

Analysis Data Reviewer's Guide

Philip Morris Products S.A.

Study ZRHM-REXA-08-US

Analysis Data Reviewer's Guide

Contents

1.	Introduction.....	4
1.1	Purpose.....	4
1.2	Acronyms	4
1.3	Study Data Standards and Dictionary Inventory	4
1.4	Source Data Used for Analysis Dataset Creation	5
2.	Protocol Description	5
2.1	Protocol Number and Title.....	5
2.2	Protocol Design in Relation to ADaM Concepts	6
3.	Analysis Considerations Related to Multiple Analysis Datasets	7
3.1	Comparison of SDTM and ADaM Content	7
3.2	Core Variables	7
3.3	Treatment Variables.....	9
3.4	Subject Issues that Require Special Analysis Rules	9
3.5	Use of Visit Windowing, Unscheduled Visits, and Record Selection	9
3.6	Imputation/Derivation Methods.....	10
4.	Analysis Data Creation and Processing Issues	11
4.1	Split Datasets	11
4.2	Data Dependencies.....	11
4.3	Intermediate Datasets	11
4.4	Variable Conventions.....	12
5.	Analysis Dataset Descriptions	13
5.1	Overview.....	13
5.2	Analysis Datasets	13
5.2.1	ADSL – Subject Level Analysis Dataset.....	18
5.2.2	ADAE – Adverse Event Analysis Dataset.....	18
5.2.3	ADBX – Biomarker Exposure Analysis Dataset	19
5.2.4	ADCM – Concomitant Medication Analysis Dataset.....	22
5.2.5	ADCO – Comments Analysis Dataset	23
5.2.6	ADDE – Device Events Analysis Dataset	23
5.2.7	ADDS - Disposition Analysis Dataset.....	23
5.2.8	ADDT - Device Tracking and Disposition Analysis Dataset	23
5.2.9	ADDV – Protocol Deviation Analysis Dataset.....	23

5.2.10 ADEG – ECG Analysis Dataset	23
5.2.11 ADEL – Eligibility Analysis Dataset.....	24
5.2.12 ADEX – Exposure Analysis Dataset	24
5.2.13 ADFA – Findings About Events or Interventions Analysis Dataset.....	24
5.2.14 ADLB – Laboratory Analysis Dataset	24
5.2.15 ADMH – Medical History Analysis Dataset	25
5.2.16 ADPC – Pharmacokinetic Concentration Analysis Dataset.....	25
5.2.17 ADPE – Physical Examination Analysis Dataset	25
5.2.18 ADPP – PK Parameters Analysis Dataset.....	25
5.2.19 ADQSDND – Nicotine Dependence Analysis Dataset	26
5.2.20 ADQSPA – Product Assessment Analysis Dataset	26
5.2.21 ADQSSU – Smoking Urges Analysis Dataset.....	27
5.2.22 ADQSSYM – Symptoms Questionnaire Analysis Dataset.....	27
5.2.23 ADSV – Visit Incidence Analysis Dataset	27
5.2.24 ADVS – Vital Signs Analysis Dataset.....	27
5.2.25 ADXP – Pulmonary Function Analysis Dataset	27
5.2.26 ADXT – Smoking Profile Analysis Dataset	27
6. Data Conformance Summary.....	30
6.1 Conformance Inputs.....	30
6.2 Issues Summary	31
7. Submission of Programs	36
8. Appendix.....	115

1. Introduction

1.1 Purpose

This document provides context for the analysis datasets and terminology that benefit from additional explanation beyond the Data Definition document (define.xml). In addition, this document provides a summary of ADaM conformance findings.

1.2 Acronyms

Acronym	Translation
FTND	Fagerström Test for Nicotine Dependence
HST	Human Smoking Topography
mCC	Menthol conventional cigarettes
MCEQ	Modified Cigarette Evaluation Questionnaire
MNWS	Minnesota Nicotine Withdrawal Scale
PD	Pharmacodynamic
PK	Pharmacokinetic
QSU	Questionnaire of Smoking Urges
SA	Smoking abstinence
SES	Socio-Economic Status
THSm2.2	Tobacco Heating System 2.2 Menthol

1.3 Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	SDTM v1.3/SDTM IG v3.1.3
ADaM	ADaM Model Document 2.1 ADaM Implementation Guide v1.0
Data Definitions	Define.xml v2.0
Socio-Economic Status Questionnaire	King et al. 2011
Fagerström Test for Nicotine Dependence	Revised version (Heatherton et al. 1991), as updated in 2012 (Fagerström et al. 2012)

Standard or Dictionary	Versions Used
Questionnaire of Smoking Urges-Brief	Cox et al. 2001
Modified Cigarette Evaluation Questionnaire	Cappelleri et al. 2007
Minnesota Nicotine Withdrawal Scale (revised edition) Questionnaire	Hughes and Hatsukami 2008
Behavioral Risk Factor Surveillance System Questionnaire 2011	CDC, 2011
Prochaska 'Stage of Change' Questionnaire	DiClemente et al. 1991 and Velicer et al. 1995
Medications Dictionary	WHO March 2013
Medical Events Dictionary	MedDRA v16.0

1.4 Source Data Used for Analysis Dataset Creation

In addition to the SDTM datasets, the source data contains CRF raw data IE_E, IE_E_ADM, IE_E_SF, IE_I, IE_I_ADM and IE_I_SF (these datasets were used in the creation of ADEL - see Section 5.2.11), and data in the form of an excel spreadsheet BANNEDMEDS.XLSX (this spreadsheet was used in the creation of ADCM to identify the half-lives for meds which impacted CYP1A2, 11-DTX-B2, and CYP2A6 - see Section 5.2.4).

2. Protocol Description

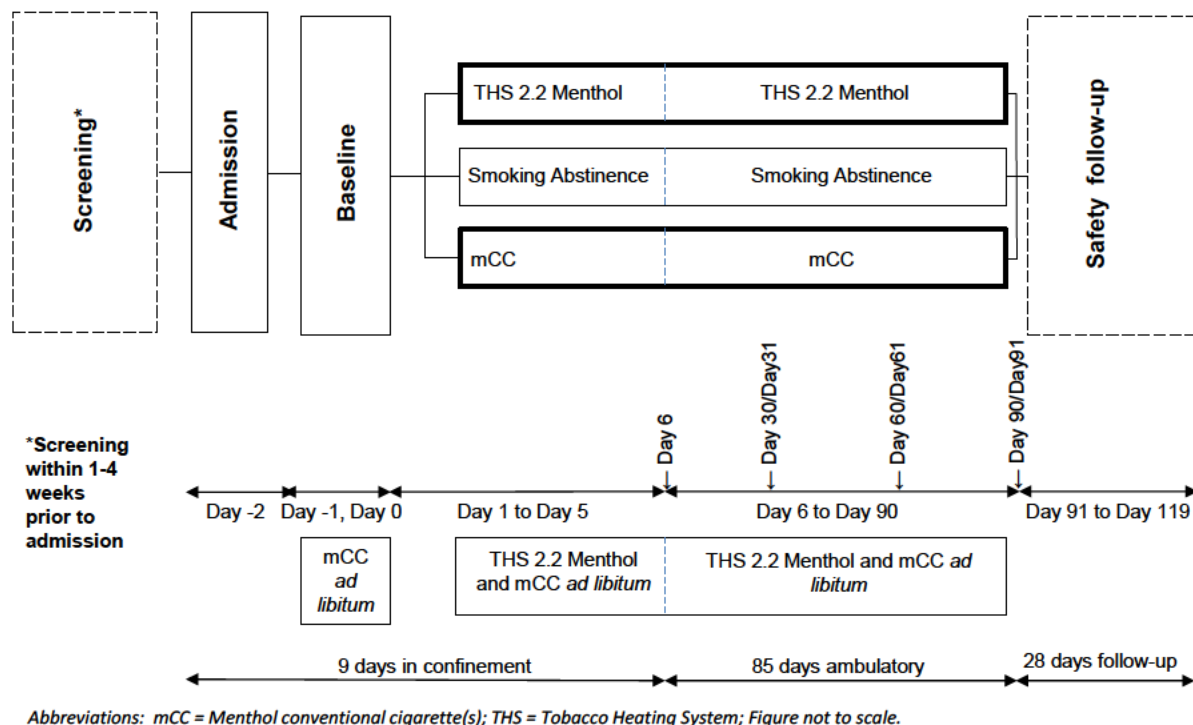
2.1 Protocol Number and Title

Protocol Number: ZRHM-REXA-08-US

Protocol Title: A randomized, controlled, open-label, 3-arm parallel group, multi center study to demonstrate reductions in exposure to selected smoke constituents in apparently healthy smokers switching to the Tobacco Heating System 2.2 Menthol (THS 2.2 Menthol) or observing smoking abstinence, compared to continuing to use menthol conventional cigarettes, for 5 days in confinement and prolonged by 86 days in an ambulatory setting

Protocol Versions: Final 5.0, 14 April 2014

2.2 Protocol Design in Relation to ADaM Concepts



Prior to enrolment on Day -2, as the last procedure of the eligibility assessments, subjects had a product test of the THS 2.2 Menthol. All subjects who tested the product, whether or not if they continued further into the study, were considered to be part of the Safety Population. On Day 0, subjects were randomized to one of 3 arms – THS 2.2 Menthol (THSm2.2), Smoking Abstinence (SA), or menthol conventional cigarettes (mCC). After subjects completed the Day 91 safety assessments (or if they were prematurely withdrawn from the study), they entered a 28-day safety follow-up period. This includes subjects who were not enrolled into the study but tested the product on Day -2.

Treatment group assignment was stored in the SDTM.DM domain. It was used in ADaM datasets to derive the treatment group (TRT01P/TRT01PN and TRT01A/TRT01AN) variables. There were no instances of subjects using a treatment other than what they were randomized to. The variables TRTP/TRTPN and TRTA/TRTAN are used on non-ADSL datasets for consistency with ADaM standards and contain the same values as TRT01P/TRT01PN and TRT01A/TRT01AN, respectively.

TRTSDTM and TRTEDTM refer to the start and end of randomized treatment use in the randomized treatment period from Day 1 to Day 91. Note that for subjects randomized to the SA arm who do not have exposure to randomized product, per the SAP, the treatment period starts on Day 1 at 10:00 AM and ends on the last visit date at 11:00 PM (unless they discharge earlier in the day).

Many of the BDS datasets also contain variables called APUPER/APUPERC and/or ASPER/ASPERC to designate the study period when the event or visit took place and these are used in analyses as needed. The confinement period of Days 1-6 (until discharge) is designated as Period 1. The ambulatory period

was broken into 3 smaller periods as Period 2 ([Day 6 ambulatory - Day 30 Visit]), Period 3 ([Day 30 Visit - Day 60 Visit]) and Period 4 ([Day 60 Visit - Day 90 Visit]).

Each ambulatory visit is comprised of 2 study days. References to the Day 30 Visit include nominal Days 30 and 31, references to the Day 60 Visit include nominal Days 60 and 61, and references to the Day 90 Visit include nominal Days 90 and 91. Depending on the parameter, data are collected at 1 of the 2 days (see protocol Study Assessments table) during each ambulatory visit. For 24-hour urine collections taken on Days x to y (e.g., Days 5 to 6), these are referred to as collected on Day x (e.g., Day 5) in the datasets.

3. Analysis Considerations Related to Multiple Analysis Datasets

3.1 Comparison of SDTM and ADaM Content

- Are data for screen failures, including data for run-in screening (for example, SDTM values of ARMCD='SCRNFAIL', or 'NOTASSGN') included in ADaM datasets?

Yes, all subjects in the SDTM database were used in ADaM datasets.

- Are data taken from an ongoing study?

No, this is a final locked database.

- Values of baseline are not always identical between SDTM domains (xxSTRESN/xxSTRESC where ABLFL='Y') and ADaM datasets (AVAL/AVALC where ABLFL='Y'). In the SDTMs, baseline refers to the last measurement on or before RFSTDTC (either the date/time of first randomized product used on Day 1 or Day 1 date for the SA arm). For the ADaMs, baseline is determined the same for the THSm2.2 and mCC arms but it is the last measurement on or before 10:00 AM on Day 1 for the SA arm. One exception is found in ADBX.PARAMCD=CO – this parameter is collected at 4 timepoints throughout the day on Days -1 to 5 during the confinement period and so baseline is defined separately for each timepoint as noted in BASETYPE.

3.2 Core Variables

Core variables are those that are represented across all/most analysis datasets.

Variable Name	Variable Description
USUBJID	Unique subject identifier
STUDYID	Study identifier used for this protocol
SUBJID	Subject Identifier for the Study
SITEID	Study Site Identifier
AGE	Age
SEX	Sex
SEXN	Sex (N)

Variable Name	Variable Description
RACE	Race
HEIGHT	Screening Height (cm)
WEIGHTBL	Baseline Weight (kg)
BMI	Baseline Body Mass Index (kg/m ²)
UCPDGR1	Usual Daily Cig Consumption Category
UCPDGR1N	Usual Daily Cig Consumption Category (N)
ENRLFL	Enrolled Population Flag
SCRFFL	Screen Failure Flag
COMPLFL	Completers Population Flag
SAFBFL	Safety Pop. Before Rand. Flag
SAFAFL	Safety Pop. After Rand. Flag
FASFL	Full Analysis Set Population Flag
PPROT1FL	Per-Protocol Population Flag - Period 1
PPROT2FL	Per-Protocol Population Flag - Period 2
PPROT3FL	Per-Protocol Population Flag - Period 3
PPROT4FL	Per-Protocol Population Flag - Period 4
RANDFL	Randomized Population Flag
EXFL	Exposed not Enrolled Flag
EXNOTRFL	Exposed not Randomized Flag
ENFL	Enrolled not Randomized Flag
TRTSDTM	Datetime of First Exposure to Treatment
TRTSDT	Date of First Exposure to Treatment
TRTEDTM	Datetime of Last Exposure to Treatment
TRTEDT	Date of Last Exposure to Treatment
TRTP	Planned Treatment
TRTPN	Planned Treatment (N)
TRTA	Actual Treatment
TRTAN	Actual Treatment (N)

3.3 Treatment Variables

ARM versus TRTxxP

- Are the values of ARM equivalent in meaning to values of TRTxxP?

For randomized subjects, ARM and TRT01P are equivalent in meaning. For non-randomized subjects, TRT01P is derived into more detail than found in ARM.

ACTARM versus TRTxxA

- If TRTxxA is used, then are the values of ACTARM equivalent in meaning to values of TRTxxA?

For randomized subjects, the values of ACTARM in SDTM are equivalent in meaning to the values of TRT01A, and TRT01A is the same as TRT01P. For non-randomized subjects, TRT01A and ACTARM are similar in meaning with TRT01A=Product Test used for subjects with ACTARM=Not Assigned, to help identify subjects who tested the product. Refer to the define.xml file for further details.

Use of ADaM Treatment Variables in Analysis

- Are both planned and actual treatment variables used in analyses?

There are no differences between the planned and actual arm for randomized subjects, therefore either can be used in analyses. For non-randomized subjects in safety summaries which contain a 'Product Test' arm (subjects who tested THSm2.2 on Day -2), then TRT01A='Product Test' is used to identify those subjects.

3.4 Subject Issues that Require Special Analysis Rules

Subject DAY-1042, randomized to THSm2.2, withdrew consent of protected health information on 26Feb2014. As a result, data entered, collected, or source data verified after that date are not in the SDTMs or ADaMs, with the exception of adverse events, medications related to adverse events, end of study and withdrawal pages, questionnaire, and dosing diary data. This subject is in the FAS population because there was exposure data in the dosing diary, however, the subject's TRTSDT (Day 1) is noted as 22Jan2014 (which is technically Study Day 6) rather than 17Jan2014 since the confinement period dosing records were removed from the database.

3.5 Use of Visit Windowing, Unscheduled Visits, and Record Selection

- Was windowing used in one or more analysis datasets?

Visit windowing was applied to data in ADBX, ADEG, ADLB, ADPE, ADQSPA, ADQSSYM, ADQSSU, ADQSND, ADXT datasets. Visit windowing was used in cases where the subject terminated early from the confinement or ambulatory period and so were assigned Day 6/Discharge Confinement or Day 91/Discharge Ambulatory Visits, respectively, in SDTMs. These visits were reassigned to the closest scheduled visit.

Assessment windows noted in SAP Section 11.1.3 (Table 23) were also used to identify records in ADaMs which were out of protocol collection windows (using DEVN and DEVWC). Most of these out-of-window records were still used in analyses with the following 2 exceptions:

- ADBX: for the sensitivity analyses of biomarkers of exposure using proc mixed (see SAP section 12.6.1.3), biomarker records which were collected outside the assessment window were set to ANL01FL=missing and not used in the sensitivity analyses.
- ADPC: plasma nicotine and cotinine records which were collected outside the assessment window were set to ANL01FL=missing and not used in analyses.

In addition, in ADBX, a time-matched algorithm was created using BASETYPE for PARAMCD=CO to align the up to 4 measurements which were collected on each day during the Confinement Period with the 4 baseline measurements (see Section 4.4 for details).

- Were unscheduled visits used in any analyses?

Unscheduled visits were used as the baseline value if they were the latest value before the treatment period. Otherwise, unscheduled visits were not summarized in any analyses.

3.6 Imputation/Derivation Methods

- If date imputation was performed, were there rules that were used in multiple analysis datasets?

