0.157	0.147	0.144	0.161
1063	0.00	0.0000662	0.364	0.281	0.236	0.194	0.151
<hr/>							
Overall							
n	10	10	10	10	10	10	10
Mean	0.00	0.09402	0.2749	0.2888	0.2216	0.2176	0.2120
SD	0.00	0.14331	0.18623	0.17894	0.071165	0.080037	0.15727
CV%	.	152.4	67.7	62.0	32.1	36.8	74.2
SEM	0.00	0.045318	0.058890	0.056585	0.022504	0.025310	0.049732
Minimum	0.00	0.0000662	0.0000968	0.101	0.133	0.129	0.000194
Median	0.00	0.008217	0.2221	0.2104	0.2195	0.2084	0.1712
Maximum	0.00	0.329	0.651	0.661	0.381	0.392	0.542

For the calculation of summary statistics, negative values are assigned a value of zero
 . = Value missing or not reportable.

Table 14.2.7.4.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)						
	Pre-Use	2	5	7	10	12	15
Female							
n	5	5	5	5	5	5	5
Mean	0.00	0.005712	0.1652	0.1680	0.1756	0.1829	0.1431
SD	0.00	0.012621	0.10879	0.042470	0.039150	0.045603	0.082429
CV%	.	221.0	65.9	25.3	22.3	24.9	57.6
SEM	0.00	0.0056441	0.048654	0.018993	0.017508	0.020394	0.036863
Minimum	0.00	0.0000673	0.0000968	0.101	0.133	0.129	0.000194
Median	0.00	0.0000678	0.1921	0.1741	0.1681	0.1872	0.1632
Maximum	0.00	0.0283	0.281	0.207	0.229	0.231	0.212
Male							
n	5	5	5	5	5	5	5
Mean	0.00	0.1823	0.3847	0.4096	0.2675	0.2524	0.2809
SD	0.00	0.16295	0.18995	0.18376	0.067716	0.096501	0.19231
CV%	.	89.4	49.4	44.9	25.3	38.2	68.5
SEM	0.00	0.072872	0.084948	0.082179	0.030283	0.043157	0.086004
Minimum	0.00	0.0000662	0.203	0.214	0.210	0.141	0.0631
Median	0.00	0.2406	0.3641	0.3612	0.2361	0.2393	0.2474
Maximum	0.00	0.329	0.651	0.661	0.381	0.392	0.542

For the calculation of summary statistics, negative values are assigned a value of zero
. = Value missing or not reportable.

Table 14.2.7.4.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)							
	20	30	45	60	90	120	150	180
1003	0.170	0.0879	0.0767	0.0886	0.278	0.0969	0.0167	0.00
1008	0.248	0.244	0.297	0.175	0.0639	0.161	0.00	0.0785
1014	0.149	0.158	0.149	0.135	0.0789	0.0591	0.0293	0.0285
1015	0.140	0.138	0.000483	0.000627	0.000915	0.00120	0.00149	0.00177
1029	0.000242	0.000338	0.000485	0.000626	0.000913	0.00120	0.00149	0.00177
1032	0.132	0.000337	0.000482	0.000627	0.000914	0.00120	0.00149	0.00177
1052	0.322	0.253	0.294	0.376	0.298	0.0472	0.0528	0.0305
1053	0.163	0.148	0.135	0.173	0.0369	0.0625	0.00	0.00
1055	0.155	0.155	0.118	0.000627	0.000914	0.00120	0.00149	0.00178
1063	0.000242	0.000336	0.000481	0.000623	0.000913	0.00120	0.00149	0.00177

Overall								
n	10	10	10	10	10	10	10	10
Mean	0.1480	0.1186	0.1073	0.09506	0.07610	0.04325	0.01063	0.01463
SD	0.097185	0.094832	0.11560	0.12363	0.11560	0.053943	0.017671	0.025332
CV%	65.7	80.0	107.8	130.1	151.9	124.7	166.2	173.1
SEM	0.030733	0.029989	0.036555	0.039094	0.036556	0.017058	0.0055881	0.0080108
Minimum	0.000242	0.000336	0.000481	0.000623	0.000913	0.00120	0.00	0.00
Median	0.1521	0.1430	0.09762	0.04460	0.01891	0.02419	0.001488	0.001773
Maximum	0.322	0.253	0.297	0.376	0.298	0.161	0.0528	0.0785

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.4.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following
 Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Subject Number	Week 6 (minutes)							
	20	30	45	60	90	120	150	180
Female								
n	5	5	5	5	5	5	5	5
Mean	0.1154	0.09056	0.05379	0.02743	0.01651	0.01278	0.007049	0.007120
SD	0.064962	0.082712	0.073795	0.059938	0.034863	0.025886	0.012435	0.011952
CV%	56.3	91.3	137.2	218.5	211.2	202.6	176.4	167.9
SEM	0.029052	0.036990	0.033002	0.026805	0.015591	0.011576	0.0055612	0.0053453
Minimum	0.000242	0.000337	0.000482	0.000626	0.000913	0.00120	0.00149	0.00177
Median	0.1402	0.1383	0.0004846	0.0006265	0.0009141	0.001202	0.001488	0.001773
Maximum	0.155	0.158	0.149	0.135	0.0789	0.0591	0.0293	0.0285
Male								
n	5	5	5	5	5	5	5	5
Mean	0.1806	0.1467	0.1608	0.1627	0.1357	0.07373	0.01421	0.02215
SD	0.11990	0.10690	0.13217	0.13915	0.14133	0.059625	0.022713	0.034057
CV%	66.4	72.9	82.2	85.5	104.2	80.9	159.8	153.8
SEM	0.053621	0.047805	0.059108	0.062229	0.063205	0.026665	0.010158	0.015231
Minimum	0.000242	0.000336	0.000481	0.000623	0.000913	0.00120	0.00	0.00
Median	0.1704	0.1477	0.1350	0.1733	0.06391	0.06252	0.001490	0.001771
Maximum	0.322	0.253	0.297	0.376	0.298	0.161	0.0528	0.0785

For the calculation of summary statistics, negative values are assigned a value of zero

Table 14.2.7.5.1 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of UB Non-Mentholated Filtered Cigarettes (Week -1) (Pharmacokinetic Population from PP)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)
1007	10.6	8.35	0.117

Table 14.2.7.5.2 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of UB Non-Mentholated Filtered Cigarettes (Week -1) (Pharmacokinetic Population from ITT)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)

1001	18.8	15.1	0.253
1013	15.4	18.4	0.116
1020	18.0	27.8	0.0860
1023	8.81	6.92	0.169
1038	13.9	11.1	0.116
1002	13.9	8.24	0.166
1007	10.6	8.35	0.117
1019	13.9	16.5	0.117
1035	7.88	6.48	0.0830
1042	6.86	14.0	0.116
1056	11.9	12.1	0.118
1058	18.2	14.3	0.116

Overall			
n	12	12	12
Mean	13.18	13.28	0.1311
SD	4.0648	5.9925	0.046066
CV%	30.8	45.1	35.1
SEM	1.1734	1.7299	0.013298
Minimum	6.86	6.48	0.0830
Median	13.90	13.08	0.1165
Maximum	18.8	27.8	0.253
Geom Mean	12.56	12.18	0.1252
Geom CV%	34.6	45.4	31.0

Table 14.2.7.5.2 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of UB Non-Mentholated Filtered Cigarettes (Week -1) (Pharmacokinetic Population from ITT)

Subject Number	Parameters		
	AUC0-180 (ng*hr/mL)	Cmax (ng/mL)	Tmax (hr)

Female			
n	5	5	5
Mean	14.97	15.86	0.1480
SD	3.9703	7.9398	0.065875
CV%	26.5	50.1	44.5
SEM	1.7756	3.5508	0.029460
Minimum	8.81	6.92	0.0860
Median	15.39	15.07	0.1160
Maximum	18.8	27.8	0.253
Geom Mean	14.48	14.27	0.1377
Geom CV%	31.0	56.2	43.5

Male			
n	7	7	7
Mean	11.90	11.44	0.1190
SD	3.8985	3.7825	0.024262
CV%	32.8	33.1	20.4
SEM	1.4735	1.4296	0.0091703
Minimum	6.86	6.48	0.0830
Median	11.93	12.11	0.1170
Maximum	18.2	16.5	0.166
Geom Mean	11.34	10.87	0.1170
Geom CV%	35.2	36.3	20.2

Table 14.2.7.6.1 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of Non-Mentholated VLN Cigarettes (Week 2) (Pharmacokinetic Population from PP)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)
1007	0.301	0.545	0.0850

Table 14.2.7.6.2 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of Non-Mentholated VLN Cigarettes (Week 2) (Pharmacokinetic Population from ITT)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)
1001	0.101	0.241	0.117
1013	0.414	0.391	0.166
1020	0.229	0.315	0.117
1023	0.0675	0.162	0.116
1038	0.0424	0.215	0.167
1002	0.577	0.301	0.199
1007	0.301	0.545	0.0850
1019	0.452	0.673	0.0830
1035	0.0412	0.274	0.0840
1042	0.0182	0.149	0.0830
1056	0.101	0.379	0.0840
1058	0.0624	0.271	0.0840
Overall			
n	12	12	12
Mean	0.2006	0.3264	0.1154
SD	0.19107	0.15367	0.040675
CV%	95.3	47.1	35.2
SEM	0.055157	0.044360	0.011742
Minimum	0.0182	0.149	0.0830
Median	0.1011	0.2873	0.1005
Maximum	0.577	0.673	0.199
Geom Mean	0.1213	0.2974	0.1097
Geom CV%	156.5	46.8	33.2

Table 14.2.7.6.2 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of Non-Mentholated VLN Cigarettes (Week 2) (Pharmacokinetic Population from ITT)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)

Female			
n	5	5	5
Mean	0.1708	0.2649	0.1366
SD	0.15363	0.089535	0.027300
CV%	90.0	33.8	20.0
SEM	0.068704	0.040041	0.012209
Minimum	0.0424	0.162	0.116
Median	0.1010	0.2411	0.1170
Maximum	0.414	0.391	0.167
Geom Mean	0.1223	0.2530	0.1345
Geom CV%	115.6	35.1	19.7

Male			
n	7	7	7
Mean	0.2218	0.3702	0.1003
SD	0.22345	0.18044	0.043534
CV%	100.7	48.7	43.4
SEM	0.084456	0.068199	0.016454
Minimum	0.0182	0.149	0.0830
Median	0.1012	0.3012	0.08400
Maximum	0.577	0.673	0.199
Geom Mean	0.1206	0.3339	0.09485
Geom CV%	212.0	53.1	33.6

Table 14.2.7.7.1 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of Non-Mentholated VLN Cigarettes (Week 6) (Pharmacokinetic Population from PP)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)
1007	0.436	0.613	0.0560

Table 14.2.7.7.2 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of Non-Mentholated VLN Cigarettes (Week 6) (Pharmacokinetic Population from ITT)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)
1001	0.461	0.488	0.334
1013	0.442	0.299	0.119
1020	0.396	0.563	0.124
1023	0.217	0.244	0.253
1038	0.335	0.312	0.194
1002	0.192	0.289	0.203
1007	0.436	0.613	0.0560
1019	0.256	0.649	0.0840
1035	0.0821	0.304	0.0840
1042	0.0188	0.218	0.0840
1056	0.241	0.519	0.0830
1058	0.0668	0.332	0.117
Overall			
n	12	12	12
Mean	0.2620	0.4026	0.1446
SD	0.15446	0.15292	0.084195
CV%	59.0	38.0	58.2
SEM	0.044589	0.044145	0.024305
Minimum	0.0188	0.218	0.0560
Median	0.2483	0.3221	0.1180
Maximum	0.461	0.649	0.334
Geom Mean	0.1956	0.3770	0.1259
Geom CV%	124.9	39.2	57.9

Table 14.2.7.7.2 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of Non-Mentholated VLN Cigarettes (Week 6) (Pharmacokinetic Population from ITT)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)

Female			
n	5	5	5
Mean	0.3703	0.3814	0.2048
SD	0.098358	0.13681	0.090861
CV%	26.6	35.9	44.4
SEM	0.043987	0.061183	0.040634
Minimum	0.217	0.244	0.119
Median	0.3963	0.3122	0.1940
Maximum	0.461	0.563	0.334
Geom Mean	0.3579	0.3626	0.1891
Geom CV%	31.3	36.4	47.1

Male			
n	7	7	7
Mean	0.1846	0.4177	0.1016
SD	0.14329	0.17249	0.048086
CV%	77.6	41.3	47.3
SEM	0.054159	0.065196	0.018175
Minimum	0.0188	0.218	0.0560
Median	0.1922	0.3321	0.08400
Maximum	0.436	0.649	0.203
Geom Mean	0.1270	0.3876	0.09412
Geom CV%	145.8	44.0	41.7

Table 14.2.7.8.1 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of UB Mentholated Filtered Cigarettes (Week -1) (Pharmacokinetic Population from PP)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)
1015	13.9	20.1	0.115
1018	9.23	12.9	0.135
1032	12.8	9.83	0.167
1063	9.09	6.95	0.116
1072	10.7	7.11	0.199

Overall			
n	5	5	5
Mean	11.16	11.36	0.1464
SD	2.1597	5.4245	0.036164
CV%	19.4	47.7	24.7
SEM	0.96584	2.4259	0.016173
Minimum	9.09	6.95	0.115
Median	10.71	9.833	0.1350
Maximum	13.9	20.1	0.199
Geom Mean	10.99	10.46	0.1430
Geom CV%	19.4	46.6	24.2

Table 14.2.7.8.1 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of UB Mentholated Filtered Cigarettes (Week -1) (Pharmacokinetic Population from PP)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)

Female			
n	3	3	3
Mean	12.00	14.25	0.1390
SD	2.4540	5.2500	0.026230
CV%	20.5	36.8	18.9
SEM	1.4168	3.0311	0.015144
Minimum	9.23	9.83	0.115
Median	12.83	12.87	0.1350
Maximum	13.9	20.1	0.167
Geom Mean	11.82	13.64	0.1374
Geom CV%	22.0	37.2	18.9

Male			
n	2	2	2
Mean	9.895	7.031	0.1575
SD	1.1456	0.11086	0.058690
CV%	11.6	1.6	37.3
SEM	0.81006	0.078386	0.041500
Minimum	9.09	6.95	0.116
Median	9.895	7.031	0.1575
Maximum	10.7	7.11	0.199
Geom Mean	9.862	7.031	0.1519
Geom CV%	11.6	1.6	39.6

Table 14.2.7.8.2 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of UB Mentholated Filtered Cigarettes (Week -1) (Pharmacokinetic Population from ITT)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)
1014	15.3	9.51	0.205
1015	13.9	20.1	0.115
1018	9.23	12.9	0.135
1029	8.67	10.6	0.117
1032	12.8	9.83	0.167
1055	13.2	10.5	0.203
1003	15.7	13.6	0.117
1008	9.70	15.5	0.116
1052	27.6	25.6	0.116
1053	17.2	13.7	0.0840
1063	9.09	6.95	0.116
1072	10.7	7.11	0.199

Overall			
n	12	12	12
Mean	13.60	12.98	0.1408
SD	5.2610	5.3932	0.041525
CV%	38.7	41.5	29.5
SEM	1.5187	1.5569	0.011987
Minimum	8.67	6.95	0.0840
Median	13.01	11.73	0.1170
Maximum	27.6	25.6	0.205
Geom Mean	12.85	12.09	0.1356
Geom CV%	34.6	40.0	29.2

Table 14.2.7.8.2 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of UB Mentholated Filtered Cigarettes (Week -1) (Pharmacokinetic Population from ITT)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)

Female			
n	6	6	6
Mean	12.20	12.23	0.1570
SD	2.6602	4.0092	0.040910
CV%	21.8	32.8	26.1
SEM	1.0860	1.6368	0.016701
Minimum	8.67	9.51	0.115
Median	13.01	10.56	0.1510
Maximum	15.3	20.1	0.205
Geom Mean	11.94	11.79	0.1526
Geom CV%	23.5	28.6	26.6

Male			
n	6	6	6
Mean	15.00	13.73	0.1247
SD	7.0077	6.8240	0.038635
CV%	46.7	49.7	31.0
SEM	2.8609	2.7859	0.015773
Minimum	9.09	6.95	0.0840
Median	13.18	13.64	0.1160
Maximum	27.6	25.6	0.199
Geom Mean	13.84	12.40	0.1204
Geom CV%	44.7	52.9	28.4

Table 14.2.7.9.1 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of Mentholated VLN Cigarettes (Week 2) (Pharmacokinetic Population from PP)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)
1015	0.0704	0.237	0.161
1063	0.0549	0.486	0.0830
1072	0.0400	0.130	0.251

Overall			
n	3	3	3
Mean	0.05510	0.2845	0.1650
SD	0.015189	0.18261	0.084071
CV%	27.6	64.2	51.0
SEM	0.0087692	0.10543	0.048539
Minimum	0.0400	0.130	0.0830
Median	0.05493	0.2371	0.1610
Maximum	0.0704	0.486	0.251
Geom Mean	0.05367	0.2467	0.1497
Geom CV%	28.9	73.8	60.3

Table 14.2.7.9.1 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of Mentholated VLN Cigarettes (Week 2) (Pharmacokinetic Population from PP)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)

Female			
n	1	1	1
Mean	0.07037	0.2371	0.1610
SD	.	.	.
CV%	.	.	.
SEM	.	.	.
Minimum	0.0704	0.237	0.161
Median	0.07037	0.2371	0.1610
Maximum	0.0704	0.237	0.161
Geom Mean	0.07037	0.2371	0.1610
Geom CV%	.	.	.

Male			
n	2	2	2
Mean	0.04746	0.3081	0.1670
SD	0.010566	0.25166	0.11879
CV%	22.3	81.7	71.1
SEM	0.0074714	0.17795	0.084000
Minimum	0.0400	0.130	0.0830
Median	0.04746	0.3081	0.1670
Maximum	0.0549	0.486	0.251
Geom Mean	0.04687	0.2516	0.1443
Geom CV%	22.7	117.5	91.9

. = Value missing or not reportable.

Table 14.2.7.9.2 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of Mentholated VLN Cigarettes (Week 2) (Pharmacokinetic Population from ITT)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)

1014	0.272	0.206	0.115
1015	0.0704	0.237	0.161
1029	0.142	0.165	0.118
1055	0.100	0.155	0.168
1003	0.279	0.678	0.249
1008	0.302	0.418	0.0850
1052	0.734	0.610	0.117
1053	0.270	0.474	0.0830
1063	0.0549	0.486	0.0830
1072	0.0400	0.130	0.251

Overall			
n	10	10	10
Mean	0.2264	0.3561	0.1430
SD	0.20588	0.20204	0.063681
CV%	90.9	56.7	44.5
SEM	0.065106	0.063889	0.020138
Minimum	0.0400	0.130	0.0830
Median	0.2058	0.3277	0.1175
Maximum	0.734	0.678	0.251
Geom Mean	0.1584	0.3029	0.1317
Geom CV%	114.7	67.8	43.9

Table 14.2.7.9.2 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of Mentholated VLN Cigarettes (Week 2) (Pharmacokinetic Population from ITT)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)

Female			
n	4	4	4
Mean	0.1462	0.1909	0.1405
SD	0.089129	0.037939	0.027887
CV%	61.0	19.9	19.8
SEM	0.044564	0.018969	0.013943
Minimum	0.0704	0.155	0.115
Median	0.1210	0.1857	0.1395
Maximum	0.272	0.237	0.168
Geom Mean	0.1285	0.1881	0.1384
Geom CV%	62.9	19.9	20.2

Male			
n	6	6	6
Mean	0.2798	0.4661	0.1447
SD	0.25093	0.19039	0.082612
CV%	89.7	40.8	57.1
SEM	0.10244	0.077728	0.033726
Minimum	0.0400	0.130	0.0830
Median	0.2741	0.4801	0.1010
Maximum	0.734	0.678	0.251
Geom Mean	0.1822	0.4161	0.1274
Geom CV%	158.2	65.3	57.9

Table 14.2.7.10.1 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of Mentholated VLN Cigarettes (Week 6) (Pharmacokinetic Population from PP)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)
1015	0.0972	0.231	0.200
1032	0.0559	0.187	0.199
1063	0.0582	0.364	0.0830
Overall			
n	3	3	3
Mean	0.07040	0.2608	0.1607
SD	0.023221	0.092116	0.067263
CV%	33.0	35.3	41.9
SEM	0.013406	0.053183	0.038834
Minimum	0.0559	0.187	0.0830
Median	0.05815	0.2312	0.1990
Maximum	0.0972	0.364	0.200
Geom Mean	0.06809	0.2507	0.1489
Geom CV%	31.6	35.0	54.1

Table 14.2.7.10.1 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
Use of Mentholated VLN Cigarettes (Week 6) (Pharmacokinetic Population from PP)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)

Female			
n	2	2	2
Mean	0.07652	0.2092	0.1995
SD	0.029215	0.031113	0.00070711
CV%	38.2	14.9	0.4
SEM	0.020658	0.022000	0.00050000
Minimum	0.0559	0.187	0.199
Median	0.07652	0.2092	0.1995
Maximum	0.0972	0.231	0.200
Geom Mean	0.07368	0.2080	0.1995
Geom CV%	40.7	15.0	0.4

Male			
n	1	1	1
Mean	0.05815	0.3641	0.08300
SD	.	.	.
CV%	.	.	.
SEM	.	.	.
Minimum	0.0582	0.364	0.0830
Median	0.05815	0.3641	0.08300
Maximum	0.0582	0.364	0.0830
Geom Mean	0.05815	0.3641	0.08300
Geom CV%	.	.	.

. = Value missing or not reportable.

Table 14.2.7.10.2 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of Mentholated VLN Cigarettes (Week 6) (Pharmacokinetic Population from ITT)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)
1014	0.284	0.281	0.0860
1015	0.0972	0.231	0.200
1029	0.0284	0.192	0.0840
1032	0.0559	0.187	0.199
1055	0.113	0.161	0.250
1003	0.328	0.278	1.50
1008	0.479	0.661	0.123
1052	0.636	0.542	0.253
1053	0.268	0.361	0.118
1063	0.0582	0.364	0.0830

Overall			
n	10	10	10
Mean	0.2348	0.3259	0.2895
SD	0.20330	0.16294	0.43017
CV%	86.6	50.0	148.6
SEM	0.064289	0.051526	0.13603
Minimum	0.0284	0.161	0.0830
Median	0.1906	0.2798	0.1610
Maximum	0.636	0.661	1.50
Geom Mean	0.1545	0.2947	0.1785
Geom CV%	139.1	48.9	106.1

Table 14.2.7.10.2 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following
 Use of Mentholated VLN Cigarettes (Week 6) (Pharmacokinetic Population from ITT)

Subject Number	Parameters		
	AUC ₀₋₁₈₀ (ng*hr/mL)	C _{max} (ng/mL)	T _{max} (hr)

Female			
n	5	5	5
Mean	0.1158	0.2106	0.1638
SD	0.099908	0.046826	0.074834
CV%	86.3	22.2	45.7
SEM	0.044680	0.020941	0.033467
Minimum	0.0284	0.161	0.0840
Median	0.09718	0.1921	0.1990
Maximum	0.284	0.281	0.250
Geom Mean	0.08695	0.2067	0.1484
Geom CV%	103.9	21.7	55.3

Male			
n	5	5	5
Mean	0.3537	0.4412	0.4152
SD	0.21822	0.15589	0.60930
CV%	61.7	35.3	146.7
SEM	0.097591	0.069718	0.27249
Minimum	0.0582	0.278	0.0830
Median	0.3282	0.3641	0.1230
Maximum	0.636	0.661	1.50
Geom Mean	0.2744	0.4202	0.2148
Geom CV%	117.1	35.8	168.3

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Table 14.2.7.11 Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters at Weeks 2 and 6 (VLN Cigarettes) Versus Week -1 (UB Cigarettes) (Pharmacokinetic Population from PP)

Parameter (Unit)	Study Week	Product Groups	-----Geometric Means -----				GMR		95%		p-Value
			Test Week (VLN)	(n)	Baseline (UB)	(n)	(Test Week /Baseline)	% Reduction	Confidence Intervals		
C _{max} (ng/mL)	Week 2	Non-mentholated	0.5451	(1)	8.352	(1)	0.065	93.5	. - .	.	
		Mentholated	0.2467	(3)	9.971	(3)	0.025	97.5	0.002 - 0.247	0.0202	
		Combined	0.3007	(4)	9.539	(4)	0.032	96.8	0.008 - 0.132	0.0046	
	Week 6	Non-mentholated	0.6131	(1)	8.352	(1)	0.073	92.7	. - .	.	
		Mentholated	0.2507	(3)	11.11	(3)	0.023	97.7	0.003 - 0.153	0.0135	
		Combined	0.3135	(4)	10.34	(4)	0.030	97.0	0.008 - 0.120	0.0039	
AUC ₀₋₁₈₀ (hr*ng/mL)	Week 2	Non-mentholated	0.3006	(1)	10.58	(1)	0.028	97.2	. - .	.	
		Mentholated	0.05367	(3)	11.06	(3)	0.005	99.5	0.003 - 0.009	0.0007	
		Combined	0.08256	(4)	10.94	(4)	0.008	99.2	0.002 - 0.032	0.0017	
	Week 6	Non-mentholated	0.4357	(1)	10.58	(1)	0.041	95.9	. - .	.	
		Mentholated	0.06809	(3)	11.75	(3)	0.006	99.4	0.003 - 0.011	0.0008	
		Combined	0.1083	(4)	11.45	(4)	0.009	99.1	0.002 - 0.047	0.0026	

 Baseline = Week -1

Subjects used their own usual brand cigarettes at Week -1.

VLN non-mentholated = Non-mentholated VLN cigarettes; VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

Analysis is based on the log-transformed data.

Paired t-test method is used to perform the analysis.

Geometric means are calculated by exponentiating the means.

Geometric Mean Ratios (GMR) are calculated by exponentiating the mean of difference from paired t-test.

95% Confidence Intervals are calculated by exponentiating the 95% Confidence Intervals of the mean difference from paired t-test.

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Table 14.2.7.12 Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters at Weeks 2 and 6 (VLN Cigarettes) Versus Week -1 (UB Cigarettes) (Pharmacokinetic Population from ITT)

Parameter (Unit)	Study Week	Product Groups	-----Geometric Means -----				GMR (Test Week /Baseline)	% Reduction	95%		p-Value
			Test Week (VLN)	(n)	Baseline (UB)	(n)			Confidence Intervals		
Cmax (ng/mL)	Week 2	Non-mentholated	0.2974	(12)	12.18	(12)	0.024	97.6	0.017 – 0.035	<.0001	
		Mentholated	0.3029	(10)	12.27	(10)	0.025	97.5	0.017 – 0.037	<.0001	
		Combined	0.2999	(22)	12.22	(22)	0.025	97.5	0.019 – 0.031	<.0001	
	Week 6	Non-mentholated	0.3770	(12)	12.18	(12)	0.031	96.9	0.023 – 0.041	<.0001	
		Mentholated	0.2947	(10)	12.67	(10)	0.023	97.7	0.017 – 0.032	<.0001	
		Combined	0.3371	(22)	12.40	(22)	0.027	97.3	0.022 – 0.033	<.0001	
AUC0-180 (hr*ng/mL)	Week 2	Non-mentholated	0.1213	(12)	12.56	(12)	0.010	99.0	0.005 – 0.018	<.0001	
		Mentholated	0.1584	(10)	13.29	(10)	0.012	98.8	0.007 – 0.020	<.0001	
		Combined	0.1370	(22)	12.88	(22)	0.011	98.9	0.007 – 0.016	<.0001	
	Week 6	Non-mentholated	0.1956	(12)	12.56	(12)	0.016	98.4	0.009 – 0.026	<.0001	
		Mentholated	0.1545	(10)	13.53	(10)	0.011	98.9	0.006 – 0.021	<.0001	
		Combined	0.1757	(22)	12.99	(22)	0.014	98.6	0.009 – 0.020	<.0001	

 Baseline = Week -1

Subjects used their own usual brand cigarettes at Week -1.

VLN non-mentholated = Non-mentholated VLN cigarettes; VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

Analysis is based on the log-transformed data.

Paired t-test method is used to perform the analysis.

Geometric means are calculated by exponentiating the means.

Geometric Mean Ratios (GMR) are calculated by exponentiating the mean of difference from paired t-test.

95% Confidence Intervals are calculated by exponentiating the 95% Confidence Intervals of the mean difference from paired t-test.

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14.2.8 Plasma Nicotine Figures

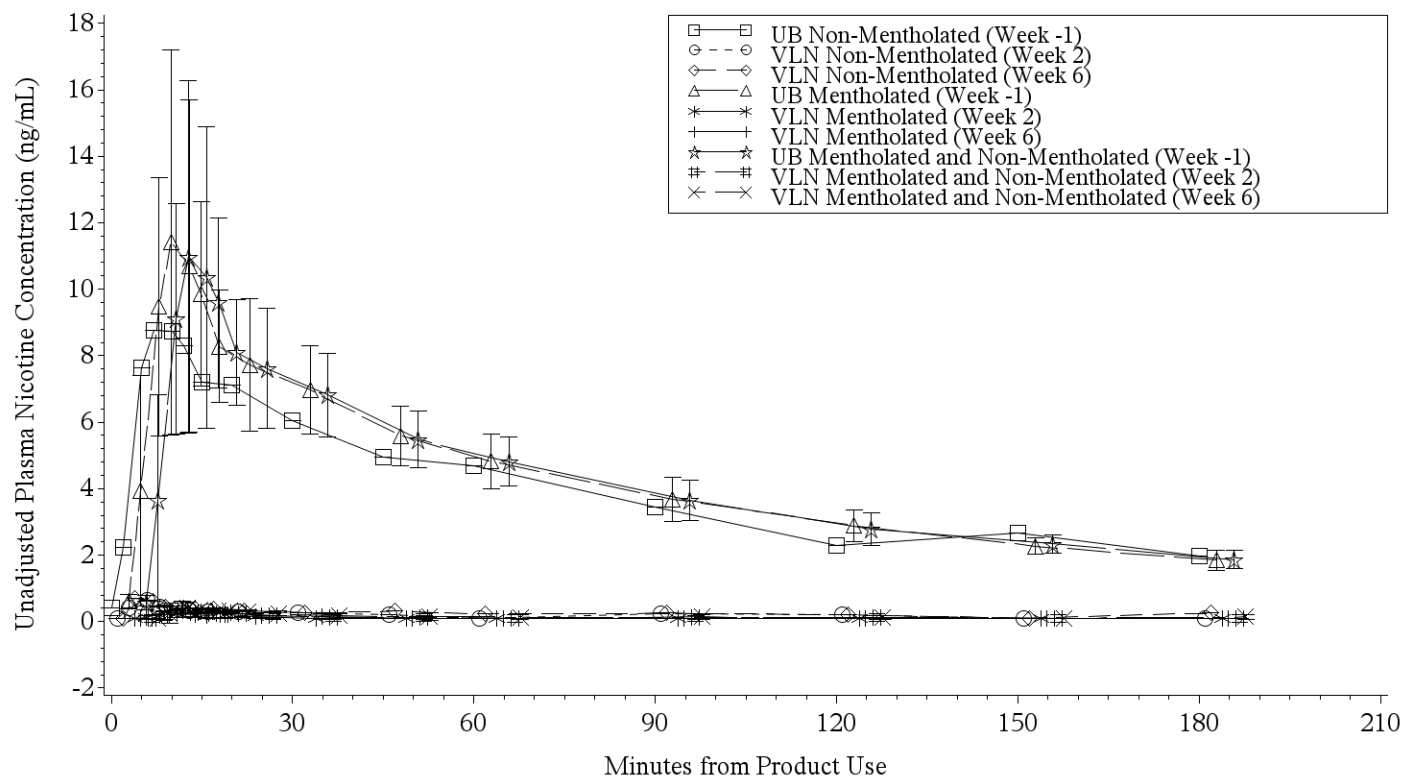
- Figure 14.2.8.1 Mean (SD) Unadjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from PP)
- Figure 14.2.8.2 Mean Unadjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from PP)
- Figure 14.2.8.3 Mean Unadjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Semi-Log Scale) (Pharmacokinetic Population from PP)
- Figure 14.2.8.4 Mean (SD) Baseline Adjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from PP)
- Figure 14.2.8.5 Mean Baseline Adjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from PP)
- Figure 14.2.8.6 Mean Baseline Adjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Semi-Log Scale) (Pharmacokinetic Population from PP)
- Figure 14.2.8.7 Mean (SD) Unadjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from ITT)
- Figure 14.2.8.8 Mean Unadjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from ITT)
- Figure 14.2.8.9 Mean Unadjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Semi-Log Scale) (Pharmacokinetic Population from ITT)
- Figure 14.2.8.10 Mean (SD) Baseline Adjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from ITT)

Figure 14.2.8.11 Mean Baseline Adjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from ITT)

Figure 14.2.8.12 Mean Baseline Adjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Semi-Log Scale) (Pharmacokinetic Population from ITT)

Figure 14.2.8.1

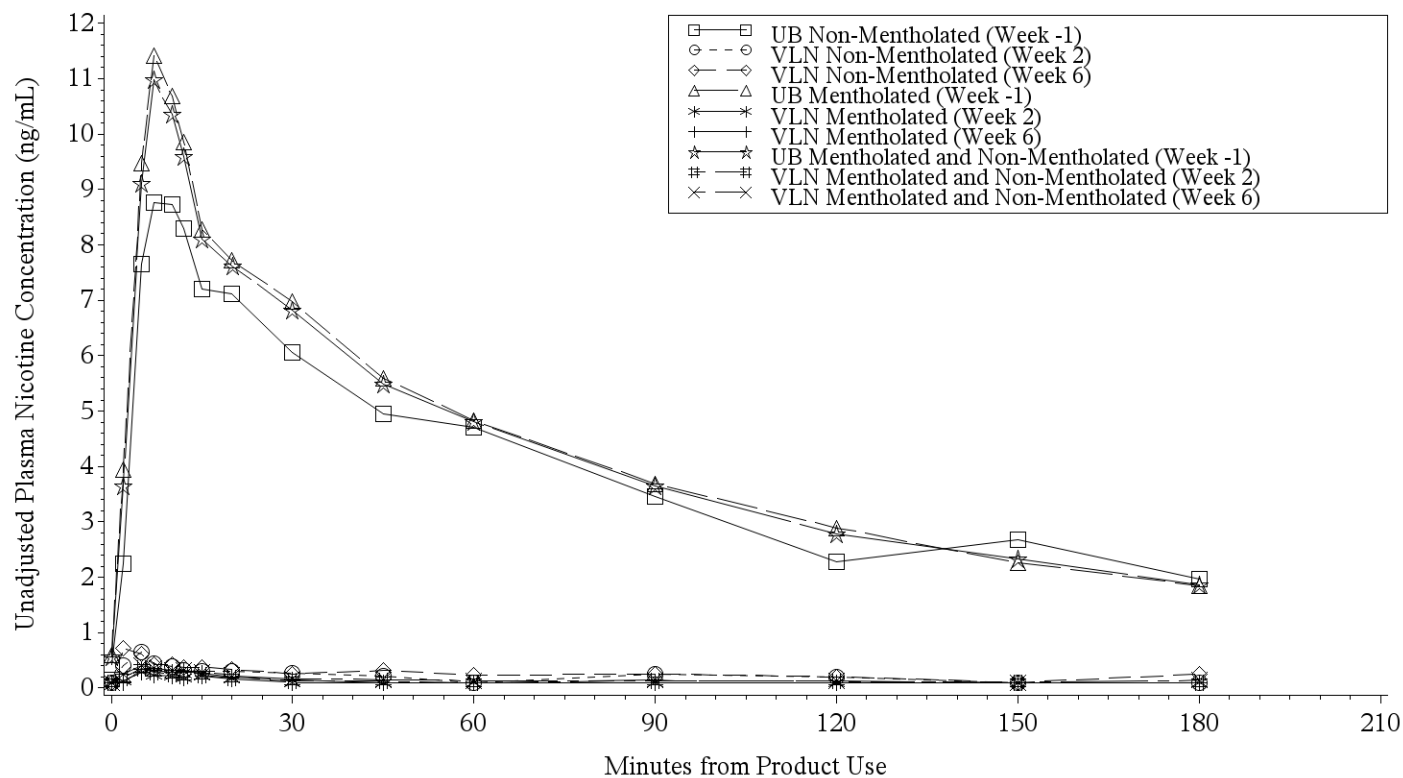
Mean (SD) Unadjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from PP)



VLN Mentholated and Non-Mentholated (Week 2 and Week 6) and UB Non-Mentholated (Week -16) are shifted to the right for ease of reading
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Figure 14.2.8.2

