

Statistical Analysis Plan

A RANDOMIZED, OPEN-LABEL, 2-SEQUENCE, 3-TREATMENT, CROSSOVER STUDY TO EVALUATE THE PHARMACOKINETICS OF SINGLE DOSES OF DIAZEPAM BUCCAL FILM (DBF) (AQUESTIVE THERAPEUTICS) COMPARED WITH DIASTAT[®] RECTAL GEL (VALEANT PHARMACEUTICALS NORTH AMERICA) IN ADULT MALE AND FEMALE SUBJECTS ON A CONCOMITANT REGIMEN OF ANTIEPILEPTIC DRUGS (AED) FOR THE TREATMENT OF EPILEPSY

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CONFIDENTIAL

SIGNATURES

Sponsor Protocol No. 180323

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Study Title: A Randomized, Open-Label, 2-Sequence, 3-Treatment, Crossover Study to Evaluate the Pharmacokinetics of Single Doses of Diazepam Buccal Film (DBF) (Aquestive Therapeutics) Compared with Diastat[®] Rectal Gel (Valeant Pharmaceuticals North America) in Adult Male and Female Subjects on a Concomitant Regimen of Antiepileptic Drugs (AED) for the Treatment of Epilepsy

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LIST OF ABBREVIATIONS

A	Abnormal
AE	Adverse event
AED	Antiepileptic drug
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
ANOVA	Analysis of variance
AST	Aspartate aminotransferase
AUC	Area under the concentration-time curve
AUC_{0-inf}	Area under the concentration-time curve from time 0 to infinity (extrapolated)
AUC_{0-t}	Area under the concentration-time curve from time 0 to the last non-zero concentration
BLQ	Below the lower limit of quantitation
BMI	Body mass index
BP	Blood Pressure
CK	Creatine Kinase
Cl/F	Apparent total clearance
Cl/F/kg	Apparent total clearance normalized for the subject body weight in kg
C_{last}	The last observed non-zero concentration
C_{max}	Maximal observed plasma concentration
CSR	Clinical study report
CV	Coefficient of variation (equivalent to C.V.)
DBF	Diazepam Buccal Film
DRG	Diastat [®] Rectal Gel
ECG	Electrocardiogram
FDA	Food and Drug Administration
H	Above normal range
HBsAg	Surface Antigen of the Hepatitis B Virus
HCV	Human Hepatitis C Virus
HEENT	Head, eyes, ears, nose and throat
HIV	Human immunodeficiency virus
HR	Heart rate
K_{el}	Terminal elimination rate constant
K_{el Lower}	The actual sampling time where K _{el} calculation begins
K_{el Upper}	The actual sampling time of the last measurable concentration used to estimate K _{el}
kg	Kilogram

L	Below normal range (conflicting with Liter)
Max	Maximum (equivalent to max.)
MDMA	3,4-methylenedioxy-N-methylamphetamine
MedDRA[®]	Medical Dictionary for Regulatory Activities
mg	Milligram
Min	Minimum (equivalent to min.)
mL	Milliliter
N	Number of observations
PCP	Phencyclidine
PK	Pharmacokinetic
PT	MedDRA [®] Preferred Term
QI	Qualified Investigator
QRS	The QRS complex is a structure on the ECG that corresponds to the depolarization of the ventricles
QT	Time from electrocardiogram Q wave to the end of the T wave corresponding to electrical systole
QTcB	QT Corrected with Bazett formula
QTcF	QT Corrected with Fridericia's formula
RR	Respiratory Rate
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS[®]	Statistical Analysis System
SD	Standard Deviation
SOC	MedDRA [®] System Organ Class
SOP	Standard Operating Procedure
TEAE	Treatment-Emergent Adverse Event
T_{1/2 el}	Elimination half-life
THC	Tetrahydrocannabinol
T_{max}	Time of maximal observed plasma concentration
vs	Versus
V_d/F	Apparent volume of distribution
V_d/F/kg	Apparent volume of distribution normalized for the subject body weight in kg
WHO DD	World Health Organization Drug Dictionary

1. Introduction

This statistical analysis plan (SAP) is intended to give a detailed description of the summaries and the analyses that will be generated for the present study by inVentiv. Analyses specified in this plan are based on Aquestive Therapeutics study Protocol No. 180323 Amendment III, dated 24 May 2019 (inVentiv Project No. 180323). Safety, tolerability and pharmacokinetic (PK) analyses will all be described.

The plan may change due to unforeseen circumstances and any changes made after the plan has been finalized will be documented. If additional analyses are required to supplement the planned analyses described in the SAP, the changes and justification for the changes will be outlined in the clinical study report (CSR). No change will be made without prior approval of the study sponsor. No revision to the SAP is required for changes which do not affect the statistical analysis methods, definitions, or rules defined in this document.

When applicable, all methodology and related processes will be conducted according to inVentiv's Standard Operating Procedures (SOPs). Protocol deviations occurring during the study will be listed.

Shells for all statistical tables, figures and listings referred to in this SAP will be displayed in a separate document.

2. Study Objectives

2.1 Primary Objective

- Evaluate the pharmacokinetics (PK) of single doses of Diazepam Buccal Film (DBF) at the recommended dose regimen (range 10 mg to 17.5 mg according to body weight) compared with Diastat[®] Rectal Gel (DRG) at the labeled dose regimen (range 10 mg to 20 mg according to body weight) in adult male and female subjects on a stable concomitant regimen of antiepileptic drugs (AED) for the treatment of epilepsy, following a moderate-fat meal.

2.2 Secondary Objectives

- Evaluate the PK of single doses of DBF following a high-fat meal compared with DRG following a moderate-fat meal at the recommended dose regimen in adult male and female subjects on a stable concomitant regimen of AED for the treatment of epilepsy.
- Assess the safety-tolerability of single doses of DBF and DRG administered to adult male and female subjects on a stable concomitant regimen of AEDs under fed conditions.

3. Study Design

3.1 General Design

This will be a randomized, multiple centers, single-dose, open-label, three-period, three treatment, two-sequence crossover study under fed conditions.

The study will evaluate single doses of DBF compared with DRG administered according to weight category in adult male and female subjects on a stable concomitant regimen of AED for the treatment of epilepsy. A stable regimen of AED is defined as no change in the prescribed AED regimen during the 30 day period prior to the first study drug administration and no change anticipated in the prescribed AED regimen over the course of study participation until the last PK blood sample collection.

Subjects will receive Treatment A and Treatment B (DBF and DRG following a moderate-fat meal) in Period 1 and Period 2 in a randomized sequence, and at a dosage specific to body weight. DBF will be administered according to the currently recommended dose regimen (derived by Aquestive from population PK modeling in healthy volunteers). DRG will be administered depending on weight category according to the current product labeling for Diastat[®]. Subjects may be asked to participate in a third period, on a voluntary basis. Subjects who volunteer to participate in a third period will receive a second dose of DBF administered in exactly the same manner as the earlier dose of DBF with the exception that DBF in Period 3 will be administered following a high-fat meal. There will be a washout of 28 days between doses.

A maximum of 32 eligible subjects will be enrolled in an effort to complete Period 2 with at least 16 subjects with representation of both genders, representation across the five weight categories of subjects taking one or more AEDs known to induce diazepam metabolism, and representation of subjects taking sodium divalproex/valproic acid. Subjects who are eligible may be enrolled without regard to weight category. Since only exploratory PK data will be gathered from treatment period 3, no more than 50% of the subjects who complete Period 1 and Period 2 will participate in Period 3.

This study is intended for filing under FDA regulations.

3.2 Study Procedures

The overall schedule of procedures and assessments is provided in the protocol.

3.3 Treatment Description

Subjects will be administered each treatment according to the 3-period, 2-sequence, block randomization scheme produced by inVentiv. At admission to the clinic, subjects who meet the inclusion/exclusion criteria will be assigned between the 2-sequence arms (ABC or BAC) according to the randomization schedule. inVentiv will inform the site about the medication to be dispensed to each particular subject at the time of subject's randomization and at the prospective

protocol visits. The clinic will administer the study treatment as described in [Table 3-1](#), according to the subject’s weight obtained at screening visit.

The randomization code will not be available to the Bioanalytical Division until the clinical and analytical phases of the study have been completed.

Table 3-1 Study Treatment Administration According to Weight Category

Product	Meal Condition	Weight Category	Weight (kg)	Dose
Test (Treatment A): Diazepam Buccal Film (Aquestive Therapeutics, USA)	Moderate-Fat Meal	A1	38-50	1 x 10 mg
		A2	51-62	1 x 12.5 mg
		A3	63-75	1 x 15 mg
		A4	76-87	1 x 15 mg
		A5	88-111*	1 x 17.5 mg
Reference (Treatment B): Diasat [®] AcuDial [™] rectal gel (Valeant Pharmaceuticals, USA)	Moderate-Fat Meal	B1	38-50	2 mL (10 mg)
		B2	51-62	2.5 mL (12.5 mg)
		B3	63-75	3 mL (15 mg)
		B4	76-87	3.5 mL (17.5 mg)
		B5	88-111*	4 mL (20 mg)
Test (Treatment C): Diazepam Buccal Film (Aquestive Therapeutics, USA)	High-Fat Meal	A1	38-50	1 x 10 mg
		A2	51-62	1 x 12.5 mg
		A3	63-75	1 x 15 mg
		A4	76-87	1 x 15 mg
		A5	88-111*	1 x 17.5 mg

*Subjects eligible for study with weights in the range of 112 to 134 kg will be dosed at the 88-111 kg weight range as shown above.

3.4 Sample Size

Subjects will be enrolled to attain a sample size of no more than 32 subjects (and a minimum of 16 completed subjects in Period 2). Because this is not a formal hypothesis testing study, the sample size is proposed based on the desired level of precision for estimating pharmacokinetic parameters and the relationship between pharmacokinetic parameters. In principle, the expected precision of the estimates of the ratios of geometric means of interest can be estimated from the intra-subject variability observed in Aquestive Study 162021 (pharmacokinetic crossover of DBF 15 mg with DRG 5, 12.5, and 20 mg in healthy volunteers). Aquestive has not undertaken a formal analysis to predict the expected precision.

3.5 Subject Withdrawal and Replacement

Subjects will be advised that they are free to withdraw from the study at any time. Over the course of the study, the Sponsor and the Investigator or a delegate may withdraw any subject from the study for one of the reasons described below:

- safety reason;
- non-compliance with protocol requirements;
- significant protocol deviation;
- positive alcohol breath test;
- positive drug screen (except for subjects using prescribed marijuana and THC containing products as AED treatment);
- positive pregnancy test.

Positive result to the urine benzodiazepine screen (urine drug screen) in Period 2 and Period 3 may derive from residual concentrations from study drug administered in the previous period(s). Therefore, it is not required that subjects with a positive result to that test in Period 2 and Period 3 be withdrawn from the study. Continued subject participation in the study will be evaluated by the Principal Investigator.

Subjects experiencing emesis within 4 hours following DBF administration will be evaluated on a case-by-case basis by the Principal Investigator/Sub-Investigator, the CRO PK Scientist, and the Sponsor, and a decision on their continued participation will be made. Subjects experiencing a bowel movement within 4 hours following DRG administration or clinically significant leakage of the rectal gel within 4 hours post-dose will be evaluated on a case-by-case basis by the Principal Investigator/Sub-Investigator, the CRO PK Scientist, and the Sponsor, and a decision on their continued participation will be made. All decisions will be made prior to the bioanalytical laboratory commencing bioanalysis.

Subjects who withdraw or are withdrawn from the study after dosing will not be replaced. However, in the event that the number of drop-outs exceeds initial expectations, subjects who withdraw or are withdrawn might be replaced at the discretion of the Sponsor. Such replacement resulting in dosing of more subjects than planned in this protocol would be documented in a protocol amendment.

Subjects who withdraw or are withdrawn will be asked to remain at the clinic until the Investigator or a delegate agrees that the subject is fine and can be discharged. As soon as subject withdrawal is confirmed, blood sampling will be stopped. Study exit procedures will be performed at the time of withdrawal from the study or as soon as possible thereafter.

4. Change From the Protocol

No changes in planned analyses were done compared to the protocol. However, for B vs C comparison, the period will not be included in the ANOVA since Treatment C is confounded with Period 3.

5. Primary and Secondary Parameters

For PK analyses (A vs B comparison), AUC_{0-t} , AUC_{0-inf} , and C_{max} calculated using diazepam plasma concentrations will be regarded as the primary endpoints. All other PK parameters (including those calculated using nordiazepam) will be regarded as secondary endpoints (refer to Section 10.3).

The safety and tolerability parameters will be regarded as secondary endpoints (refer to Section 9).

6. Analysis Populations

The analysis of safety and tolerability parameters will be based on the safety population detailed in Section 6.1 below. The analysis of PK parameters will be based on the PK population detailed in Section 6.2 below. Treatment assignment will be according to the actual treatment received.

6.1 Safety Population

The safety population is defined as all subjects who received at least one dose of the study medication.