For subjects randomized to SA, the time component of TRTSDTM and TRTEDTM were imputed. The start time on Day 1 was imputed to 10:00. The end time was imputed to 23:00 (or time of discharge if discontinued early) on the last visit date. No other dates were imputed.

Additional Content of Interest

The following values were used for DTYPE across the various ADaMs:

Controlled terminology	Definition
AVERAGE	Value derived as an average of 2 or more parameter values
BLQHALF	BLQ values set to half the LLOQ during the profile refer to SAP section 12.1.5
FUNCTION	Value derived as a function of 2 or more parameter values or a unit conversion
LOCF	Value derived using last observation carried forward
RATIO	Value derived as a ratio of 2 parameter values
SUM	Value derived as a sum of 2 or more parameter values

In particular, in the efficacy analysis, PARAMTYP='DERIVED' and DTYPE='RATIO' or 'FUNCTION' if the parameter was a combination of other existing parameters. Also, in cases where the original value was below the limit of quantification (original value contained in AVALC), a new record was created using $1/2 \times$ the lower limit in AVAL and DTYPE='BLQHALF'. Finally, DTYPE='LOCF' was used in cases where last observation carried forward was used to impute a value. Baseline values

were eligible to be carried forward to post-baseline values. For PARAMCD='CO' in which measurements on Days -1 to 5 during the confinement period were collected at 4 timepoints throughout the day, missing values were imputed using the time-matched (refer to BASETYPE) previous value (see Section 4.4).

In ADSL, there were several variables which were created using imputation. Refer to SAP Section 12.1.5 for details. In particular, if less than 75% of product use assessments over a period were available, or if product use assessments were missing over a period of more than 7 days, the Day 0 cigarette consumption data was used for the missing days to determine:

- the percentage of THS use (see SAP Section 6.3.3.1) for product use category variables PUCAT2-PUCAT4 (and GPUCAT2-GPUCAT4) for time periods 2-4, respectively. PUCAT5 (GPUCAT5) were created to determine the product use category variables over the entire ambulatory period. For subjects randomized to THSm2.2 identified as 'Primarily THS 2.2' or 'Primarily CC' (see SAP Figure 2), PUCAT2EX, PUCAT3EX, PUCAT4EX, and PUCAT5EX were used to identify whether THS 2.2. or CC were exclusively used during each respective period. PUCAT/GPUCAT variables were not available for period 1 because all subjects were compliant to the randomized product during confinement.
- compliance to randomized product (see SAP Table 21 for product compliance definition in ambulatory period) in variables CMPCP2FL-CMPCP4FL for periods 2-4, respectively

In ADSL, variables PUCAT1, GPUCAT1, and PUCAT1EX were created to capture product use categories over the entire ambulatory period without imputation. In particular, PUCAT1 was used in adverse event summaries.

4. Analysis Data Creation and Processing Issues

4.1 Split Datasets

There were no datasets that were split due to size constraints.

4.2 Data Dependencies

ADSL was used in the creation of all other analysis datasets. ADEX was used in the creation of ADQSSYM. ADCM was used in the creation of ADBX.

4.3 Intermediate Datasets

A PKMERGE intermediate dataset was used in support of the creation of ADPC as well as this file was used by the pharmacokineticist to calculate the pharmacokinetic parameters. This file was created using SDTM.DM, SDTM.SUPPDM, SDTM.DS, SDTM.DX, SDTM.EX, SDTM.PC, and SDTM.VS. This file calculated relative times from start of exposure on Study Day 5 for the nicotine and cotinine Day 5 & Day 6 concentrations in the THSm2.2 and mCC arms.

The intermediate spreadsheet, BANNEDMEDS.XLSX, was provided to the medical monitor to flag meds which could impact CYP1A2, 11-DTX-B2, and CYP2A6 assessments and to provide the corresponding half-lives for those medications. This spreadsheet was then combined with SDTM.CM in the creation of ADCM.

The raw datasets IE_E, IE_E_ADM, IE_E_SF, IE_I, IE_I_ADM and IE_I_SF coming from the EDC extract were used in the creation of ADEL so that all inclusion and exclusion responses (not just violations captured in SDTM.IE) could be included.

All intermediate datasets and spreadsheets noted above can be found in the define.xml.

4.4 Variable Conventions

In ADBX, PARAMCD='CO' is collected at 4 timepoints throughout the day on Days -1 to 5 during the confinement period and so baseline is defined as the last measurement prior to the start of treatment (for THSm2.2 and mCC arms) or 10:00 AM (for SA arm) for each timepoint as noted in BASETYPE. As such, each subject has up to 4 ABLFL='Y' values, one for each BASETYPE. For Days 6, 30, 60, and 90, in which only 1 CO measurement/day was collected, baseline was selected as the 2nd timepoint (12:00-13:30) since that generally reflected the closest timepoint. The BASE, CHG, and PCHG values were then derived using the ABLFL='Y' record on each combination of AVISIT and ATPT.

5. Analysis Dataset Descriptions

5.1 Overview

- Do the analysis datasets support all protocol- and statistical analysis plan-specified objectives?

Yes, all analyses were done using the ADaM datasets as input.

Additional Content of Interest

As noted in the SAP, this study has 4 Per Protocol flags created in ADSL and copied to other ADaMs. PPROT1FL-PPROT4FL represent the Per Protocol designation for each subject in each of the 4 study periods (see Section 2.2 above). As descriptive statistics and inferential analyses were summarized over time for the PP Set, the underlying analyses were repeated 4 times since the subjects included in each PP Set for the period was different. For example, when analyzing the endpoints for primary objectives at Day 5 and Day 90, the subjects with PPROT1FL='Y' were used in the Day 5 analysis while the subjects with PPROT4FL='Y' were used in the Day 90 analysis.

As noted in the SAP, the Compliant Population is a subset of the Per Protocol Set. As such, there were 4 flags created in ADSL and copied to ADBX, COMPP1FL-COMPP4FL, to represent the Compliant Population designation for each subject in each of the 4 study periods. These flags were used in a similar manner to that noted for the Per Protocol Set flags above.

Many of the BDS datasets also contain variables called APUPER/APUPERC and/or ASPER/ASPERC to designate the study period when the event or visit took place and these were used in analyses as needed when summarizing data by study period.

5.2 Analysis Datasets

Dataset – Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
<u>ADSL</u> : Subject Level Analysis Dataset	ADSL			X			One record per subject
<u>ADAE</u> : Adverse Event Analysis Dataset	OTHER		X				One record per subject per adverse event

Dataset – Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
<u>ADB</u> X: Biomarker Exposure Analysis Dataset	BDS	X				X	One record per subject per visit per parameter category per parameter per timepoint per date/time per lab sequence per derivation type
<u>ADCM</u> : Concomitant Medication Analysis Dataset	OTHER		X				One record per subject per concomitant medication per date
<u>ADCO</u> : Comments Analysis Dataset	OTHER			X			One record per subject per comment.
<u>ADDE</u> : Device Events Analysis Dataset	OTHER		X				One record per subject per device event
<u>ADDS</u> : Disposition Analysis Dataset	OTHER			X			One record per subject per collection date per disposition status or protocol milestone
<u>ADDT</u> : Device Tracking and Disposition Analysis Dataset	OTHER			X			One record per subject per device event category per device ID per device event per visit per sponsor-define identifier

Dataset – Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
<u>ADDV</u> : Protocol Deviation Analysis Dataset	OTHER			X			One record per subject per deviation category per deviation start date/time per visit per assessment per analysis value per sequence number
<u>ADEG</u> : ECG Analysis Dataset	BDS		X				One record per subject per visit per timepoint per parameter
<u>ADEL</u> : Eligibility Analysis Dataset	BDS			X			One record per subject per visit per parameter
<u>ADEX</u> : Exposure Analysis Dataset	OTHER		X				One record per subject per visit per parameter per product use period per treatment start date/time per treatment end date/time per source domain per source domain sequence number
<u>ADFA</u> : Findings About Events or Interventions Analysis Dataset	BDS		X	X			One record per subject per visit per parameter

Dataset – Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
<u>ADLB</u> : Laboratory Analysis Dataset	BDS	X	X				One record per subject per visit per timepoint per parameter per lab sequence number
<u>ADMH</u> : Medical History Analysis Dataset	OTHER		X	X			One record per subject per medical history category per medical history event
<u>ADPC</u> : Pharmacokinetic Concentration Analysis Dataset	BDS	X			X		One record per subject per visit per parameter per timepoint per sequence number per analysis value
<u>ADPE</u> : Physical Examination Analysis Dataset	BDS		X				One record per subject per visit per parameter per PE ID
<u>ADPP</u> : PK Parameters Analysis Dataset	BDS				X		One record per subject per visit per parameter category per parameter
<u>ADQSND</u> : Nicotine Dependence Analysis Dataset	BDS	X		X			One record per subject per visit per parameter category per parameter per start date per sequence number

Dataset – Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
<u>ADQSPA</u> : Product Assessment Analysis Dataset	BDS	X					One record per subject per visit per parameter category per parameter
<u>ADQSSU</u> : Smoking Urges Analysis Dataset	BDS	X					One record per subject per visit per parameter
<u>ADQSSYM</u> : Symptoms Questionnaire Analysis Dataset	BDS		X				One record per subject per visit per parameter
<u>ADSV</u> : Visit Incidence Analysis Dataset	OTHER			X			One record per subject per visit
<u>ADV</u> S: Vital Signs Analysis Dataset	BDS	X	X				One record per subject per visit per date/time of measurement per timepoint per parameter per analysis value
<u>ADXP</u> : Pulmonary Function Analysis Dataset	BDS		X				One record per subject per parameter category 1 per visit per timepoint per parameter
<u>ADXT</u> : Smoking Profile Analysis Dataset	BDS	X					One record per subject per visit per parameter per reference ID per sequence number per filter vial number per start date/time

5.2.1 ADSL – Subject Level Analysis Dataset

In addition to supporting all analyses, ADSL contains variables to also support baseline characteristics and disposition analyses. The population indicator variables (Enrolled Population flag ENRLFL, Screen Failure flag SCRFFL, Completers Population flag COMPLFL, Safety Population Before Randomization flag SAFBFL, Safety Population After Randomization flag SAFAFL, Full Analysis Set flag FASFL, Per Protocol Population in Period 1 flag PPROT1FL, Per Protocol Population in Period 2 flag PPROT2FL, Per Protocol Population in Period 3 flag PPROT3FL, Per Protocol Population in Period 4 flag PPROT4FL, Compliant Population in Period 1 flag COMPP1FL, Compliant Population in Period 2 flag COMPP2FL, Compliant Population in Period 3 flag COMPP3FL, Compliant Population in Period 4 flag COMPP4FL, Randomized Population flag RANDFL, Exposed Not Enrolled flag EXFL, Exposed Not Randomized flag EXNOTRFL, and Enrolled Not Randomized flag ENFL) are defined in ADSL and copied into other analysis datasets as needed. All subjects in DM were included in ADSL including screen failure subjects. All covariates used in statistical analyses of primary and secondary efficacy analysis are present in ADSL and are listed below.

Treatment group – ADSL.TRT01P (ADSL.TRTP in ADBX)

Sex – ADSL.SEX

Screening cigarette consumption – ADSL.UCPDGR1

LVISIT is recorded as the last visit attended by each subject, either Screening for subjects who did not enroll, or the last post-enrollment visit for those who did enroll. The dates associated with last visit, LVISDT and LVISDTC, are the final visit dates, including any unscheduled visit dates. LVISDAY is the number of days between first randomized product use on Day 1 and the final visit date for the subject (LVISDT-TRTSDT+1).

DSREAS is the primary term for study discontinuation as recorded in the CRF.

5.2.2 ADAE – Adverse Event Analysis Dataset

ADAE contains all observations from AE and SUPPAE. TRTEMFL = Y is used to indicate exposure emergent AEs which were used in summary tables. This data contains observations for screen failure subjects which are listed only.

The data are coded under the System Organ Class variable AEBODSYS and Preferred Term variable AEDECOD.

The following flagging variables were provided:

ANL01FL – Indicates the AE was product emergent (TRTEMFL=Y).

ANL02FL – Indicates the AE was product emergent and subject withdrew from the study due to that AE (AEACNOTH = 'DISCONTINUED STUDY').

ANL03FL – Indicates the AE was product emergent and action was taken (AEACNP1N in 1,2,3).

ANL04FL - Indicates the AE was product emergent and concomitant medication was taken for the AE (AECONTRT=Y).

ANL05FL – Indicates the AE was product emergent and other action was taken (AEACNOTH populated).

5.2.3 ADBX – Biomarker Exposure Analysis Dataset

ADBX supports the efficacy analyses of biomarkers of exposure for the primary and secondary objectives (see Protocol Table S1). ADBX contains the biomarker of exposure data captured in 24-hour urine, blood (PARAMCD='CARBHXGB'), and exhaled breath (PARAMCD='CO') found in LB. For the 24-hour urine data, each biomarker is presented as a concentration, as well as corrected for creatinine (PARAMCD ending in 'CRE') and excreted over 24 hours (PARAMCD ending in '24U'). ADBX also contains data for CYP1A2, CYP2A6, Ames mutagenicity, and risk markers in 24-hour urine (11-DTX-B2 and 8-epi-PGF-2 α) found in LB. In addition, to support some exploratory analysis, 4-hour urine fraction data were also included and these data are collected as a concentration and corrected for creatinine (PARAMCD ending in 'CRE4'). Parameters that were derived were identified with PARAMTYP='DERIVED' and DTYPE='FUNCTION' or 'RATIO'.

Most parameters in ADBX have a single baseline value. The exception is PARAMCD='CO' which is collected at 4 timepoints throughout the day on Days -1 to 5 during the confinement period and so baseline is defined for each timepoint as noted in BASETYPE. BASETYPE takes on the format of 'TIME MATCHED DAY y (x)', where x refers to the 4 time periods within a day [1='WITHIN 15 MIN PRIOR TO SMOKING' (all arms on Day 0 or for THS/mCC arms on Day 1) or '08:00 – 09:30' (for SA arm on Day 1), 2='12:00 - 13:30', 3='16:00 - 17:30', and 4='20:00 - 21:30') and y refers to the study day (-1 or 0)]. As such, each subject has up to 4 ABLFL='Y' values, one for each BASETYPE. For Days 6, 30, 60, and 90, in which only 1 CO measurement/day was collected, baseline was selected as the 2nd timepoint (12:00-13:30) since that generally reflected the closest timepoint. The BASE, CHG, and PCHG values were then derived using the ABLFL='Y' record on each combination of AVISIT and ATPT.

Some parameters had values below the limit of quantification (AVALC contains '<' and AVAL=missing and BLOQFL='Y'). In those cases, a new record was created with AVAL set to ½ x the lower limit of quantification and DTYPE='BLQHALF' and AQLFL='Y'. These newly created records were flagged for analysis with ANL02FL='Y'.

Analysis visits (AVISIT) were generally derived directly from the SDTM.VISIT value. Visit windowing was only used in cases where the subject terminated early from the confinement or ambulatory period and so were assigned Day 6/Discharge Confinement or Day 91/Discharge Ambulatory Visits, respectively, in SDTMs. These visits were reassigned to the closest scheduled visit. In cases of early termination or missed scheduled visits, LOCF records were created so that scheduled visits existed for each subject for each parameter (as expected in the protocol). These records are identified with DTYPE='LOCF' and LOCF was used in the primary proc glm analysis for the biomarkers of exposure for the primary and secondary objectives. LOCF records were not use in the proc mixed sensitivity analyses.

For the efficacy analysis variables in ADBX, ANL02FL='Y' indicates the visits used in the primary proc glm analyses. For the sensitivity analyses of biomarkers of exposure using proc mixed (see SAP section 12.6.1.3), ANL01FL='Y' was also used to only select values which occurred within the visit windows noted in SAP Table 23. Additional supportive analyses for 11-DTX-B2, 8-epi-PGF-2 α , and CYP1A2

were conducted in which assessments performed within 5 half-lives since the use of a medication impacting their results was excluded. For these analyses, ANL03FL='Y' was also used.

Therefore, AVAL records with ANL02FL='Y' are used for the primary proc glm analysis of biomarkers of exposure. AVAL records with ANL02FL='Y' and ANL01FL='Y' and DTYPE^='LOCF' were used for the proc mixed sensitivity analysis of biomarkers of exposure.

For the Per Protocol Set analyses, PPROT1FL-PPROT4FL represent the Per Protocol designation for each subject in each of the 4 study periods (see Section 2.2 above). As descriptive statistics and inferential analyses were summarized over time for the PP Set, the underlying analyses were repeated 4 times since the subjects included in each PP Set for the period was different. For example, when analyzing the endpoints for the primary objectives at Day 5 and Day 90, the subjects with PPROT1FL='Y' were used in the Day 5 analysis while the subjects with PPROT4FL='Y' were used in the Day 90 analysis. There is only 1 Full Analysis Set population flag and those analyses are designated using FASFL='Y'.

The following table shows the biomarkers of exposure analyzed.