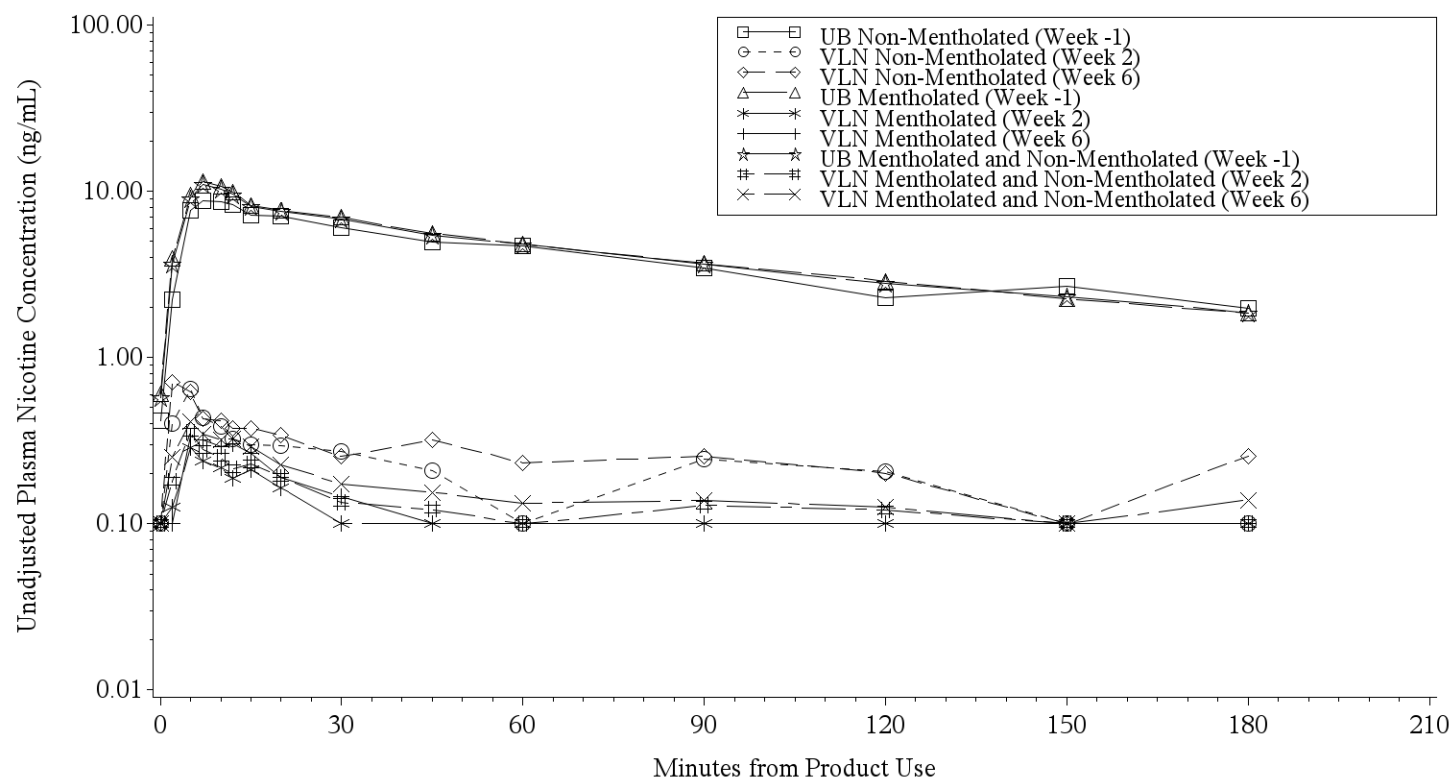
Mean Unadjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from PP)



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Figure 14.2.8.3

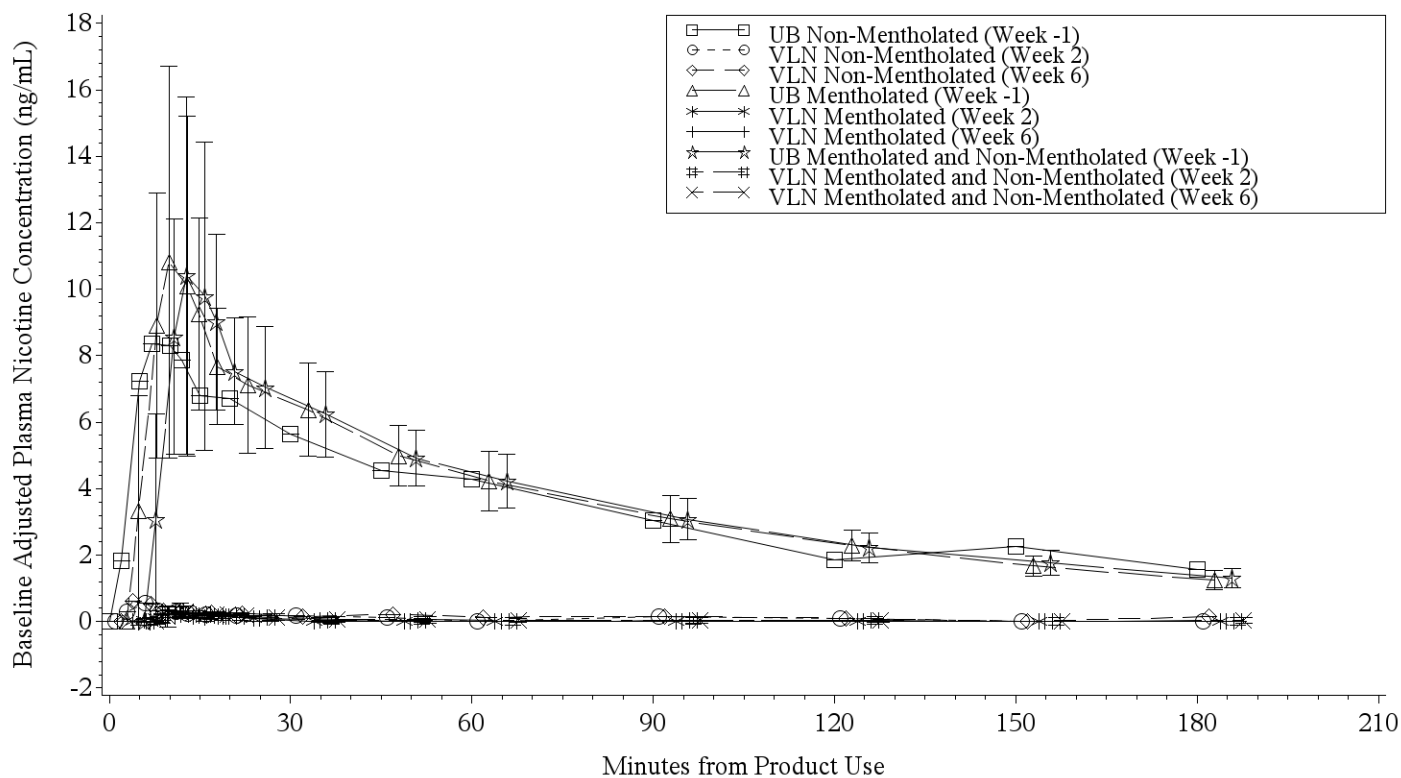
Mean Unadjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Semi-Log Scale) (Pharmacokinetic Population from PP)



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Figure 14.2.8.4

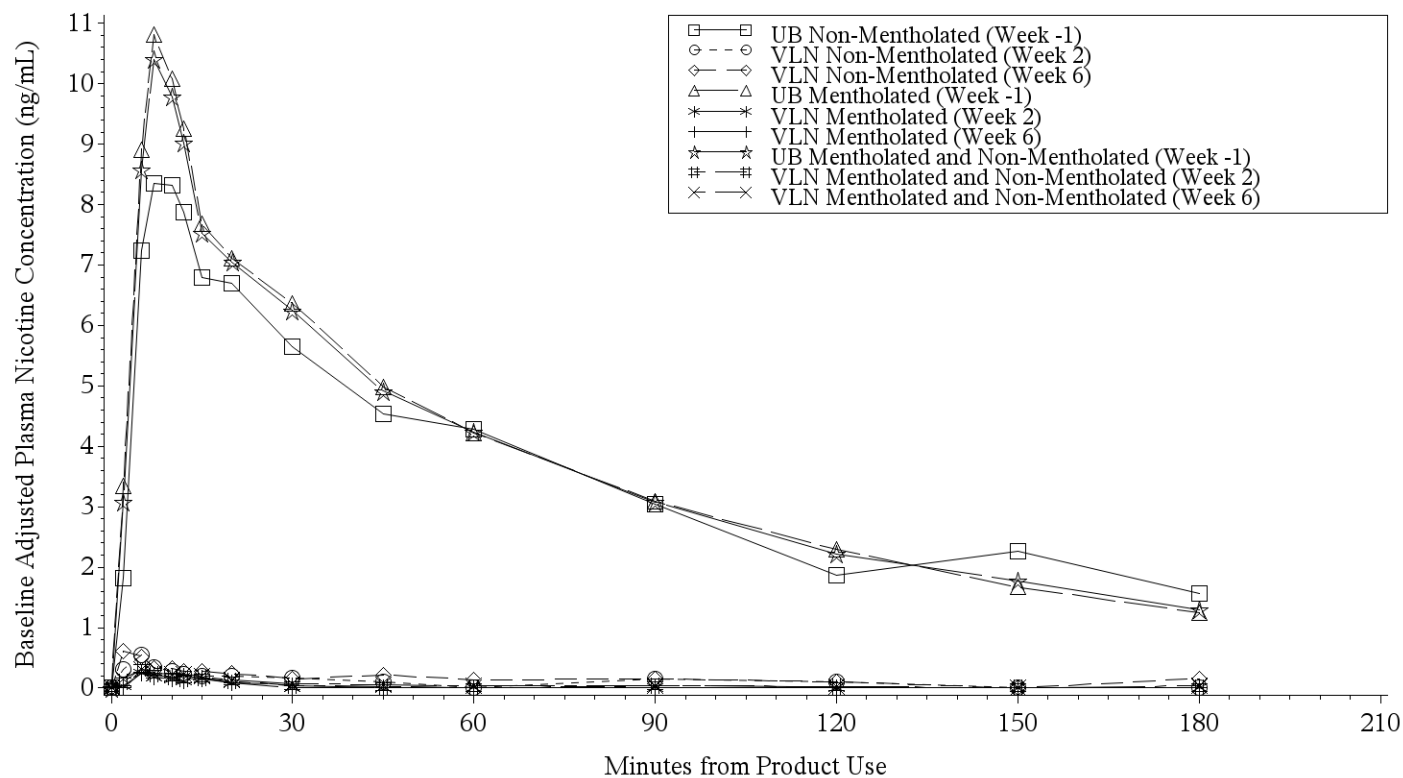
Mean (SD) Baseline Adjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from PP)



VLN Mentholated and Non-Mentholated (Week 2 and Week 6) and UB Non-Mentholated (Week -16) are shifted to the right for ease of reading
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Figure 14.2.8.5

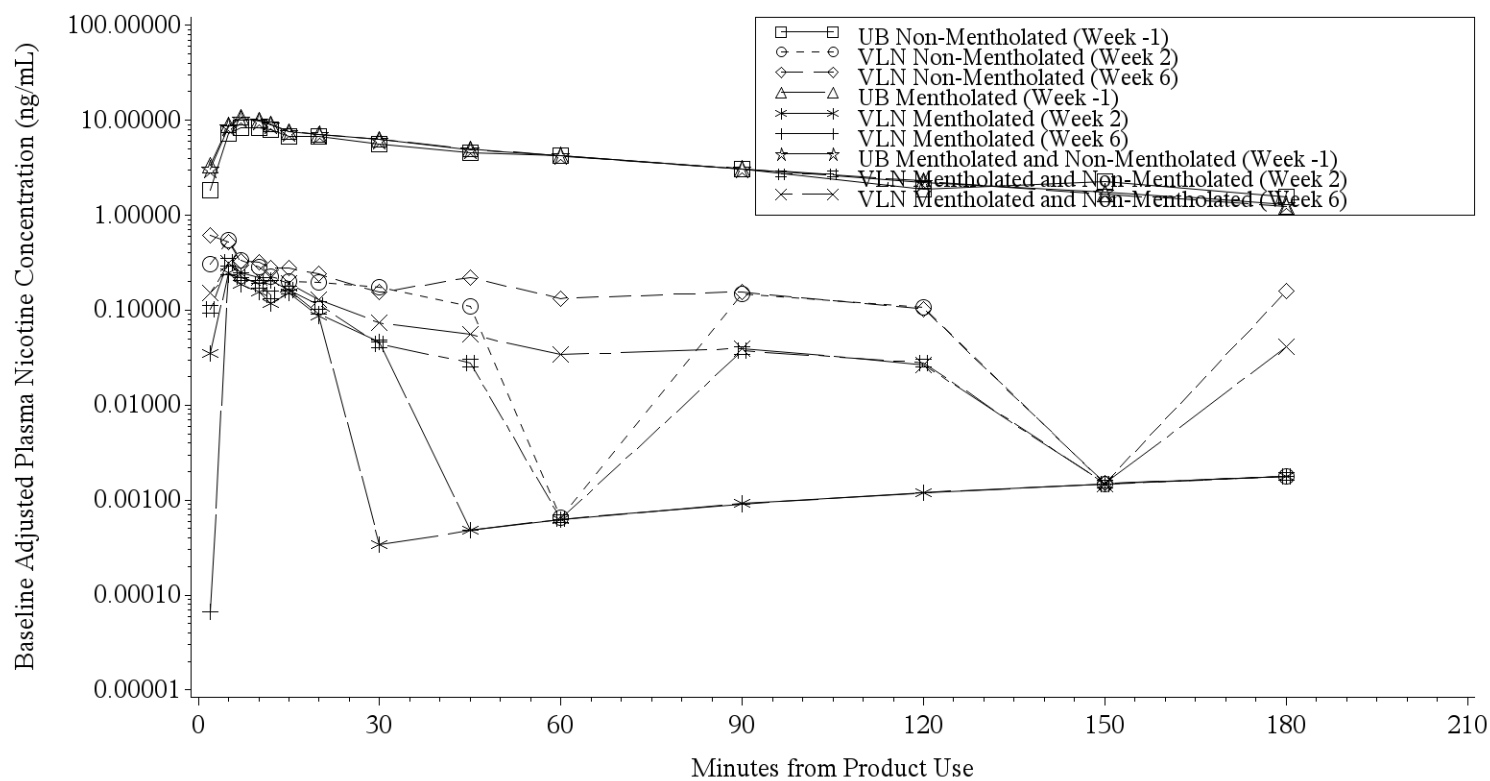
Mean Baseline Adjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from PP)



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Figure 14.2.8.6

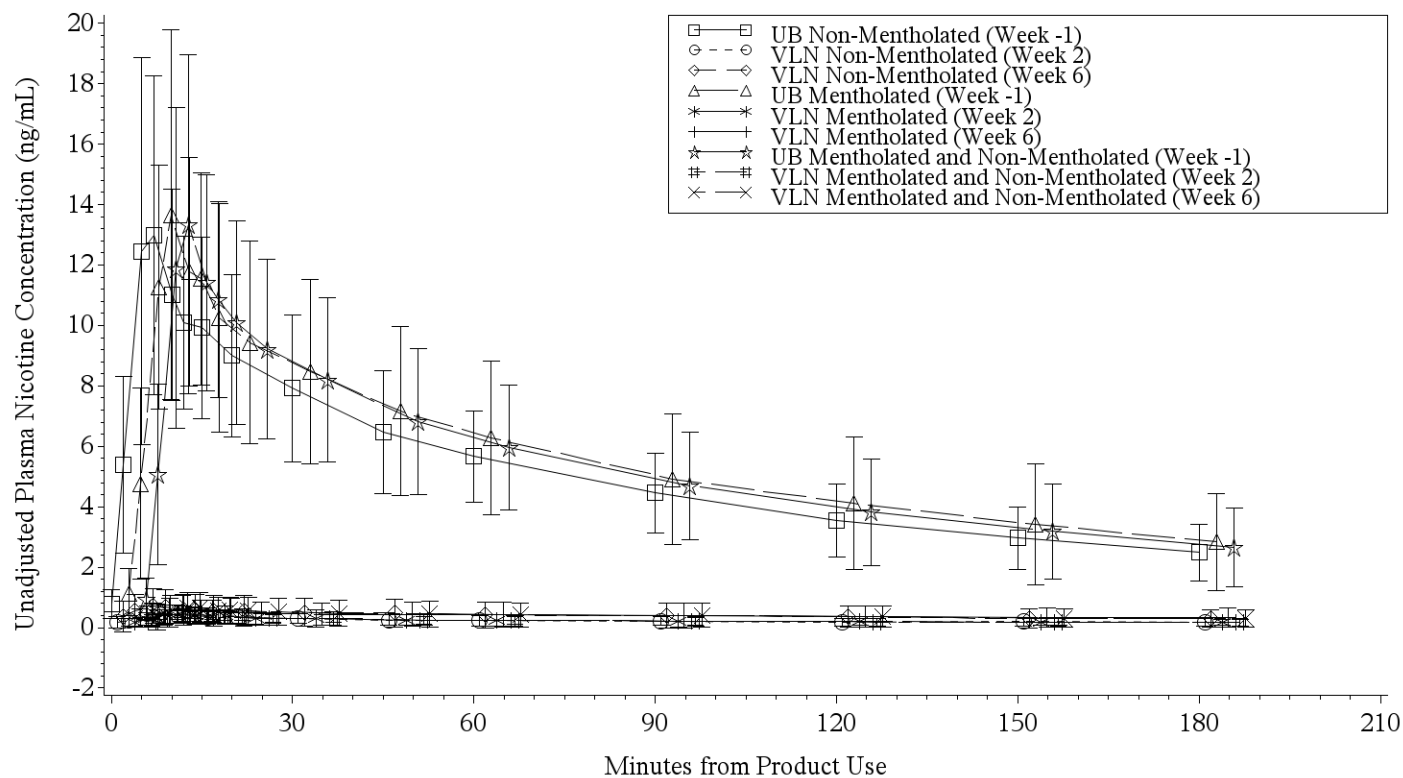
Mean Baseline Adjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Semi-Log Scale) (Pharmacokinetic Population from PP)



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Figure 14.2.8.7

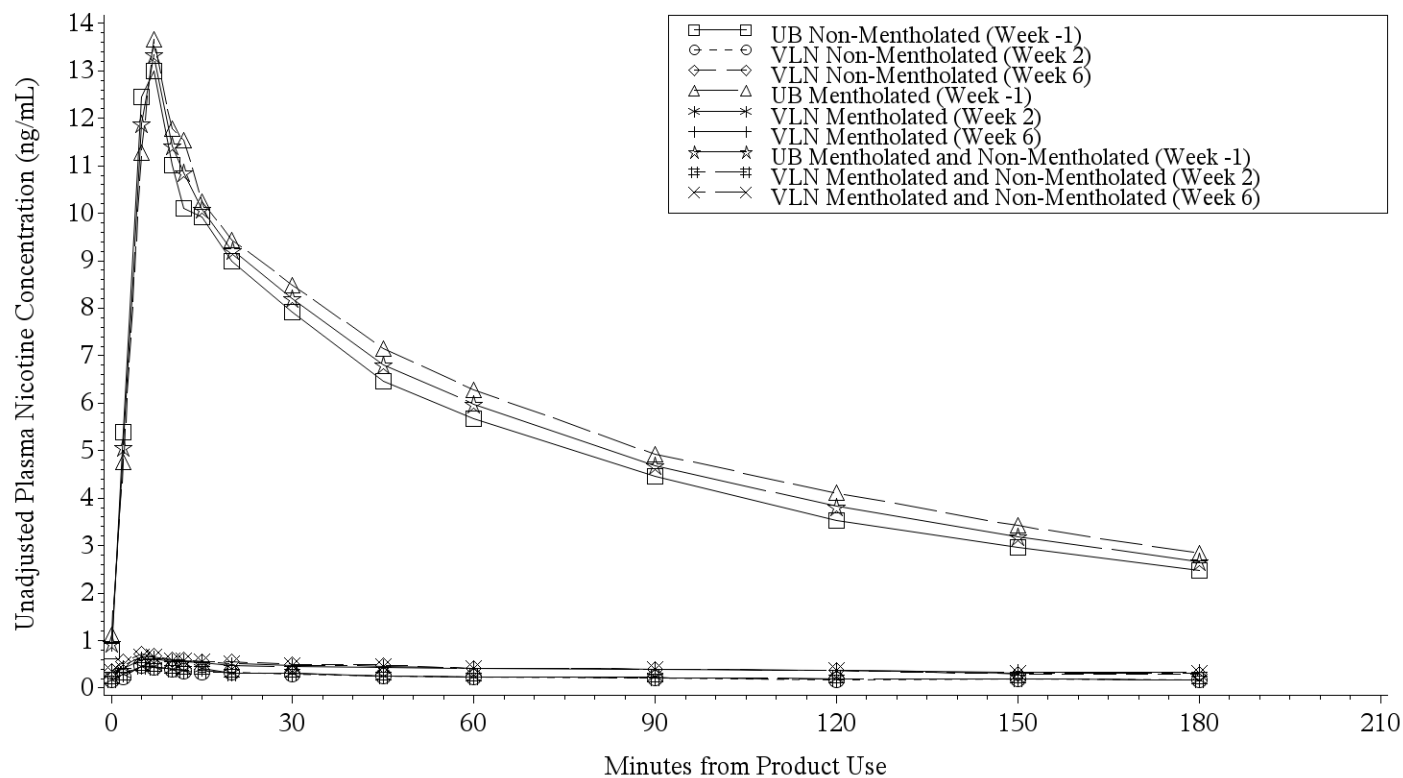
Mean (SD) Unadjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from ITT)



VLN Mentholated and Non-Mentholated (Week 2 and Week 6) and UB Non-Mentholated (Week -16) are shifted to the right for ease of reading
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Figure 14.2.8.8

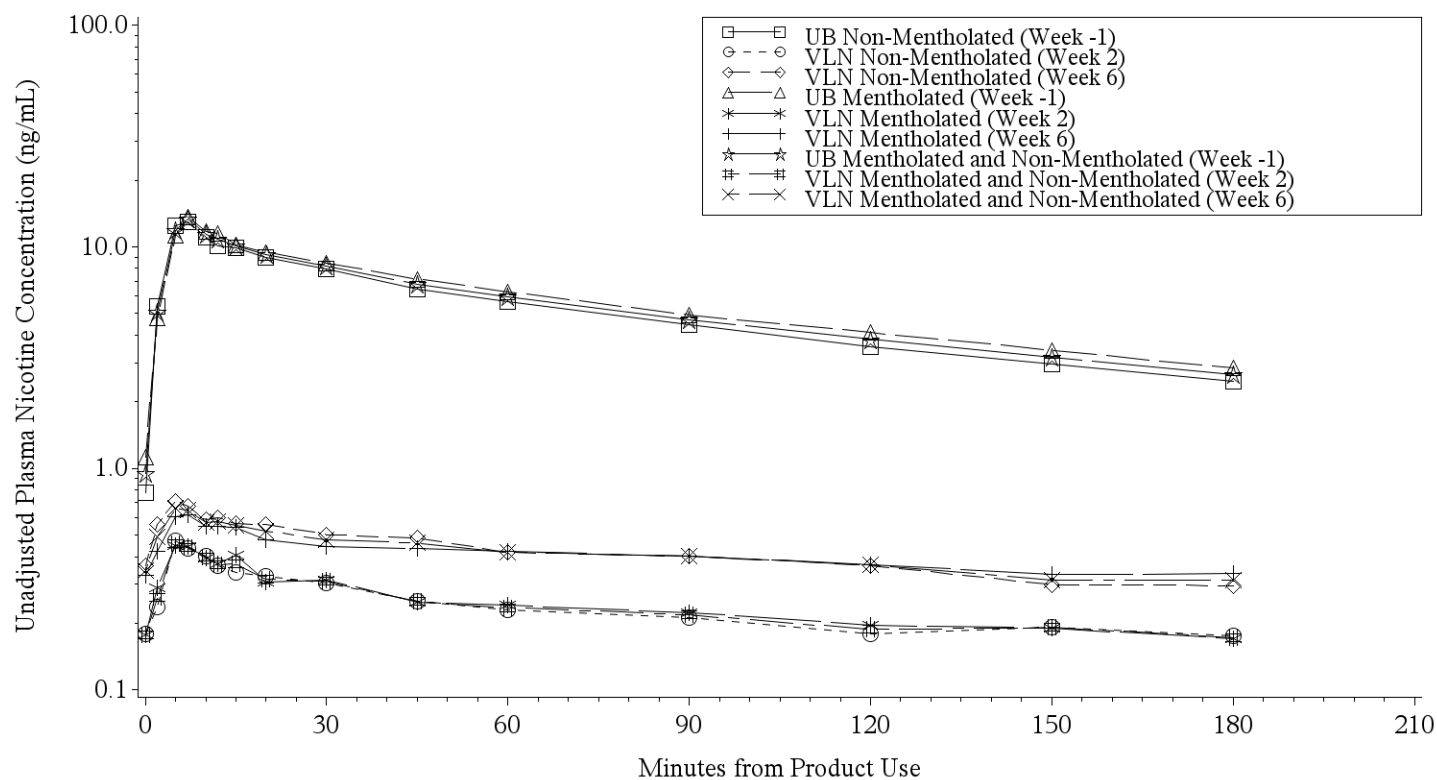
Mean Unadjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from ITT)



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Figure 14.2.8.9

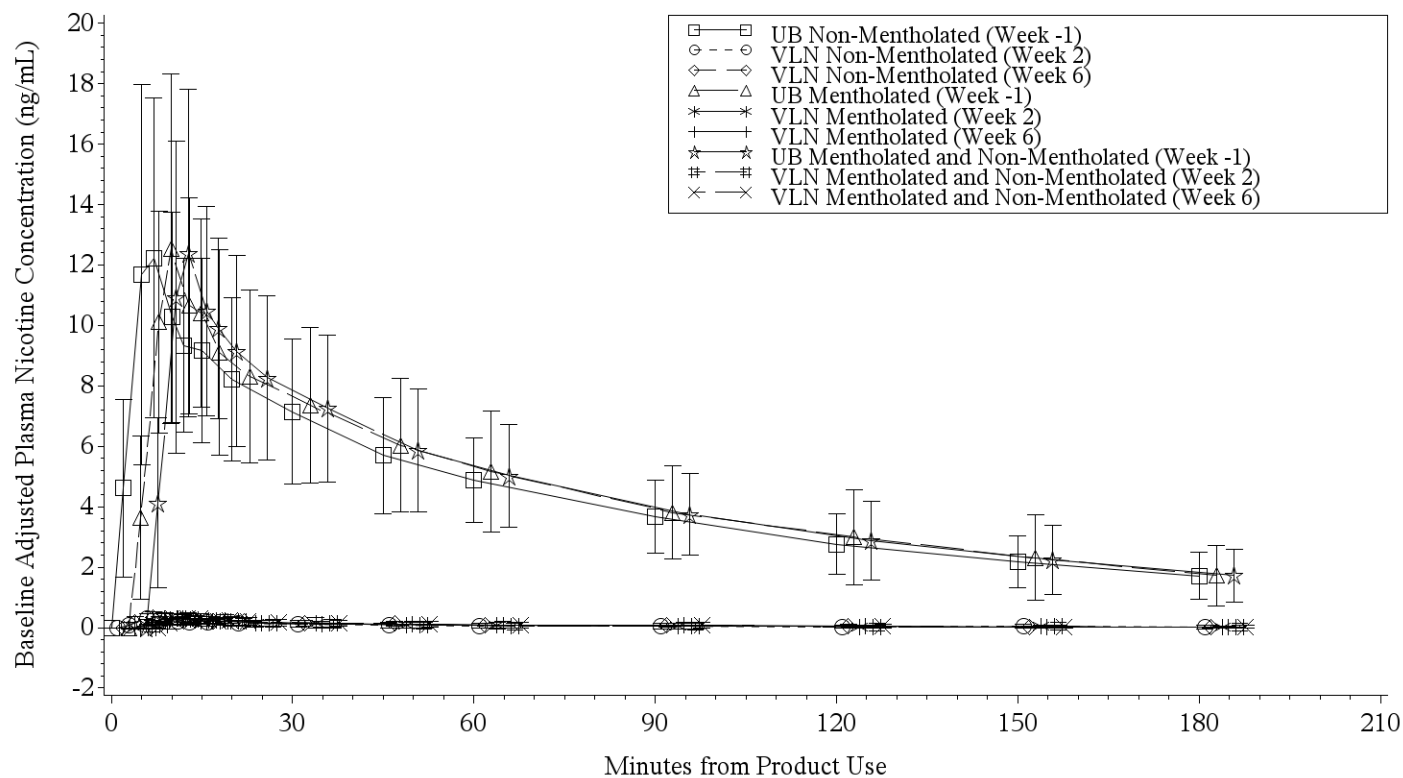
Mean Unadjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Semi-Log Scale) (Pharmacokinetic Population from ITT)



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Figure 14.2.8.10

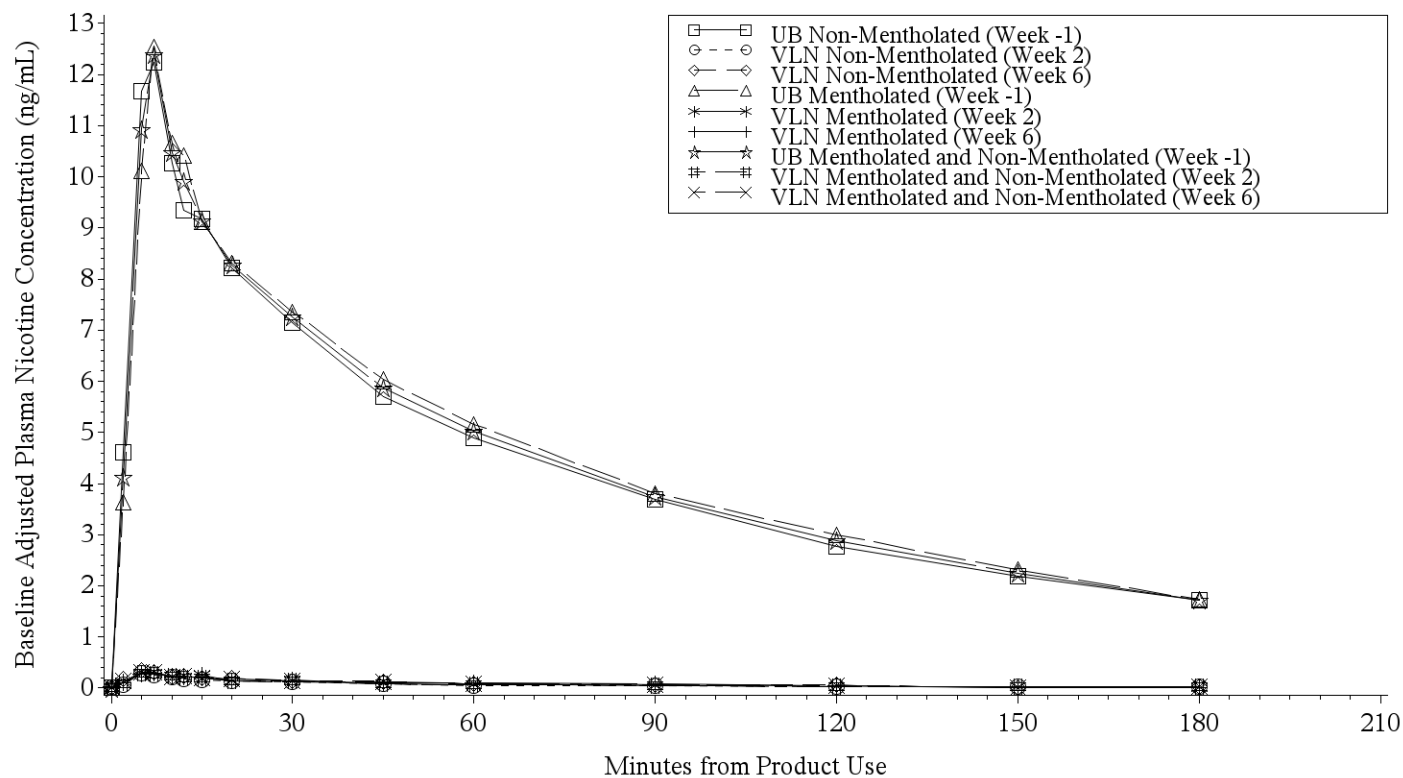
Mean (SD) Baseline Adjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from ITT)



VLN Mentholated and Non-Mentholated (Week 2 and Week 6) and UB Non-Mentholated (Week -16) are shifted to the right for ease of reading
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Figure 14.2.8.11

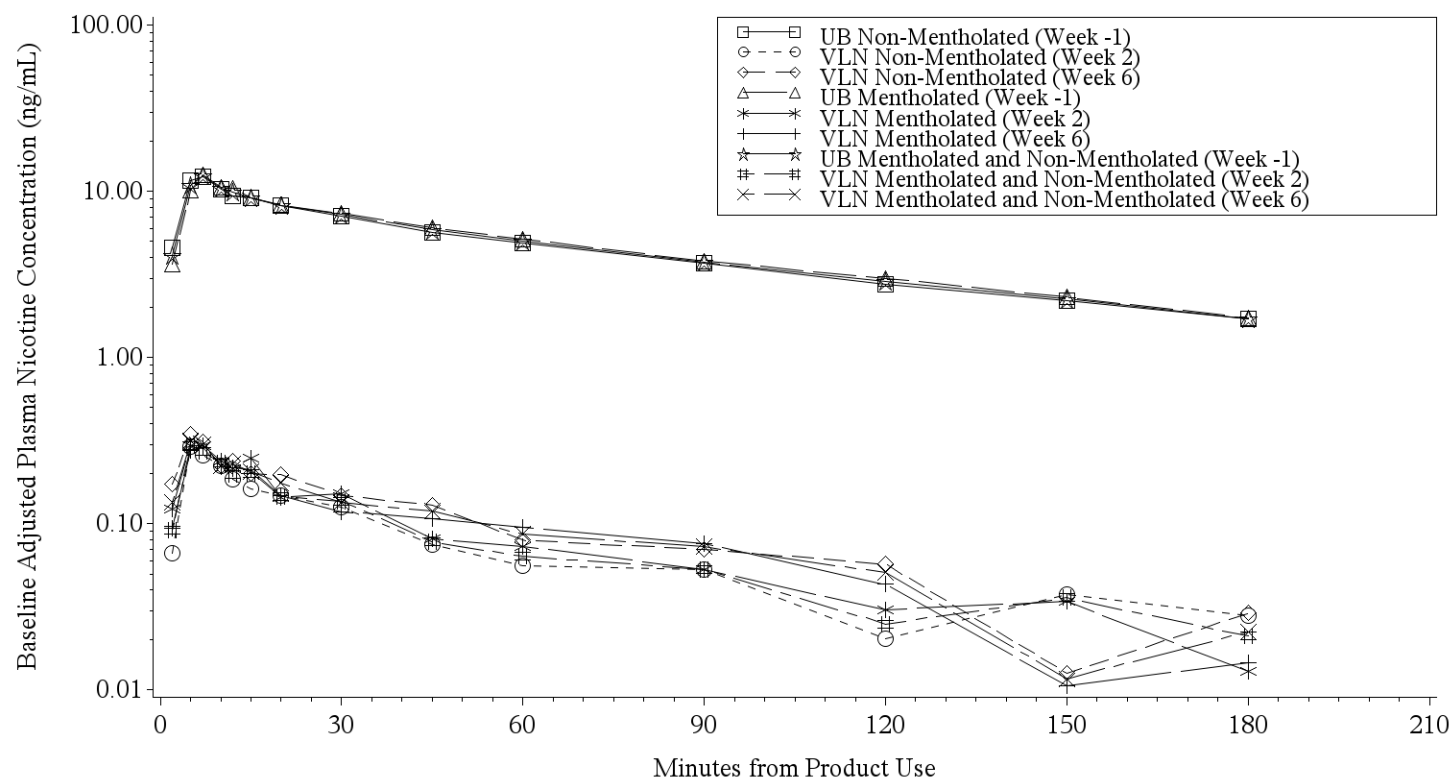
Mean Baseline Adjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from ITT)



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Figure 14.2.8.12

Mean Baseline Adjusted Plasma Nicotine Concentrations Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Semi-Log Scale) (Pharmacokinetic Population from ITT)



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14.2.9 Subjective Effect Tables

FTCD

Table 14.2.9.1.1.1 Summary of FTCD Score by Study Product Group and Study Week (PP Population)

Table 14.2.9.1.1.2 Summary of FTCD Score by Study Product Group and Study Week (ITT Population)

Table 14.2.9.1.2 Statistical Comparison of FTCD Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Table 14.2.9.1.3 Statistical Comparison of FTCD Score Among Study Product Groups at Weeks 2 and 6 (PP Population)

Table 14.2.9.1.4 Statistical Comparison of FTCD Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Table 14.2.9.1.5 Statistical Comparison of FTCD Score Among Study Product Groups at Weeks 2 and 6 (ITT Population)

QSU-Brief

Table 14.2.9.2.1.1 Summary of QSU-Brief Factor Score by Study Product Group and Study Week (PP Population)

Table 14.2.9.2.1.2 Summary of QSU-Brief Factor Score by Study Product Group and Study Week (ITT Population)

Table 14.2.9.2.2 Statistical Comparison of QSU-Brief Factor Scores at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Table 14.2.9.2.3 Statistical Comparison of QSU-Brief Factor Scores Among Study Product Groups at Weeks 2 and 6 (PP Population)

Table 14.2.9.2.4 Statistical Comparison of QSU-Brief Factor Scores at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Table 14.2.9.2.5 Statistical Comparison of QSU-Brief Factor Scores Among Study Product Groups at Weeks 2 and 6 (ITT Population)

MNWS-R

Table 14.2.9.3.1.1 Summary of MNWS-R Total Score by Study Product Group and Study Week (PP Population)

Table 14.2.9.3.1.2 Summary of MNWS-R Total Score by Study Product Group and Study Week (ITT Population)

Table 14.2.9.3.2 Statistical Comparison of MNWS-R Total Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Table 14.2.9.3.3 Statistical Comparison of MNWS-R Total Score Among Study Product Groups at Weeks 2 and 6 (PP Population)

Table 14.2.9.3.4 Statistical Comparison of MNWS-R Total Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Table 14.2.9.3.5 Statistical Comparison of MNWS-R Total Score Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Perceived Health Risk Scale

Table 14.2.9.4.1.1 Summary of Perceived Health Risk Scale by Study Product Group and Study Week (PP Population)

Table 14.2.9.4.1.2 Summary of Perceived Health Risk Scale by Study Product Group and Study Week (ITT Population)

