STATISTICAL ANALYSIS PLAN

Study CRO-PK-20-344 - Sponsor code Z7251J01

Comparative bioavailability study of a new riluzole orodispersible film vs. a marketed oral reference (Rilutek® tablets) in healthy male and female volunteers

Single centre, single dose, open-label, randomised, 2-sequence, 4-period replicate cross-over study

Test formulation:	Riluzole 50 mg orodispersible film, Aquestive Therapeutics, USA
Reference formulation:	Rilutek®, 50 mg riluzole tablets, Sanofi Mature IP, France
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Development phase:	I
Version and date:	Final version 1.0, 31MAY2021

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

This document comprises 33 pages plus appendices

VERSIONS' HISTORY

Version	Date of Issue	Reason for change
Draft version 0.1	21MAY2021	Alice Segantin issued the first draft
Draft version 0.2	28MAY2021	Alice Segantin issued the second draft after revision of MW
Final version 1.0	31MAY2021	Alice Segantin issued the final version after sponsor approval

APPROVAL AND ACKNOWLEDGEMENT

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Zambon S.p.A., Italy

Sponsor Representative (for approval and acknowledgement)
Carlo Cattaneo, Global Head Medical Affairs CNS

31st MAY 2021 — Date

Carlo Cattaneo — Signature

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31MAY2021 _____ Date

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Coordination (for acknowledgement only)
Elena Gander, Clinical Project Leader

01JUN2021 _____ Date

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STUDY/INVESTIGATION SCHEDULE

ACTIVITIES	Screening	PERIOD 1, 2, 3, 4 (wash-out≥7 days)			Final visit/ETV[12]
Visit	V1	V2, V4, V6, V8	V3, V5, V7, V9		V10[11]/ETV
	Days -14/-2	Day -1	Day 1	Day 2	Day 2[11]/ETV
Informed consent	x				
Demography	x				
Lifestyle	x				
Medical/surgical history	x				
Physical abnormalities	x				x
Previous and concomitant treatments	x	x	x	x	x
Height	x				
Body weight	x				x
Laboratory analysis[1]	x				x
Cotinine	x				
Virology	x				
Drug screening	x	x			
Vital signs	x		x [2]	x [2]	x[13]
Pregnancy test	x[3]	x[4]			
ECG	x				
Inclusion/exclusion criteria	x	x[5]			
Eligibility evaluation	x	x[5]			
Alcohol breath test		x			
Enrolment and randomisation		x[5]			
Confinement		x	x		
Discharge				x	
IMP administration			x[6]		
Palatability			x[7]		
Mouth visual inspection			x[8]		
Blood samplings [9]			x	x	
Standardised meals		x	x	x	
AEs monitoring[10]	x	x	x	x	x

1. *Haematology, blood chemistry with the exception of cotinine, urinalysis*
2. *At pre-dose and 2 and 36 h post-dose*
3. *Women only - serum β-HCG test*
4. *Women only - urine test*
5. *Period 1, visit 2*
6. *At 08:00 ± 1 h under fasting conditions*
7. *Immediately after each administration of the test product*
8. *At pre-dose and 0.5 and 1 h post-dose at each administration of the test product*
9. *At pre-dose (0) and 15, 30, 45 min, 1, 1.25, 1.5, 2, 3, 4, 6, 8, 12, 24 and 36 h post-dose*
10. *Adverse events monitored starting at the screening visit, immediately after informed consent, up to the final visit/ETV*
11. *Final visit on Day 2 of period 4 after the 36-h post-dose blood sampling*
12. *Early termination visit (ETV) in case of subject's premature discontinuation*
13. *At the ETV only*

TABLES OF CONTENTS

TABLES

ABBREVIATIONS

AE	Adverse Event
ANOVA	Analysis of Variance
AUC_{0-t}	Area under the concentration-time curve from time zero to time t
$AUC_{0-\infty}$	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∞
BE	Bioequivalence
BLQL	Below Lower Quantification Limit
BMI	Body Mass Index
BP	Blood Pressure
bpm	Beats per minute
BW	Body weight
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
C_{max}	Peak drug concentration
CPL	Clinical Project Leader
CRF	Case Report Form
CRO	Contract Research Organisation
CSP	Clinical Study Protocol
CRS	Clinical Study Report
CS	Clinically Significant
CV	Coefficient of Variation
CV_{WR}	Coefficient of Variation within-subject
DIABP	Diastolic Blood Pressure
EC	Ethics Committee
ECG	Electrocardiogram
EMA	European Medicine Agency
ETV	Early Termination Visit
FDA	Food and Drug Administration
FSFV	First Subject First Visit
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
HR	Heart Rate
ICH	International Conference on Harmonisation
IMP	Investigational Medicinal Product
IUD	Intra-Uterine Device
λ_z	Terminal elimination rate constant, calculated, if feasible, by log-linear regression using at least 3 points
LSLV	Last Subject Last Visit
MedDRA	Medical Dictionary for Regulatory Activities
min	Minute
N	Normal
NA	Not Applicable
NC	Not calculated
NCS	Not clinically significant
OTC	Over The Counter
PK	Pharmacokinetics
PT	Preferred Term

PTAE	Pre-Treatment Adverse Event
QTc	Corrected QT interval
R	Reference
SAE	Serious Adverse Event
SYSBP	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
$t_{1/2}$	Half-life
t_{max}	Time to achieve Cmax
USDA	United States Department of Agriculture
WHODDE	World Health Organisation Drug Dictionary Enhanced

1 INTRODUCTION

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

1.1 Changes with respect to the study protocol and its amendment

No change with respect to the study protocol and its amendment (5, 6) was introduced in this SAP.

2 STUDY OBJECTIVES

The objective of the study is to compare the pharmacokinetic profile of riluzole after replicate single dose of the novel orodispersible film test formulation and of the marketed reference Rilutek® tablets and to evaluate their bioequivalence.

2.1 Primary end-point

- To evaluate the bioequivalent rate (C_{max}) and extent (AUC_{0-t}) of absorption of riluzole after replicate single dose administration of test and reference.

2.2 Secondary end-points

- To describe the PK profile of riluzole after replicate single dose administration of test and reference;
- to evaluate the test product palatability;
- to collect safety and tolerability data of test and reference after replicate single dose administration.

3 INVESTIGATIONAL PLAN

3.1 Overall study design

Single centre, single dose, open-label, randomised, 2-sequence, 4-period replicate cross-over study.

3.2 Discussion of design

The study was designed in agreement with the EMA guideline "Guidance on the investigation of bioequivalence", CPMP/EWP/QWP/1401/98 Rev. 1 January 2010 (3). The well-known high variability of riluzole led to the choice of the replicate cross-over design as suggested by the current EMA guideline. According to the guideline, an enlargement of the acceptance interval for bioequivalence in terms of C_{max} is allowed up to 69.84-143.19% in relation to the actual intra-subject variability of riluzole C_{max} found in this study with the reference treatment, by keeping in consideration the favourable safety profile of the test formulation previously observed in 3 clinical studies. In detail, a C_{max} within-subject variability >30% was found in the previous pilot study and =32.66% in the previous bioequivalence study performed in USA (7). According to the 2-arm cross-over study design, each randomised subject will be allocated to one of 2 sequences of IMP administrations in the 4 study periods according to a computer generated randomisation list (see § 6.3). Balance between the sequences will be made so that subjects have the same chances to be assigned to either sequence (either RTRT or TRTR in the 4 consecutive periods).

An open-label design will be used since the primary end-point of the study is based on objective measurements of riluzole in plasma and the outcome variables could not be influenced by the subjects or investigator being aware of the administered products. The bioanalysis will be performed under blinded conditions.

The washout period of 7 days was estimated to be adequate. Based upon a half-life of 12 h (Rilutek SmPC reference: 8), it is anticipated that minimal plasma levels would be achieved in 5 days thus allowing dosing every 7 days. Blood sampling time-points were selected on the basis of the known PK profile of riluzole and on the basis of previous Phase I studies of the same test formulation administered to healthy volunteers.

The dose for the present study was selected based on EMA Rilutek® European Public Assessment Report (EPAR) (9), which recommends a dose regimen of 50 mg (one filmcoated tablet) twice a day in the common clinical practice. The dose of 50 mg is the minimal unit dose.

4 STUDY POPULATION

4.1 Target population

Healthy men and women will be enrolled in this study.

4.2 Inclusion criteria

To be enrolled in this study, subjects must fulfil 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. *Tobacco:* non-smokers for at least 6 months prior to study screening
4. *Body Mass Index (BMI):* 18.5-29 kg/m2 inclusive
5. *Vital signs: systolic* blood pressure (SBP) 100-139 mmHg, diastolic blood pressure (DBP) 50-89 mmHg, heart rate 50-90 bpm, measured after 5 min at rest in the sitting position
6. *Full comprehension:* ability to comprehend the full nature and purpose of the study,
7. including possible risks and side effects; ability to co-operate with the investigator and to comply with the requirements of the entire study
8. *Contraception and fertility (women only):* women of child-bearing potential must be using at least one of the following reliable methods of contraception:
    a. 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
    b. A male sexual partner who agrees to use a male condom with spermicide
    c. A sterile sexual partner

    Female participants of non-child-bearing potential or in post-menopausal status for at least 1 year will be admitted.
    For all women, pregnancy test result must be negative at screening.