6.2 Pharmacokinetic Population and Pharmacokinetic Analysis Data Set

The pharmacokinetic population will include all subjects completing at least Period 1 and Period 2 with no significant violation of study restrictions, and for whom the pharmacokinetic profile can be adequately characterized. Any subject who completes only one period will be presented in the concentrations and pharmacokinetic tables but excluded from descriptive statistics and ANOVA.

A violation of the requirement to maintain a stable regimen of AEDs or a stable regimen of other concomitant drugs with the potential to influence diazepam pharmacokinetics will be considered a significant violation of study restrictions. A change of drug in the prescribed AED regimen and/or change in the dose of a prescribed AED will be considered a departure from a stable regimen. Any subject who does not maintain a stable AED regimen in the course of the study will be presented in the concentrations and pharmacokinetic tables but excluded from descriptive statistics and ANOVA. For cases in which a departure from a stable AED regimen is a matter of judgment, the decision will be made by the Principal Investigator/Sub-Investigator and/or by the CRO PK Scientist in consultation with the Sponsor prior to bioanalysis.

Any subject with diazepam or nordiazepam pre-dose concentrations will be presented in the concentrations and pharmacokinetic tables but excluded from descriptive statistics and ANOVA if the pre-dose concentration is greater than 5% of the C_{max} value for that analyte of that period for that subject.

Subjects withdrawn due to vomiting episodes as per criterion established under section 3.5 or due to adverse events will be presented but excluded from the statistical analyses (i.e., descriptive statistics and ANOVA).

Data from subjects who experienced emesis during the sampling interval and who were not withdrawn as per criterion established under section 3.5 may be evaluated after completion of the pharmacokinetic analysis. Any subject who experienced emesis within 2 times median T_{max} of the current study (based on the reference product) will be excluded from the statistical analysis (i.e., descriptive statistics and ANOVA).

7. Interim Analyses

No interim analysis will be performed.

8. Study Population and Exposure

No inferential analysis will be done. Only observed data will be used.

8.1 Subject Disposition

Subject disposition will be summarized for the number of subjects who were screened, enrolled, randomized and dosed, completed the study, and who were withdrawn from the study and the reason. The data will be presented by treatment and overall (frequency and the percentage of subjects) and listed.

8.2 Protocol Deviations

The protocol deviations will be categorized and listed by subject.

8.3 Demographics and Baseline Characteristics

The descriptive statistics (mean, median, standard deviation [SD], minimum [Min], maximum [Max], and sample size) will be calculated for continuous variables (age, body mass index [BMI], height, and weight) considering last results (scheduled or unscheduled) obtained at screening. Frequency counts and percentages will be tabulated for categorical variables (age group, gender, ethnicity, and race). Results will be presented overall and by treatment group for each study population (only if populations are different). All demographic characteristics will be listed by subject.

8.4 Medical History

Medical history at screening will be listed by subject. The Medical Dictionary for Regulatory Activities (MedDRA[®]) Version 21.1 will be used to classify all medical history findings by System Organ Class (SOC) and Preferred Term (PT).

8.5 Prior and Concomitant Medications

The use of prior and/or concomitant medications will be monitored throughout the study and listed by subject. The World Health Organization Drug Dictionary (WHO DD) Version Sep2018, format B3 will be used to classify all medication reported during the study.

8.6 Study Drug Administration

The study drug administration details (including treatment received, start and end date and time of administration) will be listed by subject. The time of dosing will be set as the time the film is placed against the buccal mucosa.

9. Safety Analyses

Safety and tolerability data will be evaluated through the assessment of AEs, clinical laboratory parameters (biochemistry, hematology, and urinalysis), 12-lead electrocardiogram (ECG), vital sign (blood pressure, heart rate, respiratory rate, pulse oximetry, and oral temperature), continuous cardiac ECG monitoring, physical examination, and visual oral inspection.

Laboratory parameters, vital signs, and ECG parameters will be listed and summarized using descriptive statistics. All AEs will be listed and summarized using descriptive methodology. The incidence of AEs for each treatment will be presented by severity and association with the study drug.

Safety data will be summarized but will not be subjected to inferential analysis. The analysis of the safety variables will be based on safety population.

9.1 Physical Examination Findings

A physical examination will be performed at screening and study exit. The physical examination includes at least the following components: HEENT (head, eyes, ears, nose, and throat), neck, chest and lungs, cardiovascular, abdomen, skin, and musculoskeletal evaluation.

A brief neurologic examination will be performed at screening and study exit. The neurologic assessment involves at least the following evaluation: mental status, cranial nerves, motor system, sensory system, cerebellar disorder, gait, and reflexes.

Any abnormal findings judged to be clinically significant will be documented as medical history or as an AE, depending upon whether noted at screening, prior to dosing or after dosing, as appropriate. Any physical examination findings documented as AEs will be included in the AE summaries.

9.2 Adverse Events

Treatment-emergent AEs (TEAEs) and non-TEAEs (those occurring prior to administration of study medication or that first occurred prior to study drug administration and did not worsen in frequency or severity) will be listed. TEAEs will be defined as AEs that occur on or after the date and time of study drug administration, or those that first occur pre-dose but worsen in frequency or severity after study drug administration. AEs will be collected and documented from the signing of the ICF until at least 10 days following the last study drug administration, and as observed or reported spontaneously by study participants. TEAEs will be attributed to the most recent study drug taken. A TEAE with a start date and time during the wash-out period (ending at the time of study drug administration) will be attributed to the study drug taken during the previous treatment period. Any AEs, whether serious or non-serious, will be monitored throughout the study and followed to resolution or for up to 2 weeks after the last PK blood draw, after which the Investigator will decide the course of action.

The incidence of TEAEs will be summarized using the safety population. The MedDRA[®] dictionary Version 21.1 will be used to classify all AEs reported during the study by SOC and PT.

Incidence of subjects who experienced TEAEs (as well as number of events) will be presented by treatment and overall, by SOC, and PT, investigator-assessed relationship and also by severity. Each subject may only contribute once to each of the incidence rates, for a TEAE following a given treatment, regardless of the number of occurrences; the highest severity or highest relationship will be presented, as appropriate. In each table, SOC will be presented in descending order of overall incidence rate in terms of frequency of subjects and then in frequency of events (alphabetical order will be used in case of equal rates). For each SOC, PT will be presented the same way.

The relationship of an AE to the study drug will be assessed according to the study protocol as:

- Probable:** A clinical event, including laboratory test abnormality, with a reasonable time sequence to drug administration, unlikely to be attributed to concurrent disease or other drugs or chemicals, and which follows a clinically reasonable response on withdrawal.
- Possible:** A clinical event, including laboratory test abnormality, with a reasonable time sequence to drug administration, but which could also be explained by concurrent disease or other drugs or chemicals. Information on drug withdrawal may be lacking or unclear.
- Unlikely:** A clinical event, including laboratory test abnormality, with a temporal relationship to drug administration which makes a causal relationship improbable, and which other drugs, chemicals or underlying disease provide plausible explanation.
- Unrelated:** This category is applicable to AEs which are judged to be clearly and incontrovertibly due to extraneous causes (diseases, environment, etc.) and do not meet the criteria for drug relationship listed for the above-mentioned conditions.

The Severity of AEs will be rated as according to the study protocol as:

- Mild:** AE resulting in discomfort, but not sufficient to cause interference in normal daily activities.
- Moderate:** AE resulting in discomfort that is sufficient to cause interference in daily activities.
- Severe:** AE resulting in discomfort causing an inability to carry out normal daily activities.

A significant AE will be defined as any event (other than those reported as serious) that led to an intervention, including withdrawal of treatment, or significant additional concomitant therapy. Serious and significant AEs will be listed separately.

9.3 Laboratory Parameters

Clinical laboratory (biochemistry, hematology, and urinalysis) results will be obtained at screening, and at study exit or early termination.

Biochemistry parameters include the following: albumin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, calcium, chloride, glucose, phosphorus, potassium, creatinine, sodium, total bilirubin, CK, lactate dehydrogenase, uric acid, total protein, magnesium, bicarbonates, and ammonia.

Hematology parameters include the following: complete blood count with differential, hemoglobin, hematocrit and platelet count.

Urinalysis parameters include the following: macroscopic examination, pH, specific gravity, protein, glucose, ketones, bilirubin, occult blood, nitrite, and leukocytes. Unless otherwise specified, microscopic examination will be performed on abnormal findings and results will be listed.

Hepatitis B (HBs Ag), Hepatitis C (HCV) antibody, and HIV antigen and antibody detection will be performed at screening.

A urine drug screen (amphetamines, methamphetamines, barbiturates, benzodiazepines, tetrahydrocannabinol, cocaine, opiates, Phencyclidine (PCP), 3, 4-methylenedioxy-N-methylamphetamine (MDMA), methadone), and an alcohol breath test will be performed at screening and before dosing of each period.

A urine pregnancy test will be performed at screening and at study exit, and a serum pregnancy test will be performed at check-in of each period.

Listings of all clinical laboratory (biochemistry, hematology, and urinalysis) results will be provided with the abnormal values flagged with "L" (low) and "H" (high) for continuous parameters, and "A" (abnormal) for categorical parameters.

Descriptive statistics (mean, median, SD, Min, Max, and sample size) for each clinical laboratory test (continuous variables) will be presented overall for screening and study exit visit.

Descriptive statistics for change from screening will also be presented for study exit. Screening includes the last screening results (scheduled or unscheduled). For categorical variable (urinalysis test), the number of subjects (frequency and percentage) will be tabulated by results (e.g. negative, positive, trace...). A summary table of shifts from screening to study exit visit will be provided. Results from repeat or unscheduled tests will not be included in the summary statistics unless the repeat was required (and documented as such) due to technical reasons or an

invalid initial result, or for screening determination, if applicable. Early termination results (if any) will be included with the study exit visit for the summary statistics.

If more than one clinical laboratory is used for the study, a formula that takes into consideration the relative normal ranges of each test of laboratories used will be applied in order to normalize these data. The conversion formula used will depend on the typical distribution of the normal range for each laboratory test; the two formulae used are presented below:

Hemoglobin, hematocrit, and platelet count test results are considered to have a normal distribution ([Chuang-Stein, 1992](#)) and the following formula will be used ([Karvanen J., 2003](#)):

$$s = L_s + (x - L_x) \frac{U_s - L_s}{U_x - L_x}$$

Where U= Upper limit; L= Lower limit; s= Primary facility result; and x= Secondary facility results.

The remaining hematology, serum chemistry, and urinalysis test results are considered to have a non-normal distribution ([Chuang-Stein, 1992](#)) and the following formula will be used ([Karvanen J., 2003](#)):

$$s = \frac{x U_s}{U_x}$$

Prior to applying these formulae, if required, units will be adjusted.

9.4 Vital Signs

Vital signs measurements (blood pressure (BP), heart rate (HR), respiratory rate (RR)) and digital oxygen monitoring will be measured in a sitting position (except for safety reasons) at screening, and at study exit or early termination. Oral temperature will be measured at screening, and at study exit or early termination.

Vital signs and digital oxygen monitoring will be measured before dosing and approximately 0.5, 1, 1.5, 2, 4, and 8 hours post-dose (and beyond if clinically indicated). Vital signs will also be measured approximately 12 and 24 hours post-dose.

Descriptive statistics (mean, median, SD, Min, Max, and sample size) will be presented overall for screening and study exit, and by associated current treatment for on-study measurements for each parameter where applicable. Descriptive statistics for change from screening to study exit, and for change from baseline for on-study measurements will also be presented. Screening includes the last screening results (scheduled or unscheduled). Baseline will be defined as the last results (scheduled or unscheduled) obtained prior to drug administration in each period. Results from repeat or unscheduled tests will not be included in the summary statistics unless the repeat was required (and documented as such) due to technical reasons or an invalid initial result,

or for screening or baseline determination, if applicable. Early termination results (if any) will be included with the study exit visit for the summary statistics.

A listing of all vital signs results will be provided.

9.5 Electrocardiogram

Supine ECG will be performed at screening and study exit. Continuous ECG monitoring will be performed from approximately 1 hour prior to dosing until 8 hours post-dose (and extended if clinically indicated).

For supine ECG, descriptive statistics (mean, median, SD, Min, Max, and sample size), for each ECG parameter (heart rate, PR interval, QRS interval, QT interval, and QTcF interval) will be presented overall for screening and study exit visit. Descriptive statistics for change from screening will also be presented for study exit. Screening includes the last screening results (scheduled or unscheduled). Results from repeat or unscheduled tests will not be included in the summary statistics unless the repeat was required (and documented as such) due to technical reasons or an invalid initial result, or for screening determination, if applicable. Early termination results (if any) will be included with the study exit visit for the summary statistics.

A listing of all supine ECG results will be provided.

9.6 DBF Application Site Inspection

The Investigator or designee will make a visual inspection of the oral mucosa at screening. The application site will also be inspected prior to DBF administration and approximately 6 and 24 hours after administration. Assessments of the oral mucosa (normal/abnormal) will be conducted by the Principal Investigator/Sub-Investigator or a trained nurse. A listing will be provided.