Table 14.2.9.4.2 Statistical Comparison of Perceived Health Risk Scale at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Table 14.2.9.4.3 Statistical Comparison of Perceived Health Risk Scale Among Study Product Groups at Weeks 2 and 6 (PP Population)

Table 14.2.9.4.4 Statistical Comparison of Perceived Health Risk Scale at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Table 14.2.9.4.5 Statistical Comparison of Perceived Health Risk Scale Among Study Product Groups at Weeks 2 and 6 (ITT Population)

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Table 14.2.9.1.1.1 Summary of FTCD Score by Study Product Group and Study Week (PP Population)

Study Week	Statistics	Study Product Group					
		VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week -1*	n	17	12	29	20	22	42
	Mean	4.6	5.9	5.1	5.2	5.4	5.3
	SD	1.80	1.62	1.83	1.46	1.73	1.59
	CV (%)	39.3	27.4	35.6	28.4	32.3	30.3
	SEM	0.44	0.47	0.34	0.33	0.37	0.25
	Minimum	2	4	2	2	1	1
	Median	4.0	6.0	5.0	5.0	5.0	5.0
	Maximum	8	10	10	7	8	8
Week 2	n	13	10	23	19	21	40
	Mean	4.2	6.5	5.2	5.2	4.9	5.1
	SD	2.01	1.90	2.24	1.87	1.92	1.88
	CV (%)	47.4	29.2	42.8	35.9	39.2	37.2
	SEM	0.56	0.60	0.47	0.43	0.42	0.30
	Minimum	1	4	1	1	1	1
	Median	4.0	6.5	4.0	6.0	5.0	5.0
	Maximum	8	10	10	8	8	8

Note: * Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.9.1.1.1 Summary of FTCD Score by Study Product Group and Study Week (PP Population)

Study Week	Statistics	Study Product Group					
		VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week 4	n	10	10	20	20	19	39
	Mean	4.1	6.7	5.4	5.3	5.3	5.3
	SD	0.99	1.89	1.98	2.02	1.85	1.92
	CV (%)	24.3	28.2	36.7	38.5	35.2	36.4
	SEM	0.31	0.60	0.44	0.45	0.42	0.31
	Minimum	3	4	3	0	1	0
	Median	4.0	6.5	5.0	6.0	5.0	6.0
	Maximum	6	10	10	8	8	8
Week 6	n	9	10	19	20	19	39
	Mean	3.8	5.9	4.9	5.4	5.2	5.3
	SD	1.20	2.08	2.00	1.98	2.04	1.99
	CV (%)	31.8	35.2	40.8	36.7	39.2	37.5
	SEM	0.40	0.66	0.46	0.44	0.47	0.32
	Minimum	2	3	2	1	1	1
	Median	4.0	6.0	4.0	6.0	5.0	5.0
	Maximum	6	10	10	8	8	8

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.1.1.2 Summary of FTCD Score by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	Study Product Group					
		VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week -1*	n	49	50	99	20	22	42
	Mean	5.2	6.0	5.6	5.2	5.4	5.3
	SD	1.60	1.53	1.61	1.46	1.73	1.59
	CV (%)	30.9	25.4	28.8	28.4	32.3	30.3
	SEM	0.23	0.22	0.16	0.33	0.37	0.25
	Minimum	2	3	2	2	1	1
	Median	5.0	6.0	6.0	5.0	5.0	5.0
	Maximum	8	10	10	7	8	8
Week 2	n	46	47	93	19	21	40
	Mean	5.0	6.3	5.7	5.2	4.9	5.1
	SD	1.79	1.61	1.81	1.87	1.92	1.88
	CV (%)	35.8	25.6	32.1	35.9	39.2	37.2
	SEM	0.26	0.24	0.19	0.43	0.42	0.30
	Minimum	1	3	1	1	1	1
	Median	5.0	6.0	6.0	6.0	5.0	5.0
	Maximum	8	10	10	8	8	8

Note: * Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.1.1.2 Summary of FTCD Score by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	Study Product Group					
		VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week 4	n	41	43	84	20	19	39
	Mean	4.8	6.3	5.6	5.3	5.3	5.3
	SD	1.44	1.71	1.76	2.02	1.85	1.92
	CV (%)	30.1	27.1	31.6	38.5	35.2	36.4
	SEM	0.22	0.26	0.19	0.45	0.42	0.31
	Minimum	2	3	2	0	1	0
	Median	5.0	6.0	6.0	6.0	5.0	6.0
	Maximum	7	10	10	8	8	8
Week 6	n	42	43	85	20	19	39
	Mean	4.7	6.0	5.4	5.4	5.2	5.3
	SD	1.65	1.68	1.78	1.98	2.04	1.99
	CV (%)	34.9	27.7	33.0	36.7	39.2	37.5
	SEM	0.26	0.26	0.19	0.44	0.47	0.32
	Minimum	2	3	2	1	1	1
	Median	5.0	6.0	5.0	6.0	5.0	5.0
	Maximum	9	10	10	8	8	8

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.1.2 Statistical Comparison of FTCD Score at Weeks 2 and 6 Versus Week -1 by Study Product Group
 (PP Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	95%		p-Value
		Test Week	(n)	Baseline	(n)		Confidence Intervals		
Week 2	VLN Non-Mentholated	6.50	(10)	5.80	(10)	0.70	-0.20 -	1.60	0.1108
	VLN Mentholated	4.23	(13)	4.31	(13)	-0.08	-0.87 -	0.72	0.8372
	VLN Combined	5.22	(23)	4.96	(23)	0.26	-0.31 -	0.83	0.3542
	UB Non-Mentholated	4.90	(21)	5.33	(21)	-0.43	-0.90 -	0.04	0.0706
	UB Mentholated	5.21	(19)	5.05	(19)	0.16	-0.36 -	0.67	0.5274
	UB Combined	5.05	(40)	5.20	(40)	-0.15	-0.49 -	0.19	0.3831
Week 6	VLN Non-Mentholated	5.90	(10)	5.90	(10)	0.00	-0.67 -	0.67	1.0000
	VLN Mentholated	3.78	(9)	4.11	(9)	-0.33	-1.77 -	1.10	0.6075
	VLN Combined	4.89	(19)	5.05	(19)	-0.16	-0.84 -	0.53	0.6348
	UB Non-Mentholated	5.21	(19)	5.21	(19)	0.00	-0.36 -	0.36	1.0000
	UB Mentholated	5.40	(20)	5.15	(20)	0.25	-0.34 -	0.84	0.3828
	UB Combined	5.31	(39)	5.18	(39)	0.13	-0.21 -	0.46	0.4420

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 Paired t-test method is used to perform the analysis.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.1.3 Statistical Comparison of FTCD Score Among Study Product Groups at Weeks 2 and 6 (PP Population)

Study Week	Comparison	----- LSMeans -----		-----LSMean Difference		95%		p-value
		Test	(n)	Reference (n)	(Test - Reference)	Confidence	Intervals	
Week 2	VLN Non-mentholated vs UB Non-mentholated	6.50	(10)	4.90	(21)	1.60	0.17 - 3.03	0.0287
	VLN Mentholated vs UB Mentholated	4.23	(13)	5.28	(19)	-1.05	-2.41 - 0.31	0.1272
	VLN Combined vs UB Combined	5.37	(23)	5.09	(40)	0.27	-0.71 - 1.26	0.5805
Week 6	VLN Non-mentholated vs UB Non-mentholated	5.95	(10)	5.17	(19)	0.77	-0.71 - 2.25	0.3002
	VLN Mentholated vs UB Mentholated	3.58	(9)	5.40	(20)	-1.82	-3.26 - -0.37	0.0144
	VLN Combined vs UB Combined	4.76	(19)	5.29	(39)	-0.52	-1.56 - 0.51	0.3167

 Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.1.4 Statistical Comparison of FTCD Score at Weeks 2 and 6 Versus Week -1 by Study Product Group
 (ITT Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	95%		
		Test Week	(n)	Baseline	(n)		Confidence Intervals	p-Value	
Week 2	VLN Non-Mentholated	6.30	(47)	5.96	(47)	0.34	0.04 -	0.64	0.0278
	VLN Mentholated	5.00	(46)	5.16	(45)	-0.13	-0.46 -	0.20	0.4204
	VLN Combined	5.66	(93)	5.57	(92)	0.11	-0.12 -	0.33	0.3387
	UB Non-Mentholated	4.90	(21)	5.33	(21)	-0.43	-0.90 -	0.04	0.0706
	UB Mentholated	5.21	(19)	5.05	(19)	0.16	-0.36 -	0.67	0.5274
	UB Combined	5.05	(40)	5.20	(40)	-0.15	-0.49 -	0.19	0.3831
Week 6	VLN Non-Mentholated	6.05	(43)	6.07	(43)	-0.02	-0.37 -	0.32	0.8926
	VLN Mentholated	4.74	(42)	5.20	(41)	-0.46	-0.90 -	-0.03	0.0377
	VLN Combined	5.40	(85)	5.64	(84)	-0.24	-0.51 -	0.04	0.0887
	UB Non-Mentholated	5.21	(19)	5.21	(19)	0.00	-0.36 -	0.36	1.0000
	UB Mentholated	5.40	(20)	5.15	(20)	0.25	-0.34 -	0.84	0.3828
	UB Combined	5.31	(39)	5.18	(39)	0.13	-0.21 -	0.46	0.4420

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 Paired t-test method is used to perform the analysis.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.1.5 Statistical Comparison of FTCD Score Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Study Week	Comparison	----- LSMeans -----		-----LSMean Difference		95%		p-value
		Test	(n)	Reference (n)	(Test - Reference)	Confidence	Intervals	
Week 2	VLN Non-mentholated vs UB Non-mentholated	6.35	(47)	4.90	(21)	1.45	0.53 - 2.36	0.0021
	VLN Mentholated vs UB Mentholated	5.00	(46)	5.28	(19)	-0.28	-1.22 - 0.66	0.5566
	VLN Combined vs UB Combined	5.68	(93)	5.09	(40)	0.58	-0.07 - 1.24	0.0807
Week 6	VLN Non-mentholated vs UB Non-mentholated	6.00	(43)	5.17	(19)	0.83	-0.13 - 1.79	0.0892
	VLN Mentholated vs UB Mentholated	4.63	(42)	5.40	(20)	-0.77	-1.74 - 0.21	0.1214
	VLN Combined vs UB Combined	5.32	(85)	5.29	(39)	0.03	-0.65 - 0.72	0.9277

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.2.1.1 Summary of QSU-Brief Factor Score by Study Product Group and Study Week (PP Population)

Factor	Study Week	Statistics	Study Product Group					
			VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Factor 1	Week -1*	n	17	12	29	20	22	42
		Mean	4.5	4.4	4.4	4.5	3.8	4.1
		SD	1.86	2.29	2.01	1.50	1.26	1.41
		CV (%)	41.7	52.2	45.3	33.5	33.4	34.2
		SEM	0.45	0.66	0.37	0.34	0.27	0.22
		Minimum	2	1	1	1	2	1
		Median	4.4	4.9	4.4	4.6	3.9	4.0
		Maximum	7	7	7	7	6	7
	Week 2	n	13	10	23	19	21	40
		Mean	3.5	5.2	4.2	4.3	3.7	4.0
		SD	2.00	1.21	1.87	1.74	1.48	1.61
		CV (%)	57.2	23.3	44.3	40.6	40.0	40.6
		SEM	0.55	0.38	0.39	0.40	0.32	0.26
		Minimum	1	3	1	1	1	1
		Median	3.0	5.4	4.8	4.2	3.8	4.0
		Maximum	7	7	7	7	7	7

Note: * Subjects used their own usual brand cigarettes at Week -1.
 Factor 1: 'anticipation of pleasure from smoking'
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.2.1.1 Summary of QSU-Brief Factor Score by Study Product Group and Study Week (PP Population)

Factor	Study Week	Statistics	Study Product Group					
			VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Factor 1	Week 4	n	10	10	20	20	19	39
		Mean	3.2	4.0	3.6	3.8	3.7	3.7
		SD	1.47	1.94	1.73	1.47	1.42	1.43
		CV (%)	46.0	48.6	48.0	39.2	37.8	38.0
		SEM	0.47	0.61	0.39	0.33	0.33	0.23
		Minimum	1	2	1	1	1	1
		Median	3.0	3.8	3.5	3.6	3.8	3.8
		Maximum	5	7	7	6	7	7
	Week 6	n	9	10	19	20	19	39
		Mean	2.0	3.6	2.8	4.1	3.5	3.8
		SD	1.07	2.01	1.78	1.57	1.57	1.57
		CV (%)	54.3	56.4	63.5	38.6	44.4	41.3
		SEM	0.36	0.63	0.41	0.35	0.36	0.25
		Minimum	1	1	1	1	1	1
		Median	1.8	3.1	2.2	4.0	3.2	3.6
		Maximum	5	7	7	7	7	7

Note: Factor 1: 'anticipation of pleasure from smoking'
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.2.1.1 Summary of QSU-Brief Factor Score by Study Product Group and Study Week (PP Population)

Factor	Study Week	Statistics	Study Product Group					
			VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Factor 2	Week -1*	n	17	12	29	20	22	42
		Mean	3.3	3.2	3.2	3.7	2.9	3.3
		SD	1.89	1.85	1.84	1.49	1.00	1.30
		CV (%)	57.5	58.6	57.0	40.3	34.0	39.4
		SEM	0.46	0.53	0.34	0.33	0.21	0.20
		Minimum	1	1	1	1	1	1
		Median	2.6	3.1	2.6	3.7	2.8	3.3
		Maximum	7	7	7	6	5	6
	Week 2	n	13	10	23	19	21	40
		Mean	2.6	3.2	2.9	3.3	2.7	3.0
		SD	1.71	1.62	1.66	1.35	1.00	1.21
		CV (%)	65.4	50.9	58.0	40.5	36.9	40.3
		SEM	0.47	0.51	0.35	0.31	0.22	0.19
		Minimum	1	1	1	1	1	1
		Median	2.4	3.8	2.6	3.4	2.6	2.9
		Maximum	7	5	7	6	5	6

Note: * Subjects used their own usual brand cigarettes at Week -1.
 Factor 2: 'relief of nicotine withdrawal'
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.9.2.1.1 Summary of QSU-Brief Factor Score by Study Product Group and Study Week (PP Population)

Factor	Study Week	Statistics	Study Product Group					
			VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Factor 2	Week 4	n	10	10	20	20	19	39
		Mean	2.5	2.9	2.7	3.0	2.8	2.9
		SD	1.42	1.74	1.56	1.22	1.30	1.24
		CV (%)	56.7	60.8	58.0	41.1	45.6	42.7
		SEM	0.45	0.55	0.35	0.27	0.30	0.20
		Minimum	1	1	1	1	1	1
		Median	2.0	2.5	2.3	3.1	2.6	3.0
		Maximum	5	6	6	6	6	6
	Week 6	n	9	10	19	20	19	39
		Mean	1.6	2.4	2.0	3.3	2.7	3.0
		SD	1.09	1.23	1.21	1.33	1.00	1.20
		CV (%)	70.4	51.7	60.9	40.6	37.3	40.4
		SEM	0.36	0.39	0.28	0.30	0.23	0.19
		Minimum	1	1	1	1	1	1
		Median	1.2	2.2	1.2	3.4	2.6	3.0
		Maximum	4	4	4	6	5	6

Note: Factor 2: 'relief of nicotine withdrawal'
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.2.1.2 Summary of QSU-Brief Factor Score by Study Product Group and Study Week (ITT Population)

Factor	Study Week	Statistics	Study Product Group					
			VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Factor 1	Week -1*	n	49	50	99	20	22	42
		Mean	4.2	4.3	4.3	4.5	3.8	4.1
		SD	1.68	1.70	1.69	1.50	1.26	1.41
		CV (%)	40.4	39.1	39.6	33.5	33.4	34.2
		SEM	0.24	0.24	0.17	0.34	0.27	0.22
		Minimum	1	1	1	1	2	1
		Median	4.0	4.2	4.2	4.6	3.9	4.0
		Maximum	7	7	7	7	6	7
	Week 2	n	46	47	93	19	21	40
		Mean	3.7	5.4	4.5	4.3	3.7	4.0
		SD	1.87	1.50	1.88	1.74	1.48	1.61
		CV (%)	50.8	28.1	41.6	40.6	40.0	40.6
		SEM	0.28	0.22	0.20	0.40	0.32	0.26
		Minimum	1	2	1	1	1	1
		Median	3.3	5.2	4.4	4.2	3.8	4.0
		Maximum	7	7	7	7	7	7

Note: * Subjects used their own usual brand cigarettes at Week -1.
 Factor 1: 'anticipation of pleasure from smoking'
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.2.1.2 Summary of QSU-Brief Factor Score by Study Product Group and Study Week (ITT Population)

Factor	Study Week	Statistics	Study Product Group					
			VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Factor 1	Week 4	n	41	43	84	20	19	39
		Mean	3.8	3.9	3.8	3.8	3.7	3.7
		SD	1.68	1.47	1.56	1.47	1.42	1.43
		CV (%)	44.5	38.1	41.1	39.2	37.8	38.0
		SEM	0.26	0.22	0.17	0.33	0.33	0.23
		Minimum	1	2	1	1	1	1
		Median	3.6	3.6	3.6	3.6	3.8	3.8
		Maximum	7	7	7	6	7	7
	Week 6	n	42	43	85	20	19	39
		Mean	3.4	4.4	3.9	4.1	3.5	3.8
		SD	1.70	1.68	1.75	1.57	1.57	1.57
		CV (%)	50.1	38.2	44.9	38.6	44.4	41.3
		SEM	0.26	0.26	0.19	0.35	0.36	0.25
		Minimum	1	1	1	1	1	1
		Median	3.2	4.2	3.8	4.0	3.2	3.6
		Maximum	7	7	7	7	7	7

Note: Factor 1: 'anticipation of pleasure from smoking'
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Table 14.2.9.2.1.2 Summary of QSU-Brief Factor Score by Study Product Group and Study Week (ITT Population)

Factor	Study Week	Statistics	Study Product Group					
			VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Factor 2	Week -1*	n	49	50	99	20	22	42
		Mean	3.0	3.1	3.1	3.7	2.9	3.3
		SD	1.71	1.49	1.59	1.49	1.00	1.30
		CV (%)	56.5	47.4	51.7	40.3	34.0	39.4
		SEM	0.24	0.21	0.16	0.33	0.21	0.20
		Minimum	1	1	1	1	1	1
		Median	2.6	3.0	2.8	3.7	2.8	3.3
		Maximum	7	7	7	6	5	6
	Week 2	n	46	47	93	19	21	40
		Mean	2.6	3.9	3.2	3.3	2.7	3.0
		SD	1.64	1.52	1.69	1.35	1.00	1.21
		CV (%)	62.6	39.5	52.1	40.5	36.9	40.3
		SEM	0.24	0.22	0.18	0.31	0.22	0.19
		Minimum	1	1	1	1	1	1
		Median	2.2	3.8	3.2	3.4	2.6	2.9
		Maximum	7	7	7	6	5	6

Note: * Subjects used their own usual brand cigarettes at Week -1.
Factor 2: 'relief of nicotine withdrawal'
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.2.1.2 Summary of QSU-Brief Factor Score by Study Product Group and Study Week (ITT Population)

Factor	Study Week	Statistics	Study Product Group					
			VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Factor 2	Week 4	n	41	43	84	20	19	39
		Mean	2.6	2.8	2.7	3.0	2.8	2.9
		SD	1.40	1.32	1.36	1.22	1.30	1.24
		CV (%)	54.4	47.9	50.8	41.1	45.6	42.7
		SEM	0.22	0.20	0.15	0.27	0.30	0.20
		Minimum	1	1	1	1	1	1
		Median	2.4	2.6	2.6	3.1	2.6	3.0
		Maximum	7	6	7	6	6	6
	Week 6	n	42	43	85	20	19	39
		Mean	2.4	3.2	2.8	3.3	2.7	3.0
		SD	1.54	1.54	1.59	1.33	1.00	1.20
		CV (%)	65.4	47.7	56.9	40.6	37.3	40.4
		SEM	0.24	0.23	0.17	0.30	0.23	0.19
		Minimum	1	1	1	1	1	1
		Median	1.8	3.2	2.4	3.4	2.6	3.0
		Maximum	7	7	7	6	5	6

Note: Factor 2: 'relief of nicotine withdrawal'
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.2.2 Statistical Comparison of QSU-Brief Factor Scores at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Factor	Study Week	Product Group	Means				Difference (Test Week - Baseline)	95%		p-Value
			Test Week	(n)	Baseline	(n)		Confidence Intervals		
Factor 1	Week 2	VLN Non-Mentholated	5.18	(10)	4.42	(10)	0.76	-0.28 -	1.80	0.1327
		VLN Mentholated	3.49	(13)	3.97	(13)	-0.48	-1.39 -	0.43	0.2760
		VLN Combined	4.23	(23)	4.17	(23)	0.06	-0.62 -	0.74	0.8551
		UB Non-Mentholated	3.70	(21)	3.69	(21)	0.01	-0.58 -	0.60	0.9736
		UB Mentholated	4.28	(19)	4.45	(19)	-0.17	-0.68 -	0.34	0.4961
		UB Combined	3.97	(40)	4.05	(40)	-0.07	-0.45 -	0.30	0.6899
	Week 6	VLN Non-Mentholated	3.56	(10)	4.46	(10)	-0.90	-2.95 -	1.15	0.3474
		VLN Mentholated	1.98	(9)	3.89	(9)	-1.91	-2.88 -	-0.94	0.0019
		VLN Combined	2.81	(19)	4.19	(19)	-1.38	-2.47 -	-0.29	0.0159
		UB Non-Mentholated	3.54	(19)	3.65	(19)	-0.12	-0.71 -	0.48	0.6859
		UB Mentholated	4.06	(20)	4.47	(20)	-0.41	-0.81 -	-0.01	0.0434
		UB Combined	3.81	(39)	4.07	(39)	-0.27	-0.61 -	0.07	0.1199

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 Paired t-test method is used to perform the analysis.
 Factor 1: 'anticipation of pleasure from smoking'
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.2.2 Statistical Comparison of QSU-Brief Factor Scores at Weeks 2 and 6 Versus Week -1 by Study Product Group
 (PP Population)

Factor	Study Week	Product Group	Means				Difference (Test Week - Baseline)	95% Confidence Intervals		p-Value
			Test Week	(n)	Baseline	(n)				
Factor 2	Week 2	VLN Non-Mentholated	3.18	(10)	3.18	(10)	0.00	-0.80 - 0.80		1.0000
		VLN Mentholated	2.62	(13)	2.91	(13)	-0.29	-0.89 - 0.31		0.3105
		VLN Combined	2.86	(23)	3.03	(23)	-0.17	-0.61 - 0.28		0.4536
		UB Non-Mentholated	2.70	(21)	2.96	(21)	-0.27	-0.63 - 0.09		0.1391
		UB Mentholated	3.35	(19)	3.72	(19)	-0.37	-0.71 - -0.03		0.0362
		UB Combined	3.01	(40)	3.32	(40)	-0.32	-0.55 - -0.08		0.0111
	Week 6	VLN Non-Mentholated	2.38	(10)	3.22	(10)	-0.84	-2.41 - 0.73		0.2557
		VLN Mentholated	1.56	(9)	2.58	(9)	-1.02	-1.79 - -0.26		0.0152
		VLN Combined	1.99	(19)	2.92	(19)	-0.93	-1.74 - -0.11		0.0278
		UB Non-Mentholated	2.67	(19)	2.97	(19)	-0.29	-0.79 - 0.20		0.2261
		UB Mentholated	3.28	(20)	3.70	(20)	-0.42	-0.75 - -0.09		0.0145
		UB Combined	2.98	(39)	3.34	(39)	-0.36	-0.64 - -0.08		0.0133

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 Paired t-test method is used to perform the analysis.
 Factor 2: 'relief of nicotine withdrawal'
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.2.3 Statistical Comparison of QSU-Brief Factor Scores Among Study Product Groups at Weeks 2 and 6 (PP Population)

Factor	Study Week	Comparison	-----LSMeans-----LSMean Difference			95%		p-value
			Test	(n) Reference (n)	(Test - Reference)	Confidence Intervals		
Factor 1	Week 2	VLN Non-mentholated vs UB Non-mentholated	5.30(10)	3.70(21)	1.60	0.36	- 2.84	0.0125
		VLN Mentholated vs UB Mentholated	3.49(13)	4.27(19)	-0.78	-1.95	- 0.40	0.1916
		VLN Combined vs UB Combined	4.39(23)	3.98(40)	0.41	-0.44	- 1.27	0.3388
	Week 6	VLN Non-mentholated vs UB Non-mentholated	3.49(10)	3.50(19)	-0.01	-1.24	- 1.21	0.9824
		VLN Mentholated vs UB Mentholated	1.98 (9)	4.06(20)	-2.08	-3.31	- -0.85	0.0012
		VLN Combined vs UB Combined	2.73(19)	3.78(39)	-1.05	-1.91	- -0.18	0.0187
Factor 2	Week 2	VLN Non-mentholated vs UB Non-mentholated	3.22(10)	2.70(21)	0.53	-0.51	- 1.56	0.3113
		VLN Mentholated vs UB Mentholated	2.62(13)	3.36(19)	-0.75	-1.72	- 0.23	0.1325
		VLN Combined vs UB Combined	2.92(23)	3.03(40)	-0.11	-0.82	- 0.60	0.7602
	Week 6	VLN Non-mentholated vs UB Non-mentholated	2.26(10)	2.67(19)	-0.40	-1.34	- 0.53	0.3907
		VLN Mentholated vs UB Mentholated	1.65 (9)	3.28(20)	-1.63	-2.56	- -0.70	0.0009
		VLN Combined vs UB Combined	1.96(19)	2.97(39)	-1.02	-1.67	- -0.36	0.0031

Note: LSMeans, LMean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 Factor 1: 'anticipation of pleasure from smoking'
 Factor 2: 'relief of nicotine withdrawal'
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.2.4 Statistical Comparison of QSU-Brief Factor Scores at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Factor	Study Week	Product Group	Means				Difference (Test Week - Baseline)	95% Confidence Intervals		p-Value
			Test Week	(n)	Baseline	(n)				
Factor 1	Week 2	VLN Non-Mentholated	5.35	(47)	4.32	(47)	1.03	0.56 -	1.50	<.0001
		VLN Mentholated	3.69	(46)	3.99	(45)	-0.31	-0.75 -	0.13	0.1631
		VLN Combined	4.53	(93)	4.16	(92)	0.37	0.03 -	0.72	0.0354
		UB Non-Mentholated	3.70	(21)	3.69	(21)	0.01	-0.58 -	0.60	0.9736
		UB Mentholated	4.28	(19)	4.45	(19)	-0.17	-0.68 -	0.34	0.4961
		UB Combined	3.97	(40)	4.05	(40)	-0.07	-0.45 -	0.30	0.6899
	Week 6	VLN Non-Mentholated	4.39	(43)	4.39	(43)	-0.00	-0.63 -	0.62	0.9882
		VLN Mentholated	3.40	(42)	3.98	(41)	-0.57	-1.16 -	0.02	0.0577
		VLN Combined	3.90	(85)	4.19	(84)	-0.28	-0.71 -	0.15	0.1945
		UB Non-Mentholated	3.54	(19)	3.65	(19)	-0.12	-0.71 -	0.48	0.6859
		UB Mentholated	4.06	(20)	4.47	(20)	-0.41	-0.81 -	-0.01	0.0434
		UB Combined	3.81	(39)	4.07	(39)	-0.27	-0.61 -	0.07	0.1199

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 Paired t-test method is used to perform the analysis.
 Factor 1: 'anticipation of pleasure from smoking'
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.2.4 Statistical Comparison of QSU-Brief Factor Scores at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Factor	Study Week	Product Group	Means				Difference (Test Week - Baseline)	95% Confidence Intervals		p-Value
			Test Week	(n)	Baseline	(n)				
Factor 2	Week 2	VLN Non-Mentholated	3.86	(47)	3.14	(47)	0.71	0.33 -	1.09	0.0005
		VLN Mentholated	2.63	(46)	2.88	(45)	-0.28	-0.60 -	0.03	0.0758
		VLN Combined	3.25	(93)	3.02	(92)	0.22	-0.04 -	0.49	0.0962
		UB Non-Mentholated	2.70	(21)	2.96	(21)	-0.27	-0.63 -	0.09	0.1391
		UB Mentholated	3.35	(19)	3.72	(19)	-0.37	-0.71 -	-0.03	0.0362
		UB Combined	3.01	(40)	3.32	(40)	-0.32	-0.55 -	-0.08	0.0111
	Week 6	VLN Non-Mentholated	3.23	(43)	3.21	(43)	0.02	-0.57 -	0.60	0.9492
		VLN Mentholated	2.35	(42)	2.81	(41)	-0.45	-0.87 -	-0.03	0.0369
		VLN Combined	2.80	(85)	3.01	(84)	-0.21	-0.57 -	0.15	0.2498
		UB Non-Mentholated	2.67	(19)	2.97	(19)	-0.29	-0.79 -	0.20	0.2261
		UB Mentholated	3.28	(20)	3.70	(20)	-0.42	-0.75 -	-0.09	0.0145
		UB Combined	2.98	(39)	3.34	(39)	-0.36	-0.64 -	-0.08	0.0133

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 Paired t-test method is used to perform the analysis.
 Factor 2: 'relief of nicotine withdrawal'
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.2.5 Statistical Comparison of QSU-Brief Factor Scores Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Factor	Study Week	Comparison	-----LSMeans -----LSMean Difference			95%		p-value
			Test	(n) Reference (n)	(Test - Reference)	Confidence Intervals		
Factor 1	Week 2	VLN Non-mentholated vs UB Non-mentholated	5.39(47)	3.70(21)	1.69	0.83	- 2.56	0.0002
		VLN Mentholated vs UB Mentholated	3.69(46)	4.27(19)	-0.58	-1.48	- 0.31	0.1994
		VLN Combined vs UB Combined	4.54(93)	3.98(40)	0.56	-0.07	- 1.18	0.0795
	Week 6	VLN Non-mentholated vs UB Non-mentholated	4.31(43)	3.51(19)	0.80	-0.09	- 1.69	0.0765
		VLN Mentholated vs UB Mentholated	3.39(42)	4.06(20)	-0.67	-1.55	- 0.22	0.1407
		VLN Combined vs UB Combined	3.85(85)	3.78(39)	0.07	-0.56	- 0.70	0.8293
Factor 2	Week 2	VLN Non-mentholated vs UB Non-mentholated	3.89(47)	2.70(21)	1.19	0.43	- 1.96	0.0025
		VLN Mentholated vs UB Mentholated	2.63(46)	3.36(19)	-0.73	-1.52	- 0.06	0.0689
		VLN Combined vs UB Combined	3.26(93)	3.03(40)	0.23	-0.32	- 0.78	0.4086
	Week 6	VLN Non-mentholated vs UB Non-mentholated	3.16(43)	2.67(19)	0.49	-0.29	- 1.26	0.2143
		VLN Mentholated vs UB Mentholated	2.37(42)	3.28(20)	-0.91	-1.69	- -0.13	0.0230
		VLN Combined vs UB Combined	2.76(85)	2.97(39)	-0.21	-0.76	- 0.34	0.4538

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 Factor 1: 'anticipation of pleasure from smoking'
 Factor 2: 'relief of nicotine withdrawal'
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.3.1.1 Summary of MNWS-R Total Score by Study Product Group and Study Week (PP Population)

Study Week	Statistics	Study Product Group					
		VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week -1*	n	17	12	29	20	22	42
	Mean	10.9	10.8	10.9	10.6	9.2	9.9
	SD	10.36	7.69	9.19	9.68	7.49	8.52
	CV (%)	94.7	70.9	84.4	91.3	81.5	86.4
	SEM	2.51	2.22	1.71	2.16	1.60	1.31
	Minimum	1	2	1	0	0	0
	Median	8.0	10.0	8.0	7.5	8.0	8.0
	Maximum	33	23	33	36	26	36
Week 2	n	13	10	23	19	21	40
	Mean	14.0	12.2	13.2	8.1	9.0	8.6
	SD	11.91	9.67	10.79	9.02	6.94	7.90
	CV (%)	85.1	79.3	81.6	112.0	77.1	92.4
	SEM	3.30	3.06	2.25	2.07	1.51	1.25
	Minimum	0	3	0	0	0	0
	Median	9.0	9.5	9.0	4.0	8.0	6.5
	Maximum	33	29	33	34	25	34

Note: * Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.3.1.1 Summary of MNWS-R Total Score by Study Product Group and Study Week (PP Population)

Study Week	Statistics	Study Product Group					
		VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week 4	n	10	10	20	20	19	39
	Mean	10.8	10.1	10.5	8.4	7.8	8.1
	SD	10.03	9.00	9.28	8.76	7.10	7.89
	CV (%)	92.9	89.1	88.8	104.9	90.5	97.4
	SEM	3.17	2.85	2.08	1.96	1.63	1.26
	Minimum	0	0	0	0	0	0
	Median	9.5	8.5	9.5	6.5	6.0	6.0
	Maximum	26	23	26	30	25	30
Week 6	n	9	10	19	20	19	39
	Mean	6.8	6.2	6.5	7.5	8.3	7.9
	SD	7.36	5.90	6.45	7.32	7.53	7.33
	CV (%)	108.6	95.2	99.6	97.5	91.1	93.1
	SEM	2.45	1.87	1.48	1.64	1.73	1.17
	Minimum	0	0	0	0	0	0
	Median	5.0	4.0	5.0	5.5	7.0	6.0
	Maximum	20	15	20	27	25	27

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.3.1.2 Summary of MNWS-R Total Score by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	Study Product Group					
		VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week -1*	n	49	50	99	20	22	42
	Mean	8.1	13.0	10.6	10.6	9.2	9.9
	SD	7.56	8.77	8.52	9.68	7.49	8.52
	CV (%)	93.6	67.5	80.7	91.3	81.5	86.4
	SEM	1.08	1.24	0.86	2.16	1.60	1.31
	Minimum	0	0	0	0	0	0
	Median	6.0	13.0	8.0	7.5	8.0	8.0
	Maximum	33	38	38	36	26	36
Week 2	n	46	47	93	19	21	40
	Mean	8.4	16.0	12.3	8.1	9.0	8.6
	SD	8.53	9.74	9.88	9.02	6.94	7.90
	CV (%)	101.1	60.8	80.5	112.0	77.1	92.4
	SEM	1.26	1.42	1.02	2.07	1.51	1.25
	Minimum	0	2	0	0	0	0
	Median	6.0	15.0	9.0	4.0	8.0	6.5
	Maximum	33	35	35	34	25	34

Note: * Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.3.1.2 Summary of MNWS-R Total Score by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	Study Product Group					
		VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week 4	n	41	43	84	20	19	39
	Mean	6.5	13.5	10.1	8.4	7.8	8.1
	SD	7.67	10.55	9.86	8.76	7.10	7.89
	CV (%)	118.2	77.9	97.7	104.9	90.5	97.4
	SEM	1.20	1.61	1.08	1.96	1.63	1.26
	Minimum	0	0	0	0	0	0
	Median	3.0	14.0	6.0	6.5	6.0	6.0
	Maximum	30	33	33	30	25	30
Week 6	n	42	43	85	20	19	39
	Mean	5.4	13.4	9.5	7.5	8.3	7.9
	SD	6.17	10.01	9.22	7.32	7.53	7.33
	CV (%)	114.2	74.5	97.4	97.5	91.1	93.1
	SEM	0.95	1.53	1.00	1.64	1.73	1.17
	Minimum	0	0	0	0	0	0
	Median	3.0	13.0	8.0	5.5	7.0	6.0
	Maximum	20	46	46	27	25	27

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.3.2 Statistical Comparison of MNWS-R Total Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	95%		p-Value
		Test Week	(n)	Baseline	(n)		Confidence Intervals		
Week 2	VLN Non-Mentholated	12.20	(10)	11.00	(10)	1.20	-4.11 -	6.51	0.6214
	VLN Mentholated	14.00	(13)	10.08	(13)	3.92	-3.60 -	11.44	0.2779
	VLN Combined	13.22	(23)	10.48	(23)	2.74	-1.77 -	7.25	0.2213
	UB Non-Mentholated	9.00	(21)	9.29	(21)	-0.29	-3.11 -	2.54	0.8353
	UB Mentholated	8.05	(19)	10.00	(19)	-1.95	-4.88 -	0.98	0.1795
	UB Combined	8.55	(40)	9.63	(40)	-1.07	-3.03 -	0.88	0.2741
Week 6	VLN Non-Mentholated	6.20	(10)	11.10	(10)	-4.90	-9.44 -	-0.36	0.0374
	VLN Mentholated	6.78	(9)	10.22	(9)	-3.44	-10.09 -	3.20	0.2663
	VLN Combined	6.47	(19)	10.68	(19)	-4.21	-7.75 -	-0.67	0.0224
	UB Non-Mentholated	8.26	(19)	8.84	(19)	-0.58	-4.15 -	3.00	0.7377
	UB Mentholated	7.50	(20)	10.60	(20)	-3.10	-5.14 -	-1.06	0.0050
	UB Combined	7.87	(39)	9.74	(39)	-1.87	-3.85 -	0.11	0.0629

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 Paired t-test method is used to perform the analysis.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.3.3 Statistical Comparison of MNWS-R Total Score Among Study Product Groups at Weeks 2 and 6 (PP Population)

