16.1.9 Documentation of statistical and pharmacokinetic methods

The following document is enclosed:

- Statistical analysis plan including table and listing shells, Final version 1.0, 10FEB21

STATISTICAL ANALYSIS PLAN

Study CRO-PK-20-345 - Sponsor code LDX0219

Influence of Food on the Oral Bioavailability of Ladarixin 200 mg Capsule in Healthy Volunteers of Both Sexes. A Single dose (400 mg), Randomized, Open Label, Two-Way Crossover Study

Single center, single dose, open label, randomized, two-way, crossover, food effect study

Test treatment (fed conditions):	Ladarixin 200 mg hard gelatin capsules, Dompé farmaceutici S.p.A., Italy
Reference treatment (fasting conditions):	Ladarixin 200 mg hard gelatin capsules, Dompé farmaceutici S.p.A., Italy
Sponsor:	Dompé farmaceutici S.p.A., via Santa Lucia 6; 20122 Milan, Italy Phone: +39 02.58383.1 Fax: +39 02.58383.324 Email: pieradelchi.ruffini@dompe.com Sponsor Medical Expert: Pier Adelchi Ruffini, MD -Global Clinical Development Director
Investigator:	Milko Radicioni, MD - Principal investigator CROSS Research S.A., Phase I Unit Via F.A. Giorgioli 14 CH-6864 Arzo, Switzerland Phone: +41.91.64.04.450 Fax: +41.91.64.04.451 Email: clinic@croalliance.com
Development phase:	Phase I
Version and date:	Final version 1.0, 10FEB2021

This study will be conducted in accordance with current version of Good Clinical Practice (GCP), ICH topic E6 (R2)

This document comprises 34 pages plus appendices

VERSIONS' HISTORY

Version	Date of Issue	Reason for change
Draft version 0.1	31DEC2020	Francesca Morano issued the first draft
Draft version 0.2	15JAN2021	Francesca Morano issue the second draft after internal revision
Pre-final version 0.3	02FEB2021	Francesca Morano issued pre-final version 0.3 after sponsor revision
Final version 1.0	10FEB2021	Francesca Morano issued final version 1.0 after sponsor approval

APPROVAL AND ACKNOWLEDGEMENT

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STUDY SCHEDULE

ACTIVITIES	Screening		PERIOD 1			(wash-out≥14 days)	PERIOD 2				Final visit/ETV[1]
Visit	V1	V1.1	V2	V3			V4	V5	V6		
	Day -21/-2	Day -3 or -2	Day -1	Day 1	Days 2, 3, 4		Day -3 or -2	Day -1	Day 1	Days 2, 3, 4	Day 4 of period 2[2] or early termination
Informed consent	x										
Demography	x										
Lifestyle	x										
Medical history and underlying disease	x										
Physical abnormalities	x				x[3]			x			x
Previous and concomitant medications	x	x	x	x	x	x	x	x	x	x	x
Height and Body Mass Index	x										
Body Weight	x				x[3]			x			x
Laboratory analysis[4]	x										x
Virology	x										
SARS-COV2 test		x					x				
Pregnancy test	x[5]		x[6]					x[6]			x[5]
Urine drug screening[7]	x		x					x			x
Alcohol breath test	x		x					x			x
Coagulation	x										
Vital signs[10]	x		x	x[8]	x[9]			x	x[8]	x[9]	x[11]
ECG	x		x	x[8]	x[9]			x	x[8]	x[9]	x[11]
Inclusion/exclusion criteria	x		x					x			
Subject eligibility	x		x					x			
Enrolment / randomization			x								
Confinement			x	x	x			x	x	x	
Discharge					x[12]						x
Study dosing				x[13]					x[13]		
Blood samplings				x[14]	x[14]				x[14]	x[14]	
Standardized meals			x[15]	x[16]	x[17]			x[15]	x[16]	x[17]	
Adverse events monitoring[18]	x	x	x	x	x	x	x	x	x	x	x

1. *Early termination visit (ETV) in case of premature discontinuation*
2. *Final visit on day 4 of period 2 after the 72-h post-dose blood sampling*
3. *On day 4 of period 1, upon discharge*
4. *Hematology, blood chemistry and urinalysis*
5. *Serum β-HCG test (women only)*
6. *Urine pregnancy test (women only)*
7. *Multi-drug kit (cocaine, amphetamine, methamphetamine, cannabinoids [Δ-9-tetrahydrocannabinol-THC], opiates and ecstasy)*
8. *At pre-dose*
9. *At 72 h post-dose (corresponding to the final visit assessment in period 2)*
10. *Blood pressure, heart rate, body temperature*
11. *ETV only*
12. *In the morning of day 4 of period 1*
13. *At 08:00±1 h*
14. *At pre-dose (0), 0.25, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 8, 10, 12, 18, 24, 30, 36, 48, 54, 60 and 72 h post-dose*
15. *Standardized low-fat dinner served in the evening*
16. *Subjects allocated to the fed condition (T treatment) only: a high-fat and high-caloric breakfast to be started 30 min pre-dose and completed within 30 min. Standardized lunch and dinner at approximately 13:00 (5 h post-dose on day 1) and 20:00 (12 h post-dose on day 1) in both periods*
17. *Standardized breakfast, lunch and dinner served on days 2 and 3 at approximately 09:00, 13:00 and 20:00, respectively*
18. *Adverse events monitored starting at the screening visit, immediately after informed consent, up to the final visit/ETV*

TABLES OF CONTENTS

ABBREVIATIONS

β-HCG	human chorionic gonadotropin β
λ_z	Terminal elimination rate constant, calculated, if feasible, by log-linear regression using at least 3 points
ADaM	Analysis Data Model
AE	Adverse Event
ANOVA	Analysis of Variance
AUC_{0-t}	Area under the concentration-time curve from time zero to time t
AUC∞	Area under the concentration versus time curve up to infinity
$\%AUC_{extra}$	Percentage of the residual area extrapolated to infinity in relation to the AUC∞
BLQL	Below Lower Quantification Limit
BMI	Body Mass Index
BP	Blood Pressure
BT	Body Temperature
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
C_{max}	Peak drug concentration
CPL	Clinical Project Leader
CRA	Clinical Research Associate
CRO	Contract Research Organisation
CSR	Clinical Study Report
CS	Clinically Significant
CV	Coefficient of Variation
DBP	Diastolic Blood Pressure
ECG	Electrocardiogram
eCRF	electronic Case Report Form
EMA	European Medicines Agency
ETV	Early Termination Visit
FDA	Food and Drug Administration
F_{rel}	Relative Bioavailability
FSFV	First Subject First Visit
GCP	Good Clinical Practice
HBs Ag	Hepatitis B virus surface antigen
HCV Ab	Hepatitis C virus antibodies
HIV	Human Immunodeficiency Virus
HR	Heart Rate
IB	Investigator's Brochure
ICH	International Conference on Harmonisation
IMP	Investigational Medicinal Product
INDs	Investigational New Drug applications
IUD	Intra-Uterine Device
LSLV	Last Subject Last Visit
MedDRA	Medical Dictionary for Regulatory Activities
NC	Not calculated
NDAs	New Drug Applications
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
OTC	Over The Counter
PE	Point Estimate

PK	Pharmacokinetics
PT	Preferred Term
PTAE	Pre-Treatment Adverse Event
R	Reference
SAP	Statistical Analysis Plan
SBP	Systolic Blood Pressure
SD	Standard Deviation
SOC	System Organ Class
SOP	Standard Operating Procedure
SDTM	Study Data Tabulation Model
SUSAR	Suspected Unexpected Serious Adverse Reaction
T	Test
TEAE	Treatment-Emergent Adverse Event
THC	delta-9-tetrahydrocannabinol
$t_{1/2}$	Half-life
t_{max}	Time to achieve C_{max}
USDA	United States Department of Agriculture
WHODDE	World Health Organisation Drug Dictionary Enhanced

1 INTRODUCTION

Statistical analysis will be performed by the Contract Research Organization (CRO) Biometry Unit. The end-points and methods of analysis specified in this SAP are consistent with ICH E6 (R2) and E9 guidelines (1, 2), with EMA guideline on the investigation of bioequivalence (3, 4) and on the investigation of drug interactions (5). The SAP has been compiled by the CRO Biometry Unit on the basis of the final version 1.0 of the clinical study protocol (6), reviewed by the Sponsor and finalized before the database lock.

1.1 Changes with respect to the study protocol

The following changes were introduced into the SAP with respect to the study protocol (6):

- the gender effect on bioavailability of ladarixin and its metabolites will be analysed for T and R separately using a non-parametric Wilcoxon signed ranks test on C_{max}, AUC_{0-t} and $AUC_{0-\infty}$. This analysis replaces the ANOVA including sequence, period, treatment, subject within sequence, sex and sex*treatment interaction as fixed effect. The replacement has been done with the objective to better identify the gender effect when the same treatment is administered.

2 STUDY OBJECTIVES

2.1 Objectives

2.1.1 Primary objective

Primary objective of the study is to investigate the effect of food on the bioavailability of DF 2156Y after single dose administration of 400 mg of ladarixin to healthy male and female volunteers under fed and fasting conditions.

2.1.2 Secondary objectives

- to investigate the effect of gender on the bioavailability of DF 2156Y and its metabolites (DF 2108Y and DF 2227Y) after single dose administration of 400 mg of ladarixin to healthy male and female volunteers
- to evaluate safety and tolerability of a single dose administration of 400 mg ladarixin to healthy male and female volunteers

2.2 End-points

2.2.1 Primary end-point

- to evaluate and compare the rate (C_{max}) and extent (AUC_{0-t}; $AUC_{0-\infty}$) of absorption of DF 2156Y after single dose administration of 400 mg of ladarixin under fed and fasting conditions

2.2.2 Secondary end-points

- to evaluate and compare between genders the rate (C_{max}) and extent (AUC_{0-t}; $AUC_{0-\infty}$) of absorption of DF 2156Y and its metabolites (DF 2108Y and DF 2227Y) after single dose administration of 400 mg of ladarixin to healthy male and female volunteers
- to describe the pharmacokinetic profile of DF 2156Y (total and unbound) and its metabolites (DF 2108Y and DF 2227Y) after single dose administration of 400 mg of ladarixin under fed and fasting conditions
- to collect safety and tolerability data of a single oral dose administration of 400 mg of ladarixin

3 INVESTIGATIONAL PLAN

3.1 Overall study design

Single center, single dose, open label, randomized, two-way, crossover, food effect study.

3.2 Discussion of design

The study has been designed in agreement with the ICH E6 (R2) and E9 guidelines (1, 2), with EMA guideline on the investigation of bioequivalence (3, 4) and FDA guidance on the Assessing the Effects of Food on Drugs in INDs and NDAs (7).

The sample size was not calculated through any statistical calculation. The planned sample size is estimated as sufficient for the descriptive purposes of the study in compliance with the relevant EMA guideline for PK studies (3).

Each randomized subject will be allocated to a sequence of treatments (fasting [R] or fed [T]) in the two study periods (TR or RT) according to a computer generated randomization list.

The dose of 400 mg planned for the present study was selected because it proved to be well tolerated in the previous Phase I and II clinical studies (8).

The EMA Guideline on the Investigation of Drug Interactions (5) has been taken into account for the study administration of the IMP in fed conditions.

The wash-out interval of 14 days is considered appropriate according to the known half-life of ladarixin.

The open-label design was chosen since the study endpoints are based on the objective measurement of ladarixin and its active metabolites in plasma. The outcome variables are not influenced by the subjects or investigator being aware of the administered treatment.

4 STUDY POPULATION

4.1 Target population

The study population included healthy volunteers (men and women), aged 18-55 years inclusive.

4.2 Inclusion criteria

To be enrolled in this study, subjects had to fulfill all these criteria:

1. *Informed consent*: signed written informed consent before inclusion in the study
2. *Sex and Age*: men/women, 18-55 years old inclusive
3. *Body Mass Index (BMI)*: 18.5-30 kg/m^2 inclusive
4. *Vital signs*: systolic blood pressure (SBP) 100-139 mmHg, diastolic blood pressure (DBP) 50-89 mmHg, heart rate (HR) 50-90 bpm and body temperature (BT) 35.5-37.5° C, measured after 5 min at rest in the sitting position
5. *Full comprehension*: ability to comprehend the full nature and purpose of the study, including possible risks and side effects; ability to co-operate with the investigator and to comply with the requirements of the entire study
6. *Contraception and fertility (women only)*: women of child-bearing potential must not wish to get pregnant within 30 days after the end of the study and must be using at least one of the following reliable methods of contraception:
   a. Hormonal oral, implantable, transdermal, or injectable contraceptives for at least 2 months before the screening visit until 30 days after final visit
   b. A non-hormonal intrauterine device [IUD] or female condom with spermicide or contraceptive sponge with spermicide or diaphragm with spermicide or cervical cap with spermicide for at least 2 months before the screening visit until 30 days after final visit
   c. A male sexual partner who agrees to use a male condom with spermicide until 30 days after final visit
   d. A sterile sexual partner

   Women participants of non-childbearing potential or in post-menopausal status for at least one year will be admitted.

   For all women, pregnancy test result must be negative at screening and day -1.

4.3 Exclusion criteria

Subjects meeting any of these criteria were not enrolled in the study:

1. *Electrocardiogram (ECG)* 12-leads (supine position): clinically significant abnormalities
2. *Physical findings*: clinically significant abnormal physical findings which could interfere with the objectives of the study

3. *Laboratory analyses:* clinically significant abnormal laboratory values indicative of physical illness
4. *Allergy:* ascertained or presumptive hypersensitivity to the active principles (ladarixin or derivatives) and/or formulations' ingredients; known hypersensitivity to non-steroidal anti-inflammatory drugs (NSAIDs); history of hypersensitivity to drugs (in particular methanesulfonyl propanamide) or allergic reactions in general, which the Investigator considers may affect the outcome of the study
5. *Diseases*: hypoalbuminemia or significant history of renal, hepatic, gastrointestinal, respiratory, skin, hematological, endocrine, neurological or cardiovascular diseases that may interfere with the aim of the study
6. *Medications*: medications, including over the counter drugs (in particular NSAIDs), herbal remedies and food supplements taken 14 days before the start of the study (in any case at least 5 times the half-life of the drug or a minimum of 14 days, whichever is longer), with the exception of paracetamol. Hormonal contraceptives and hormonal replacement therapy for women will be allowed
7. *Investigative drug studies:* participation in the evaluation of any investigational product for 3 months before this study. The 3-month interval is calculated as the time between the first calendar day of the month that follows the last visit of the previous study and the first day of the present study
8. *Blood donation:* blood donations for 3 months before this study
9. *Drug, alcohol, caffeine, tobacco:* history of drug, alcohol (>1 drink/day for women and >2 drinks/day for men, defined according to the USDA Dietary Guidelines 2015-2020], caffeine (>5 cups coffee/tea/day) or tobacco abuse (≥10 cigarettes/day)
10. *SARS-COV2 test:* positive SARS-COV2 test on day -3 or -2 of each study period
11. Positive to one of these test: Hepatitis B (HBs antigen), Hepatitis C (HCV antibodies), HIV 1/2 (HIV Ag/Ab combo) at screening.
12. *Drug test:* positive result at the drug test at screening or day -1 of each study period
13. *Alcohol test:* positive alcohol breath test at screening or day -1 of each study period
14. *Diet:* abnormal diets (<1600 or >3500 kcal/day) or substantial changes in eating habits in the 4 weeks before this study; vegetarians; vegans
15. *Pregnancy (women only)*: positive or missing pregnancy test at screening or day -1 of each period, pregnant or lactating women

4.3.1 Not allowed treatments

No medication, including over the counter drugs (in particular NSAIDs), herbal remedies and food supplements, is allowed for 14 days before the start of the study (in any case at least 5 times the half-life of the drug or a minimum of 14 days, whichever is longer), and during the whole study duration. Paracetamol is allowed as therapeutic counter-measure (maximum 2 g per day) for AEs according to the investigator's opinion. Hormonal contraceptives and hormonal replacement therapy for women are allowed.

The intake of any other medication is reported as a protocol deviation. However, it leads to subject's discontinuation from the study only if the investigator, together with the Sponsor, considers it could affect the study assessments or outcome.

5 STUDY SCHEDULE

The schedule of the study is summarised at page 5.

5.1 Study visits and procedures

Each study subject undergoes 8 visits.

The study protocol foresees 2 periods separated by a wash-out interval of at least 14 days. Minimum study duration is 20 days, screening visit included. A written informed consent is obtained before any study assessment or procedure.

The first subject first visit (FSFV) is defined as the 1st visit performed at the Phase I Unit by the 1st screened subject. The last subject last visit (LSLV) is defined as the last visit performed at the Phase I Unit by the last subject, i.e. the last visit foreseen by the study protocol, independently of the fact that the subject is a completer or a withdrawn subject.