4.3 Exclusion criteria

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

1. *Electrocardiogram (ECG) 12-leads:* (supine position) clinically significant abnormalities; QTc interval > 450 msec
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. *Cotinine:* positive cotinine test at screening

5. *Allergy:* ascertained or presumptive hypersensitivity to the active principle and/or formulations' ingredients; history of anaphylaxis to drugs or allergic reactions in general, which the investigator considers may affect the outcome of the study
6. *Diseases:* clinically significant history or presence of renal, hepatic, gastrointestinal, cardiovascular, cerebrovascular, immunological, musculoskeletal, respiratory, skin, haematological, endocrine, psychiatric or neurological diseases or surgeries that may interfere with the aim of the study. Gastrointestinal pathologies include any clinically significant disorder of the mouth, e.g. impairment of swallowing, lesions, ulcerations, deformities, untreated dental caries
7. *Dentures:* presence of mouth jewellery, dentures, braces, piercings that may interfere with successful completion of the dosing
8. *Medications:* medications, including over the counter (OTC) medications and herbal remedies for 2 weeks before study screening; central nervous system depressants, including opioids, benzodiazepines, general anaesthetics and anticonvulsants, or CYP inhibitors, including cimetidine, fluoxetine, quinidine, erythromycin, ciprofloxacin, fluconazole, ketoconazole, diltiazem and antiretroviral agents, or strong CYP inducers, including barbiturates, carbamazepine, glucocorticoids, phenytoin, St John's wort and rifampin, or hormonal oral or transdermal contraceptives for 30 days before study screening; implanted, injected, intravaginal or intrauterine hormonal contraceptives for 6 months before study screening
9. *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
10. *Blood donation:* blood donations for 3 months before this study
11. *Drug, alcohol, caffeine, tobacco:* history of drug, alcohol [>1 drink/day for females and >2 drinks/day for males, defined according to the USDA Dietary Guidelines 2015 (10)], caffeine (>5 cups coffee/tea/day) or tobacco use including any tobacco product like ecigarettes and vaping products
12. *Drug test:* positive result at the drug test at screening or Day -1
13. *Alcohol test:* positive alcohol breath test at Day -1
14. *Diet:* abnormal diets (<1600 or >3500 kcal/day) or substantial changes in eating habits in the 4 weeks before this study; vegetarians and vegans
15. *Pregnancy (women only):* positive or missing pregnancy test at screening or Day -1, pregnant or lactating women

4.3.1 Not allowed treatments

No medication, including OTC and herbal remedies, will be allowed for 2 weeks before the start of the study and during the whole study duration.

Central nervous system depressants, including opioids, benzodiazepines, general anaesthetics and anticonvulsants, or CYP inhibitors, including cimetidine, fluoxetine, quinidine, erythromycin, ciprofloxacin, fluconazole, ketoconazole, diltiazem and antiretroviral agents, or strong CYP inducers, including barbiturates, carbamazepine, glucocorticoids, phenytoin, St John's wort and rifampin, or hormonal oral or transdermal contraceptives will be forbidden for 30 days before study screening and during the whole study duration.

Implanted, injected, intravaginal or intrauterine hormonal contraceptives will be forbidden for

6 months before study screening and during the whole study duration.

Paracetamol will be allowed as therapeutic counter-measure for adverse events (AEs) according to the investigator's opinion.

The intake of any other medication will be reported as a protocol deviation. However, it will lead 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/investigation is summarised at page 5.

5.1 Study visits and procedures

Each study subject will undergo 10 visits.

The study protocol foresees 4 periods separated by wash-out intervals of at least 7 days. Minimum study duration will be 25 days, screening visit included. A written informed consent will be 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, and it corresponds to the study completion.

The following phases, visits and procedures will be performed:

- Screening phase
  - Screening – visit 1: between Day -14 and Day -2
  - Period 1 – visit 2: Day -1

- Interventional phase
  - Period 1 – visit 3: Days 1-2
  - Wash-out interval of at least 7 days
  - Period 2 – visit 4: Day -1
  - Period 2 – visit 5: Days 1-2
  - Wash-out interval of at least 7 days
  - Period 3 – visit 6: Day -1
  - Period 3 – visit 7: Days 1-2
  - Wash-out interval of at least 7 days
  - Period 4 – visit 8: Day -1
  - Period 4 – visit 9: Days 1-2

- Final phase
  - Period 4 – visit 10: Day 2 - Final visit or early termination visit (ETV) in case of early discontinuation

		Day	Procedures/Assessments	Notes
Screening phase	**Screening – visit 1**	*From Day -14 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, vital signs, physical abnormalities) ➢ ECG recording ➢ Laboratory analyses: haematology, blood chemistry, cotinine, urinalysis, virology and serum pregnancy test (women only) ➢ 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
Period 1	**Visit 2**	*Day -1*	➢ Alcohol breath test ➢ Urine multi-drug kit test ➢ Urine pregnancy test (women only) ➢ AE and concomitant medications ➢ Inclusion/exclusion criteria evaluation ➢ Eligibility evaluation ➢ Enrolment and randomisation	Arrival at the Phase I Unit in the evening Confinement until the evening of Day 2 Standardised low-fat dinner Fasting for at least 10 h (overnight) up to dosing
	Visit 3	*Day 1*	➢ IMP administration at 08:00 ± 1 h ➢ Palatability of the test product immediately after administration ➢ Mouth visual inspections after administration of the test investigational medicinal product, at pre-dose and 0.5 and 1 h post-dose ➢ Vital signs measurement ➢ Blood sample collection for PK analysis ➢ AE and concomitant medications	Fasting until about 5 h post-dose Standardised lunch at about 13:00 Standardised dinner at about 20:00 (12 h post-dose)
		Day 2	➢ Vital signs measurement ➢ Blood sample collection for PK analysis ➢ AE and concomitant medications	Standardised breakfast at about 8:00 and lunch at about 13:00 Discharge from the Phase I Unit in the evening after the 36-h post-dose blood sample collection and vital signs check
Wash-out		*At least 7 days*	A wash-out interval of at least 7 days between 2 consecutive administrations	

		Day	Procedures/Assessments	Notes
Period 2	**Visit 4**	*Day -1*	As visit 2, excluding inclusion/exclusion criteria evaluation, enrolment and randomisation	As visit 2
	Visit 5	*Day 1*	As visit 3. Test or reference IMP administered according to the randomisation list and cross-over design	As visit 3
		Day 2	As visit 3	As visit 3
Wash-out		*At least 7 days*	A wash-out interval of at least 7 days between 2 consecutive administrations	
Period 3	**Visit 6**	*Day -1*	As visit 2, excluding inclusion/exclusion criteria evaluation, enrolment and randomisation	As visit 2
	Visit 7	*Day 1*	As visit 3. Test or reference IMP administered according to the randomisation list and cross-over design	As visit 3
		Day 2	As visit 3	As visit 3
Wash-out		*At least 7 days*	A wash-out interval of at least 7 days between 2 consecutive administrations	
Period 4	**Visit 8**	*Day -1*	As visit 2, excluding inclusion/exclusion criteria evaluation, enrolment and randomisation	As visit 2
	Visit 9	*Day 1*	As visit 3. Test or reference IMP administered according to the randomisation list and cross-over design	As visit 3
Period 4	**Visit 9**	*Day 2*	As visit 3	As visit 3

		Day	Procedures/Assessments	Notes
Final phase	**Visit 10 - Final Visit or ETV**	*Day 2 of period 4 / at ETV in case of discontinuation*	➢ Full physical examination (body weight and physical abnormalities; also vital signs in case of ETV) ➢ Laboratory analyses as at screening, with the exception of cotinine, virology, urine drug test and pregnancy test ➢ AE and concomitant medications In case of clinically significant results at the final visit, the subjects will be followed-up by the investigator until the normalisation 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

During confinement, the subjects will not take any food or drinks (except water) for about 10 h (i.e. overnight) before IMP administration and for about 5 h afterwards. On Day -1 of each study period, a standardised low-fat dinner will be served. Water will be allowed as desired, except for one h before and one h after IMP administration. In order to maintain an adequate hydration, the subjects will be 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 of each study period, the subjects will remain fasted until about 5 h post-dose. Standardised lunch and dinner will be served at approximately 5 h and 12 h post-dose. On Day 2 of each study period, standardised breakfast and lunch will be served at about 8:00 and 13:00, respectively. The meals' composition will be standardised on Days -1 and 1 in each study period (see the study protocol (5) for further details).

Coffee, tea or food containing xanthines (i.e. coke, chocolate, etc.), smoking, alcohol and grapefruit will be forbidden during confinement. In particular, alcohol and grapefruit will be forbidden for 24 h before the first IMP administration until the end of the study.

Only non-smokers will be included in the study.

During confinement, routine ambulant daily activities will be strongly recommended.

5.3 Restrictions

During each study period, the subjects will be confined from the evening preceding the IMP administration (study Day -1) until the evening of Day 2.

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

During confinement, hazardous, strenuous or athletic activities will not be permitted.

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 will be coded with "unique subject identifiers" when data are extracted from the study database into the domains of the CDISC SDTM and ADaM models. The unique subject identifier consists of the sponsor study code (i.e. Z7251J01), the 3-digit centre number (e.g. 001, 002, etc), the 4-digit screening number (e.g. S001, S002, etc.) and the 3-digit randomisation number (e.g. 001, 002, etc., when applicable). Study code, centre number, screening number and randomisation number (when applicable) are separated by slashes ("/").

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 randomisation 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 clinical study report and will be used to identify the subjects in in-text tables or wording (if applicable).

6.3 Randomisation

The randomisation list was computer-generated by the Biometry Unit of the Clinical Contract Research Organization (CRO), using the PLAN procedure of the SAS® version 9.3 (TS1M1) (11). The randomisation list was supplied to the study site and to STM Pharma PRO Srl., Italy for the preparation of the IMP individual kits before study start and will be attached to the final clinical study report.

6.4 Treatment allocation

The study subjects will be assigned to one of 2 sequences of treatments (either RTRT or TRTR) according to their randomisation number. Randomisation number will be given to the subjects on study Day -1, period 1, as soon as they are definitely enrolled in the study.

6.5 Blinding

This is an open study. No masking procedure will be applied.

7 STUDY EVALUATION PARAMETERS

7.1 Study variables

7.1.1 Primary variables

- C_{max} and AUC_{0-t} of plasma riluzole after replicate single dose administration of test and reference formulation.