Study Week	Comparison	----- LSMeans -----		-----LSMean Difference		95%		p-value
		Test	(n)	Reference	(n)	(Test - Reference)	Confidence Intervals	
Week 2	VLN Non-mentholated vs UB Non-mentholated	12.38	(10)	9.00	(21)	3.38	-3.57 - 10.33	0.3344
	VLN Mentholated vs UB Mentholated	14.00	(13)	8.58	(19)	5.42	-1.17 - 12.00	0.1051
	VLN Combined vs UB Combined	13.19	(23)	8.79	(40)	4.40	-0.39 - 9.18	0.0710
Week 6	VLN Non-mentholated vs UB Non-mentholated	6.12	(10)	8.14	(19)	-2.02	-7.43 - 3.39	0.4574
	VLN Mentholated vs UB Mentholated	6.97	(9)	7.50	(20)	-0.53	-5.89 - 4.83	0.8435
	VLN Combined vs UB Combined	6.54	(19)	7.82	(39)	-1.28	-5.08 - 2.53	0.5050

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.3.4 Statistical Comparison of MNWS-R Total Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	95% Confidence Intervals		p-Value
		Test Week	(n)	Baseline	(n)				
Week 2	VLN Non-Mentholated	16.02	(47)	12.57	(47)	3.45	0.69 -	6.21	0.0155
	VLN Mentholated	8.43	(46)	7.58	(45)	0.87	-1.48 -	3.22	0.4615
	VLN Combined	12.27	(93)	10.13	(92)	2.18	0.38 -	3.99	0.0182
	UB Non-Mentholated	9.00	(21)	9.29	(21)	-0.29	-3.11 -	2.54	0.8353
	UB Mentholated	8.05	(19)	10.00	(19)	-1.95	-4.88 -	0.98	0.1795
	UB Combined	8.55	(40)	9.63	(40)	-1.07	-3.03 -	0.88	0.2741
Week 6	VLN Non-Mentholated	13.44	(43)	12.81	(43)	0.63	-2.42 -	3.68	0.6800
	VLN Mentholated	5.40	(42)	7.37	(41)	-1.95	-3.90 -	-0.00	0.0497
	VLN Combined	9.47	(85)	10.15	(84)	-0.63	-2.44 -	1.18	0.4907
	UB Non-Mentholated	8.26	(19)	8.84	(19)	-0.58	-4.15 -	3.00	0.7377
	UB Mentholated	7.50	(20)	10.60	(20)	-3.10	-5.14 -	-1.06	0.0050
	UB Combined	7.87	(39)	9.74	(39)	-1.87	-3.85 -	0.11	0.0629

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 Paired t-test method is used to perform the analysis.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.3.5 Statistical Comparison of MNWS-R Total Score Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Study Week	Comparison	----- LSMeans -----		-----LSMean Difference-----		95%		p-value
		Test	(n)	Reference	(n)	(Test - Reference)	Confidence Intervals	
Week 2	VLN Non-mentholated vs UB Non-mentholated	16.43	(47)	9.00	(21)	7.43	2.73 - 12.13	0.0022
	VLN Mentholated vs UB Mentholated	8.43	(46)	8.45	(19)	-0.02	-4.87 - 4.84	0.9950
	VLN Combined vs UB Combined	12.43	(93)	8.73	(40)	3.71	0.33 - 7.09	0.0317
Week 6	VLN Non-mentholated vs UB Non-mentholated	13.61	(43)	8.14	(19)	5.46	1.15 - 9.78	0.0134
	VLN Mentholated vs UB Mentholated	5.75	(42)	7.50	(20)	-1.75	-6.07 - 2.57	0.4239
	VLN Combined vs UB Combined	9.68	(85)	7.82	(39)	1.86	-1.20 - 4.91	0.2310

 Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.4.1.1 Summary of Perceived Health Risk Scale by Study Product Group and Study Week (PP Population)

Study Week	Statistics	Study Product Group					
		VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week -1*	n	17	12	29	20	22	42
	Mean	6.6	7.7	7.1	6.6	7.7	7.1
	SD	1.93	2.19	2.07	2.09	2.25	2.23
	CV (%)	29.1	28.5	29.3	31.9	29.4	31.2
	SEM	0.47	0.63	0.38	0.47	0.48	0.34
	Minimum	3	4	3	2	3	2
	Median	7.0	8.0	8.0	7.0	8.0	7.0
	Maximum	10	10	10	10	10	10
Week 2	n	13	10	23	19	21	40
	Mean	4.1	5.3	4.6	6.8	7.0	6.9
	SD	2.72	2.83	2.78	2.07	2.68	2.38
	CV (%)	66.8	53.4	60.2	30.5	38.3	34.5
	SEM	0.75	0.90	0.58	0.47	0.59	0.38
	Minimum	1	1	1	3	1	1
	Median	5.0	5.5	5.0	7.0	8.0	7.0
	Maximum	9	10	10	10	10	10

Note: * Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.4.1.1 Summary of Perceived Health Risk Scale by Study Product Group and Study Week (PP Population)

Study Week	Statistics	Study Product Group					
		VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week 4	n	10	10	20	20	19	39
	Mean	2.7	3.8	3.3	6.7	7.4	7.0
	SD	2.91	2.94	2.90	2.37	2.55	2.45
	CV (%)	107.7	77.3	89.2	35.6	34.3	34.9
	SEM	0.92	0.93	0.65	0.53	0.58	0.39
	Minimum	1	1	1	1	2	1
	Median	1.0	3.0	2.0	7.0	8.0	7.0
	Maximum	9	10	10	10	10	10
Week 6	n	9	10	19	20	19	39
	Mean	2.6	4.0	3.3	6.6	6.9	6.7
	SD	2.65	3.56	3.16	1.70	2.54	2.12
	CV (%)	103.7	89.0	95.4	25.7	36.8	31.5
	SEM	0.88	1.13	0.73	0.38	0.58	0.34
	Minimum	1	1	1	3	2	2
	Median	1.0	2.5	2.0	7.0	7.0	7.0
	Maximum	9	10	10	10	10	10

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.4.1.2 Summary of Perceived Health Risk Scale by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	Study Product Group					
		VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week -1*	n	49	50	99	20	22	42
	Mean	7.0	7.6	7.3	6.6	7.7	7.1
	SD	2.17	2.04	2.12	2.09	2.25	2.23
	CV (%)	31.0	26.7	28.9	31.9	29.4	31.2
	SEM	0.31	0.29	0.21	0.47	0.48	0.34
	Minimum	2	3	2	2	3	2
	Median	7.0	8.0	8.0	7.0	8.0	7.0
	Maximum	10	10	10	10	10	10
Week 2	n	46	47	93	19	21	40
	Mean	3.4	4.0	3.7	6.8	7.0	6.9
	SD	2.73	3.02	2.88	2.07	2.68	2.38
	CV (%)	79.5	74.7	77.0	30.5	38.3	34.5
	SEM	0.40	0.44	0.30	0.47	0.59	0.38
	Minimum	1	1	1	3	1	1
	Median	3.0	3.0	3.0	7.0	8.0	7.0
	Maximum	10	10	10	10	10	10

Note: * Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.4.1.2 Summary of Perceived Health Risk Scale by Study Product Group and Study Week (ITT Population)

Study Week	Statistics	Study Product Group					
		VLN Mentholated	VLN Non-Mentholated	VLN Combined	UB Mentholated	UB Non-Mentholated	UB Combined
Week 4	n	41	43	84	20	19	39
	Mean	3.4	3.4	3.4	6.7	7.4	7.0
	SD	2.86	2.55	2.69	2.37	2.55	2.45
	CV (%)	83.3	75.0	78.7	35.6	34.3	34.9
	SEM	0.45	0.39	0.29	0.53	0.58	0.39
	Minimum	1	1	1	1	2	1
	Median	3.0	2.0	3.0	7.0	8.0	7.0
	Maximum	10	10	10	10	10	10
Week 6	n	42	43	85	20	19	39
	Mean	3.2	3.6	3.4	6.6	6.9	6.7
	SD	2.89	2.79	2.83	1.70	2.54	2.12
	CV (%)	90.0	78.4	83.5	25.7	36.8	31.5
	SEM	0.45	0.43	0.31	0.38	0.58	0.34
	Minimum	1	1	1	3	2	2
	Median	2.0	3.0	2.0	7.0	7.0	7.0
	Maximum	10	10	10	10	10	10

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.4.2 Statistical Comparison of Perceived Health Risk Scale at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	95%		p-Value
		Test Week	(n)	Baseline	(n)		Confidence Intervals		
Week 2	VLN Non-Mentholated	5.30	(10)	7.40	(10)	-2.10	-4.81 -	0.61	0.1132
	VLN Mentholated	4.08	(13)	6.38	(13)	-2.31	-4.02 -	-0.59	0.0126
	VLN Combined	4.61	(23)	6.83	(23)	-2.22	-3.60 -	-0.83	0.0031
	UB Non-Mentholated	7.00	(21)	7.57	(21)	-0.57	-1.33 -	0.18	0.1305
	UB Mentholated	6.79	(19)	6.53	(19)	0.26	-0.70 -	1.23	0.5725
	UB Combined	6.90	(40)	7.08	(40)	-0.18	-0.77 -	0.42	0.5536
Week 6	VLN Non-Mentholated	4.00	(10)	7.70	(10)	-3.70	-7.32 -	-0.08	0.0459
	VLN Mentholated	2.56	(9)	6.78	(9)	-4.22	-5.97 -	-2.47	0.0005
	VLN Combined	3.32	(19)	7.26	(19)	-3.95	-5.82 -	-2.07	0.0003
	UB Non-Mentholated	6.89	(19)	7.58	(19)	-0.68	-1.61 -	0.24	0.1371
	UB Mentholated	6.60	(20)	6.55	(20)	0.05	-0.94 -	1.04	0.9169
	UB Combined	6.74	(39)	7.05	(39)	-0.31	-0.97 -	0.35	0.3494

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 Paired t-test method is used to perform the analysis.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.4.3 Statistical Comparison of Perceived Health Risk Scale Among Study Product Groups at Weeks 2 and 6 (PP Population)

Study Week	Comparison	----- LSMeans -----		-----LSMean Difference		95%		p-value
		Test	(n) Reference (n)	(Test - Reference)		Confidence Intervals		
Week 2	VLN Non-mentholated vs UB Non-mentholated	5.24(10)	7.00(21)	-1.76		-3.69 - 0.16		0.0721
	VLN Mentholated vs UB Mentholated	4.08(13)	6.77(19)	-2.69		-4.51 - -0.88		0.0043
	VLN Combined vs UB Combined	4.66(23)	6.89(40)	-2.23		-3.55 - -0.90		0.0013
Week 6	VLN Non-mentholated vs UB Non-mentholated	4.10(10)	6.86(19)	-2.76		-4.69 - -0.84		0.0057
	VLN Mentholated vs UB Mentholated	3.04 (9)	6.60(20)	-3.56		-5.50 - -1.62		0.0005
	VLN Combined vs UB Combined	3.57(19)	6.73(39)	-3.16		-4.53 - -1.79		<.0001

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.4.4 Statistical Comparison of Perceived Health Risk Scale at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

Study Week	Product Group	Means				Difference (Test Week - Baseline)	95% Confidence Intervals		p-Value
		Test Week	(n)	Baseline	(n)				
Week 2	VLN Non-Mentholated	4.04	(47)	7.57	(47)	-3.53	-4.63	-2.43	<.0001
	VLN Mentholated	3.43	(46)	6.98	(45)	-3.62	-4.56	-2.68	<.0001
	VLN Combined	3.74	(93)	7.28	(92)	-3.58	-4.29	-2.86	<.0001
	UB Non-Mentholated	7.00	(21)	7.57	(21)	-0.57	-1.33	0.18	0.1305
	UB Mentholated	6.79	(19)	6.53	(19)	0.26	-0.70	1.23	0.5725
	UB Combined	6.90	(40)	7.08	(40)	-0.18	-0.77	0.42	0.5536
Week 6	VLN Non-Mentholated	3.56	(43)	7.81	(43)	-4.26	-5.37	-3.14	<.0001
	VLN Mentholated	3.21	(42)	7.12	(41)	-3.88	-4.93	-2.83	<.0001
	VLN Combined	3.39	(85)	7.48	(84)	-4.07	-4.82	-3.32	<.0001
	UB Non-Mentholated	6.89	(19)	7.58	(19)	-0.68	-1.61	0.24	0.1371
	UB Mentholated	6.60	(20)	6.55	(20)	0.05	-0.94	1.04	0.9169
	UB Combined	6.74	(39)	7.05	(39)	-0.31	-0.97	0.35	0.3494

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 Paired t-test method is used to perform the analysis.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.2.9.4.5 Statistical Comparison of Perceived Health Risk Scale Among Study Product Groups at Weeks 2 and 6 (ITT Population)

Study Week	Comparison	----- LSMeans -----		-----LSMean Difference	95%		p-value
		Test	(n)	Reference (n)	(Test - Reference)	Confidence Intervals	
Week 2	VLN Non-mentholated vs UB Non-mentholated	4.10(47)		7.00(21)	-2.90	-4.32 - -1.47	<.0001
	VLN Mentholated vs UB Mentholated	3.43(46)		6.77(19)	-3.33	-4.80 - -1.86	<.0001
	VLN Combined vs UB Combined	3.77(93)		6.88(40)	-3.11	-4.14 - -2.09	<.0001
Week 6	VLN Non-mentholated vs UB Non-mentholated	3.52(43)		6.86(19)	-3.34	-4.74 - -1.94	<.0001
	VLN Mentholated vs UB Mentholated	3.37(42)		6.60(20)	-3.23	-4.63 - -1.82	<.0001
	VLN Combined vs UB Combined	3.45(85)		6.73(39)	-3.28	-4.28 - -2.29	<.0001

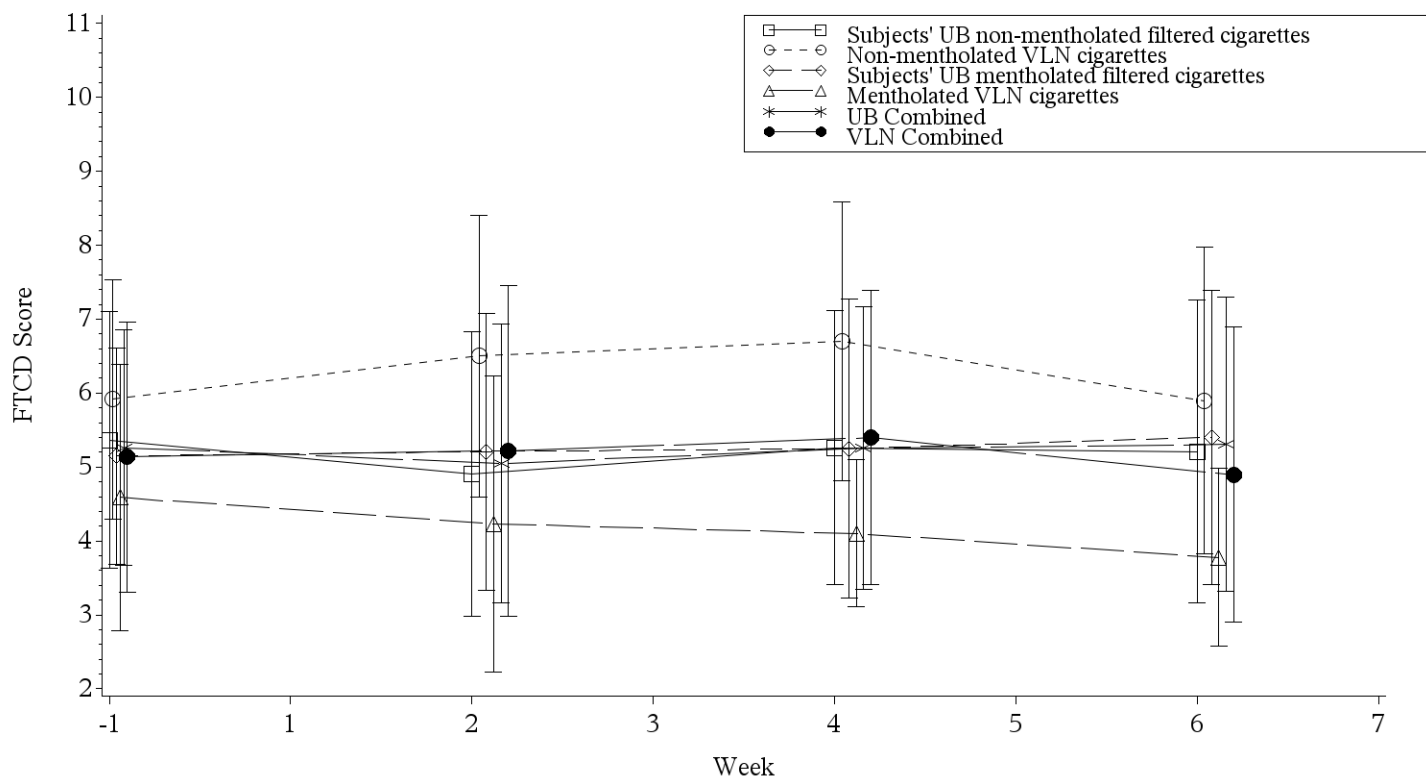
 Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis
 Test = The first product in the comparison
 Reference = The second product in the comparison
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

14.2.10 Subject Effect Figures

- Figure 14.2.10.1.1 Mean (\pm SD) of FTCD Score by Study Product Group and Study Week (PP Population)
- Figure 14.2.10.1.2 Mean FTCD Score by Study Product Group and Study Week (PP Population)
- Figure 14.2.10.1.3 Mean (\pm SD) of FTCD Score by Study Product Group and Study Week (ITT Population)
- Figure 14.2.10.1.4 Mean FTCD Score by Study Product Group and Study Week (ITT Population)
- Figure 14.2.10.2.1.1 Mean (\pm SD) of QSU-Brief Factor Score (Factor 1) by Study Product Group and Study Week (PP Population)
- Figure 14.2.10.2.1.2 Mean QSU-Brief Factor Score (Factor 1) by Study Product Group and Study Week (PP Population)
- Figure 14.2.10.2.1.3 Mean (\pm SD) of QSU-Brief Factor Score (Factor 1) by Study Product Group and Study Week (ITT Population)
- Figure 14.2.10.2.1.4 Mean QSU-Brief Factor Score (Factor 1) by Study Product Group and Study Week (ITT Population)
- Figure 14.2.10.2.2.1 Mean (\pm SD) of QSU-Brief Factor Score (Factor 2) by Study Product Group and Study Week (PP Population)
- Figure 14.2.10.2.2.2 Mean QSU-Brief Factor Score (Factor 2) by Study Product Group and Study Week (PP Population)
- Figure 14.2.10.2.2.3 Mean (\pm SD) of QSU-Brief Factor Score (Factor 2) by Study Product Group and Study Week (ITT Population)
- Figure 14.2.10.2.2.4 Mean QSU-Brief Factor Score (Factor 2) by Study Product Group and Study Week (ITT Population)
- Figure 14.2.10.3.1 Mean (\pm SD) of MNWS-R Total Score by Study Product Group and Study Week (PP Population)
- Figure 14.2.10.3.2 Mean MNWS-R Total Score by Study Product Group and Study Week (PP Population)
- Figure 14.2.10.3.3 Mean (\pm SD) of MNWS-R Total Score by Study Product Group and Study Week (ITT Population)
- Figure 14.2.10.3.4 Mean MNWS-R Total Score by Study Product Group and Study Week (ITT Population)
- Figure 14.2.10.4.1 Mean (\pm SD) of Perceived Health Risk Scale by Study Product Group and Study Week (PP Population)
- Figure 14.2.10.4.2 Mean Perceived Health Risk Scale by Study Product Group and Study Week (PP Population)
- Figure 14.2.10.4.3 Mean (\pm SD) of Perceived Health Risk Scale by Study Product Group and Study Week (ITT Population)
- Figure 14.2.10.4.4 Mean Perceived Health Risk Scale by Study Product Group and Study Week (ITT Population)

Figure 14.2.10.1.1

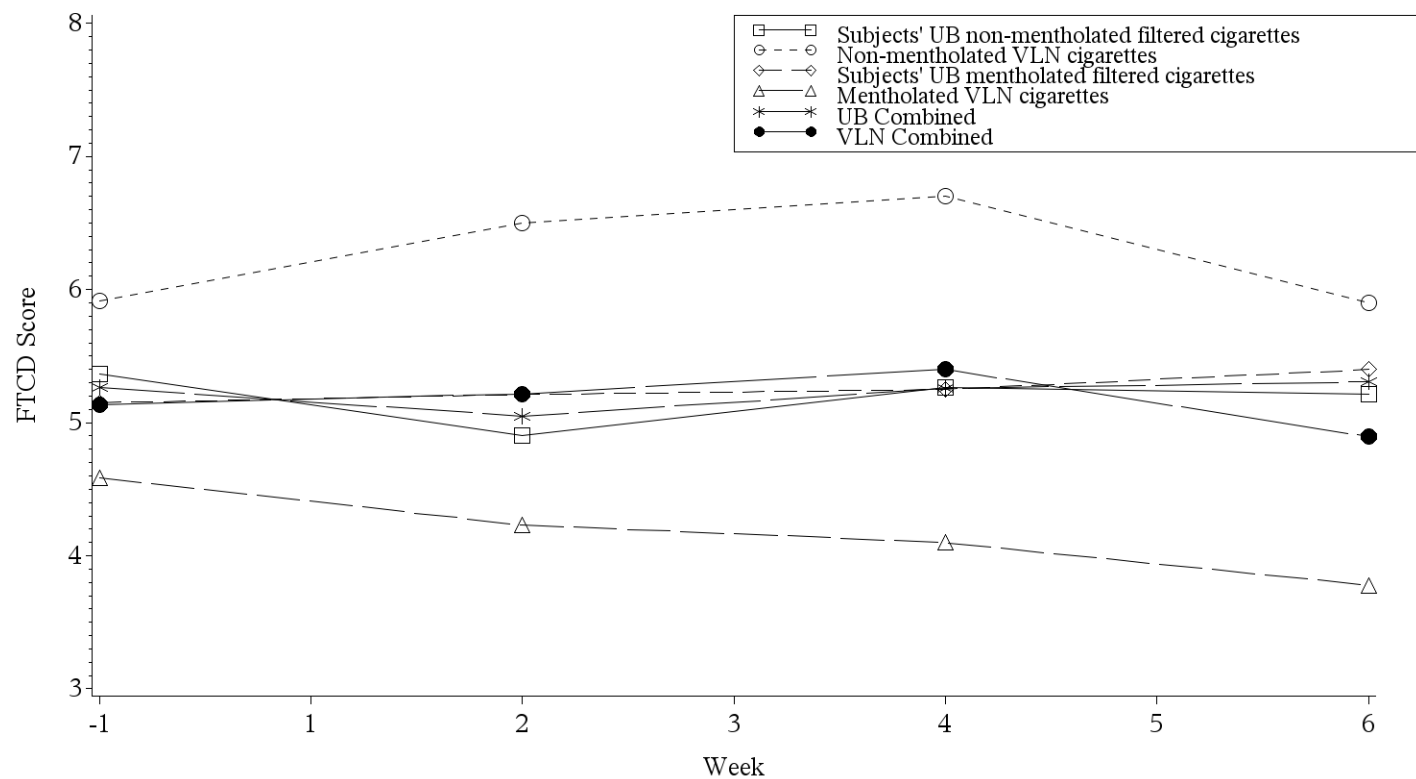
Mean (\pm SD) of FTCD Score by Study Product Group and Study Week (PP Population)



All products except Subjects' UB non-mentholated filtered cigarettes are shifted to the right for ease of reading.
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Figure 14.2.10.1.2

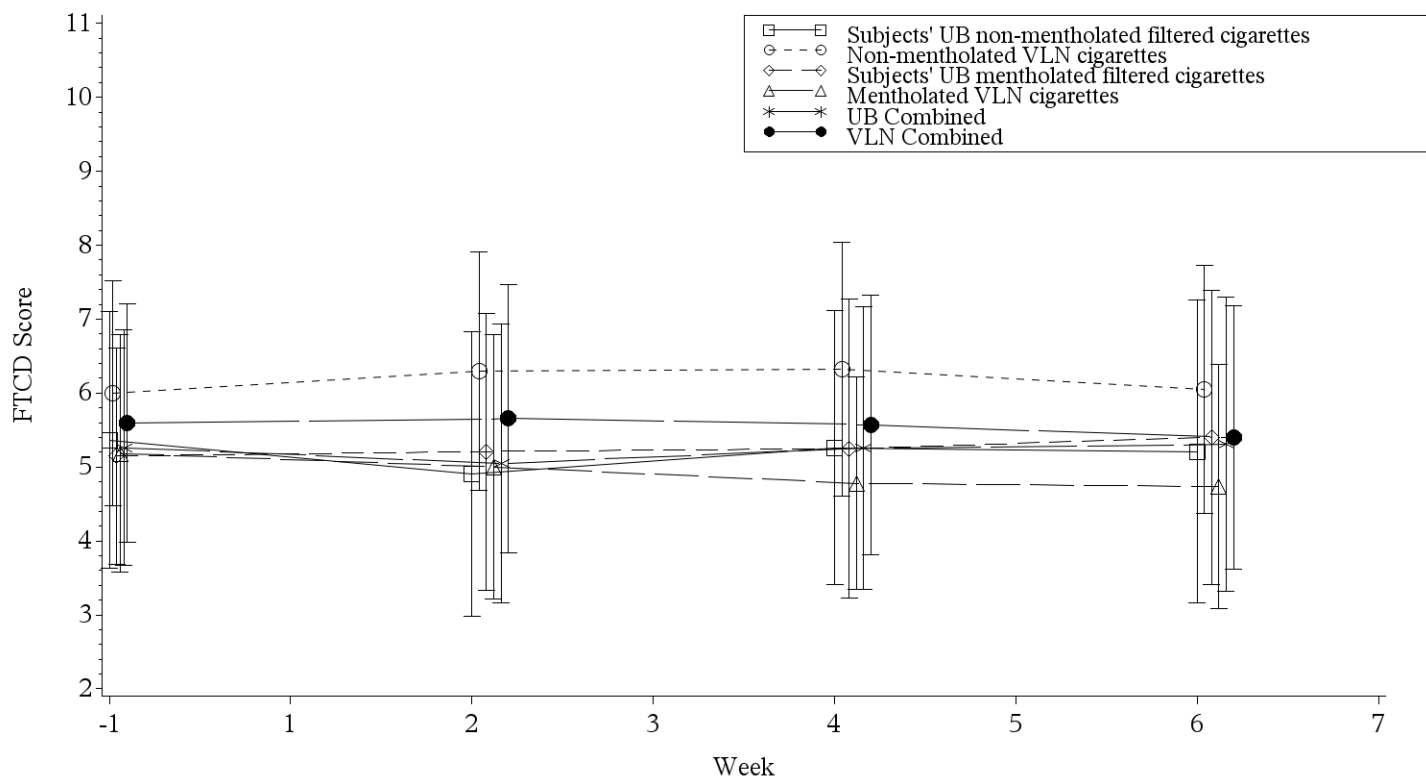
Mean FTCD Score by Study Product Group and Study Week (PP Population)



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Figure 14.2.10.1.3

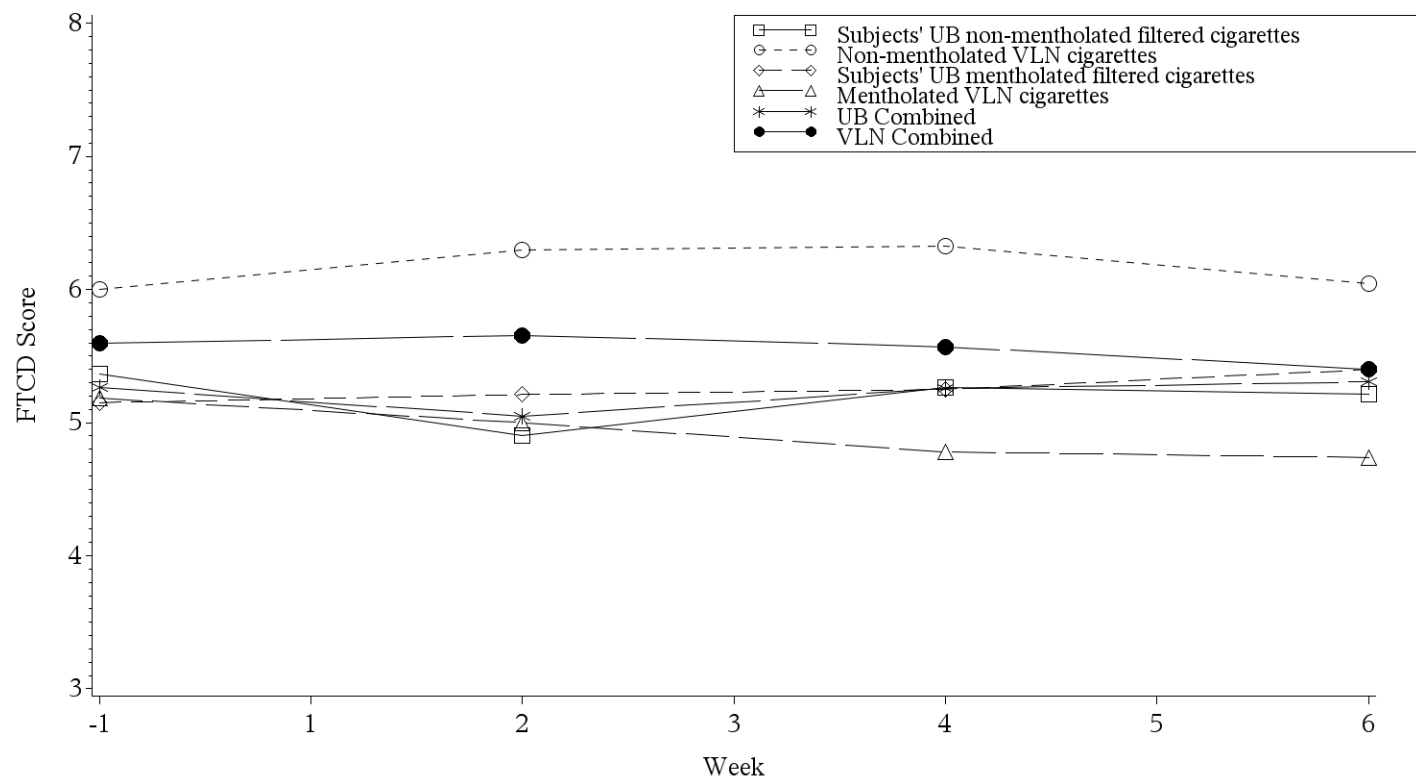
Mean (\pm SD) of FTCD Score by Study Product Group and Study Week (ITT Population)



All products except Subjects' UB non-mentholated filtered cigarettes are shifted to the right for ease of reading.
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Figure 14.2.10.1.4

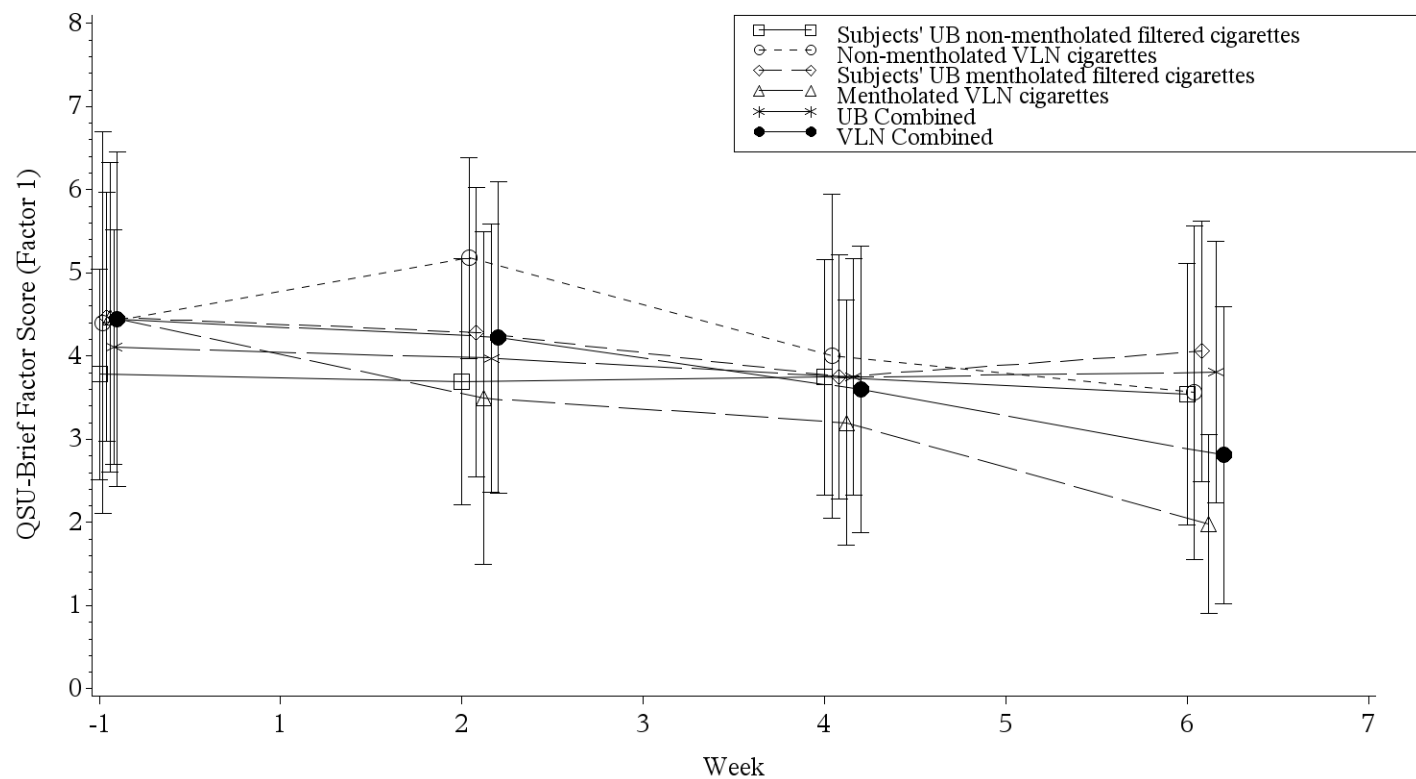
Mean FTCD Score by Study Product Group and Study Week (ITT Population)



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Figure 14.2.10.2.1.1

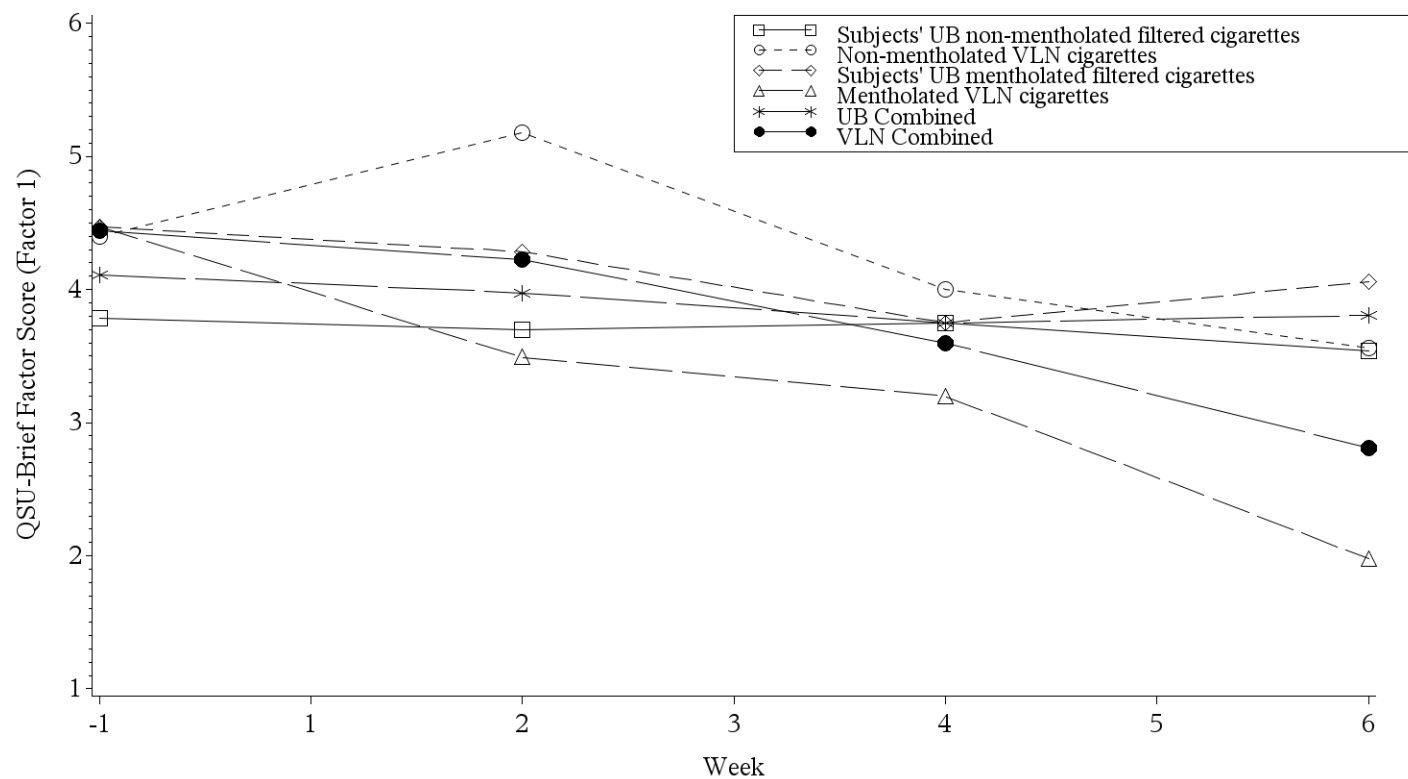
Mean (\pm SD) of QSU-Brief Factor Score (Factor 1) by Study Product Group and Study Week (PP Population)



All products except Subjects' UB non-mentholated filtered cigarettes are shifted to the right for ease of reading.
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Figure 14.2.10.2.1.2