The following phases, visits and procedures are performed:

- Screening phase
  - Screening – visit 1: between day -21 and day -2
  - Screening – visit 1.1: day -3 or day -2
  - Period 1 – visit 2: day -1

- Interventional phase
  - Period 1 – visit 3: days 1-4
  - Wash-out interval of at least 14 days
  - Period 2 – visit 4: day -3 or day -2
  - Period 2 – visit 5: day -1
  - Period 2 – visit 6: days 1-4

- Final phase
  - Final visit/early termination visit (ETV). In case of early discontinuation, discontinued subjects will undergo an ETV

	Day	Procedures/Assessments	Notes
Screening – Visit 1	*From day -21 to day -2*	➢ Explanation to the subject of study aims, procedures and possible risks ➢ Informed consent signature ➢ Screening number (as S001, S002, etc.) ➢ Demographic data and life style recording ➢ Medical/surgical history ➢ Previous/concomitant medications ➢ Full physical examination (body weight, height, physical abnormalities) ➢ Vital signs measurement including blood pressure (BP), heart rate (HR) and body temperature (BT) ➢ ECG recording ➢ Laboratory analyses: hematology, blood chemistry, urinalysis, serum virology and serum pregnancy test (women only) ➢ Alcohol breath test ➢ Urine multi-drug kit test ➢ AE monitoring ➢ Inclusion/exclusion criteria evaluation ➢ Eligibility evaluation	*Note:* The first two letters of the surname followed by the first two letters of the first name will be used in the Phase I Unit source document only and will not be transferred to the Sponsor.
Screening – Visit 1.1	*Day -3 or -2*	➢ Nasal and pharyngeal swab for SARS-COV2 test ➢ Adverse events monitoring ➢ Previous/concomitant medications	
Period 1 - Visit 2	*Day -1*	➢ Alcohol breath test ➢ Urine pregnancy test (women only) ➢ Urine multi-drug kit test ➢ ECG recording ➢ Vital signs measurement ➢ AE and concomitant medications ➢ Inclusion/exclusion criteria evaluation ➢ Eligibility evaluation ➢ Enrolment and randomization	Arrival at the Phase I Unit in the evening. Confinement until the morning of day 4. Standardized low-fat dinner. Fasting for at least 10 h (overnight).

	Day	Procedures/Assessments	Notes
Period 1 - Visit 3	*Day 1*	➢ Investigational medicinal product administration at 8:00 ± 1 h ➢ Vital signs measurement at pre-dose ➢ ECG recording at pre-dose ➢ Blood sample collection for PK analysis at pre-dose (0) and 0.25 (15 min), 0.5 (30 min), 1, 1.5, 2, 3, 4, 5, 6, 8, 10, 12 and 18 h post-dose ➢ AE and concomitant medications	Standardized high-fat and high caloric breakfast starting at 30 min pre-dose for subjects receiving the investigational medicinal product under fed conditions in this study period. Breakfast must be completed within 30 min. Subjects receiving the investigational medicinal product under fasting conditions will not have breakfast. Standardized lunch and dinner at about 13:00 (5 h post-dose) and 20:00 (12 h post-dose), respectively
	Days 2 and 3	➢ Blood sample collection for PK analysis at 24, 30, 36, 48, 54 and 60 h post-dose ➢ AE and concomitant medications	Standardized breakfast, lunch and dinner at about 9:00, 13:00 and 20:00, respectively
	Day 4	➢ Vital signs measurement upon discharge 72 h post-dose ➢ ECG recording upon discharge 72 h post-dose ➢ Blood sample collection for PK analysis at 72 h post-dose ➢ AE and concomitant medications ➢ Full physical examination (body weight and physical abnormalities) upon discharge	Discharge from the Phase I Unit in the morning, after the 72-h post-dose blood sample collection, ECG recording, vital signs check and full physical examination. Upon leaving, the subjects will be instructed to contact immediately the investigator in case of occurrence of any adverse reactions.
Wash-out	*At least 14 days*	A wash-out interval of at least 14 days between the two administrations of the two study periods	
Period 2 - Visit 4	*Day -3 or -2*	*As visit 1.1, day -3 or -2*	

	Day	Procedures/Assessments	Notes
Period 2 - Visit 5	*Day -1*	As visit 2, excluding enrolment and randomization. In addition full physical examination (body weight and physical abnormalities) will be performed.	As visit 2
Period 2 - Visit 6	*Days 1-4*	As visit 3. IMP administered according to the randomization list and crossover design	As visit 3
Final Visit/ETV	*Day 4 of period 2 /at ETV in case of discontinuation*	➢ Full physical examination (body weight and physical abnormalities; also vital signs and ECG in case of ETV) ➢ Alcohol breath test ➢ Urine multi-drug kit test ➢ Laboratory analyses as at screening, with the exception of virology, coagulation, microbiology, albumin and globulin ➢ AEs and concomitant medications In case of clinically significant results at the final visit, the subjects will be followed-up by the investigator until the normalization of the concerned clinical parameter(s)	Upon leaving, the subjects will be instructed to contact immediately the investigator in case of occurrence of any adverse reactions.

5.2 Diet and lifestyle

On day -1 of each period, a standardized low-fat dinner is served after confinement. On day 1 of each study period, all the subjects do not take any food or drinks (except water) for at least 10 h (i.e. overnight). The subjects allocated to the fed conditions, after the overnight fasting period, receive a high-fat and high-caloric breakfast [see § 6.2.1 of the study protocol (6) for details] starting 30 min pre-dose and complete their breakfast within 30 min, while the subjects allocated to the fasting conditions fast overnight and then receive their treatment. Water is allowed as desired, except for 1 h before and 1 h after IMP administration. In order to maintain an adequate hydration, the subjects are encouraged to drink at least 150 mL of still mineral water every 2 h for 5 h post-dose, starting at 1 h post-dose.

On day 1, all subjects remain fasted until 5 h post-dose. A standardized lunch and dinner is served at approximately 5 h and 12 h post-dose (at approximately 13:00 and 20:00).
On days 2 and 3, standardized breakfast, lunch and dinner are served to all subjects at about 9:00, 13:00 and 20:00, respectively.

One cup of coffee or tea is allowed after each meal only; any other coffee, tea or food containing xanthines (i.e. coke, chocolate, etc.), alcohol and grapefruit is forbidden during confinement. In particular, grapefruit and alcohol are forbidden for 24 h before the first IMP administration until the end of the study.

The subjects are allowed to smoke 9 cigarettes during confinement, one after each meal, with the exclusion of the high-fat and high-caloric breakfast.

During confinement, routine ambulant daily activities are strongly recommended.

5.3 Restrictions

During each study period, the subjects are confined from the evening preceding the IMP administration (study day -1) until the morning of day 4.

For the 4 h following the administration, when not involved in study activities, the subjects remain seated. They are not allowed to lie down.

During confinement, hazardous, strenuous or athletic activities are not permitted.

5.4 Protocol deviations

All un-intended departures from the approved protocol, from other agreed study documents, from relevant ICH guidelines, from other applicable regulatory requirements or from SOPs will be treated as deviations.

A deviation is defined major when it is significant and could, indirectly or over time, negatively influence the quality or the authenticity of the data, or the privacy, safety and security of the participants in a clinical trial.

6 STUDY SUBJECT IDENTIFICATION METHOD AND TREATMENT ASSIGNMENT METHOD

6.1 Unique subject identifier

All the subjects who sign the informed consent form for the present study are coded with "unique subject identifiers" when data are extracted from the study database into the domains of the CDISC SDTM model. The unique subject identifier consists of the sponsor study code (i.e. LDX0219), the 3-digit site number (i.e. 001), the 4-digit screening number (e.g. S001, S002, etc.) and, if applicable, the 3-digit subject randomization number (e.g. 001, 002, etc.). Study code, site number, screening number and subject randomization number are separated by slashes ("/") [example: LDX0219/001/S001/001].

6.2 Subject identifier for the study

The last 8 digits of the unique subject identifier (enrolled subjects), corresponding to the subject screening and subject randomization numbers separated by a slash, or the last 4 digits of the unique subject identifier (not enrolled subjects), corresponding to the subject screening number, will appear as subject identifier in the individual listings and figures of the CSR and will be used to identify the subjects in in-text tables or wording (if applicable).

6.3 Randomisation

The randomization list was computer-generated by the Biometry Unit of the CRO, using the PLAN procedure of SAS® version 9.3 (TS1M1) (9). The randomization list was supplied to the study site before study start and will be attached to the final CSR.
Randomization was stratified by sex in order to have the same number of men and women for every sequence of treatments.

6.4 Treatment allocation

Subjects were assigned to one sequence of treatments (e.g. TR or RT) i.e. to receive the IMP in fed conditions (T treatment) during period 1 and in fasting conditions (R treatment) in period 2 or vice versa according to their randomization number.
Randomization number was given to the subjects on study Day -1 of period 1 and was used to assign the treatment sequence.

6.5 Blinding

This is an open-label trial. No masking procedure will be applied since an open-label design was considered adequate for evaluating objective measures such as pharmacokinetic parameters. All the personnel involved in the analytical determinations of ladarixin and its metabolites in plasma samples collected from the volunteers will be maintained in blind conditions.

7 STUDY EVALUATION PARAMETERS

7.1 Study variables

7.1.1 Primary variables

C_{max} and AUC_{0-t} of plasma DF 2156Y after single dose administration of 400 mg of ladarixin under fed and fasting conditions.

7.1.2 Secondary variables

- $AUC_{0-\infty}$, t_{max}, $t_{1/2}$, λ_z and F_{rel} of plasma DF 2156Y after single dose administration of 400 mg of ladarixin under fed and fasting conditions
- C_{max}, AUC_{0-t}, $AUC_{0-\infty}$, t_{max}, $t_{1/2}$, λ_z and F_{rel} of plasma DF 2156Y and its metabolites (DF 2108Y and DF 2227Y) after single dose of 400 mg of ladarixin under fed and fasting conditions measured and calculated in healthy men and healthy women
- Treatment-emergent adverse events (TEAEs), vital signs (BP, HR, BT), body weight, ECGs, physical examinations, laboratory parameters (hematology, blood chemistry and urine analysis)

7.2 PK assessments

The following PK parameters will be measured and/or calculated for DF 2156Y and its metabolites, DF 2108Y and DF 2227Y.

7.2.1 PK parameters

C_{max}: Maximum plasma concentration

t_{max}: Time to achieve C_{max}

λ_z: Terminal rate constant, calculated, if feasible, by log-linear regression using at least 3 points

$t_{1/2}$: Half-life, calculated, if feasible, as $\ln 2/\lambda_z$

AUC_{0-t}: Area under the concentration-time curve from administration to the last observed concentration time t, calculated with the linear trapezoidal method

$AUC_{0-\infty}$: Area under the concentration-time curve extrapolated to infinity, calculated, if feasible, as $AUC_{0-t} + C_t/\lambda_z$, where C_t is the last measurable drug concentration

$\%AUC_{extra}$: Percentage of the residual area (C_t/λ_z) extrapolated to infinity in relation to the total $AUC_{0-\infty}$, calculated, if feasible, as $100\times[(C_t/\lambda_z)/AUC_{0-\infty}]$

F_{rel}: Relative bioavailability, calculated as ratio AUC_{0-t}(T)/ AUC_{0-t}(R)

The sampling schedule is considered adequate if the ratio $AUC_{0-t}/AUC_{0-\infty}$ equals or exceeds a factor of 0.8 (i.e. if $\%AUC_{extra}$ is <20%) for more than 80% of the individual PK profiles. This assures that the primary variable AUC_{0-t} covers a sufficient percentage of the theoretical total extent of exposure. AUC truncated at 72 h (AUC_{0-72h}) may be used as an alternative to AUC_{0-t} for comparison of extent of exposure as the absorption phase has been covered by 72 h for immediate release formulations.

The quality of log-linear regression (and, consequently, the reliability of the extrapolated PK parameters) should be demonstrated by a determination coefficient $R^2 > 0.8$. Individual extrapolated parameters, when considered unreliable, will be reported as NC (not calculated).

7.3 Safety assessments

Safety and general tolerability of the IMP will be based on TEAEs, physical examinations including body weight, vital signs, routine hematology, blood chemistry, urinalysis laboratory tests and ECGs.

7.4 COVID-19 implications

The presence of protocol deviations and/or adverse events related to the COVID-19 pandemic will be captured and listed in the same listings, but with a clear description identifying the COVID-19 pandemic relationship.

8 STATISTICAL METHOD

The statistical analysis of demographic, baseline and background characteristics, safety and tolerability data will be performed using SAS® version 9.3 (TS1M1) (9).

The PK analysis and the statistical analysis of PK parameters will be performed using Phoenix WinNonlin® version 6.3 (10) and SAS® version 9.3 (TS1M1).

The data documented in this study and the parameters measured will be evaluated and compared using classic descriptive statistics, i.e. geometric mean (PK data only), arithmetic mean, SD, CV (%), minimum, median and maximum values for quantitative variables and frequencies for qualitative variables.
Not available data will be evaluated as “missing values”.

8.1 Tables, listings and figures layout

Tables, listings and figures will be provided according to the following settings:

- Background: White
- Foreground: Black
- Font face: Times
- Font style: Roman
- Font size: 10 pt
- Font weight: Medium (data, footers and notes), Bold (titles and headers)
- Font width: Normal
- Layout: Landscape
- Top Margin: 2.5 cm
- Bottom Margin: 2.5 cm
- Left Margin: 0.8 cm
- Right Margin: 0.8 cm
- Test label: Ladarixin fed (T)
- Reference label: Ladarixin fasting (R)
- Date format: ddMMMyyyy
- Means, standard deviations, percent coefficient of variations, medians, lower confidence limits and upper confidence limits will be rounded to one digit more than the original data
- Minima and maxima will keep the same number of decimal digits as the source values
- Two-sided p-values will be rounded to the fourth decimal digit and will be flagged by an asterisk (*) in case of statistical significance (i.e. p-value < 0.05 or, in case of centre by treatment interaction, p-value < 0.10)
- p-values lower than 0.0001 will be reported as "<.0001 *".

The data and results of Ladarixin fed (T) will be presented before the data and results of Ladarixin fasting (R) in all listings and tables.

8.2 Analysis sets

8.2.1 Definitions

A subject will be defined as screened after the signature of the informed consent, regardless of the completion of all the screening procedures.

A subject will be defined as eligible if he/she meets all the inclusion/exclusion criteria. Otherwise he/she will be defined as a screen failure.

A subject will be defined as enrolled in the study if he/she is included into the interventional phase of the study. The enrolment will be performed through randomised allocation to one treatment sequence.

An eligible but not enrolled subject will be defined as a reserve.

In the present study, randomized subjects will be the same as enrolled subjects.

Analysis sets are defined as follows:

- Enrolled set: all enrolled subjects. This analysis set will be used for demographic, baseline and background characteristics
- Safety set: all subjects who receive at least one dose of study treatments. This analysis set will be used for the safety and tolerability analyses
- PK set 1: all subjects randomized who fulfill the study protocol requirements in terms of investigational treatment intake and have evaluable PK data readouts for DF 2156Y with no major deviations that may affect the PK results. This analysis set will be used for the statistical analysis of the PK results for DF 2156Y.
- PK set 2: all subjects randomized who fulfill the study protocol requirements in terms of investigational treatment intake and have evaluable PK data readouts for DF 2108Y and DF 2227Y, with no major deviations that may affect the PK results. This analysis set will be used for the statistical analysis of the PK results for DF 2108Y and DF 2227Y.

Each subject will be coded by the CRO Biometry Unit as valid or not valid for the safety set and the PK sets. Subjects will be evaluated according to the treatment they actually receive.

8.2.2 Reasons for exclusion from the PK sets

Reasons for the exclusion of subjects from the PK sets before the bioanalysis are the following:

- vomiting and diarrhea before or after drug intake which could render the plasma concentration-time profile unreliable
- intake of concomitant medications which could render the plasma concentration-time profile unreliable
- AEs which could render the plasma concentration-time profile unreliable
- administration errors which could render the plasma concentration-time profile unreliable
- other events which could render the plasma concentration-time profile unreliable

If one of these events occurred, it was to be noted in the eCRF as the study was being conducted.

Reason for the exclusion of subjects from the PK sets after the bioanalysis is the following:

- in case of more than 5 randomized patients affected by COVID-19 during the study, these subjects will be excluded from the Statistical comparison of PK parameters (§8.6.3)

8.3 Sample size and power considerations

The sample size was not calculated through any statistical calculation. A sample size of 36 subjects (18 men and 18 women) was estimated as sufficient for the descriptive purposes of the present study in compliance with the relevant EMA guideline for PK studies (3).

Drop-out subjects will not be replaced.

8.4 Demographic, baseline and background characteristics

Demographic, baseline and background characteristics will be reported for all the enrolled subjects and analyses will be performed according to the treatment they actually received.

8.4.1 Subjects' disposition

The disposition of all subjects enrolled in the study will be listed (Listing 16.2.4.1) and summarised (Table 14.1.1.1). The number and proportion of subjects enrolled, treated and completing the study, the number and proportion of withdrawals and the reasons for withdrawal will be presented.