7.1.2 Secondary variables

- $AUC_{0-\infty}$, $t_{1/2}$, t_{max}, AUC_{extra}, λ_z, of riluzole after replicate single dose administration of test and reference;
- Palatability score
- TEAEs, vital signs (BP, HR), laboratory parameters, physical examination including BW

7.2 Pharmacokinetic assessments

The following PK parameters will be measured and/or calculated for riluzole, using the validated software Phoenix WinNonlin® version 6.3 (12) or higher (actual version will be stated in the final report).

7.2.1 Pharmacokinetic parameters

- C_{max} Maximum plasma concentration
- t_{max} Time to achieve C_{max}
- λ_z Terminal elimination 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
- %AUCextra Percentage of the residual area (C_t/λ_z) extrapolated to infinity in relation to the total $AUC_{0-\infty}$, calculated, if feasible, as $100\times[(C_t/\lambda_z)/AUC_{0-\infty}]$

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.

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

7.3 Safety and tolerability parameters

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

8 STATISTICAL METHOD

The statistical analysis of demographic and safety data will be performed using SAS® version 9.3 (TS1M1) (11) or higher (the actual versions will be stated in the final report).

The statistical analysis of PK parameters will be performed using Phoenix WinNonlin® version 6.3 (12) or higher and SAS® version 9.3 (TS1M1) or higher.

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.

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: Riluzole 50 mg orodispersible film (T)
- Reference/Placebo label: Rilutek®, 50 mg riluzole tablets (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
- 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 Riluzole 50 mg orodispersible film (T) will be presented before the data and results of Rilutek®, 50 mg riluzole tablets (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 treatments sequence.

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

A subject will be defined as randomised in the study when he/she is assigned to a randomised treatments sequence.

The following analysis sets are defined:

- *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 the investigational medicinal products. This analysis set will be used for the safety analyses
- *PK Set*: all randomised subjects who fulfil the study protocol requirements in terms of investigational medicinal product intake and have evaluable PK data readouts for the planned treatment comparisons, with no major deviations that may affect the PK results. This analysis set will be used for the statistical analysis of the PK results

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

8.2.1.1 Reasons for exclusion from the PK Set before bioanalysis

Reasons for the exclusion of subjects from the PK set are the following:

- vomiting and diarrhoea 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 occurs, it will be noted in the CRF as the study is being conducted.

8.2.1.2 Reasons for exclusion from the PK Set after bioanalysis

Exclusion of subjects on the basis of pharmacokinetic reasons is possible only for:

- subjects with lack of any measurable concentrations or only very low plasma concentrations for the reference medicinal product. A subject is considered to have very low plasma concentrations if his/her AUC is less than 5% of the reference medicinal product geometric mean AUC (which should be calculated without inclusion of data from the outlying subject)
- subjects with implausible concentrations (i.e. different from the known, expected concentration profiles) for the reference medicinal product. The exclusion of these subjects must be justified on the basis of sound scientific reasons and mutually agreed between the CRO and the Sponsor
- subjects with non-zero baseline concentrations > 5% of C_{max}

The samples from the subjects excluded from the PK set should still be assayed and the results listed. Subjects should not be excluded from the PK set if the AUC_{0-t} covers less than 80% of the $AUC_{0-\infty}$.

8.3 Sample size and power considerations

Data from previous PK studies of the test product, 1897 and 162020 (see the study protocol (5) for further details) were used to calculate the sample size of the present study, as shown in the table below.

Table 9.4.1 - Sample size calculation

Parameter	δ	CV_{WR}	α	β	n	N=2n
C_{max}	1.11	0.3266	0.1	0.2	26	52
AUC_{0-t}	1.0917	0.1265	0.1	0.2	4	9

δ: ratio of geometric means of the considered parameter; CV_{WR}%: within-subject variability; α: type 1 error; β: type 2 error; n: number of subjects per sequence; N: total sample size

Variability of AUC_{0-t} and C_{max} (CV_{WR}) actually observed in study 162020 (§ 1.4.2) was used in the calculation. The actual ratio of geometric means of AUC_{0-t} of study 162020 was 1.0917, whilst that of C_{max} observed in study 162020 was 1.1582. This high ratio did not prevent the demonstration of bioequivalence of the formulations in study 162020 also for C_{max}. However, the calculation of the sample size for the present study using a δ of 1.1582 would be 126 subjects. Considering that the enrolment of at least 126 subjects in a bioequivalence study would be hardly justifiable, that bioequivalence between the test IMP and Rilutek® 50 mg tablets available in US was demonstrated in study 162020 in 30 subjects, who completed the study, and t hat t he a ctual δ o f C_{max} obtained in the previous pilot study 1897 was 0.9436, which is notably nearer the equality, i.e. ratio = 1.00, than the ratio 1.1582 observed later in study 162020, a ratio of 1.11 was postulated in the present sample size calculation. Indeed, maintaining CV_{WR}, α and β unchanged and assuming as C_{max} ratios, alternately, 1.05 and 1.10, sample sizes of 26 and 46 subjects, respectively, would be necessary to demonstrate bioequivalence in terms of C_{max}.

Taking into account this premise, when the sample size in each sequence group is 26 (and the

total sample size is 52), a replicate crossover design will have 80% power to reject both the null hypothesis that the ratio of the test mean to the reference mean of C_{max} is below 0.800 and the null hypothesis that the ratio of test mean to the reference mean of C_{max} is above 1.250 (i.e. that the test and standard are not equivalent, in favour of the alternative hypothesis that the means of the two treatments are equivalent) assuming that data will be analysed in the natural log scale using t-tests for differences in means and that each t-test will be made at the 5.0% significance level.

In conclusion, 54 subjects will be enrolled in order to have 52 completed subjects.

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 (Safety Set and PK Set).

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, randomised, 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 (Table 14.1.1.2) by treatment group.

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 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. race) and descriptive statistics (mean, SD, CV%, minimum, median and maximum) for continuous variables (e.g. age, weight) will be presented.

8.4.7 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).

8.4.8 ECG

The date/time of ECG assessments, the value of parameters and the overall investigator's interpretation (as normal, abnormal, not clinically significant or abnormal, clinically significant) will be listed (Listing 16.2.4.5).

The overall investigator's interpretations will be summarised using contingency tables at screening (Table 14.1.1.6).

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 24.0, 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) March 2021 and listed (Listing 16.2.10.4).

8.4.11 Subjects' study visits

The dates of all subjects study visits and date/time of home discharge at the end of each period will be listed (Listing 16.2.10.5).

8.4.12 Fertility status and contraceptive method

The fertility status and the contraceptive method used by the subjects will be listed (Listing 16.2.10.6).

8.4.13 Alcohol breath test, pregnancy test, cotinine test and urine drug test

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

8.4.14 Tobacco consumption

Individual tobacco consumption habits history collected at screening will be listed (Listing 16.2.4.6).

8.4.15 Meals

The start date/time of the standardised meals will be listed (Listing 16.2.10.7).

8.5 IMP administration

The date and time of all IMP administrations, of film dissolution, of accidental film swallowing and reference tablet administrations will be listed (Listing 16.2.5.1). Dosing time is defined as the time the film is placed on the subject's tongue.

The actual time of film dissolution will be summarised by descriptive statistics (Table 14.2.4.1).

8.5.1 Dose per body weight

The dose per body weight of riluzole will be listed (Listing 16.2.5.2) and summarised using descriptive statistics (Table 14.3.5.5).

The body weight collected at the screening visit will be used for the calculation.

8.5.2 Wash-out

The minimum and maximum number of days of wash-out between periods will be presented (Table 14.3.5.6).

8.6 PK and Palatability analysis

The date/time and score of palatability (for test only) will be listed (Listing 16.2.6.2) and summarised in tables of frequency (Table 14.2.4.2) on the safety set.

The PK analysis will be performed on the subjects included into the PK Set. 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/pharmacodynamics

A descriptive PK will be presented.

Individual subject concentrations of riluzole will be presented in data listings (Listing 16.2.5.4) and summarised at each time point by treatment (Table 14.2.1.1).

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.

PK parameters of riluzole will be listed (Listing 16.2.6.1) and summarised by treatment (Table 14.2.2.1).

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

According to the current European Guideline on the Investigation of Bioequivalence (3), plasma riluzole AUC_{0-t}, $AUC_{0-\infty}$ and C_{max} will be analysed using analysis of variance (ANOVA) (Table 14.2.3.1).

A mixed linear model will be used to make statistical inferences about the values of C_{max} and AUC_{0-t}. In order to correctly assume normality and homoscedasticity, the data will be transformed prior to analysis using a neperian logarithmic transformation in compliance with the EMA guideline.

The 90% CI of the ratio of the population means (test/reference), for the parameters under consideration will be calculated. This method is equivalent to the corresponding two one-sided test procedure with the null hypothesis of bioequivalence at the 5% significance level.

- The statistical analysis will take into account treatment, period, sequence and subject within sequence as fixed effects.
- Acceptance criterion for bioequivalence in terms of extent of absorption (AUC_{0-t} as primary variable and $AUC_{0-\infty}$ as secondary variable) will be that the 90% CI of this ratio has to lie within the range 80.00-125.00%.
- Due to the replicate design of the study, if the within-subject variability (CV_{WR}%) of C_{max} of plasma riluzole after administration of the reference formulation is >30%, the reference-scaled BE approach will be used. Bioequivalence acceptance range for C_{max} will be widened, in compliance with the guideline, as exemplified in Table 8.9.3.1.
- CV_{WR}% will be calculated by applying the formula $CV_{WR}(\%) = 100\sqrt{e^{S^2_{WR}} - 1}$, where S^2_{WR} is the within-subject variation plasma riluzole after administration of the reference formulation only.
- The extent of the widening will be defined on the basis of the within-subject variability actually observed in the study according to [U, L] = exp [±k·S_{WR}], where U is the upper limit of the acceptance range, L is the lower limit of the acceptance range, k is the regulatory constant set to 0.760 and S_{WR} is the within-subject standard deviation of the log-transformed values of C_{max} of plasma riluzole after administration of the reference formulation.