Abnormalities observed before dosing will be recorded and evaluated regarding exclusion criteria but will not be considered AEs. Any post-dose abnormalities will be reported as AEs and followed until resolution.

10. Pharmacokinetic Analyses

10.1 Handling of the Below the Lower Limit of Quantitation (BLQ) and the No Reportable Concentration Values

All concentration values BLQ will be set to zero, except when they occur between two non-BLQ concentrations where they will be considered as missing for pharmacokinetic calculations. Samples with no reportable value occurring prior to dosing for a given period will be replaced by “0.00”, otherwise they will be set to missing for tabulation, graphical representation and calculation purposes. All samples with no reportable value observed after dosing will be set to missing.

10.2 Handling of the Difference Between the Scheduled and the Actual Sampling Times

The actual clock time for dosing and the actual clock time for each collection time for the PK samples will be recorded using the electronic data capture. For all sampling times, the actual sampling times will be calculated as the difference between the sample collection actual clock time and the actual clock time of dosing. The actual post-dose sampling times expressed in hours and rounded off to three decimal digits will be used to calculate the PK parameters, except for pre-dose samples occurring prior to dosing, which will always be reported as zero (0.000), regardless of the time difference. In the PK section of the report, scheduled sampling times will be presented in concentration tables and mean graphs while actual times are presented for the individual graphs. A listing of the actual times for PKs will be provided for PK samples.

10.3 Pharmacokinetic Parameters

In each period, a total of 19 blood samples will be drawn from each subject for pharmacokinetic analyses. Blood samples will be collected prior to study drug administration (0.00 hour) and 0.500, 0.750, 1.00, 1.50, 2.00, 3.00, 4.00, 6.00, 9.00, 12.0, 24.0, 48.0, 72.0, 96.0, 120, 144, 192, and 240 hours post-dose (3 mL for each sampling time). The time tolerance window for blood samples collected during the confinement period will be ± 1 minute for all samples collected before 8 hours post-dose and ± 3 minutes for subsequent samples. The time tolerance window for return visit samples will be ± 60 minutes. Blood samples will be collected as close as possible to nominal times; exact sample collection times will be recorded on the appropriate source documents and reported for each subject. The actual time of blood sample collection will be used for PK and statistical analysis.

Plasma concentrations from diazepam and nordiazepam will be used to calculate the following PK parameters by standard non-compartmental methods:

AUC_{0-t}	Area under the concentration-time curve from time zero to the last non-zero concentration and it is calculated using the linear trapezoidal method.
AUC_{0-inf}	Area under the concentration-time curve from time zero to infinity (extrapolated), calculated as $AUC_{0-t} + C_{last} / K_{el}$, where C_{last} is the last observed non-zero concentration.

C_{max}	Maximal observed plasma concentration.
Residual Area	Residual area, calculated as $100 \cdot (1 - AUC_{0-t} / AUC_{0-inf})$.
T_{max}	Time when the maximal plasma concentration is observed.
K_{el}	Elimination rate constant. This parameter will be the negative of the estimated slope of the linear regression of the ln-transformed concentration versus time profile in the elimination phase. Four non-zero observations during the elimination phase (excluding the C_{max}) will be used to calculate K_{el} , or a minimum of 3 concentration points will be used if fewer than four observations are available. The time point where ln-linear K_{el} calculation begins ($K_{el\ Lower}$), and the actual sampling time of the last quantifiable concentration used to estimate the K_{el} ($K_{el\ Upper}$) will be reported with the correlation coefficient from the linear regression to calculate K_{el} (Correlation).
$T_{1/2\ el}$	Elimination half-life, calculated as $\ln(2) / K_{el}$.
Cl/F	Apparent total clearance, calculated as $Dose / AUC_{0-inf}$.
Cl/F/kg	Apparent total clearance normalized for the subject body weight in kg, calculated as $(Cl/F) / weight$.
V_d/F	Apparent volume of distribution, calculated as $Dose / (K_{el} \times AUC_{0-inf})$
$V_d/F/kg$	Apparent volume of distribution normalized for the subject body weight in kg, calculated as $(V_d/F) / weight$.

For subjects with missing or non-reportable concentrations for three or more of the last samples (e.g. timepoints past T_{max}), the data will be reviewed on a case-by-case basis by inVentiv pharmacokinetic scientist and/or sponsor to determine if the data are reliable for C_{max} and T_{max} . If so, only the C_{max} and T_{max} will be presented and included in the statistical analysis. Other PK parameters will not be reported. Explanations for PK parameters that could not be estimated will be provided in the CSR.

Additional PK analysis may be performed.

10.4 Statistical Analyses

Individual and mean plasma concentration versus time curves will be presented for both linear and semi-log scales for diazepam and nordiazepam. Descriptive statistics (arithmetic and geometric means, SD, coefficient of variation [CV (%)], Min, Max, and median) of the plasma concentrations versus time will be presented as well for the PK parameters for diazepam and nordiazepam.

10.4.1 Treatment Comparison DBF (Test) versus DRG (Reference) Following a Moderate-Fat Meal

The statistical analyses below will include only data from subjects completing both Treatments A and B.

For diazepam and nordiazepam, using GLM procedures in SAS, ANOVA will be performed on untransformed T_{max} , K_{el} , and $T_{1/2\ el}$ and on ln-transformed AUC_{0-t} , AUC_{0-inf} , C_{max} , Cl/F , $Cl/F/kg$, V_d/F , and $V_d/F/kg$ at the alpha level of 0.05. Factors incorporated in the model will include: Sequence, Subject(Sequence), Period, and Treatment. T_{max} will be analyzed using an additional non-parametric test (Wilcoxon signed-rank test).

The ratio of geometric means will be calculated for AUC_{0-t} , AUC_{0-inf} , and C_{max} for the Test product versus the Reference product (Treatment A/Treatment B) irrespective of weight category. The 90% confidence interval for the ratio of geometric means, based on least-squares means from the ANOVA of the ln-transformed data will also be calculated. Intra and inter-subject coefficient of variation will be estimated.

10.4.2 Treatment Comparison DBF (Test) versus DRG (Reference) Following Different Meal Conditions

An exploratory pair-wise analysis comparing DBF following a high-fat meal (Treatment C) with DRG following a moderate-fat meal (Treatment B) will be conducted and reported. The statistical analyses below will include only data from subjects completing both Treatments B and C.

For diazepam and nordiazepam, using GLM procedures in SAS, ANOVA will be performed on untransformed T_{max} , K_{el} , and $T_{1/2\ el}$ and on ln-transformed AUC_{0-t} , AUC_{0-inf} , C_{max} , Cl/F , $Cl/F/kg$, V_d/F , and $V_d/F/kg$ at the alpha level of 0.05. Factors incorporated in the model will include: Sequence, Subject(Sequence), and Treatment. T_{max} will be analyzed using an additional non-parametric test (Wilcoxon signed-rank test).

The ratio of geometric means will be calculated for AUC_{0-t} , AUC_{0-inf} , and C_{max} for Treatment C versus Treatment B, irrespective of weight category. The 90% confidence interval for the ratio of geometric means, based on least-squares means from the ANOVA of the ln-transformed data will also be calculated. Intra and inter-subject coefficient of variation will be estimated.

Additional analyses may be performed.

11. Percentages and Decimal Places

If not otherwise specified, the following rules will be applied, with the exception of PK tables and listings described below:

- Percentages will be presented to one decimal point.
- Percentages equal to 0 or 100 will be presented as such without a decimal point.
- Minimum and maximum will be presented with the same precision as the original values and, mean, standard deviation, and median will be presented with one more decimal place than the original values.

All digits will be used for pharmacokinetic and statistical PK calculations. For PK tables and listings, the final reportable results or data will be presented by rounding off to two decimal digits, except for the following situations (this applies to individual data and descriptive statistics):

- K_{el} data: rounded off to four decimal digits.
- Pharmacokinetic parameters related to time such as T_{max} must be reported with the same precision as the actual sampling time: rounded off to 3 decimal digits.
- Concentration versus time data, as well as C_{max} : reported as they appear in corresponding dataset.
- Ratios and 90% confidence intervals, CV (%), Inter-CV%, Intra-CV% will be presented to two decimal places.

12. Data Handling

The PK plasma concentrations, safety and tolerability data will be received as SAS[®] datasets from the inVentiv data management facility. Screening failures and ineligible volunteer's data (subject disposition) will be received from the clinical site as source data.

13. Handling of Missing Data

For PK, only observed data will be used in the data analysis except for concentration values BLQ and samples with no reportable value occurring prior to dosing as described in Section 10.1. No attempt will be made to extrapolate or interpolate estimates for missing data.

For safety,

- If an AE is recorded with an onset date corresponding to a dosing day, but the time is missing, then the AE will be assigned to the treatment.
- If an AE is recorded with an onset date that does not correspond to the dosing day, but the time is missing, then the AE will be assigned to the treatment if AE onset date is after dosing date.
- If an AE is recorded with an onset date where day and time are both missing, then the AE allocation to the treatment will be done on a case by case basis considering available information (e.g., AE onset date, AE end date, AE comments, subject disposition).

14. Software to be Used

PK analysis will be performed using Phoenix WinNonlin[®] version 8.0 or higher, which is validated for bioequivalence/bioavailability studies by inVentiv. Inferential statistical analyses will be performed using SAS[®] according to FDA guidelines. The safety data tables and listings, as well as PK tables and listings will be created using SAS[®], release 9.2 or a higher version. PK figures will be created using R version 3.5. The report text will be created using Microsoft[®] Office Word 2010, or a higher version.

15. Reference List

- Chuang-Stein C. Summarizing laboratory data with different reference ranges in multi-center clinical trials. *Drug Information Journal*. 1992; 26:77-84.
- Karvanen J. The statistical basis of laboratory data normalization. *Drug Information Journal*. 2003; 37:101-107.

Table/Figure/Listing Shells



Table/Figure/Listing Shells

A RANDOMIZED, OPEN-LABEL, 2-SEQUENCE, 3-TREATMENT, CROSSOVER STUDY TO EVALUATE THE PHARMACOKINETICS OF SINGLE DOSES OF DIAZEPAM BUCCAL FILM (DBF) (AQUESTIVE THERAPEUTICS) COMPARED WITH DIASTAT[®] RECTAL GEL (VALEANT PHARMACEUTICALS NORTH AMERICA) IN ADULT MALE AND FEMALE SUBJECTS ON A CONCOMITANT REGIMEN OF ANTIEPILEPTIC DRUGS (AED) FOR THE TREATMENT OF EPILEPSY

Sponsor Protocol No. 180323

inVentiv Health Clinical Inc. Project No. 180323

Final Version: 1.0

Date: 28-JUN-2019

Contract Research Organization:
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a Syneos Health company
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Sponsor:
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30 Technology Drive
Warren, NJ 07059
USA

CONFIDENTIAL


SIGNATURES

Sponsor Protocol No. 180323

inVentiv Project No.: 180323

Study Title: A Randomized, Open-Label, 2-Sequence, 3-Treatment, Crossover Study to Evaluate the Pharmacokinetics of Single Doses of Diazepam Buccal Film (DBF) (Aquestive Therapeutics) Compared With Diastat® Rectal Gel (Valeant Pharmaceuticals North America) in Adult Male and Female Subjects on a Concomitant Regimen of Antiepileptic Drugs (AED) for the Treatment of Epilepsy

Author: **Siva Durga Prasad Sattu, M.Sc.**
Statistician
inVentiv

Signature: 
Date: 01 Jul 2019

Sponsor's
Representative: **Allen H Heller, MD, MPH**
Founder and CEO, Pharma Study
Design LLC (Consultant to Aquestive
Therapeutics)

Signature: 
Date: 28 June 2019



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1. Tables, Figures and Data Listings Formatting

The table, figure, and data listing (TFL) shells are presented in order to provide a framework for displaying the study data. The shells may change due to unforeseen circumstances. The shells may not be truly representative of every aspect of the study (e.g., sampling time points, assessed laboratory parameters, calculated parameters, units), but are intended to illustrate the general layout of the tables, figures, and data listings that will be included in the final report.

The default tables, listings, and figures layout will be as presented in [Table 1-1](#):

Table 1-1 Layout Specifications

Orientation	Portrait	Landscape
Paper Size	Letter	Letter
Margins	Top: 3.05 cm Bottom: 2.54 cm Left: 2.54 cm Right: 2.54 cm	Top: 3.05 cm Bottom: 2.2 cm Left: 1.9 cm Right: 1.9 cm
Font	Table text: Times new Roman 9 or 10 pts Table title: Times new Roman 12 pts Table legend: Times new Roman 10 pts	

The font size may be reduced as necessary to allow additional columns to be presented, but not at the expense of clarity. Also the orientation may be changed to portrait if appropriate.

Except for pharmacokinetic (PK) tables, descriptive statistics for minimum and maximum will be presented with the same decimal digits as the original values, and with one more decimal place than the original data for mean, standard Deviation, and median. For PK tables, the data presentation will be as per the appropriate inVentiv SOP.