8.4.2 Analysis sets

The subjects included in each analysis sets will be listed (Listing 16.2.4.2) and summarised by treatment group (Table 14.1.1.2).

8.4.3 Subjects excluded from PK and/or safety analysis

All subjects excluded from the PK and/or safety analysis will be listed (Listing 16.2.3.1) and the reasons for exclusion will be reported.

8.4.4 Discontinued subjects

All subjects who discontinued the clinical trial (if any) will be listed (Listing 16.2.1.1). Last IMP administered before discontinuation, gender, age, last visit performed before discontinuation, time elapsed from last IMP administration (days), date of premature discontinuation and primary reason for subject premature discontinuation will be reported.

8.4.5 Protocol deviations

All the protocol deviations reported during the clinical trial will be listed (Listing 16.2.2.1) and summarised by severity (major and minor) (Table 14.1.1.5). The number and proportion of subjects for each deviation will be reported.

8.4.6 Treatment mismatch

All subjects with actual treatment sequence different from the assigned one will be listed (Listing 16.2.2.2).

8.4.7 Demography

Demographic data will be listed (Listing 16.2.4.3) and summarised (Table 14.1.1.3). The number and proportion of subjects in each category for categorical variables (e.g. gender, race) and descriptive statistics (mean, SD, CV%, minimum, median and maximum) for continuous variables (e.g. age, weight) will be presented.

8.4.8 Inclusion/exclusion criteria not met

All the unmet inclusion/exclusion criteria will be listed (Listing 16.2.4.4) and summarised (Table 14.1.1.4).

8.4.9 Medical and surgical history

All the diseases of medical history and the surgeries of all subjects enrolled in the study will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 23.1 and listed (Listing 16.2.10.1).

8.4.10 Prior and concomitant medication

All prior and concomitant medications will be coded using the World Health Organization Drug Dictionary Enhanced (WHODDE) version March 2020 and listed (Listing 16.2.10.3).

8.4.11 Subjects' study visits

The dates of all subjects study visits will be listed (Listing 16.2.10.4).

8.4.12 Fertility status and contraceptive method

The fertility status and the contraceptive method used by the subjects will be listed (Listing 16.2.10.5).

8.4.13 Alcohol breath test, pregnancy test, SARS-COV2 test and urine drug test

The date/time and the result of alcohol breath test, pregnancy test, SARS-COV2 test and urine drug test will be listed (Listing 16.2.8.1).

8.4.14 Meals

The start date/time of the standardised meals will be listed (Listing 16.2.10.6).

8.5 IMP administration

8.5.1 IMP administration date/time

The date and time of all IMP administrations will be listed (Listing 16.2.5.1).

8.5.2 Dose per body weight

The dose per body weight of ladarixin will be listed (Listing 16.2.5.2) and summarised using descriptive statistics (Table 14.3.5.6).
The body weight collected at the screening visit will be used for the calculation.

8.5.3 Wash-out

The minimum and maximum number of days of wash-out between periods will be presented (Table 14.3.5.7).

8.6 PK analysis

The PK analysis will be performed on the subjects included into the PK Sets.

Subjects will be analysed according to the treatment they actually received.

8.6.1 PK blood samples collection

The actual date/time of PK blood samples collection will be listed (Listing 16.2.5.3).

8.6.2 Descriptive pharmacokinetics

A descriptive PK will be presented for plasma total and unbound DF 2156Y and its metabolites DF 2108Y and DF 2227Y.

Individual subject concentrations of total and unbound DF 2156Y and its metabolites DF 108Y and DF 2227Y will be presented in data listings (Listing 16.2.5.4, Listing 16.2.5.5, Listing 16.2.5.6, Listing 16.2.5.7) and summarised at each time point by treatment (Table 14.2.1.1, Table 14.2.1.2, Table 14.2.1.3, Table 14.2.1.4).

Individual (figures in section 16.2.5) and mean curves (+SD at sampling times) (figures in section 14.2.1), indicating inter-subject variability, will be plotted. Mean curves will be presented by treatment and by treatment and sex.

PK parameters of total plasma DF 2156Y and its metabolites DF 2108Y and DF 2227Y will be listed (Listing 16.2.6.1, Listing 16.2.6.2, Listing 16.2.6.3, Listing 16.2.6.4) and summarised by treatment and by treatment and sex (Table 14.2.2.1, Table 14.2.2.2, 14.2.2.3, 14.2.2.4).

Data below the lower quantification limit (BLQL) will be considered as 0 in the calculations and presented as BLQL in listings and tables. As a consequence of BLQL (i.e. 0) values, calculated geometric means (if requested) could be null. For this reason, in the presence of any null value, the geometric mean will be reported as NC. If for an individual PK curve, a log-linear regression with a correlation coefficient $R^2 > 0.8$ cannot be obtained, the

extrapolated PK parameters will be reported as NC and considered missing in the calculations of descriptive statistics.

8.6.3 Statistical comparison of pharmacokinetic parameters

For the primary end-point evaluation of food effect, C_{max}, AUC_{0-t} and $AUC_{0-\infty}$ of total plasma DF 2156Y will be compared between fed and fasting conditions (T vs. R) using analysis of variance (ANOVA) for a cross-over design on log-transformed data for evaluation of the food effect. Period, treatment, sequence and subject within sequence will be taken in account as sources of variation and they will be treated as fixed effect (Table 14.2.3.1).

The 90% confidence intervals (CI) will be calculated for the point estimates (PE, i.e. the T/R ratio of least square geometric means) of the PK parameters.

Established criteria for the absence of a food effect are that the 90% CI for the T/R ratio of the geometric means of the PK parameters under consideration are within the 80.00-125.00% range.

For the purpose of exploring the gender effect on bioavailability of ladarixin and its metabolites, C_{max}, AUC_{0-t} and $AUC_{0-\infty}$ of total plasma DF 2156Y and of DF 2108Y and DF 2227Y will be analysed for T and R separately using a non-parametric Wilcoxon signed ranks test (Table 14.2.3.2, Table 14.2.3.3, Table 14.2.3.4).

8.7 Safety and tolerability analysis

The safety and tolerability analysis will be performed on the subjects included into the Safety Set.

Subjects will be analysed according to the treatment they actually received.

8.7.1 Adverse events

AEs will be coded by System Organ Class (SOC) and Preferred Term (PT), using the Medical Dictionary for Regulatory Activities (MedDRA).
AEs will be classified as pre-treatment AEs (PTAEs) and TEAEs, according to the period of occurrence, as follows:

- PTAEs: all AEs occurring after informed consent signature by the enrolled subject but before the first dose of IMP and not negatively affected by the first dose of IMP
- TEAEs: all AEs occurring or worsening after the administration of the first dose of IMP

Individual PTAEs and TEAEs will be listed in subject data listings (Listing 16.2.7.2, Listing 16.2.7.1). No summary table will be provided for PTAEs.

TEAEs will be summarised by treatment group and overall. The number and percentage of subjects with any TEAE and the number of TEAEs will be tabulated by SOC and PT, seriousness, relationship to treatment and severity.

For TEAEs that change intensity during the study (e.g. from mild to moderate or from moderate to mild), the most severe intensity will be reported in the summary tables (Table 14.3.1.1, Table 14.3.1.2, Table 14.3.1.3, Table 14.3.1.4).

Should any serious TEAE occur, the number and percentage of subjects with any serious TEAE, the number of serious TEAEs, the number and percentage of subjects with any serious TEAE related to study drug and the number of serious TEAEs related to study drug will be presented (Table 14.3.1.5, Table 14.3.1.6).

All TEAEs leading to death will be listed, all Serious TEAEs will be listed and all TEAEs leading to discontinuation will be listed, if applicable (Table 14.3.2.1).

8.7.2 Vital signs

The date/time of vital signs assessments and the values of vital signs will be listed (Listing 16.2.9.1) and summarised using descriptive statistics at screening, day -1 and end of study (Table 14.3.5.2) and by treatment during the study (Table 14.3.5.3).
A table of all the abnormal vital signs' values will be presented (Table 14.3.5.1).

8.7.3 Body weight

Body weight values will be listed (Listing 16.2.9.1) and summarised using descriptive statistics at screening and end of study (Table 14.3.5.2).

8.7.4 ECG

The date/time of ECG assessments and the overall investigator’s interpretation (as normal, abnormal, not clinically significant or abnormal, clinically significant) and all abnormalities found (if any) will be listed (Listing 16.2.9.2, Listing 16.2.9.3).
The overall investigator's interpretations will be summarised using contingency tables at screening, day -1 and end of study (Table 14.3.5.4) and by treatment during the study (Table 14.3.5.5).

8.7.5 Laboratory data

Date/time of samples collection, overall Investigator’s interpretation (as normal or abnormal and, if abnormal, clinically significant or not clinically significant) and clinically significant findings (if any) will be listed (Listing 16.2.8.2).
All laboratory results will be listed (Listing 16.2.8.1) and a table of all the abnormal values will be presented (Table 14.3.4.1). The overall Investigator’s interpretation will be summarised using tables of frequency (Table 14.3.4.2).

8.7.6 Physical examination

Date of the physical examination, overall Investigator’s interpretation (as normal or abnormal and, if abnormal, clinically significant or not clinically significant) and clinically significant abnormalities (if any) will be listed (Listing 16.2.10.2).

8.8 Analysis datasets

Analysis datasets will be created according to the version 2.1 of the ADaM model of CDISC (11).

9 REFERENCES

1 ICH Topic E6 (R2): Good clinical practice.

2 ICH Topic E9: Statistical principles for clinical trials.

3 Guidance on the investigation of bioequivalence. CPMP/EWP/QWP/1401/98 Rev. 1/Corr **, 20 January 2010

4 Questions & Answers: Positions on specific questions addressed to the pharmacokinetics working party. EMA/618604/2008 Rev. 8, 10 October 2013

5 Guideline on the investigation of drug interactions. CPMP/EWP/560/95/Rev. 1 Corr. 2**, 21JUN2012

6 Study Protocol CRO-PK-20-345. "Influence of Food on the Oral Bioavailability of Ladarixin 200 mg Capsule in Healthy Volunteers of Both Sexes. A Single dose (400 mg), Randomized, Open Label, Two-Way Crossover Study". Final version 1.0, 28MAY2020

7 Guidance for industry. Assessing the Effects of Food on Drugs in INDs and NDAs — Clinical Pharmacology Considerations. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research. CDER, February 2019

8 Dompé, Ladarixin (DF 2156A – formerly meraxin) Investigator's Brochure, final version No. 7, 09APR20

9 SAS/STAT® User's Guide

10 Phoenix 1.3 User's Guide, Pharsight Corporation

11 CDISC Analysis Data Model Version 2.1

10 APPENDICES

1. Section 14 - Tables Shells
2. Section 16.2 - Individual Subject Data Listings Shells

Section 14 - Tables Shells

Section 14 - Tables Shells

Table 14.1.1.1 - Subjects' disposition - Enrolled set

	Overall n (%)
Enrolled	nn (xx.x)
Discontinued before treatment [1]	nn (xx.x)
Treated [1]	nn (xx.x)
Completed [2]	nn (xx.x)
Discontinued [2]	nn (xx.x)
Adverse event [2]	nn (xx.x)
Withdrawal by subject [2]	nn (xx.x)
...	...

Note: The number and the proportion of subjects of each disposition event are reported
Note 1: The denominator for calculating the proportions is the number of enrolled subjects
Note 2: The denominator for calculating the proportions is the number of enrolled and treated subjects
Source: Listing 16.2.4.1 - Subjects' disposition
Program: Tables\k345-ds-tbl.sas

Table 14.1.1.2 - Analysis sets - Enrolled set

	Enrolled Set		
	Ladarixin fed (T) N=XX n (%)	**Ladarixin fasting (R) N=XX n (%)**	**Overall N=XX n (%)**
Safety Set	nn (xx.x)	nn (xx.x)	nn (xx.x)
PK Set 1	nn (xx.x)	nn (xx.x)	nn (xx.x)
PK Set 2	nn (xx.x)	nn (xx.x)	nn (xx.x)

Note: Subjects are summarised according to the product they were assigned to
The number and the proportion of subjects included in each analysis set are reported
The denominator for calculating the proportions is the number of subjects in the enrolled set of each treatment group and overall
Source: Listing 16.2.4.2 - Analysis sets
Program: Tables\k345-ds-tbl.sas

Table 14.1.1.3 - Demography - Enrolled set, Safety set, PK set 1 and PK set 2

		Statistics	Enrolled Set N=XX	Safety Set N=XX	PK Set 1 N=XX	PK Set 2 N=XX
Sex	Female	n (%)	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
	Male	n (%)	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Race	American Indian or Alaska Native	n (%)	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
	Asian	n (%)	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
	Native Hawaiian or Other Pacific Islander	n (%)	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
	Black or African American	n (%)	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
	White	n (%)	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
	Other	n (%)	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Age (years)		N	nn	nn	nn	nn
		Mean	xx.x	xx.x	xx.x	xx.x
		SD	xx.x	xx.x	xx.x	xx.x
		CV%	xx.x	xx.x	xx.x	xx.x
		Min	xx	xx	xx	xx
		Median	xx.x	xx.x	xx.x	xx.x
		Max	xx	xx	xx	xx
Weight (kg)		N	nn	nn	nn	nn
		Mean	xx.xx	xx.xx	xx.xx	xx.xx
		SD	xx.xx	xx.xx	xx.xx	xx.xx
		CV%	xx.xx	xx.xx	xx.xx	xx.xx
		Min	xx.x	xx.x	xx.x	xx.x
		Median	xx.xx	xx.xx	xx.xx	xx.xx
		Max	xx.x	xx.x	xx.x	xx.x

Note: The number and the proportion of subjects of each sex and race are reported
The denominator for calculating the proportions is the number of subjects in each analysis set
Source: Listing 16.2.4.3 - Demography
Program: Tables\k345-dm-tbl.sas

Table 14.1.1.3 - Demography - Enrolled set, Safety set, PK set 1 and PK set 2

	Statistics	Enrolled Set N=XX	Safety Set N=XX	PK Set 1 N=XX	PK Set 2 N=XX
Body Mass Index (kg/m^2)	N	nn	nn	nn	nn
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	CV%	xx.xx	xx.xx	xx.xx	xx.xx
	Min	xx.x	xx.x	xx.x	xx.x
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Max	xx.x	xx.x	xx.x	xx.x

Note: The number and the proportion of subjects of each sex and race are reported
The denominator for calculating the proportions is the number of subjects in each analysis set
Source: Listing 16.2.4.3 - Demography
Program: Tables\k345-dm-tbl.sas

Table 14.1.1.4 - Inclusion/exclusion criteria not met - Enrolled set, Safety set, PK set 1 and PK set 2

	Enrolled Set N=XX	Safety Set N=XX	PK Set 1 N=XX	PK Set 2 N=XX
Number of subjects with any inclusion/exclusion criteria not met	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Inclusion	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Inclusion criterion 1	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Inclusion criterion 2	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
...	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Exclusion	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Exclusion criterion 1	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Exclusion criterion 2	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
...	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)

Note: The number and the proportion of subjects for any criterion not met are reported
The denominator for calculating the proportions is the number of subjects in each analysis set
Source: Listing 16.2.4.4 - Inclusion/Exclusion criteria not met
Program: Tables\k345-ie-tbl.sas

Table 14.1.1.5 - Protocol deviations - Enrolled set, Safety set, PK set 1 and PK set 2

	Enrolled Set N=XX	**Safety Set N=XX**	**PK Set 1 N=XX**	**PK Set 2 N=XX**
Number of subjects with any protocol deviation	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Major	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Treatment deviation	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Inclusion criteria violation	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Exclusion criteria violation	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Medication not admitted	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
...	...	...	...	...
Minor	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Deviation from scheduled sampling time	nn (xx.x)	nn (xx.x)	nn (xx.x)	nn (xx.x)
...	...	...	...	...