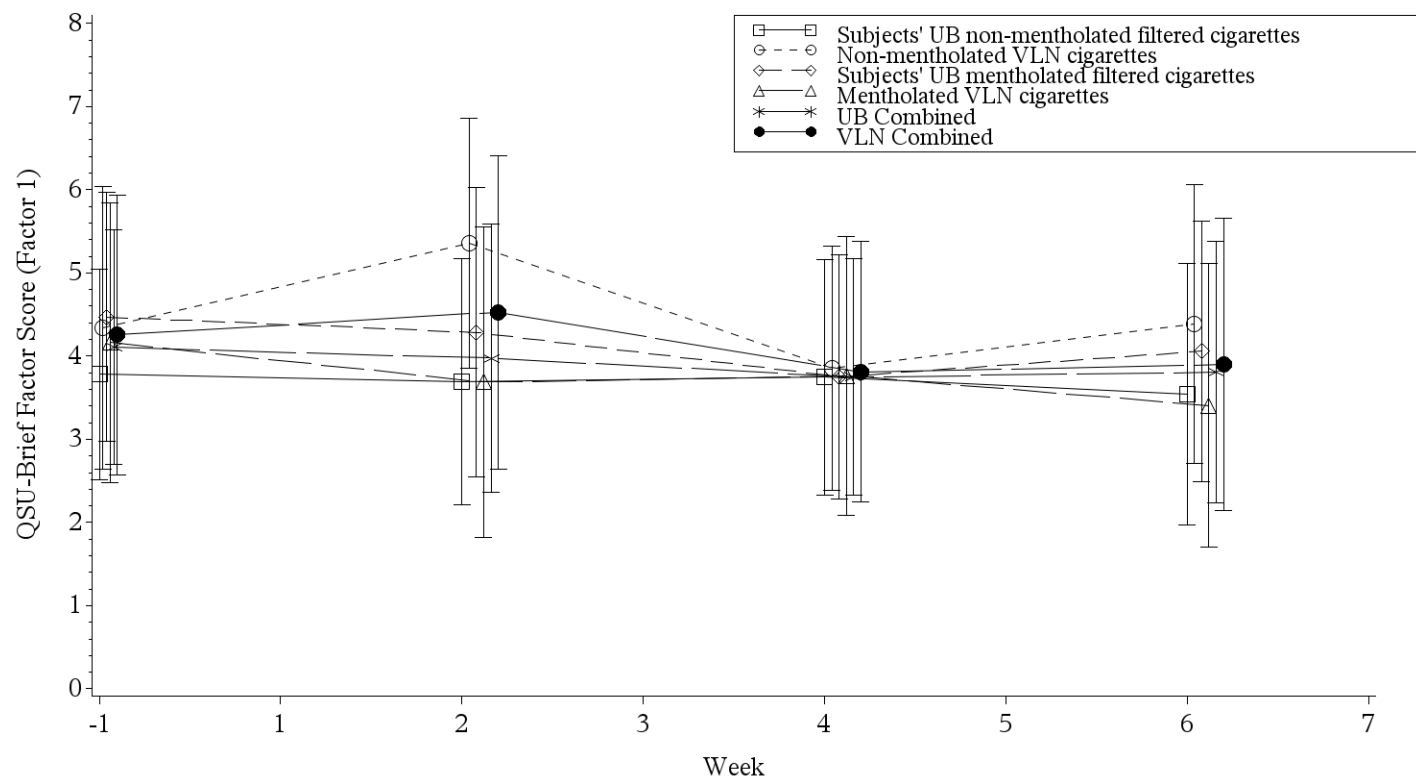
Mean QSU-Brief Factor Score (Factor 1) by Study Product Group and Study Week (PP Population)



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Figure 14.2.10.2.1.3

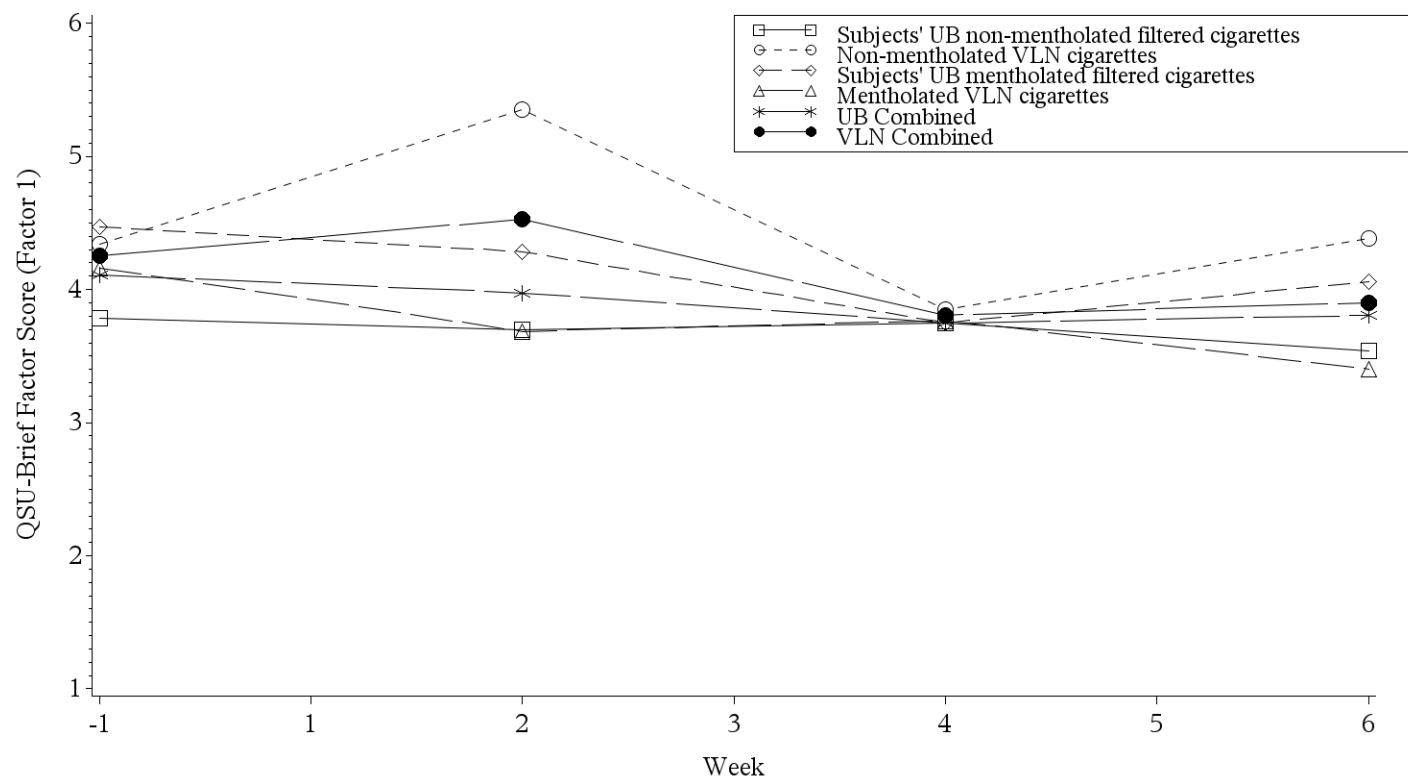
Mean (\pm SD) of QSU-Brief Factor Score (Factor 1) by Study Product Group and Study Week (ITT Population)



All products except Subjects' UB non-mentholated filtered cigarettes are shifted to the right for ease of reading.
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Figure 14.2.10.2.1.4

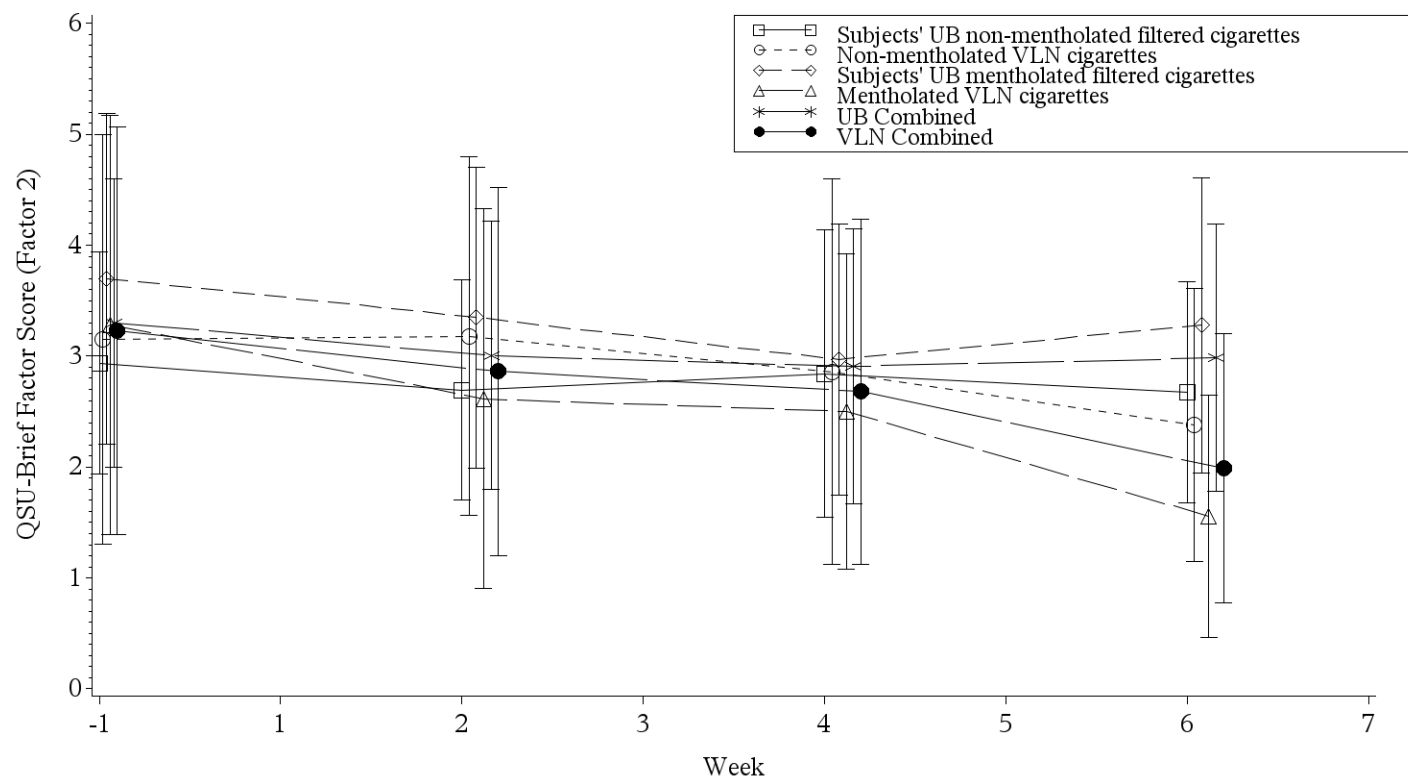
Mean QSU-Brief Factor Score (Factor 1) by Study Product Group and Study Week (ITT Population)



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Figure 14.2.10.2.2.1

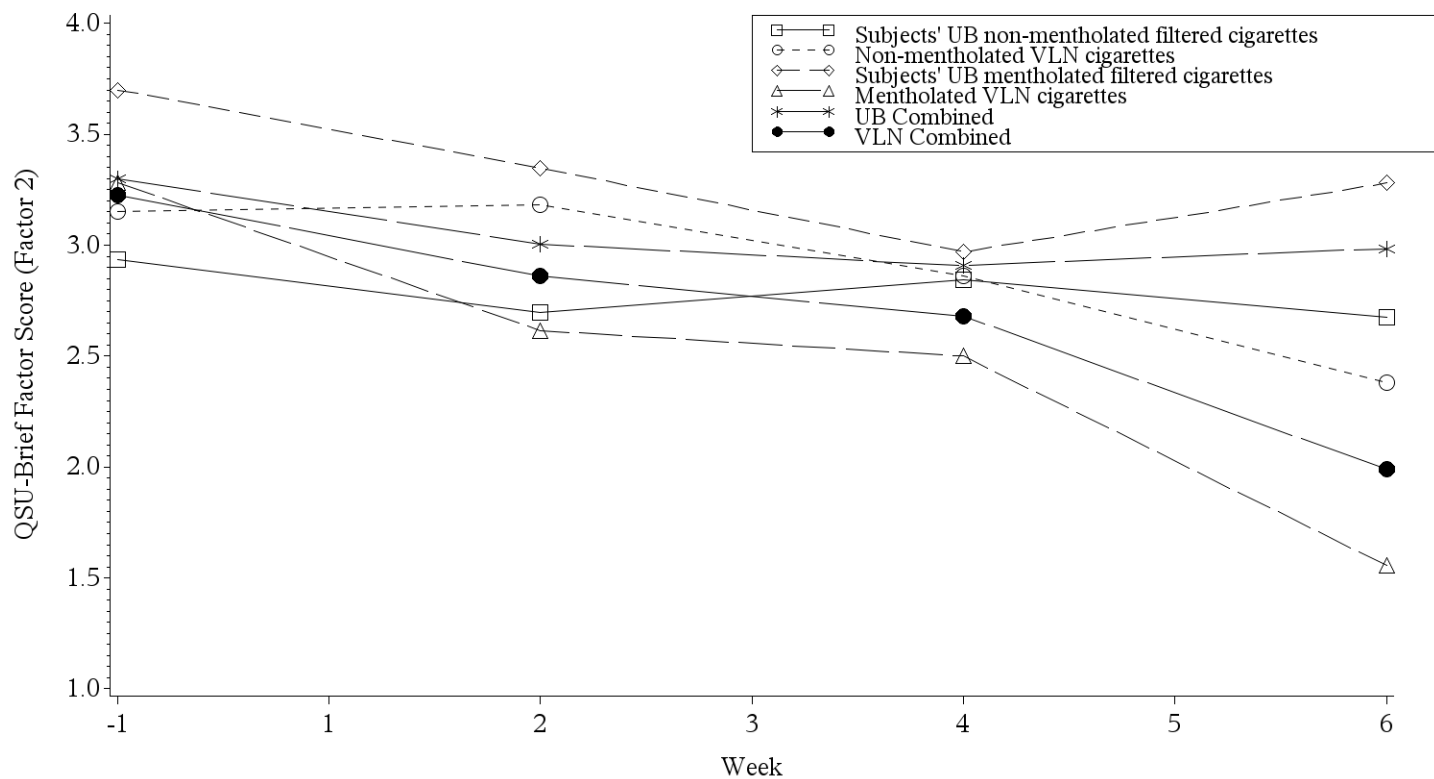
Mean (\pm SD) of QSU-Brief Factor Score (Factor 2) by Study Product Group and Study Week (PP Population)



All products except Subjects' UB non-mentholated filtered cigarettes are shifted to the right for ease of reading.
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Figure 14.2.10.2.2.2

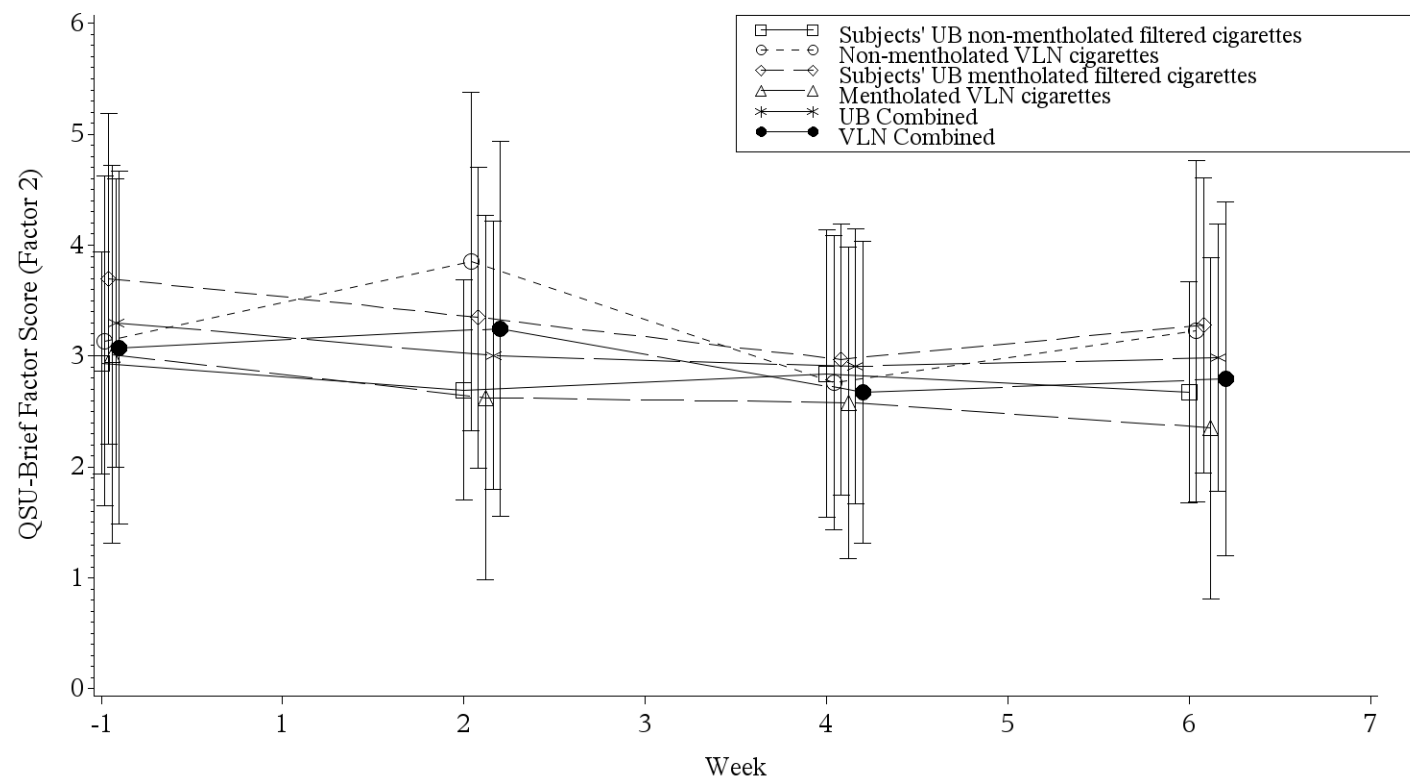
Mean QSU-Brief Factor Score (Factor 2) by Study Product Group and Study Week (PP Population)



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Figure 14.2.10.2.2.3

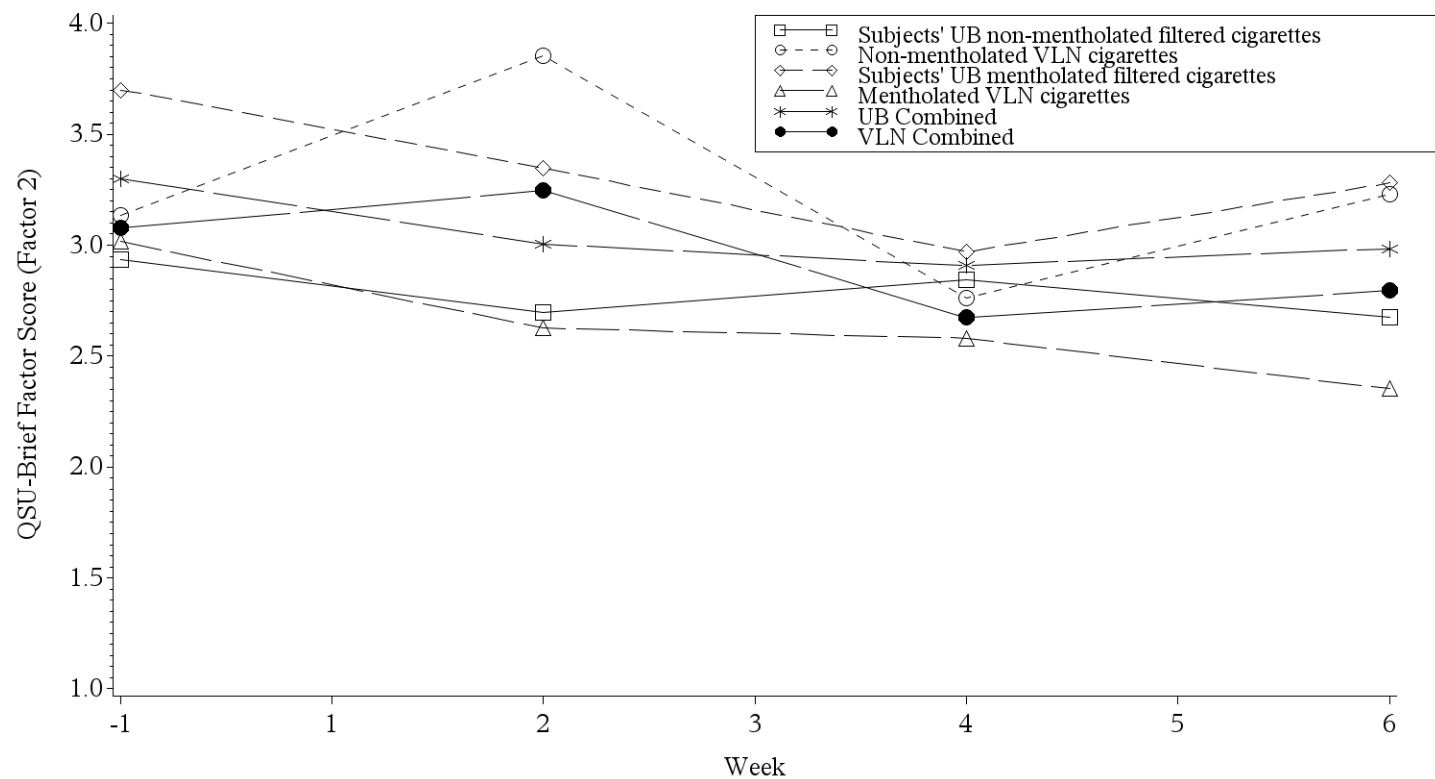
Mean (\pm SD) of QSU-Brief Factor Score (Factor 2) by Study Product Group and Study Week (ITT Population)



All products except Subjects' UB non-mentholated filtered cigarettes are shifted to the right for ease of reading.
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Figure 14.2.10.2.2.4

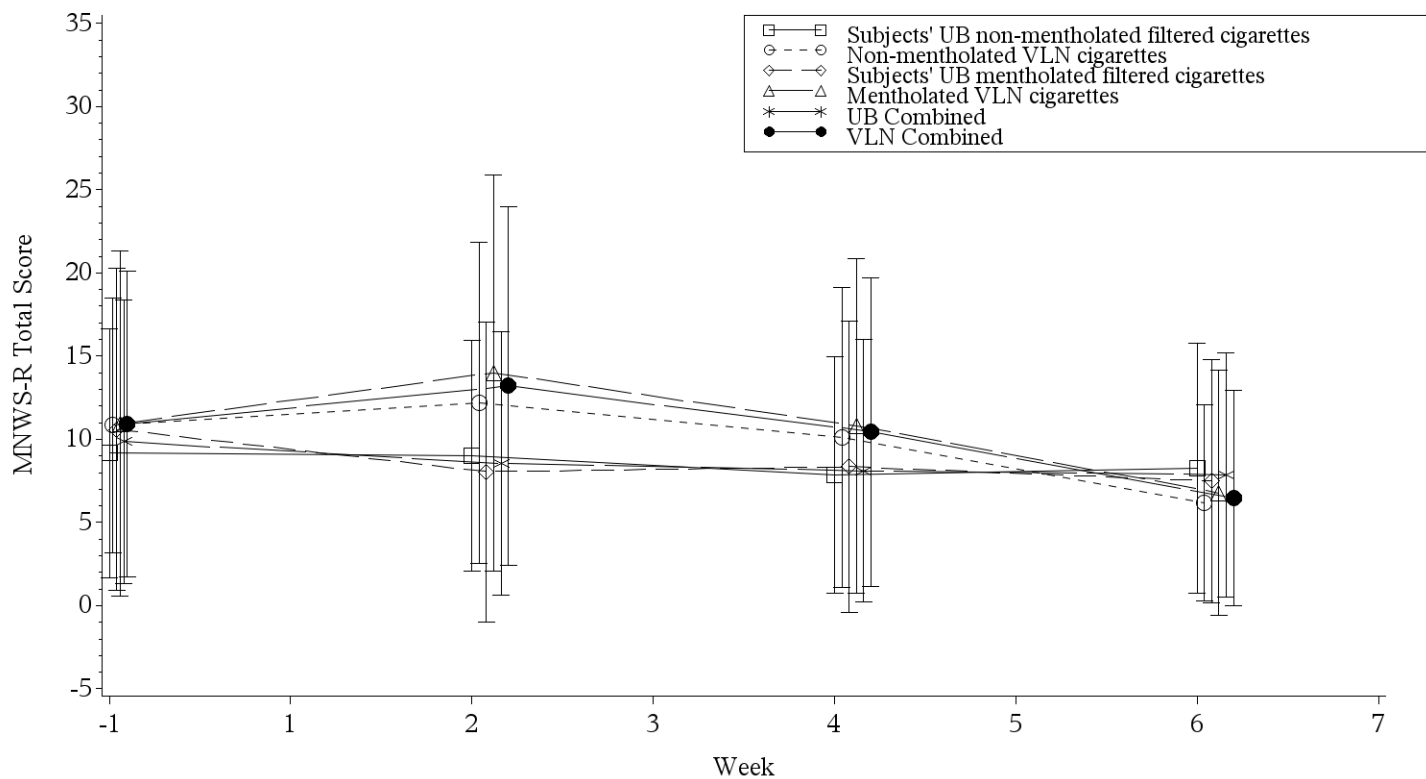
Mean QSU-Brief Factor Score (Factor 2) by Study Product Group and Study Week (ITT Population)



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Figure 14.2.10.3.1

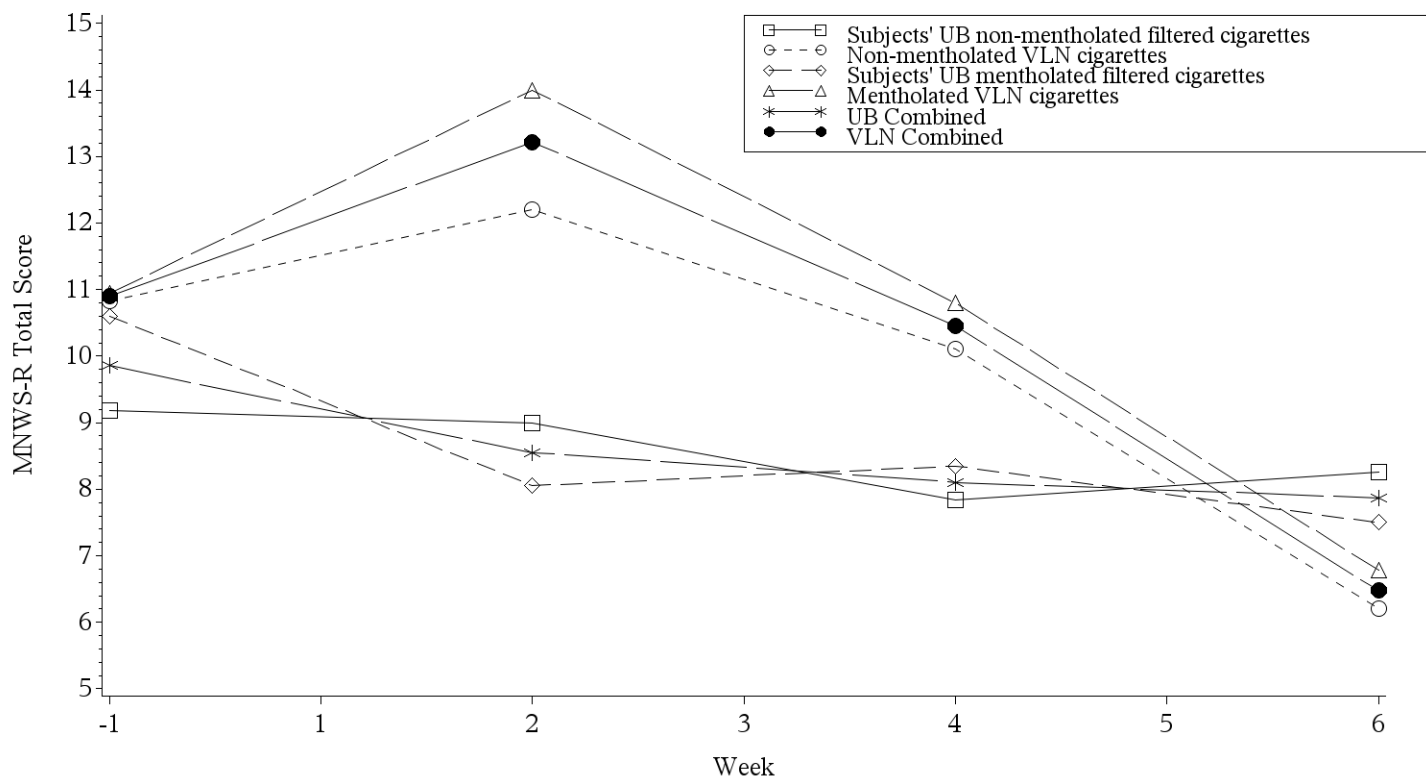
Mean (\pm SD) of MNWS-R Total Score by Study Product Group and Study Week (PP Population)



All products except Subjects' UB non-mentholated filtered cigarettes are shifted to the right for ease of reading.
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Figure 14.2.10.3.2

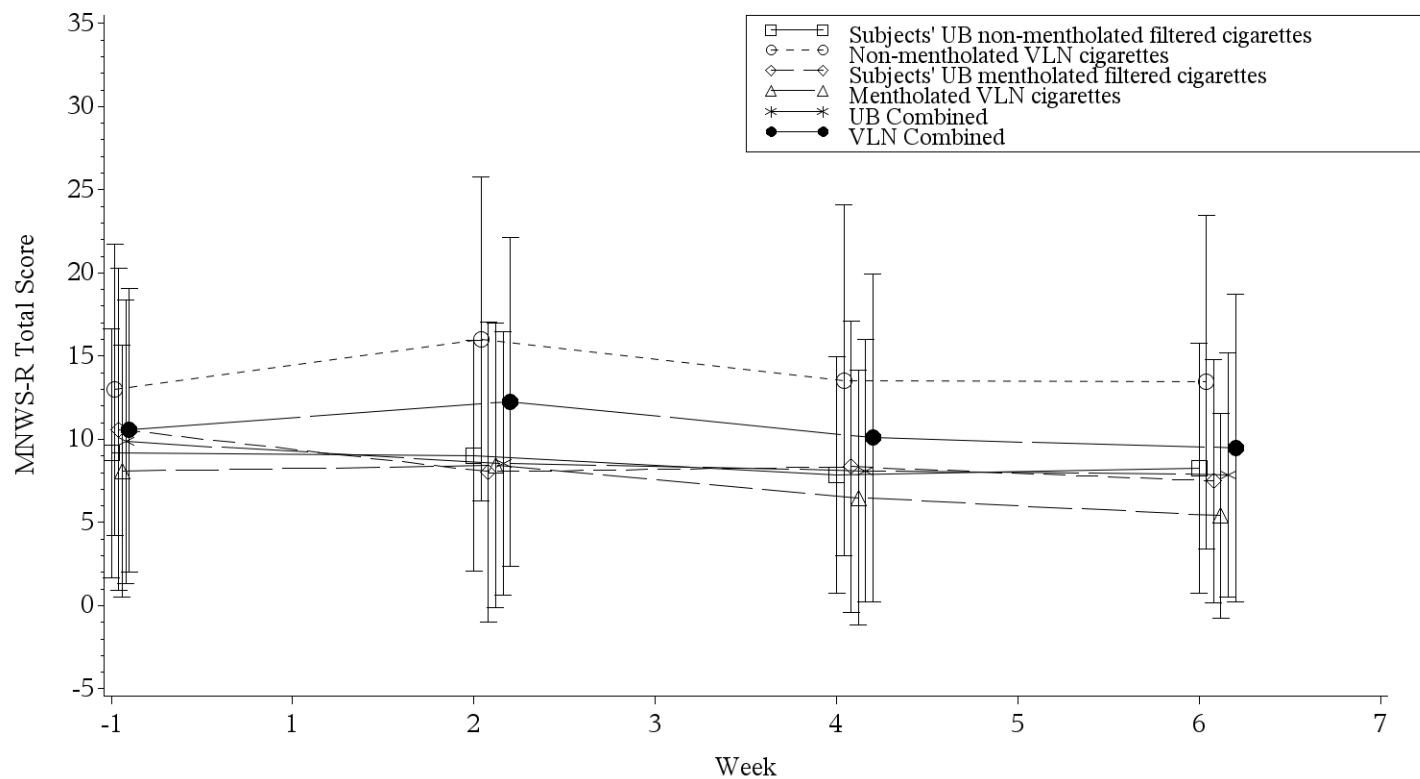
Mean MNWS-R Total Score by Study Product Group and Study Week (PP Population)



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Figure 14.2.10.3.3

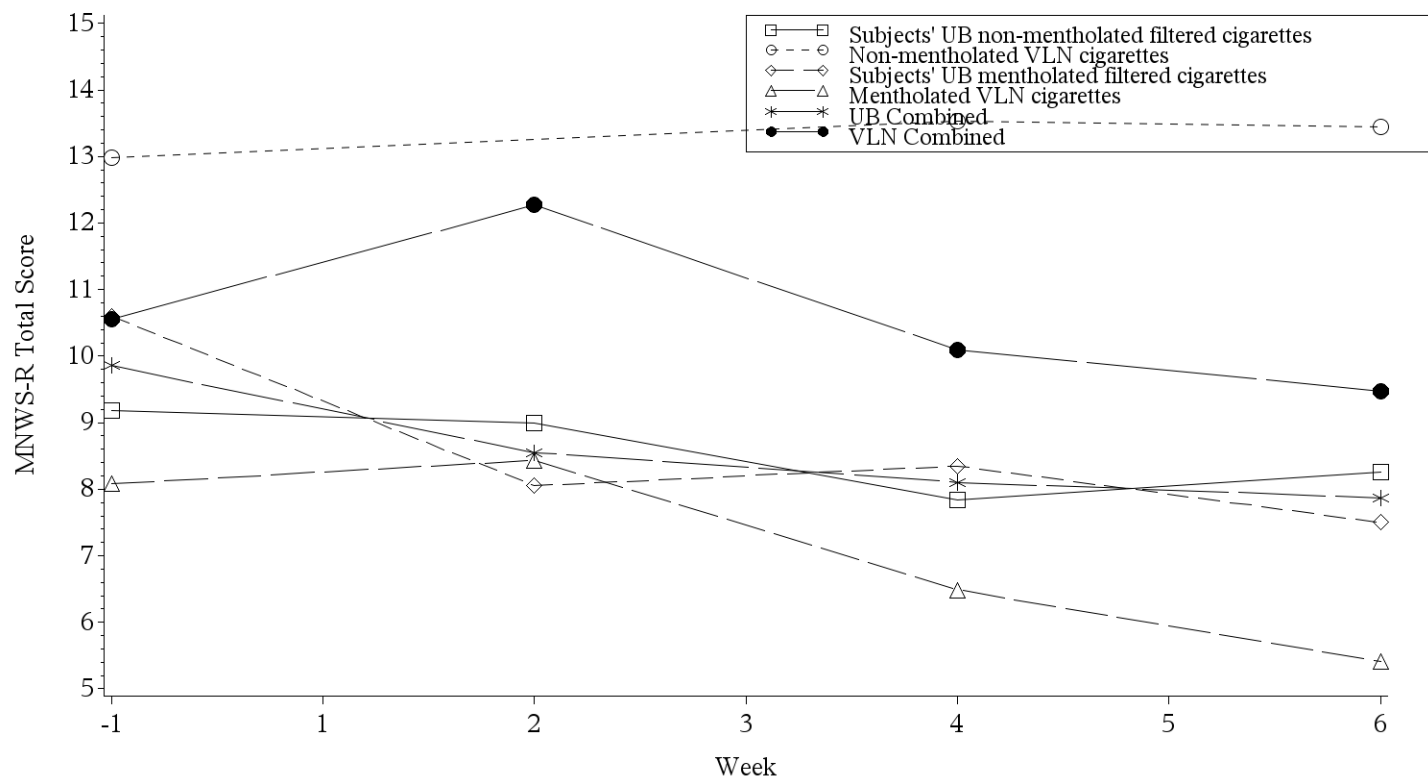
Mean (\pm SD) of MNWS-R Total Score by Study Product Group and Study Week (ITT Population)



All products except Subjects' UB non-mentholated filtered cigarettes are shifted to the right for ease of reading.
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Figure 14.2.10.3.4