Table 8.9.3.1 Examples of widened bioequivalence acceptance limits of C_{max} according to its actual CV_{WR}

CV_{WR} %*	Lower Limit	Upper Limit
30	80.00	125.00
35	77.23	129.48
40	74.62	134.02
45	72.15	138.59
≥50	69.84	143.19

*: $CVWR(\%) = 100\sqrt{e^{s^2_{WR}} - 1}$; source: reference (3)

The value of within-subject variability of C_{max} (after administration of the reference formulation), obtained using the formula above, will be reported in the table 14.2.3.2.

t_{max} and $t_{1/2}$ will be compared between treatments by the non-parametric Friedman test (Table 14.2.3.3).

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

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 treatment-emergent AEs (TEAEs), according to the period of occurrence, as follows:

- PTAEs: all AEs occurring before the first dose of IMP and not worsening after the first dose of IMP
- TEAEs: all AEs occurring or worsening after the first dose of IMP

Individual PTAEs and TEAEs will be listed in subject data listings (Listing 16.2.7.1, Listing 16.2.7.2).

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 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 Laboratory data

Date/time of samples collection and 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).

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).
The overall Investigator's interpretation will be summarised using tables of frequency (Table 14.3.4.2).

8.7.4 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).

8.7.5 Mouth Visual Inspection

The date/time of mouth visual inspection, 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 16.2.10.3).

The overall Investigator's interpretation will be summarised using tables of frequency (Table 14.3.5.4) at each time point.

8.8 Analysis datasets

Analysis datasets will be created according to the version 2.1 of the ADaM model of CDISC (13).

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 Radicioni M. Protocol CRO-PK-20-344. "Comparative bioavailability study of a new riluzole orodispersible film vs. a marketed oral reference (Rilutek® tablets) in healthy male and female volunteers". Final version 1.0, 28APR2020, CROSS Research, Switzerland, 2020

6 Radicioni M. Protocol amendment CRO-PK-20-344. "Comparative bioavailability study of a new riluzole orodispersible film vs. a marketed oral reference (Rilutek® tablets) in healthy male and female volunteers". Final version 1.0, 17FEB2021, CROSS Research, Switzerland, 2020

7 Riluzole orodispersible film. Investigator's Brochure, Edition 3.0, Aquestive Therapeutics

8 Rilutek SmPC, Rilutek EPAR 14 August 2019 - EMEA/H/C/000109 - IAIN/0060, last updated 11 November 2019

9 European Public Assessment Report (EPAR), Rilutek. EMEA/H/C/109

10 U.S. Department of Health and Human Services and U.S. Department of Agriculture, Nutrition and your health: 2015-2020 Dietary Guidelines, Appendix 9

11 SAS/STAT® User's Guide

12 Phoenix 1.3 User's Guide, Pharsight Corporation

13 CDISC Analysis Data Model Version 2.1

10 APPENDICES

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

Section 14 - Tables Shells

Table 14.1.1.1 - Subjects' disposition - Enrolled set

	Overall n (%)
Enrolled	nn
Enrolled but not randomised [1]	nn (xx.x)
Randomised [1]	nn (xx.x)
Discontinued before treatment [2]	nn (xx.x)
Treated [2]	nn (xx.x)
Completed [3]	nn (xx.x)
Discontinued [3]	nn (xx.x)
Adverse event [3]	nn (xx.x)
Withdrawal by subject [3]	nn (xx.x)
...	nn (xx.x)

Note: The number and the proportion of subjects of each disposition event are reported
Note 1: The denominator for calculating the proportion is the number of enrolled subjects
Note 2: The denominator for calculating the proportion is the number of randomised subjects
Note 3: The denominator for calculating the proportion is the number of randomised and treated subjects
Source: Listing 16.2.4.1 - Subjects' disposition
Program: Tables\k344-ds-tbl.sas

Table 14.1.1.2 - Analysis sets - Enrolled set

	Enrolled Set		
	Riluzole 50 mg orodispersible film (T) N=XX n (%)	**Rilutek®, 50 mg riluzole tablets (R) N=XX n (%)**	**Overall N=XX n (%)**
Safety Set	nn (xx.x)	nn (xx.x)	nn (xx.x)
PK Set	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\k344-ds-tbl.sas

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

		Statistics	Enrolled Set N=XX	Safety Set N=XX	PK Set N=XX
Sex	Female	n (%)	nn (xx.x)	nn (xx.x)	nn (xx.x)
	Male	n (%)	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)
	Asian	n (%)	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)
	Black or African American	n (%)	nn (xx.x)	nn (xx.x)	nn (xx.x)
	White	n (%)	nn (xx.x)	nn (xx.x)	nn (xx.x)
	Other	n (%)	nn (xx.x)	nn (xx.x)	nn (xx.x)
Age (years)		N	nn	nn	nn
		Mean	xx.x	xx.x	xx.x
		SD	xx.x	xx.x	xx.x
		CV%	xx.x	xx.x	xx.x
		Min	xx	xx	xx
		Median	xx.x	xx.x	xx.x
		Max	xx	xx	xx
Body Weight (kg)		N	nn	nn	nn
		Mean	xx.xx	xx.xx	xx.xx
		SD	xx.xx	xx.xx	xx.xx
		CV%	xx.xx	xx.xx	xx.xx
		Min	xx.x	xx.x	xx.x
		Median	xx.xx	xx.xx	xx.xx
		Max	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\k344-dm-tbl.sas

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

	Statistics	Enrolled Set N=XX	Safety Set N=XX	PK Set N=XX
Body Mass Index (kg/m^2)	N	nn	nn	nn
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	CV%	xx.xx	xx.xx	xx.xx
	Min	xx.x	xx.x	xx.x
	Median	xx.xx	xx.xx	xx.xx
	Max	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\k344-dm-tbl.sas

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

	Enrolled Set N=XX	**Safety Set N=XX**	**PK Set N=XX**
Number of subjects with any inclusion/exclusion criteria not met	nn (xx.x)	nn (xx.x)	nn (xx.x)
Inclusion	nn (xx.x)	nn (xx.x)	nn (xx.x)
Inclusion criterion 1	nn (xx.x)	nn (xx.x)	nn (xx.x)
Inclusion criterion 2	nn (xx.x)	nn (xx.x)	nn (xx.x)
...	...	...	...
Exclusion	nn (xx.x)	nn (xx.x)	nn (xx.x)
Exclusion criterion 1	nn (xx.x)	nn (xx.x)	nn (xx.x)
Exclusion criterion 2	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\k344-ie-tbl.sas

Table 14.1.1.5 - Protocol deviations - Enrolled set, Safety set, PK set

	Enrolled Set N=XX	**Safety Set N=XX**	**PK Set N=XX**
Number of subjects with any protocol deviation	nn (xx.x)	nn (xx.x)	nn (xx.x)
Major	nn (xx.x)	nn (xx.x)	nn (xx.x)
Treatment deviation	nn (xx.x)	nn (xx.x)	nn (xx.x)
Inclusion criteria violation	nn (xx.x)	nn (xx.x)	nn (xx.x)
Exclusion criteria violation	nn (xx.x)	nn (xx.x)	nn (xx.x)
Medication not admitted	nn (xx.x)	nn (xx.x)	nn (xx.x)
...	...	...	...
Minor	nn (xx.x)	nn (xx.x)	nn (xx.x)
Deviation from scheduled sampling time	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\k344-dv-tbl.sas

Table 14.1.1.6 - Contingency tables of investigator's interpretation of ECG at screening - Enrolled set

Time Point	Investigator's interpretation	Enrolled Set N=XX
Screening	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 enrolled set
Source: Listing 16.2.4.5 - Investigator's interpretation of ECG
Program: Tables\k344-eg-tbl.sas

Table 14.2.1.1 - Riluzole concentrations (ng/mL) measured in plasma - PK Set

Investigational Medicinal Product: Riluzole 50 mg orodispersible film (T)

Statistics	Pre dose	0.25 h	0.5 h	0.75 h	1 h	1.25 h	1.5 h	2 h	3 h	4 h	6 h	8 h	12 h	18 h	24 h
N	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
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
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
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
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
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
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

BLQL: Below Lower Quantification Limit (x.xx ng/mL)
Source: Listing 16.2.5.4 - Riluzole concentrations (ng/mL) measured in plasma
Program: pk-analysis\k344-tlf.sas

Table 14.2.1.1 - Riluzole concentrations (ng/mL) measured in plasma - PK Set

Investigational Medicinal Product: Rilutek®, 50 mg riluzole tablets (R)

Statistics	Pre dose	0.25 h	0.5 h	0.75 h	1 h	1.25 h	1.5 h	2 h	3 h	4 h	6 h	8 h	12 h	18 h	24 h
N	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
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
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
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
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
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
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

BLQL: Below Lower Quantification Limit (x.xx ng/mL)
Source: Listing 16.2.5.4 - Riluzole concentrations (ng/mL) measured in plasma
Program: pk-analysis\k344-tlf.sas

Table 14.2.2.1 - Riluzole plasma PK parameters - PK Set

Investigational Medicinal Product: Riluzole 50 mg orodispersible film (T)

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

Source: Listing 16.2.6.1 - Riluzole plasma PK parameters
Program: pk-analysis\k344-tlf.sas

Table 14.2.2.1 - Riluzole plasma PK parameters - PK Set

Investigational Medicinal Product: Rilutek®, 50 mg riluzole tablets (R)

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

Source: Listing 16.2.6.1 - Riluzole plasma PK parameters
Program: pk-analysis\k344-tlf.sas

Table 14.2.3.1 - Statistical analysis on riluzole plasma PK parameters - PK set

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: Riluzole 50 mg orodispersible film (T)
R: Rilutek®, 50 mg riluzole tablets (R) _
Program: pk-analysis\k344-tlf.sas

Table 14.2.3.2 - Within-subject variability of C_{max} (after administration of the reference formulation) - PK Set

AINGR	Dependent Variable	S^2_{WR}	Within-subject variability CV_{WR}(%)
Riluzole	Ln(C_{max})	xxx.xxx	xx.xx