2. Summary TFLs

Table 2-1 List of Table Shells

Table Number	Title
	In-Text Table
10.1-1	Subject Disposition
11.4.2.3-1	Summary of Pharmacokinetic Parameters of Diazepam– PK Population
11.4.2.3-2	Ratios (A/B), 90% Geometric Confidence Intervals, Intra-Subjects CV (%), Inter-Subjects CV (%) and P-values for Plasma Pharmacokinetic Parameters of Diazepam – PK Population
11.4.2.3-3	Ratios (C/B), 90% Geometric Confidence Intervals, Intra-Subjects CV (%), Inter-Subjects CV (%) and P-values for Plasma Pharmacokinetic Parameters of Diazepam – PK Population
11.4.2.3-4	Summary of Pharmacokinetic Parameters Nordiazepam – PK Population
11.4.2.3-5	Ratios (A/B), 90% Geometric Confidence Intervals, Intra-Subjects CV (%), Inter-Subjects CV (%) and P-values for Plasma Pharmacokinetic Parameters of Nordiazepam – PK Population
11.4.2.3-6	Ratios (C/B), 90% Geometric Confidence Intervals, Intra-Subjects CV (%), Inter-Subjects CV (%) and P-values for Plasma Pharmacokinetic Parameters of Nordiazepam – PK Population
	Demographic Data Summary Tables
14.1-1	Summary of Demographic Characteristics of Subjects Included in the Safety Population
14.1-2	Summary of Demographic Characteristics of Subjects Included in the Pharmacokinetic Population
	Pharmacokinetic Tables
14.2.1-1	Descriptive Statistics for Plasma Concentration over Nominal Time by Treatment– PK Population
14.2.1-2	Descriptive Statistics of Plasma Pharmacokinetic Parameters by Treatment - PK Population
14.2.1-3	Descriptive Statistics of Individual Ratios or Individual Differences between Treatments for Pharmacokinetic Parameters - PK Population
14.2.1-4	Ratios (A/B), 90% Geometric Confidence Intervals, Intra-Subjects CV (%) and P-values for Diazepam – PK Population
14.2.1-5	Ratios (C/B), 90% Geometric Confidence Intervals, Intra-Subjects CV (%) and P-values for Diazepam – PK Population
14.2.1-6	Ratios (A/B), 90% Geometric Confidence Intervals, Intra-Subjects CV (%) and P-values for Nordiazepam – PK Population
14.2.1-7	Ratios (C/B), 90% Geometric Confidence Intervals, Intra-Subjects CV (%) and P-values for Nordiazepam – PK Population
	Safety Data Summary Tables
14.3.1-1	Frequency of Subjects Experiencing Treatment-Emergent Adverse Events and Number of Events Summarized per Treatment – Safety Population
14.3.1-2	Frequency of Subjects Experiencing Treatment-Emergent Adverse Events Summarized per Treatment and Severity – Safety Population
14.3.1-3	Number of Treatment-Emergent Adverse Events Summarized per Treatment and Severity – Safety Population



14.3.1-4	Frequency of Subjects Experiencing Treatment-Emergent Adverse Events Summarized per Treatment and Relationship – Safety Population
14.3.1-5	Number of Treatment-Emergent Adverse Events Summarized per Treatment and Relationship – Safety Population
14.3.4-1	Biochemistry Summary Descriptive Statistics and Change from Screening to Study Exit – Safety Population
14.3.4-2	Frequency of Subjects – Biochemistry Shifts from Screening to Study Exit – Safety Population
14.3.4-3	Hematology Summary Descriptive Statistics and Change from Screening to Study Exit – Safety Population
14.3.4-4	Frequency of Subjects - Hematology Shifts from Screening to Study Exit – Safety Population
14.3.4-5	Urinalysis Summary Descriptive Statistics and Change from Screening to Study Exit – Safety Population
14.3.4-6	Frequency of Subjects - Urinalysis Shifts from Screening to Study Exit, pH and Specific Gravity – Safety Population
14.3.4-7	Urinalysis Frequency Summary: Categorical Results – Safety Population
14.3.4-8	Frequency of Subjects - Urinalysis Shifts from Screening to Study Exit : Categorical Results – Safety Population
14.3.4-9	Vital Signs Summary Descriptive Statistics – Safety Population
14.3.4-10	Electrocardiogram Summary Descriptive Statistics – Safety Population

Table 2-2 List of Figures Shells

Figure Number*	Title
14.2.2-1a to 14.2.2-32a**	Plasma Concentrations of Diazepam for Subject XX - Linear Scale
14.2.2-1b to 14.2.2-32b**	Plasma Concentrations of Diazepam for Subject XX - Semi-Log Scale
14.2.2-33a	Mean (\pm SD) Plasma Concentrations of Diazepam - Linear Scale
14.2.2-33b	Mean (\pm SD) Plasma Concentrations of Diazepam - Semi-Log Scale
14.2.2-34a	Overlay of Individual and Mean Plasma Concentrations of Diazepam by Treatment - Linear Scale
14.2.2-34b	Overlay of Individual and Mean Plasma Concentrations of Diazepam by Treatment - Semi-Log Scale
14.2.2-35a to 14.2.2-66a**	Plasma Concentrations of Nordiazepam for Subject XX - Linear Scale
14.2.2-35b to 14.2.2-66b**	Plasma Concentrations of Nordiazepam for Subject XX - Semi-Log Scale
14.2.2-67a	Mean (\pm SD) Plasma Concentrations of Nordiazepam - Linear Scale
14.2.2-67b	Mean (\pm SD) Plasma Concentrations of Nordiazepam - Semi-Log Scale
14.2.2-68a	Overlay of Individual and Mean Plasma Concentrations of Nordiazepam by Treatment - Linear Scale
14.2.2-68b	Overlay of Individual and Mean Plasma Concentrations of Nordiazepam by Treatment - Semi-Log Scale

* Depending on the number of subjects included in the PK population, the figure numbering presented here may change in the report.

** Similar figures will be presented for each subject who received study medication

Table 2-3 List of Data Listings Shells

Listing Number	Title
	Documentation of Statistical Methods
16.1.9-1	ANOVA for Treatment Comparison of Diazepam – PK Population
16.1.9-2	ANOVA for Treatment Comparison of Nordiazepam – PK Population
16.1.9-3	Wilcoxon Signed-Rank Test for T_{max} for Treatment Comparison of Diazepam – PK Population
16.1.9-4	Wilcoxon Signed-Rank Test for T_{max} for Treatment Comparison of Nordiazepam – PK Population
	Subject Characteristics Listings
16.2.1-1	Subjects Completion and Discontinuation Information
16.2.2-1	Protocol Deviations
16.2.4-1	Demographics
16.2.4-2	Medical History Findings at Screening
16.2.4-3	Prior and Concomitant Medications
16.2.4-4	Study Drug Administration
16.2.4-5	Assignment to Analysis Populations
	PK Data Listings
16.2.6-1	Listing of Individual Actual Sampling Times and Pharmacokinetic Concentrations
16.2.6-2	Listing of Individual Pharmacokinetic Parameters
16.2.6-3	Listing of Individual Ratios or Differences between Treatment for Pharmacokinetic Parameters
	Safety Data Listings
16.2.7-1	Non-Treatment-Emergent Adverse Events
16.2.7-2	Treatment-Emergent Adverse Events
16.2.7-3	Serious Adverse Events
16.2.7-4	Significant Adverse Events
16.2.8-1	Clinical Laboratory – Biochemistry
16.2.8-2	Clinical Laboratory – Hematology
16.2.8-3	Clinical Laboratory – Urinalysis
16.2.8-4	Vital Signs Result
16.2.8-5	Electrocardiogram Result
16.2.8-6	DBF Application Site Visual Inspection



3. CSR In-text Tables



Table 10.1-1 Subject Disposition

Category	Treatment A	Treatment B	Treatment C	Overall
Screened	-	-	-	XX
Screening Failures ^{1,2}	-	-	-	X (XX.X)
Not Enrolled ^{1,3}	-	-	-	X (XX.X)
Enrolled ^{1,4}	-	-	-	X (XX.X)
Dosed	XX	XX	XX	XX
Not Dosed	XX	XX	XX	XX
Completed ⁵	X (XX.X)	X (XX.X)	X (XX.X)	-
Completed All Treatment Periods ⁶	-	-	-	X (XX.X)
Number of Subjects Discontinued ^{7, 8}	XX	XX	XX	XX
Primary Reason for Discontinuation ^{7, 8, 9}				
Adverse Event	X (XX.X)	X (XX.X)	X (XX.X)	X (XX.X)
Lost to Follow-up	X (XX.X)	X (XX.X)	X (XX.X)	X (XX.X)
Non-Compliance with Protocol Requirements	X (XX.X)	X (XX.X)	X (XX.X)	X (XX.X)
Positive Alcohol Breath Test	X (XX.X)	X (XX.X)	X (XX.X)	X (XX.X)
Positive Drug Screen	X (XX.X)	X (XX.X)	X (XX.X)	X (XX.X)
Positive Pregnancy Test	X (XX.X)	X (XX.X)	X (XX.X)	X (XX.X)
Safety Reason	X (XX.X)	X (XX.X)	X (XX.X)	X (XX.X)
Significant Protocol Deviation	X (XX.X)	X (XX.X)	X (XX.X)	X (XX.X)
Study Terminated by Sponsor	X (XX.X)	X (XX.X)	X (XX.X)	X (XX.X)
Other	X (XX.X)	X (XX.X)	X (XX.X)	X (XX.X)
Informed Consent Withdrawn	X (XX.X)	X (XX.X)	X (XX.X)	X (XX.X)
Investigator's decision	X (XX.X)	X (XX.X)	X (XX.X)	X (XX.X)

Programming Note:

if a subject was withdrawn from one period or more but he is included in next period(s) please add a footnote 10 to clarify, e.g.

“¹⁰ Subject No. XX completed Period 1 (Treatment A) but was discontinued before dosing in Period 2 (Treatment B) and was dosed in Periods 3 (Treatment C).”

¹ Percentage based on the number of screened subjects.



² Screening failures include volunteers who did not meet project criteria.

³ Not enrolled include volunteers who were judged eligible but decided not to participate on study or who were not selected to participate in the study since there was already a sufficient number of subjects.

⁴ Enrolled include volunteers who were judged eligible and accepted to participate in the trial after having signed the approved final version of the study informed consent form and also those identified as standby who may replace subjects who withdraw from the study before dosing.

⁵ Percentage based on the number of dosed subjects for a given treatment.

⁶ Percentage based on the overall number of subjects dosed (safety population).

⁷ Includes subjects who discontinued during the washout period or during the baseline assessment; these subjects are included under the last treatment received prior to discontinuation.

⁸ Overall, each subject could only contribute once to each reason for discontinuation, regardless of the number of occurrences.

⁹ Percentage based on the number of discontinued subjects per treatment group or overall, as appropriate.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content),

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Data source: [Listings 16.2.1-1](#) and [16.2.4-4](#).



Table 11.4.2.3-1 Summary of Plasma Pharmacokinetic Parameters of Diazepam – PK Population

Parameter(unit)	Treatment A				Treatment B				Treatment C			
	N	Mean	SD	CV%	N	Mean	SD	CV%	N	Mean	SD	CV%
AUC _{0-t} (h*ng/mL)												
AUC _{0-inf} (h*ng/mL)												
Residual area (%)												
C _{max} (ng/mL)												
T _{1/2 el} (h)												
K _{el} (/h)												
Cl/F												
V _d /F												
Cl/F/kg												
V _d /F/kg												
Parameter (unit)	Treatment A				Treatment B				Treatment C			
	N	Median	Min	Max	N	Median	Min	Max	N	Median	Min	Max
T _{max} (h)												

N: Number of observations; SD: Standard Deviation; CV = Coefficient of Variation; Min = Minimum, Max = Maximum; ‘.’ : Not calculated.

Residual area (%) = 100*(1- AUC_{0-t}/ AUC_{0-inf}).

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Note: Similar layout will be used for Tables 11.4.2.3-4. Please adapt title and footnotes accordingly.

Table 11.4.2.3-2 Ratios (A/B), 90% Geometric Confidence Intervals, Intra-Subjects CV (%), Inter-Subjects CV (%) and p-values for Plasma Pharmacokinetic Parameters of Diazepam – PK Population

Parameter (unit)	Geometric LSM		Ratio ¹ (%)	90% Geometric C.I. ²		Intra-Subject CV (%) ³	Inter-Subject CV (%) ⁴	p-values		
	Treatment A	Treatment B		Lower (%)	Upper (%)			Sequence	Period	Treatment
AUC _{0-t} (h*ng/mL)										
AUC _{0-inf} (h*ng/mL)										
C _{max} (ng/mL)										

¹ Calculated using least-squares means according to the formula: $\exp(\text{DIFFERENCE}) * 100$.

² 90% Geometric Confidence Interval calculated according to the formula: $\exp(\text{DIFFERENCE} \pm t_{(\text{dfResidual})} * SE_{\text{DIFFERENCE}})$

³ Calculated according to formula: $\text{SQRT}(\exp(\text{MSE}) - 1) * 100$

⁴ Calculated according to formula: $\text{SQRT}(\exp((\text{MS}_{\text{SUBJECT}(\text{SEQ})} - \text{MSE})/2) - 1) * 100$

LSM: Least Square Mean.