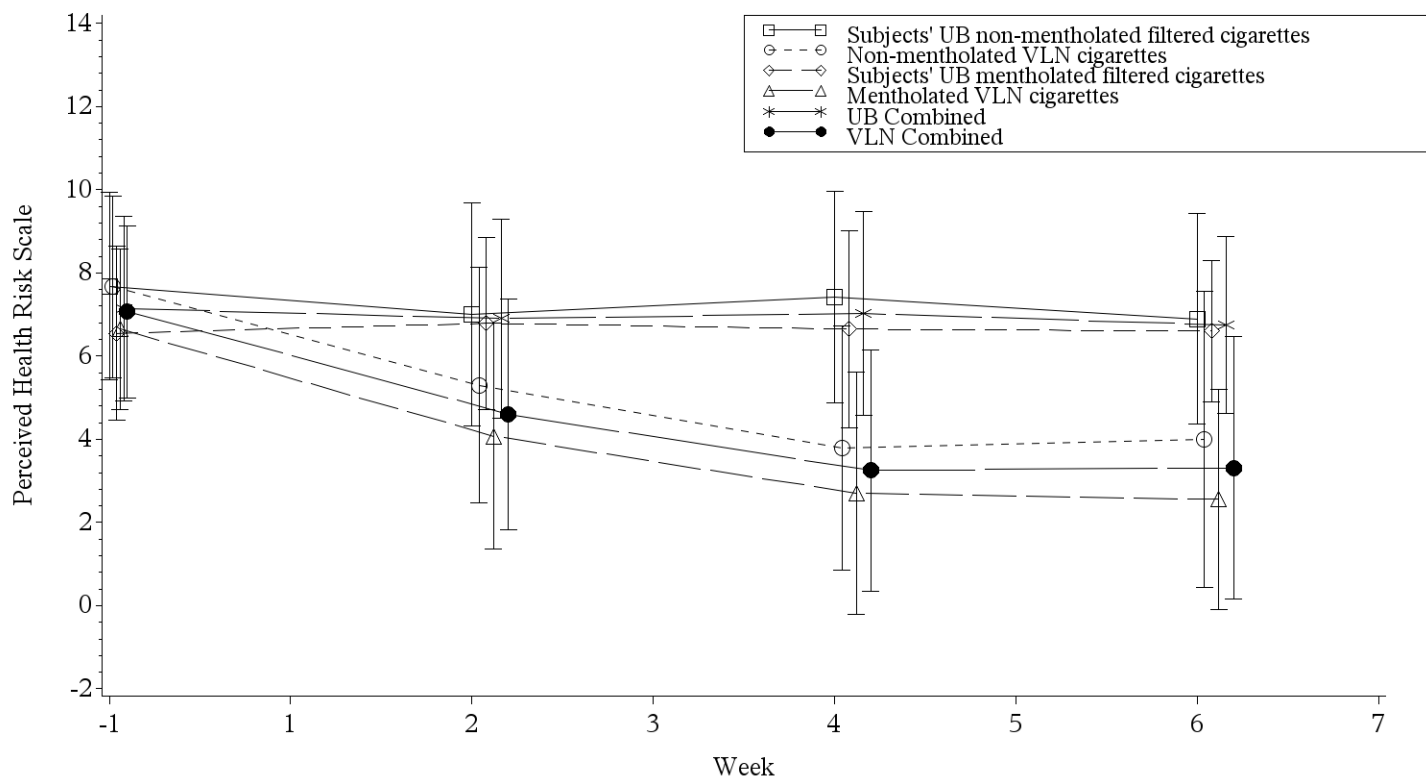
Mean MNWS-R Total Score by Study Product Group and Study Week (ITT Population)



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Figure 14.2.10.4.1

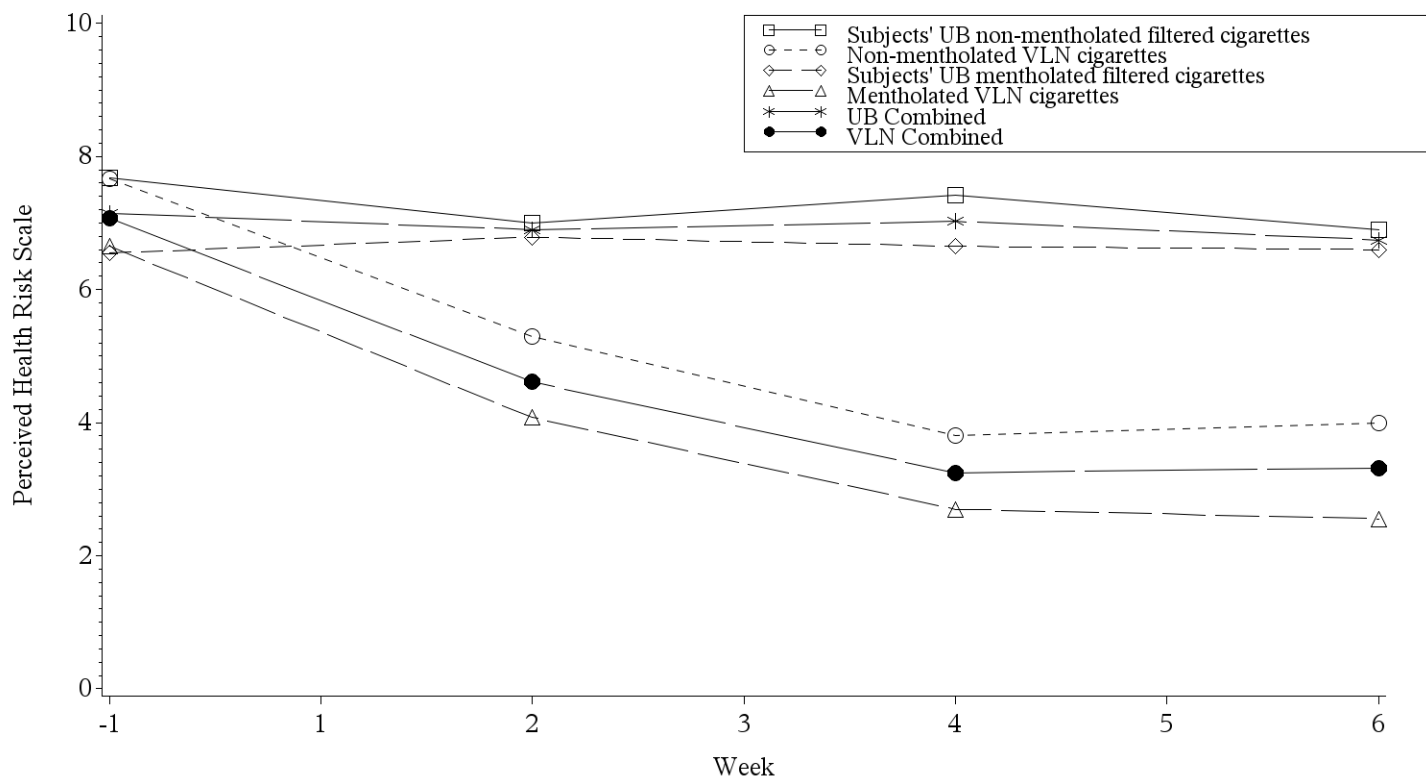
Mean (\pm SD) of Perceived Health Risk Scale by Study Product Group and Study Week (PP Population)



All products except Subjects' UB non-mentholated filtered cigarettes are shifted to the right for ease of reading.
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Figure 14.2.10.4.2

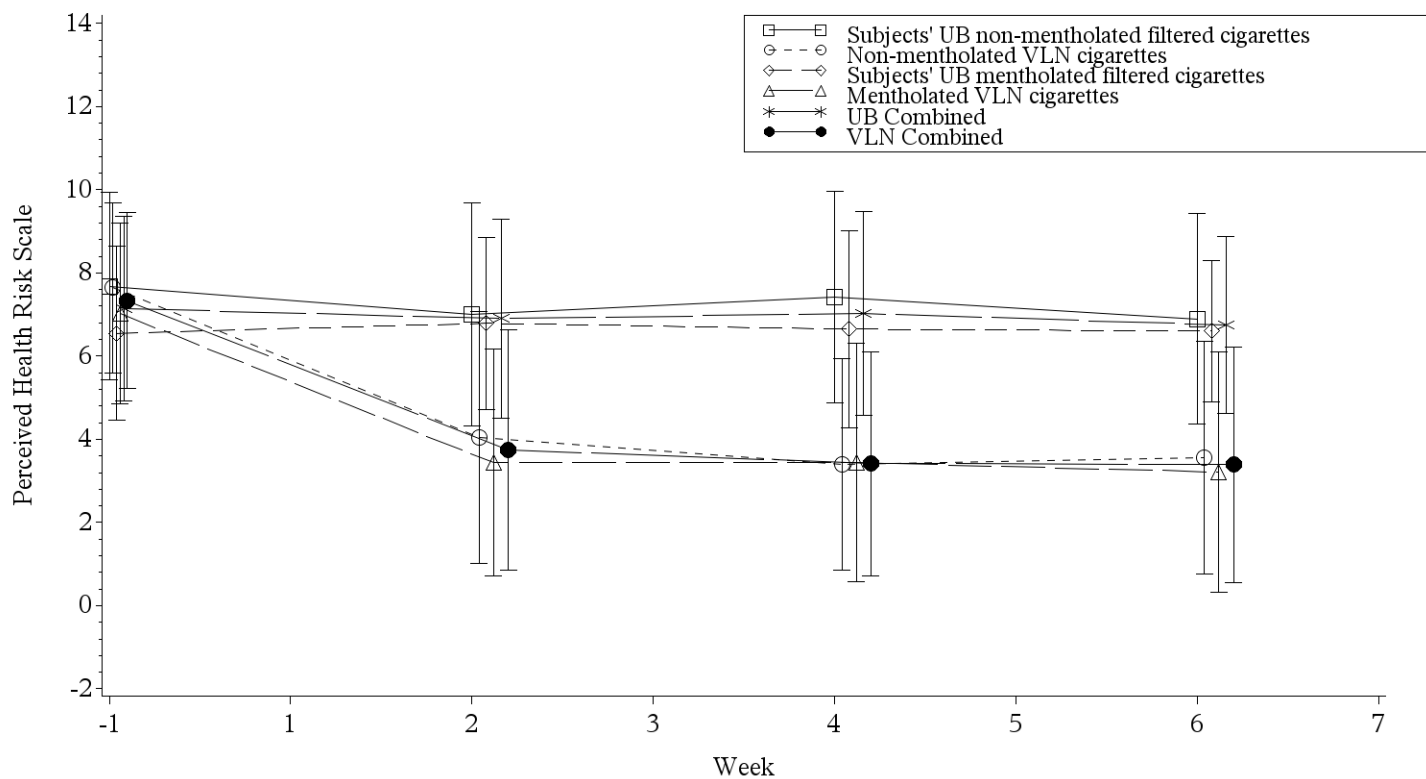
Mean Perceived Health Risk Scale by Study Product Group and Study Week (PP Population)



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Figure 14.2.10.4.3

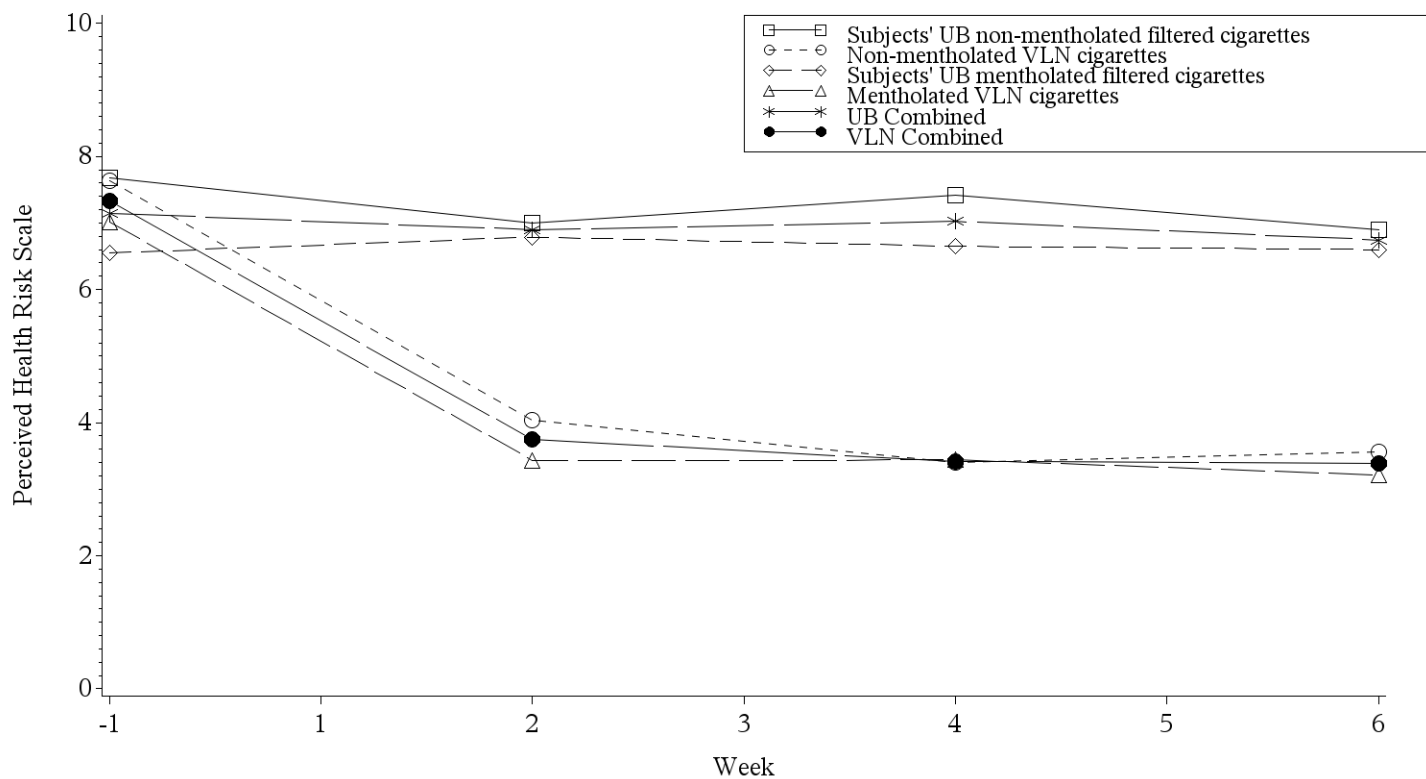
Mean (\pm SD) of Perceived Health Risk Scale by Study Product Group and Study Week (ITT Population)



All products except Subjects' UB non-mentholated filtered cigarettes are shifted to the right for ease of reading.
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Figure 14.2.10.4.4

Mean Perceived Health Risk Scale by Study Product Group and Study Week (ITT Population)



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14.3 Safety Data Summary Tables

14.3.1 Displays of Adverse Events

Table 14.3.1.1	Product-Use-Emergent Adverse Event Frequency– Number of Subjects Reporting the Event (% of Subjects (% of Subject Used Study Product) (Safety Population)
Table 14.3.1.2	Product-Use-Emergent Adverse Event Frequency – Number of Adverse Events (% of Total Adverse Events) (Safety Population)
Table 14.3.1.3	Product-Use-Emergent Adverse Event Frequency by Severity and Relationship to Study Product - Number of Subjects Reporting Adverse Events (Safety Population)

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Table 14.3.1.1 Product-Use-Emergent Adverse Event Frequency-
 Number of Subjects Reporting the Event (% of Subjects (% of Subject Used Study Product) (Safety Population)

Adverse Event*	Study Product					Overall#
	Baseline	UB Non-Mentholated	VLN Non-Mentholated	UB Mentholated	VLN Mentholated	
Number of Subjects Use Study Product	142 (100%)	22 (100%)	50 (100%)	20 (100%)	50 (100%)	142 (100%)
Number of Subjects With PUEAEs^	19 (13.4%)	9 (40.9%)	16 (32.0%)	5 (25.0%)	15 (30.0%)	45 (31.7%)
Number of Subjects Without PUEAEs^	123 (86.6%)	13 (59.1%)	34 (68.0%)	15 (75.0%)	35 (70.0%)	97 (68.3%)
Eye disorders	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Erythema of eyelid	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Eye pruritus	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lacrimation increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ocular hyperaemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gastrointestinal disorders	5 (3.5%)	2 (9.1%)	2 (4.0%)	0 (0.0%)	4 (8.0%)	8 (5.6%)
Abdominal discomfort	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Constipation	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)
Diarrhoea	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.0%)	2 (1.4%)
Dyspepsia	2 (1.4%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Gastrooesophageal reflux disease	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nausea	0 (0.0%)	1 (4.5%)	1 (2.0%)	0 (0.0%)	1 (2.0%)	3 (2.1%)
Oral discomfort	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)
Toothache	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)
Vomiting	1 (0.7%)	2 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.4%)
General disorders and administration site conditions	1 (0.7%)	0 (0.0%)	2 (4.0%)	0 (0.0%)	4 (8.0%)	6 (4.2%)
Chest discomfort	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)
Fatigue	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.0%)	2 (1.4%)
Pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)
Vessel puncture site pain	1 (0.7%)	0 (0.0%)	2 (4.0%)	0 (0.0%)	2 (4.0%)	4 (2.8%)

Note: * Adverse events are classified according to MedDRA Version 21.0. ^ = Product-use-emergent adverse events
 Subject used their usual brand at Baseline (Week -1).
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 # Overall includes AEs after the start of Week1 product use.

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Table 14.3.1.1 Product-Use-Emergent Adverse Event Frequency-
Number of Subjects Reporting the Event (% of Subjects (% of Subject Used Study Product) (Safety Population)

Adverse Event*	Study Product					Overall#
	Baseline	UB Non-Mentholated	VLN Non-Mentholated	UB Mentholated	VLN Mentholated	
Infections and infestations	0 (0.0%)	1 (4.5%)	2 (4.0%)	1 (5.0%)	0 (0.0%)	4 (2.8%)
Nasal abscess	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	1 (0.7%)
Tooth infection	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Upper respiratory tract infection	0 (0.0%)	1 (4.5%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	2 (1.4%)
Injury, poisoning and procedural complications	1 (0.7%)	1 (4.5%)	1 (2.0%)	1 (5.0%)	2 (4.0%)	5 (3.5%)
Arthropod bite	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.0%)	2 (1.4%)
Contusion	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Laceration	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Meniscus injury	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	1 (0.7%)
Subarachnoid haemorrhage	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Metabolism and nutrition disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)
Increased appetite	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)
Musculoskeletal and connective tissue disorders	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	2 (4.0%)	3 (2.1%)
Back pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)
Neck pain	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	2 (1.4%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Skin papilloma	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Nervous system disorders	13 (9.2%)	5 (22.7%)	10 (20.0%)	3 (15.0%)	6 (12.0%)	24 (16.9%)
Dizziness	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.0%)	2 (1.4%)
Headache	12 (8.5%)	5 (22.7%)	8 (16.0%)	3 (15.0%)	6 (12.0%)	22 (15.5%)
Lethargy	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)
Migraine	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Presyncope	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Tremor	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)

Note: * Adverse events are classified according to MedDRA Version 21.0. ^ = Product-use-emergent adverse events
Subject used their usual brand at Baseline (Week -1).
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Overall includes AEs after the start of Week1 product use.

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Table 14.3.1.1 Product-Use-Emergent Adverse Event Frequency-
 Number of Subjects Reporting the Event (% of Subjects (% of Subject Used Study Product) (Safety Population)

Adverse Event*	Study Product					Overall#
	Baseline	UB Non-Mentholated	VLN Non-Mentholated	UB Mentholated	VLN Mentholated	
Psychiatric disorders	0 (0.0%)	0 (0.0%)	3 (6.0%)	1 (5.0%)	5 (10.0%)	9 (6.3%)
Anxiety	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)
Depressed mood	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)
Insomnia	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.0%)	2 (1.4%)
Irritability	0 (0.0%)	0 (0.0%)	3 (6.0%)	0 (0.0%)	4 (8.0%)	7 (4.9%)
Nightmare	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)
Stress	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	1 (0.7%)
Respiratory, thoracic and mediastinal disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.0%)	2 (1.4%)
Oropharyngeal pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)
Throat irritation	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (0.7%)
Skin and subcutaneous tissue disorders	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.0%)	2 (1.4%)
Erythema	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Palmar erythema	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pruritus	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.0%)	2 (1.4%)
Vascular disorders	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Presyncope	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Note: * Adverse events are classified according to MedDRA Version 21.0. ^ = Product-use-emergent adverse events
 Subject used their usual brand at Baseline (Week -1).
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 # Overall includes AEs after the start of Week1 product use.

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Table 14.3.1.2 Product-Use-Emergent Adverse Event Frequency -
Number of Adverse Events (% of Total Adverse Events) (Safety Population)

Adverse Event*	Study Product					Overall#
	Baseline	UB Non-Mentholated	VLN Non-Mentholated	UB Mentholated	VLN Mentholated	
Number of PUEAEs	30 (100%)	13 (100%)	22 (100%)	6 (100%)	42 (100%)	83 (100%)
Eye disorders	4 (13.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Erythema of eyelid	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Eye pruritus	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lacrimation increased	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ocular hyperaemia	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gastrointestinal disorders	5 (16.7%)	4 (30.8%)	2 (9.1%)	0 (0.0%)	5 (11.9%)	11 (13.3%)
Abdominal discomfort	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Constipation	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	1 (1.2%)
Diarrhoea	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	1 (2.4%)	2 (2.4%)
Dyspepsia	2 (6.7%)	1 (7.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
Gastrooesophageal reflux disease	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nausea	0 (0.0%)	1 (7.7%)	1 (4.5%)	0 (0.0%)	1 (2.4%)	3 (3.6%)
Oral discomfort	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	1 (1.2%)
Toothache	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	1 (1.2%)
Vomiting	1 (3.3%)	2 (15.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.4%)
General disorders and administration site conditions	1 (3.3%)	0 (0.0%)	2 (9.1%)	0 (0.0%)	8 (19.0%)	10 (12.0%)
Chest discomfort	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.8%)	2 (2.4%)
Fatigue	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.8%)	2 (2.4%)
Pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	1 (1.2%)
Vessel puncture site pain	1 (3.3%)	0 (0.0%)	2 (9.1%)	0 (0.0%)	3 (7.1%)	5 (6.0%)
Infections and infestations	0 (0.0%)	1 (7.7%)	2 (9.1%)	1 (16.7%)	0 (0.0%)	4 (4.8%)
Nasal abscess	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	1 (1.2%)
Tooth infection	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
Upper respiratory tract infection	0 (0.0%)	1 (7.7%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	2 (2.4%)

Note: * Adverse events are classified according to MedDRA Version 21.0. ^ = Product-use-emergent adverse events
Subject used their usual brand at Baseline (Week -1).
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Overall includes AEs after the start of Week1 product use.

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Table 14.3.1.2 Product-Use-Emergent Adverse Event Frequency -
Number of Adverse Events (% of Total Adverse Events) (Safety Population)

Adverse Event*	Study Product					Overall#
	Baseline	UB Non-Mentholated	VLN Non-Mentholated	UB Mentholated	VLN Mentholated	
Injury, poisoning and procedural complications	1 (3.3%)	1 (7.7%)	1 (4.5%)	1 (16.7%)	2 (4.8%)	5 (6.0%)
Arthropod bite	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.8%)	2 (2.4%)
Contusion	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Laceration	0 (0.0%)	1 (7.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
Meniscus injury	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	1 (1.2%)
Subarachnoid haemorrhage	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
Metabolism and nutrition disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	1 (1.2%)
Increased appetite	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	1 (1.2%)
Musculoskeletal and connective tissue disorders	0 (0.0%)	1 (7.7%)	0 (0.0%)	0 (0.0%)	2 (4.8%)	3 (3.6%)
Back pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	1 (1.2%)
Neck pain	0 (0.0%)	1 (7.7%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	2 (2.4%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0 (0.0%)	1 (7.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
Skin papilloma	0 (0.0%)	1 (7.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
Nervous system disorders	13 (43.3%)	5 (38.5%)	11 (50.0%)	3 (50.0%)	10 (23.8%)	29 (34.9%)
Dizziness	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	1 (2.4%)	2 (2.4%)
Headache	12 (40.0%)	5 (38.5%)	9 (40.9%)	3 (50.0%)	7 (16.7%)	24 (28.9%)
Lethargy	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	1 (1.2%)
Migraine	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Presyncope	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
Tremor	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	1 (1.2%)
Psychiatric disorders	0 (0.0%)	0 (0.0%)	4 (18.2%)	1 (16.7%)	9 (21.4%)	14 (16.9%)
Anxiety	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.8%)	2 (2.4%)
Depressed mood	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	1 (1.2%)
Insomnia	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	1 (2.4%)	2 (2.4%)

Note: * Adverse events are classified according to MedDRA Version 21.0. ^ = Product-use-emergent adverse events
Subject used their usual brand at Baseline (Week -1).
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Overall includes AEs after the start of Week1 product use.

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Table 14.3.1.2 Product-Use-Emergent Adverse Event Frequency -
 Number of Adverse Events (% of Total Adverse Events) (Safety Population)

Adverse Event*	Study Product					Overall#
	Baseline	UB Non-Mentholated	VLN Non-Mentholated	UB Mentholated	VLN Mentholated	
Irritability	0 (0.0%)	0 (0.0%)	3 (13.6%)	0 (0.0%)	4 (9.5%)	7 (8.4%)
Nightmare	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	1 (1.2%)
Stress	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	1 (1.2%)
Respiratory, thoracic and mediastinal disorders	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.8%)	2 (2.4%)
Oropharyngeal pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	1 (1.2%)
Throat irritation	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	1 (1.2%)
Skin and subcutaneous tissue disorders	5 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (7.1%)	3 (3.6%)
Erythema	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Palmar erythema	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pruritus	3 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (7.1%)	3 (3.6%)
Vascular disorders	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Presyncope	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Note: * Adverse events are classified according to MedDRA Version 21.0. ^ = Product-use-emergent adverse events
 Subject used their usual brand at Baseline (Week -1).
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 # Overall includes AEs after the start of Week1 product use.

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Table 14.3.1.3 Product-Use-Emergent Adverse Event Frequency by Severity and Relationship to Study Product -
Number of Subjects Reporting Adverse Events (Safety Population)

Adverse Event*	Product	Number of Subjects with PUEAEs	Number of PUEAEs	Severity			Relationship to Study Product			
				Mild	Moderate	Severe	Not Related	Unlikely	Possible	Likely
Abdominal discomfort	Baseline	1	1	1	0	0	1	0	0	0
Anxiety	VLN Mentholated	1	2	1	0	0	0	0	1	0
Arthropod bite	VLN Mentholated	2	2	1	1	0	2	0	0	0
Back pain	VLN Mentholated	1	1	1	0	0	1	0	0	0
Chest discomfort	VLN Mentholated	1	2	1	0	0	0	0	1	0
Constipation	VLN Mentholated	1	1	1	0	0	0	0	1	0
Contusion	Baseline	1	1	1	0	0	1	0	0	0
Depressed mood	VLN Mentholated	1	1	1	0	0	0	0	1	0
Diarrhoea	VLN Mentholated	1	1	1	0	0	1	0	0	0
	VLN Non Mentholated	1	1	1	0	0	0	1	0	0
Dizziness	VLN Mentholated	1	1	1	0	0	1	0	0	0
	VLN Non Mentholated	1	1	1	0	0	1	0	0	0
Dyspepsia	Baseline	2	2	2	0	0	1	0	1	0
	UB Non Mentholated	1	1	1	0	0	1	0	0	0
Erythema	Baseline	1	1	1	0	0	1	0	0	0
Erythema of eyelid	Baseline	1	1	1	0	0	1	0	0	0
Eye pruritus	Baseline	1	1	1	0	0	1	0	0	0
Fatigue	VLN Mentholated	2	2	2	0	0	1	0	1	0
Gastrooesophageal reflux disease	Baseline	1	1	1	0	0	1	0	0	0
Headache	Baseline	12	12	12	0	0	7	4	1	0
	UB Mentholated	3	3	3	0	0	3	0	0	0
	UB Non Mentholated	5	5	4	1	0	4	1	0	0
	VLN Mentholated	6	7	4	2	0	2	2	2	0

Note: * Adverse events are classified according to MedDRA Version 21.0.
When a subject experienced the same AE at more than one level of severity, only the most severe occurrence was counted.
When a subject experienced the same AE at more than one level of product relationship, only the the most closely related to study product was counted.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.1.3 Product-Use-Emergent Adverse Event Frequency by Severity and Relationship to Study Product -
Number of Subjects Reporting Adverse Events (Safety Population)

Adverse Event*	Product	Number of Subjects with PUEAEs	Number of PUEAEs	Severity			Relationship to Study Product			
				Mild	Moderate	Severe	Not Related	Unlikely	Possible	Likely
Headache	VLN Non Mentholated	8	9	6	2	0	2	3	3	0
Increased appetite	VLN Mentholated	1	1	1	0	0	0	0	1	0
Insomnia	VLN Mentholated	1	1	1	0	0	0	0	1	0
Irritability	VLN Non Mentholated	1	1	1	0	0	0	0	1	0
	VLN Mentholated	4	4	4	0	0	0	0	4	0
	VLN Non Mentholated	3	3	3	0	0	1	0	2	0
Laceration	UB Non Mentholated	1	1	1	0	0	1	0	0	0
Lacrimation increased	Baseline	1	1	1	0	0	1	0	0	0
Lethargy	VLN Mentholated	1	1	1	0	0	0	0	1	0
Meniscus injury	UB Mentholated	1	1	0	1	0	1	0	0	0
Migraine	Baseline	1	1	0	1	0	1	0	0	0
Nasal abscess	UB Mentholated	1	1	0	1	0	1	0	0	0
Nausea	UB Non Mentholated	1	1	1	0	0	1	0	0	0
	VLN Mentholated	1	1	1	0	0	0	0	1	0
	VLN Non Mentholated	1	1	1	0	0	0	0	0	1
Neck pain	UB Non Mentholated	1	1	1	0	0	1	0	0	0
	VLN Mentholated	1	1	1	0	0	1	0	0	0
Nightmare	VLN Mentholated	1	1	1	0	0	0	0	1	0
Ocular hyperaemia	Baseline	1	1	1	0	0	1	0	0	0
Oral discomfort	VLN Mentholated	1	1	1	0	0	0	0	1	0
Oropharyngeal pain	VLN Mentholated	1	1	1	0	0	1	0	0	0
Pain	VLN Mentholated	1	1	1	0	0	0	0	1	0
Palmar erythema	Baseline	1	1	1	0	0	1	0	0	0
Presyncope	Baseline	1	1	0	1	0	1	0	0	0

Note: * Adverse events are classified according to MedDRA Version 21.0.

When a subject experienced the same AE at more than one level of severity, only the most severe occurrence was counted.

When a subject experienced the same AE at more than one level of product relationship, only the the most closely related to study product was counted.

VLN non-mentholated = Non-mentholated VLN cigarettes

VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.1.3 Product-Use-Emergent Adverse Event Frequency by Severity and Relationship to Study Product -
Number of Subjects Reporting Adverse Events (Safety Population)

Adverse Event*	Product	Number of Subjects with PUEAEs	Number of PUEAEs	Severity			Relationship to Study Product			
				Mild	Moderate	Severe	Not Related	Unlikely	Possible	Likely
Presyncope	VLN Non Mentholated	1	1	1	0	0	1	0	0	0
Pruritus	Baseline	1	3	1	0	0	1	0	0	0
	VLN Mentholated	2	3	2	0	0	1	1	0	0
Skin papilloma	UB Non Mentholated	1	1	0	1	0	1	0	0	0
Stress	UB Mentholated	1	1	1	0	0	1	0	0	0
Subarachnoid haemorrhage	VLN Non Mentholated	1	1	0	0	1	1	0	0	0
Throat irritation	VLN Mentholated	1	1	1	0	0	0	0	1	0
Tooth infection	VLN Non Mentholated	1	1	0	1	0	1	0	0	0
Toothache	VLN Mentholated	1	1	1	0	0	1	0	0	0
Tremor	VLN Mentholated	1	1	1	0	0	0	0	1	0
Upper respiratory tract infection	UB Non Mentholated	1	1	1	0	0	1	0	0	0
	VLN Non Mentholated	1	1	1	0	0	1	0	0	0
Vessel puncture site pain	Baseline	1	1	1	0	0	1	0	0	0
	VLN Mentholated	2	3	2	0	0	2	0	0	0
	VLN Non Mentholated	2	2	2	0	0	2	0	0	0
Vomiting	Baseline	1	1	0	1	0	1	0	0	0
	UB Non Mentholated	2	2	2	0	0	2	0	0	0
Baseline		19	30	16	3	0	14	4	1	0
UB Mentholated		5	6	3	2	0	5	0	0	0
UB Non Mentholated		9	13	7	2	0	8	1	0	0
VLN Mentholated		15	42	12	3	0	7	1	7	0
VLN Non Mentholated		16	22	13	2	1	6	4	5	1

Note: * Adverse events are classified according to MedDRA Version 21.0.

When a subject experienced the same AE at more than one level of severity, only the most severe occurrence was counted.

When a subject experienced the same AE at more than one level of product relationship, only the the most closely related to study product was counted.

VLN non-mentholated = Non-mentholated VLN cigarettes

VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.1.3 Product-Use-Emergent Adverse Event Frequency by Severity and Relationship to Study Product -
 Number of Subjects Reporting Adverse Events (Safety Population)

Adverse Event*	Product	Number of Subjects with PUEAEs	Number of PUEAEs	Severity			Relationship to Study Product			
				Mild	Moderate	Severe	Not Related	Unlikely	Possible	Likely
Overall		45	83	35	9	1	26	6	12	1

Note: * Adverse events are classified according to MedDRA Version 21.0.
 When a subject experienced the same AE at more than one level of severity, only the most severe occurrence was counted.
 When a subject experienced the same AE at more than one level of product relationship, only the the most closely related to study product was counted.
 VLN non-mentholated = Non-mentholated VLN cigarettes
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14.3.2 Listings of Deaths, Other Serious and Significant Adverse Events

Table 14.3.2.1 Serious Adverse Events

Table 14.3.2.1 Serious Adverse Events

Subject Number	Study Product	System Organ Class >Preferred Term* UE?^ >>Adverse Event	Time From start of Product Use ----- (DD:HH:MM)	Onset Date/ Resolved Date	Freq#	Severity	Serious	Outcome	Relationship to Study Product	Action
1023	B	Yes Injury, poisoning and procedural complications >Subarachnoid haemorrhage >>SUBARACHNOID HEMORRHAGE	44:00:00	15SEP2018/ 02OCT2018	Cont.	Severe	Yes	Resolved	Not Related	Dose Not Changed

Note: Product A = Product H6 unbranded combustible menthol cigarette (Test Cigarette)
 Product B = Product N7 unbranded combustible menthol cigarette (Reference Cigarette)

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14.3.3 Narratives of Deaths, Other Serious and Certain Other Significant Adverse Events

The narratives can be found in [Sections 12.2.2](#) and [12.2.3](#).