PARAMCD Value	PARAM Value	Endpoints for Primary/Secondary/Exploratory Objectives
UMHBMCRE	MHBMA (pg/mg creat)	Primary
UMHBM24U	MHBMA (ng)	Secondary
U3HPMCRE	3-HPMA (ng/mg creat)	Primary
U3HPM24U	3-HPMA (ug)	Secondary
USPMACRE	S-PMA (pg/mg creat)	Primary
USPMA24U	S-PMA (ng)	Secondary
CARBHXGB	Carboxyhemoglobin (%)	Primary
UNNALCRE	Total NNAL (pg/mg creat)	Primary
UNNAL24U	Total NNAL (ng)	Secondary
CO	Exhaled CO (ppm)	Secondary

PARAMCD Value	PARAM Value	Endpoints for Primary/Secondary/Exploratory Objectives
U1OHPCRE	Total 1-OHP (pg/mg creat)	Secondary
U1OHP24U	Total 1-OHP (ng)	Secondary
UNNNCRE	NNN (pg/mg creat)	Secondary
UNNN24U	NNN (ng)	Secondary
U4ABPCRE	4-ABP (pg/mg creat)	Secondary
U4ABP24U	4-ABP (ng)	Secondary
U1NACRE	1-NA (pg/mg creat)	Secondary
U1NA24U	1-NA (ng)	Secondary
U2NACRE	2-NA (pg/mg creat)	Secondary
U2NA24U	2-NA (ng)	Secondary
UOTOLCRE	o-tol (pg/mg creat)	Secondary
UOTOL24U	o-tol (ng)	Secondary
UCEMACRE	CEMA (ng/mg creat)	Secondary
UCEMA24U	CEMA (ug)	Secondary
UHEMACRE	HEMA (pg/mg creat)	Secondary
UHEMA24U	HEMA (ng)	Secondary
UBAPCRE	B[a]P (fg/mg creat)	Secondary
UBAP24U	B[a]P (pg)	Secondary

PARAMCD Value	PARAM Value	Endpoints for Primary/Secondary/Exploratory Objectives
UHMPMCRE	HMPMA (ng/mg creat)	Secondary
UHMPM24U	HMPMA (ug)	Secondary
USBMACRE	S-BMA (pg/mg creat)	Secondary
USBMA24U	S-BMA (ng)	Secondary
UNEQCRE	NEQ (mg/g creat)	Secondary
UNEQ24U	NEQ (mg)	Secondary
UPGF2CRE	Prostaglandin F2 Alpha (pg/mg creat)	Secondary
UPGF224U	Prostaglandin F2 Alpha (ng)	Secondary
UTXB2CRE	11-Dehydro-Thromboxane B2 (pg/mg creat)	Secondary
UTXB224U	11-Dehydro-Thromboxane B2 (ng)	Secondary
CYP1A2	CYP1A2 Activity (%)	Secondary
CYP2A6	CYP2A6 Activity (%)	Exploratory

5.2.4 ADCM – Concomitant Medication Analysis Dataset

ADCM contains all observations and required variables from CM and SUPPCM. Refer to an external spreadsheet BANNEDMEDS.XLSX (see Section 4.3) for the list of medications impacting CYP2A6, CYP1A2, and 11-DTX-B2, and this is used to populate CRIT1FL, CRIT2FL, CRIT3FL, and HALFLIFE. CRIT1FL=Y indicates if any medication affects CYP2A6, CRIT2FL=Y indicates if any medication affects CYP1A2, and CRIT3FL=Y indicates if any medication affects 11-DTX-B2. HALFLIFE is the corresponding half-life of the medication which impacts at least one of those 3 parameters. CMFL=Y indicates the medication is concomitant. PMFL=Y indicates the medication is prior. This dataset includes medications recorded for screen failure subjects.

5.2.5 ADCO – Comments Analysis Dataset

ADCO contains all observations from CO. ADOMAIN indicates the source dataset and ASEQ indicates the sequence number from the source dataset for traceability.

5.2.6 ADDE – Device Events Analysis Dataset

ADDE contains all observations and required variables from DE and SUPPDE and includes a record for any subject who took part in the device test and enrolled into the study, even if they didn't experience a device event (note that subject DAY-1023, who did not experience a device event, was not included in this dataset even though they did take the product test – this subject was the only subject who took the product test but didn't enroll into the study). The variable ANYDEFL=Y indicates a device event was experienced.

5.2.7 ADDS - Disposition Analysis Dataset

ADDS contains all observations from DS and SUPPDS. Follow-up has not been included as a visit as it was undertaken as a telephone call so information on subjects taking part in the followup assessments are included in this dataset. This dataset includes observations for screen failure subjects.

5.2.8 ADDT - Device Tracking and Disposition Analysis Dataset

ADDT contains all observations from DT for the identification of devices and collection, distribution, and replacement information from the CRF.

5.2.9 ADDV – Protocol Deviation Analysis Dataset

ADDV contains all observations from DV except that deviations with DV.DVCAT=MIS-USE OF PRODUCT were removed and replaced by records coming from ADSL (which used compliance imputation rules as defined in SAP). In particular, deviations with ADDV.DVCAT= MIS-USE OF PRODUCT IN PERIOD x were created from ADSL when CMPCPxFL=N and PPREASx ^= 'Discontinued in previous period' (for the same value of 'x'). These 'mis-use of product' deviations were based on SAP Table 21 to determine major product compliance deviations in each study period according to imputation rules noted in SAP Section 12.1.5. PARAMCD and PARAM are derived from the SAP tables 21 and 22. This dataset contains observations for screen failure subjects which are listed only.

DVSIG indicates if the protocol deviation category is (Minor/Major). For any major protocol deviations, the EVALCAT indicates if it impacts (EVALCAT=NON EVALUABLE) or does not impact (EVALCAT=EVALUABLE) the evaluability of the subject for the Per Protocol populations.

5.2.10 ADEG – ECG Analysis Dataset

ADEG contains all observations from EG and SUPPEG. Fridericia's Correction Formula (QTcF) is derived and included in all output for ECG data. ANL01FL=Y is used to indicate which values are used in summary statistics. Reference ranges were not used to assess this data.

5.2.11 ADEL – Eligibility Analysis Dataset

The CRF datasets IE_E, IE_E_ADM, IE_E_SF, IE_I, IE_I_ADM and IE_I_SF are used to create this dataset as only abnormal responses are stored in SDTM.IE. The description of the eligibility criteria is defined in the Parameter Value Level Metadata section contained within the define.xml. This dataset contains observations for screen failure subjects which are listed only.

5.2.12 ADEX – Exposure Analysis Dataset

ADEX contains all observations from EX/SUPPEX and DX/SUPPDX, as well as records from SU with SUCAT in ('NRT_USE', 'TOB_USE'). Exposure records from both the product administration log used during the confinement period (PARCAT2='PRODUCT USE CONFINEMENT') as well as the product diary used during the ambulatory period (PARCAT2='PRODUCT USE DIARY – ELECTRONIC' or 'PRODUCT USE DIARY – PAPER') are included.

During confinement, each THSm2.2 stick and/or each mCC used by a subject are recorded separately and derivations are then performed to calculate the number of THSm2.2 sticks and the number of mCC used by a subject each day (PARAMCD='DTHS2_2' or 'DMCC'). During the ambulatory period, the number of THSm2.2 sticks, the number of mCC, and the number of other tobacco products are recorded per day. Derivations are then done to calculate the average number of daily products used in Periods 2, 3, and 4 (PARAMCD starting with 'PD' and period noted by APUPER) as well as the average number of daily products used over the entire ambulatory period (PARAMCD starting with 'AD').

Records with ANL01FL='Y' are used to flag the maximum daily use by subject for each product in each period for Periods 2, 3, and 4. Records with ANL02FL='Y' are used to flag the maximum daily use by subject for each product across the entire ambulatory period.

5.2.13 ADFA – Findings About Events or Interventions Analysis Dataset

ADFA contains all observations from FA and SUPPFA. This dataset contains observations for screen failure subjects which are listed only.

5.2.14 ADLB – Laboratory Analysis Dataset

ADLB contains all observation from LB and SUPPLB identified under LBCAT of HAEMATOLOGY, CLINICAL CHEMISTRY, SEROLOGY, COTININE SCREENING, ALCOHOL TEST, DRUG SCREEN, PREGNANCY, URINALYSIS (excluding LBTESTCD=VOLUME), and BIOMARKERS (records with LBGRPID=RISK MARKERS). ANL01FL=Y indicates the values to be used in summary statistics. This dataset contains observations for screen failure subjects which are listed only. ANRIND contains the normal range indicator while ACLSIG contains the clinical significance. Some parameters had values below the limit of quantification (BLOQFL='Y'). In those cases, AVAL was set to ½ x the lower limit of quantification found in AVALC.

PARCAT3='Risk Markers' identify lab parameters used in risk marker analyses. Subjects with missing risk marker data at scheduled visits have records with DTYPE=LOCF to identify records which are carried forward from an earlier visit.

PARCAT4 is used to identify whether lab tests are evaluated for toxicity grading in a single direction (high or low) or bi-directional. For those parameters with PARCAT4='Single-directional (High) CTC grade parameter', then LBTOXH indicates the toxicity name for the summary table. The grades for baseline appear in BTOXGRH, for post-baseline in ATOXGRH, and for the shift in SHIFT2. For those parameters with PARCAT4='Single-directional (Low) CTC grade parameter', then LBTOXL indicates the toxicity name for the summary table. The grades for baseline appear in BTOXGRL, for post-baseline in ATOXGRL, and for the shift in SHIFT3. For those parameters with PARCAT4='Bi-directional CTC grade parameter', then LBTOXH, BTOXGRH, ATOXGRH, and SHIFT2 indicate the high toxicities and separate summaries for LBTOXL, BTOXGRL, ATOXGRL, and SHIFT3 indicate the low toxicities.

5.2.15 ADMH – Medical History Analysis Dataset

ADMH contains all observation from MH. ANYMHFL=Y indicates the observation is a medical history. ANYCDFL=Y indicates the observation is a concomitant disease. MHONGFL=Y indicates the concurrent disease is ongoing during the study.

The data are coded under the System Organ Class variable MHBODSYS and Preferred Term variable MHDECOD.

5.2.16 ADPC – Pharmacokinetic Concentration Analysis Dataset

ADPC supports the secondary analyses of biomarkers of exposure to nicotine (PARAMCD=NIC) and cotinine (PARAMCD=COT) in plasma. ADPC is created from the PC domain as well as from an intermediate dataset PKMERGE. PKMERGE was created to calculate relative times from start of exposure on Day 5 for the THSm2.2 and mCC arms. Nicotine and cotinine are collected in the evening (ATPT= 08:00 PM - 09:30 PM) on Days 0 to 4, collected over a 24-hour interval starting on Day 5 (every 2 hours out to 16 hours on Day 5 and 2 more times on Day 6), and then once per day at the Day 30, 60, and 90 study visits. Baseline for each parameter is the Day 0 evening measurement. Values outside of the protocol-allowed collection window were not flagged for analysis (i.e., records with DEVWC=missing had ANL01FL=''). Records with ANL01FL='Y' were used in analysis. In addition, for the analysis of covariance statistical summary, ANL02FL='Y' was used to identify the evening (08:00 PM - 09:30 PM) records selected for analysis during the Confinement Period.

Some parameters had values below the limit of quantification (AVALC contains 'BLQ' and AVAL=missing). In those cases, a new record was created with AVAL set to $\frac{1}{2}$ x the lower limit of quantification and DTYPE='BLQHALF'. These newly created records were flagged for analysis with ANL01FL='Y' (as long as DEVWC=missing).

5.2.17 ADPE – Physical Examination Analysis Dataset

ADPE contains all observations from PE. ANL01FL='Y' indicates values to be used in summary tables.

5.2.18 ADPP – PK Parameters Analysis Dataset

ADPP is a sponsor-defined analysis dataset following the ADaM BDS supporting the secondary analyses of biomarkers of exposure to nicotine and cotinine in plasma. ADPP contains 6 PK parameters (3 for nicotine [PARAMCD=NCAVG, NCMAX, and NTMAX] and 3 for cotinine [PARAMCD=CCAVG,

CCMAX, and CTMAX]) on Day 5 for subjects randomized to the THSm2.2 and mCC arms. Records with ANL01FL='Y' were used in analysis.

5.2.19 ADQSND – Nicotine Dependence Analysis Dataset

ADQSND contains data from QS for the Fagerström Test for Nicotine Dependence (FTND), the Minnesota Nicotine Withdrawal Scale (MNWS) Questionnaire, the Socio-Economic Status (SES) Questionnaire, the Behavioral Risk Factor Surveillance System Questionnaire, the Smoking Questionnaire and Supplemental Questions, and the Prochaska Stage of Change Questionnaire. ANL01FL=Y indicates values used in summary statistics and analysis.

For PARCAT1=Socio Economic Status Questionnaire, PARCAT1=Behavioral Risk Factor Surveillance System Questionnaire, PARCAT1=Smoking Questionnaire, PARCAT1=Supplemental Question, and PARCAT1= Prochaska Stage Of Change Questionnaire, individual responses are captured for each question identified by PARAMCD/PARAM and the response is captured in AVALC.

For PARCAT1=Fagerstrom Test For Nicotine Dependence Questionnaire, the total score has been derived as detailed in SAP section 7.3.2 with PARAMCD=FTNDSC, numeric total score is in AVAL and the category is recorded under AVALCAT1.

For PARCAT1=Minnesota Nicotine Dependence/Withdrawal Scale, the total score has been derived as detailed in SAP section 7.3.5 with PARAMCD=MNWSRWDS and numeric total score is in AVAL.

5.2.20 ADQSPA – Product Assessment Analysis Dataset

ADQSPA contains data from QS for the Modified Cigarette Evaluation Questionnaire (MCEQ) and the Human Smoking Topography (HST) Questionnaire. ANL01FL=Y indicates values used in summary statistics and analysis.

For PARCAT1=Human Smoking Topography Questionnaire, individual responses are captured for each question identified by PARAMCD/PARAM and the response is captured in AVALC.

For PARCAT1=Modified Cigarette Evaluation Questionnaire, subscale scores have been derived into AVAL according to SAP section 7.3.4.

The subscale parameter information are in the following table:

Subscale	PARAMCD
Aversion Subscale	MCEQA
Craving Reduction Subscale	MCEQCR
Enjoyment of Respiratory Tract Sensation Subscale	MCEQERTS
Psychological Reward Subscale	MCEQPR
Smoking Satisfaction Subscale	MCEQSS

5.2.21 ADQSSU – Smoking Urges Analysis Dataset

ADQSSU contains data from QS for the Questionnaire On Smoking Urges (QSU)-Brief. Factor scores have been derived into AVAL according to SAP section 7.3.3 (Reward has PARAMCD= QSUFACT1, Relief has PARAMCD= QSUFACT2 and total score has PARAMCD= QSUTOTAL). ANL01FL=Y indicates values used in summary statistics and analysis.

5.2.22 ADQSSYM – Symptoms Questionnaire Analysis Dataset

ADQSSYM contains data from QS for the Cough Assessment Questionnaire. ANL01FL=Y indicates values used in summary statistics.

5.2.23 ADSV – Visit Incidence Analysis Dataset

ADSV contains all visit information from SV. It does not contain information on the telephone followup visit. This information is contained within ADDS. This dataset contains observations for screen failure subjects.

5.2.24 ADVS – Vital Signs Analysis Dataset

ADVS contains all observations from VS and SUPPVS. Reference ranges were not used to assess this data. ANL01FL=Y indicates values used in summary statistics. Subjects with missing blood pressure and waist circumference data (for risk marker analysis) at scheduled visits have DTYPE=LOCF to identify records which are carried forward from an earlier visit.

5.2.25 ADXP – Pulmonary Function Analysis Dataset

ADXP contains all lung function observations from XP. The ratio between FEV₁ and FVC was included in the CRF for assessment of eligibility, to continue the comparison of subsequent timepoints to baseline, this parameter has also been derived for all timepoints. PARCAT2 can be used to determine if the assessment was prior to or after the bronchodilator dose. ANL01FL=Y indicates values used in summary statistics. Subjects with missing lung function data at scheduled visits have DTYPE=LOCF to identify records which are carried forward from an earlier visit (note these records are not used in analysis).

5.2.26 ADXT – Smoking Profile Analysis Dataset

ADXT contains all observations from XT, including records from XTCAT=Topography, Filter Analysis, and Visual Inspection Of Tobacco Plug.

For PARCAT1=Visual Inspection Of Tobacco Plug, all records are used in the summary table. AVAL contains values of 0 (= No overheating), 1 (= White spot(s) inside the tobacco plug), and 2 (= Ashes inside the tobacco plug and burnt paper).

For PARCAT1=Topography, this includes the per-puff parameters noted in SAP Table 13, the derived per-cigarette parameters identified in SAP Table 14, and the derived average daily per-cigarette parameters used in analysis. Records with ANL02FL='Y' are used in summary statistics and analysis.

The following table shows the parameters from SAP Tables 13 and 14 as well as the parameters used in analysis.