Probability (p) values are derived from Type III sums of squares. p-value for the Sequence effect is tested using the Subject(Sequence) effect as the error term.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content).

Note: Similar layout will be used for Tables 11.4.2.3-3, 11.4.2.3-5 and 11.4.2.3-6. Please adapt title and footnotes accordingly.



4. Summary Tables



Table 14.1-1 Summary of Demographic Characteristics of Subjects Included in the Safety Population

Category	Statistic	Treatment A	Treatment B	Treatment C	Overall
Age (years)	N	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.x	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx-xx	xx-xx	xx-xx	xx-xx
Age Groups					
<18	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
18-40	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
> 40	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Sex					
Female	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Male	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Ethnicity					
Hispanic or Latino	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Not Hispanic or Latino	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Not Reported	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Unknown	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Race					
Am Indian	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Asian	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Black	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Hawaiian	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Islander	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
White	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Other	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Height (cm)	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.x-xx.x	xx.x-xx.x	xx.x-xx.x	xx.x-xx.x
Weight (kg)	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx



	Median Min, Max	xx.xx xx.x-xx.x	xx.xx xx.x-xx.x	xx.xx xx.x-xx.x	xx.xx xx.x-xx.x
BMI (kg/m ²)	N	xx	xx	xx	xx
	Mean	xx.xxx	xx.xxx	xx.xxx	xx.xxx
	SD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
	Median	xx.xxx	xx.xxx	xx.xxx	xx.xxx
	Min, Max	xx.xx-xx.xx	xx.xx-xx.xx	xx.xx-xx.xx	xx.xx-xx.xx

Programming Note:

- 1) Refer to the note below for additional instructions

N: Number of subjects dosed; n (%): Number and percent of subjects; SD: Standard Deviation.

Am Indian: American Indian or Alaskan Native; Black: Black or African American; Hawaiian: Native Hawaiian or Pacific Islander;

BMI: body mass index.

Last results (scheduled or unscheduled) obtained at screening were used to generate this table.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Data source: [Listing 16.2.4-1](#)

Note: This table will be repeated for Table 14.1-2 only if PK Population is not the same as Safety Population. Otherwise, the title will be updated accordingly.



Table 14.2.1-1 Descriptive Statistics for Plasma Concentration over Nominal Time by Treatment– PK Population

Analyte	Treatment	Nominal Time	Time Unit	N	Mean	SD	CV%	Min	Median	Max	Geometric Mean	Concentration Unit	
Diazepam	A	0.000	h										
		0.500	h										
		0.750	h										
		1.00	h										
		1.50	h										
		2.00	h										
		3.00	h										
		4.00	h										
		6.00	h										
		9.00	h										
		12.0	h										
		24.0	h										
		48.0	h										
		72.0	h										
		96.0	h										
		120	h										
144	h												
192	h												
240	h												
...	...												

N: Number of observations; SD: Standard Deviation; CV: Coefficient of Variation; Min: Minimum, Max: Maximum.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Data source: [Listing 16.2.6-1](#)



Table 14.2.1-2 Descriptive Statistics of Plasma Pharmacokinetic Parameters by Treatment - PK Population

Analyte	Treatment	Parameter(unit)	N	Mean	SD	CV%	Min	Median	Max	Geometric Mean
Diazepam	A	AUC _{0-t} (ng*h/mL)								
		AUC _{0-inf} (ng*h/mL)								
		Residual Area (%)								
		C _{max} (ng/mL)								
		T _{max} (h)								
		T _{1/2 el} (h)								
		K _{el} (/h)								
		Cl/F(h)								
		Vd/F(h)								
		Cl/F/kg								
		Vd/F/kg								
							

N: Number of observations; SD: Standard Deviation; CV = Coefficient of Variation; Min = Minimum, Max = Maximum; ‘.’ : Not calculated.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Data source: [Listing 16.2.6-2](#)

Table 14.2.1-3 Descriptive Statistics of Individual Ratios or Individual Differences between Treatments for Pharmacokinetic Parameters - PK Population

Analyte	Comparison	Parameter	Ratio/Difference (unit)	N	Mean	SD	CV%	Min	Median	Max	Geometric Mean
Diazepam	A vs B	AUC _{0-t}	A/B (%)								
		AUC _{0-inf}	A/B (%)								
		Residual Area	A - B (%)								
		C _{max}	A/B (%)								
		T _{max}	A - B (h)								
		T _{1/2 el}	A/B (%)								
		K _{el}	A/B (%)								
	...										

N: Number of observations; SD: Standard Deviation; CV = Coefficient of Variation; Min = Minimum, Max = Maximum; '.': Not calculated.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Data source: [Listing 16.2.6-3](#)



Table 14.2.1-4 Ratios (A/B), 90% Geometric Confidence Intervals, Intra-Subjects CV (%) and P-values for Diazepam – PK Population

Comparison (Test vs. Ref.)	Parameter(unit)	Geometric LSM		Ratio ¹ (%)	90% Geometric C.I. ²		Intra-Subject CV (%) ³	Inter-Subject CV (%) ⁴	p-values		
		Test	Ref.		Lower (%)	Upper (%)			Sequence	Period	Treatment
A vs B	AUC _{0-t} (h*ng/mL)										
	AUC _{0-inf} (h*ng/mL)										
	C _{max} (ng/mL)										

¹ Calculated using least-squares means according to the formula: $\exp(\text{DIFFERENCE}) * 100$.

² 90% Geometric Confidence Interval calculated according to the formula: $\exp(\text{DIFFERENCE} \pm t_{(df_{\text{Residual}})} * SE_{\text{DIFFERENCE}})$

³ Calculated according to formula: $\text{SQRT}(\exp(\text{MSE}) - 1) * 100$

⁴ Calculated according to formula: $\text{SQRT}(\exp((\text{MS}_{\text{SUBJECT (SEQ)}} - \text{MSE})/2) - 1) * 100$

LSM: Least Square Mean; Ref.: Reference.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content).

Data Source: [Listing 16.1.9-1](#)

Note: Similar layout will be used for Table 14.2.1-5, 14.2.1-6 and 14.2.1-7. Please adapt title and footnotes accordingly.



Table 14.3.1-1 Frequency of Subjects Experiencing Treatment-Emergent Adverse Events and Number of Events Summarized per Treatment – Safety Population

MedDRA [®] System Organ Class MedDRA [®] Preferred Term	Statistic	Treatment A (N=XX)	Treatment B (N=XX)	Treatment C (N=XX)	Overall (N=XX)
Number of TEAEs	E	xx	xx	xx	xx
Number of Subjects with TEAEs	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] System Organ Class 1	n(%) E	x (xx.x) x	x (xx.x) x	x (xx.x) x	x (xx.x) x
MedDRA [®] Preferred Term 1	n(%) E	x (xx.x) x	x (xx.x) x	x (xx.x) x	x (xx.x) x
MedDRA [®] Preferred Term 2	n(%) E	x (xx.x) x	x (xx.x) x	x (xx.x) x	x (xx.x) x
MedDRA [®] System Organ Class 2	n(%) E	x (xx.x) x	x (xx.x) x	x (xx.x) x	x (xx.x) x
MedDRA [®] Preferred Term 1	n(%) E	x (xx.x) x	x (xx.x) x	x (xx.x) x	x (xx.x) x
MedDRA [®] Preferred Term 2	n(%) E	x (xx.x) x	x (xx.x) x	x (xx.x) x	x (xx.x) x
MedDRA [®] System Organ Class 3	n(%) E	x (xx.x) x	x (xx.x) x	x (xx.x) x	x (xx.x) x
MedDRA [®] Preferred Term 1	n(%) E	x (xx.x) x	x (xx.x) x	x (xx.x) x	x (xx.x) x
MedDRA [®] Preferred Term 2	n(%) E	x (xx.x) x	x (xx.x) x	x (xx.x) x	x (xx.x) x

Programming Notes:

1) SOC will be presented in descending order of overall incidence rate in terms of frequency of subjects and then in frequency of events (alphabetical order will be used in case of equal rates). For each SOC, PT will be presented the same way.

2) Refer to footnotes for additional instructions.

E: Number of TEAEs; N: Number of subjects dosed; n (%): Number and percent of subjects with TEAE; MedDRA[®]: Medical Dictionary for Regulatory Activities, version 21.1; TEAEs: Treatment-Emergent Adverse Events.

Each subject could only contribute once to each of the incidence rates, regardless of the number of occurrences.

Overall: Included results from all treatment groups.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Data source: [Listing 16.2.7-2](#)

Table 14.3.1-2 Frequency of Subjects Experiencing Treatment-Emergent Adverse Events Summarized per Treatment and Severity – Safety Population

MedDRA [®] System Organ Class MedDRA [®] Preferred Term n (%)	Treatment A (N=XX)			Treatment B (N=XX)		
	Mild	Moderate	Severe	Mild	Moderate	Severe
MedDRA [®] System Organ Class 1	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 1	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 2	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] System Organ Class 2	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 1	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 2	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)

Programming Notes:

- 1) SOC will be presented in descending order of overall incidence rate in terms of frequency of subjects and then in frequency of events (alphabetical order will be used in case of equal rates). For each SOC, PT will be presented the same way.
- 2) If the distribution of treatments is presented on more than one page, preserve the order of the SOC and PT as defined in the generation of the global table without severity.
- 3) Refer to footnotes for additional instructions.

N: Number of subjects dosed; n (%): Number and percent of subjects with treatment-emergent adverse events; MedDRA[®]: Medical Dictionary for Regulatory Activities, version 21.1.

Each subject could only contribute once to each of the incidence rates, regardless of the number of occurrence; the highest severity is presented.

Overall: Included results from all treatment groups.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Data source: [Listing 16.2.7-2](#)

Table 14.3.1-2 Frequency of Subjects Experiencing Treatment-Emergent Adverse Events Summarized per Treatment and Severity – Safety Population

MedDRA [®] System Organ Class MedDRA [®] Preferred Term n (%)	Treatment C (N=XX)			Overall (N=XX)		
	Mild	Moderate	Severe	Mild	Moderate	Severe
MedDRA [®] System Organ Class 1	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 1	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 2	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] System Organ Class 2	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 1	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 2	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)

Programming Notes:

- 1) SOC will be presented in descending order of overall incidence rate in terms of frequency of subjects and then in frequency of events (alphabetical order will be used in case of equal rates). For each SOC, PT will be presented the same way.
- 2) If the distribution of treatments is presented on more than one page, preserve the order of the SOC and PT as defined in the generation of the global table without severity.
- 3) Refer to footnotes for additional instructions.

N: Number of subjects dosed; n (%): Number and percent of subjects with treatment-emergent adverse events; MedDRA[®]: Medical Dictionary for Regulatory Activities, version 21.1.

Each subject could only contribute once to each of the incidence rates, regardless of the number of occurrence; the highest severity is presented.

Overall: Included results from all treatment groups.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Data source: [Listing 16.2.7-2](#)



Table 14.3.1-3 Number of Treatment-Emergent Adverse Events Summarized per Treatment and Severity – Safety Population

MedDRA [®] System Organ Class MedDRA [®] Preferred Term	E	Treatment A (N=XX)			Treatment B (N=XX)		
		Mild	Moderate	Severe	Mild	Moderate	Severe
MedDRA [®] System Organ Class 1		x	x	x	x	x	x
MedDRA [®] Preferred Term 1		x	x	x	x	x	x
MedDRA [®] Preferred Term 2		x	x	x	x	x	x
MedDRA [®] System Organ Class 2		x	x	x	x	x	x
MedDRA [®] Preferred Term 1		x	x	x	x	x	x
MedDRA [®] Preferred Term 2		x	x	x	x	x	x

Programming Notes:

- 1) SOC will be presented in descending order of overall incidence rate in terms of frequency of subjects and then in frequency of events (alphabetical order will be used in case of equal rates). For each SOC, PT will be presented the same way.
- 2) If the distribution of treatments is presented on more than one page, preserve the order of the SOC and PT as defined in the generation of the global table without severity.

E: Number of treatment-emergent adverse event; N: Number of subjects dosed; MedDRA[®]: Medical Dictionary for Regulatory Activities, version 21.1.

Overall: Included results from all treatment groups.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Data source: [Listing 16.2.7-2](#)



Table 14.3.1-3 Number of Treatment-Emergent Adverse Events Summarized per Treatment and Severity – Safety Population

MedDRA [®] System Organ Class MedDRA [®] Preferred Term	E	Treatment C (N=XX)			Overall (N=XX)		
		Mild	Moderate	Severe	Mild	Moderate	Severe
MedDRA [®] System Organ Class 1		x	x	x	x	x	x
MedDRA [®] Preferred Term 1		x	x	x	x	x	x
MedDRA [®] Preferred Term 2		x	x	x	x	x	x
MedDRA [®] System Organ Class 2		x	x	x	x	x	x
MedDRA [®] Preferred Term 1		x	x	x	x	x	x
MedDRA [®] Preferred Term 2		x	x	x	x	x	x

Programming Notes:

- 1) SOC will be presented in descending order of overall incidence rate in terms of frequency of subjects and then in frequency of events (alphabetical order will be used in case of equal rates). For each SOC, PT will be presented the same way.
- 2) If the distribution of treatments is presented on more than one page, preserve the order of the SOC and PT as defined in the generation of the global table without severity.