Note: The number and the proportion of subjects for any protocol violation are reported
The denominator for calculating the proportions is the number of subjects in each analysis set
Source: Listing 16.2.2.1 - Protocol deviations
Program: Tables\k345-dv-tbl.sas

Table 14.2.1.1 - Total DF 2156Y concentrations (µg/mL) measured in plasma - PK Set 1

Investigational Medicinal Product: Ladarixin fed (T)

Statistics	Pre dose	0.25 h	0.5 h	1 h	1.5 h	2 h	3 h	4 h	5 h	6 h	8 h	10 h	12 h	18 h	24 h	30 h	36 h	48 h	54 h	60 h	72 h
N	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Geo.Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
SD	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
CV%	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Min	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x
Median	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Max	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Source: Listing 16.2.5.4 - Total DF 2156Y concentrations (µg/mL) measured in plasma
Program: pk-analysis\k345-tlf.sas

Table 14.2.1.1 - Total DF 2156Y concentrations (µg/mL) measured in plasma - PK Set 1

Investigational Medicinal Product: Ladarixin fasting (R)

Statistics	Pre dose	0.25 h	0.5 h	1 h	1.5 h	2 h	3 h	4 h	5 h	6 h	8 h	10 h	12 h	18 h	24 h	30 h	36 h	48 h	54 h	60 h	72 h
N	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Geo.Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
SD	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
CV%	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Min	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x
Median	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Max	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Source: Listing 16.2.5.4 - Total DF 2156Y concentrations (µg/mL) measured in plasma
Program: pk-analysis\k345-tlf.sas

Table 14.2.1.2 - Unbound DF 2156Y concentrations (µg/mL) measured in plasma - PK Set 1

Investigational Medicinal Product: Ladarixin fed (T)

Statistics	1 h	3 h	6 h	12 h	24 h
N	xx	xx	xx	xx	xx
Geo.Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
SD	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
CV%	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Min	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x
Median	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Max	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Source: Listing 16.2.5.5 - Unbound DF 2156Y concentrations (µg/mL) measured in plasma
Program: pk-analysis\k345-tlf.sas

Table 14.2.1.2 - Unbound DF 2156Y concentrations (µg/mL) measured in plasma - PK Set 1

Investigational Medicinal Product: Ladarixin fasting (R)

Statistics	1 h	3 h	6 h	12 h	24 h
N	xx	xx	xx	xx	xx
Geo.Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
SD	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
CV%	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Min	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x
Median	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Max	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Source: Listing 16.2.5.5 - Unbound DF 2156Y concentrations (µg/mL) measured in plasma
Program: pk-analysis\k345-tlf.sas

Table 14.2.1.3 - DF 2108Y concentrations (µg/mL) measured in plasma - PK Set 2

Investigational Medicinal Product: Ladarixin fed (T)

Statistics	Pre dose	0.25 h	0.5 h	1 h	1.5 h	2 h	3 h	4 h	5 h	6 h	8 h	10 h	12 h	18 h	24 h	30 h	36 h	48 h	54 h	60 h	72 h
N	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Geo.Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
SD	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
CV%	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Min	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x
Median	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Max	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Source: Listing 16.2.5.6 - DF 2108Y concentrations (µg/mL) measured in plasma
Program: pk-analysis\k345-tlf.sas

Table 14.2.1.3 - DF 2108Y concentrations (µg/mL) measured in plasma - PK Set 2

Investigational Medicinal Product: Ladarixin fasting (R)

Statistics	Pre dose	0.25 h	0.5 h	1 h	1.5 h	2 h	3 h	4 h	5 h	6 h	8 h	10 h	12 h	18 h	24 h	30 h	36 h	48 h	54 h	60 h	72 h
N	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Geo.Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
SD	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
CV%	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Min	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x
Median	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Max	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Source: Listing 16.2.5.6 - DF 2108Y concentrations (µg/mL) measured in plasma
Program: pk-analysis\k345-tlf.sas

Table 14.2.1.4 - DF 2227Y concentrations (µg/mL) measured in plasma - PK Set 2

Investigational Medicinal Product: Ladarixin fed (T)

Statistics	Pre dose	0.25 h	0.5 h	1 h	1.5 h	2 h	3 h	4 h	5 h	6 h	8 h	10 h	12 h	18 h	24 h	30 h	36 h	48 h	54 h	60 h	72 h
N	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Geo.Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
SD	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
CV%	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Min	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x
Median	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Max	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Source: Listing 16.2.5.7 - DF 2227Y concentrations (µg/mL) measured in plasma
Program: pk-analysis\k345-tlf.sas

Table 14.2.1.4 - DF 2227Y concentrations (µg/mL) measured in plasma - PK Set 2

Investigational Medicinal Product: Ladarixin fasting (R)

Statistics	Pre dose	0.25 h	0.5 h	1 h	1.5 h	2 h	3 h	4 h	5 h	6 h	8 h	10 h	12 h	18 h	24 h	30 h	36 h	48 h	54 h	60 h	72 h
N	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Geo.Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Mean	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
SD	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
CV%	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Min	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x
Median	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Max	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Source: Listing 16.2.5.7 - DF 2227Y concentrations (µg/mL) measured in plasma
Program: pk-analysis\k345-tlf.sas

Table 14.2.2.1 - Total DF 2156Y plasma PK parameters - PK Set 1

Investigational Medicinal Product: Ladarixin fed (T)

Sex	Statistics	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	$t_{½}$ (h)	λ_z (1/h)
Males	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Females	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx

Source: Listing 16.2.6.1 - Total DF 2156Y plasma PK parameters
Program: pk-analysis\k345-tlf.sas

Table 14.2.2.1 - Total DF 2156Y plasma PK parameters - PK Set 1

Investigational Medicinal Product: Ladarixin fed (T)

Sex	Statistics	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	$t_{½}$ (h)	λ_z (1/h)
Males and Females	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx

Source: Listing 16.2.6.1 - Total DF 2156Y plasma PK parameters
Program: pk-analysis\k345-tlf.sas

Table 14.2.2.1 - Total DF 2156Y plasma PK parameters - PK Set 1

Investigational Medicinal Product: Ladarixin fasting (R)

Sex	Statistics	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	$t_{½}$ (h)	λ_z (1/h)
Males	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Females	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx

Source: Listing 16.2.6.1 - Total DF 2156Y plasma PK parameters
Program: pk-analysis\k345-tlf.sas

Table 14.2.2.1 - Total DF 2156Y plasma PK parameters - PK Set 1

Investigational Medicinal Product: Ladarixin fasting (R)

Sex	Statistics	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	$t_{½}$ (h)	λ_z (1/h)
Males and Females	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx

Source: Listing 16.2.6.1 - Total DF 2156Y plasma PK parameters
Program: pk-analysis\k345-tlf.sas

Table 14.2.2.2 - DF 2108Y plasma PK parameters - PK Set 2

Investigational Medicinal Product: Ladarixin fed (T)

Sex	Statistics	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	$t_{½}$ (h)	λ_z (1/h)
Males	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Females	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx

Source: Listing 16.2.6.2 - DF 2108Y plasma PK parameters
Program: pk-analysis\k345-tlf.sas

Table 14.2.2.2 - DF 2108Y plasma PK parameters - PK Set 2

Investigational Medicinal Product: Ladarixin fed (T)

Sex	Statistics	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	$t_{½}$ (h)	λ_z (1/h)
Males and Females	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx

Source: Listing 16.2.6.2 - DF 2108Y plasma PK parameters
Program: pk-analysis\k345-tlf.sas

Table 14.2.2.2 - DF 2108Y plasma PK parameters - PK Set 2

Investigational Medicinal Product: Ladarixin fasting (R)

Sex	Statistics	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	$t_{½}$ (h)	λ_z (1/h)
Males	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Females	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx

Source: Listing 16.2.6.2 - DF 2108Y plasma PK parameters
Program: pk-analysis\k345-tlf.sas

Table 14.2.2.2 - DF 2108Y plasma PK parameters - PK Set 2

Investigational Medicinal Product: Ladarixin fasting (R)

Sex	Statistics	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	$t_{½}$ (h)	λ_z (1/h)
Males and Females	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx

Source: Listing 16.2.6.2 - DF 2108Y plasma PK parameters
Program: pk-analysis\k345-tlf.sas

Table 14.2.2.3 - DF 2227Y plasma PK parameters - PK Set 2

Investigational Medicinal Product: Ladarixin fed (T)

Sex	Statistics	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	$t_{½}$ (h)	λ_z (1/h)
Males	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Females	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx

Source: Listing 16.2.6.3 - DF 2227Y plasma PK parameters
Program: pk-analysis\k345-tlf.sas

Table 14.2.2.3 - DF 2227Y plasma PK parameters - PK Set 2

Investigational Medicinal Product: Ladarixin fed (T)

Sex	Statistics	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	$t_{½}$ (h)	λ_z (1/h)
Males and Females	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx

Source: Listing 16.2.6.3 - DF 2227Y plasma PK parameters
Program: pk-analysis\k345-tlf.sas

Table 14.2.2.3 - DF 2227Y plasma PK parameters - PK Set 2

Investigational Medicinal Product: Ladarixin fasting (R)

Sex	Statistics	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	$t_{½}$ (h)	λ_z (1/h)
Males	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
Females	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx

Source: Listing 16.2.6.3 - DF 2227Y plasma PK parameters
Program: pk-analysis\k345-tlf.sas

Table 14.2.2.3 - DF 2227Y plasma PK parameters - PK Set 2

Investigational Medicinal Product: Ladarixin fasting (R)

Sex	Statistics	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	$t_{½}$ (h)	λ_z (1/h)
Males and Females	N	xx	xx	xx	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx

Source: Listing 16.2.6.3 - DF 2227Y plasma PK parameters
Program: pk-analysis\k345-tlf.sas

Table 14.2.2.4 - Total DF 2156Y, DF 2108Y and DF 2227Y relative bioavailability in plasma calculated as AUC_{0-t} T/R ratio - PK Sets 1 and 2

Sex	Statistics	DF 2156Y F_{rel} [1] (%)	DF 2108Y F_{rel} [2] (%)	DF 2227Y F_{rel} [2] (%)
Males	N	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx
Females	N	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx

T: Ladarixin fed (T)
R: Ladarixin fasting (R)
Note 1: PK set 1
Note 2: PK set 2
Source: Listing 16.2.6.4 - Total DF 2156Y, DF 2108Y and DF 2227Y relative bioavailability in plasma calculated as AUC_{0-t} T/R ratio
Program: pk-analysis\k345-tlf.sas

Table 14.2.2.4 - Total DF 2156Y, DF 2108Y and DF 2227Y relative bioavailability in plasma calculated as AUC_{0-t} T/R ratio - PK Sets 1 and 2

Sex	Statistics	DF 2156Y F_{rel} [1] (%)	DF 2108Y F_{rel} [2] (%)	DF 2227Y F_{rel} [2] (%)
Males and Females	N	xx	xx	xx
	Geo.Mean	xxx.xxx	xxx.xxx	xxx.xxx
	Mean	xxx.xxx	xxx.xxx	xxx.xxx
	SD	xxx.xxx	xxx.xxx	xxx.xxx
	CV%	xxx.xxx	xxx.xxx	xxx.xxx
	Min	xxx.xx	xxx.xx	xxx.xx
	Median	xxx.xxx	xxx.xxx	xxx.xxx
	Max	xxx.xx	xxx.xx	xxx.xx

T: Ladarixin fed (T)
R: Ladarixin fasting (R)
Note 1: PK set 1
Note 2: PK set 2
Source: Listing 16.2.6.4 - Total DF 2156Y, DF 2108Y and DF 2227Y relative bioavailability in plasma calculated as AUC_{0-t} T/R ratio
Program: pk-analysis\k345-tlf.sas

Table 14.2.3.1 - Statistical analysis on total DF 2156Y plasma PK parameters - PK set 1

Analysis	Dependent Variable	Comparison	Point Estimate	90% Confidence Interval Lower Limit	90% Confidence Interval Upper Limit	Effect	p Value
ANOVA	Ln(AUC_{0-inf})	T vs R	xxx.xx	xxx.xx	xxx.xx		
						Sequence	x.xxxx
						Treatment	x.xxxx
						Period	x.xxxx
ANOVA	Ln(AUC_{0-t})	T vs R	xxx.xx	xxx.xx	xxx.xx		
						Sequence	xxxxx
						Treatment	x.xxxx
						Period	x.xxxx
ANOVA	Ln(C_{max})	T vs R	xxx.xx	xxx.xx	xxx.xx		
						Sequence	x.xxxx
						Treatment	x.xxxx
						Period	x.xxxx

T: Ladarixin fed (T)
R: Ladarixin fasting (R)
Program: pk-analysis\k345-tlf.sas

Table 14.2.3.2 - Statistical analysis of gender effect on total DF 2156Y plasma PK parameters - PK set 1

Analysis	Treatment	Dependent Variable	Comparison	p Value
Wilcoxon	Ladarixin fed (T)	$AUC_{0\text{-}inf}$	Males vs Females	x.xxxx
		$AUC_{0\text{-}t}$	Males vs Females	x.xxxx
		C_{max}	Males vs Females	x.xxxx
Wilcoxon	Ladarixin fasting (R)	$AUC_{0\text{-}inf}$	Males vs Females	x.xxxx
		$AUC_{0\text{-}t}$	Males vs Females	x.xxxx
		C_{max}	Males vs Females	x.xxxx

Program: pk-analysis\k345-tlf.sas

Table 14.2.3.3 - Statistical analysis of gender effect on DF 2108Y plasma PK parameters - PK set 2

Analysis	Treatment	Dependent Variable	Comparison	p Value
Wilcoxon	Ladarixin fed (T)	$AUC_{0\text{-}inf}$	Males vs Females	x.xxxx
		$AUC_{0\text{-}t}$	Males vs Females	x.xxxx
		C_{max}	Males vs Females	x.xxxx
Wilcoxon	Ladarixin fasting (R)	$AUC_{0\text{-}inf}$	Males vs Females	x.xxxx
		$AUC_{0\text{-}t}$	Males vs Females	x.xxxx
		C_{max}	Males vs Females	x.xxxx

Program: pk-analysis\k345-tlf.sas

Table 14.2.3.4 - Statistical analysis of gender effect on DF 2227Y plasma PK parameters - PK set 2

Analysis	Treatment	Dependent Variable	Comparison	p Value
Wilcoxon	Ladarixin fed (T)	$AUC_{0\text{-}inf}$	Males vs Females	x.xxxx
		$AUC_{0\text{-}t}$	Males vs Females	x.xxxx
		C_{max}	Males vs Females	x.xxxx
Wilcoxon	Ladarixin fasting (R)	$AUC_{0\text{-}inf}$	Males vs Females	x.xxxx
		$AUC_{0\text{-}t}$	Males vs Females	x.xxxx
		C_{max}	Males vs Females	x.xxxx

Program: pk-analysis\k345-tlf.sas

Table 14.3.1.1 - Global incidence of subjects with treatment-emergent adverse events - Safety set

	Safety Set **Ladarixin fed (T)** **N=XX** **n (%) [n AE]**	**Ladarixin fasting (R)** **N=XX** **n (%) [n AE]**	**Overall** **N=XX** **n (%) [n AE]**
Treatment-emergent Adverse Events	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Relationship	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Related	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Not related	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Intensity	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Mild	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Moderate	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Severe	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Leading to discontinuation	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]

Note: Subjects are summarised according to the product they actually received
Subjects are summarised according to the each level of relationship and intensity reported in each treatment group and overall
The number and the proportion of subjects with any adverse event and the number of adverse events for each classification level are reported
The denominator for calculating the proportions is the number of subjects in the safety set of each treatment group and overall
Source: Listing 16.2.7.1 - Treatment-emergent adverse events
Program: Tables\k345-ae-01-tbl.sas

Table 14.3.1.1 - Global incidence of subjects with treatment-emergent adverse events - Safety set

	Safety Set **Ladarixin fed (T)** **N=XX** **n (%) [n AE]**	**Ladarixin fasting (R)** **N=XX** **n (%) [n AE]**	**Overall** **N=XX** **n (%) [n AE]**
Serious Treatment-emergent Adverse Events	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Relationship	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Related	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Not related	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Intensity	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Mild	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Moderate	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Severe	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Leading to discontinuation	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]

Note: Subjects are summarised according to the product they actually received
Subjects are summarised according to the each level of relationship and intensity reported in each treatment group and overall
The number and the proportion of subjects with any adverse event and the number of adverse events for each classification level are reported
The denominator for calculating the proportions is the number of subjects in the safety set of each treatment group and overall
Source: Listing 16.2.7.1 - Treatment-emergent adverse events
Program: Tables\k345-ae-01-tbl.sas

Table 14.3.1.2 - Subjects with treatment-emergent adverse events by system organ class and preferred term - Safety set

System Organ Class [1] **Preferred Term [1]**	**Safety Set** **Ladarixin fed (T)** **N=XX** **n (%) [n AE]**	**Ladarixin fasting (R)** **N=XX** **n (%) [n AE]**	**Overall** **N=XX** **n (%) [n AE]**
Treatment-emergent Adverse Events	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Nervous system disorders	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Headache	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
...	...	...	...
Gastrointestinal disorders	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Abdominal pain upper	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Diarrhoea	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
...	...	...	...