PARAMCD Value	PARAM Value	Per-Puff/Per-Cigarette/Per-Cigarette Averaged Over Visit
NPC	Total number of puffs	Per-Cigarette
TVOL	Total puff volume (mL)	Per-Cigarette
AVGVI	Average puff volume (mL)	Per-Cigarette
AVGDI	Average puff duration (s)	Per-Cigarette
TDI	Total puff duration (s)	Per-Cigarette
AVGQMI	Average flow (mL/s)	Per-Cigarette
AVGQCI	Average Peak flow (mL/s)	Per-Cigarette
TII	Total inter puff interval (s)	Per-Cigarette
AVGII	Average inter puff interval (s)	Per-Cigarette
TDFI	Total smoking duration (s)	Per-Cigarette
TWI	Total Work (mJ)	Per-Cigarette
AVGWI	Average Work (mJ)	Per-Cigarette
AVGPMI	Average pressure drop (mmWg)	Per-Cigarette
AVGPCI	Average Peak pressure drop (mmWg)	Per-Cigarette
SMINT	Smoking Intensity (mL/s)	Per-Cigarette
PTI	Puffing Time Index (%)	Per-Cigarette
PFEQ	Puff Frequency (puffs/min)	Per-Cigarette

PARAMCD Value	PARAM Value	Per-Puff/Per-Cigarette/Per-Cigarette Averaged Over Visit
NI	Puff Number	Per-Puff
VI	Puff volume (mL)	Per-Puff
DI	Puff Duration (S)	Per-Puff
QMI	Average Flow [Vi/Di] (mL/s)	Per-Puff
QCI	Peak Flow (mL/s)	Per-Puff
II	Inter Puff Interval (S)	Per-Puff
DFI	Sum of li and Di (S)	Per-Puff
WI	Work [INT Pmi*FinalFlow*dt] (mJ)	Per-Puff
PMI	Average Pressure Drop (mmWG)	Per-Puff
PCI	Peak Pressure Drop (mmWG)	Per-Puff
RMI	Average Resistance [Pmi/Qmi] (mmWG/mL/s)	Per-Puff
RCI	Peak Resistance [Pci/Qci] (mmWG/mL/s)	Per-Puff
ANPC	Total number of puffs (average over visit)	Per-Cigarette Averaged Over Visit
ATVOL	Total puff volume (mL) (average over visit)	Per-Cigarette Averaged Over Visit
AAVGVI	Average puff volume (mL) (average over visit)	Per-Cigarette Averaged Over Visit
AAVGDI	Average puff duration (s) (average over visit)	Per-Cigarette Averaged Over Visit
ATDI	Total puff duration (s) (average over visit)	Per-Cigarette Averaged Over Visit

PARAMCD Value	PARAM Value	Per-Puff/Per-Cigarette/Per-Cigarette Averaged Over Visit
AAVGQMI	Average flow (mL/s) (average over visit)	Per-Cigarette Averaged Over Visit
AAVGQCI	Average Peak flow (mL/s) (average over visit)	Per-Cigarette Averaged Over Visit
ATII	Total inter puff interval (s) (average over visit)	Per-Cigarette Averaged Over Visit
AAVGII	Average inter puff interval (s) (average over visit)	Per-Cigarette Averaged Over Visit
ATDFI	Total smoking duration (s) (average over visit)	Per-Cigarette Averaged Over Visit
ATWI	Total Work (mJ) (average over visit)	Per-Cigarette Averaged Over Visit
AAVGWI	Average Work (mJ) (average over visit)	Per-Cigarette Averaged Over Visit
AAVGPMI	Average pressure drop (mmWg) (average over visit)	Per-Cigarette Averaged Over Visit
AAVGPCI	Average Peak pressure drop (mmWg) (average over visit)	Per-Cigarette Averaged Over Visit
ASMINT	Smoking Intensity (mL/s) (average over visit)	Per-Cigarette Averaged Over Visit
APTI	Puffing Time Index (%) (average over visit)	Per-Cigarette Averaged Over Visit
APFEQ	Puff Frequency (puffs/min) (average over visit)	Per-Cigarette Averaged Over Visit

6. Data Conformance Summary

6.1 Conformance Inputs

- Were the analysis datasets evaluated for conformance with CDISC ADaM Validation Checks?

If yes:

- Version of CDISC ADaM Validation Checks:
- Specify software used:
 - OpenCDISC Validator Version 1.5
- Were the ADaM datasets evaluated in relation to define.xml? Yes, see below
- Was define.xml evaluated? Yes, see below

CDISC Controlled Terminology Version 20141219

6.2 Issues Summary

(insert your text here and/or use following table)

Dataset(s)	Diagnostic Message and/or Check ID	Severity	Count and/or Issue Rate	Explanation
ADAE	Neither AVAL nor AVALC are present in dataset	Error	1	ADAE is not a BDS domain and as such AVAL and AVALC are not required as per CDISC ADaM Data Structure for Adverse Event Analysis Version 1.0. Not amended as this is an OpenCDISC issue where it has not yet had appropriate class information for the ADAE domain.
ADAE	Required variable is not present	Error	2	As above, PARAM and PARAMCD are not required under CDISC ADaM Data Structure for Adverse Event Data Analysis version 1.0.
ADBX	Inconsistent value for PARCAT2 within a unique PARAMCD	Error	1	"when PARAMCD=BLBALL, we have PARCAT2=BIOMARKER OF EXPOSURE PARCAT2=RISK MARKERS depending on which form was not completed"
ADBX	calculation error: PCHG != (AVAL - BASE)/BASE * 100	Error	11	the SAP says that when the baseline values is 0, 1 will be

Dataset(s)	Diagnostic Message and/or Check ID	Severity	Count and/or Issue Rate	Explanation
	present in dataset			used in the denominator for calculating the percent change from baseline
ADCM	Neither AVAL nor AVALC are present in dataset	Error	1	It was determined that the BDS format was not appropriate to this data type and as such AVAL and AVALC are not appropriate. Structure was based upon ADAE and SDTM.CM structure
ADCM	Required variable is not present	Error	2	It was determined that the BDS format was not appropriate to this data type and as such PARAM and PARAMCD are not appropriate. Structure was based upon ADAE and SDTM.CM structure
ADCO	Required variable is not present	Error	2	PARAM and PARAMCD were not applicable to this data type due to the collection method of the comments. Data structure reflects BDS domain as closely as possible
ADDE	Neither AVAL nor AVALC are present in dataset	Error	1	AVAL and AVALC were not applicable to this data type. Data structure reflects ADAE domain as closely as possible as these are event data type..
ADDE	Required variable is not present	Error	2	PARAM and PARAMCD were not applicable to this data. Data structure

Dataset(s)	Diagnostic Message and/or Check ID	Severity	Count and/or Issue Rate	Explanation
				reflects ADAE domain as closely as possible as these are event data type.
ADDS	Neither AVAL nor AVALC are present in dataset	Error	1	AVAL and AVALC were not applicable to this data type. Data structure reflects ADAE domain as closely as possible as this reflected the data type.
ADDS	Required variable is not present	Error	2	PARAM and PARAMCD were not applicable to this data type. Data structure reflects ADAE domain as closely as possible as this reflected the data
ADDT	Neither AVAL nor AVALC are present in dataset	Error	1	AVAL and AVALC were not applicable to this data type. Data structure reflects ADAE domain as closely as possible as this reflected the data type.
ADDT	Required variable is not present	Error	2	PARAM and PARAMCD were not applicable to this data type. Data structure reflects ADAE domain as closely as possible as this reflected the data type.
ADEX	Inconsistent value for PARCAT2 within a unique PARAMCD	Error	6760	we have multiple values of PARCAT2 depending on if captured during the confinement period or on the electronic diary
ADLB	Inconsistent value for AVALC	Error	7	"As per the spec if values are presented as ""<xxxx"" or ""<=xxxx"", then AVAL=xxxx/2;

Dataset(s)	Diagnostic Message and/or Check ID	Severity	Count and/or Issue Rate	Explanation
				<p>or</p> <p>values are presented as <code>"">xxxx""</code> or <code>"">=xxxx""</code>, then AVAL=xxxx; Here for Paramcd =BILLI AVAL=0.1 for values AVALC=0.1 and AVAL=<0.2"</p>
ADMH	Neither AVAL nor AVALC are present in dataset	Error	1	ADMH is not a BDS domain. It is based upon ADAE domain and as detailed under ADAE OpenCDISC does not take this into account yet.
ADMH	Required variable is not present	Error	2	ADMH is not a BDS domain. It is based upon ADAE domain and as detailed under ADAE OpenCDISC does not take this into account yet.
ADQSND	Inconsistent value for AVALC	Error	229	AVAL values are derived based on the value level meta data in specifications
ADQSND	calculation error: $PCHG \neq (AVAL - BASE)/BASE * 100$	Error	1572	the SAP says that when the baseline values is 0, 1 will be used in the denominator for calculating the percent change from baseline
ADQSPA	Inconsistent value for PARCAT1 within a unique PARAMCD	Error	82	when PARAMCD=QSALL, we have PARCAT1=Modified Cigarette Evaluation Questionnaire and PARCAT1=Human Smoking Topography Questionnaire

Dataset(s)	Diagnostic Message and/or Check ID	Severity	Count and/or Issue Rate	Explanation
				depending on which form was not completed
ADSV	Neither AVAL nor AVALC are present in dataset	Error	1	Structure is not a BDS domain for this data type. Data is not used for any analysis but can be used for supporting information.
ADSV	Required variable is not present	Error	2	PARAM and PARAMCD are not appropriate for this data type. Data is not used for any analysis in its own right but can be used for information.
ADXP	Inconsistent value for PARCAT1 within a unique PARAMCD	Error	904	the parcat1 values are populated based on the forms collected
ADXP	Inconsistent value for PARCAT2 within a unique PARAMCD	Error	885	the parcat2 values are populated based on the forms collected
ADXP	Inconsistent value for PARAMN	Error	38	paramn values are populated based on valuelevel meta data tab in specifications change from baseline
ADXT	calculation error: $PCHG \neq (AVAL - BASE)/BASE * 100$	Error	27462	the SAP says that when the baseline values is 0, 1 will be used in the denominator for calculating the percent change from baseline

7. Submission of Programs

ADaM dataset production programs have been submitted and referred to in the define.xml.

Programs for the production of primary and secondary analysis, descriptive statistics tables and figures and associated macros have also been submitted and are defined below. Submitted programs will execute on a SAS version 9.3. Library definitions will need to be modified to reflect the actual environment where run.

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.1.1	Forest Plot of Statistical Analysis of Biomarkers of Exposure on Day 5 and Day 90 - PP Set.	F_FOREST_BM	ADSL ADBX	USUBJID, PROT1FL, PPROT4FL PARAMN, PARAM, PARAMCD, AVALU, SUBJID, BASE, TRTP, AVAL, SEX, UCPDGR, AVISIT, ANL02FL, PPROT1FL, PPROT4FL, AVISITN, ATPT, UCPDGR1

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.1.2	Biomarkers of Exposure Geometric Mean and 95% CI – PP Set	F BIOMARK	ADSL	USUBJID, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, TRT01PN, TRT01AN
			ADBx	ANL02FL, PARCAT, PARAM, PARAMN, PARAMCD, LBSPEC, TRTPN, TRTP, ABLFL, AVISIT, ATPT, ATPTN, AVISITN, AVAL, PCHG, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AQLFL, AVALC, APUPER, APUPERC, AVALU, LBSPEC, TRTAN, PARCAT1
			ADXt	DTYPE, AVISIT, AVISITN, PARAMN, PARAMCD, PARAM, USUBJID, TRTP, BASE, UCPDGR1, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, SEX, AVAL

[illegible]

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.2.1.1	Plasma Nicotine and Cotinine Profile (ng/mL) over the 90 Days Geometric Mean and 95% CI – PP Set	F_PNIC_PP	ADSL ADPC	PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, USUBJID, TRT01AN AVAL, AVISITN, ATPTN, BASE, PARAMCD, ANL01FL, ABLFL, AVISIT, APUPER, APUPERC, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AVALU, ATPT, ATPTN, PARAMN, TRTPN, PARAM
15.1.2.1.2	Plasma Nicotine and Cotinine Profile (ng/mL) over the 90 Days Geometric Mean and 95% CI – FAS	F_PNIC_FAS	ADSL ADPC	FASFL, USUBJID, TRT01AN AVAL, AVISITN, ATPTN, BASE, PARAMCD, ANL01FL, ABLFL, AVISIT, APUPER, APUPERC, FASFL, AVALU, ATPT, ATPTN, PARAMN, TRTPN, PARAM
15.1.2.2	Forest Plot of Statistical Analysis of Risk Markers – PP Set	F_FOREST_RM	ADBx	PARAM, PARAMCD, AVISITN, DIFFTYPE, PARAMN, DIFF, LCLM, UCLM, AVISIT

[illegible]

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.2.4.1	QSU-brief Total Scores Arithmetic Mean and 95% CI – PP Set	F QSUTOTAL P P	ADSL ADQSSU	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, ANL01FL, ABLFL, TRTPN, PARCAT2N, PARCAT2, AVISITN, AVISIT, AVALC, AVAL, APUPERC, APUPER CHG, PCHG
15.1.2.4.2	QSU-brief Total Scores Arithmetic Mean and 95% CI – FAS	F QSUTOTAL F AS	ADSL ADQSSU	USUBJID, TRT01PN, FASFL FASFL, ANL01FL, ABLFL, TRTPN, PARCAT2N, PARCAT2, AVISITN, AVISIT, AVALC, AVAL,
15.1.2.5.1	QSU-brief Total Scores Least Squares Means Differences and 95% CI – PP Set	F QSU LS PP	ADQSSU	DTYPE, ANL01FL, AVISIT, , BASE, UCPDGR1, PARCAT2, PARCAT2N, AVISITN, TRTP, USUBJID, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AVAL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.2.5.2	QSU-brief Total Scores Least Squares Means Differences and 95% CI – FAS	F QSU LS FAS	ADQSSU	DTYPE, ANL01FL, AVISIT, BASE, UCPDGR1, PARCAT2, PARCAT2N, AVISITN, TRTP, USUBJID, FASFL, ABLFL, AVAL
15.1.2.6.1	MCEQ Subscales Arithmetic Mean and 95% CI – PP Set	F MCEQ PP	ADQSPA	DTYPE, ANL01FL, AVISIT, PARAMTYP, PARAM, PARAMN, USUBJID, TRTP, AVISITN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AVAL, SEX, UCPDGR1, BASE
15.1.2.6.2	MCEQ Subscales Arithmetic Mean and 95% CI – FAS	F MCEQ FAS	ADSL ADQSPA	USUBJID, TRT01PN, FASFL FASFL, AVISITN, PARAMCD, ABLFL, AVISITN, AVISIT, APUPER, APUPER, PARAM, PARAMN, AVALC, USUBJID, TRTPN, AVAL, PCHG, ANL01FL,

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.2.7.1	MCEQ Subscales Least Squares Means Differences and 95% CI – PP Set	F MCEQ LS PP	ADQSPA	DTYPE, ANL01FL, AVISIT, PARAMTYP, PARAM, PARAMN, USUBJID, TRTP, AVISITN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AVAL, SEX, UCPDGR1, BASE
15.1.2.7.2	MCEQ Subscales Least Squares Means Differences and 95% CI – FAS	F MCEQ LS FAS	ADQSPA	DTYPE, ANL01FL, AVISIT, PARAMTYP, PARAM, PARAMN, USUBJID, TRTP, AVISITN, FASFL, AVAL, SEX, UCPDGR1, BASE
15.1.2.8.1	MNWS Total Score Arithmetic Mean and 95% CI – PP Set	F MNWS PP	ADSL ADQSND	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, AVISITN, AVISIT, PARAM, PARAMN, AVALC, USUBJID, TRTPN, AVAL, PCHG, ANL01FL, APUPER, APUPERC,

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.2.8.2	MNWS Total Score Arithmetic Mean and 95% CI – FAS	F MNWS FAS	ADSL ADQSND	USUBJID, TRT01PN, FASFL FASFL, PARAMCD, ABLFL, AVISITN, AVISIT, PARAM, PARAMN, AVALC, USUBJID, TRTPN, AVAL, PCHG, ANL01FL,
15.1.2.9.1	MNWS Total Score Least Squares Means Differences and 95% CI – PP Set	F MNWS LS PP	ADQSND	DTYPE, ANL01FL, AVISIT, PARAM, PARAMN, USUBJID, TRTP, AVISITN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AVAL, SEX, UCPDGR1, BASE
15.1.2.9.2	MNWS Total Score Least Squares Means Differences and 95% CI – FAS	F MNWS LS FAS	ADQSND	DTYPE, ANL01FL, AVISIT, PARAM, PARAMN, USUBJID, TRTP, AVISITN, FASFL, AVAL, SEX, UCPDGR1, BASE, ABLFL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.2.10	HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set	F HST PP	ADSL ADXT	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AVISITN, PARAMCD, ABLFL, AVISITN, AVISIT, APUPER, APUPERC, PARAM, PARAMN, AVALC, USUBJID, TRTPN, AVAL, PCHG
15.1.2.10.1	HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI	f1501021001_Z RHM-REXA- 08_US_v1_PMI	ADXT	PARAMCD PARAMN PARAM TRTA AVAL ANL02FL PPROT1FL PPROT2FL
15.1.2.11.1	Oxysterol Parameters Arithmetic Mean and 95% CI – PP Set	F OXY PP	ADSL ADBX	TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, USUBJID PPROT1FL, PPROT4FL, ANL02FL, PARAMCD, TRTPN, AVAL, ABLFL, AVISIT, AQLFL, PARAM, PARAMN, AVISITN, PCHG, ATPTN, ATPT, USUBJID, AVALC
15.1.2.11.2	Oxysterol Parameters Arithmetic Mean and 95% CI – FAS	F OXY FAS	ADSL ADBX	TRT01PN, FASFL FASFL, ANL02FL, PARAMCD, TRTPN, AVAL, ABLFL, AVISIT, AQLFL, PARAM, PARAMN, AVISITN, PCHG, ATPTN, ATPT, USUBJID, AVALC