Note: CV_{WR}% was calculated by applying the formula 100*sqrt[exp(S^2_{WR})-1]
Program: pk-analysis\k344-tlf.sas

Table 14.2.3.3 - Non-parametric Friedman test on t_{max} and $t_{1/2}$ - PK set

Analysis	Dependent Variable	Comparison	p Value
Friedman	t_{max}	T vs R	x.xxxx
	$t_{1/2}$	T vs R	x.xxxx

Program: pk-analysis\k344-tlf.sas

Table 14.2.4.1 - Descriptive statistics of dissolution time (Safety set)

			Safety Set	
		Statistics	**Riluzole 50 mg orodispersible film (T) 1st adm. N=XX**	**Riluzole 50 mg orodispersible film (T) 2nd adm. N=XX**
Was the film accidentally swallowed within 5 min after dosing?	Yes	n (%)	nn (xx.x)	nn (xx.x)
	No	n (%)	nn (xx.x)	nn (xx.x)
Was the film undissolved at 5 min after dosing and had to be swallowed?	Yes	n (%)	nn (xx.x)	nn (xx.x)
	No	n (%)	nn (xx.x)	nn (xx.x)
Dissolution Time [min]		N	nn	nn
		Mean	xxx.xx	xxx.xx
		SD	xxx.xx	xxx.xx
		CV%	xxx.xx	xxx.xx
		Min	xxx.x	xxx.x
		Median	xxx.xx	xxx.xx
		Max	xxx.x	xxx.x

Note: Subjects are summarised according to the product they actually received
The number and the proportion of subjects for each question are reported
The denominator for calculating the proportions is the number of subjects in the safety set of Riluzole 50 mg orodispersible film (T) of each administration
Source: Listing 16.2.5.1 - Investigational medicinal products administration
Program: Tables\k344-ex-tbl.sas

Table 14.2.4.2 - Contingency tables of palatability - Safety set

Time Point	Palatability Score	Safety Set	
		Riluzole 50 mg orodispersible film (T) 1st adm. N=XX	**Riluzole 50 mg orodispersible film (T) 2nd adm. N=XX**
Immediately after administration	0 - very unpleasant	xx (xx.x)	nn (xx.x)
	1 - unpleasant	xx (xx.x)	nn (xx.x)
	2 - acceptable	xx (xx.x)	nn (xx.x)
	3 - good	xx (xx.x)	nn (xx.x)
	4 - very good	xx (xx.x)	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 of Riluzole 50 mg orodispersible film (T) of each administration
Source: Listing 16.2.6.2 - Palatability
Program: Tables\k344-fa-tbl.sas

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

	Safety Set		
	Riluzole 50 mg orodispersible film (T) N=XX n (%) [n AE]	**Rilutek®, 50 mg riluzole tablets (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\k344-ae-01-tbl.sas

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

	Safety Set **Riluzole 50 mg orodispersible film (T)** **N=XX** **n (%) [n AE]**	 **Rilutek®, 50 mg riluzole tablets (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\k344-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 Riluzole 50 mg orodispersible film (T) N=XX n (%) [n AE]	Rilutek®, 50 mg riluzole tablets (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 24.0
Source: Listing 16.2.7.1 - Treatment-emergent adverse events
Program: Tables\k344-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								
	Riluzole 50 mg orodispersible film (T) N=XX			Rilutek®, 50 mg riluzole tablets (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 24.0
Source: Listing 16.2.7.1 - Treatment-emergent adverse events
Program: Tables\k344-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 Riluzole 50 mg orodispersible film (T) N=XX n (%) [n AE]	Safety Set Rilutek®, 50 mg riluzole tablets (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 24.0
Source: Listing 16.2.7.1 - Treatment-emergent adverse events
Program: Tables\k344-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 Riluzole 50 mg orodispersible film (T) N=XX n (%) [n AE]	Safety Set Rilutek®, 50 mg riluzole tablets (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 24.0
Source: Listing 16.2.7.1 - Treatment-emergent adverse events
Program: Tables\k344-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 Riluzole 50 mg orodispersible film (T) N=XX n (%) [n AE]	Safety Set Rilutek®, 50 mg riluzole tablets (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 24.0
Source: Listing 16.2.7.1 - Treatment-emergent adverse events
Program: Tables\k344-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: Riluzole 50 mg orodispersible film (T)

Subject ID	Adverse Event ID		
S001/001	1	Description:	Headache
		Body Area Affected:	Head
		Preferred Term [1]:	Headache
		System Organ Class [1]:	Nervous system disorders
		Acknowledgment Date/Time (Day)	ddMMMyyyy hh:mm (j)
		Start - End Date/Time (Day):	ddMMMyyyy hh:mm (k) - ddMMMyyyy hh:mm (k+n)
		Has the Adverse Event Started After the Administration of the Study Drug?	Y
		Last Study Drug Administration Date/Time Before Onset	ddMMMyyyy hh:mm
		Reasonable Possibility of a Causal Relationship with the Study Drug?	Y
		Other Causal Relationship	---
		Severity:	Severe
		Pattern:	Continuous
		Serious?	N
		Seriousness criteria:	---
		Action taken with Study Drug:	None
		Concomitant therapy?	N
		Caused Study Discontinuation?	Y
		Other Action Taken:	None
		Outcome:	Recovered/Resolved
		Comments:	---
...	...	...	...

Note: Subjects are listed according to the product they actually received
Note 1: MedDRA version 24.0.
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\k344-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: Rilutek®, 50 mg riluzole tablets (R)

Subject ID	Adverse Event ID		
S001/001	2	Description:	Headache
		Body Area Affected:	Head
		Preferred Term [1]:	Headache
		System Organ Class [1]:	Nervous system disorders
		Acknowledgment Date/Time (Day)	ddMMMyyyy hh:mm (j)
		Start - End Date/Time (Day):	ddMMMyyyy hh:mm (k) - ddMMMyyyy hh:mm (k+n)
		Has the Adverse Event Started After the Administration of the Study Drug?	Y
		Last Study Drug Administration Date/Time Before Onset	ddMMMyyyy hh:mm
		Reasonable Possibility of a Causal Relationship with the Study Drug?	Y
		Other Causal Relationship	---
		Severity:	Severe
		Pattern:	Continuous
		Serious?	N
		Seriousness criteria:	---
		Action taken with Study Drug:	None
		Concomitant therapy?	N
		Caused Study Discontinuation?	Y
		Other Action Taken:	None
		Outcome:	Recovered/Resolved
		Comments:	---
...	...	...	...

Note: Subjects are listed according to the product they actually received
Note 1: MedDRA version 24.0.
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\k344-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\k344-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\k344-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\k344-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\k344-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 - 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\k344-vs-tbl.sas

Table 14.3.5.2 - Descriptive statistics of vital signs at screening 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]	End of Study	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Min	xxx
		Median	xxx.x
		Max	xxx
Diastolic Blood Pressure [mmHg]	Screening	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Min	xxx
		Median	xxx.x
		Max	xxx

Note: End of Study = Visit 9 - Day 2 - 36 hours 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
Program: Tables\k344-vs-tbl.sas

Table 14.3.5.2 - Descriptive statistics of vital signs at screening and end of study - Safety set

Parameter	Time Point	Statistics	Safety Set N=XX
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
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]	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 9 - Day 2 - 36 hours 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
Program: Tables\k344-vs-tbl.sas

Table 14.3.5.2 - Descriptive statistics of vital signs at screening and end of study - Safety set

Parameter	Time Point	Statistics	Safety Set N=XX
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
		Median	xxx.x
		Max	xxx

Note: End of Study = Visit 9 - Day 2 - 36 hours 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
Program: Tables\k344-vs-tbl.sas

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

Parameter	Time Point	Statistics	Safety Set			
			Riluzole 50 mg orodispersible film (T) 1st adm. N=XX	**Riluzole 50 mg orodispersible film (T) 2nd adm. N=XX**	**Rilutek®, 50 mg riluzole tablets (R) 1st adm. N=XX**	**Rilutek®, 50 mg riluzole tablets (R) 2nd adm. N=XX**
Systolic Blood Pressure [mmHg]	Pre-dose	N	nn	nn	nn	nn
		Mean	xxx.x	xxx.x	xxx.x	xxx.x
		SD	xxx.x	xxx.x	xxx.x	xxx.x
		CV%	xxx.x	xxx.x	xxx.x	xxx.x
		Min	xxx	xxx	xxx.x	xxx.x
		Median	xxx.x	xxx.x	xxx.x	xxx.x
		Max	xxx	xxx	xxx.x	xxx.x
Systolic Blood Pressure [mmHg]	2 hours post-dose	N	nn	nn	nn	nn
		Mean	xxx.x	xxx.x	xxx.x	xxx.x
		SD	xxx.x	xxx.x	xxx.x	xxx.x
		CV%	xxx.x	xxx.x	xxx.x	xxx.x
		Min	xxx	xxx	xxx.x	xxx.x
		Median	xxx.x	xxx.x	xxx.x	xxx.x
		Max	xxx	xxx	xxx.x	xxx.x
Systolic Blood Pressure [mmHg]	36 hours post-dose	N	nn	nn	nn	nn
		Mean	xxx.x	xxx.x	xxx.x	xxx.x
		SD	xxx.x	xxx.x	xxx.x	xxx.x
		CV%	xxx.x	xxx.x	xxx.x	xxx.x
		Min	xxx	xxx	xxx.x	xxx.x
		Median	xxx.x	xxx.x	xxx.x	xxx.x
		Max	xxx	xxx	xxx.x	xxx.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\k344-vs-tbl.sas