E: Number of treatment-emergent adverse event; N: Number of subjects dosed; MedDRA[®]: Medical Dictionary for Regulatory Activities, version 21.1.

Overall: Included results from all treatment groups.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Data source: [Listing 16.2.7-2](#)



Table 14.3.1-4 Frequency of Subjects Experiencing Treatment-Emergent Adverse Events Summarized per Treatment and Relationship – Safety Population

MedDRA [®] System Organ Class MedDRA [®] Preferred Term n (%)	Treatment A (N=XX)				Treatment B (N=XX)			
	Unrelated	Unlikely	Possible	Probable	Unrelated	Unlikely	Possible	Probable
MedDRA [®] System Organ Class 1	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 1	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 2	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] System Organ Class 2	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 1	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 2	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)

Programming Notes:

- 1) SOC will be presented in descending order of overall incidence rate in terms of frequency of subjects and then in frequency of events (alphabetical order will be used in case of equal rates). For each SOC, PT will be presented the same way.
- 2) If the distribution of treatments is presented on more than one page, preserve the order of the SOC and PT as defined in the generation of the global table without relationship.
- 3) Refer to footnotes for additional instructions.

N: Number of subjects dosed; n (%): Number and percent of subjects with treatment-emergent adverse event; MedDRA[®]: Medical Dictionary for Regulatory Activities, version 21.1.

Each subject could only contribute once to each of the incidence rates, regardless of the number of occurrence; the highest relationship is presented.

Overall: Included results from all treatment groups.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Data source: [Listing 16.2.7-2](#)

Table 14.3.1-4 Frequency of Subjects Experiencing Treatment-Emergent Adverse Events Summarized per Treatment and Relationship – Safety Population

MedDRA [®] System Organ Class MedDRA [®] Preferred Term n (%)	Treatment C (N=XX)				Overall (N=XX)			
	Unrelated	Unlikely	Possible	Probable	Unrelated	Unlikely	Possible	Probable
MedDRA [®] System Organ Class 1	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 1	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 2	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] System Organ Class 2	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 1	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
MedDRA [®] Preferred Term 2	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)

Programming Notes:

- 1) SOC will be presented in descending order of overall incidence rate in terms of frequency of subjects and then in frequency of events (alphabetical order will be used in case of equal rates). For each SOC, PT will be presented the same way.
- 2) If the distribution of treatments is presented on more than one page, preserve the order of the SOC and PT as defined in the generation of the global table without relationship.
- 3) Refer to footnotes for additional instructions.

N: Number of subjects dosed; n (%): Number and percent of subjects with treatment-emergent adverse event; MedDRA[®]: Medical Dictionary for Regulatory Activities, version 21.1.

Each subject could only contribute once to each of the incidence rates, regardless of the number of occurrence; the highest relationship is presented.

Overall: Included results from all treatment groups.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Data source: [Listing 16.2.7-2](#)



Table 14.3.1-5 Number of Treatment-Emergent Adverse Events Summarized per Treatment and Relationship – Safety Population

MedDRA [®] System Organ Class MedDRA [®] Preferred Term	E	Treatment A (N=XX)				Treatment B (N=XX)			
		Unrelated	Unlikely	Possible	Probable	Unrelated	Unlikely	Possible	Probable
MedDRA [®] System Organ Class 1		x	x	x	x	x	x	x	x
MedDRA [®] Preferred Term 1		x	x	x	x	x	x	x	x
MedDRA [®] Preferred Term 2		x	x	x	x	x	x	x	x
MedDRA [®] System Organ Class 2		x	x	x	x	x	x	x	x
MedDRA [®] Preferred Term 1		x	x	x	x	x	x	x	x
MedDRA [®] Preferred Term 2		x	x	x	x	x	x	x	x

Programming Notes:

- 4) SOC will be presented in descending order of overall incidence rate in terms of frequency of subjects and then in frequency of events (alphabetical order will be used in case of equal rates). For each SOC, PT will be presented the same way.
- 5) If the distribution of treatments is presented on more than one page, preserve the order of the SOC and PT as defined in the generation of the global table without relationship.

E: Number of treatment-emergent adverse event; N: Number of subjects dosed; MedDRA[®]: Medical Dictionary for Regulatory Activities, version 21.1.

Overall: Included results from all treatment groups.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Data source: [Listing 16.2.7-2](#)



Table 14.3.1-5 Number of Treatment-Emergent Adverse Events Summarized per Treatment and Relationship – Safety Population

MedDRA [®] System Organ Class MedDRA [®] Preferred Term	E	Treatment C (N=XX)				Overall (N=XX)			
		Unrelated	Unlikely	Possible	Probable	Unrelated	Unlikely	Possible	Probable
MedDRA [®] System Organ Class 1		x	x	x	x	x	x	x	x
MedDRA [®] Preferred Term 1		x	x	x	x	x	x	x	x
MedDRA [®] Preferred Term 2		x	x	x	x	x	x	x	x
MedDRA [®] System Organ Class 2		x	x	x	x	x	x	x	x
MedDRA [®] Preferred Term 1		x	x	x	x	x	x	x	x
MedDRA [®] Preferred Term 2		x	x	x	x	x	x	x	x

Programming Notes:

- 1) SOC will be presented in descending order of overall incidence rate in terms of frequency of subjects and then in frequency of events (alphabetical order will be used in case of equal rates). For each SOC, PT will be presented the same way.
- 2) If the distribution of treatments is presented on more than one page, preserve the order of the SOC and PT as defined in the generation of the global table without relationship.

E: Number of treatment-emergent adverse event; N: Number of subjects dosed; MedDRA[®]: Medical Dictionary for Regulatory Activities, version 21.1.

Overall: Included results from all treatment groups.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Data source: [Listing 16.2.7-2](#)

Table 14.3.4-1 Biochemistry Summary Descriptive Statistics and Change from Screening to Study Exit – Safety Population

Parameter (unit) Normal Range	Visit	Statistic	Overall (N=XX)
Parameter 1 (xxx) XX-XX	Screening	n	xx
		Mean	xx.x
		SD	xx.x
		Median	xx.x
		Min, Max	xx, xx
	Study Exit	n	xx
		Mean	xx.x
		SD	xx.x
		Median	xx.x
		Min, Max	xx, xx
	Study Exit - CFS	n	xx
		Mean	xx.x
		SD	xx.x
		Median	xx.x
		Min, Max	xx, xx
...			

Programming Notes:

- 1) Refer to study protocol for laboratory tests to be presented.
- 2) Urinalysis parameters (quantitative results) expected and sorted as: pH (PH) and Specific Gravity (SPGRAV).
- 3) For each parameter provide normal range of primary facility and, for gender specific parameters, use the same sorting of sex from demographic table.
- 4) If multiple laboratories involved, refer to the SAP instructions for results normalization.
- 5) Evaluate individually for each table if some standard results were not quantifiable and, if applicable, add footnote: Not quantifiable values outside of limit of quantitation (<x or >y) will be set to missing for calculation of summary statistics.
- 6) Refer to footnotes for additional instructions.
- 7) Adapt Data Source to the appropriate laboratory category listing.

CFS: Change from screening; N: Number of subjects dosed; n: number of subjects; SD: Standard Deviation.

Screening is defined as the last screening results (scheduled or unscheduled).

Data source: [Listing 16.2.8-1](#)

Note: This table will be repeated for Tables 14.3.4-3, 14.3.4-5 and Table 14.3.4-10. Please adapt title and data source footnote accordingly.

**Table 14.3.4-2 Frequency of Subjects – Biochemistry Shifts from Screening to Study Exit -
– Safety Population**

Parameter (unit)	Screening	Study Exit		
		Low n (%)	Normal n (%)	High n (%)
Parameter 1 (xxx)	Low	x (xx.x)	x (xx.x)	x (xx.x)
	Normal	x (xx.x)	x (xx.x)	x (xx.x)
	High	x (xx.x)	x (xx.x)	x (xx.x)
Parameter 2 (xxx)	Low	x (xx.x)	x (xx.x)	x (xx.x)
	Normal	x (xx.x)	x (xx.x)	x (xx.x)
	High	x (xx.x)	x (xx.x)	x (xx.x)

Programming Notes:

- 1) Refer to study protocol for parameters to be presented.
- 2) Preserve parameters and sorting defined in Summary Descriptive Statistics Table
- 3) Refer to footnotes for additional instructions.
- 4) Adapt Data Source to the appropriate laboratory category listing.

n (%): Number and percentage of subjects.

Percentage based on the number of subjects having available results at screening and at study exit.

Screening is defined as the last screening results (scheduled or unscheduled).

Data source: [Listing 16.2.8-1](#)

Note: This table will be repeated for Tables 14.3.4-4, and 14.3.4-6. Please adapt title and data source accordingly.

Table 14.3.4-7 Urinalysis Frequency Summary: Categorical Results – Safety Population

Parameter (unit) Normal range	Visit	Result	Overall n (%)
Parameter 1 (xxx) [Normal range]	Screening	Clear	x (xx.x)
		Cloudy	x (xx.x)
		Turbid	x (xx.x)
	Study Exit	Clear	x (xx.x)
		Cloudy	x (xx.x)
		Turbid	x (xx.x)
Parameter 2 (xxx) [Normal range]	Screening	+	x (xx.x)
		Negative	x (xx.x)
	Study Exit	Negative	x (xx.x)
Parameter 3 (xxx) [Normal range]	Screening	+	x (xx.x)
		Negative	x (xx.x)
		Trace	x (xx.x)
	Study Exit	+	x (xx.x)
		Negative	x (xx.x)
		Trace	x (xx.x)

Programming Notes:

- 1) Refer to study protocol for parameters to be presented.
- 2) Urine Microscopy parameters will not be presented in this table.
- 3) Evaluate if the units must be added to parameter name if a numeric result was observed. Remove (Units) from column header if no numeric results were observed.
- 4) For each parameter provide normal range of primary facility and, for gender specific parameters, use the same sorting of sex from demographic table.
- 5) Independently for each parameter test, sort results by gradation.
- 6) Refer to footnotes for additional instructions.

n (%): Number and percentage of subjects.

Percentage based on the number of subjects having available results at screening and at study exit.

Data source: [Listing 16.2.8-3](#)



Table 14.3.4-8 Frequency of Subjects - Urinalysis Shifts from Screening to Study Exit: Categorical Results – Safety Population

Parameter	Screening	Study Exit	
		Normal n (%)	Abnormal n (%)
Parameter 1	Normal	x (xx.x)	x (xx.x)
	Abnormal	x (xx.x)	x (xx.x)
Parameter 2	Normal	x (xx.x)	x (xx.x)
	Abnormal	x (xx.x)	x (xx.x)
Parameter 3	Normal	x (xx.x)	x (xx.x)
	Abnormal	x (xx.x)	x (xx.x)

Programming Notes:

- 1) Refer to study protocol for parameters to be presented.
- 2) Preserve parameters and sorting defined in Summary Descriptive Statistics Table
- 3) Refer to footnotes for additional instructions.

n (%): Number and percentage of subjects.
Percentage based on the number of subjects having available results at screening and at study exit.
Screening is defined as the last screening results (scheduled or unscheduled).
Data source: [Listing 16.2.8-3](#)



Table 14.3.4-9 Vital Signs Summary Descriptive Statistics - Safety Population

Parameter (unit) Normal Range	Timepoint	Statistic	Treatment A (N=XX)	Treatment B (N=XX)	Treatment C (N=XX)	Overall (N=XX)
Parameter 1 (xxx) XX-XX	Screening	n	-	-	-	XX
		Mean	-	-	-	XX.X
		SD	-	-	-	XX.X
		Median	-	-	-	XX.X
		Min, Max	-	-	-	XX, XX
	Pre-dose	n	XX	XX	XX	-
		Mean	XX.X	XX.X	XX.X	-
		SD	XX.X	XX.X	XX.X	-
		Median	XX.X	XX.X	XX.X	-
		Min, Max	XX, XX	XX, XX	XX, XX	-
	Baseline	n	XX	XX	XX	-
		Mean	XX.X	XX.X	XX.X	-
		SD	XX.X	XX.X	XX.X	-
		Median	XX.X	XX.X	XX.X	-
		Min, Max	XX, XX	XX, XX	XX, XX	-
	0.5H Post-Dose	n	XX	XX	XX	-
		Mean	XX.X	XX.X	XX.X	-
		SD	XX.X	XX.X	XX.X	-
		Median	XX.X	XX.X	XX.X	-
		Min, Max	XX, XX	XX, XX	XX, XX	-
0.5H Post-Dose – CFB	n	XX	XX	XX	-	
	Mean	XX	XX	XX	-	
	SD	XX	XX	XX	-	
	Median	XX	XX	XX	-	
	Min, Max	XX, XX	XX, XX	XX, XX	-	



1.00H Post-Dose	n	XX	XX	XX	-
	Mean	XX.X	XX.X	XX.X	-
	SD	XX.X	XX.X	XX.X	-
	Median	XX.X	XX.X	XX.X	-
	Min, Max	XX, XX	XX, XX	XX, XX	-
1.00H Post-Dose – CFB	N	XX	XX	XX	-
	Mean	XX	XX	XX	-
	SD	XX	XX	XX	-
	Median	XX	XX	XX	-
	Min, Max	XX, XX	XX, XX	XX, XX	-
....					
Study Exit	n	-	-	-	XX
	Mean	-	-	-	XX.X
	SD	-	-	-	XX.X
	Median	-	-	-	XX.X
	Min, Max	-	-	-	XX, XX
Study Exit - CFS	n	-	-	-	XX
	Mean	-	-	-	XX.X
	SD	-	-	-	XX.X
	Median	-	-	-	XX.X
	Min, Max	-	-	-	XX, XX

Programming Notes:

- 1) *Preserve parameters and sorting defined in Summary Descriptive Statistics Table*
- 2) *Independently for each parameter, if Baseline assessment is composed by the same visit and timepoint for all subjects, identify this timepoint with Baseline between parentheses. ex. Day 1 Pre-Dose (Baseline)*
- 3) *Refer to footnotes for additional instructions.*

CFB: Change from Baseline; CFS: Change from Screening; N: Number of subjects dosed; n: Number of subjects; SD: Standard Deviation.