14.3.4 Abnormal Laboratory Value Listing (Each Subject)

Table 14.3.4.1.1	Out-of-Range Values and Recheck Results - Serum Chemistry (I of IV) (Safety Population)
Table 14.3.4.1.2	Out-of-Range Values and Recheck Results - Serum Chemistry (II of IV) (Safety Population)
Table 14.3.4.1.3	Out-of-Range Values and Recheck Results - Serum Chemistry (III of IV) (Safety Population)
Table 14.3.4.1.4	Out-of-Range Values and Recheck Results - Serum Chemistry (IV of IV) (Safety Population)
Table 14.3.4.2.1	Out-of-Range Values and Recheck Results - Hematology (I of IV) (Safety Population)
Table 14.3.4.2.2	Out-of-Range Values and Recheck Results - Hematology (II of IV) (Safety Population)
Table 14.3.4.2.3	Out-of-Range Values and Recheck Results - Hematology (III of IV) (Safety Population)
Table 14.3.4.2.4	Out-of-Range Values and Recheck Results - Hematology (IV of IV) (Safety Population)
Table 14.3.4.3.1	Out-of-Range Values and Recheck Results - Urinalysis (I of VI) (Safety Population)
Table 14.3.4.3.2	Out-of-Range Values and Recheck Results - Urinalysis (II of VI) (Safety Population)
Table 14.3.4.3.3	Out-of-Range Values and Recheck Results - Urinalysis (III of VI) (Safety Population)
Table 14.3.4.3.4	Out-of-Range Values and Recheck Results - Urinalysis (IV of VI) (Safety Population)
Table 14.3.4.3.5	Out-of-Range Values and Recheck Results - Urinalysis (V of VI) (Safety Population)
Table 14.3.4.3.6	Out-of-Range Values and Recheck Results - Urinalysis (VI of VI) (Safety Population)
Table 14.3.4.4	Clinically Significant Values and Recheck Results (Safety Population)

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Table 14.3.4.1.1 Out-of-Range Values and Recheck Results - Serum Chemistry (I of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Carbon Dioxide 001: 24-33.2 002: 20-29 (mmol/L)	Potassium 001: 3.7-5.2 002: 3.5-5.2 (mmol/L)	Albumin 001: 39-50 002: 35-55 002: 36-48 (g/L)	Creatinine	
		Name	Date					001: F: 44.209-79.576 002: F: 50.398-88.417 001: M: 61.008-106.101 002: M: 67.197-112.29 (umol/L)	
1010	32/M	End Of Study	06SEP2018	UB Mentholated			52 HN		
1011	36/M	End Of Study	06SEP2018	UB Non Mentholated			52 HN		
1014	36/F	End Of Study	14SEP2018	VLN Mentholated	23.5 LN				
1016	54/M	End Of Study	13SEP2018	UB Non Mentholated				56.587 LN	
1018	41/F	Screening	17JUL2018					85.765 HN	
		End Of Study	15AUG2018	VLN Mentholated				87.533 HN	
1021	49/F	End Of Study	13SEP2018	UB Non Mentholated	23 LN				
1029	35/F	End Of Study	11OCT2018	VLN Mentholated	23.3 LN				
1032	53/F	End Of Study	11OCT2018	VLN Mentholated				43.324 LN	
1034	45/M	Screening	13AUG2018					55.703 LN	
		End Of Study	10OCT2018	VLN Non Mentholated				57.471 LN	
1035	44/M	Screening	13AUG2018					110.522 HN	
1045	58/M	Screening	14AUG2018			5.7 HN			

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 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.1.1 Out-of-Range Values and Recheck Results - Serum Chemistry (I of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Carbon Dioxide 001: 24-33.2 002: 20-29 (mmol/L)	Potassium 001: 3.7-5.2 002: 3.5-5.2 (mmol/L)	Albumin 001: 39-50 002: 35-55 002: 36-48 (g/L)	Creatinine	
		Name	Date					001: F: 44.209-79.576 002: F: 50.398-88.417 001: M: 61.008-106.101 002: M: 67.197-112.29 (umol/L)	
1051	36/F	Screening	14AUG2018		23.2 LN				
		End Of Study	10OCT2018	UB Mentholated	23.2 LN				
1055	39/F	End Of Study	11OCT2018	VLN Mentholated				42.44	LN
1077	49/F	Screening	28AUG2018			5.3 HN			
1079	33/M	End Of Study	24OCT2018	VLN Mentholated			38 LN		
1083	54/F	Screening	04SEP2018			5.3 HN			
1089	60/F	End Of Study	31OCT2018	UB Non Mentholated				80.46	HN
1092	43/F	End Of Study	31OCT2018	VLN Mentholated	23 LN				
1095	55/F	End Of Study	31OCT2018	VLN Mentholated				86.649	HN
1097	30/M	End Of Study	31OCT2018	VLN Mentholated				53.935	LN
1098	63/M	End Of Study	16NOV2018	VLN Non Mentholated		5.5 HN			
1099	46/F	End Of Study	16NOV2018	VLN Non Mentholated			38 LN		

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 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.1.1 Out-of-Range Values and Recheck Results - Serum Chemistry (I of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Carbon Dioxide 001: 24-33.2 002: 20-29 (mmol/L)	Potassium 001: 3.7-5.2 002: 3.5-5.2 (mmol/L)	Albumin 001: 39-50 002: 35-55 002: 36-48 (g/L)	Creatinine 001: F: 44.209-79.576 002: F: 50.398-88.417 001: M: 61.008-106.101 002: M: 67.197-112.29 (umol/L)
		Name	Date					
1109	58/M	Screening	21SEP2018		21.2 LN			
		End Of Study	16NOV2018	UB Non Mentholated	23.5 LN			
2002	49/M	Screening	29JUN2018			5.4 HN		
		End Of Study	05SEP2018	UB Mentholated		5.3 HN		
2007	57/F	Screening	29JUN2018			5.5 HN		
2025	59/M	Screening	03JUL2018					60.124 LN
2028	36/M	End Of Study	29AUG2018	VLN Non Mentholated		5.5 HN		
2052	54/M	End Of Study	20SEP2018	VLN Mentholated		5.3 HN		
2057	52/M	Screening	23JUL2018		32 HN			
2067	52/M	Screening	23JUL2018		30 HN	6 HN		
		End Of Study	20SEP2018	VLN Non Mentholated	31 HN			
2076	42/M	End Of Study	14OCT2018	VLN Mentholated				116.711 HN
2092	50/F	Screening	06AUG2018			5.5 HN		

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 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.1.1 Out-of-Range Values and Recheck Results - Serum Chemistry (I of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Carbon Dioxide 001: 24-33.2 002: 20-29 (mmol/L)	Potassium 001: 3.7-5.2 002: 3.5-5.2 (mmol/L)	Albumin 001: 39-50 002: 35-55 002: 36-48 (g/L)	Creatinine	
		Name	Date					001: F: 44.209-79.576 002: F: 50.398-88.417 001: M: 61.008-106.101 002: M: 67.197-112.29 (umol/L)	
2099	52/M	End Of Study	14OCT2018	VLN Non Mentholated				66.313	LN
2108	60/F	Screening	13AUG2018					48.63	LN
2119	48/M	Screening	20AUG2018			5.3	HN		
2140	56/F	End Of Study	06NOV2018	UB Non Mentholated	30	HN			
2142	30/F	End Of Study	08OCT2018	VLN Non Mentholated	19	LN			
2159	37/M	End Of Study	02DEC2018	VLN Non Mentholated			34	LN	
2170	51/F	Screening	28SEP2018			5.8	HN	92.838	HN
2175	40/F	Screening	01OCT2018			5.3	HN		
2211	29/F	End Of Study	02DEC2018	VLN Mentholated			34	LN	
2235	26/F	End Of Study	16DEC2018	VLN Mentholated	19	LN			

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 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.1.2 Out-of-Range Values and Recheck Results - Serum Chemistry (II of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Glucose 001: 4.1-5.8 002: 3.6-5.5 (mmol/L)	Alkaline Phosphatase 001: F: 37-115 001: M: 45-120 002: 39-117 (IU/L)	Alanine Amino- transferase 001: 10-67 002: F: 0-32 002: M: 0-44 (IU/L)	Aspartate Amino- transferase 001: 14-48 002: 0-40 (IU/L)
		Name	Date					
1001	59/F	Screening	02JUL2018	VLN Non Mentholated		141 HN		
		End Of Study	07SEP2018			130 HN		
1008	48/M	Screening	12JUL2018	VLN Mentholated	6.4 HN			
		End Of Study	07SEP2018		6 HN			
1013	36/F	End Of Study	14SEP2018	VLN Non Mentholated			8 LN	13 LN
1014	36/F	Screening	16JUL2018			126 HN		
1020	36/F	Screening	17JUL2018					13 LN
1021	49/F	End Of Study	13SEP2018	UB Non Mentholated				10 LN
1023	50/F	End Of Study	14SEP2018	VLN Non Mentholated	6 HN			
1034	45/M	Screening	13AUG2018		6.5 HN			
1038	39/F	Screening	13AUG2018					13 LN
1045	58/M	Screening	14AUG2018	UB Non Mentholated		145 HN		
		End Of Study	10OCT2018			121 HN		

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 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.1.2 Out-of-Range Values and Recheck Results - Serum Chemistry (II of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Glucose 001: 4.1-5.8 002: 3.6-5.5 (mmol/L)	Alkaline Phosphatase 001: F: 37-115 001: M: 45-120 002: 39-117 (IU/L)	Alanine Amino- transferase 001: 10-67 002: F: 0-32 002: M: 0-44 (IU/L)	Aspartate Amino- transferase 001: 14-48 002: 0-40 (IU/L)
		Name	Date					
1046	45/M	Screening	14AUG2018		5.9 HN			
1052	31/M	Screening	14AUG2018				7 LN	10 LN
		End Of Study	11OCT2018	VLN Mentholated			8 LN	11 LN
1055	39/F	Screening	14AUG2018					12 LN
		End Of Study	11OCT2018	VLN Mentholated				11 LN
1060	55/M	Screening	27AUG2018					13 LN
		End Of Study	24OCT2018	VLN Mentholated				13 LN
1069	40/F	End Of Study	24OCT2018	UB Non Mentholated				13 LN
1070	53/M	Screening	28AUG2018		6 HN			
		End Of Study	24OCT2018	VLN Non Mentholated	6.1 HN			
1071	42/M	Screening	28AUG2018		6 HN			
1075	26/F	End Of Study	24OCT2018	UB Non Mentholated				13 LN
1083	54/F	End Of Study	31OCT2018	VLN Non Mentholated				13 LN

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 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.1.2 Out-of-Range Values and Recheck Results - Serum Chemistry (II of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Glucose 001: 4.1-5.8 002: 3.6-5.5 (mmol/L)	Alkaline Phosphatase 001: F: 37-115 001: M: 45-120 002: 39-117 (IU/L)	Alanine Amino- transferase 001: 10-67 002: F: 0-32 002: M: 0-44 (IU/L)	Aspartate Amino- transferase 001: 14-48 002: 0-40 (IU/L)
		Name	Date					
1089	60/F	Screening	04SEP2018				9 LN	
1094	46/M	Screening	05SEP2018				8 LN	12 LN
		End Of Study	31OCT2018	VLN Mentholated			8 LN	
1095	55/F	Screening	07SEP2018		6.2 HN			
		End Of Study	31OCT2018	VLN Mentholated			9 LN	11 LN
1098	63/M	End Of Study	16NOV2018	VLN Non Mentholated				13 LN
1099	46/F	Screening	18SEP2018		5.9 HN			
		End Of Study	16NOV2018	VLN Non Mentholated	6.2 HN			13 LN
1101	41/M	Screening	18SEP2018				78 HN	64 HN
		End Of Study	16NOV2018	VLN Non Mentholated			90 HN	75 HN
1105	47/F	Screening	19SEP2018				0 LN	13 LN
1112	59/F	Screening	21SEP2018			130 HN		
		End Of Study	16NOV2018	VLN Non Mentholated		128 HN		
1114	26/F	Screening	24SEP2018			132 HN		

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 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.1.2 Out-of-Range Values and Recheck Results - Serum Chemistry (II of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Glucose 001: 4.1-5.8 002: 3.6-5.5 (mmol/L)	Alkaline Phosphatase 001: F: 37-115 001: M: 45-120 002: 39-117 (IU/L)	Alanine Amino- transferase 001: 10-67 002: F: 0-32 002: M: 0-44 (IU/L)	Aspartate Amino- transferase 001: 14-48 002: 0-40 (IU/L)
		Name	Date					
1114	26/F	End Of Study	16NOV2018	UB Non Mentholated		120 HN		
2002	49/M	Screening	29JUN2018		5.8 HN			
2008	42/M	End Of Study	29AUG2018	VLN Mentholated	3.5 LN			
2014	37/M	Screening	02JUL2018		5.6 HN			
2021	31/M	Screening	02JUL2018					53 HN
		End Of Study	29AUG2018	VLN Mentholated				42 HN
2023	35/M	Screening	02JUL2018				50 HN	
2024	26/M	Screening	03JUL2018				51 HN	169 HN
2025	59/M	End Of Study	29AUG2018	UB Non Mentholated	5.7 HN			
2028	36/M	End Of Study	29AUG2018	VLN Non Mentholated	5.6 HN			
2029	56/M	End Of Study	05SEP2018	UB Mentholated	5.8 HN			
2050	57/M	Screening	20JUL2018		6.2 HN			

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 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.1.2 Out-of-Range Values and Recheck Results - Serum Chemistry (II of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Glucose 001: 4.1-5.8 002: 3.6-5.5 (mmol/L)	Alkaline Phosphatase 001: F: 37-115 001: M: 45-120 002: 39-117 (IU/L)	Alanine Amino- transferase 001: 10-67 002: F: 0-32 002: M: 0-44 (IU/L)	Aspartate Amino- transferase 001: 14-48 002: 0-40 (IU/L)
		Name	Date					
2050	57/M	End Of Study	20SEP2018	UB Mentholated	7.7 HN			
2052	54/M	Screening	20JUL2018		5.8 HN			
		End Of Study	20SEP2018	VLN Mentholated	6 HN			
2057	52/M	Screening	23JUL2018		5.9 HN			
		End Of Study	20SEP2018	VLN Mentholated	5.7 HN			
2075	34/M	Screening	30JUL2018				91 HN	71 HN
		End Of Study	22AUG2018	VLN Mentholated			80 HN	63 HN
2076	42/M	Screening	30JUL2018		5.6 HN			
2108	60/F	Screening	13AUG2018		5.8 HN			
		End Of Study	14OCT2018	VLN Non Mentholated	5.6 HN			
2120	62/F	Screening	20AUG2018		6 HN			
		End Of Study	20OCT2018	VLN Non Mentholated	7.4 HN			
2125	35/M	End Of Study	20OCT2018	UB Mentholated		37 LN		
2136	64/M	Screening	27AUG2018		5.7 HN			

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 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
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Table 14.3.4.1.2 Out-of-Range Values and Recheck Results - Serum Chemistry (II of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Glucose 001: 4.1-5.8 002: 3.6-5.5 (mmol/L)	Alkaline Phosphatase 001: F: 37-115 001: M: 45-120 002: 39-117 (IU/L)	Alanine Amino- transferase 001: 10-67 002: F: 0-32 002: M: 0-44 (IU/L)	Aspartate Amino- transferase 001: 14-48 002: 0-40 (IU/L)
		Name	Date					
2142	30/F	Screening	31AUG2018				37	HN
2244	31/M	End Of Study	16DEC2018	VLN Non Mentholated	5.7	HN		

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 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.1.3 Out-of-Range Values and Recheck Results - Serum Chemistry (III of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Protein 001: 6.3-8.1 002: 6-8.5 (g/dL)	Sodium 001: 135-143 002: 134-144 (mmol/L)	Bilirubin 001: 0.2-1.6 002: 0-1.2 (mg/dL)	Urate	
		Name	Date					001: F: 2.3-5.9 002: F: 2.5-7.1 001: M: 3.5-7.8 002: M: 3.7-8.6 (mg/dL)	
1001	59/F	Screening	02JUL2018			144 HN			
		End Of Study	07SEP2018	VLN Non Mentholated			0 LN		
1002	30/M	Screening	02JUL2018			144 HN			
1003	38/M	End Of Study	07SEP2018	VLN Mentholated			0 LN		
1007	37/M	End Of Study	07SEP2018	VLN Non Mentholated			0 LN		
1011	36/M	Screening	13JUL2018					8.3 HN	
1013	36/F	End Of Study	14SEP2018	VLN Non Mentholated			0 LN		
1015	49/F	End Of Study	14SEP2018	VLN Mentholated			0 LN		
1020	36/F	Screening	17JUL2018					7.9 HN	
		End Of Study	14SEP2018	VLN Non Mentholated			0 LN	6.6 HN	
1029	35/F	End Of Study	11OCT2018	VLN Mentholated		134 LN	0 LN		
1032	53/F	End Of Study	11OCT2018	VLN Mentholated			0 LN		
1036	38/F	End Of Study	10OCT2018	UB Mentholated			0 LN		

Note: \$Age is derived from birth date to date of informed consent
 001 = Lincoln, 002 = High Point, F = Female, M = Male
 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.1.3 Out-of-Range Values and Recheck Results - Serum Chemistry (III of IV) (Safety Population)

Subject Number	Age\$/Sex	Visit		Product Group	Protein	Sodium	Bilirubin	Urate
		Name	Date		001: 6.3-8.1 002: 6-8.5 (g/dL)	001: 135-143 002: 134-144 (mmol/L)	001: 0.2-1.6 002: 0-1.2 (mg/dL)	001: F: 2.3-5.9 002: F: 2.5-7.1 001: M: 3.5-7.8 002: M: 3.7-8.6 (mg/dL)
1050	33/F	End Of Study	10OCT2018	VLN Non Mentholated	6.2 LN		0 LN	
1055	39/F	End Of Study	11OCT2018	VLN Mentholated			0 LN	
1069	40/F	End Of Study	24OCT2018	UB Non Mentholated			0 LN	
1077	49/F	End Of Study	24OCT2018	VLN Non Mentholated			0 LN	
1079	33/M	End Of Study	24OCT2018	VLN Mentholated	5.7 LN			
1083	54/F	Screening End Of Study	04SEP2018 31OCT2018	VLN Non Mentholated		144 HN	0 LN	
1089	60/F	Screening	04SEP2018			144 HN		
1094	46/M	Screening	05SEP2018			145 HN		
1095	55/F	Screening	07SEP2018					7 HN
1096	42/F	End Of Study	31OCT2018	VLN Non Mentholated			0 LN	
1097	30/M	End Of Study	31OCT2018	VLN Mentholated			0 LN	2.6 LN

Note: \$Age is derived from birth date to date of informed consent
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 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.1.3 Out-of-Range Values and Recheck Results - Serum Chemistry (III of IV) (Safety Population)

Subject Number	Age\$/Sex	Visit		Product Group	Protein 001: 6.3-8.1 002: 6-8.5 (g/dL)	Sodium 001: 135-143 002: 134-144 (mmol/L)	Bilirubin 001: 0.2-1.6 002: 0-1.2 (mg/dL)	Urate	
		Name	Date					001: F: 2.3-5.9 002: F: 2.5-7.1 001: M: 3.5-7.8 002: M: 3.7-8.6 (mg/dL)	
1099	46/F	Screening	18SEP2018						
		End Of Study	16NOV2018	VLN Non Mentholated			0 LN		6.2 HN
1109	58/M	End Of Study	16NOV2018	UB Non Mentholated		144 HN			
1112	59/F	End Of Study	16NOV2018	VLN Non Mentholated			0 LN		
1115	29/M	Screening	24SEP2018		8.2 HN				
2011	32/F	End Of Study	29AUG2018	VLN Mentholated	5.9 LN				
2015	57/F	End Of Study	29AUG2018	UB Mentholated	5.9 LN				
2020	60/F	Screening	02JUL2018			149 HN			
2076	42/M	Screening	30JUL2018			146 HN			
2092	50/F	Screening	06AUG2018			147 HN			
2110	41/F	Screening	13AUG2018						8.3 HN
		End Of Study	20OCT2018	UB Mentholated					8 HN
2122	60/M	Screening	20AUG2018						3.6 LN

Note: \$Age is derived from birth date to date of informed consent
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 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
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Table 14.3.4.1.3 Out-of-Range Values and Recheck Results - Serum Chemistry (III of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Protein 001: 6.3-8.1 002: 6-8.5 (g/dL)	Sodium 001: 135-143 002: 134-144 (mmol/L)	Bilirubin 001: 0.2-1.6 002: 0-1.2 (mg/dL)	Urate 001: F: 2.3-5.9 002: F: 2.5-7.1 001: M: 3.5-7.8 002: M: 3.7-8.6 (mg/dL)
		Name	Date					
2140	56/F	Screening	30AUG2018			146 HN		
2142	30/F	End Of Study	08OCT2018	VLN Non Mentholated		128 LN		
2159	37/M	End Of Study	02DEC2018	VLN Non Mentholated	5.1 LN			
2168	32/F	End Of Study	02DEC2018	VLN Non Mentholated	5.8 LN			
2175	40/F	End Of Study	02DEC2018	UB Mentholated	5.9 LN			
2211	29/F	End Of Study	02DEC2018	VLN Mentholated	5.6 LN			
2259	49/M	End Of Study	19JAN2019	UB Mentholated	5.6 LN			

Note: \$Age is derived from birth date to date of informed consent
 001 = Lincoln, 002 = High Point, F = Female, M = Male
 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.1.4 Out-of-Range Values and Recheck Results - Serum Chemistry (IV of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Urea Nitrogen 001: F: 6-17 001: M: 7-20 002: 6-20 002: 6-24 002: 8-27 (mg/dL)
		Name	Date		
1002	30/M	Screening	02JUL2018		4 LN
1034	45/M	Screening	13AUG2018		6 LN
1042	47/M	Screening	13AUG2018		21 HN
1055	39/F	Screening	14AUG2018		5 LN
1100	59/M	End Of Study	16NOV2018	VLN Non Mentholated	22 HN
1105	47/F	End Of Study	16NOV2018	VLN Non Mentholated	18 HN
1109	58/M	End Of Study	16NOV2018	UB Non Mentholated	21 HN
2067	52/M	Screening	23JUL2018		5 LN
2108	60/F	Screening	13AUG2018		7 LN
2142	30/F	Screening	31AUG2018		4 LN
		End Of Study	08OCT2018	VLN Non Mentholated	4 LN
2159	37/M	Screening	19SEP2018		5 LN

Note: \$Age is derived from birth date to date of informed consent
 001 = Lincoln, 002 = High Point, F = Female, M = Male
 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.1.4 Out-of-Range Values and Recheck Results - Serum Chemistry (IV of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Urea Nitrogen (mg/dL)
		Name	Date		
2168	32/F	Screening	28SEP2018		4 LN
		End Of Study	02DEC2018	VLN Non Mentholated	5 LN

Note: \$Age is derived from birth date to date of informed consent
 001 = Lincoln, 002 = High Point, F = Female, M = Male
 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.2.1 Out-of-Range Values and Recheck Results - Hematology (I of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit ----- Name	Product Group	Hemoglobin		Hematocrit		Platelet Count	Red Blood Cell Count	
				001: F: 120-159	002: F: 111-159	001: F: 3.53-4.7	002: F: 3.4-4.66		001: F: 3.95-5.21	002: F: 3.77-5.28
		Date		001: M: 136-174	002: M: 130-177	001: M: 4.06-5.23	002: M: 3.75-5.1	001: 155-361	001: M: 4.43-5.81	002: M: 4.14-5.8
				(g/L)		(v/v)		(thou/uL)	(mil/uL)	
1001	59/F	Screening 02JUL2018								
		End Of Study 07SEP2018	VLN Non Mentholated					490 HN		
								507 HN		
1008	48/M	End Of Study 07SEP2018	VLN Mentholated							4.34 LN
1013	36/F	End Of Study 14SEP2018	VLN Non Mentholated		114 LN					
1014	36/F	End Of Study 14SEP2018	VLN Mentholated		118 LN					3.53 LN
1018	41/F	End Of Study 15AUG2018	VLN Mentholated				4.81 HN			
1020	36/F	End Of Study 14SEP2018	VLN Non Mentholated		118 LN					
1032	53/F	Screening 13AUG2018								
		End Of Study 11OCT2018	VLN Mentholated					105 LN		
								127 LN		
1034	45/M	Screening 13AUG2018								4.27 LN
		End Of Study 10OCT2018	VLN Non Mentholated							4.06 LN
1035	44/M	Screening 13AUG2018		188 HN			5.39 HN			
1052	31/M	End Of Study 11OCT2018	VLN Mentholated		135 LN					

Note: \$Age is derived from birth date to date of informed consent
 001 = Lincoln, 002 = High Point, F = Female, M = Male
 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.2.1 Out-of-Range Values and Recheck Results - Hematology (I of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Hemoglobin	Hematocrit	Platelet	Red Blood Cell Count
		Name	Date		001: F: 120-159 002: F: 111-159 001: M: 136-174 002: M: 130-177 (g/L)	001: F: 3.53-4.7 002: F: 3.4-4.66 001: M: 4.06-5.23 002: M: 3.75-5.1 (v/v)	Count 001: 155-361 002: 150-379 (thou/uL)	001: F: 3.95-5.21 002: F: 3.77-5.28 001: M: 4.43-5.81 002: M: 4.14-5.8 (mil/uL)
1053	42/M	Screening	14AUG2018		135 LN	3.96 LN		4.28 LN
		End Of Study	11OCT2018	VLN Mentholated		4.02 LN		4.35 LN
1060	55/M	Screening	27AUG2018		132 LN			
		End Of Study	24OCT2018	VLN Mentholated	124 LN	4.02 LN		
1066	62/M	End Of Study	24OCT2018	VLN Non Mentholated	132 LN			
1075	26/F	Screening	29AUG2018				138 LN	
		End Of Study	24OCT2018	UB Non Mentholated			139 LN	
1083	54/F	Screening	04SEP2018			4.77 HN		
1089	60/F	Screening	04SEP2018					5.31 HN
1101	41/M	Screening	18SEP2018				148 LN	
2075	34/M	Screening	30JUL2018					4.08 LN
		End Of Study	22AUG2018	VLN Mentholated	118 LN	3.61 LN		3.58 LN
2092	50/F	Screening	06AUG2018				391 HN	

Note: \$Age is derived from birth date to date of informed consent
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 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.2.1 Out-of-Range Values and Recheck Results - Hematology (I of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Hemoglobin		Hematocrit		Platelet Count	Red Blood Cell Count	
		Name	Date		001: F: 120-159 002: F: 111-159 001: M: 136-174 002: M: 130-177 (g/L)		001: F: 3.53-4.7 002: F: 3.4-4.66 001: M: 4.06-5.23 002: M: 3.75-5.1 (v/v)		001: 155-361 002: 150-379 (thou/uL)	001: F: 3.95-5.21 002: F: 3.77-5.28 001: M: 4.43-5.81 002: M: 4.14-5.8 (mil/uL)	
2125	35/M	Screening	21AUG2018	UB Mentholated					121 LN		
		End Of Study	20OCT2018						131 LN		
2126	37/M	End Of Study	20OCT2018	VLN Mentholated					406 HN		
2136	64/M	End Of Study	19OCT2018	VLN Non Mentholated							4.13 LN
2142	30/F	Screening	31AUG2018		167 HN		4.72 HN				
2143	63/M	End Of Study	06NOV2018	VLN Non Mentholated					133 LN		
2159	37/M	Unscheduled	04OCT2018		147		4.3		283		4.68

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 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.2.2 Out-of-Range Values and Recheck Results - Hematology (II of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	White Blood Cell Count	Basophils	Absolute Basophils	Absolute Eosinophils
		----- Name	----- Date		001: 3.7-11.5 002: 3.4-10.8 (thou/uL)	001: 0-2 002: Not Estab. (%)	001: 0-0.1 002: 0-0.2 (thou/uL)	001: 0-0.5 002: 0-0.4 (thou/uL)
1001	59/F	End Of Study	07SEP2018	VLN Non Mentholated	12.2 HN			
1003	38/M	End Of Study	07SEP2018	VLN Mentholated				0.8 HN
1008	48/M	Unscheduled	16JUL2018		7	0.3	0	0.1
1014	36/F	Unscheduled	23JUL2018		9.6			
1034	45/M	Screening	13AUG2018					0.7 HN
		End Of Study	10OCT2018	VLN Non Mentholated				0.8 HN
1051	36/F	Screening	14AUG2018		12.8 HN			
		End Of Study	10OCT2018	UB Mentholated	12.5 HN			
1066	62/M	End Of Study	24OCT2018	VLN Non Mentholated	3.6 LN			
1069	40/F	Screening	28AUG2018		11.9 HN			
		End Of Study	24OCT2018	UB Non Mentholated	13 HR			
1079	33/M	End Of Study	24OCT2018	VLN Mentholated				1.1 HN
1099	46/F	Screening	18SEP2018					0.7 HN

Note: \$Age is derived from birth date to date of informed consent
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 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.2.2 Out-of-Range Values and Recheck Results - Hematology (II of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	White Blood Cell Count	Basophils	Absolute Basophils	Absolute Eosinophils
		----- Name	Date		001: 3.7-11.5 002: 3.4-10.8 (thou/uL)	001: 0-2 002: Not Estab. (%)	001: 0-0.1 002: 0-0.2 (thou/uL)	001: 0-0.5 002: 0-0.4 (thou/uL)
1105	47/F	Screening	19SEP2018		13.1 HN			
1107	45/M	Unscheduled End Of Study	25SEP2018 16NOV2018	VLN Non Mentholated	10.9 12.1 HN	0.4	0	0.4
1109	58/M	Unscheduled	25SEP2018		7.9	0.4	0	0.1
2028	36/M	Screening End Of Study	06JUL2018 29AUG2018	VLN Non Mentholated				0.7 HN 0.5 HN
2064	52/M	Screening	23JUL2018		11.3 HN			
2066	30/F	End Of Study	20SEP2018	VLN Mentholated				0.5 HN
2122	60/M	Screening	20AUG2018		3.1 LN			
2159	37/M	Unscheduled	04OCT2018		6.7	0	0	0.1
2235	26/F	Screening	19OCT2018		11.5 HN			
2251	27/M	Screening End Of Study	09NOV2018 19JAN2019	UB Non Mentholated				1.1 HN 0.9 HN

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 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.2.3 Out-of-Range Values and Recheck Results - Hematology (III of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Eosinophils	Absolute Lymphocytes	Lymphocytes	Absolute Monocytes
		Name	Date		001: 0.5-7.4 002: Not Estab. (%)	001: 1.1-3.2 002: 0.7-3.1 (thou/uL)	001: 15.8-45.8 002: Not Estab. (%)	001: 0.3-0.9 002: 0.1-0.9 (thou/uL)
1001	59/F	End Of Study	07SEP2018	VLN Non Mentholated		3.5 HN		
1002	30/M	Screening	02JUL2018					0.2 LN
1003	38/M	End Of Study	07SEP2018	VLN Mentholated	9.2 HN			
1008	48/M	Unscheduled End Of Study	16JUL2018 07SEP2018	VLN Mentholated	1.3	4.9 HN 5 HN	69.3 HN 48.8 HN	0.3
1017	41/F	End Of Study	13SEP2018	UB Mentholated		3.5 HN		
1019	30/M	Screening End Of Study	17JUL2018 14SEP2018	VLN Non Mentholated		3.5 HN 3.8 HN		
1021	49/F	End Of Study	13SEP2018	UB Non Mentholated		3.6 HN		
1029	35/F	End Of Study	11OCT2018	VLN Mentholated		3.7 HN		
1034	45/M	End Of Study	10OCT2018	VLN Non Mentholated	9 HN			
1042	47/M	End Of Study	11OCT2018	VLN Non Mentholated			14.4 LN	
1046	45/M	End Of Study	10OCT2018	UB Mentholated		3.4 HN		

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 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.2.3 Out-of-Range Values and Recheck Results - Hematology (III of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Eosinophils	Absolute Lymphocytes	Lymphocytes	Absolute Monocytes
		Name	Date		001: 0.5-7.4 002: Not Estab. (%)	001: 1.1-3.2 002: 0.7-3.1 (thou/uL)	001: 15.8-45.8 002: Not Estab. (%)	001: 0.3-0.9 002: 0.1-0.9 (thou/uL)
1051	36/F	Screening	14AUG2018			3.3 HN		
		End Of Study	10OCT2018	UB Mentholated		4.3 HN		
1052	31/M	End Of Study	11OCT2018	VLN Mentholated				0.2 LN
1054	56/M	Screening	14AUG2018					1 HN
		End Of Study	10OCT2018	UB Non Mentholated		3.5 HN		
1059	38/M	End Of Study	24OCT2018	UB Non Mentholated		3.4 HN	46.6 HN	
1066	62/M	Screening	27AUG2018			0.9 LN		
1072	59/M	Screening	28AUG2018		0.4 LN	3.8 HN		
		End Of Study	22OCT2018	VLN Mentholated		4.1 HN		
1074	42/M	End Of Study	24OCT2018	VLN Non Mentholated		3.3 HN		
1077	49/F	End Of Study	24OCT2018	VLN Non Mentholated		4.3 HR	55.9 HN	
1079	33/M	End Of Study	24OCT2018	VLN Mentholated	10.7 HN			1 HN
1083	54/F	End Of Study	31OCT2018	VLN Non Mentholated		4.4 HR	52.8 HN	

Note: \$Age is derived from birth date to date of informed consent
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 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.2.3 Out-of-Range Values and Recheck Results - Hematology (III of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Eosinophils	Absolute Lymphocytes	Lymphocytes	Absolute Monocytes
		Name	Date		001: 0.5-7.4 002: Not Estab. (%)	001: 1.1-3.2 002: 0.7-3.1 (thou/uL)	001: 15.8-45.8 002: Not Estab. (%)	001: 0.3-0.9 002: 0.1-0.9 (thou/uL)
1089	60/F	End Of Study	31OCT2018	UB Non Mentholated		4.3 HR	49.8 HN	
1092	43/F	End Of Study	31OCT2018	VLN Mentholated		3.3 HN	49.5 HN	
1095	55/F	Screening	07SEP2018			3.5 HN		
		End Of Study	31OCT2018	VLN Mentholated		4.1 HR	58.6 HR	
1097	30/M	End Of Study	31OCT2018	VLN Mentholated				1.4 HN
1099	46/F	Screening	18SEP2018		8 HN			
		End Of Study	16NOV2018	VLN Non Mentholated		3.3 HN		
1100	59/M	End Of Study	16NOV2018	VLN Non Mentholated		3.7 HN		
1105	47/F	Screening	19SEP2018		0.4 LN			
1107	45/M	Unscheduled	25SEP2018		3.5	2.5	22.7	1 HN
		End Of Study	16NOV2018	VLN Non Mentholated		3.9 HN		
1109	58/M	Unscheduled	25SEP2018		0.8	1.3	16.2	0.4
		End Of Study	16NOV2018	UB Non Mentholated		3.3 HN		
2015	57/F	Screening	02JUL2018			4.8 HN		

Note: \$Age is derived from birth date to date of informed consent
 001 = Lincoln, 002 = High Point, F = Female, M = Male
 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.2.3 Out-of-Range Values and Recheck Results - Hematology (III of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Eosinophils	Absolute Lymphocytes	Lymphocytes	Absolute Monocytes
		Name	Date		001: 0.5-7.4 002: Not Estab. (%)	001: 1.1-3.2 002: 0.7-3.1 (thou/uL)	001: 15.8-45.8 002: Not Estab. (%)	001: 0.3-0.9 002: 0.1-0.9 (thou/uL)
2015	57/F	End Of Study	29AUG2018	UB Mentholated		4.2 HN		
2017	30/M	End Of Study	29AUG2018	VLN Mentholated		4.5 HN		
2059	56/F	Screening	23JUL2018			3.7 HN		
2110	41/F	Screening	13AUG2018			3.2 HN		
2113	51/F	Screening	15AUG2018			3.4 HN		
2115	46/F	Screening	15AUG2018			3.5 HN		
2126	37/M	Screening	21AUG2018			3.5 HN		
		End Of Study	20OCT2018	VLN Mentholated		3.8 HN		
2159	37/M	Unscheduled	04OCT2018		2	1.8	27	0.5
2164	65/F	Screening	27SEP2018			4.4 HN		
		End Of Study	02DEC2018	VLN Non Mentholated		3.4 HN		
2168	32/F	Screening	28SEP2018			3.2 HN		
		End Of Study	02DEC2018	VLN Non Mentholated		3.5 HN		

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 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
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Table 14.3.4.2.3 Out-of-Range Values and Recheck Results - Hematology (III of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Eosinophils	Absolute Lymphocytes	Lymphocytes	Absolute Monocytes
		Name	Date		001: 0.5-7.4 002: Not Estab. (%)	001: 1.1-3.2 002: 0.7-3.1 (thou/uL)	001: 15.8-45.8 002: Not Estab. (%)	001: 0.3-0.9 002: 0.1-0.9 (thou/uL)
2175	40/F	Screening	01OCT2018	UB Mentholated		3.4 HN		
		End Of Study	02DEC2018			3.2 HN		
2215	59/F	Screening	10OCT2018			3.6 HN		
2235	26/F	Screening	19OCT2018	VLN Mentholated		4.3 HN		
		End Of Study	16DEC2018			3.4 HN		
2244	31/M	Screening	25OCT2018	VLN Non Mentholated		3.3 HN		
		End Of Study	16DEC2018			3.6 HN		

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 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.2.4 Out-of-Range Values and Recheck Results - Hematology (IV of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Monocytes	Absolute Neutrophils	Neutrophils
		Name	Date		001: 4.9-12.8 002: Not Estab. (%)	001: 1.6-7.7 002: 1.4-7 (thou/uL)	001: 38.4-74.2 002: Not Estab. (%)
1001	59/F	Screening	02JUL2018		4.2 LN		
		End Of Study	07SEP2018	VLN Non Mentholated	4.4 LN	7.9 HN	
1002	30/M	Screening	02JUL2018		4.1 LN		
1008	48/M	Unscheduled	16JUL2018		4.9	1.7	24.1 LN
		End Of Study	07SEP2018	VLN Mentholated	4.6 LN		
1016	54/M	End Of Study	13SEP2018	UB Non Mentholated	15.2 HN		
1018	41/F	Screening	17JUL2018		4.6 LN		
1020	36/F	Screening	17JUL2018		4.4 LN		
		End Of Study	14SEP2018	VLN Non Mentholated	4.4 LN		
1023	50/F	Screening	17JUL2018		4.5 LN		
		End Of Study	14SEP2018	VLN Non Mentholated	4.3 LN		
1029	35/F	End Of Study	11OCT2018	VLN Mentholated	3.2 LN		
1042	47/M	End Of Study	11OCT2018	VLN Non Mentholated		7.8 HN	77.1 HN
1051	36/F	Screening	14AUG2018			8.3 HN	

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PI interpretation: N = Not Clinically Significant, R = To be rechecked
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.2.4 Out-of-Range Values and Recheck Results - Hematology (IV of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Monocytes	Absolute Neutrophils	Neutrophils
		Name	Date		001: 4.9-12.8 002: Not Estab. (%)	001: 1.6-7.7 002: 1.4-7 (thou/uL)	001: 38.4-74.2 002: Not Estab. (%)
1052	31/M	End Of Study	11OCT2018	VLN Mentholated	4.3 LN		
1053	42/M	End Of Study	11OCT2018	VLN Mentholated	4.4 LN		
1059	38/M	Screening	27AUG2018		4.4 LN		
1066	62/M	Screening	27AUG2018		13 HN		
1069	40/F	Screening	28AUG2018			8.2 HN	
		End Of Study	24OCT2018	UB Non Mentholated		8.6 HR	
1074	42/M	Screening	28AUG2018		4.3 LN		
1077	49/F	End Of Study	24OCT2018	VLN Non Mentholated			31.8 LR
1083	54/F	End Of Study	31OCT2018	VLN Non Mentholated			35.5 LN
1086	54/M	Screening	04SEP2018		4.5 LN		
1089	60/F	End Of Study	31OCT2018	UB Non Mentholated	4.4 LN		
1092	43/F	Screening	05SEP2018		4.6 LN		
		End Of Study	31OCT2018	VLN Mentholated	3.9 LN		

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 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.2.4 Out-of-Range Values and Recheck Results - Hematology (IV of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Monocytes	Absolute Neutrophils	Neutrophils
		Name	Date		001: 4.9-12.8 002: Not Estab. (%)	001: 1.6-7.7 002: 1.4-7 (thou/uL)	001: 38.4-74.2 002: Not Estab. (%)
1094	46/M	End Of Study	31OCT2018	VLN Mentholated	4.5 LN		
1095	55/F	End Of Study	31OCT2018	VLN Mentholated			32.3 LR
1097	30/M	End Of Study	31OCT2018	VLN Mentholated	16.2 HN		
1105	47/F	Screening	19SEP2018			9.4 HN	
1107	45/M	Unscheduled	25SEP2018		9	7	64
1109	58/M	Unscheduled	25SEP2018		5.3	6.1	77 HN
2028	36/M	Screening	06JUL2018			7.4 HN	
2058	37/F	End Of Study	20SEP2018	VLN Mentholated		1 LN	
2060	37/F	Screening	23JUL2018			7.6 HN	
2064	52/M	Screening	23JUL2018			7.3 HN	
2143	63/M	End Of Study	06NOV2018	VLN Non Mentholated		7.1 HN	
2159	37/M	Unscheduled	04OCT2018		8	4.3	64

Note: \$Age is derived from birth date to date of informed consent
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 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.2.4 Out-of-Range Values and Recheck Results - Hematology (IV of IV) (Safety Population)