Note: Subjects are summarised according to the product they actually received
The number and the proportion of subjects with any adverse event and the number of adverse events for each classification level are reported
The denominator for calculating the proportions is the number of subjects in the safety set of each treatment group and overall
Note 1: MedDRA version 23.1
Source: Listing 16.2.7.1 - Treatment-emergent adverse events
Program: Tables\k345-ae-02-tbl.sas

Table 14.3.1.3 - Subjects with treatment-emergent adverse events by intensity, system organ class and preferred term - Safety set

	Safety Set								
	Ladarixin fed (T) N=XX			Ladarixin fasting (R) N=XX			Overall N=XX		
System Organ Class [1] Preferred Term [1]	**Mild n (%) [n AE]**	**Moderate n (%) [n AE]**	**Severe n (%) [n AE]**	**Mild n (%) [n AE]**	**Moderate n (%) [n AE]**	**Severe n (%) [n AE]**	**Mild n (%) [n AE]**	**Moderate n (%) [n AE]**	**Severe n (%) [n AE]**
Treatment-emergent Adverse Events	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]
Nervous system disorders	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]
Headache	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]
...	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]
Gastrointestinal disorders	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]
Abdominal pain upper	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]
Diarrhoea	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]
...	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]	nn (x.x) [kk]

Note: Subjects are summarised according to the treatment they actually received
The number and the proportion of subjects with any adverse event and the number of adverse events for each classification level are reported
The denominator for calculating the proportions is the number of subjects in the safety set of each treatment group and overall
Note 1: MedDRA version 23.1
Source: Listing 16.2.7.1 - Treatment-emergent adverse events
Program: Tables\k345-ae-02-tbl.sas

Table 14.3.1.4 - Subjects with treatment-emergent adverse events related to the IMP by system organ class and preferred term - Safety set

System Organ Class [1] Preferred Term [1]	Safety Set Ladarixin fed (T) N=XX n (%) [n AE]	Ladarixin fasting (R) N=XX n (%) [n AE]	Overall N=XX n (%) [n AE]
Treatment-emergent Adverse Events related to the IMP	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Nervous system disorders	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Headache	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
...	...	...	...
Gastrointestinal disorders	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Abdominal pain upper	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Diarrhoea	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
...	...	...	...

Note: Subjects are summarised according to the product they actually received
The number and the proportion of subjects with any related adverse event and the number of related adverse events for each classification level are reported
The denominator for calculating the proportions is the number of subjects in the safety set of each treatment group and overall
Note 1: MedDRA version 23.1
Source: Listing 16.2.7.1 - Treatment-emergent adverse events
Program: Tables\k345-ae-02-tbl.sas

Table 14.3.1.5 - Subjects with serious treatment-emergent adverse events by system organ class and preferred term - Safety set

System Organ Class [1] **Preferred Term [1]**	**Safety Set** **Ladarixin fed (T)** **N=XX** **n (%) [n AE]**	**Ladarixin fasting (R)** **N=XX** **n (%) [n AE]**	**Overall** **N=XX** **n (%) [n AE]**
Serious Treatment-emergent Adverse Events	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Nervous system disorders	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Headache	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
...	...	...	...
Gastrointestinal disorders	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Abdominal pain upper	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Diarrhoea	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
...	...	...	...

Note: Subjects are summarised according to the product they actually received
The number and the proportion of subjects with any serious adverse event and the number of serious adverse events for each classification level are reported
The denominator for calculating the proportions is the number of subjects in the safety set of each treatment group and overall
Note 1: MedDRA version 23.1
Source: Listing 16.2.7.1 - Treatment-emergent adverse events
Program: Tables\k345-ae-02-tbl.sas

Table 14.3.1.6 - Subjects with serious treatment-emergent adverse events related to the IMP by system organ class and preferred term - Safety set

System Organ Class [1] **Preferred Term [1]**	**Safety Set** **Ladarixin fed (T)** **N=XX** **n (%) [n AE]**	**Ladarixin fasting (R)** **N=XX** **n (%) [n AE]**	**Overall** **N=XX** **n (%) [n AE]**
Serious Treatment-emergent Adverse Events related to the IMP	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Nervous system disorders	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Headache	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
...	...	...	...
Gastrointestinal disorders	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Abdominal pain upper	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
Diarrhoea	nn (xx.x) [kk]	nn (xx.x) [kk]	nn (xx.x) [kk]
...	...	...	...

Note: Subjects are summarised according to the product they actually received
The number and the proportion of subjects with any serious related adverse event and the number of serious related adverse events for each classification level are reported
The denominator for calculating the proportions is the number of subjects in the safety set of each treatment group and overall
Note 1: MedDRA version 23.1
Source: Listing 16.2.7.1 - Treatment-emergent adverse events
Program: Tables\k345-ae-02-tbl.sas

Table 14.3.2.1 - Treatment emergent adverse events leading to death, serious adverse events or treatment emergent adverse events leading to discontinuation - Safety set

Investigational Medicinal Product: Ladarixin fed (T)

Subject ID	Adverse Event ID	Follow Up ID		
S001/001	1		Description:	Headache
			Preferred Term [1]:	Headache
			System Organ Class [1]:	Nervous system disorders
			Start Date/Time - End Date/Time (Day):	ddMMMyyyy hh:mm (k) - ddMMMyyyy hh:mm (j)
			IMP last administration before AE onset Date and Time:	ddMMMyyyy hh:mm
			Time Elapsed form Last Study Drug intake before AE	hh:mm
			Relationship to Study Drug Treatment (IMP):	N
			Severity	Mild
			AE frequency	Intermittent
			Serious Adverse Event?	N
			Seriousness criteria:	---
			Action Taken with Study Drug Treatment (IMP):	Dose not changed
			Any Concomitant Medication?:	Y
			Caused study discontinuation	Y
			Other Action Taken:	---
			Outcome:	Recovered/Resolved
			Comments:	---
...	...	...	...	...

Note: Subjects are listed according to the product they actually received
Note 1: MedDRA version 23.1.
Sources: Listing 16.2.7.1 - Treatment-emergent adverse events, Listing 16.2.7.2 - Pre-treatment adverse events (for serious adverse events only)
Program: Tables\k345-ae-03-tbl.sas

Table 14.3.2.1 - Treatment emergent adverse events leading to death, serious adverse events or treatment emergent adverse events leading to discontinuation - Safety set

Investigational Medicinal Product: Ladarixin fasting (R)

Subject ID	Adverse Event ID	Follow Up ID		
S001/001	2		Description:	Headache
			Preferred Term [1]:	Headache
			System Organ Class [1]:	Nervous system disorders
			Start Date/Time - End Date/Time (Day):	ddMMMyyyy hh:mm (k) - ddMMMyyyy hh:mm (j)
			IMP last administration before AE onset Date and Time:	ddMMMyyyy hh:mm
			Time Elapsed form Last Study Drug intake before AE	hh:mm
			Relationship to Study Drug Treatment (IMP):	N
			Severity	Mild
			AE frequency	Intermittent
			Serious Adverse Event?	N
			Seriousness criteria:	---
			Action Taken with Study Drug Treatment (IMP):	Dose not changed
			Any Concomitant Medication?:	Y
			Caused study discontinuation	Y
			Other Action Taken:	---
			Outcome:	Recovered/Resolved
			Comments:	---
...	...	...	...	...

Note: Subjects are listed according to the product they actually received
Note 1: MedDRA version 23.1.
Sources: Listing 16.2.7.1 - Treatment-emergent adverse events, Listing 16.2.7.2 - Pre-treatment adverse events (for serious adverse events only)
Program: Tables\k345-ae-03-tbl.sas

Table 14.3.4.1 - Abnormal laboratory values - Safety set

Category of Laboratory Parameters: BLOOD CHEMISTRY

Subject ID	Time Point	Collection Date/time	Parameter	Value and Abnormality [1]	Normal Range or Reference Value	Clinically Significant?
S001/001	Screening	ddMMMyyyy hh:mm	Phosphate [mmol/L]	0.84 [L]	0.87 - 1.45	N
...	...	...	...	...	...	...
S001/001	End of Study	ddMMMyyyy hh:mm	Phosphate [mmol/L]	0.84 [L]	0.87 - 1.45	N
...	...	...	...	...	...	...

Note 1: H=Higher than upper normal limit, L=Lower than lower normal limit
Source: Listing 16.2.8.1 - Individual laboratory measurements
Program: Tables\k345-lb-tbl.sas

Table 14.3.4.1 - Abnormal laboratory values - Safety set

Category of Laboratory Parameters: HEMATOLOGY

Subject ID	Time Point	Collection Date/time	Parameter	Value and Abnormality [1]	Normal Range or Reference Value	Clinically Significant?
S001/001	Screening	ddMMMyyyy hh:mm	Leukocytes [10^9/L]	10.02 [H]	4.00 - 10.00	N
...	...	...	...	...	...	...
S001/001	End of Study	ddMMMyyyy hh:mm	Leukocytes [10^9/L]	10.02 [H]	4.00 - 10.00	N
...	...	...	...	...	...	...

Note 1: H=Higher than upper normal limit, L=Lower than lower normal limit
Source: Listing 16.2.8.1 - Individual laboratory measurements
Program: Tables\k345-lb-tbl.sas

Table 14.3.4.1 - Abnormal laboratory values - Safety set

Category of Laboratory Parameters: COAGULATION

Subject ID	Time Point	Collection Date/time	Parameter	Value and Abnormality [1]	Normal Range or Reference Value	Clinically Significant?
S001/001	Screening	ddMMMyyyy hh:mm	Prothrombin time [sec]	9.00 [L]	10.00 - 13.00	N
...	...	...	...	...	...	...

Note 1: H=Higher than upper normal limit, L=Lower than lower normal limit
Source: Listing 16.2.8.1 - Individual laboratory measurements
Program: Tables\k345-lb-tbl.sas

Table 14.3.4.1 - Abnormal laboratory values - Safety set

Category of Laboratory Parameters: URINE ANALYSIS

Subject ID	Time Point	Collection Date/time	Parameter	Value and Abnormality [1]	Normal Range or Reference Value	Clinically Significant?
S001/001	Screening	ddMMMyyyy hh:mm	Urinary Hemoglobin	+++ [A]	Absent	N
...	...	...	...	...	...	...
S001/001	End of Study	ddMMMyyyy hh:mm	Urinary Hemoglobin	+++ [A]	Absent	N
...	...	...	...	...	...	...

Note 1: A=Different from reference value
Source: Listing 16.2.8.1 - Individual laboratory measurements
Program: Tables\k345-lb-tbl.sas

Table 14.3.4.2 - Contingency tables of investigator's interpretation of laboratory test results - Safety set

Time Point	Investigator's interpretation	Safety Set N=XX
Screening	Normal	nn (xx.x)
	Abnormal, Not Clinically Significant	nn (xx.x)
	Abnormal, Clinically Significant	nn (xx.x)
End of Study	Normal	nn (xx.x)
	Abnormal, Not Clinically Significant	nn (xx.x)
	Abnormal, Clinically Significant	nn (xx.x)

Note: The number and the proportion of subjects for each classification level are reported
The denominator for calculating the proportions is the number of subjects in the safety set
Source: Listing 16.2.8.2 - Investigator's interpretation of laboratory test results
Program: Tables\k345-lb-tbl.sas

Table 14.3.5.1 - Abnormal vital signs - Safety set

Subject ID	Time Point	Assessment Date/Time	Parameter	Value and Abnormality [1]	Normal Range	Clinically Significant?
S001/001	Screening	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 3 - Day 1 - Pre-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
...	...	...	...	...	...	...

Note 1: H=Higher than upper normal limit, L=Lower than lower normal limit
Source: Listing 16.2.9.1 - Vital signs and body weight
Program: Tables\k345-vs-tbl.sas

Table 14.3.5.2 - Descriptive statistics of vital signs and body weight at screening, day -1 and end of study - Safety set

Parameter	Time Point	Statistics	Safety Set N=XX
Systolic Blood Pressure [mmHg]	Screening	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Min	xxx
		Median	xxx.x
		Max	xxx
Systolic Blood Pressure [mmHg]	Day -1	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Min	xxx
		Median	xxx.x
		Max	xxx
Systolic Blood Pressure [mmHg]	End of Study	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Min	xxx
		Median	xxx.x
		Max	xxx

Note: End of Study = Visit 6 - Day 4 - 72 hour post-dose or early termination visit for vital signs, final visit or early termination visit for body weight
Source: Listing 16.2.9.1 - Vital signs and body weight
Program: Tables\k345-vs-tbl.sas

Table 14.3.5.2 - Descriptive statistics of vital signs and body weight at screening, day -1 and end of study - Safety set

Parameter	Time Point	Statistics	Safety Set N=XX
Diastolic Blood Pressure [mmHg]	Screening	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Min	xxx
		Median	xxx.x
		Max	xxx
Diastolic Blood Pressure [mmHg]	Day -1	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Min	xxx
		Median	xxx.x
		Max	xxx
Diastolic Blood Pressure [mmHg]	End of Study	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Min	xxx
		Median	xxx.x
		Max	xxx

Note: End of Study = Visit 6 - Day 4 - 72 hour post-dose or early termination visit for vital signs, final visit or early termination visit for body weight
Source: Listing 16.2.9.1 - Vital signs and body weight
Program: Tables\k345-vs-tbl.sas

Table 14.3.5.2 - Descriptive statistics of vital signs and body weight at screening, day -1 and end of study - Safety set

Parameter	Time Point	Statistics	Safety Set N=XX
Heart Rate [beats/min]	Screening	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Min	xxx
		Median	xxx.x
		Max	xxx
Heart Rate [beats/min]	Day -1	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Min	xxx
		Median	xxx.x
		Max	xxx
Heart Rate [beats/min]	End of Study	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Min	xxx
		Median	xxx.x
		Max	xxx

Note: End of Study = Visit 6 - Day 4 - 72 hour post-dose or early termination visit for vital signs, final visit or early termination visit for body weight
Source: Listing 16.2.9.1 - Vital signs and body weight
Program: Tables\k345-vs-tbl.sas

Table 14.3.5.2 - Descriptive statistics of vital signs and body weight at screening, day -1 and end of study - Safety set

Parameter	Time Point		Statistics	Safety Set N=XX
Temperature [C]	Screening		N	nn
			Mean	xxx.x
			SD	xxx.x
			CV%	xxx.x
			Min	xxx
			Median	xxx.x
			Max	xxx
Temperature [C]	Screening	< 37.5	n (%)	nn (xx.x)
		>= 37.5	n (%)	nn (xx.x)
Temperature [C]	Day -1		N	nn
			Mean	xxx.x
			SD	xxx.x
			CV%	xxx.x
			Min	xxx
			Median	xxx.x
			Max	xxx
Temperature [C]	Day -1	< 37.5	n (%)	nn (xx.x)
		>= 37.5	n (%)	nn (xx.x)
Temperature [C]	End of Study		N	nn

Note: End of Study = Visit 6 - Day 4 - 72 hour post-dose or early termination visit for vital signs, final visit or early termination visit for body weight
Source: Listing 16.2.9.1 - Vital signs and body weight
Program: Tables\k345-vs-tbl.sas

Table 14.3.5.2 - Descriptive statistics of vital signs and body weight at screening, day -1 and end of study - Safety set

Parameter	Time Point		Statistics	Safety Set N=XX
Temperature [C]	End of Study		Mean	xxx.x
			SD	xxx.x
			CV%	xxx.x
			Min	xxx
			Median	xxx.x
			Max	xxx
Temperature [C]	End of Study	< 37.5	n (%)	nn (xx.x)
		>= 37.5	n (%)	nn (xx.x)
Weight [kg]	Screening		N	nn
			Mean	xxx.x
			SD	xxx.x
			CV%	xxx.x
			Min	xxx
			Median	xxx.x
			Max	xxx
Weight [kg]	End of Study		N	nn
			Mean	xxx.x
			SD	xxx.x
			CV%	xxx.x
			Min	xxx

Note: End of Study = Visit 6 - Day 4 - 72 hour post-dose or early termination visit for vital signs, final visit or early termination visit for body weight
Source: Listing 16.2.9.1 - Vital signs and body weight
Program: Tables\k345-vs-tbl.sas

Table 14.3.5.2 - Descriptive statistics of vital signs and body weight at screening, day -1 and end of study - Safety set

Parameter	Time Point	Statistics	Safety Set N=XX
Weight [kg]	End of Study	Median	xxx.x
		Max	xxx

Note: End of Study = Visit 6 - Day 4 - 72 hour post-dose or early termination visit for vital signs, final visit or early termination visit for body weight
Source: Listing 16.2.9.1 - Vital signs and body weight
Program: Tables\k345-vs-tbl.sas

Table 14.3.5.3 - Descriptive statistics of vital signs during the study - Safety set

			Safety Set	
Parameter	**Time Point**	**Statistics**	**Ladarixin fed (T) N=XX**	**Ladarixin fasting (R) N=XX**
Systolic Blood Pressure [mmHg]	Day 1 - Pre-dose	N	nn	nn
		Mean	xxx.x	xxx.x
		SD	xxx.x	xxx.x
		CV%	xxx.x	xxx.x
		Min	xxx	xxx
		Median	xxx.x	xxx.x
		Max	xxx	xxx
Systolic Blood Pressure [mmHg]	Day 4 - 72 hour post-dose	N	nn	nn
		Mean	xxx.x	xxx.x
		SD	xxx.x	xxx.x
		CV%	xxx.x	xxx.x
		Min	xxx	xxx
		Median	xxx.x	xxx.x
		Max	xxx	xxx
Diastolic Blood Pressure [mmHg]	Day 1 - Pre-dose	N	nn	nn
		Mean	xxx.x	xxx.x
		SD	xxx.x	xxx.x
		CV%	xxx.x	xxx.x
		Min	xxx	xxx
		Median	xxx.x	xxx.x
		Max	xxx	xxx