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.2.12.1	ScatterPlot of Urinary MHBMA Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC MHBMA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.12.2	Bland-Altman Plot for Concordance of Urinary MHBMA Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA MHBMA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.13.1	ScatterPlot of Urinary 3-HPMA Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC 3HPMA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.13.2	Bland-Altman Plot for Concordance of Urinary 3-HPMA Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA 3HPMA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.14.1	ScatterPlot of Urinary S-PMA Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC SPMA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.14.2	Bland-Altman Plot for Concordance of Urinary S-PMA Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA SPMA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.2.15.1	ScatterPlot of Urinary Total NNAL Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC NNAL	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.15.2	Bland-Altman Plot for Concordance of Urinary Total NNAL Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA NNAL	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.16.1	ScatterPlot of Urinary Total 1-OHP Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC 1OHP	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.16.2	Bland-Altman Plot for Concordance of Urinary Total 1-OHP Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA 1OHP	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.17.1	ScatterPlot of Urinary Total NNN Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC NNN	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.17.2	Bland-Altman Plot for Concordance of Urinary Total NNN Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA NNN	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.2.18.1	ScatterPlot of Urinary 4-ABP Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC 4ABP	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.18.2	Bland-Altman Plot for Concordance of Urinary 4-ABP Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA 4ABP	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.19.1	ScatterPlot of Urinary 1-NA Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC 1NA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.19.2	Bland-Altman Plot for Concordance of Urinary 1-NA Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA 1NA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.20.1	ScatterPlot of Urinary 2-NA Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC 2NA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.20.2	Bland-Altman Plot for Concordance of Urinary 2-NA Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA 2NA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.2.21.1	ScatterPlot of Urinary o-tol Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC OTOL	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.21.2	Bland-Altman Plot for Concordance of Urinary o-tol Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA OTOL	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.22.1	ScatterPlot of Urinary CEMA Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC CEMA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.22.2	Bland-Altman Plot for Concordance of Urinary CEMA Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA CEMA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.23.1	ScatterPlot of Urinary HEMA Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC HEMA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.23.2	Bland-Altman Plot for Concordance of Urinary HEMA Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA HEMA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.2.24.1	ScatterPlot of Urinary B[a]P Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC BAP	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.24.2	Bland-Altman Plot for Concordance of Urinary B[a]P Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA BAP	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.25.1	ScatterPlot of Urinary HMPMA Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC HMPMA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.25.2	Bland-Altman Plot for Concordance of Urinary HMPMA Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA HMPMA	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.26.1	ScatterPlot of Urinary NEQ Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC NEQ	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.26.2	Bland-Altman Plot for Concordance of Urinary NEQ Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA NEQ	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.2.27.1	ScatterPlot of Urinary 8-epi-PGF2 α Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC 8EPI	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.27.2	Bland-Altman Plot for Concordance of Urinary 8-epi-PGF2 α Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA 8EPI	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.28.1	ScatterPlot of Urinary 11-DTX-B2 Concentration Adjusted for Creatinine from 24 hour Urine Collection versus 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F SC 11DTX	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, TRTA, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.28.2	Bland-Altman Plot for Concordance of Urinary 11-DTX-B2 Concentration Adjusted for Creatinine from 24 hour Urine Collection and 4 hour Urine Fraction at Baseline and Day 90 Visit – FAS	F BA 11DTX	ADBx	USUBJID, AVISITN, PARCAT2, PARAMCD, AVAL, BASE, AVISIT, TRTP, TRTPN, LBSPEC, FASFL, ANL02FL
15.1.2.30	Full Lung Function Results Mean and 95% CI – Safety Population	F LUNGF SAF	ADSL ADXP	TRT01A, TRT01AN, ANL01FL, SAF AFL, DTYPE, AVALC, TRTA, TRTAN, ABLFL, AVISIT, AVISITN, USUBJID, PARAMN, PARAM, PARAMCD, XPCLSIG, AVAL, AVALC, AVALU,

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.1.2.31	Full Lung Function Results Arithmetic Mean and 95% CI – PP Set	F_LUNGF_PP	ADSL ADXP	USUBJID, TRT01PN, PPROT1FL ANL01FL, PARAM, PARAMN, PPROT1FL, PPROT4FL, AVISITN, AVISIT, ABLFL, APUPER, APUPERC, AVAL, PARAMCD, TRTPN, TRTP
15.2.1.1	Summary of Subject Disposition – All Screened Subjects	T_DISP	ADSL ADFA	DTESTDTM, STUDYID, SCRFFL, SAFBFL, DISFUCAT, DSREAS, ENRFL, ENFL, RANDFL, TRT01AN, TRT01A, DISCCAT USUBJID, SCRFFL, SAFBFL, PARAMCD, AVAL, PARCAT1
15.2.1.2	Summary of Reasons for Discontinuations – FAS	T_RSDISCON	ADSL ADDS	USUBJID, TRT01PN, TRT01P, FASFL RANDFL, FASFL, COMPLFL, DSCAT, DSDECOD, USUBJID, DSSEQ, TRTPN, TRTP
15.2.1.3.1	Summary of Protocol Deviations – Safety Population	T_PROTVIOL	ADSL ADDV	USUBJID, TRT01AN, SAFBFL, SAF AFL SAFBFL, SAF AFL, TRTAN, USUBJID, EVALCAT, DVCAT, DVSIG,

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.1.3.2	Analysis Sets and Reasons for Exclusions from Analyses	T_ANALSET	ADSL	DISTINCT, USUBJID, TRT01AN, TRT01A, SCRFFL SAFBFL, SAFBREA, RANDFL, FASFL, FASREAS, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PPREAS1, PPREAS2, PPREAS3, PPREAS4, COMPP1FL, COMPP2FL, COMPP3FL, COMPP4F
15.2.1.4.1	Summary of Demographics and Other Baseline Characteristics – Safety Population	T_DEMOG_SAF	ADSL	PRODPREF, SAFBFL, TRT01AN, TRT01A, UCPDGR1N, UCPDGR1, HEIGHT, AGE USUBJID, SEXN, SEXC, SEX, RACEN, RACE, BMIGR1N, BMIGR1, BMI
			ADV S	PARAMCD, SAFBFL, AVALC, AVAL, USUBJID, TRTAN, TRTA, AVISIT
			ADQSN D	PARAMCD, SAFBFL, AVAL, AVALC, USUBJID, TRTAN, TRTA, AVISIT, AVALCAT1

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.1.4.2	Summary of Demographics and Other Baseline Characteristics – FAS	T_DEMOG_FAS	ADSL	PRODPREF, TRT01AN, USUBJID, SEXN, SEXC, SEX, RACEN, RACE, BMIGR1N, BMIGR1, UCPDGR1N, UCPDGR1, HEIGHT, AGE, BMI
			ADV_S	PARAMCD, FASFL, TRTAN, TRTA, AVISIT, AVAL, AVALC, USUBJID,
			ADQSN_D	PARAMCD, FASFL, TRTAN, TRTA, AVISIT, AVAL, AVALC, USUBJID, AVALCAT1
15.2.1.4.3	Summary of Demographics and Other Baseline Characteristics – PP Set	T_DEMOG_PP	ADSL	PRODPREF, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, TRT01AN, TRT01A, USUBJID, SEXN, SEXC, SEX, RACEN, RACE, BMIGR1N, BMIGR1, BMI, UCPDGR1N, UCPDGR1, HEIGHT, AGE
			ADV_S	PARAMCD, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AVALC, AVAL, USUBJID, TRTAN, TRTA, AVISIT,
			ADQSN_D	PARAMCD, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AVAL, AVALC, USUBJID, TRTAN, TRTA, AVISIT, AVALCAT1

[illegible]

[illegible]

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.1.7	Summary of Concomitant Diseases – Safety Population	T_CONDIS_NEW	ADSL ADMH	TRT01A, TRT01AN, SAFAFL, RANDFL, SAFBFL SAFAFL, SAFBFL, MHCAT, ANYCDFL, TRTAN, TRTA, MHBODSYS, SUBJIDN, MHDECOD
15.2.2.1.1	Summary of Daily Product Use in Confinement Period – FAS	T_PRODUSE_FAS	ADEX ADFA	FASFL, PARCAT3, PARAMCD, TRTPN, USUBJID, AVISITN, AVISIT, APUPER FASFL, PARAMCD, USUBJID, AVAL, TRTPN
15.2.2.1.2	Summary of Daily Product Use in Confinement Period – PP Set	T_PRODUSE_PP	ADEX ADFA	PProt1FL, PARCAT3, PARAMCD, TRTPN, USUBJID, AVISITN, AVISIT, APUPER PProt1FL, PARAMCD, USUBJID, AVAL, TRTPN
15.2.2.2	Summary of Maximum Daily Product Use in Ambulatory Period – FAS	T_MAX_PRDUSE_FAS	ADEX ADSL	PARCAT3, ANL01FL, ANL02FL, FASFL, PARAMCD, PARAM, APUPER, APUPERC, TRTPN, USUBJID, AVAL USUBJID, TRT01PN, FASFL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.2.3.1	Summary of Average Daily Product Use in Ambulatory Period – FAS	T_AVG_PRDUSE_FAS	ADSL ADEX	USUBJID, TRT01PN, SAFAFL USUBJID, PARAMCD, SAFAFL, APUPERC, APUPER, PARAM, TRTPN, TRT01P, TRT01PN, AVAL
15.2.2.3.2	Summary of Average Daily Product Use in Ambulatory Period – PP Set	T_AVG_PRDUSE_PP	ADSL ADEX	USUBJID, TRT01PN, TRT01P, PPROT2FL, PPROT3FL, PPROT4FL USUBJID, PARAMCD, PPROT2FL, PPROT3FL, PPROT4FL, TRTPN, TRT01P, TRT01PN, AVAL, APUPER, APUPERC, PARAM
15.2.2.4	Summary of Product Use by Product Use Category in Ambulatory Period – FAS	T_PRDUSE_PRD_CAT_FAS	ADSL	FASFL, TRT01AN, GPUCAT1, PUCAT1, PUCAT1EX, GPUCAT2, PUCAT2, PUCAT2EX, GPUCAT3, PUCAT3, PUCAT3EX, GPUCAT4, PUCAT4, PUCAT4EX, GPUCAT5, PUCAT5, PUCAT5EX
15.2.2.5.1	Summary of Average Daily Product Use by Product Use Category in Ambulatory Period – FAS	T_AVG_PRDUSE_CAT_FAS	ADSL ADEX	FASFL, TRT01PN AVAL, FASFL, PARCAT3, PARAMCD, TRTAN, GPUCAT2, GPUCAT3, GPUCAT4, GPUCAT5, APUPERC

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.2.5.2	Summary of Average Daily Product Use by Product Use Category During the Ambulatory Period – PP Set	T_AVG_PRDUSE CAT_PP	ADEX	AVAL, PARCAT3, PARAMCD, TRTAN, GPUCAT2, GPUCAT3, GPUCAT4, APUPERC, PPROT2FL, PPROT3FL, PPROT4FL, PUCAT2, PUCAT3, PUCAT4, , PUCAT2EX, PUCAT3EX, PUCAT4EX
15.2.3.1.1	Analysis of COHb MHBMA 3-HPMA S-PMA and Total NNAL on Day 5/90 Visit for THS 2.2 Menthol versus mCC for the Primary Objective – PP Set	T_ANL_BOEXP	ADBX	PARAMCD, PARAM, PARAMN, AVALU, SUBJID; BASE, TRTP, SEX, UCPDGR1, AVAL, SEX ANL02FL, PPROT1FL, PPROT4FL, VISITN, ATPT, PPROT1FL, PPROT4FL
15.2.3.1.2	Sensitivity Analysis of COHb MHBMA 3-HPMA S-PMA and Total NNAL on Day 5/90 Visit for THS 2.2 Menthol versus mCC for the Primary Objective using Mixed Model- PP Set	T_SENANL_BOE XP	ADBX	PARAMCD, PARAM, PARAMN, AVALU, DTYPE, ANL02FL, ANL01FL, SUBJID, BASE, TRTP, AVAL, SEX, UCPDGR1

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.3.1.3	Sensitivity Analysis of COHb MHBMA 3-HPMA S-PMA and Total NNAL on Day 5/90 Visit for THS 2.2 Menthol versus mCC for the Primary Objective - Compliant Population	T ANL BOEXP	ADBX	PARAMCD, PARAM, PARAMN, AVALU, SUBJID; BASE, TRTP, SEX, UCPDGR1, AVAL, SEX ANL02FL, PPROT1FL, PPROT4FL, VISITN, ATPT, COMPP1FL, COMPP4FL
15.2.3.2	Analysis of COHb MHBMA 3-HPMA S-PMA and Total NNAL on Day 5/90 Visit for THS 2.2 Menthol versus mCC and SA for the Secondary Objective-PP Set	T ANLCOHB	ADBX	PARAMN, PARAM, PARAMCD, AVALU, SUBJID, BASE, TRTP, AVAL, SEX, UCPDGR, AVISIT, ANL02FL, PPROT1FL, PPROT4FL, AVISITN, ATPT
15.2.3.3	Analysis of COHb MHBMA 3-HPMA S-PMA and Total NNAL on Day 5/90 Visit for THS 2.2 Menthol versus mCC and SA for the Secondary Objective – FAS	T ANLCOHB	ADBX	PARAMN, PARAM, PARAMCD, AVALU, SUBJID, BASE, TRTP, AVAL, SEX, UCPDGR, AVISIT, ANL02FL, FASFL, AVISITN, ATPT

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.3.4	Analysis of Additional Biomarkers of Exposure versus mCC and SA on Day 5/90 Visit – PP Set	T ANABIOEXP	ADSL ADBx	USUBJID, PPROT1FL, PPROT4FL USUBJID, AVISITN, AVISIT, ANL02FL, BASE, UCPDGR1, PARAMCD, PARAMN, PARAM, ATPTN, TRTP, AVAL, TRTPN, SEXC
15.2.3.5	Analysis of Additional Biomarkers of Exposure versus mCC and SA on Day 5/90 Visit – FAS	T ANABIOEXP	ADSL ADBx	USUBJID, FASFL USUBJID, AVISITN, AVISIT, ANL02FL, BASE, UCPDGR1, PARAMCD, PARAMN, PARAM, ATPTN, TRTP, AVAL, TRTPN, SEXC

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.3.6	Sensitivity Analysis of Additional Biomarkers of Exposure versus mCC and SA using Mixed Model on Day 5/90 Visit – PP Set	T_ANABIOEXP MIX	ADSL ADBX	USUBJID, PPROT1FL, , PPROT4FL USUBJID, AVISITN, AVISIT, ANL02FL, BASE, UCPDGR1, PARAMCD, PARAMN, PARAM, ATPTN, TRTP, AVAL, TRTPN, SEX, ANL01FL, DTYPE
15.2.3.7	Sensitivity Analysis of Additional Biomarkers of Exposure versus mCC and SA on Day 5/90 Visit – Compliant Population	T_ANABIOEXP	ADSL ADBX	USUBJID, COMPP1FL, COMPP4FL USUBJID, AVISITN, AVISIT, ANL02FL, BASE, UCPDGR1, PARAMCD, PARAMN, PARAM, ATPTN, TRTP, AVAL, TRTPN, SEXC

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.1.1	Descriptive Statistics of Blood COHb (%) – PP Set	T_COHB_PP	ADBX ADSL	USUBJID, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, TRT01PN ANL02FL, PARCAT, PARAM, PARAMN, PARAMCD, LBSPEC, TRTPN, ABLFL, AVISIT, ATPT, ATPTN, AVISITN, AVAL, PCHG, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AQLFL, AVALC, APUPER, APUPERC, AVALU
15.2.4.1.1.1	Descriptive Statistics of Blood COHb (%) by Sex – PP Set	T_COHB_PP_SEX	ADSL ADBX	USUBJID, PPROT1FL, PPROT4FL, TRT01PN, UCPDGR1 ANL02FL, PARCAT, PARAM, LBSPEC, TRTPN, ABLFL, AVISIT, ATPT, ATPTN, AVISITN, AVAL, PCHG, PPROT1FL, PPROT4FL, AQLFL, AVALC, , UCPDGR1, SEXC

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.1.1.2	Descriptive Statistics of Blood COHb (%) by Cigarette Consumption – PP Set	T_COHB_PP_CC	ADSL ADBX	USUBJID, PPROT1FL, PPROT4FL, TRT01PN, UCPDGR1 ANL02FL, PARCAT, PARAM, LBSPEC, TRTPN, ABLFL, AVISIT, ATPT, ATPTN, AVISITN, AVAL, PCHG, PPROT1FL, PPROT4FL, AQLFL, AVALC, UCPDGR1
15.2.4.1.2	Descriptive Statistics of Blood COHb (%)– FAS	T_COHB_FAS	ADSL ADBX	FASFL, TRT01PN ANL02FL, PARCAT1, PARAM, PARAMN, PARAMCD, AVALU, TRTP, TRTPN, LBSPEC, AVISITN, FASFL, TRTPN, ABLFL, AVISIT, ATPT, ATPTN, AVAL, PCHG, AQLFL, AVALC