Screening is defined as the last screening results (scheduled or unscheduled).

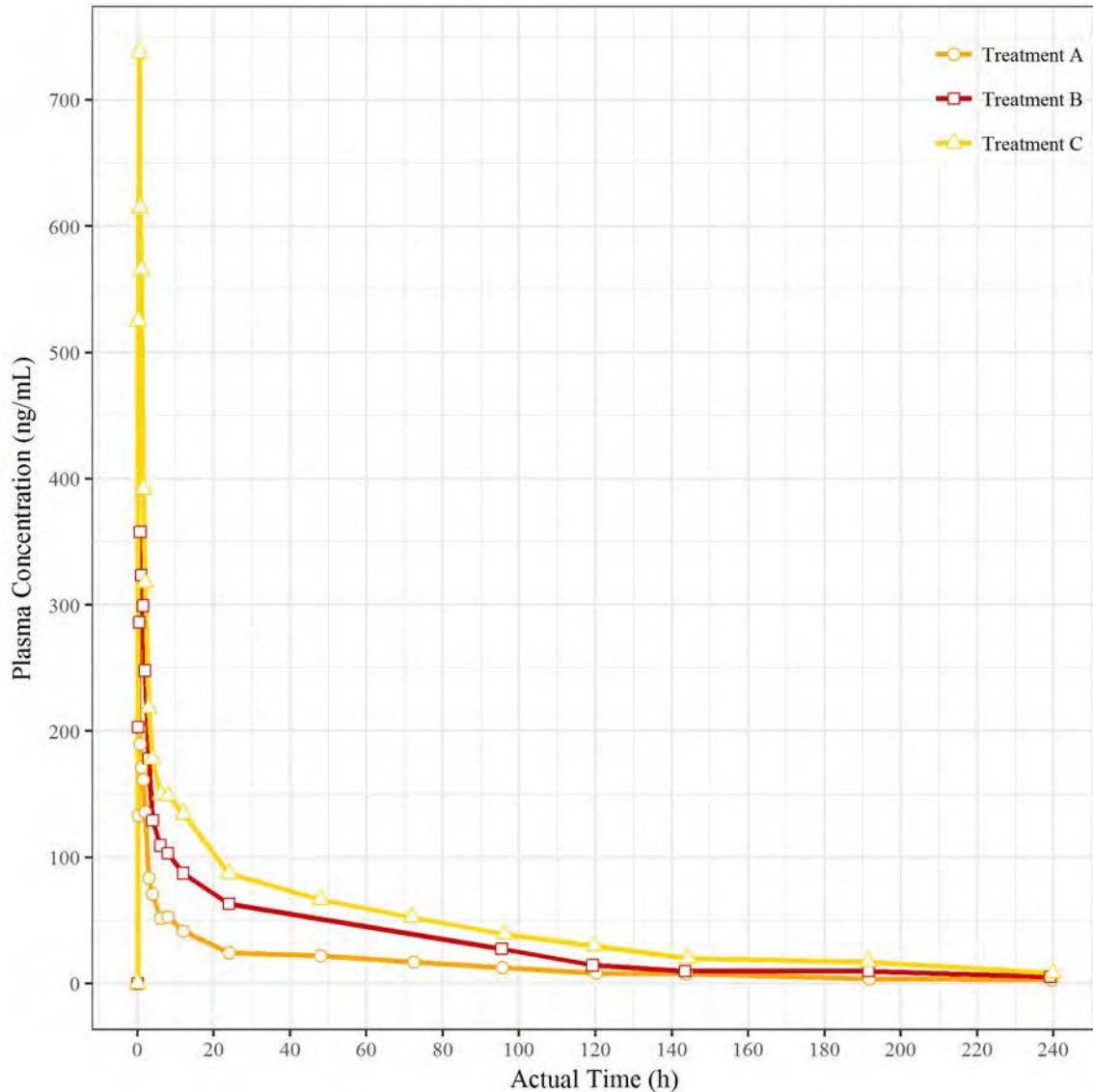
Baseline is defined as the last results (scheduled or unscheduled) obtained prior to drug administration in each period.

Data source: [Listing 16.2.8-4](#)



5. Figures

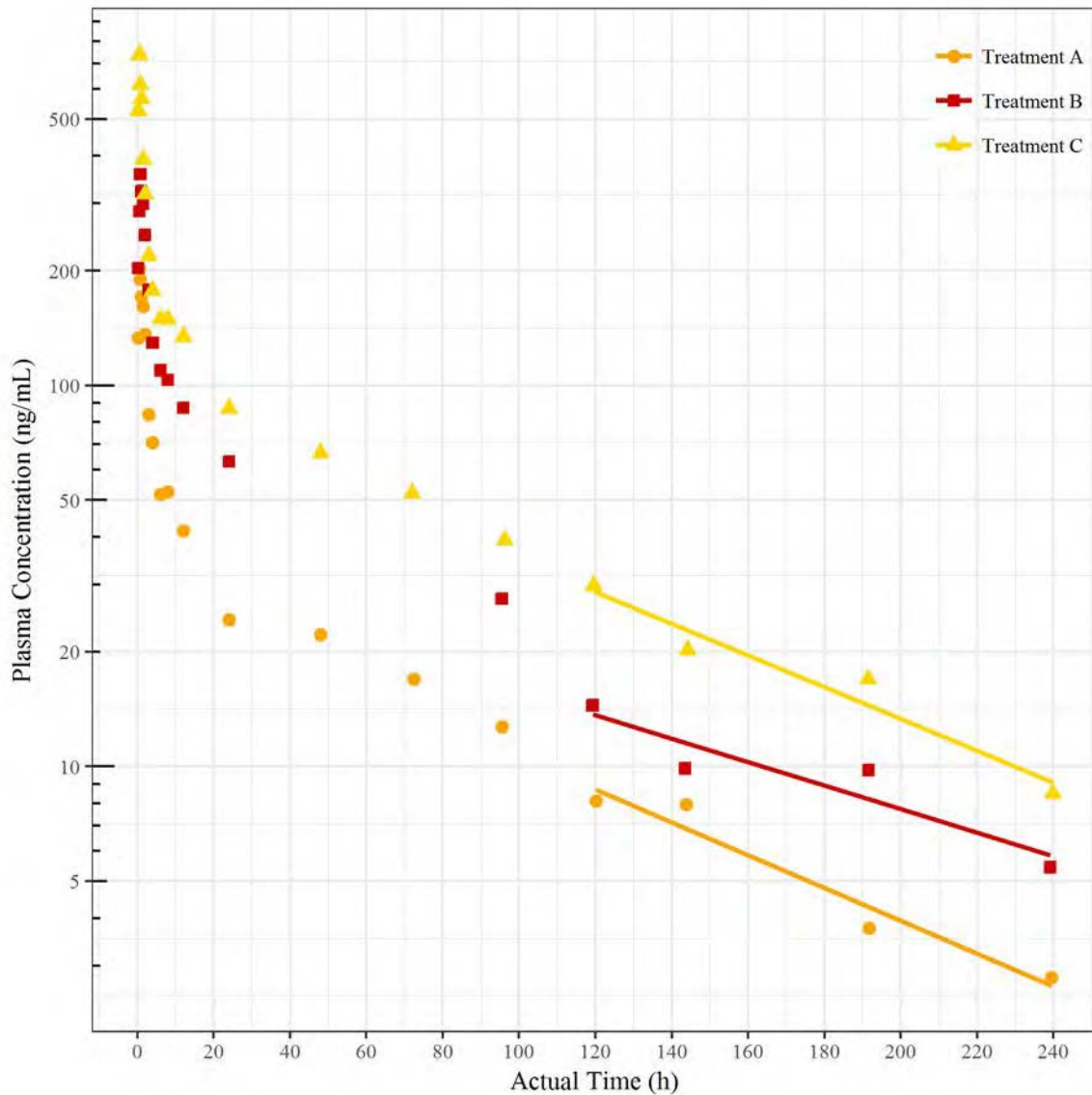
Figure 14.2.2-1a: Plasma Concentrations of Diazepam for Subject XX - Linear Scale



Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);
 Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);
 Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Note: This figure will be repeated for each subject included in the PK population, and for nordiazepam.

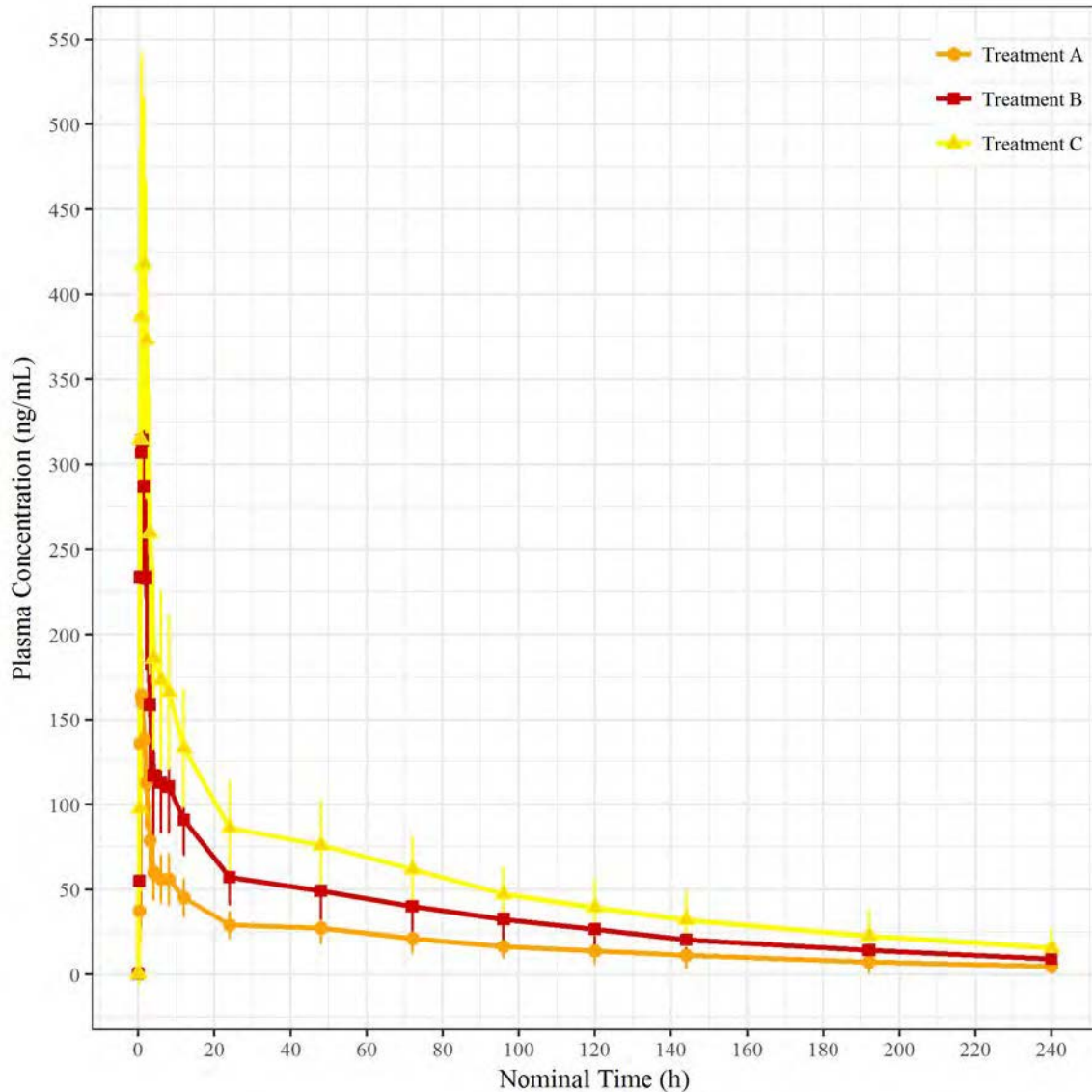
Figure 14.2.2-1b: Plasma Concentrations of Diazepam for Subject XX – Semi-Log Scale



Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);
 Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);
 Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Note: This figure will be repeated for each subject included in the PK population, and for nordiazepam.