Note: Subjects are summarised according to the product they actually received
Source: Listing 16.2.9.1 - Vital signs and body weight
Program: Tables\k345-vs-tbl.sas

Table 14.3.5.3 - Descriptive statistics of vital signs during the study - Safety set

			Safety Set	
Parameter	**Time Point**	**Statistics**	**Ladarixin fed (T) N=XX**	**Ladarixin fasting (R) N=XX**
Diastolic Blood Pressure [mmHg]	Day 4 - 72 hour post-dose	N	nn	nn
		Mean	xxx.x	xxx.x
		SD	xxx.x	xxx.x
		CV%	xxx.x	xxx.x
		Min	xxx	xxx
		Median	xxx.x	xxx.x
		Max	xxx	xxx
Heart Rate [beats/min]	Day 1 - Pre-dose	N	nn	nn
		Mean	xxx.x	xxx.x
		SD	xxx.x	xxx.x
		CV%	xxx.x	xxx.x
		Min	xxx	xxx
		Median	xxx.x	xxx.x
		Max	xxx	xxx
Heart Rate [beats/min]	Day 4 - 72 hour post-dose	N	nn	nn
		Mean	xxx.x	xxx.x
		SD	xxx.x	xxx.x
		CV%	xxx.x	xxx.x
		Min	xxx	xxx
		Median	xxx.x	xxx.x
		Max	xxx	xxx

Note: Subjects are summarised according to the product they actually received
Source: Listing 16.2.9.1 - Vital signs and body weight
Program: Tables\k345-vs-tbl.sas

Table 14.3.5.3 - Descriptive statistics of vital signs during the study - Safety set

				Safety Set	
Parameter	**Time Point**		**Statistics**	**Ladarixin fed (T) N=XX**	**Ladarixin fasting (R) N=XX**
Temperature [C]	Day 1 - Pre-dose		N	nn	nn
			Mean	xxx.x	xxx.x
			SD	xxx.x	xxx.x
			CV%	xxx.x	xxx.x
			Min	xxx	xxx
			Median	xxx.x	xxx.x
			Max	xxx	xxx
Temperature [C]	Day 1 - Pre-dose	< 37.5	n (%)	nn (xx.x)	nn (xx.x)
		>= 37.5	n (%)	nn (xx.x)	nn (xx.x)
Temperature [C]	Day 4 - 72 hour post-dose		N	nn	nn
			Mean	xxx.x	xxx.x
			SD	xxx.x	xxx.x
			CV%	xxx.x	xxx.x
			Min	xxx	xxx
			Median	xxx.x	xxx.x
			Max	xxx	xxx
Temperature [C]	Day 4 - 72 hour post-dose	< 37.5	n (%)	nn (xx.x)	nn (xx.x)
		>= 37.5	n (%)	nn (xx.x)	nn (xx.x)

Note: Subjects are summarised according to the product they actually received
Source: Listing 16.2.9.1 - Vital signs and body weight
Program: Tables\k345-vs-tbl.sas

Table 14.3.5.4 - Contingency tables of investigator's interpretation of ECG at screening, day -1 and end of study - Safety set

Time Point	Investigator's interpretation	Safety Set N=XX
Screening	Normal	nn (xx.x)
	Abnormal, Not Clinically Significant	nn (xx.x)
	Abnormal, Clinically Significant	nn (xx.x)
Day -1	Normal	nn (xx.x)
	Abnormal, Not Clinically Significant	nn (xx.x)
	Abnormal, Clinically Significant	nn (xx.x)
End of Study	Normal	nn (xx.x)
	Abnormal, Not Clinically Significant	nn (xx.x)
	Abnormal, Clinically Significant	nn (xx.x)

Note: End of Study = Visit 6 - Day 4 - 72 hour post-dose or early termination visit
The number and the proportion of subjects for each classification level are reported
The denominator for calculating the proportions is the number of subjects in the safety set
Source: Listing 16.2.9.2 - Investigator's interpretation of ECG
Program: Tables\k345-eg-tbl.sas

Table 14.3.5.5 - Contingency tables of investigator's interpretation of ECG during the study - Safety set

		Safety Set	
Time Point	**Investigator's interpretation**	**Ladarixin fed (T) N=XX**	**Ladarixin fasting (R) N=XX**
Day 1 - Pre-dose	Normal	nn (xx.x)	nn (xx.x)
	Abnormal, Not Clinically Significant	nn (xx.x)	nn (xx.x)
	Abnormal, Clinically Significant	nn (xx.x)	nn (xx.x)
Day 4 - 72 hour post-dose	Normal	nn (xx.x)	nn (xx.x)
	Abnormal, Not Clinically Significant	nn (xx.x)	nn (xx.x)
	Abnormal, Clinically Significant	nn (xx.x)	nn (xx.x)

NoteThe number and the proportion of subjects for each classification level are reported
The denominator for calculating the proportions is the number of subjects in the safety set of each treatment group
Source: Listing 16.2.9.2 - Investigator's interpretation of ECG
Program: Tables\k345-eg-tbl.sas

Table 14.3.5.6 - Descriptive statistics of dose per body weight - Safety set

Parameter	Sex	Statistics	Safety Set N=XX
Dose per body weight [mg/kg]	Females	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Median	xxx.x
		Min	xxx
		Max	xxx
Dose per body weight [mg/kg]	Males	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Median	xxx.x
		Min	xxx
		Max	xxx
Dose per body weight [mg/kg]	Females and males	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Median	xxx.x
		Min	xxx
		Max	xxx

Note: The dose per body weight was calculated using the screening body weight
Source: Listing 16.2.5.2 - Dose per body weight
Program: Tables\k345-ex-tbl.sas

Table 14.3.5.7 - Descriptive statistics of wash-out - Safety set

Parameter	Statistics	Safety Set N=XX
Wash-out between IMP administration of Period 1 and Period 2 [days]	N	nn
	Min	xxx
	Max	xxx

Note: The wash-out is calculated as the difference in days between the dates of product administrations
Source: Listing 16.2.5.1 - Investigational medicinal products administration
Program: Tables\k345-ex-tbl.sas

Section 16.2 - Individual Subject Data Listings Shells

Section 16.2 - Individual Subject Data Listings Shells

Listing 16.2.1.1 - Discontinued subjects

Subject ID	Last IMP before discontinuation	Sex	Age (years)	Last visit	Time elapsed from last drug administration (days)	Date of premature discontinuation	Primary reason for subject premature study termination
S001/001	Ladarixin fed (T)	M	30	Visit 3	1	ddMMMyyyy	Withdrawal by subject
S003/002	Ladarixin fasting (R)	F	27	Visit 5	2	ddMMMyyyy	Adverse event
S005/004	Ladarixin fasting (R)	M	18	Visit 3	2	ddMMMyyyy	Physician decision
S007/006	Ladarixin fed (T)	F	27	Visit 5	2	ddMMMyyyy	Adverse event
S011/010	Ladarixin fasting (R)	M	18	Visit 3	2	ddMMMyyyy	Physician decision
...	...	...		...	...	...	...

Note: Subjects are listed according to the last product they actually received before discontinuation
Program: Listings\k345-ds-lst.sas

Listing 16.2.2.1 - Protocol deviations

Subject ID	Deviation Number	Deviation Category	Deviation Coded Term	Deviation Description
S001/001	1	Minor	Deviation from scheduled sampling time	Sample number 2 was collected outside the window of 15 min post-dose
S007/006	1	Major	Inclusion criteria violation	Inclusion criteria violation
...		...	...	...

Program: Listings\k345-dv-lst.sas

Listing 16.2.2.2 - Assigned and actual sequence of treatments mismatches

Subject ID	Assigned Sequence of Treatments	Actual Sequence of Treatments
S003/002	Ladarixin fed (T) - Ladarixin fasting (R)	Ladarixin fasting (R) - Ladarixin fed (T)
...	...	...

Program: Listings\k345-ds-lst.sas

Listing 16.2.3.1 - Subjects excluded from PK and/or safety analysis

Subject ID	Sex	Age (years)	Enrolled Set	Safety Set	PK Set 1	PK Set 2	Reason for the exclusion
S010/008	F	30	Y	N	N	N	Lack of IMP administration
S015/013	F	20	Y	Y	Y	Y	Major protocol deviations
...	...		.	.	.	.	...

Program: Listings\k345-ds-lst.sas

Listing 16.2.4.1 - Subjects' disposition

Subject ID	Date of Informed Consent	Date of Screening	Date of Enrolment	Date of First Administration	Date of Last Administration	Completed or Discontinued	Date of Study Completion or Discontinuation	Date of End of Participation	Reason for discontinuation
S001/001	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	Discontinued	ddMMMyyyy	ddMMMyyyy	Withdrawal by subject
S002/002	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	Completed	ddMMMyyyy	ddMMMyyyy	
S005/003	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	Discontinued	ddMMMyyyy	ddMMMyyyy	Adverse event
...	...	...	...	...	...	...	...	...	...

Program: Listings\k345-ds-lst.sas

Listing 16.2.4.2 - Analysis sets

Subject ID	Planned Sequence	Enrolled Set	Safety Set	PK Set 1	PK Set 2	Reason for the exclusion
S001/001	Ladarixin fed (T) - Ladarixin fasting (R)	Y	N	N	N	Lack of IMP intake
S003/002	Ladarixin fasting (R) - Ladarixin fed (T)	Y	Y	Y	Y	
...	...	.	.	.	.	...

Note: Subjects are listed according to the sequence they were assigned to
Program: Listings\k345-ds-lst.sas

Listing 16.2.4.3 - Demography

Subject ID	Sex	Race	Birth Year	Age (years)	Height (cm)	Body Weight (kg)	Body Mass Index (kg/m^2)
S001/001	F	White	2001	19	170	55.0	19.0
S002/002	M	White	1990	30	187	91.0	26.0
...	...	...	...		...	...	...

Note:Program:Listings\k345-dm-lst.sas

Listing 16.2.4.4 - Inclusion/Exclusion criteria not met

Subject ID	Criterion	Verbatim
S001/001	Inclusion criterion 3	Body Mass Index (BMI): 18.5-30 kg/m2 inclusive
...	...	...

Program: Listings\k345-ie-lst.sas

Listing 16.2.5.1 - Investigational medicinal products administration

Investigational Medicinal Product: Ladarixin fed (T)

Subject ID	Adm. Nr.	Administration Time Point	Administration Date/time	Breakfast Start Date/time	Time from Start of Breakfast	Fasting Conditions Start Date/time	Time from Start of Fasting Conditions	Fasting Conditions From 10 h before IMP Administration?
S001/001	1	Visit 3 - Day 1 - 08:00 ± 1 hour	ddMMMyyyy hh:mm	ddMMMyyyy hh:mm	xx min	---	---	---
...	...	...	...	...	...	...	...	...

Note: Subjects are listed according to the product they actually received
Program: Listings\k345-ex-lst.sas

Listing 16.2.5.1 - Investigational medicinal products administration

Investigational Medicinal Product: Ladarixin fasting (R)

Subject ID	Adm. Nr.	Administration Time Point	Administration Date/time	Breakfast Start Date/time	Time from Start of Breakfast	Fasting Conditions Start Date/time	Time from Start of Fasting Conditions	Fasting Conditions From 10 h before IMP Administration?
S001/001	2	Visit 6 - Day 1 - 08:00 ± 1 hour	ddMMMyyyy hh:mm	---	---	ddMMMyyyy hh:mm	xx h xx min	Y
...	...	...	...	...	...	...	...	...

Note: Subjects are listed according to the product they actually received
Program: Listings\k345-ex-lst.sas

Listing 16.2.5.2 - Dose per body weight

Subject ID	Active Ingredient	Dose Administered (mg)	Body Weight at Screening (kg)	Dose per Body Weight (mg/kg)
S001/001	Ladarixin	800	55.0	14.54
...	...	...	...	...

Note: The dose per body weight is calculated using the screening body weight
Program: Listings\k345-ex-lst.sas

Listing 16.2.5.3 - PK samples collection dates and times

Investigational Medicinal Product: Ladarixin fed (T)

Subject ID	IMP Administration Date/Time	IMP Adm Nr.	Time Point	Sample Number	Collection Date/time	Time from IMP Administration
S001/001	ddMMMyyyy hh:mm	1	Pre-dose - Within 30 min before IMP administration	1	ddMMMyyyy hh:mm	-xx min
S001/001	ddMMMyyyy hh:mm	1	15 min post-dose	2	ddMMMyyyy hh:mm	xx min
S001/001	ddMMMyyyy hh:mm	1	30 min post-dose ± 1 min	3	ddMMMyyyy hh:mm	xx min
S001/001	ddMMMyyyy hh:mm	1	1 hour post-dose ± 3 min	4	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	1.5 hour post-dose ± 3 min	5	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	2 hours post-dose ± 5 min	6	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	3 hours post-dose ± 5 min	7	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	4 hours post-dose ± 5 min	8	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	5 hours post-dose ± 5 min	9	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	6 hours post-dose ± 5 min	10	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	8 hours post-dose ± 10 min	11	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	10 hours post-dose ± 10 min	12	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	12 hours post-dose ± 10 min	13	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	18 hours post-dose ± 10 min	14	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	24 hours post-dose ± 10 min	15	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	30 hours post-dose ± 10 min	16	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	36 min post-dose ± 30 min	17	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	48 hour post-dose ± 30 min	18	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	54 hour post-dose ± 30 min	19	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	60 hours post-dose ± 30 min	20	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	72 hours post-dose ± 30 min	21	ddMMMyyyy hh:mm	xx h xx min
...	...	...	...	...	...	...

Note: Subjects are listed according to the product they actually received
Program: Listings\k345-pc-lst.sas

Listing 16.2.5.3 - PK samples collection dates and times

Investigational Medicinal Product: Ladarixin fasting (R)

Subject ID	IMP Administration Date/Time	IMP Adm Nr.	Time Point	Sample Number	Collection Date/time	Time from IMP Administration
S001/001	ddMMMyyyy hh:mm	2	Pre-dose - Within 30 min before IMP administration	22	ddMMMyyyy hh:mm	-xx min
S001/001	ddMMMyyyy hh:mm	2	15 min post-dose	23	ddMMMyyyy hh:mm	xx min
S001/001	ddMMMyyyy hh:mm	2	30 min post-dose ± 1 min	24	ddMMMyyyy hh:mm	xx min
S001/001	ddMMMyyyy hh:mm	2	1 hour post-dose ± 3 min	25	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	1.5 hour post-dose ± 3 min	26	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	2 hours post-dose ± 5 min	27	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	3 hours post-dose ± 5 min	28	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	4 hours post-dose ± 5 min	29	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	5 hours post-dose ± 5 min	30	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	6 hours post-dose ± 5 min	31	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	8 hours post-dose ± 10 min	32	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	10 hours post-dose ± 10 min	33	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	12 hours post-dose ± 10 min	34	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	18 hours post-dose ± 10 min	35	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	24 hours post-dose ± 10 min	36	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	30 hours post-dose ± 10 min	37	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	36 min post-dose ± 30 min	38	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	48 hour post-dose ± 30 min	39	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	54 hour post-dose ± 30 min	40	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	60 hours post-dose ± 30 min	41	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	72 hours post-dose ± 30 min	42	ddMMMyyyy hh:mm	xx h xx min
...	...	...	...	...	...	...

Note: Subjects are listed according to the product they actually received
Program: Listings\k345-pc-lst.sas

Listing 16.2.5.4 - Total DF 2156Y concentrations (µg/mL) measured in plasma

Investigational Medicinal Product: Ladarixin fed (T)

Subject ID	Period	Pre dose	0.25 h	0.5 h	1 h	1.5 h	2 h	3 h	4 h	5 h	6 h	8 h	10 h	12 h	18 h	24 h	30 h	36 h	48 h	54 h	60 h	72 h
S001/001	1	BLQL	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
...		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Program: pk-analysis\k345-tlf.sas

Listing 16.2.5.4 - Total DF 2156Y concentrations (µg/mL) measured in plasma

Investigational Medicinal Product: Ladarixin fasting (R)

Subject ID	Period	Pre dose	0.25 h	0.5 h	1 h	1.5 h	2 h	3 h	4 h	5 h	6 h	8 h	10 h	12 h	18 h	24 h	30 h	36 h	48 h	54 h	60 h	72 h
S001/001	2	BLQL	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
...		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Program: pk-analysis\k345-tlf.sas

Listing 16.2.5.5 - Unbound DF 2156Y concentrations (µg/mL) measured in plasma

Investigational Medicinal Product: Ladarixin fed (T)

Subject ID	Period	1 h	3 h	6 h	12 h	24 h
S001/001	1	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
...		...	...	...	...	...

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Program: pk-analysis\k345-tlf.sas

Listing 16.2.5.5 - Unbound DF 2156Y concentrations (µg/mL) measured in plasma

Investigational Medicinal Product: Ladarixin fasting (R)

Subject ID	Period	1 h	3 h	6 h	12 h	24 h
S001/001	2	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
...		...	...	...	...	...