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.1.3	Descriptive Statistics of Blood COHb (%)– Compliant Population	T_COHB_COMP	ADSL ADBX	USUBJID, COMPP1FL, COMPP2FL, COMPP3FL, COMPP4FL, TRT01PN ANL02FL, PARCAT1, PARAM, PARAMCD, PARAMN, AVALU, LBSPEC, AVISITN, TRTPN, ABLFL, AVISIT, ATPT, ATPTN, AVAL, PCHG, AQLFL, COMPP1FL, COMPP2FL, COMPP3FL, COMPP4FL, APUPERC, APUPER, TRTP
15.2.4.2.1	Descriptive Statistics of MHBMA in 24-hour Urine Collection – PP Set	T_MHBMA_PP	ADBX ADSL	PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, ANL02FL, TRTP, TRTPN, PARAMCD, PARAMN, AVISITN, AVISIT, APUPER, APUPERC, ABLFL, PCHG, AVAL, AQLFL TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, USUBJID
15.2.4.2.1.1	Descriptive Statistics of MHBMA Urinary Concentration Adjusted for Creatinine (units) in 24-hour Urine Collection by Sex – PP Set	T_MHBMA_SEX_PP	ADBX ADSL	PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, ANL02FL, TRTP, TRTPN, PARAMCD, ABLFL, PARAMN, AVISITN, AVISIT, APUPER, APUPERC, PCHG, AVAL, USUBJID, AQLFL, SEX, PARAM, AVALU USUBJID, SEX,

[illegible]

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.3.1	Descriptive Statistics of 3-HPMA in 24-hour Urine Collection – PP Set	T HPMA PP	ADSL ADBX	USUBJID, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, TRT01PN USUBJID, ANL02FL, PARAM, PARAMN, PARAMCD, LBSPEC, TRTPN, ABLFL, AVISIT, AVISITN, , AVAL, PCHG, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AQLFL, AVALC, TRTP, APUPER, APUPERC, AVALU
15.2.4.3.1.1	Descriptive Statistics of 3-HPMA Urinary Concentration Adjusted for Creatinine (units) in 24-hour Urine Collection by Sex – PP Set	T HPMA SEX P	ADSL ADBX	USUBJID, SEX, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, TRT01PN USUBJID, ANL02FL, PARAM, PARAMN, PARAMCD, LBSPEC, TRTPN, ABLFL, AVISIT, AVISITN, AVAL, PCHG, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AQLFL, AVALC, TRTP, APUPER, APUPERC, AVALU
15.2.4.3.1.2	Descriptive Statistics of 3-HPMA Urinary Concentration Adjusted for Creatinine (units) in 24-hour Urine Collection by Cigarette Consumption – PP Set	T HPMA CC PP	ADSL ADBX	USUBJID, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, TRT01PN USUBJID, ANL02FL, PARAM, PARAMN, PARAMCD, LBSPEC, TRTPN, ABLFL, AVISIT, AVISITN, , AVAL, PCHG, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AQLFL, AVALC, TRTP, UCPDGR1N, APUPER,

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
				APUPERC, AVAL
15.2.4.3.2	Descriptive Statistics of 3-HPMA in 24-hour Urine Collection – FAS	T HPMA FAS	ADSL ADBX	USUBJID, FASFL, TRT01PN USUBJID, ANL02FL, PARAM, PARAMN, PARAMCD, LBSPEC, TRTPN, ABLFL, AVISIT, AVISITN, AVAL, PCHG, FASFL, AQLFL, AVALC, TRTP, APUPER, APUPERC, AVALU
15.2.4.3.3	Descriptive Statistics of 3-HPMA in 24-hour Urine Collection – Compliant Population	T HPMA CP	ADSL ADBX	USUBJID, COMPP1FL, COMPP2FL, COMPP3FL, COMPP4FL, TRT01PN USUBJID, ANL02FL, PARAM, PARAMN, PARAMCD, LBSPEC, TRTPN, ABLFL, AVISIT, AVISITN, , AVAL, PCHG, COMPP1FL, COMPP2FL, COMPP3FL, COMPP4FL, AQLFL, AVALC, TRTP, APUPER, APUPERC, AVALU

[illegible]

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.5.1	Descriptive Statistics of Total NNAL in 24-hour Urine Collection – PP Set	T NNAL PP	ADSL ADBx	USUBJID, TRT01AN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL ANL02FL, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, TRTAN, PARCAT1, PARAMCD, PARAM, LBSPEC, ABLFL, AVISIT, AVISITN, AVAL, PCHG, AQLFL
15.2.4.5.1.1	Descriptive Statistics of Total NNAL Urinary Concentration Adjusted for Creatinine (units) in 24-hour Urine Collection by Sex – PP Set	T NNAL SEX	ADSL ADBx	TRT01PN, PPROT1FL, PPROT4FL, SEXC ANL02FL, PPROT1FL, PPROT4FL, TRTPN, PARCAT1, PARAMCD, PARAM, LBSPEC, ABLFL, AVISIT, AVISITN, AVAL, PCHG, AQLFL, SEXC
15.2.4.5.1.2	Descriptive Statistics of Total NNAL Urinary Concentration Adjusted for Creatinine (units) in 24-hour Urine Collection by CC Consumption – PP Set	T NNAL CC	ADSL ADBx	PPROT1FL, PPROT4FL, TRT01PN, UCPDGR1 ANL02FL, PARCAT1, PARAMCD, PARAM, LBSPEC, TRTPN, ABLFL, AVISIT, AVISITN, AVAL, PCHG, PPROT1FL, PPROT4FL, UCPDGR1
15.2.4.5.2	Descriptive Statistics of Total NNAL in 24-hour Urine Collection – FAS	T NNAL FAS	ADSL ADBx	FASFL, TRT01PN ANL02FL, PARCAT1, PARAMCD, PARAM, LBSPEC, FASFL, TRTPN, ABLFL, AVISIT, AVISITN, AVAL, PCHG, AQLFL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.5.3	Descriptive Statistics of Total NNAL in 24-hour Urine Collection – Compliant Population	T_NNAL_COMP	ADSL ADBX	USUBJID, TRT01PN, COMPP1FL, COMPP2FL, COMPP3FL, COMPP4FL ANL02FL, COMPP1FL, COMPP2FL, COMPP3FL, COMPP4FL, PARCAT1, PARAMCD, PARAM, LBSPEC, TRTPN, ABLFL, AVISIT, AVISITN, AVAL, PCHG, AQLFL
15.2.4.6.1	Descriptive Statistics of Exhaled CO (ppm) – PP Set	T_CO_PP	ADSL ADBX	USUBJID, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, TRT01PN ANL02FL, PARCAT1, PARAMCD, LBSPEC, TRTPN, ABLFL, AVISIT, ATPT, ATPTN, AVISITN, BASETYPE, AVAL, PCHG, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AQLFL, AVALC
15.2.4.6.2	Descriptive Statistics of Exhaled CO (ppm) – FAS	T_CO_FAS	ADSL ADBX	FASFL, TRT01PN ANL02FL, PARCAT1, PARAMCD, LBSPEC, AVISITN, FASFL, TRTPN, ABLFL, AVISIT, ATPT, ATPTN, AVAL, PCHG, AQLFL, AVALC

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.7.1	Descriptive Statistics of 1-OHP in 24-hour Urine Collection – PP Set	T BIOMARK	ADSL ADBX	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.7.2	Descriptive Statistics of 1-OHP in 24-hour Urine Collection – FAS	T BIOMARK FAS	ADSL ADBX	USUBJID, TRT01AN, FASFL ANL02FL, FASFL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.8.1	Descriptive Statistics of Total NNN in 24-hour Urine Collection – PP Set	T BIOMARK	ADSL ADBX	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.8.2	Descriptive Statistics of Total NNN in 24-hour Urine Collection – FAS	T BIOMARK FAS	ADSL ADBX	USUBJID, TRT01AN, FASFL ANL02FL, FASFL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.9.1	Descriptive Statistics of 4-ABP in 24-hour Urine Collection – PP Set	T BIOMARK	ADSL ADBX	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.9.2	Descriptive Statistics of 4-ABP in 24-hour Urine Collection – FAS	T BIOMARK FAS	ADSL ADBX	USUBJID, TRT01AN, FASFL ANL02FL, FASFL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.10.1	Descriptive Statistics of 1-NA in 24-hour Urine Collection – PP Set	T BIOMARK	ADSL ADBX	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.10.2	Descriptive Statistics of 1-NA in 24-hour Urine Collection – FAS	T BIOMARK FAS	ADSL ADBX	USUBJID, TRT01AN, FASFL ANL02FL, FASFL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.11.1	Descriptive Statistics of 2-NA in 24-hour Urine Collection – PP Set	T BIOMARK	ADSL ADBX	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.11.2	Descriptive Statistics of 2-NA in 24-hour Urine Collection – FAS	T BIOMARK FAS	ADSL ADBX	USUBJID, TRT01AN, FASFL ANL02FL, FASFL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.12.1	Descriptive Statistics of o-tol in 24-hour Urine Collection – PP Set	T BIOMARK	ADSL ADBX	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.12.2	Descriptive Statistics of o-tol in 24-hour Urine Collection – FAS	T BIOMARK FAS	ADSL ADBX	USUBJID, TRT01AN, FASFL ANL02FL, FASFL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.13.1	Descriptive Statistics of CEMA in 24-hour Urine Collection – PP Set	T BIOMARK	ADSL ADBX	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.13.2	Descriptive Statistics of CEMA in 24-hour Urine Collection – FAS	T BIOMARK FAS	ADSL ADBX	USUBJID, TRT01AN, FASFL ANL02FL, FASFL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.14.1	Descriptive Statistics of HEMA in 24-hour Urine Collection – PP Set	T BIOMARK	ADSL ADBX	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.14.2	Descriptive Statistics of HEMA in 24-hour Urine Collection – FAS	T BIOMARK FAS	ADSL ADBX	USUBJID, TRT01AN, FASFL ANL02FL, FASFL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.15.1	Descriptive Statistics of B[a]P in 24-hour Urine Collection – PP Set	T BIOMARK	ADSL ADBX	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.15.2	Descriptive Statistics of B[a]P in 24-hour Urine Collection – FAS	T BIOMARK FAS	ADSL ADBX	FASFL, TRT01PN, USUBJID, TRT01AN ANL02FL, PARCAT1, PARAM, PARAMN, PARAMCD, AVALU, TRTP, TRTPN, LBSPEC, AVISITN, FASFL, TRTPN, ABLFL, AVISIT, ATPT, ATPTN, AVAL, AVALU, AVALC, , PCHG, AQLFL, AVALC, USUBJID, PAUPER, APUPERC
15.2.4.16.1	Descriptive Statistics of HMPMA in 24-hour Urine Collection – PP Set	T BIOMARK	ADSL ADBX	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.16.2	Descriptive Statistics of HMPMA in 24-hour Urine Collection – FAS	T BIOMARK FAS	ADSL ADBX	USUBJID, TRT01AN, FASFL ANL02FL, FASFL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.17.1	Descriptive Statistics of S-BMA in 24-hour Urine Collection – PP Set	T BIOMARK	ADSL ADBX	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.17.2	Descriptive Statistics of S-BMA in 24-hour Urine Collection – FAS	T BIOMARK FAS	ADSL ADBX	USUBJID, TRT01AN, FASFL ANL02FL, FASFL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.18.1	Descriptive Statistics of NEQ in 24-hour Urine Collection – PP Set	T BIOMARK	ADSL ADBX	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.18.2	Descriptive Statistics of NEQ in 24-hour Urine Collection – FAS	T_BIOMARK_FAS	ADSL ADBx	USUBJID, TRT01AN, FASFL ANL02FL, FASFL, PARAMCD, ABLFL, PARAM, AQLFL, TRTPN, PARAMN, PARAM, AVALU, AVISITN, AVISIT, ATPTN, ATPT
15.2.4.19.1	Descriptive Statistics of Plasma Nicotine and Cotinine Concentrations (ng/mL) – PP Set	T_DESC_NC	ADSL ADPC	PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, USUBJID, TRT01AN, AVAL, AVISITN, ATPTN, BASE, PARAMCD, ANL01FL, ABLFL, AVISIT, APUPER, APUPERC, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AVALU, ATPT, ATPTN, PARAMN, TRTPN, PARAM
15.2.4.19.2	Descriptive Statistics of Plasma Nicotine and Cotinine Concentrations (ng/mL) – FAS	T_DESC_NC	ADSL ADPC	FASFL, USUBJID, TRT01AN, AVAL, AVISITN, ATPTN, BASE, PARAMCD, ANL01FL, ABLFL, AVISIT, APUPER, APUPERC, FASFL, AVALU, ATPT, ATPTN, PARAMN, TRTPN, PARAM
15.2.4.20.1	Analysis of Plasma Nicotine and Cotinine Concentrations (ng/mL) over the 90 Days – PP Set	T_ANL_NC	ADPC	AVAL, BASE, TRTP, PARAMN, TRTPN, SEX, UCPDGR1, PARAM, PARAMCD, AVISIT, AVISITN, ATPT, ATPTN, , ANL01FL, ANL02FL, DTYPE, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.20.2	Analysis of Plasma Nicotine and Cotinine Concentrations (ng/mL) over the 90 Days – FAS	T ANL NC	ADPC	AVAL, BASE, TRTP, PARAMN, TRTPN, SEX, UCPDGR1, PARAM, PARAMCD, AVISIT, AVISITN, ATPT, ATPTN, , ANL01FL, ANL02FL, DTYPE, FASFL
15.2.4.21.1	Descriptive Statistics of Plasma Nicotine and Cotinine PK Parameters on Day 5 – PP Set	T DESC NC PK	ADSL ADPP	PPROT1FL, USUBJID, TRT01AN, PPROT1FL, AVAL, PARAMN, PARAM, AVALU, AVISITN, AVISIT, TRTAN, ANL01FL,
15.2.4.21.2	Descriptive Statistics of Plasma Nicotine and Cotinine PK Parameters on Day 5 – FAS	T DESC NC PK	ADSL ADPP	FASFL, USUBJID, TRT01AN, FASFL, AVAL, PARAMN, PARAM, AVALU, AVISITN, AVISIT, TRTAN, ANL01FL,
15.2.4.22.1	Analysis of Plasma Nicotine and Cotinine Concentration PK Parameters on Day 5 – PP Set	T ANL NC PK	ADPP	AVAL, BASE, TRTP, PARAMN, TRTPN, SEX, UCPDGR1, PARAM, PARAMCD, AVISIT, AVISITN, ATPT, ATPTN, ANL01FL, , PPROT1FL
15.2.4.22.2	Analysis of Plasma Nicotine and Cotinine Concentration PK Parameters on Day 5 – FAS	T ANL NC PK	ADPP	AVAL, BASE, TRTP, PARAMN, TRTPN, SEX, UCPDGR1, PARAM, PARAMCD, AVISIT, AVISITN, ATPT, ATPTN, ANL01FL, FASFL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.23.1	Descriptive Statistics of CYP1A2 Activity (%) – PP Set	T_CYP1A2L_PP	ADSL ADBX	PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, TRT01AN, USUBJID ANL02FL, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, , PARAM, AVISIT, ABLFL, AVAL, PCHG, AVISITN, TRTAN, TRTA, ATPTN, ATPT, AQLFL
15.2.4.23.1.1	Descriptive Statistics of CYP1A2 Activity (%) Excluding Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP1A2 Activity – PP Set	T_CYP1A2_EXCL_PP	ADSL ADBX	TRT01AN, USUBJID, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, ANL02FL, ANL03FL, , PARAMCD, PARAM, AVISIT, ABLFL, AVAL, PCHG, AVISITN, TRTAN, TRTA, ATPTN, ATPT, BLOQFL, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AULQFL
15.2.4.23.2	Descriptive Statistics of CYP1A2 Activity (%) – FAS	T_CYP1A2_FAS	ADSL ADBX	FASFL, TRT01AN, TRT01A, SUBJID ANL02FL, FASFL, PARAMCD, PARAM, AVISIT, ABLFL, AVAL, PCHG, AVISITN, TRTAN, TRTA, ATPTN, ATPT, BLOQFL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.23.2. 1	Descriptive Statistics of CYP1A2 Activity (%) Excluding Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP1A2 Activity – FAS	T_CYP1A2_EXCL_FAS	ADSL ADBX	FASFL, TRT01AN, TRT01A, SUBJID ANL02FL, ANL03FL, FASFL, PARAMCD, PARAM, AVISIT, ABLFL, AVAL, PCHG, AVISITN, TRTAN, TRTA, ATPTN, ATPT, BLOQFL
15.2.4.24.1	Analysis of CYP1A2 Activity (%) – PP Set	T_ANL_CYP	ADBX	AVAL, PARAMN, USUBJID, PARAMCD, PARAM, AVISITN, AVISIT, TRTP, ANL02FL, DTYPE, BASE, UCPDGR1, PPROT1FL, PPROT4FL
15.2.4.24.1. 1	Analysis of CYP1A2 Activity (%) Excluding Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP1A2 Activity – PP Set	T_ANL_CYP	ADBX	AVAL, PARAMN, USUBJID, PARAMCD, PARAM, AVISITN, AVISIT, TRTP, ANL02FL, DTYPE, BASE, UCPDGR1, PPROT1FL, PPROT4FL
15.2.4.24.2	Analysis of CYP1A2 Activity (%) – FAS	T_ANL_CYP	ADBX	AVAL, PARAMN, USUBJID, PARAMCD, PARAM, AVISITN, AVISIT, TRTP, ANL02FL, DTYPE, BASE, UCPDGR1, FASFL

[illegible]