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

Parameter	Time Point	Statistics	Safety Set			
			Riluzole 50 mg orodispersible film (T) 1st adm. N=XX	Riluzole 50 mg orodispersible film (T) 2nd adm. N=XX	Rilutek®, 50 mg riluzole tablets (R) 1st adm. N=XX	Rilutek®, 50 mg riluzole tablets (R) 2nd adm. N=XX
Diastolic Blood Pressure [mmHg]	Pre-dose	N	nn	nn	nn	nn
		Mean	xxx.x	xxx.x	xxx.x	xxx.x
		SD	xxx.x	xxx.x	xxx.x	xxx.x
		CV%	xxx.x	xxx.x	xxx.x	xxx.x
		Min	xxx	xxx	xxx.x	xxx.x
		Median	xxx.x	xxx.x	xxx.x	xxx.x
		Max	xxx	xxx	xxx.x	xxx.x
Diastolic Blood Pressure [mmHg]	2 hours post-dose	N	nn	nn	nn	nn
		Mean	xxx.x	xxx.x	xxx.x	xxx.x
		SD	xxx.x	xxx.x	xxx.x	xxx.x
		CV%	xxx.x	xxx.x	xxx.x	xxx.x
		Min	xxx	xxx	xxx.x	xxx.x
		Median	xxx.x	xxx.x	xxx.x	xxx.x
		Max	xxx	xxx	xxx.x	xxx.x
Diastolic Blood Pressure [mmHg]	36 hours post-dose	N	nn	nn	nn	nn
		Mean	xxx.x	xxx.x	xxx.x	xxx.x
		SD	xxx.x	xxx.x	xxx.x	xxx.x
		CV%	xxx.x	xxx.x	xxx.x	xxx.x
		Min	xxx	xxx	xxx.x	xxx.x
		Median	xxx.x	xxx.x	xxx.x	xxx.x
		Max	xxx	xxx	xxx.x	xxx.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\k344-vs-tbl.sas

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

Parameter	Time Point	Statistics	Safety Set			
			Riluzole 50 mg orodispersible film (T) 1st adm. N=XX	Riluzole 50 mg orodispersible film (T) 2nd adm. N=XX	Rilutek®, 50 mg riluzole tablets (R) 1st adm. N=XX	Rilutek®, 50 mg riluzole tablets (R) 2nd adm. N=XX
Heart Rate [beats/min]	Pre-dose	N	nn	nn	nn	nn
		Mean	xxx.x	xxx.x	xxx.x	xxx.x
		SD	xxx.x	xxx.x	xxx.x	xxx.x
		CV%	xxx.x	xxx.x	xxx.x	xxx.x
		Min	xxx	xxx	xxx.x	xxx.x
		Median	xxx.x	xxx.x	xxx.x	xxx.x
		Max	xxx	xxx	xxx.x	xxx.x
Heart Rate [beats/min]	2 hours post-dose	N	nn	nn	nn	nn
		Mean	xxx.x	xxx.x	xxx.x	xxx.x
		SD	xxx.x	xxx.x	xxx.x	xxx.x
		CV%	xxx.x	xxx.x	xxx.x	xxx.x
		Min	xxx	xxx	xxx.x	xxx.x
		Median	xxx.x	xxx.x	xxx.x	xxx.x
		Max	xxx	xxx	xxx.x	xxx.x
Heart Rate [beats/min]	36 hours post-dose	N	nn	nn	nn	nn
		Mean	xxx.x	xxx.x	xxx.x	xxx.x
		SD	xxx.x	xxx.x	xxx.x	xxx.x
		CV%	xxx.x	xxx.x	xxx.x	xxx.x
		Min	xxx	xxx	xxx.x	xxx.x
		Median	xxx.x	xxx.x	xxx.x	xxx.x
		Max	xxx	xxx	xxx.x	xxx.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\k344-vs-tbl.sas

Table 14.3.5.4 - Contingency tables of investigator's interpretation of mouth visual inspection during the study - Safety set

Time Point	Investigator's interpretation	Safety Set Riluzole 50 mg orodispersible film (T) 1st adm. N=XX	Safety Set Riluzole 50 mg orodispersible film (T) 2nd adm. N=XX
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)
0.5 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)
1 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)

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 of Riluzole 50 mg orodispersible film (T) of each administration
Source: Listing 16.2.10.3 - Mouth Visual Inspection
Program: Tables\k344-pe-tbl.sas

Table 14.3.5.5 - 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
		Min	xxx
		Median	xxx.x
		Max	xxx
Dose per body weight [mg/kg]	Males	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Min	xxx
		Median	xxx.x
		Max	xxx
Dose per body weight [mg/kg]	Females and males	N	nn
		Mean	xxx.x
		SD	xxx.x
		CV%	xxx.x
		Min	xxx
		Median	xxx.x
		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\k344-ex-tbl.sas

Table 14.3.5.6 - 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
Wash-out between IMP administration of Period 2 and Period 3 [days]	N	nn
	Min	xxx
	Max	xxx
Wash-out between IMP administration of Period 3 and Period 4 [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\k344-ex-tbl.sas

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	Riluzole 50 mg orodispersible film (T)	M	30	Visit 3	1	ddMMMyyyy	Withdrawal by subject
S003/002	Rilutek®, 50 mg riluzole tablets (R)	F	27	Visit 5	2	ddMMMyyyy	Adverse event
S005/004	Rilutek®, 50 mg riluzole tablets (R)	M	18	Visit 3	2	ddMMMyyyy	Physician decision
S007/006	Riluzole 50 mg orodispersible film (T)	F	27	Visit 5	2	ddMMMyyyy	Adverse event
S011/010	Rilutek®, 50 mg riluzole tablets (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\k344-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\k344-dv-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	Reason for the exclusion
S010/008	F	30	Y	N	N	Lack of IMP administration
S015/013	F	20	Y	Y	N	Major protocol deviations
...	...		.	.	.	...

Program: Listings\k344-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\k344-ds-lst.sas

Listing 16.2.4.2 - Analysis sets

Subject ID	Planned Sequence	Enrolled Set	Safety Set	PK Set	Reason for the exclusion
S001/001	TRTR	Y	N	N	Lack of IMP intake
S003/002	RTRT	Y	Y	Y	
...	...	.	.	.	...

Note: Subjects are listed according to the sequence they were assigned to
T: Riluzole 50 mg orodispersible film (T)
R: Rilutek®, 50 mg riluzole tablets (R)
Program: Listings\k344-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	20	170	55.0	19.0
S002/002	M	White	1990	31	187	91.0	26.0
...	...	...	...		...	...	...

Note:Program:Listings\k344-dm-lst.sas

Listing 16.2.4.4 - Inclusion/Exclusion criteria not met

Subject ID	Criterion	Verbatim
S001/001	Inclusion criterion 4	Body Mass Index (BMI): 18.5-29 kg/m2 inclusive
...	...	...

Program: Listings\k344-ie-lst.sas

Listing 16.2.4.5 - Investigator's interpretation of ECG

Subject ID	Time Point	Assessment Date/Time	Investigator's Interpretation	Clinically Significant Abnormalites
S001/001	Screening	ddMMMyyyy hh:mm	Abnormal, Not Clinically Significant	---
S005/002	Screening	ddMMMyyyy hh:mm	Normal	---
...	...	...	...	...

Program: Listings\k344-eg-lst.sas

Listing 16.2.4.6 - Tobacco consumption

Subject ID	Tobacco Consumption	End of consumption Date
S001/001	Non smoker	---
S003/003	Ex Smoker	2019
...	...	...

Program: Listings\k344-su-lst.sas

Listing 16.2.5.1 - Investigational medicinal products administration

Investigational Medicinal Product: Riluzole 50 mg orodispersible film (T)

Subject ID	Adm. Nr.	Adm. Visit	Administration Date/time	Dissolution Start Time	Dissolution End Time	Film swallowed within 5 min?	If yes, accidental swallowing time	Film undissolved at 5 min after Adm.?	Fasting Conditions From 10 h before IMP Adm.?	Fasting Conditions Start Date/time	Time from Start of Fasting Conditions
S001/001	1	Visit 3	ddMMMyyyy hh:mm	hh:mm:ss	hh:mm:ss	N	---	N	Y	ddMMMyyyy hh:mm	xx min
S001/001	3	Visit 7	ddMMMyyyy hh:mm	hh:mm:ss	hh:mm:ss	N	---	N	Y	ddMMMyyyy hh:mm	xx min
...	...	...	...	...	...	...	...	...	...	...	...

Note: Subjects are listed according to the product they actually received
Program: Listings\k344-ex-lst.sas

Listing 16.2.5.1 - Investigational medicinal products administration

Investigational Medicinal Product: Rilutek®, 50 mg riluzole tablets (R)

Subject ID	Adm. Nr.	Adm. Visit	Administration Date/time	Dissolution Start Time	Dissolution End Time	Film swallowed within 5 min?	If yes, accidental swallowing time	Film undissolved at 5 min after Adm.?	Fasting Conditions From 10 h before IMP Adm.?	Fasting Conditions Start Date/time	Time from Start of Fasting Conditions
S001/001	2	Visit 5	ddMMMyyyy hh:mm	---	---	---	---	---	Y	ddMMMyyyy hh:mm	xx min
S001/001	4	Visit 9	ddMMMyyyy hh:mm	---	---	---	---	---	Y	ddMMMyyyy hh:mm	xx min
...	...	...	...	...	...	...	...	...	...	...	...

Note: Subjects are listed according to the product they actually received
Program: Listings\k344-ex-lst.sas

Listing 16.2.5.2 - Dose per body weight

Investigational Medicinal Product: Riluzole 50 mg orodispersible film (T)

Subject ID	Active Ingredient	Dose Administered (mg)	Body Weight at Screening (kg)	Dose per Body Weight (mg/kg)
S001/001	Riluzole	200	55.0	3.63
...	...	...	...	...