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Program: pk-analysis\k345-tlf.sas

Listing 16.2.5.6 - DF 2108Y concentrations (µg/mL) measured in plasma

Investigational Medicinal Product: Ladarixin fed (T)

Subject ID	Period	Pre dose	0.25 h	0.5 h	1 h	1.5 h	2 h	3 h	4 h	5 h	6 h	8 h	10 h	12 h	18 h	24 h	30 h	36 h	48 h	54 h	60 h	72 h
S001/001	1	BLQL	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
...		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Program: pk-analysis\k345-tlf.sas

Listing 16.2.5.6 - DF 2108Y concentrations (µg/mL) measured in plasma

Investigational Medicinal Product: Ladarixin fasting (R)

Subject ID	Period	Pre dose	0.25 h	0.5 h	1 h	1.5 h	2 h	3 h	4 h	5 h	6 h	8 h	10 h	12 h	18 h	24 h	30 h	36 h	48 h	54 h	60 h	72 h
S001/001	2	BLQL	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
...		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Program: pk-analysis\k345-tlf.sas

Listing 16.2.5.7 - DF 2227Y concentrations (µg/mL) measured in plasma

Investigational Medicinal Product: Ladarixin fed (T)

Subject ID	Period	Pre dose	0.25 h	0.5 h	1 h	1.5 h	2 h	3 h	4 h	5 h	6 h	8 h	10 h	12 h	18 h	24 h	30 h	36 h	48 h	54 h	60 h	72 h
S001/001	1	BLQL	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
...		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Program: pk-analysis\k345-tlf.sas

Listing 16.2.5.7 - DF 2227Y concentrations (µg/mL) measured in plasma

Investigational Medicinal Product: Ladarixin fasting (R)

Subject ID	Period	Pre dose	0.25 h	0.5 h	1 h	1.5 h	2 h	3 h	4 h	5 h	6 h	8 h	10 h	12 h	18 h	24 h	30 h	36 h	48 h	54 h	60 h	72 h
S001/001	2	BLQL	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
...		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...

BLQL: Below Lower Quantification Limit (x.xx µg/mL)
Program: pk-analysis\k345-tlf.sas

Listing 16.2.6.1 - Total DF 2156Y plasma PK parameters

Investigational Medicinal Product: Ladarixin fed (T)

Subject ID	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	AUC_{extra} (%)	$t_{½}$ (h)	λ_z (1/h)	Points	R^2
S001/001	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
...	...	...	...	...	...	...	...	...	...

Note: Only subjects included in PK Set 1 are listed
Program: pk-analysis\k345-tlf.sas

Listing 16.2.6.1 - Total DF 2156Y plasma PK parameters

Investigational Medicinal Product: Ladarixin fasting (R)

Subject ID	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	AUC_{extra} (%)	$t_{½}$ (h)	λ_z (1/h)	Points	R^2
S001/001	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
...	...	...	...	...	...	...	...	...	...

Note: Only subjects included in PK Set 1 are listed
Program: pk-analysis\k345-tlf.sas

Listing 16.2.6.2 - DF 2108Y plasma PK parameters

Investigational Medicinal Product: Ladarixin fed (T)

Subject ID	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	AUC_{extra} (%)	$t_{½}$ (h)	λ_z (1/h)	Points	R^2
S001/001	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
...	...	...	...	...	...	...	...	...	...

Note: Only subjects included in PK Set 2 are listed
Program: pk-analysis\k345-tlf.sas

Listing 16.2.6.2 - DF 2108Y plasma PK parameters

Investigational Medicinal Product: Ladarixin fasting (R)

Subject ID	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	AUC_{extra} (%)	$t_{½}$ (h)	λ_z (1/h)	Points	R^2
S001/001	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
...	...	...	...	...	...	...	...	...	...

Note: Only subjects included in PK Set 2 are listed
Program: pk-analysis\k345-tlf.sas

Listing 16.2.6.3 - DF 2227Y plasma PK parameters

Investigational Medicinal Product: Ladarixin fed (T)

Subject ID	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	AUC_{extra} (%)	$t_{½}$ (h)	λ_z (1/h)	Points	R^2
S001/001	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
...	...	...	...	...	...	...	...	...	...

Note: Only subjects included in PK Set 2 are listed
Program: pk-analysis\k345-tlf.sas

Listing 16.2.6.3 - DF 2227Y plasma PK parameters

Investigational Medicinal Product: Ladarixin fasting (R)

Subject ID	C_{max} (µg/mL)	t_{max} (h)	AUC_{0-t} (h*µg/mL)	AUC_{0-inf} (h*µg/mL)	AUC_{extra} (%)	$t_{½}$ (h)	λ_z (1/h)	Points	R^2
S001/001	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
...	...	...	...	...	...	...	...	...	...

Note: Only subjects included in PK Set 2 are listed
Program: pk-analysis\k345-tlf.sas

Listing 16.2.6.4 - Total DF 2156Y, DF 2108Y and DF 2227Y relative bioavailability in plasma calculated as AUC_{0-t} T/R ratio

Subject ID	DF 2156Y F_{rel} (%)	DF 2108Y F_{rel} (%)	DF 2227Y F_{rel} (%)
S001/001	xxx.xx	xxx.xx	xxx.xx
...	...	...	...

T: Ladarixin fed (T)
R: Ladarixin fasting (R)
Program: pk-analysis\k345-tlf.sas

Listing 16.2.7.1 - Treatment-emergent adverse events

Investigational Product: Ladarixin fed (T)

Subject ID	Adverse Event ID		
S001/001	1	Description:	Headache
		AE Record date and time:	ddMMMyyyy hh:mm
		Body Location:	Head
		Preferred Term [1]:	Headache
		System Organ Class [1]:	Nervous system disorders
		Serious?	N
		Frequency:	Continuous
		Severity:	Mild
		Action taken with Study Drug:	Dose not changed
		Relationship with Investigational Study Drug?	Unlikely (remote)
		Corrective therapy?	Y
		Other Action Taken:	---
		Outcome:	Resolved
		Start - End Date/Time (Day):	ddMMMyyyy hh:mm (k) - ddMMMyyyy hh:mm (k+n)
		Did this Adverse Event result in discontinuation of the subject from the study?	N
...	...	...	...

Note: Subjects are listed according to the product they actually received
Note 1: MedDRA version 23.1
Program: Listings\k345-ae-lst.sas

Listing 16.2.7.1 - Treatment-emergent adverse events

Investigational Product: Ladarixin fasting (R)

Subject ID	Adverse Event ID		
S001/001	2	Description:	Headache
		AE Record date and time:	ddMMMyyyy hh:mm
		Body Location:	Head
		Preferred Term [1]:	Headache
		System Organ Class [1]:	Nervous system disorders
		Serious?	N
		Frequency:	Continuous
		Severity:	Mild
		Action taken with Study Drug:	Dose not changed
		Relationship with Investigational Study Drug?	Unlikely (remote)
		Corrective therapy?	Y
		Other Action Taken:	---
		Outcome:	Resolved
		Start - End Date/Time (Day):	ddMMMyyyy hh:mm (k) - ddMMMyyyy hh:mm (k+n)
		Did this Adverse Event result in discontinuation of the subject from the study?	N
...	...	...	...

Note: Subjects are listed according to the product they actually received
Note 1: MedDRA version 23.1
Program: Listings\k345-ae-lst.sas

Listing 16.2.7.2 - Pre-treatment adverse events

Subject ID	Adverse Event ID		
S001/001	1	Description:	Headache
		AE Record date and time:	ddMMMyyyy hh:mm
		Body Location:	Head
		Preferred Term [1]:	Headache
		System Organ Class [1]:	Nervous system disorders
		Serious?	N
		Frequency:	Continuous
		Severity:	Mild
		Action taken with Study Drug:	Dose not changed
		Relationship with Investigational Study Drug?	Unlikely (remote)
		Corrective therapy?	Y
		Other Action Taken:	---
		Outcome:	Resolved
		Start - End Date/Time (Day):	ddMMMyyyy hh:mm (k) - ddMMMyyyy hh:mm (k+n)
		Did this Adverse Event result in discontinuation of the subject from the study?	N
...	...	...	...

Note 1: MedDRA version 23.1
Program: Listings\k345-ae-lst.sas

Listing 16.2.8.1 - Individual laboratory measurements

Category of Laboratory Parameters: BLOOD CHEMISTRY

Subject ID	Time Point	Collection Date/time	Parameter	Value and Abnormality [1]	Normal Range or Reference Value	Clinically Significant?
S001/001	Screening	ddMMMyyyy hh:mm	Sodium [mmol/L]	138 [N]	136 - 145	N
S001/001	Screening	ddMMMyyyy hh:mm	Potassium [mmol/L]	4.4 [N]	3.5 - 5.1	N
S001/001	Screening	ddMMMyyyy hh:mm	Calcium [mmol/L]	2.27 [N]	2.10 - 2.55	N
S001/001	Screening	ddMMMyyyy hh:mm	Chloride [mmol/L]	103 [N]	96 - 110	N
S001/001	Screening	ddMMMyyyy hh:mm	Phosphate [mmol/L]	0.84 [L]	0.87 - 1.45	N
S001/001	Screening	ddMMMyyyy hh:mm	Alkaline Phosphatase [U/L]	95 [N]	<= 129	N
S001/001	Screening	ddMMMyyyy hh:mm	Gamma Glutamyl Transferase [U/L]	17 [N]	<= 66	N
S001/001	Screening	ddMMMyyyy hh:mm	Aspartate Aminotransferase [U/L]	24 [N]	<= 50	N
S001/001	Screening	ddMMMyyyy hh:mm	Alanine Aminotransferase [U/L]	30 [N]	<= 50	N
...	...	...	...	...	...	...
S001/001	End of Study	ddMMMyyyy hh:mm	Sodium [mmol/L]	138 [N]	136 - 145	N
S001/001	End of Study	ddMMMyyyy hh:mm	Potassium [mmol/L]	4.4 [N]	3.5 - 5.1	N
S001/001	End of Study	ddMMMyyyy hh:mm	Calcium [mmol/L]	2.27 [N]	2.10 - 2.55	N
S001/001	End of Study	ddMMMyyyy hh:mm	Chloride [mmol/L]	103 [N]	96 - 110	N
S001/001	End of Study	ddMMMyyyy hh:mm	Phosphate [mmol/L]	0.84 [L]	0.87 - 1.45	N
S001/001	End of Study	ddMMMyyyy hh:mm	Alkaline Phosphatase [U/L]	95 [N]	<= 129	N
S001/001	End of Study	ddMMMyyyy hh:mm	Gamma Glutamyl Transferase [U/L]	17 [N]	<= 66	N
S001/001	End of Study	ddMMMyyyy hh:mm	Aspartate Aminotransferase [U/L]	24 [N]	<= 50	N
S001/001	End of Study	ddMMMyyyy hh:mm	Alanine Aminotransferase [U/L]	30 [N]	<= 50	N
...	...	...	...	...	...	...

Note 1: N=Normal, H=Higher than upper normal limit, L=Lower than lower normal limit
Program: Listings\k345-lb-lst.sas

Listing 16.2.8.1 - Individual laboratory measurements

Category of Laboratory Parameters: HEMATOLOGY

Subject ID	Time Point	Collection Date/time	Parameter	Value and Abnormality [1]	Normal Range or Reference Value	Clinically Significant?
S001/001	Screening	ddMMMyyyy hh:mm	Leukocytes [10^9/L]	10.02 [H]	4.00 - 10.00	N
S001/001	Screening	ddMMMyyyy hh:mm	Erythrocytes [10^12/L]	5.19 [N]	4.30 - 5.90	N
S001/001	Screening	ddMMMyyyy hh:mm	Hemoglobin [g/dL]	15.4 [N]	14.0 - 18.0	N
S001/001	Screening	ddMMMyyyy hh:mm	Hemoglobin [mmol/L]	9.6 [N]	8.7 - 11.2	N
S001/001	Screening	ddMMMyyyy hh:mm	Hematocrit [%]	44 [N]	42 - 52	N
S001/001	Screening	ddMMMyyyy hh:mm	Ery. Mean Corpuscular Volume [fL]	84 [N]	83 - 100	N
S001/001	Screening	ddMMMyyyy hh:mm	Ery. Mean Corpuscular Hemoglobin [pg]	30 [N]	27 - 34	N
S001/001	Screening	ddMMMyyyy hh:mm	Ery. Mean Corpuscular HGB Concentration [g/dL]	35 [N]	32 - 36	N
...	...	...	...	...	...	...
S001/001	End of Study	ddMMMyyyy hh:mm	Leukocytes [10^9/L]	10.02 [H]	4.00 - 10.00	N
S001/001	End of Study	ddMMMyyyy hh:mm	Erythrocytes [10^12/L]	5.19 [N]	4.30 - 5.90	N
S001/001	End of Study	ddMMMyyyy hh:mm	Hemoglobin [g/dL]	15.4 [N]	14.0 - 18.0	N
S001/001	End of Study	ddMMMyyyy hh:mm	Hemoglobin [mmol/L]	9.6 [N]	8.7 - 11.2	N
S001/001	End of Study	ddMMMyyyy hh:mm	Hematocrit [%]	44 [N]	42 - 52	N
S001/001	End of Study	ddMMMyyyy hh:mm	Ery. Mean Corpuscular Volume [fL]	84 [N]	83 - 100	N
S001/001	End of Study	ddMMMyyyy hh:mm	Ery. Mean Corpuscular Hemoglobin [pg]	30 [N]	27 - 34	N
S001/001	End of Study	ddMMMyyyy hh:mm	Ery. Mean Corpuscular HGB Concentration [g/dL]	35 [N]	32 - 36	N
...	...	...	...	...	...	...

Note 1: N=Normal, H=Higher than upper normal limit, L=Lower than lower normal limit
Program: Listings\k345-lb-lst.sas

Listing 16.2.8.1 - Individual laboratory measurements

Category of Laboratory Parameters: COAGULATION

Subject ID	Time Point	Collection Date/time	Parameter	Value and Abnormality [1]	Normal Range or Reference Value	Clinically Significant?
S001/001	Screening	ddMMMyyyy hh:mm	Prothrombin time [sec]	12.00 [N]	10.00 - 13.00	N
S001/001	Screening	ddMMMyyyy hh:mm	aPTT [sec]	31.00 [N]	30.00 - 40.00	N
...	...	...	...	...	...	...

Note 1: N=Normal, H=Higher than upper normal limit, L=Lower than lower normal limit
Program: Listings\k345-lb-lst.sas

Listing 16.2.8.1 - Individual laboratory measurements

Category of Laboratory Parameters: URINE ANALYSIS

Subject ID	Time Point	Collection Date/time	Parameter	Value and Abnormality [1]	Normal Range or Reference Value	Clinically Significant?
S001/001	Screening	ddMMMyyyy hh:mm	Urobilinogen	Normal [N]	Normal	N
S001/001	Screening	ddMMMyyyy hh:mm	Urinary Bilirubin	Absent [N]	Absent	N
S001/001	Screening	ddMMMyyyy hh:mm	Ketones	Absent [N]	Absent	N
S001/001	Screening	ddMMMyyyy hh:mm	Urinary Hemoglobin	+++ [A]	Absent	N
S001/001	Screening	ddMMMyyyy hh:mm	Urinary Leukocytes	Absent [N]	Absent	N
S001/001	Screening	ddMMMyyyy hh:mm	Sediment Examination	Checked		
S001/001	Screening	ddMMMyyyy hh:mm	Urinary Sediment Leukocytes	Absent [N]	Absent or 0-2 per field	N
S001/001	Screening	ddMMMyyyy hh:mm	Urinary Sediment Erythrocytes	0-2 per field [N]	Absent or 0-2 per field	N
...	...	...	...	...	...	...
S001/001	End of Study	ddMMMyyyy hh:mm	Urobilinogen	Normal [N]	Normal	N
S001/001	End of Study	ddMMMyyyy hh:mm	Urinary Bilirubin	Absent [N]	Absent	N
S001/001	End of Study	ddMMMyyyy hh:mm	Ketones	Absent [N]	Absent	N
S001/001	End of Study	ddMMMyyyy hh:mm	Urinary Hemoglobin	+++ [A]	Absent	N
S001/001	End of Study	ddMMMyyyy hh:mm	Urinary Leukocytes	Absent [N]	Absent	N
S001/001	End of Study	ddMMMyyyy hh:mm	Sediment Examination	Checked		
S001/001	End of Study	ddMMMyyyy hh:mm	Urinary Sediment Leukocytes	Absent [N]	Absent or 0-2 per field	N
S001/001	End of Study	ddMMMyyyy hh:mm	Urinary Sediment Erythrocytes	0-2 per field [N]	Absent or 0-2 per field	N
...	...	...	...	...	...	...