Subject Number	Age\$/ Sex	Visit		Product Group	Monocytes	Absolute Neutrophils	Neutrophils
		Name	Date		001: 4.9-12.8 002: Not Estab. (%)	001: 1.6-7.7 002: 1.4-7 (thou/uL)	001: 38.4-74.2 002: Not Estab. (%)
2170	51/F	End Of Study	02DEC2018	UB Non Mentholated		7.6 HN	

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 H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.3.1 Out-of-Range Values and Recheck Results - Urinalysis (I of VI) (Safety Population)

Subject Number	Age\$/ Sex	Visit			Product Group	Urobilinogen 001: NEGATIVE	Occult Blood 001: F: NEG, TRAC 001: M: NEGATIVE 002: Negative	pH, Urine 001: 5-8 002: 5-7.5
		Name	Date	Time				
1059	38/M	Screening	27AUG2018	10:00				8.5 HN
1069	40/F	End Of Study	24OCT2018	19:58	UB Non Mentholated		1+ *R	
1089	60/F	End Of Study	31OCT2018	20:19	UB Non Mentholated		1+ *R	
1097	30/M	Unscheduled	10SEP2018	8:01		NEGATIVE	NEGATIVE	6
1098	63/M	End Of Study	16NOV2018	19:04	VLN Non Mentholated		TRACE *N	
1099	46/F	End Of Study	16NOV2018	19:12	VLN Non Mentholated		3+ *R	
2007	57/F	Screening	29JUN2018	10:52			Trace *N	
2024	26/M	Screening	03JUL2018	9:41				8.5 HN
2060	37/F	Screening	23JUL2018	9:47			3+ *N	
2122	60/M	Screening	20AUG2018	10:52			Trace *N	
		End Of Study	19OCT2018	14:02	UB Non Mentholated			8 HN
2168	32/F	End Of Study	01DEC2018	14:13	VLN Non Mentholated		Trace *N	

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* = No Range, H = Above Normal Range

PI interpretation: N = Not Clinically Significant, R = To be rechecked, Y = Clinically Significant

VLN non-mentholated = Non-mentholated VLN cigarettes

VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.3.1 Out-of-Range Values and Recheck Results - Urinalysis (I of VI) (Safety Population)

Subject Number	Age\$/ Sex	Visit			Product Group	Urobilinogen 001: NEGATIVE	Occult Blood 001: F: NEG, TRAC 001: M: NEGATIVE 002: Negative	pH, Urine 001: 5-8 002: 5-7.5
		Name	Date	Time				
2170	51/F	Screening	28SEP2018	10:31	UB Non Mentholated		2+ *N	
		End Of Study	01DEC2018	14:02				
2211	29/F	Screening	10OCT2018	11:05	VLN Mentholated		1+ *N	
		End Of Study	01DEC2018	14:03				

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* = No Range, H = Above Normal Range

PI interpretation: N = Not Clinically Significant, R = To be rechecked, Y = Clinically Significant

VLN non-mentholated = Non-mentholated VLN cigarettes

VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.3.2 Out-of-Range Values and Recheck Results - Urinalysis (II of VI) (Safety Population)

Subject Number	Age\$/ Sex	Visit			Product Group	Specific Gravity	Leukocyte Esterase	Nitrite
		Name	Date	Time		001: 1.005-1.03 002: 1.005-1.03	001: NEG, TRACE 002: Negative	001: NEGATIVE 002: Negative
1002	30/M	End Of Study	07SEP2018	11:20	VLN Non Mentholated	1.003 LN		
1003	38/M	Screening	03JUL2018	10:26		1.035 HN		
		End Of Study	07SEP2018	11:17	VLN Mentholated	1.035 HN		
1013	36/F	End Of Study	14SEP2018	12:19	VLN Non Mentholated	1.003 LN		
1014	36/F	Screening	16JUL2018	10:48		1.003 LN		
1015	49/F	Screening	16JUL2018	11:14		1.002 LN		
		End Of Study	14SEP2018	11:19	VLN Mentholated	1.004 LN		
1016	54/M	Screening	16JUL2018	11:16		1.004 LN		
		End Of Study	13SEP2018	20:20	UB Non Mentholated		1+ *N	
1017	41/F	Screening	17JUL2018	11:20		1.002 LN		
1018	41/F	Screening	17JUL2018	11:18		1.002 LN		
1019	30/M	Screening	17JUL2018	12:16		1.031 HN		
1023	50/F	Screening	17JUL2018	12:22		1.004 LN		

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 VLN non-mentholated = Non-mentholated VLN cigarettes
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Table 14.3.4.3.2 Out-of-Range Values and Recheck Results - Urinalysis (II of VI) (Safety Population)

Subject Number	Age\$/ Sex	Visit			Product Group	Specific Gravity	Leukocyte Esterase	Nitrite
		Name	Date	Time		001: 1.005-1.03 002: 1.005-1.03	001: NEG, TRACE 002: Negative	001: NEGATIVE 002: Negative
1029	35/F	Screening	26JUL2018	9:54	VLN Mentholated	1.004 LN		
		End Of Study	11OCT2018	10:48		1.003 LN		
1036	38/F	Screening	13AUG2018	10:01		1.004 LN		
1037	29/M	Screening	13AUG2018	9:40		1.003 LN		
1038	39/F	Screening	13AUG2018	10:04		1.002 LN		
1051	36/F	End Of Study	10OCT2018	19:53	UB Mentholated		1+ *R	
1052	31/M	End Of Study	11OCT2018	10:52	VLN Mentholated		1+ *N	
1054	56/M	End Of Study	10OCT2018	20:02	UB Non Mentholated		1+ *R	
1055	39/F	Screening	14AUG2018	10:39		1.004 LN		
1056	48/M	Screening	14AUG2018	10:36		1.003 LN		
1070	53/M	Screening	28AUG2018	10:20		1.003 LN		
1072	59/M	Screening	28AUG2018	10:02		1.004 LN		

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 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.3.2 Out-of-Range Values and Recheck Results - Urinalysis (II of VI) (Safety Population)

Subject Number	Age\$/ Sex	Visit			Product Group	Specific Gravity	Leukocyte Esterase	Nitrite
		Name	Date	Time		001: 1.005-1.03 002: 1.005-1.03	001: NEG, TRACE 002: Negative	001: NEGATIVE 002: Negative
1075	26/F	End Of Study	24OCT2018	20:05	UB Non Mentholated		3+ *R	
1077	49/F	End Of Study	24OCT2018	20:03	VLN Non Mentholated		2+ *R	
1084	42/M	Screening	04SEP2018	9:59		1.003 LN		
1096	42/F	End Of Study	31OCT2018	20:39	VLN Non Mentholated		1+ *R	
1097	30/M	Unscheduled	10SEP2018	8:01		1.018	NEGATIVE	NEGATIVE
1099	46/F	End Of Study	16NOV2018	19:12	VLN Non Mentholated		1+ *R	
1101	41/M	Screening	18SEP2018	10:59		1.003 LN		
2003	41/F	End Of Study	28AUG2018	13:14	VLN Mentholated		1+ *N	
2015	57/F	End Of Study	28AUG2018	13:30	UB Mentholated	>=1.030 *N		
2023	35/M	End Of Study	28AUG2018	13:38	VLN Mentholated	>=1.030 *N		
2050	57/M	Screening	20JUL2018	10:04			Trace *N	
2058	37/F	Screening	23JUL2018	9:31			Trace *N	

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VLN non-mentholated = Non-mentholated VLN cigarettes
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UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.3.2 Out-of-Range Values and Recheck Results - Urinalysis (II of VI) (Safety Population)

Subject Number	Age\$/ Sex	Visit			Product Group	Specific Gravity	Leukocyte Esterase	Nitrite
		Name	Date	Time		001: 1.005-1.03 002: 1.005-1.03	001: NEG, TRACE 002: Negative	001: NEGATIVE 002: Negative
2064	52/M	Screening	23JUL2018	10:34		<=1.005 *N		
2075	34/M	Screening	30JUL2018	10:11			Trace *N	
		End Of Study	22AUG2018	19:17	VLN Mentholated	<=1.005 *N		
2092	50/F	Screening	06AUG2018	9:43		<=1.005 *N		
2100	48/F	End Of Study	13OCT2018	13:26	UB Mentholated	>=1.030 *N		
2110	41/F	Screening	13AUG2018	9:49			2+ *N	
		End Of Study	19OCT2018	13:48	UB Mentholated		2+ *N	
2119	48/M	Screening	20AUG2018	9:42		>=1.030 *N		
		End Of Study	19OCT2018	13:52	VLN Mentholated			Positive *N
2126	37/M	End Of Study	19OCT2018	14:13	VLN Mentholated	>=1.030 *N		
2136	64/M	End Of Study	19OCT2018	14:18	VLN Non Mentholated		1+ *N	Positive *N
2140	56/F	Screening	30AUG2018	10:06			1+ *N	
2142	30/F	Screening	31AUG2018	10:24			Trace *N	
		End Of Study	08OCT2018	13:25	VLN Non Mentholated	<=1.005 *N		

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 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.3.2 Out-of-Range Values and Recheck Results - Urinalysis (II of VI) (Safety Population)

Subject Number	Age\$/ Sex	Visit			Product Group	Specific Gravity	Leukocyte Esterase	Nitrite
		Name	Date	Time		001: 1.005-1.03 002: 1.005-1.03	001: NEG, TRACE 002: Negative	001: NEGATIVE 002: Negative
2164	65/F	Screening	27SEP2018	10:13	VLN Non Mentholated		2+ *N	
		End Of Study	01DEC2018	14:21			Trace *N	
2215	59/F	End Of Study	01DEC2018	14:11	UB Mentholated		Trace *N	
2220	37/M	Screening	11OCT2018	9:23		>=1.030 *N		
2247	28/M	End Of Study	28DEC2018	15:13	VLN Mentholated		Trace *N	
2259	49/M	End Of Study	19JAN2019	15:09	UB Mentholated		Trace *N	

Note: \$Age is derived from birth date to date of informed consent
 001 = Lincoln, 002 = High Point, F = Female, M = Male
 * = No Range, H = Above Normal Range, L = Below Normal Range
 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.3.3 Out-of-Range Values and Recheck Results - Urinalysis (III of VI) (Safety Population)

Subject Number	Age\$/ Sex	Visit			Product Group	Bilirubin		Epithelial Cells 002: 0 - 10 (/HPF)	Glucose	
		----- Name	----- Date	----- Time		001: NEGATIVE 002: Negative			001: NEGATIVE 002: Negative	
1097	30/M	Unscheduled	10SEP2018	8:01		NEGATIVE			NEGATIVE	
2017	30/M	Screening	02JUL2018	9:45					Trace	*N
2050	57/M	End Of Study	20SEP2018	13:32	UB Mentholated				Trace	*N
2110	41/F	End Of Study	19OCT2018	13:48	UB Mentholated			>10	*N	
2126	37/M	End Of Study	19OCT2018	14:13	VLN Mentholated				Trace	*N
2142	30/F	Screening	31AUG2018	10:24				>10	*N	
2213	29/M	End Of Study	01DEC2018	14:05	VLN Mentholated				Trace	*N

Note: \$Age is derived from birth date to date of informed consent
 001 = Lincoln, 002 = High Point, F = Female, M = Male
 * = No Range
 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.3.4 Out-of-Range Values and Recheck Results - Urinalysis (IV of VI) (Safety Population)

Subject Number	Age\$/ Sex	Visit			Product Group	RBC	WBC	Protein
		Name	Date	Time		001: 0-3 002: 0 - 2 (/HPF)	001: 0-7 002: 0 - 5 (/HPF)	001: NEG, TRACE 002: Negative/Trace
1016	54/M	End Of Study	13SEP2018	20:20	UB Non Mentholated		10 HN	
1051	36/F	End Of Study	10OCT2018	19:53	UB Mentholated	4 HR		
1052	31/M	End Of Study	11OCT2018	10:52	VLN Mentholated		11 HN	
1054	56/M	End Of Study	10OCT2018	20:02	UB Non Mentholated		10 HR	
1075	26/F	End Of Study	24OCT2018	20:05	UB Non Mentholated	6 HR	54 HR	
1077	49/F	End Of Study	24OCT2018	20:03	VLN Non Mentholated	6 HR		
1097	30/M	Screening Unscheduled	07SEP2018 10SEP2018	9:23 8:01			16 HR	Negative
1099	46/F	End Of Study	16NOV2018	19:12	VLN Non Mentholated	53 HR		
2003	41/F	End Of Study	28AUG2018	13:14	VLN Mentholated		6-10 *N	
2060	37/F	Screening	23JUL2018	9:47		11-30 *N		
2110	41/F	Screening	13AUG2018	9:49			6-10 *N	
2136	64/M	End Of Study	19OCT2018	14:18	VLN Non Mentholated	3-10 *N	6-10 *N	

Note: \$Age is derived from birth date to date of informed consent
 001 = Lincoln, 002 = High Point, F = Female, M = Male
 * = No Range, H = Above Normal Range
 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.3.4 Out-of-Range Values and Recheck Results - Urinalysis (IV of VI) (Safety Population)

Subject Number	Age\$/ Sex	Visit			Product Group	RBC	WBC	Protein
		Name	Date	Time		001: 0-3 002: 0 - 2 (/HPF)	001: 0-7 002: 0 - 5 (/HPF)	001: NEG, TRACE 002: Negative/Trace
2140	56/F	Screening	30AUG2018	10:06			6-10 *N	
2170	51/F	Screening	28SEP2018	10:31		11-30 *N		
		End Of Study	01DEC2018	14:02	UB Non Mentholated	11-30 *N		
2211	29/F	Screening	10OCT2018	11:05		3-10 *N		

Note: \$Age is derived from birth date to date of informed consent
 001 = Lincoln, 002 = High Point, F = Female, M = Male
 * = No Range, H = Above Normal Range
 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.3.5 Out-of-Range Values and Recheck Results - Urinalysis (V of VI) (Safety Population)

Subject Number	Age\$/ Sex	Visit			Product Group	Ketones 001: NEG, TRACE 002: Negative	Bacteria 001: NEGATIVE 002: None seen/Few	Casts 001: 0-1 (/LPF)
		Name	Date	Time				
1051	36/F	End Of Study	10OCT2018	19:53	UB Mentholated			2 HR
1052	31/M	End Of Study	11OCT2018	10:52	VLN Mentholated			3 HN
1054	56/M	End Of Study	10OCT2018	20:02	UB Non Mentholated			3 HR
1069	40/F	End Of Study	24OCT2018	19:58	UB Non Mentholated			2 HR
1075	26/F	End Of Study	24OCT2018	20:05	UB Non Mentholated		1+ *N	4 HR
1089	60/F	End Of Study	31OCT2018	20:19	UB Non Mentholated		1+ *N	2 HR
1097	30/M	Screening Unscheduled	07SEP2018 10SEP2018	9:23 8:01		NEGATIVE		5 HR
1099	46/F	End Of Study	16NOV2018	19:12	VLN Non Mentholated			4 HR
2008	42/M	End Of Study	28AUG2018	13:30	VLN Mentholated	Trace *N		
2014	37/M	Screening End Of Study	02JUL2018 28AUG2018	9:20 13:26	VLN Mentholated	Trace *N Trace *N		
2017	30/M	Screening	02JUL2018	9:45		Trace *N		

Note: \$Age is derived from birth date to date of informed consent
 001 = Lincoln, 002 = High Point, F = Female, M = Male
 * = No Range, H = Above Normal Range
 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.3.5 Out-of-Range Values and Recheck Results - Urinalysis (V of VI) (Safety Population)

Subject Number	Age\$/ Sex	Visit			Product Group	Ketones		Bacteria		Casts	
		Name	Date	Time		001: NEG, TRACE	002: Negative	001: NEGATIVE	002: None seen/Few	001: 0-1	(/LPF)
2100	48/F	End Of Study	13OCT2018	13:26	UB Mentholated		Trace *N				
2119	48/M	Screening	20AUG2018	9:42			Trace *N				
2136	64/M	End Of Study	19OCT2018	14:18	VLN Non Mentholated		Trace *N				
2143	63/M	End Of Study	05NOV2018	14:24	VLN Non Mentholated		Trace *N				
2189	28/M	Screening	04OCT2018	10:35			Trace *N				
2211	29/F	Screening	10OCT2018	11:05			1+ *N				

Note: \$Age is derived from birth date to date of informed consent
 001 = Lincoln, 002 = High Point, F = Female, M = Male
 * = No Range, H = Above Normal Range
 PI interpretation: N = Not Clinically Significant, R = To be rechecked
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.3.6 Out-of-Range Values and Recheck Results - Urinalysis (VI of VI) (Safety Population)

Subject Number	Age\$/ Sex	Visit			Product Group	Hyaline Casts 002: None seen (/LPF)
		Name	Date	Time		
2119	48/M	End Of Study	19OCT2018	13:52	VLN Mentholated	Present *N

Note: \$Age is derived from birth date to date of informed consent
 001 = Lincoln, 002 = High Point, F = Female, M = Male
 * = No Range
 PI interpretation: N = Not Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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Table 14.3.4.4 Clinically Significant Values and Recheck Results (Safety Population)

Subject Number	Age\$/ Sex	Visit			Product Group	Day	Deptment	Test	Result	Reference	Range
		Name	Date	Time							
2211	29/F	End Of Study	01DEC2018	14:03	VLN Mentholated	42	Urinalysis	Occult Blood	2+	*Y	Negative

Note: * = No Match to Reference Range
 PI Interpretation: Y = Clinically Significant
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

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14.3.5 Displays of Other Laboratory, Vital Signs, Electrocardiogram, Physical Examination, and Other Safety Data

Table 14.3.5.1	Clinical Laboratory Summary – Serum Chemistry (Safety Population)
Table 14.3.5.2	Clinical Laboratory Summary – Hematology (Safety Population)
Table 14.3.5.3	Clinical Laboratory Summary – Urinalysis (Safety Population)
Table 14.3.5.4	Vital Sign Summary (Safety Population)

Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

Laboratory Test (units)	Reference Range	Statistic	Time Point	
			Screening	End of Study
Carbon Dioxide (mmol/L) - Blood	20-33.2 #	n	142	133
		Mean	25.80	25.40
		SD	2.425	2.173
		Minimum	20.0	19.0
		Median	25.95	25.10
		Maximum	32.0	31.0
Potassium (mmol/L)	3.5-5.2 #	n	142	133
		Mean	4.59	4.45
		SD	0.393	0.337
		Minimum	3.6	3.7
		Median	4.50	4.40
		Maximum	6.0	5.5
Albumin (g/L)	35-50 #	n	142	133
		Mean	45.5	42.9
		SD	2.50	3.33
		Minimum	39	34
		Median	46.0	43.0
		Maximum	52	52

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.
 Test values reported as <0.2 for Bilirubin were not included in the calculation

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

Laboratory Test (units)	Reference Range	Statistic	Time Point	
			Screening	End of Study
Creatinine (umol/L)	44.209-112.29 #	n	142	133
		Mean	74.8060	74.1243
		SD	13.79597	14.87021
		Minimum	48.630	42.440
		Median	74.7130	73.3860
		Maximum	112.290	116.711
Glucose (mmol/L)	3.6-5.8 #	n	142	133
		Mean	5.13	5.17
		SD	0.462	0.550
		Minimum	4.2	3.5
		Median	5.10	5.20
		Maximum	6.5	7.7
Alkaline Phosphatase (IU/L)	37-120 #	n	142	133
		Mean	77.6	73.4
		SD	19.36	17.84
		Minimum	42	37
		Median	77.0	71.0
		Maximum	145	130

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.
Test values reported as <0.2 for Bilirubin were not included in the calculation

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

Laboratory Test (units)	Reference Range	Statistic	Time Point	
			Screening	End of Study
Alanine Aminotransferase (IU/L)	0-67 #	n	142	133
		Mean	22.5	19.8
		SD	13.22	11.22
		Minimum	0	5
		Median	20.5	18.0
		Maximum	91	90
Aspartate Aminotransferase (IU/L)	0-48 #	n	142	133
		Mean	22.2	18.6
		SD	15.12	8.00
		Minimum	10	9
		Median	19.0	17.0
		Maximum	169	75
Protein (g/dL)	6-8.1 #	n	142	133
		Mean	7.10	6.67
		SD	0.372	0.462
		Minimum	6.0	5.1
		Median	7.10	6.60
		Maximum	8.2	7.8

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.
Test values reported as <0.2 for Bilirubin were not included in the calculation

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

Laboratory Test (units)	Reference Range	Statistic	Time Point	
			Screening	End of Study
Sodium (mmol/L)	134-143 #	n	142	133
		Mean	141.0	140.3
		SD	2.22	2.29
		Minimum	135	128
		Median	141.0	141.0
		Maximum	149	144
Bilirubin (mg/dL)	0-1.6 #	n	136	128
		Mean	0.44	0.32
		SD	0.200	0.215
		Minimum	0.2	0.0
		Median	0.40	0.30
		Maximum	1.2	1.1
Urate (mg/dL)	2.3-8.6 #	n	142	133
		Mean	5.24	5.07
		SD	1.135	1.188
		Minimum	3.0	2.5
		Median	5.10	5.10
		Maximum	8.3	8.2

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.
Test values reported as <0.2 for Bilirubin were not included in the calculation

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

Laboratory Test (units)	Reference Range	Statistic	Time Point	
			Screening	End of Study
Urea Nitrogen (mg/dL)	6-27 #	n	142	133
		Mean	11.1	13.1
		SD	3.30	3.25
		Minimum	4	4
		Median	11.0	13.0
		Maximum	22	22

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.
 Test values reported as <0.2 for Bilirubin were not included in the calculation

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Table 14.3.5.2 Clinical Laboratory Summary - Hematology (Safety Population)

Laboratory Test (units)	Reference Range	Statistic	Time Point	
			Screening	End of Study
Hemoglobin (g/L)	111-174 #	n	142	133
		Mean	147.9	142.2
		SD	12.85	13.44
		Minimum	115	114
		Median	148.0	143.0
		Maximum	188	174
Hematocrit (v/v)	3.4-5.23 #	n	142	133
		Mean	4.404	4.301
		SD	0.3280	0.3540
		Minimum	3.71	3.53
		Median	4.395	4.290
		Maximum	5.39	5.01
Platelet Count (thou/uL)	150-361 #	n	142	133
		Mean	256.5	247.0
		SD	55.73	55.13
		Minimum	105	127
		Median	251.0	240.0
		Maximum	490	507

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.

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Table 14.3.5.2 Clinical Laboratory Summary - Hematology (Safety Population)

Laboratory Test (units)	Reference Range	Statistic	Time Point	
			Screening	End of Study
Red Blood Cell Count (mil/uL)	3.77-5.81 #	n	142	133
		Mean	4.845	4.675
		SD	0.3630	0.3949
		Minimum	4.08	3.53
		Median	4.865	4.730
		Maximum	5.76	5.53
White Blood Cell Count (thou/uL)	3.4-11.5 #	n	142	133
		Mean	7.75	7.45
		SD	1.802	1.978
		Minimum	3.1	3.4
		Median	7.70	7.20
		Maximum	13.1	13.0
Basophils (%)	0-2	n	142	133
		Mean	0.27	0.32
		SD	0.327	0.368
		Minimum	0.0	0.0
		Median	0.20	0.20
		Maximum	1.0	2.0

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.

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Table 14.3.5.2 Clinical Laboratory Summary - Hematology (Safety Population)

Laboratory Test (units)	Reference Range	Statistic	Time Point	
			Screening	End of Study
Absolute Basophils (thou/uL)	0-0.2 #	n	142	133
		Mean	0.01	0.01
		SD	0.031	0.028
		Minimum	0.0	0.0
		Median	0.00	0.00
		Maximum	0.1	0.1
Absolute Eosinophils (thou/uL)	0-0.5 #	n	142	133
		Mean	0.20	0.21
		SD	0.154	0.162
		Minimum	0.0	0.0
		Median	0.20	0.20
		Maximum	1.1	1.1
Eosinophils (%)	0.5-7.4	n	142	133
		Mean	2.44	2.93
		SD	1.832	2.094
		Minimum	0.0	0.0
		Median	2.00	2.30
		Maximum	15.0	15.0

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.

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Table 14.3.5.2 Clinical Laboratory Summary - Hematology (Safety Population)

Laboratory Test (units)	Reference Range	Statistic	Time Point	
			Screening	End of Study
Absolute Lymphocytes (thou/uL)	0.7-3.2 #	n	142	133
		Mean	2.42	2.58
		SD	0.744	0.821
		Minimum	0.9	1.0
		Median	2.30	2.50
		Maximum	4.9	5.0
Lymphocytes (%)	15.8-45.8	n	142	133
		Mean	31.60	35.17
		SD	8.791	9.168
		Minimum	14.0	14.4
		Median	29.35	34.40
		Maximum	69.3	64.0
Absolute Monocytes (thou/uL)	0.1-0.9 #	n	142	133
		Mean	0.54	0.53
		SD	0.167	0.188
		Minimum	0.2	0.2
		Median	0.50	0.50
		Maximum	1.0	1.4

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.

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Table 14.3.5.2 Clinical Laboratory Summary - Hematology (Safety Population)

Laboratory Test (units)	Reference Range	Statistic	Time Point	
			Screening	End of Study
Monocytes (%)	4.9-12.8	n	142	133
		Mean	7.02	7.31
		SD	1.836	2.279
		Minimum	4.0	3.0
		Median	7.00	7.00
		Maximum	13.0	16.2
Absolute Neutrophils (thou/uL)	1.4-7.7 #	n	142	133
		Mean	4.58	4.10
		SD	1.432	1.494
		Minimum	1.5	1.0
		Median	4.50	3.90
		Maximum	9.4	8.6
Neutrophils (%)	38.4-74.2	n	142	133
		Mean	58.40	54.09
		SD	8.438	9.348
		Minimum	24.1	26.0
		Median	60.25	55.00
		Maximum	77.0	77.1

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.

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Table 14.3.5.3 Clinical Laboratory Summary - Urinalysis (Safety Population)

Laboratory Test (units)	Reference Range	Statistic	Time Point	
			Screening	End of Study
pH, Urine	5-8 #	n	142	133
		Mean	6.25	6.18
		SD	0.809	0.757
		Minimum	5.0	5.0
		Median	6.00	6.00
		Maximum	8.5	8.0
Specific Gravity	1.005-1.03	n	138	127
		Mean	1.0145	1.0179
		SD	0.00841	0.00701
		Minimum	1.002	1.003
		Median	1.0140	1.0190
		Maximum	1.035	1.035

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.
 Test values reported as ≥ 1.030 , ≤ 1.005 for Specific Gravity were not included in the calculation

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Table 14.3.5.4 Vital Sign Summary (Safety Population)

Measurement (unit)	Study Week	Statistic	Study Product Group			
			Non-Mentholated	Mentholated	Non-Mentholated	Mentholated
Systolic Blood Pressure (mmHg)	Screening	n	50	50	22	20
		Mean	122.3	122.6	125.6	123.9
		SD	14.09	10.69	12.80	11.52
		Minimum	100	93	106	106
		Median	120.5	123.0	124.5	125.0
		Maximum	149	143	150	141
	Start Of Week -1	n	50	50	22	20
		Mean	120.6	120.0	118.7	120.1
		SD	14.43	12.15	11.12	10.13
		Minimum	100	94	104	103
		Median	119.0	120.0	116.0	120.0
		Maximum	163	146	148	141
	End Of Week -1	n	50	50	22	20
		Mean	121.8	120.4	120.2	119.9
		SD	15.53	12.89	10.65	15.46
		Minimum	97	97	102	90
		Median	118.5	117.0	121.0	118.5
		Maximum	155	148	146	146
	End Of Week 2	n	50	47	21	20
		Mean	121.3	117.8	120.6	119.9
		SD	16.65	13.48	17.57	11.63
		Minimum	97	95	96	99
		Median	118.5	116.0	119.0	119.5
		Maximum	161	154	175	138

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
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Table 14.3.5.4 Vital Sign Summary (Safety Population)

Measurement (unit)	Study Week	Statistic	Study Product Group			
			VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated
Systolic Blood Pressure (mmHg)	End Of Week 4	n	49	43	19	20
		Mean	121.1	120.2	118.2	118.2
		SD	15.18	13.10	11.24	9.77
		Minimum	94	94	101	95
		Median	120.0	121.0	116.0	118.0
		Maximum	159	145	149	132
	End Of Week 6	n	44	42	19	20
		Mean	120.8	117.7	122.6	116.1
		SD	15.41	13.07	13.68	10.41
		Minimum	90	92	103	99
		Median	121.5	116.5	120.0	118.5
		Maximum	168	147	150	139
	End Of Study	n	45	47	19	20
		Mean	119.7	115.9	120.9	116.0
		SD	14.75	13.70	18.24	12.72
		Minimum	88	91	91	94
		Median	121.0	116.0	117.0	114.5
		Maximum	155	153	174	142
Diastolic Blood Pressure (mmHg)	Screening	n	50	50	22	20
		Mean	81.4	81.5	82.6	80.9
		SD	8.60	6.80	7.40	6.17
		Minimum	64	61	71	70
		Median	81.0	82.0	82.0	80.5
		Maximum	96	95	95	90

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Table 14.3.5.4 Vital Sign Summary (Safety Population)

Measurement (unit)	Study Week	Statistic	Study Product Group			
			VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated
Diastolic Blood Pressure (mmHg)	Start Of Week -1	n	50	50	22	20
		Mean	78.3	77.8	77.0	77.9
		SD	7.81	7.79	7.64	6.13
		Minimum	64	61	58	69
		Median	78.0	78.0	77.5	76.5
		Maximum	94	93	93	94
	End Of Week -1	n	50	50	22	20
		Mean	78.0	77.0	77.5	76.6
		SD	8.15	7.79	5.98	8.00
		Minimum	58	62	65	62
		Median	78.0	75.5	79.5	76.5
		Maximum	94	95	88	92
	End Of Week 2	n	50	47	21	20
		Mean	76.9	75.5	76.7	76.5
		SD	9.36	8.70	10.02	6.70
		Minimum	61	63	62	65
		Median	76.0	73.0	76.0	78.0
		Maximum	104	100	111	88
	End Of Week 4	n	49	43	19	20
		Mean	77.7	77.6	77.1	77.9
		SD	7.95	8.14	6.76	7.30
		Minimum	62	59	67	60
		Median	78.0	78.0	78.0	78.0
		Maximum	99	91	91	92

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Table 14.3.5.4 Vital Sign Summary (Safety Population)

Measurement (unit)	Study Week	Statistic	Study Product Group			
			Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated
Diastolic Blood Pressure (mmHg)	End Of Week 6	n	44	42	19	20
		Mean	76.9	75.1	79.6	74.7
		SD	9.45	8.60	8.02	6.66
		Minimum	56	57	70	64
		Median	77.0	74.0	79.0	75.5
		Maximum	98	100	101	88
	End Of Study	n	45	47	19	20
		Mean	77.0	74.6	78.0	76.6
		SD	8.59	8.43	10.34	6.95
		Minimum	60	56	58	61
		Median	77.0	74.0	76.0	75.5
		Maximum	95	96	110	92
Pulse Rate (bpm)	Screening	n	50	50	22	20
		Mean	71.0	70.4	72.0	69.0
		SD	10.78	9.10	8.85	11.19
		Minimum	51	53	60	47
		Median	70.5	70.0	71.0	68.5
		Maximum	98	90	90	87
	Start Of Week -1	n	50	50	22	20
		Mean	73.3	76.8	74.2	74.6
		SD	9.65	9.00	8.54	10.39
		Minimum	57	56	63	51
		Median	72.5	75.0	71.0	75.0
		Maximum	98	96	88	92

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Table 14.3.5.4 Vital Sign Summary (Safety Population)

Measurement (unit)	Study Week	Statistic	Study Product Group			
			VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated
Pulse Rate (bpm)	End Of Week -1	n	50	50	22	20
		Mean	80.3	81.6	78.1	77.2
		SD	10.43	11.08	10.67	12.20
		Minimum	58	51	58	49
		Median	79.0	80.0	78.5	80.5
		Maximum	99	108	93	93
	End Of Week 2	n	50	47	21	20
		Mean	77.2	76.1	81.8	78.0
		SD	13.54	11.70	9.10	9.51
		Minimum	50	44	63	60
		Median	75.5	76.0	80.0	79.0
		Maximum	103	102	99	96
	End Of Week 4	n	49	43	19	20
		Mean	74.3	74.1	77.7	74.8
		SD	11.17	9.37	9.02	11.66
		Minimum	55	56	64	55
		Median	74.0	74.0	75.0	75.0
		Maximum	111	101	96	101
	End Of Week 6	n	44	42	19	20
		Mean	78.7	78.7	83.3	80.6
		SD	10.92	10.54	9.90	9.95
		Minimum	57	59	67	60
		Median	76.5	78.5	82.0	83.0
		Maximum	101	98	105	94

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Table 14.3.5.4 Vital Sign Summary (Safety Population)

Measurement (unit)	Study Week	Statistic	Study Product Group			
			Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated
Pulse Rate (bpm)	End Of Study	n	45	47	19	20
		Mean	69.9	68.0	74.7	69.4
		SD	12.20	9.41	10.03	9.93
		Minimum	45	52	58	50
		Median	67.0	66.0	73.0	69.0
		Maximum	98	96	94	85
Respiration Rate (rpm)	Screening	n	50	50	22	20
		Mean	15.6	15.7	15.3	15.9
		SD	2.12	1.72	1.84	1.86
		Minimum	10	12	12	12
		Median	16.0	16.0	16.0	16.0
		Maximum	22	19	18	19
	Start Of Week -1	n	50	50	22	20
		Mean	14.3	15.4	14.3	14.7
		SD	2.92	2.04	2.38	2.11
		Minimum	8	12	10	10
		Median	14.0	16.0	15.0	16.0
		Maximum	22	22	18	18
	End Of Week -1	n	50	50	22	20
		Mean	15.1	15.8	14.5	15.7
		SD	1.87	1.82	2.48	1.59
		Minimum	12	12	10	12
		Median	16.0	16.0	14.0	16.0
		Maximum	18	20	20	18

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Table 14.3.5.4 Vital Sign Summary (Safety Population)

Measurement (unit)	Study Week	Statistic	Study Product Group			
			VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated
Respiration Rate (rpm)	End Of Week 2	n	50	47	21	20
		Mean	15.4	15.3	15.4	14.4
		SD	2.65	2.48	2.50	2.11
		Minimum	10	8	10	12
		Median	16.0	16.0	16.0	14.0
		Maximum	22	20	20	20
	End Of Week 4	n	49	42	19	20
		Mean	14.9	15.1	14.6	14.8
		SD	2.28	2.14	2.43	2.19
		Minimum	10	10	10	12
		Median	14.0	16.0	14.0	15.0
		Maximum	20	19	18	20
	End Of Week 6	n	44	42	19	20
		Mean	14.7	14.8	15.2	14.9
		SD	2.40	1.77	2.85	1.65
		Minimum	10	12	10	12
		Median	14.0	16.0	16.0	16.0
		Maximum	20	18	20	18
	End Of Study	n	45	47	19	20
		Mean	14.8	15.8	13.9	15.7
		SD	3.10	2.31	2.38	2.08
		Minimum	10	12	10	12
		Median	14.0	16.0	14.0	16.0
		Maximum	24	21	18	20

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Table 14.3.5.4 Vital Sign Summary (Safety Population)

Measurement (unit)	Study Week	Statistic	Study Product Group			
			VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated
Temperature (°C)	Screening	n	50	50	22	20
		Mean	36.759	36.758	36.810	36.764
		SD	0.2384	0.2304	0.1713	0.2201
		Minimum	36.33	36.00	36.61	36.39
		Median	36.720	36.720	36.750	36.805
		Maximum	37.44	37.39	37.28	37.11
	Start Of Week -1	n	50	50	22	20
		Mean	36.744	36.836	36.725	36.861
		SD	0.1791	0.2061	0.1526	0.1455
		Minimum	36.44	36.50	36.39	36.61
		Median	36.720	36.780	36.780	36.860
		Maximum	37.22	37.50	36.89	37.11
	End Of Week -1	n	50	50	22	20
		Mean	36.885	36.914	36.879	36.895
		SD	0.1903	0.1841	0.2218	0.2620
		Minimum	36.44	36.17	36.39	36.28
		Median	36.890	36.940	36.890	36.915
		Maximum	37.39	37.33	37.28	37.33
	End Of Week 2	n	50	47	21	20
		Mean	36.844	36.850	36.894	36.856
		SD	0.2094	0.1756	0.1999	0.2486
		Minimum	36.33	36.44	36.56	36.33
		Median	36.805	36.830	36.890	36.890
		Maximum	37.44	37.39	37.44	37.22

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Table 14.3.5.4 Vital Sign Summary (Safety Population)

Measurement (unit)	Study Week	Statistic	Study Product Group			
			VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated
Temperature (°C)	End Of Week 4	n	49	43	19	20
		Mean	36.766	36.811	36.806	36.801
		SD	0.1568	0.1977	0.1248	0.2113
		Minimum	36.50	36.28	36.61	36.39
		Median	36.780	36.830	36.780	36.750
		Maximum	37.11	37.17	37.11	37.39
	End Of Week 6	n	44	42	19	20
		Mean	36.811	36.896	36.846	36.884
		SD	0.2254	0.2272	0.2220	0.2177
		Minimum	36.33	36.39	36.33	36.56
		Median	36.780	36.830	36.890	36.860
		Maximum	37.28	37.44	37.17	37.44
	End Of Study	n	45	47	19	20
		Mean	36.757	36.800	36.815	36.770
		SD	0.2095	0.1781	0.1946	0.1483
		Minimum	36.33	36.39	36.39	36.50
		Median	36.780	36.780	36.830	36.780
		Maximum	37.28	37.33	37.11	37.17

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