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.25.2	Analysis of Risk Markers – FAS	T_ANLRISK	ADBX ADLB	USUBJID, AVAL, BASE, CHG, ABLFL, AVISIT, AVISITN, SEXC, UCPDGR1, PARAMN, PARAM, PARAMCD, ANL02FL, PARCAT2, TRTP, PARCAT1, SEXC, TRTPN, UCPDGR1, FASFL USUBJID, AVAL, BASE, CHG, ABLFL, AVISIT, AVISITN, SEXC, UCPDGR1, PARAMN, PARAM, PARAMCD
15.2.4.25.2.1	Analysis of 11-DTX-B2 (units) Excluding Assessments within 5 Half-Lives of a Concomitant Medication Affecting the Production of 11-DTX-B2 – FAS	T_ANL_DTX	ADBX	AVAL, BASE, TRTP, PARAMN, TRTPN, SEXC, UCPDGR1, PARAM, PARAMCD, AVISIT, AVISITN, ANL03FL, PARCAT2, FASFL
15.2.4.26.1	Descriptive Statistics of Blood Pressure (mmHg) – PP Set	T_VS_BP_PP	ADSL ADVS	USUBJID, TRT01AN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL ANL01FL, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, TRTAN, TRTA, PCHG, AVAL
15.2.4.26.2	Descriptive Statistics of Blood Pressure (mmHg) – FAS	T_VS_BP_FAS	ADSL ADVS	FASFL, USUBJID, TRT01AN, TRT01A ANL01FL, FASFL, PARAMCD, ABLFL, AVISIT, AVISITN, TRTAN, TRTA, PCHG, AVAL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.27.1	Descriptive Statistics of hs-CRP (units) homocysteine (units) blood glucose (units) LDL (units) HDL (units) TG (units) and TC (units) – PP Set	T LB BC PP	ADSL ADLB	PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, USUBJID, TRT01AN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, ANL01FL, PARAMCD, ABLFL, TRTAN, TRTA, AVISITN, AVISIT, ATPTN, ATPT, AVALC, AVAL, PCHG
15.2.4.27.2	Descriptive Statistics of hs-CRP (units) homocysteine (units) blood glucose (units) LDL (units) HDL (units) TG (units) and TC (units) – FAS	T LB BC FAS	ADSL ADLB	FASFL, USUBJID, TRT01AN, TRT01A FASFL, ANL01FL, PARAMCD, ABLFL, TRTAN, TRTA, AVISITN, AVISIT, ATPTN, ATPT, AVALC, AVAL, PCHG
15.2.4.28.1	Descriptive Statistics of Fibrinogen (units) – PP Set	T FIBRINO PP	ADSL ADLB	PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, TRT01PN, USUBJID PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ANL01FL, ABLFL, AVISITN, AVISIT, TRTPN, PARAM, PARAMN, AVAL, PCHG, APUPER, APUPERC
15.2.4.28.2	Descriptive Statistics of Fibrinogen (units) – FAS	T FIBRINO FAS	ADSL ADLB	FASFL, TRT01PN, USUBJID FASFL, PARAMCD, ANL01FL, ABLFL, AVISITN, AVISIT, TRTPN, PARAM, PARAMN, ATPT,

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
				ATPTN, AVAL, PCHG
15.2.4.29.1	Descriptive Statistics of HbA1c (units) – PP Set	T_HBA1C_PP	ADSL ADLB	PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, TRT01PN, USUBJID PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ANL01FL, ABLFL, AVISITN, AVISIT, TRTPN, PARAM, PARAMN, AVAL, PCHG, APUPER, APUPERC
15.2.4.29.2	Descriptive Statistics of HbA1c (units) – FAS	T_HBA1C_FAS	ADSL ADLB	FASFL, TRT01PN, USUBJID FASFL, PARAMCD, ANL01FL, ABLFL, AVISITN, AVISIT, TRTPN, PARAM, PARAMN, AVAL, PCHG, ATPT, ATPTN
15.2.4.30.1	Descriptive Statistics of sICAM (units) – PP Set	T_ICAM1_PP	ADSL ADLB	PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, TRT01PN, USUBJID PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ANL01FL, ABLFL, AVISITN, AVISIT, TRTPN, PARAM, PARAMN, AVAL, PCHG, APUPER, APUPERC, AQLFL,

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.30.2	Descriptive Statistics of sICAM (units) – FAS	T ICAM1 FAS	ADSL ADLB	FASFL, TRT01PN, USUBJID FASFL, PARAMCD, ANL01FL, ABLFL, AVISITN, AVISIT, TRTPN, PARAM, PARAMN, AVAL, PCHG, ATPT, ATPTN, AQLFL,
15.2.4.31.1	Descriptive Statistics of Total WBC Count (units) Neutrophils Counts (units) Basophils Counts (Units) Eosinophils Counts (units) Lymphocytes Counts (units) Monocytes Counts (units) and Platelet Count (units) – PP Set	T LAB PP	ADLB ADSL	PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ANL01FL, AVISITN, AVISIT, TRTPN, PARAMN, PARAM, ATPTN, ATPT, AVAL, PCHG, APUPER, APUPER, ABLFL USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL
15.2.4.31.2	Descriptive Statistics of Total WBC Count (units) Neutrophils Counts (units) Basophils Counts (Units) Eosinophils Counts (units) Lymphocytes Counts (units) Monocytes Counts (units) and Platelet Count (units) – FAS	T LAB FAS	ADLB ADSL	FASFL, PARAMCD, ANL01FL, AVISITN, AVISIT, TRTPN, PARAMN, PARAM, ATPTN, ATPT, AVAL, PCHG USUBJID, TRT01PN, FASFL
15.2.4.32.1	Descriptive Statistics of 8-epi-PGF2 α (units) and 11 DTX-B2 (units) – PP Set	T BX BM PP	ADSL ADBX	USUBJID, TRT01AN, TRT01A, , PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL ANL02FL, PARAMCD, ABLFL, AVISIT, AVISITN, TRTAN, TRTA, AVAL, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PCHG,

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.32.1. 1	Descriptive Statistics of 11-DTX-B2 (units) Excluding Assessments within 5 Half-Lives of a Concomitant Medication Affecting the Production of 11-DTX-B2 – PP Set	T BX BM EXCL PP	ADSL ADBX	USUBJID, TRT01AN, TRT01A, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL ANL02FL, ANL03FL, PARAMCD, ABLFL, AVISIT, AVISITN, TRTAN, TRTA, AVAL, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PCHG,
15.2.4.32.2	Descriptive Statistics of 8-epi-PGF2 α (units) and 11 DTX-B2 (units) – FAS	T BX BM FAS	ADSL ADBX	FASFL, USUBJID, TRT01AN, TRT01A ANL02FL, FASFL, PARAMCD, ABLFL, AVISIT, AVISITN, TRTAN, TRTA, AVAL, PCHG
15.2.4.32.2. 1	Descriptive Statistics of 11-DTX-B2 (units) Excluding Assessments within 5 Half-Lives of a Concomitant Medication Affecting the Production of 11-DTX-B2 – FAS	T BX BM EXCL FAS	ADSL ADBX	FASFL, USUBJID, TRT01AN, TRT01A ANL02FL, FASFL, ANL03FL, PARAMCD, ABLFL, AVISIT, AVISITN, TRTAN, TRTA, AVAL, PCHG
15.2.4.33.1	Descriptive Statistics of Body weight (kg) and waist circumference (cm) – PP Set	T VS BWWC P P	ADSL ADVS	USUBJID, TRT01AN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL ANL01FL, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, TRTAN, TRTA, PCHG, AVAL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.33.2	Descriptive Statistics of Body weight (kg) and waist circumference (cm) – FAS	T VS BWWC F AS	ADSL ADVS	FASFL, USUBJID, TRT01AN, TRT01A, ANL01FL, FASFL, PARAMCD, ABLFL, AVISIT, AVISITN, TRTAN, TRTA, PCHG, AVAL
15.2.4.34	Analysis of Biomarkers of Exposure in 4-hour Fraction versus mCC and SA on Day 90 Visit – PP Set	T ANL EXP	ADBX	TRTP, PARAMN, PARAM, BASE, UCPDGR1, ANL02FL, AVISITN, PPROT4FL, AVAL, AVISIT, SEX
15.2.4.35	Descriptive Statistics of MHBMA in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL
15.2.4.36	Descriptive Statistics of 3-HPMA in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL
15.2.4.37	Descriptive Statistics of S-PMA in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.38	Descriptive Statistics of NNAL in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL
15.2.4.39	Descriptive Statistics of 1-OHP in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL
15.2.4.40	Descriptive Statistics of Total NNN in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL
15.2.4.41	Descriptive Statistics of 4-ABP in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.42	Descriptive Statistics of 1-NA in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL
15.2.4.42.1	Descriptive Statistics of HST Parameters per Cigarette	t1502044201 Z RHM-REXA-08 US v1 PMI	ADSL ADXT	USUBJID TRT01A PPROT1FL PPROT2FL PPROT3FL PPROT4FL TRTA AVISITN AVAL PARAMCD PARAMN AVISIT
15.2.4.43	Descriptive Statistics of 2-NA in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL
15.2.4.43.1	Analysis of HST Parameters per Cigarette	t1502044301 Z RHM-REXA-08 US v1 PMI	ADSL ADXT	USUBJID, TRT01A, PPROT1FL PARAM PARAMN PARAMCD AVISITN AVAL AVISIT AVISITN APUPER PPROT1FL PPROT2FL PPROT3FL PPROT4FL ANL02FL TRTP

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.44	Descriptive Statistics of o-tol in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL
15.2.4.45	Descriptive Statistics of CEMA in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL
15.2.4.46	Descriptive Statistics of HEMA in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL
15.2.4.47	Descriptive Statistics of B[a]P in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.48	Descriptive Statistics of HMPMA in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL
15.2.4.49	Descriptive Statistics of S-BMA in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL
15.2.4.50	Descriptive Statistics of NEQ in 4-hour Urine Fraction – PP Set	T URINBX PP	ADSL ADBX	USUBJID, TRT01AN, PPROT4FL ANL02FL, PPROT4FL, PARAMCD, ABLFL, AVISIT, AVISITN, ATPTN, ATPT, TRTAN, TRTA, PCHG, AVAL
15.2.4.51.1	Descriptive Statistics of Fagerström Test for Nicotine Dependence Results – PP Set	T FAGER PP	ADSL ADQSND	USUBJID, TRT01PN, PPROT4FL, ABLFL, TRTAN, PARAMCD, PARAM, AVISITN, AVISIT, AVAL, CHG, AVALCAT1, SHIFT1
15.2.4.51.2	Descriptive Statistics of Fagerström Test for Nicotine Dependence Results – FAS	T FAGER FAS	ADSL ADQSND	FASFL, TRT01PN ABLFL, FASFL, TRTAN, PARAMCD, PARAM, AVISITN, AVISIT, AVAL, CHG, AVALCAT1, SHIFT1

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.51.3	Descriptive Statistics of Fagerström Test for Nicotine Dependence Results – Compliant Population	T_FAGER_COMP	ADSL ADQSND	USUBJID, TRT01PN, COMPP4FL, COMPP1FL, PPROT2FL, PPROT3FL ABLFL, TRTAN, PARAMCD, PARAM, AVISITN, AVISIT, AVAL, CHG, AVALCAT1, SHIFT1
15.2.4.52.1	Descriptive Statistics of QSU- brief Factors and Total Scores – PP Set	T_QSU_PP	ADSL ADQSSU	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, ANL01FL, ABLFL, TRTPN, PARCAT2N, PARCAT2, AVISITN, AVISIT, AVALC, AVAL, APUPERC, APUPER CHG, PCHG
15.2.4.52.2	Descriptive Statistics of QSU- brief Factors and Total Scores – FAS	T_QSU_FAS	ADSL ADQSSU	USUBJID, TRT01PN, FASFL FASFL, ANL01FL, ABLFL, TRTPN, PARCAT2N, PARCAT2, AVISITN, AVISIT, AVALC, AVAL
15.2.4.53.1	Analysis of QSU-brief Factors and Total Scores – PP Set	T_ANL_QSU	ADQSSU	DTYPE, ANL01FL, AVISIT, , BASE, UCPDGR1, PARCAT2, PARCAT2N, AVISITN, TRTP, USUBJID, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AVAL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.53.2	Analysis of QSU-brief Factors and Total Scores – FAS	T ANL QSU	ADQSSU	DTYPE, ANL01FL, AVISIT, , BASE, UCPDGR1, PARCAT2, PARCAT2N, AVISITN, TRTP, USUBJID, FASFL, ABLFL, AVAL
15.2.4.54.1	Descriptive Statistics of MCEQ Subscales – PP Set	T MCEQ PP	ADSL ADQSPA	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, AVISITN, AVISIT, APUPER, APUPERC, PARAM, PARAMN, AVALC, USUBJID, TRTPN, AVAL, PCHG, ANL01FL
15.2.4.54.2	Descriptive Statistics of MCEQ Subscales – FAS	T MCEQ FAS	ADSL ADQSPA	USUBJID, TRT01PN, FASFL FASFL, AVISITN, PARAMCD, ABLFL, AVISITN, AVISIT, APUPER, APUPERC, PARAM, PARAMN, AVALC, USUBJID, TRTPN, AVAL, PCHG, ANL01FL
15.2.4.55.1	Analysis of MCEQ Subscales – PP Set	T ANL MCEQ	ADQSPA	DTYPE, ANL01FL, AVISIT, PARAMTYP, PARAM, PARAMN, USUBJID, TRTP, AVISITN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AVAL, SEX, UCPDGR1, BASE

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.55.2	Analysis of MCEQ Subscales – FAS	T ANL MCEQ	ADQSPA	DTYPE, ANL01FL, AVISIT, PARAMTYP, PARAM, PARAMN, USUBJID, TRTP, AVISITN, FASFL, AVAL, SEX, UCPDGR1, BASE
15.2.4.56.1	Descriptive Statistics of MNWS Total Scores – PP Set	T MNWS PP	ADSL ADQSND	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, PARAMCD, ABLFL, AVISITN, AVISIT, PARAM, PARAMN, AVALC, USUBJID, TRTPN, AVAL, PCHG, ANL01FL, APUPER, APUPERC
15.2.4.56.2	Descriptive Statistics of MNWS Total Scores – FAS	T MNWS FAS	ADSL ADQSND	USUBJID, TRT01PN, FASFL FASFL, PARAMCD, ABLFL, AVISITN, AVISIT, PARAM, PARAMN, AVALC, USUBJID, TRTPN, AVAL, PCHG, ANL01FL
15.2.4.57.1	Analysis of MNWS Total Scores – PP Set	T ANL MNWS	ADQSND	DTYPE, ANL01FL, AVISIT, PARAM, PARAMN, USUBJID, TRTP, AVISITN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AVAL, SEX, UCPDGR1, BASE
15.2.4.57.2	Analysis of MNWS Total Scores – FAS	T ANL MNWS	ADQSND	DTYPE, ANL01FL, AVISIT, PARAM, PARAMN, USUBJID, TRTP, AVISITN, FASFL, AVAL, SEX, UCPDGR1, BASE, ABLFL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.58	Descriptive Statistics of HST Questionnaire Data – PP Set	T_HST_PP	ADSL ADQSPA	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, , PARAMCD, ABLFL, AVISITN, AVISIT, APUPER, APUPERC, PARAM, PARAMN, AVALC, USUBJID, TRTPN, AVAL, PCHG, ANL01FL
15.2.4.59.1	Descriptive Statistics of Prochaska 'Stage of Change' Questionnaire Results – FAS	T_PROCH_FAS	ADSL ADQSND	FASFL, USUBJID, TRT01PN FASFL, AVISITN, PARAMCD, ANL01FL, ABLFL, AVISIT, APUPER, APUPERC, PARAMN, PARAM, TRTPN, AVAL, AVALC
15.2.4.59.2	Descriptive Statistics of Prochaska 'Stage of Change' Questionnaire Results – Compliant Population	T_PROCH_COM P	ADSL ADQSND	COMPP1FL, COMPP2FL, COMPP3FL, COMPP4FL, USUBJID, TRT01PN COMPP1FL, COMPP2FL, COMPP3FL, COMPP4FL, AVISITN, PARAMCD, ANL01FL, ABLFL, AVISIT, APUPER, APUPERC, PARAMN, PARAM, TRTPN, AVAL, AVALC