Note 1: N=Normal, A=Different from reference value
Program: Listings\k345-lb-lst.sas

Listing 16.2.8.1 - Individual laboratory measurements

Category of Laboratory Parameters: URINE DRUG SCREENING

Subject ID	Time Point	Collection Date/time	Parameter	Value and Abnormality [1]	Normal Range or Reference Value	Clinically Significant?
S001/001	Screening	ddMMMyyyy hh:mm	Amphetamine	Negative [N]	Negative	N
S001/001	Screening	ddMMMyyyy hh:mm	Cannabinoids	Negative [N]	Negative	N
S001/001	Screening	ddMMMyyyy hh:mm	Cocaine	Negative [N]	Negative	N
S001/001	Screening	ddMMMyyyy hh:mm	Ecstasy	Negative [N]	Negative	N
S001/001	Screening	ddMMMyyyy hh:mm	Methamphetamine	Negative [N]	Negative	N
S001/001	Screening	ddMMMyyyy hh:mm	Opiate	Negative [N]	Negative	N
...	...	...	...	...	...	...

Note 1: N=Normal, A=Different from reference value_
Program: Listings\k345-lb-lst.sas

Listing 16.2.8.1 - Individual laboratory measurements

Category of Laboratory Parameters: VIROLOGY

Subject ID	Time Point	Collection Date/time	Parameter	Value and Abnormality [1]	Normal Range or Reference Value	Clinically Significant?
S001/001	Screening	ddMMMyyyy hh:mm	Hepatitis B Virus Surface Antigen	Negative [N]	Negative	N
S001/001	Screening	ddMMMyyyy hh:mm	Hepatitis C Virus Antibody	Negative [N]	Negative	N
S001/001	Screening	ddMMMyyyy hh:mm	HIV Ag/Ab Combo	Negative [N]	Negative	N
...	...	...	...	...	...	...

Note 1: N=Normal, A=Different from reference value
Program: Listings\k345-lb-lst.sas

Listing 16.2.8.1 - Individual laboratory measurements

Category of Laboratory Parameters: ALCOHOL BREATH TEST AND PREGNANCY TEST

Subject ID	Time Point	Collection Date/time	Parameter	Value and Abnormality [1]	Normal Range or Reference Value	Clinically Significant?
S001/001	Screening	ddMMMyyyy hh:mm	Pregnancy Test	Negative [N]	Negative	N
S001/001	Visit 2 - Day -1	ddMMMyyyy hh:mm	Pregnancy Test	Negative [N]	Negative	N
S001/001	Visit 2 - Day -1	ddMMMyyyy hh:mm	Alcohol Breath Test	Negative [N]	Negative	N
S001/001	Visit 4 - Day -1	ddMMMyyyy hh:mm	Pregnancy Test	Negative [N]	Negative	N
S001/001	Visit 4 - Day -1	ddMMMyyyy hh:mm	Alcohol Breath Test	Negative [N]	Negative	N
...	...	...	...	...	...	...

Note 1: N=Normal, A=Different from reference value_
Program: Listings\k345-lb-lst.sas

Listing 16.2.8.1 - Individual laboratory measurements

Category of Laboratory Parameters: MICROBIOLOGICAL ANALYSIS

Subject ID	Time Point	Collection Date/time	Parameter	Value and Abnormality [1]	Normal Range or Reference Value	Clinically Significant?
S001/001	Visit 1.1 - Day -3/-2	ddMMMyyyy hh:mm	Coronavirus SARS-COV-2	Negative [N]	Negative	N
S001/001	Visit 4 - Day -3/-2	ddMMMyyyy hh:mm	Coronavirus SARS-COV-2	Negative [N]	Negative	N
...	...	...	...	...	...	...

Note 1: N=Normal, A=Different from reference value
Program: Listings\k345-lb-lst.sas

Listing 16.2.8.2 - Investigator's interpretation of laboratory test results

Subject ID	Time Point	Assessment Date	Investigator's Interpretation	Clinically Significant Abnormalites
S001/001	Screening	ddMMMyyyy	Abnormal, Not Clinically Significant	---
S001/001	End of Study	ddMMMyyyy	Abnormal, Not Clinically Significant	---
...	...	...	...	...

Program: Listings\k345-lb-lst.sas

Listing 16.2.9.1 - Vital signs and body weight

Subject ID	Time Point	Assessment Date/Time	Parameter	Value and Abnormality [1]	Normal Range	Clinically Significant?
S001/001	Screening	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Screening	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	60-89	N
S001/001	Screening	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Screening	ddMMMyyyy hh:mm	Temperature [C]	36.5 [N]	35.7 - 37.5	N
S001/001	Screening	ddMMMyyyy hh:mm	Weight [kg]	55.5	---	N
S001/001	Visit 2 - Day -1	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 2 - Day -1	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	60-89	N
S001/001	Visit 2 - Day -1	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 2 - Day -1	ddMMMyyyy hh:mm	Temperature [C]	36.5 [N]	35.7 - 37.5	N
S001/001	Visit 3 - Day 1 - Pre-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 3 - Day 1 - Pre-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	60-89	N
S001/001	Visit 3 - Day 1 - Pre-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 3 - Day 1 - Pre-dose	ddMMMyyyy hh:mm	Temperature [C]	36.5 [N]	35.7 - 37.5	N
S001/001	Visit 3 - Day 4 - 72 hour post-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 3 - Day 4 - 72 hour post-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	60-89	N
S001/001	Visit 3 - Day 4 - 72 hour post-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 3 - Day 4 - 72 hour post-dose	ddMMMyyyy hh:mm	Temperature [C]	36.5 [N]	35.7 - 37.5	N
S001/001	Visit 5 - Day -1	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 5 - Day -1	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	60-89	N
S001/001	Visit 5 - Day -1	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 5 - Day -1	ddMMMyyyy hh:mm	Temperature [C]	36.5 [N]	35.7 - 37.5	N
S001/001	Visit 6 - Day 1 - Pre-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 6 - Day 1 - Pre-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	60-89	N
S001/001	Visit 6 - Day 1 - Pre-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 6 - Day 1 - Pre-dose	ddMMMyyyy hh:mm	Temperature [C]	36.5 [N]	35.7 - 37.5	N

Note 1: N=Normal, H=Higher than upper normal limit, L=Lower than lower normal limit
Program: Listings\k345-vs-lst.sas

Listing 16.2.9.1 - Vital signs and body weight

Subject ID	Time Point	Assessment Date/Time	Parameter	Value and Abnormality [1]	Normal Range	Clinically Significant?
S001/001	Visit 6 - Day 4 - 72 hour post-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 6 - Day 4 - 72 hour post-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	60-89	N
S001/001	Visit 6 - Day 4 - 72 hour post-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 6 - Day 4 - 72 hour post-dose	ddMMMyyyy hh:mm	Temperature [C]	36.5 [N]	35.7 - 37.5	N
S001/001	End of Study	ddMMMyyyy hh:mm	Weight [kg]	55.5	---	N
...	...	...	...	...	...	...

Note 1: N=Normal, H=Higher than upper normal limit, L=Lower than lower normal limit
Program: Listings\k345-vs-lst.sas

Listing 16.2.9.2 - Investigator's interpretation of ECG

Subject ID	Time Point	Assessment Date/Time	Investigator's Interpretation
S001/001	Screening	ddMMMyyyy hh:mm	Abnormal, Not Clinically Significant
S001/001	Visit 2 - Day -1	ddMMMyyyy hh:mm	Normal
S001/001	Visit 3 - Day 1 - Pre-dose	ddMMMyyyy hh:mm	Normal
S001/001	Visit 3 - Day 4 - 72 hour post-dose	ddMMMyyyy hh:mm	Abnormal, Not Clinically Significant
S001/001	Visit 5 - Day -1	ddMMMyyyy hh:mm	Normal
S001/001	Visit 6 - Day 1 - Pre-dose	ddMMMyyyy hh:mm	Abnormal, Not Clinically Significant
S001/001	Visit 6 - Day 4 - 72 hour post-dose	ddMMMyyyy hh:mm	Normal
...	...	...	...

Program: Listings\k345-eg-lst.sas

Listing 16.2.9.3 - Abnormal ECG parameters

Subject ID	Time Point	Assessment Date/Time	Parameter	Value and Abnormality [1]	Clinically Significant?	If CS, AE number
S001/001	Screening	ddMMMyyyy hh:mm	Heart Rate [beats/min]	xx [L]	N	---
S001/001	Visit 3 - Day 4 - 72 hour post-dose	ddMMMyyyy hh:mm	QRS Duration [msec]	xx [H]	Y	1
S001/001	Visit 3 - Day 4 - 72 hour post-dose	ddMMMyyyy hh:mm	QT Interval [msec]	xx [L]	N	---
S001/001	Visit 6 - Day 1 - Pre-dose	ddMMMyyyy hh:mm	QTcF Interval [msec]	xx [L]	N	---
...	...	...	...	...	...	...

Note 1: H=Higher than upper normal limit, L=Lower than lower normal limit
Program: Listings\k345-eg-lst.sas

Listing 16.2.10.1 - Medical and surgical history

Subject ID	Category	Disease/Surgery ID		
S001/001	Medical History	M1	Verbatim:	Left shoulder luxation
			Preferred Term [1]:	Joint dislocation
			System Organ Class [1]:	Injury, poisoning and procedural complications
			Disease Start - End Date:	2012 - 2012
	Surgery	S1	Verbatim:	Right knee meniscectomy
			Preferred Term [1]:	Meniscus removal
			System Organ Class [1]:	Surgical and medical procedures
			Surgery Date:	04NOV1980
	...	...	...	...

Note 1: MedDRA version 23.1
Program: Listings\k345-mh-lst.sas

Listing 16.2.10.2 - Physical examination

Subject ID	Time Point	Physical Examination Date		
S001/001	Screening	ddMMMyyyy	Investigator's Interpretation	Normal
	Visit 3 - Day 4 - 72 hour post-dose	ddMMMyyyy	Investigator's Interpretation	Normal
	Visit 5 - Day -1	ddMMMyyyy	Investigator's Interpretation	Normal
	End of Study	ddMMMyyyy	Investigator's Interpretation:	Abnormal, Clinically Significant
			Clinically Significant Abnormalities:	Left shoulder luxation
			Preferred Term [1]:	Joint dislocation
			System Organ Class [1]:	Injury, poisoning and procedural complications
...	...	...	...	...

Note 1: MedDRA version 23.1
Program: Listings\k345-pe-lst.sas

Listing 16.2.10.3 - Prior and concomitant medications

Subject ID	Category	Medication ID		
S001/001	Prior	1	Verbatim:	Alerid
			Standardised Medication Name [1]:	Alerid
			Active Ingredients [1]:	Cetirizine hydrochloride
			Medication Class [1, 2]:	Piperazine derivatives (R06AE)
			Indication:	Pollinosis
			Dose:	10 mg
			Start - End Date/Time:	2013 - Ongoing
			Frequency - Route:	1 time per day - Oral
			Related to AE (AE nr.):	N (-)
			Related to MH (MH nr.):	Y (Disease M1)
			Related to SG (SG nr.):	N (-)
	Concomitant	2	Verbatim:	Paracen
			Standardised Medication Name [1]:	Paracen
			Active Ingredients [1]:	Paracetamol
			Medication Class [1, 2]:	Anilides (N02BE)
			Indication:	Headache
			Dose:	500 mg
			Start - End Date/Time:	15JUN2019 19:08 - 15JUN2019 19:08
			Frequency - Route:	Once - Oral
			Related to AE (AE nr.):	Y (Adverse Event 1)
			Related to MH (MH nr.):	N (-)
			Related to SG (SG nr.):	N (-)
	...	...	...	...

Note 1: WHO Drug Dictionary Enhanced March 1, 2020
Note 2: Anatomical Therapeutic Chemical classification, 4th level term
Program: Listings\k345-cm-lst.sas

Listing 16.2.10.4 - Subjects study visits

Subject ID	Visit	Visit Start Date (Day)	Visit End Date (Day)
S001/001	Visit 1 - Screening - Day -21/-2	ddMMMyyyy (-j)	---
S001/001	Visit 1.1 –Screening - Day -3/-2	ddMMMyyyy (-y)	---
S001/001	Period 1 - Visit 2 - Day -1	ddMMMyyyy (-1)	---
S001/001	Period 1 - Visit 3 - Days 1-4	ddMMMyyyy (1)	ddMMMyyyy (4)
S001/001	Period 2 - Visit 4 - Day -3/-2	ddMMMyyyy (k-y)	---
S001/001	Period 2 - Visit 5 - Day -1	ddMMMyyyy (k-1)	---
S001/001	Period 2 - Visit 6 - Days 1-4	ddMMMyyyy (k+1)	ddMMMyyyy (k+4)
S001/001	Final Visit	ddMMMyyyy (k+4)	---
...	...	...	...

Program: Listings\k345-sv-lst.sas

Listing 16.2.10.5 - Fertility status and contraception

Subject ID	Chilbearing Potential?	Non-childbearing Potential Status Onset	Menopausal Status?	Date of Menopause	Surgical Sterilisation?	Surgical Sterilisation Date	Reliable Contraceptive Method Used?
S001/001	No	ddMMMyyyy	Yes	MMMyyyy	Yes	ddMMMyyyy	---
...	...	...	...	...	...	...	...

Note: Only female subjects are listed
Program: Listings\k345-rp-lst.sas

Listing 16.2.10.6 - Meals

Investigational Medicinal Product: Ladarixin fed (T)

Subject ID	Reference Date/Time [1]	Meal Nr	Standardised Meal	Time Point	Meal Served?	Meal Start Date/time	Elapsed Time	Fasting Conditions From 10 h before Breakfast?	Breakfast completely eaten within 30 min?
S001/001	ddMMMyyyy hh:mm	1	Breakfast	Day 1 –30 min before IMP admin	Y	ddMMMyyyy hh:mm	xx h xx min	Y	Y
S001/001	ddMMMyyyy hh:mm	2	Lunch	Day 1 –5 hours post-dose	Y	ddMMMyyyy hh:mm	xx h xx min	---	---
S001/001	ddMMMyyyy hh:mm	3	Dinner	Day 1 –12 hours post-dose	Y	ddMMMyyyy hh:mm	xx h xx min	---	---
S001/001	---	4	Breakfast	Day 2 –at about 09:00	Y	ddMMMyyyy hh:mm	---	---	---
S001/001	---	5	Lunch	Day 2 - at about 13:00	Y	ddMMMyyyy hh:mm	---	---	---
S001/001	---	6	Dinner	Day 2 - at about 20:00	Y	ddMMMyyyy hh:mm	---	---	---
S001/001	---	7	Breakfast	Day 3 - at about 09:00	Y	ddMMMyyyy hh:mm	---	---	---
S001/001	---	8	Lunch	Day 3 - at about 13:00	Y	ddMMMyyyy hh:mm	---	---	---
S001/001	---	9	Dinner	Day 3 - at about 20:00	Y	ddMMMyyyy hh:mm	---	---	---
...	...		...	...	...	...	...	---	---

Note 1: Reference Date/time is Fasting conditions Start Date/Time for Day 1 –Breakfast (Test only) and IMP Administration Date/Time for Day 1 - Lunch and Day 1 - Dinner
Note: Subjects are listed according to the product they actually received
Program: Listings\k345-ml-lst.sas

Listing 16.2.10.6 - Meals

Investigational Medicinal Product: Ladarixin fasting (R)

Subject ID	Reference Date/Time [1]	Meal Nr	Standardised Meal	Time Point	Meal Served?	Meal Start Date/time	Elapsed Time	Fasting Conditions From 10 h before Breakfast?	Breakfast completely eaten within 30 min?
S001/001	ddMMMyyyy hh:mm	11	Lunch	Day 1 –5 hours post-dose	Y	ddMMMyyyy hh:mm	xx h xx min	---	---
S001/001	ddMMMyyyy hh:mm	12	Dinner	Day 1 –12 hours post-dose	Y	ddMMMyyyy hh:mm	xx h xx min	---	---
S001/001	---	13	Breakfast	Day 2 –at about 09:00	Y	ddMMMyyyy hh:mm	---	---	---
S001/001	---	14	Lunch	Day 2 - at about 13:00	Y	ddMMMyyyy hh:mm	---	---	---
S001/001	---	15	Dinner	Day 2 - at about 20:00	Y	ddMMMyyyy hh:mm	---	---	---
S001/001	---	16	Breakfast	Day 3 - at about 09:00	Y	ddMMMyyyy hh:mm	---	---	---
S001/001	---	17	Lunch	Day 3 - at about 13:00	Y	ddMMMyyyy hh:mm	---	---	---
S001/001	---	18	Dinner	Day 3 - at about 20:00	Y	ddMMMyyyy hh:mm	---	---	---
...	...		...	...	...	...	...	---	---

Note 1: Reference Date/time is Fasting conditions Start Date/Time for Day 1 –Breakfast (Test only) and IMP Administration Date/Time for Day 1 - Lunch and Day 1 - Dinner
Note: Subjects are listed according to the product they actually received
Program: Listings\k345-ml-lst.sas