Note: The dose per body weight is calculated using the screening body weight
Program: Listings\k344-ex-lst.sas

Listing 16.2.5.3 - PK samples collection dates and times

Investigational Medicinal Product: Riluzole 50 mg orodispersible film (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	45 min post-dose ± 2 min	4	ddMMMyyyy hh:mm	xx min
S001/001	ddMMMyyyy hh:mm	1	1 hour post-dose ± 3 min	5	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	1.25 hours post-dose ± 3 min	6	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	1.5 hours post-dose ± 3 min	7	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	2 hours post-dose ± 5 min	8	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	3 hours post-dose ± 5 min	9	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	4 hours post-dose ± 5 min	10	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	6 hours post-dose ± 10 min	11	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	8 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	24 hours post-dose ± 10 min	14	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	1	36 hours post-dose ± 10 min	15	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	3	Pre-dose - Within 30 min before IMP administration	31	ddMMMyyyy hh:mm	-xx min
S001/001	ddMMMyyyy hh:mm	3	15 min post-dose	32	ddMMMyyyy hh:mm	xx min
S001/001	ddMMMyyyy hh:mm	3	30 min post-dose ± 1 min	33	ddMMMyyyy hh:mm	xx min

Note: Subjects are listed according to the product they actually received
Program: Listings\k344-pc-lst.sas

Listing 16.2.5.3 - PK samples collection dates and times

Investigational Medicinal Product: Riluzole 50 mg orodispersible film (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	3	45 min post-dose ± 2 min	34	ddMMMyyyy hh:mm	xx min
S001/001	ddMMMyyyy hh:mm	3	1 hour post-dose ± 3 min	35	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	3	1.25 hours post-dose ± 3 min	36	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	3	1.5 hours post-dose ± 3 min	37	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	3	2 hours post-dose ± 5 min	38	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	3	3 hours post-dose ± 5 min	39	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	3	4 hours post-dose ± 5 min	40	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	3	6 hours post-dose ± 10 min	41	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	3	8 hours post-dose ± 10 min	42	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	3	12 hours post-dose ± 10 min	43	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	3	24 hours post-dose ± 10 min	44	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	3	36 hours post-dose ± 10 min	45	ddMMMyyyy hh:mm	xx h xx min
...	...	...	...	...	...	...

Note: Subjects are listed according to the product they actually received
Program: Listings\k344-pc-lst.sas

Listing 16.2.5.3 - PK samples collection dates and times

Investigational Medicinal Product: Rilutek®, 50 mg riluzole tablets (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	16	ddMMMyyyy hh:mm	-xx min
S001/001	ddMMMyyyy hh:mm	2	15 min post-dose	17	ddMMMyyyy hh:mm	xx min
S001/001	ddMMMyyyy hh:mm	2	30 min post-dose ± 1 min	18	ddMMMyyyy hh:mm	xx min
S001/001	ddMMMyyyy hh:mm	2	45 min post-dose ± 2 min	19	ddMMMyyyy hh:mm	xx min
S001/001	ddMMMyyyy hh:mm	2	1 hour post-dose ± 3 min	20	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	1.25 hours post-dose ± 3 min	21	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	1.5 hours post-dose ± 3 min	22	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	2 hours post-dose ± 5 min	23	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	3 hours post-dose ± 5 min	24	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	4 hours post-dose ± 5 min	25	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	6 hours post-dose ± 10 min	26	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	8 hours post-dose ± 10 min	27	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	12 hours post-dose ± 10 min	28	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	24 hours post-dose ± 10 min	29	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	36 hours post-dose ± 10 min	30	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	4	Pre-dose - Within 30 min before IMP administration	46	ddMMMyyyy hh:mm	-xx min
S001/001	ddMMMyyyy hh:mm	4	15 min post-dose	47	ddMMMyyyy hh:mm	xx min
S001/001	ddMMMyyyy hh:mm	4	30 min post-dose ± 1 min	48	ddMMMyyyy hh:mm	xx min

Note: Subjects are listed according to the product they actually received
Program: Listings\k344-pc-lst.sas

Listing 16.2.5.3 - PK samples collection dates and times

Investigational Medicinal Product: Rilutek®, 50 mg riluzole tablets (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	4	45 min post-dose ± 2 min	49	ddMMMyyyy hh:mm	xx min
S001/001	ddMMMyyyy hh:mm	4	1 hour post-dose ± 3 min	50	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	4	1.25 hours post-dose ± 3 min	51	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	4	1.5 hours post-dose ± 3 min	52	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	4	2 hours post-dose ± 5 min	53	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	4	3 hours post-dose ± 5 min	54	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	4	4 hours post-dose ± 5 min	55	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	4	6 hours post-dose ± 10 min	56	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	4	8 hours post-dose ± 10 min	57	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	4	12 hours post-dose ± 10 min	58	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	4	24 hours post-dose ± 10 min	59	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	4	36 hours post-dose ± 10 min	60	ddMMMyyyy hh:mm	xx h xx min
...	...	...	...	...	...	...

Note: Subjects are listed according to the product they actually received
Program: Listings\k344-pc-lst.sas

Listing 16.2.5.4 - Riluzole concentrations (ng/mL) measured in plasma

Investigational Medicinal Product: Riluzole 50 mg orodispersible film (T)

Subject ID	Period	Pre dose	0.25 h	0.5 h	0.75 h	1 h	1.25 h	1.5 h	2 h	3 h	4 h	6 h	8 h	12 h	24 h	36 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
S001/001	3	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
...		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...

BLQL: Below Lower Quantification Limit (xx.xx ng/mL)
Program: pk-analysis\k344-tlf.sas

Listing 16.2.5.4 - Riluzole concentrations (ng/mL) measured in plasma

Investigational Medicinal Product: Rilutek®, 50 mg riluzole tablets (R)

Subject ID	Period	Pre dose	0.25 h	0.5 h	0.75 h	1 h	1.25 h	1.5 h	2 h	3 h	4 h	6 h	8 h	12 h	24 h	36 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
S001/001	4	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
...		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...

BLQL: Below Lower Quantification Limit (xx.xx ng/mL)
Program: pk-analysis\k344-tlf.sas

Listing 16.2.6.1 - Riluzole plasma PK parameters

Investigational Medicinal Product: Riluzole 50 mg orodispersible film (T)

Subject ID	Period	C_{max} (ng/mL)	t_{max} (h)	AUC_{0-t} (h*ng/mL)	AUC_{0-inf} (h*ng/mL)	AUC_{extra} (%)	$t_{½}$ (h)	λ_z (1/h)	Points	R^2
S001/001	1	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
S001/001	3	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 are listed
Program: pk-analysis\k344-tlf.sas

Listing 16.2.6.1 - Riluzole plasma PK parameters

Investigational Medicinal Product: Rilutek®, 50 mg riluzole tablets (R)

Subject ID	Period	C_{max} (ng/mL)	t_{max} (h)	AUC_{0-t} (h*ng/mL)	AUC_{0-inf} (h*ng/mL)	AUC_{extra} (%)	$t_{½}$ (h)	λ_z (1/h)	Points	R^2
S001/001	2	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx	xxx.xx
S001/001	4	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 are listed
Program: pk-analysis\k344-tlf.sas

Listing 16.2.6.2 - Palatability

Subject ID	IMP Administration Date/Time	IMP Administration Number	Time Point	Assessment Date/Time	Palatability Score
S001/001	ddMMMyyyy hh:mm	1	Visit 3 - Day 1 - Immediately after administration	ddMMMyyyy hh:mm	0 - Very unpleasant
S001/001	ddMMMyyyy hh:mm	3	Visit 7 - Day 1 - Immediately after administration	ddMMMyyyy hh:mm	1 - Unpleasant
...	...	...	...	...	...

Note: Palatability has been evaluated only for Riluzole 50 mg orodispersible film (T)
Program: Listings\k344-pc-lst.sas

Listing 16.2.7.1 - Treatment-emergent adverse events

Investigational Product: Riluzole 50 mg orodispersible film (T)

Subject ID	Adverse Event ID		
S001/001	1	Description:	Headache
		Body Area Affected:	Head
		Preferred Term [1]:	Headache
		System Organ Class [1]:	Nervous system disorders
		Acknowledgment Date/Time (Day)	ddMMMyyyy hh:mm (j)
		Start - End Date/Time (Day):	ddMMMyyyy hh:mm (k) - ddMMMyyyy hh:mm (k+n)
		Has the Adverse Event Started After the Administration of the Study Drug?	Y
		Last Study Drug Administration Date/Time Before Onset	ddMMMyyyy hh:mm
		Reasonable Possibility of a Causal Relationship with the Study Drug?	Y
		Other Causal Relationship	---
		Severity:	Mild
		Pattern:	Continuous
		Serious?	N
		Seriousness criteria:	---
		Action taken with Study Drug:	None
		Concomitant therapy?	N
		Caused Study Discontinuation?	N
		Other Action Taken:	None
		Outcome:	Recovered/Resolved
		Comments:	---
...	...	...	...

Note: Subjects are listed according to the product they actually received
Note 1: MedDRA version 24.0
Program: Listings\k344-ae-lst.sas

Listing 16.2.7.1 - Treatment-emergent adverse events

Investigational Product: Rilutek®, 50 mg riluzole tablets (R)

Subject ID	Adverse Event ID		
S001/001	2	Description:	Headache
		Body Area Affected:	Head
		Preferred Term [1]:	Headache
		System Organ Class [1]:	Nervous system disorders
		Acknowledgment Date/Time (Day)	ddMMMyyyy hh:mm (j)
		Start - End Date/Time (Day):	ddMMMyyyy hh:mm (k) - ddMMMyyyy hh:mm (k+n)
		Has the Adverse Event Started After the Administration of the Study Drug?	Y
		Last Study Drug Administration Date/Time Before Onset	ddMMMyyyy hh:mm
		Reasonable Possibility of a Causal Relationship with the Study Drug?	Y
		Other Causal Relationship	---
		Severity:	Mild
		Pattern:	Continuous
		Serious?	N
		Seriousness criteria:	---
		Action taken with Study Drug:	None
		Concomitant therapy?	N
		Caused Study Discontinuation?	N
		Other Action Taken:	None
		Outcome:	Recovered/Resolved
		Comments:	---
...	...	...	...