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.60	Descriptive Statistics of HST Parameters per Cigarette – PP Set	T_HST_CIG_PP	ADSL ADXT	USUBJID, TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, AVISITN, PARAMCD, ABLFL, AVISITN, AVISIT, APUPER, APUPERC, PARAM, PARAMN, AVALC, USUBJID, TRTPN, AVAL, PCHG
15.2.4.61	Analysis of HST Parameters per Cigarette – PP Set	T_ANL_HST	ADXT	DTYPE, AVISIT, AVISITN, PARAMN, PARAMCD, PARAM, USUBJID, TRTP, BASE, UCPDGR1, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, SEX, AVAL
15.2.4.62.1	Descriptive Statistics of CYP2A6 Activity (%) – PP Set	T_CYP2A6_PP	ADSL ADBx	TRT01AN, USUBJID, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL ANL02FL, PARAMCD, ABLFL, AVAL, PCHG, TRTAN, TRTA, AVISITN, AVISIT, ATPTN, ATPT, AQLFL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.62.1. 1	Descriptive Statistics of CYP2A6 Activity (%) Excluding Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP2A6 Activity – PP Set	T_CYP2A6_EXCL_PP	ADSL ADBX	TRT01AN, USUBJID, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL ANL02FL, ANL03FL, PARAMCD, ABLFL, AVAL, PCHG, TRTAN, TRTA, AVISITN, AVISIT, ATPTN, ATPT, AQLFL
15.2.4.62.2	Descriptive Statistics of CYP2A6 Activity (%) – FAS	T_CYP2A6_FAS	ADSL ADBX	TRT01AN, TRT01A, SUBJID, FASFL ANL02FL, FASFL, PARAMCD, ABLFL, AVISIT, AVAL, PCHG, TRTAN, TRTA, AVISITN, AVISIT, ATPTN, ATPT, AQLFL
15.2.4.62.2. 1	Descriptive Statistics of CYP2A6 Activity (%) Excluding Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP2A6 Activity – FAS	T_CYP2A6_EXCL_FAS	ADSL ADBX	TRT01AN, TRT01A, SUBJID, FASFL ANL02FL, ANL03FL, FASFL, PARAMCD, ABLFL, AVISIT, AVAL, PCHG, TRTAN, TRTA, AVISITN, AVISIT, ATPTN, ATPT, AQLFL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.63.1	Analysis of CYP2A6 Activity (%) – PP Set	T_ANL_CYP	ADBX	AVAL, PARAMN, USUBJID, PARAMCD, PARAM, AVISITN, AVISIT, TRTP ANL02FL, DTYPE, BASE, UCPDGR1, PPROT1FL, PPROT4FL
15.2.4.63.1.1	Analysis of CYP2A6 Activity (%) Excluding Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP2A6 Activity – PP Set	T_ANL_CYP	ADBX	AVAL, PARAMN, USUBJID, PARAMCD, PARAM, AVISITN, AVISIT, TRTP ANL02FL, DTYPE, BASE, UCPDGR1, PPROT1FL, PPROT4FL
15.2.4.63.2	Analysis of CYP2A6 Activity (%) – FAS	T_ANL_CYP	ADBX	AVAL, PARAMN, USUBJID, PARAMCD, PARAM, AVISITN, AVISIT, TRTP ANL02FL, DTYPE, BASE, UCPDGR1, FASFL
15.2.4.63.2.1	Analysis of CYP2A6 Activity (%) Excluding Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP2A6 Activity – FAS	T_ANL_CYP	ADBX	AVAL, PARAMN, USUBJID, PARAMCD, PARAM, AVISITN, AVISIT, TRTP ANL02FL, DTYPE, BASE, UCPDGR1, FASFL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.64.1	Descriptive Statistics of Ames Mutagenicity Test (YG1024+S9) (units) – PP Set	T AMES PP	ADSL ADBX	USUBJID, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL USUBJID, ABLFL, ANL02FL, PPROT1FL, PPROT4FL, AVISIT, PARAMCD, PARAM, AVISITN, PERIOD
15.2.4.64.2	Descriptive Statistics of Ames Mutagenicity Test (YG1024+S9) (units) – FAS	T AMES FAS	ADSL ADBX	USUBJID, FASFL, TRT01PN USUBJID, ANL02FL, PARAMCD, FASFL, TRTPN, ABLFL, AVISIT, AVAL, AQLFL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.65	Descriptive Statistics of Visual Inspection of the THS 2.2 Menthol Tobacco Plugs Data – FAS	T_PLUG	ADSL ADXT	FASFL, TRT01P, USUBJID FASFL, PARCAT1, PARAMCD, TRTPN, AVAL, AVISITN, AVISIT, USUBJID, TRTP, AVALC
15.2.4.66.1	Descriptive Statistics of Oxysterol Parameters – PP set	T_OXYST_PP	ADSL ADBX	TRT01PN, PPROT1FL, PPROT2FL, PPROT3FL, PPROT4FL, USUBJID PPROT1FL, PPROT4FL, ANL02FL, PARAMCD, TRTPN, AVAL, ABLFL, AVISIT, AQLFL, PARAM, PARAMN, AVISITN, PCHG, ATPTN, ATPT, USUBJID, AVALC
15.2.4.66.2	Descriptive Statistics of Oxysterol Parameters – FAS	T_OXYST_FAS	ADSL ADBX	TRT01PN, FASFL FASFL, ANL02FL, PARAMCD, TRTPN, AVAL, ABLFL, AVISIT, AQLFL, PARAM, PARAMN, AVISITN, PCHG, ATPTN, ATPT, USUBJID, AVALC
15.2.4.67	Descriptive Statistics of Average Daily Product Use in Ambulatory Period by Preferred Product Declared at Admission – FAS	T_PROD_AMB_FAS	ADSL ADEX	FASFL, TRT01PN, PRODPREF, USUBJID, TRT01P, PUCAT5N, PUCAT5, GPUCAT5N, GPUCAT5 TRTPN, FASFL, PARAMCD, PARCAT3N, APUPER, APUPERC, PRODPREF, PARAM, AVAL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.4.68	Descriptive Statistics of Product Use Categories by Preferred Product Declared at Admission – FAS	T_PRODUSE_PR EF_FAS	ADSL	FASFL, TRT01PN, TRT01P, PRODPREF, USUBJID, GPUCAT5N, GPUCAT5, PUCAT5N, PUCAT5, PUCAT5EX
15.2.4.70	Descriptive Statistics of Full Lung Function Results – PP Set	t_desc_lung_pp	ADSL ADXP	USUBJID, TRT01PN, PPROT1FL ANL01FL, PARAM, PARAMN, PPROT1FL, PPROT4FL, AVISITN, AVISIT, ABLFL, APUPER, APUPERC, AVAL, PARAMCD
15.2.4.71	Analysis of Full Lung Function Results – PP Set	t_anal_lung_pp	ADSL ADXP	USUBJID, TRT01PN, PPROT1FL ANL01FL, PARAM, PARAMN, PPROT1FL, PPROT4FL, AVISITN, AVISIT, ABLFL, APUPER, APUPERC, AVAL, PARAMCD, TRTPN, TRTP
15.2.5.1	Summary of Compliance as Measured by Exhaled CO (ppm) During Confinement Period – FAS in the SA Arm	T_COMP_CO	ADSL ADBX	TRT01PN, TRT01P, SUBJID, FASFL FASFL, ANL01FL, LBSTAT, COMPP1FL, AVALCAT1, PARAMCD, AVISITN, AVISIT, ATPTN, ATPT
15.2.5.2	Summary of Compliance by Period and Overall – FAS	T_COMP	ADSL	TRT01PN, TRT01P, SUBJID, FASFL, COMPP1FL, COMPP2FL, COMPP3FL, COMPP4FL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.6.1	Summary of Adverse Events – Safety Population	T AE SUM	ADSL ADAE	USUBJID, TRT01A, TRT01AN, SAFAFL, SAFBFL USUBJID, SAFBFL, ANYAEFL, ANL01FL, ASPER, AEDECOD, TRTAN, AESER, AEREL, AERELSP, AESEV, AECONTRT, ACNP1
15.2.6.2	Summary of Adverse Events by Product Use Category in Ambulatory – Safety Population	T AE SUM PRO DUSE	ADSL ADAE	USUBJID, TRT01A, TRT01AN, SAFAFL, SAFBFL, GPUCAT1, GPUCAT1N USUBJID, SAFAFL, ANYAEFL, ANL01FL, ASPER, TRTAN, GPUCAT1N, AEBODSYS, AEDECOD, AEEXPEC, AERELSP, AEACNP1

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.6.3	Summary of Adverse Events by System Organ Class and Preferred Term – Safety Population	T AE SOC SUM	ADSL ADAE	USUBJID, TRT01A,TRT01A, SAFAFL,SAFBFL, GPUCAT1,GPUCAT1N USUBJID,SAFAFL,ANYAE FL, ANL01FL, ASPER,TRTAN, GPUCAT1N, AEBODSYS,AEDECOD, AEEXPEC, AERELSP, AEACNP1,
15.2.6.3.1	Summary of Adverse Events (Incidence >5% in any Study Arm) by System Organ Class and Preferred Term – Safety Population	T AE SOC DIS	ADSL ADAE	USUBJID, TRT01A, TRT01AN, SAFBFL, SAFAFL USUBJID, SAFAFL, SAFBFL, ANYAEFL, ANL01FL, ASPER, TRTAN, TRTA, AEDECOD, AEBODSYS

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.6.4	Summary of Adverse Events by Product Use Category System Organ Class and Preferred Term – Safety Population	T AE SOC SUM PRODUSE	ADSL ADAE	USUBJID, TRT01A, TRT01AN, SAFAFL, SAFBFL, GPUCAT1, GPUCAT1N USUBJID, SAFAFL, ANYAEFL, ANL01FL, ASPER, TRTAN, TRTAN, AEBODSYS, AEDECOD
15.2.6.5	Summary of Adverse Events by System Organ Class Preferred Term and Relationship to Study Product Exposure and Expectedness – Safety Population	T AE SOC IP1	ADSL ADAE	USUBJID, TRT01A, TRT01AN, SAFAFL USUBJID, SAFBFL, ANYAEFL, ANL01FL, ASPER, TRTAN, TRTA, AEDECOD, AEBODSYS, AEREL, AEEXPEC

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.6.6	Summary of Adverse Events by Product Use Category System Organ Class Preferred Term and Relationship to Study Product Exposure and Expectedness – Safety Population	T AE606	ADSL ADAE	USUBJID, TRT01A, TRT01AN, SAFAFL, GPUCAT1, GPUCAT1N USUBJID,SAFBFL,ANYAEFL,ANL01FL,ASPER,TRTAN,AEEXPEC,AEREL,AEBODSYS,AEDECOD
15.2.6.7	Summary of Adverse Events Leading to Study Product Discontinuation Interruption or Reduction by System Organ Class and Preferred Term – Safety Population	T AE607	ADSL ADAE	USUBJID, TRT01A, TRT01AN, SAFAFL, SAFBFL, USUBJID,SAFBFL,ANYAEFL,ANL01FL,ASPER,TRTAN,AEBODSYS,AEDECOD

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.6.8	Summary of Adverse Events Leading to Study Product Discontinuation Interruption or Reduction by Product Use Category System Organ Class and Preferred Term – Safety Population	T AE608	ADSL ADAE	USUBJID, TRT01A, TRT01AN, SAF AFL, GPUCAT1, GPUCAT1N USUBJID, SAF AFL, SAFBFL, ANYAEFL, ANL01FL, ASPER, TRTAN, TRTA, AEDECOD, AEBODSYS, AEREL, AEEXPEC
15.2.6.9	Summary of Adverse Events Related to Study Procedure by System Organ Class and Preferred Term – Safety Population	T AE609	ADSL ADAE	USUBJID, TRT01A, TRT01AN, SAF AFL, SAFBFL USUBJID, SAFBFL, ANYAEFL, ANL01FL, ASPER, TRTAN, TRTA, AEDECOD, AEBODSYS, AERELSP

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.6.10	Summary of Adverse Events by System Organ Class Preferred Term and Severity – Safety Population	T AE6010	ADSL ADAE	USUBJID, TRT01A, TRT01AN, SAF AFL, SAFBFL USUBJID, SAFBFL, ANYAEFL, ANL01FL, ASPER, TRTAN, AEBODSYS, AEDECOD, AESEV
15.2.6.11	Summary of Adverse Events by Product Use Category System Organ Class Preferred Term and Severity – Safety Population	T AE6011	ADSL ADAE	USUBJID, TRT01A, TRT01AN, SAF AFL USUBJID, ANL01FL, ASPER, TRTAN, AEBODSYS, AEDECOD, AESEV, GPUCAT1N

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.6.12	Summary of Serious Adverse Events by System Organ Class and Preferred Term – Safety Population	T AE6012	ADSL ADAE	USUBJID, TRT01A, TRT01AN, SAFAFL, SAFBFL USUBJID, SAFBFL, ANL01FL, ASPER, AESER, TRTAN, AEDECOD, AEBODSYS
15.2.6.13	Summary of Adverse Events Leading to Study Discontinuation by System Organ Class and Preferred Term – Safety Population	T AE6013	ADSL ADAE	USUBJID, TRT01A, TRT01AN, SAFAFL, SAFBFL USUBJID, SAFBFL, ANYAEFL, ANL01FL, ASPER, ANL02FL, AESER, TRTA, TRTAN, AEDECOD, AEBODSYS

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.6.14	Summary of Adverse Events Leading to Study Discontinuation by Product Use Category System Organ Class and Preferred Term – Safety Population	T_AE6014	ADSL ADAE	USUBJID, TRT01A, TRT01AN, SAFAFL USUBJID, SAFAFL, ANYAEFL, ANL01FL, ASPER, TRTAN, ANL02FL, TRTAN, AEDECOD, AEBODSYS, GPUCAT1N
15.2.6.15	Summary of THS 2.2 Menthol Device Events – Safety Population	T_DEVICE	ADSL ADDE	TRT01A, TRT01AN, SAFBFL, USUBJID, SAFAFL TRTA, TRTAN, USUBJID, AEREL, DESEV, DEDECOD, ASPER, SAFBFL, SAFAFL

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.6.16	Summary of Clinical Chemistry Parameters – Safety Population	T_LABCHEM	ADLB ADSL	SFAFL, PARCAT1, ANL01FL, DTYPE, PARAMCD, PARAMN, PARAM, AVISITN, AVISIT, ABLFL, ANRLO, ANRHI, SEXC, SFBFL, TRTA, AVALC, AVAL, CHG, LBFAST TRTAN, TRTA, ANRIND, ACLSIG, SHIFT1 SFBFL, SFAFL, TRT01AN, TRT01A,
15.2.6.17	Summary of Hematology Parameters – Safety Population	T_LABHEMA	ADLB ADSL	SFAFL, PARCAT1, ANL01FL, DTYPE, PARAMCD, PARAMN, PARAM, AVISITN, AVISIT, ABLFL, ANRLO, ANRHI, SEXC, SFBFL, TRTA, AVALC, AVAL, CHG TRTAN, TRTA, ANRIND, ACLSIG, SHIFT1 SFBFL, SFAFL, TRT01AN, TRT01A
15.2.6.18	Summary of Urinalysis Parameters – Safety Population	T_LABURIN	ADLB ADSL	SFAFL, PARCAT1, ANL01FL, DTYPE, PARAMCD, PARAMN, PARAM, AVISITN, AVISIT, ABLFL, ANRLO, ANRHI, SEXC, SFBFL, TRTA, AVALC, AVAL, CHG TRTAN, TRTA, ANRIND, ACLSIG, SHIFT1 SFBFL, SFAFL, TRT01AN, TRT01A,

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.6.19.1	Summary of Concomitant Medication by Anatomical Therapeutic Classes (ATC) 1 and 2 – Safety Population	T_CONMED_ATC	ADSL ADCM	TRTA, TRTAN, USUBJID, SAFBFL, TRT01AN, TRT01A, SAFAFL TRTA, TRTAN, USUBJID, CMFL, SAFBFL, SAFAFL, ASPER, CMATC1, CMATC2,
15.2.6.19.2	Summary of Concomitant Medication by Preferred Drug Name – Safety Population	T_CONMED	ADSL ADCM	TRTA, TRTAN, USUBJID, SAFBFL, TRT01AN, TRT01A, SAFAFL TRTA, TRTAN, USUBJID, CMFL, CMDECOD, SAFBFL, SAFAFL, ASPER
15.2.6.20	Summary of Supine Vital Signs – Safety Population	T_SUPINE	ADSL ADVS	USUBJID, TRT01A, TRT01AN, SAFBFL, SAFAFL ABLFL, ANL0IFL, AVISIT, AVISITN, TRTA, SAFAFL, ANL01FL, VSDTC

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.6.21	Summary of ECG Results – Safety Population	T_ECG	ADSL ADEG	TRT01AN, TRT01A, SAFAFL ABLFL, ANL01FL, TRTA, TRTAN, SAFAFL, AVISITN, AVISIT, ASPER, USUBJID, PARAMCD, PARAM, PARAMN, EGCLSIG, AVAL, AVALC, EGDTC
15.2.6.22	Summary of Full Lung Function Results – Safety Population	T_SPIRO	ADSL ADXP	TRT01A, TRT01AN, ANL01FL, SAFAFL, DTYPE, AVALC, TRTA, TRTAN, ABLFL, AVISIT, AVISITN, USUBJID, PARAMN, PARAM, PARAMCD, XPCLSIG, AVAL, AVALC, AVALU
15.2.6.23	Summary of Physical Examination of Body Systems – Safety Population	T_PE	ADSL ADPE	TRT01A, SAFAFL, TRT01AN SAFAFL, AVISITN, AVISIT, ABLFL, AVALC, PECLSIG, SHIFT1, TRTAN, TRTA, PARAMN, PARAMCD, PARAM
15.2.6.24	Summary of Weight Waist Circumference and BMI Results – Safety Population	T_WT_WC_BMI	ADSL ADVS	TRT01A, SAFAFL ABLFL, AVISITN, AVISIT, ANL01FL, TRTA, SAFAFL, VSDTC, USUBJID, PARAMCD, PARAM, PARAMN, AVALCAT1, OVERALL_SAFETY, TRTAN, AVALU

Table / Figure Number	Title	Program	Analysis Dataset	Analysis Variable(s)
15.2.6.25	Summary of Cough Assessments Over Study – Safety Population	T_COUGH	ADSL ADQSSY M	USUBJID, SAFBFL, TRT01AN, SAFAFL TRTA, TRTAN, PARAMN, AVAL, AVALC, SUBJID, USUBJID, ASPER, SAFBFL, SAFAFL
15.2.6.25.1	Summary of Cough Assessments by Study Day – Safety Population	T_COUGH2	ADSL ADQSSY M	USUBJID, SAFBFL, TRT01AN, SAFAFL TRTA, TRTAN, PARAMN, PARAM, AVAL, AVALC, SUBJID, USUBJID, ASPER, SAFBFL, SAFAFL, AVISITN, AVISIT

8. Appendix

Not applicable.