Note: Subjects are listed according to the product they actually received
Note 1: MedDRA version 24.0
Program: Listings\k344-ae-lst.sas

Listing 16.2.7.2 - Pre-treatment adverse events

Subject ID	Adverse Event ID		
S001/001	1	Description:	Headache
		Body Area Affected:	Head
		Preferred Term [1]:	Headache
		System Organ Class [1]:	Nervous system disorders
		Acknowledgment Date/Time (Day)	ddMMMyyyy hh:mm (j)
		Start - End Date/Time (Day):	ddMMMyyyy hh:mm (k) - ddMMMyyyy hh:mm (k+n)
		Has the Adverse Event Started After the Administration of the Study Drug?	N
		Last Study Drug Administration Date/Time Before Onset	---
		Reasonable Possibility of a Causal Relationship with the Study Drug?	N
		Other Causal Relationship	Other, stress period
		Severity:	Mild
		Pattern:	Continuous
		Serious?	N
		Seriousness criteria:	---
		Action taken with Study Drug:	None
		Concomitant therapy?	N
		Caused Study Discontinuation?	N
		Other Action Taken:	None
		Outcome:	Recovered/Resolved
		Comments:	---
...	...	...	...

Note 1: MedDRA version 24.0
Program: Listings\k344-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\k344-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\k344-lb-lst.sas

Listing 16.2.8.1 - Individual laboratory measurements

Category of Laboratory Parameters: COTININE

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	Cotinine	Negative [N]	Negative	N
...	...	...	...	...	...	...

Note 1: N=Normal, A=Different from reference value
Program: Listings\k344-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\k344-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\k344-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\k344-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
...	...	...	...	...	...	...

Note 1: N=Normal, A=Different from reference value
Program: Listings\k344-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\k344-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]	50-89	N
S001/001	Screening	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Screening	ddMMMyyyy hh:mm	Weight [kg]	55.5	---	N
S001/001	Visit 3 - Pre-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 3 - Pre-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	50-89	N
S001/001	Visit 3 - Pre-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 3 - 2 hours post-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 3 - 2 hours post-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	50-89	N
S001/001	Visit 3 - 2 hours post-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 3 - 36 hours post-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 3 - 36 hours post-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	50-89	N
S001/001	Visit 3 - 36 hours post-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 5 - Pre-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 5 - Pre-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	50-89	N
S001/001	Visit 5 - Pre-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 5 - 2 hours post-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 5 - 2 hours post-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	50-89	N
S001/001	Visit 5 - 2 hours post-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 5 - 36 hours post-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 5 - 36 hours post-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	50-89	N
S001/001	Visit 5 - 36 hours post-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 7 - Pre-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 7 - Pre-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	50-89	N
S001/001	Visit 7 - Pre-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N

Note 1: N=Normal, H=Higher than upper normal limit, L=Lower than lower normal limit
Program: Listings\k344-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 7 - 2 hours post-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 7 - 2 hours post-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	50-89	N
S001/001	Visit 7 - 2 hours post-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 7 - 36 hours post-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 7 - 36 hours post-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	50-89	N
S001/001	Visit 7 - 36 hours post-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 9 - Pre-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 9 - Pre-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	50-89	N
S001/001	Visit 9 - Pre-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 9 - 2 hours post-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 9 - 2 hours post-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	50-89	N
S001/001	Visit 9 - 2 hours post-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	N
S001/001	Visit 9 - 36 hours post-dose	ddMMMyyyy hh:mm	Systolic Blood Pressure [mmHg]	96 [L]	100-139	N
S001/001	Visit 9 - 36 hours post-dose	ddMMMyyyy hh:mm	Diastolic Blood Pressure [mmHg]	58 [N]	50-89	N
S001/001	Visit 9 - 36 hours post-dose	ddMMMyyyy hh:mm	Heart Rate [beats/min]	88 [N]	50-90	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\k344-vs-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 24.0
Program: Listings\k344-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
	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 24.0
Program: Listings\k344-pe-lst.sas

Listing 16.2.10.3 - Mouth Visual Inspection

Subject ID	Time Point	Physical Examination Date		
S001/001	Visit 3 - Pre-dose	ddMMMyyyy	Investigator's Interpretation	Normal
S001/001	Visit 3 - 0.5 hour post-dose	ddMMMyyyy	Investigator's Interpretation	Abnormal, Not Clinically Significant
S001/001	Visit 3 - 1 hour post-dose	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
S001/001	Visit 7 - Pre-dose	ddMMMyyyy	Investigator's Interpretation	Normal
S001/001	Visit 7 - 0.5 hour post-dose	ddMMMyyyy	Investigator's Interpretation	Abnormal, Not Clinically Significant
S001/001	Visit 7 - 1 hour post-dose	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: Mouth visual inspection has been evaluated only for Riluzole 50 mg orodispersible film (T)
Note 1: MedDRA version 24.0
Program: Listings\k344-pe-lst.sas

Listing 16.2.10.4 - 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 - Dosage Form - Route:	1 time per day - Tablet - Oral
			Related to:	Disease M1
	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:	15JUN2016 19:08 - 15JUN2016 19:08
			Frequency - Dosage Form - Route:	Once - Tablet - Oral
			Related to:	Adverse Event 1
	...	...	...	...

Note 1: WHO Drug Dictionary Enhanced March 1, 2021
Note 2: Anatomical Therapeutic Chemical classification, 4th level term
Program: Listings\k344-cm-lst.sas

Listing 16.2.10.5 - Subjects study visits

Subject ID	Visit	Visit Start Date (Day)	Visit End Date (Day)	Home discharge Date/time
S001/001	Visit 1 - Screening - Day -14/-2	ddMMMyyyy (-j)	---	---
S001/001	Period 1 - Visit 2 - Day -1	ddMMMyyyy (-1)	---	---
S001/001	Period 1 - Visit 3 - Days 1-2	ddMMMyyyy (1)	ddMMMyyyy (2)	ddMMMyyyy (2) hh:mm
S001/001	Period 1 - Visit 4 - Day -1	ddMMMyyyy (k-1)	---	---
S001/001	Period 2 - Visit 5 - Days 1-2	ddMMMyyyy (k)	ddMMMyyyy (k+1)	ddMMMyyyy (k+1) hh:mm
S001/001	Period 1 - Visit 6 - Day -1	ddMMMyyyy (n-1)	---	---
S001/001	Period 2 - Visit 7 - Days 1-2	ddMMMyyyy (n)	ddMMMyyyy (n+1)	ddMMMyyyy (n+1) hh:mm
S001/001	Period 1 - Visit 8 - Day -1	ddMMMyyyy (p-1)	---	---
S001/001	Period 2 - Visit 9 - Days 1-2	ddMMMyyyy (p)	ddMMMyyyy (p+1)	---
S001/001	Final Visit	ddMMMyyyy (p+1)	---	ddMMMyyyy (p+1) hh:mm
...	...	...	...	...

Program: Listings\k344-sv-lst.sas

Listing 16.2.10.6 - 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\k344-rp-lst.sas

Listing 16.2.10.7 - Meals

Investigational Medicinal Product: Riluzole 50 mg orodispersible film (T)

Subject ID	IMP Administration Date/Time	Meal Nr	Standardised Meal	Time Point	Meal Served?	Meal Start Date/time	Elapsed Time
S001/001	ddMMMyyyy hh:mm	1	Lunch	Visit 3 - Day 1 –5 hours post-dose	Y	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	2	Dinner	Visit 3 - Day 1 –12 hours post-dose	Y	ddMMMyyyy hh:mm	xx h xx min
S001/001	---	3	Breakfast	Visit 3 - Day 2 –at about 08:00	Y	ddMMMyyyy hh:mm	---
S001/001	---	4	Lunch	Visit 3 - Day 2 - at about 13:00	Y	ddMMMyyyy hh:mm	---
S001/001	ddMMMyyyy hh:mm	9	Lunch	Visit 7 - Day 1 –5 hours post-dose	Y	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	10	Dinner	Visit 7 - Day 1 –12 hours post-dose	Y	ddMMMyyyy hh:mm	xx h xx min
S001/001	---	11	Breakfast	Visit 7 - Day 2 –at about 08:00	Y	ddMMMyyyy hh:mm	---
S001/001	---	12	Lunch	Visit 7 - Day 2 - at about 13:00	Y	ddMMMyyyy hh:mm	---
...	...		...	...	...	...	...

Note: Subjects are listed according to the product they actually received
Program: Listings\k344-ml-lst.sas

Listing 16.2.10.7 - Meals

Investigational Medicinal Product: Rilutek®, 50 mg riluzole tablets (R)

Subject ID	IMP Administration Date/Time	Meal Nr	Standardised Meal	Time Point	Meal Served?	Meal Start Date/time	Elapsed Time
S001/001	ddMMMyyyy hh:mm	5	Lunch	Visit 5 - Day 1 –5 hours post-dose	Y	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	6	Dinner	Visit 5 - Day 1 –12 hours post-dose	Y	ddMMMyyyy hh:mm	xx h xx min
S001/001	---	7	Breakfast	Visit 5 - Day 2 –at about 08:00	Y	ddMMMyyyy hh:mm	---
S001/001	---	8	Lunch	Visit 5 - Day 2 - at about 13:00	Y	ddMMMyyyy hh:mm	---
S001/001	ddMMMyyyy hh:mm	13	Lunch	Visit 9 - Day 1 –5 hours post-dose	Y	ddMMMyyyy hh:mm	xx h xx min
S001/001	ddMMMyyyy hh:mm	14	Dinner	Visit 9 - Day 1 –12 hours post-dose	Y	ddMMMyyyy hh:mm	xx h xx min
S001/001	---	15	Breakfast	Visit 9 - Day 2 –at about 08:00	Y	ddMMMyyyy hh:mm	---
S001/001	---	16	Lunch	Visit 9 - Day 2 - at about 13:00	Y	ddMMMyyyy hh:mm	---
...	...		...	...	...	...	...

Note: Subjects are listed according to the product they actually received
Program: Listings\k344-ml-lst.sas