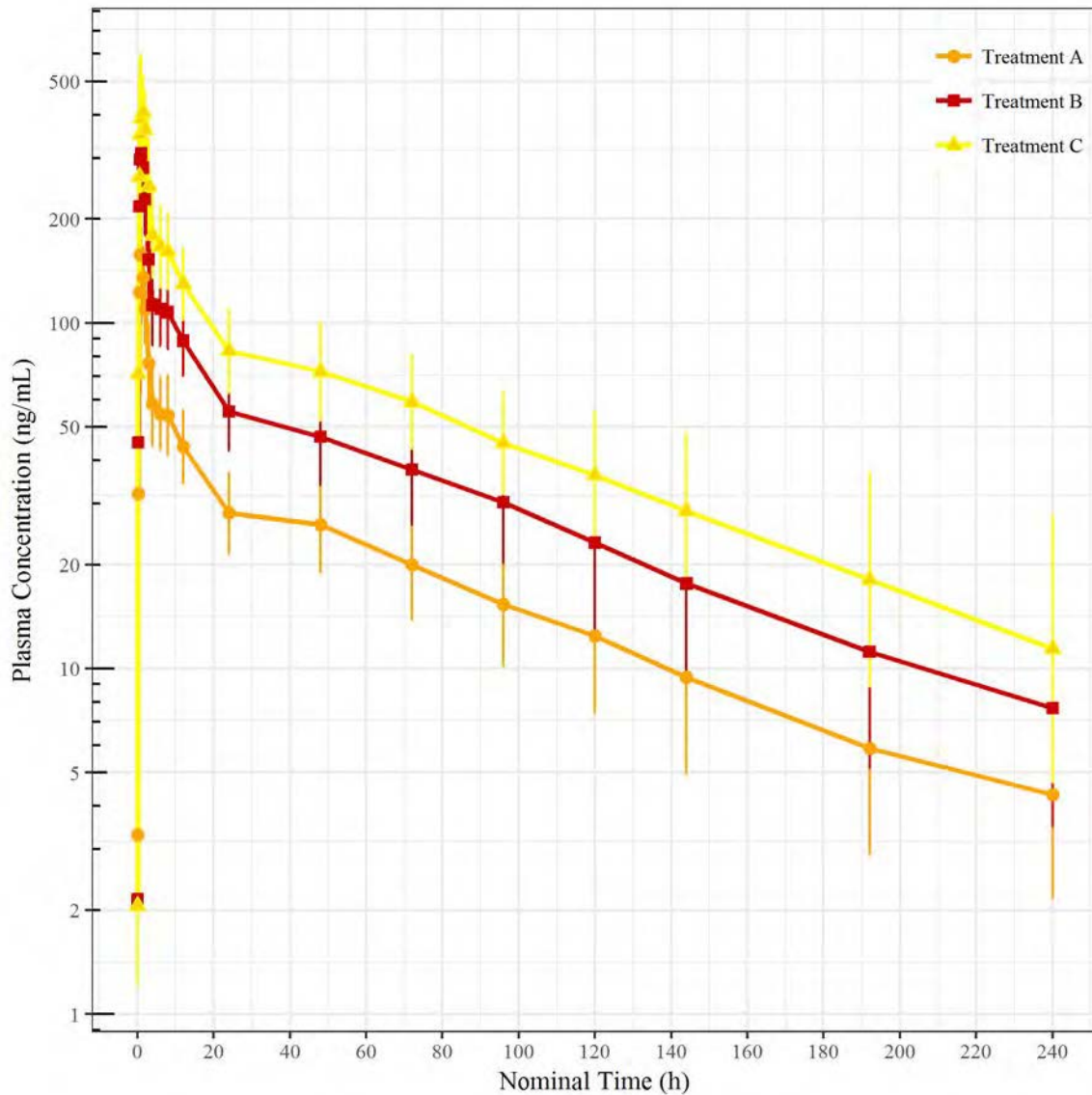
Figure 14.2.2-33a: Mean (\pm SD) Plasma Concentrations of Diazepam - Linear Scale



Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);
 Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);
 Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Note: This figure will be repeated for nordiazepam.

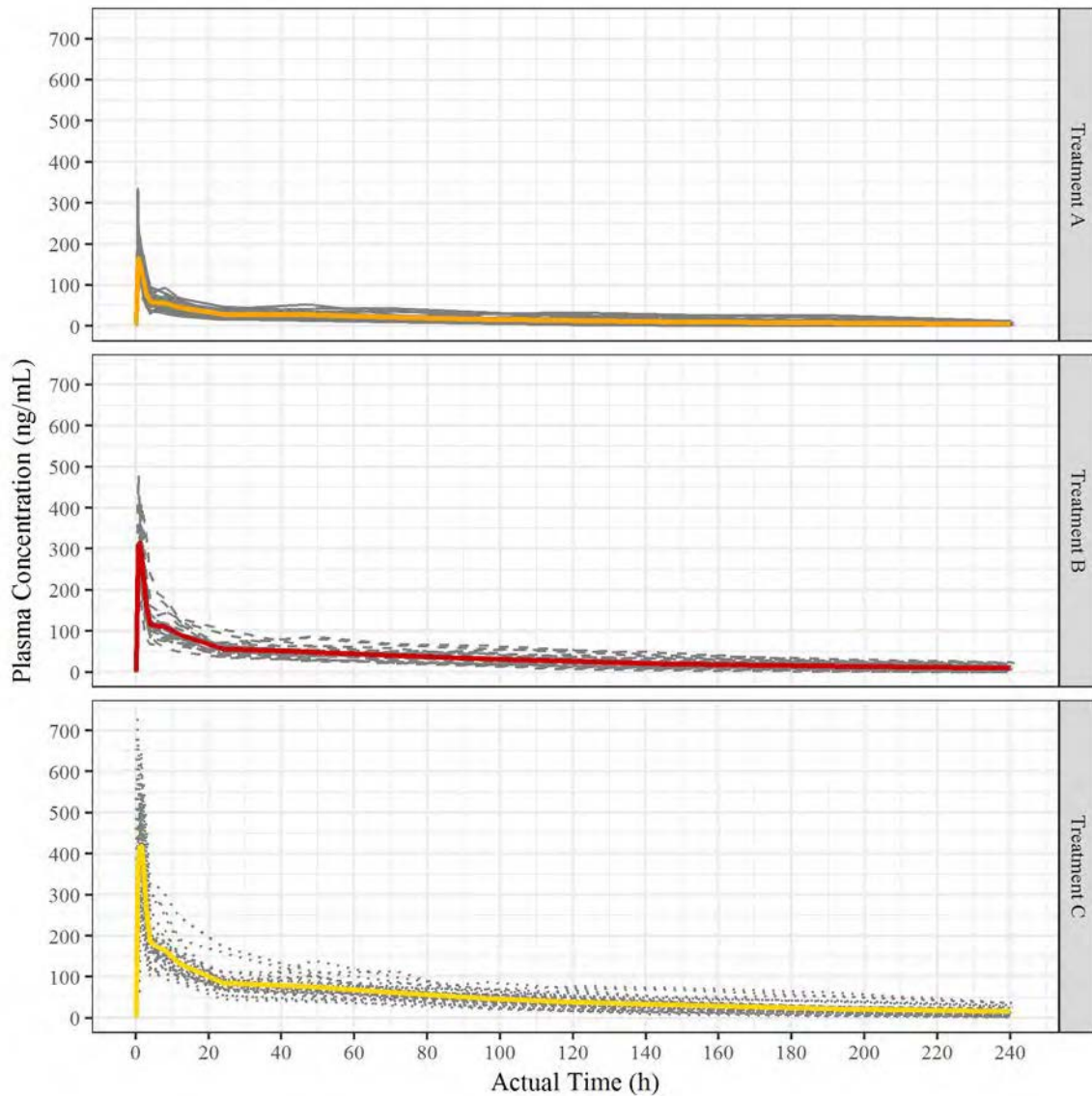
Figure 14.2.2-33b: Mean (\pm SD) Plasma Concentrations of Diazepam - Semi-Log Scale



Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);
 Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);
 Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Note: This figure will be repeated for nordiazepam.

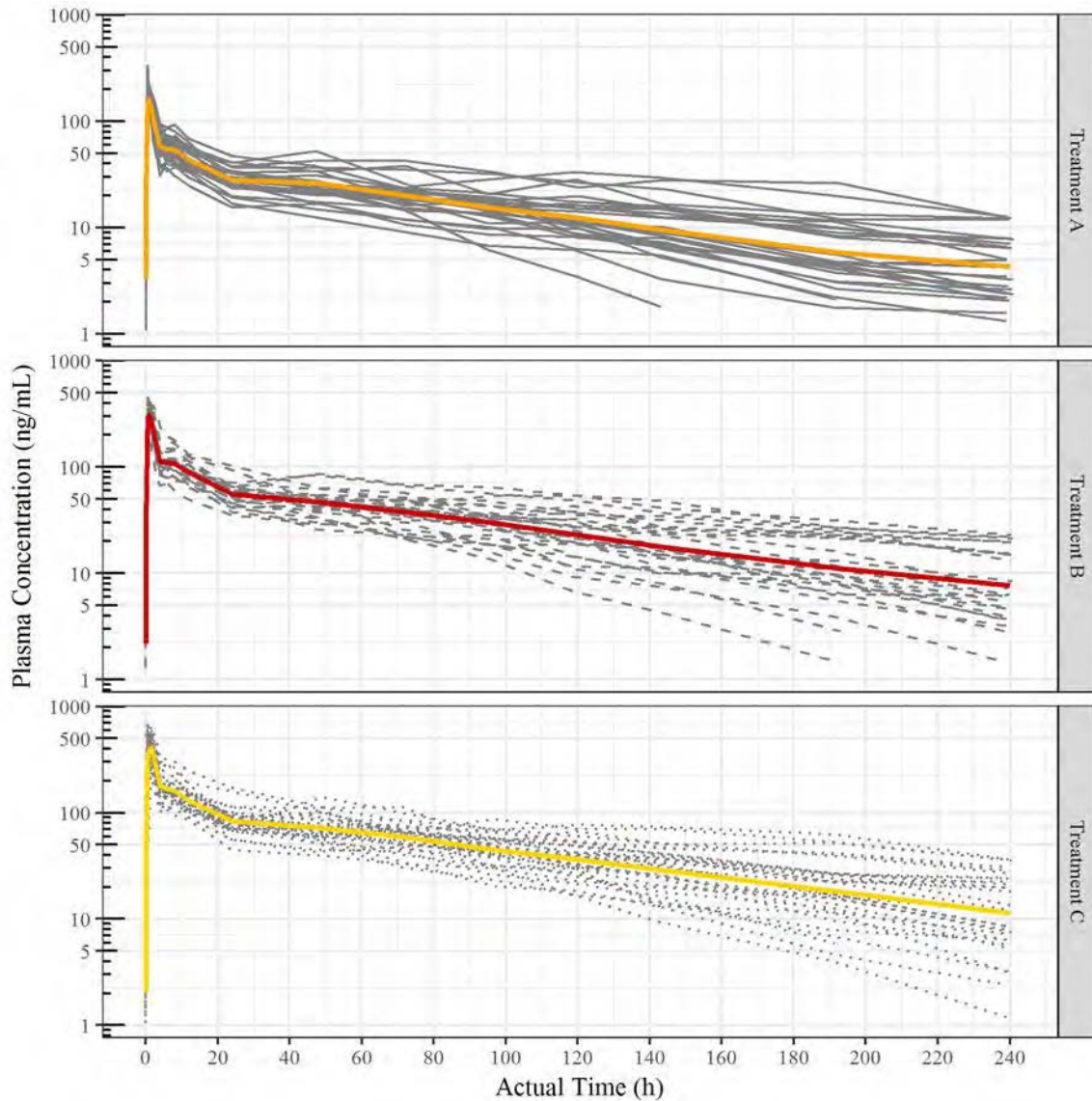
Figure 14.2.2-34a: Overlay of Individual and Mean Plasma Concentrations of Diazepam by Treatment - Linear Scale



Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);
 Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);
 Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Note: This figure will be repeated for nordiazepam.

Figure 14.2.2-34b: Overlay of Individual and Mean Plasma Concentrations of Diazepam by Treatment - Semi-Log Scale



Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);
 Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);
 Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Note: This figure will be repeated for nordiazepam.



6. Listings



Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam – PK Population

Comparison: A vs B
Dependent Variable: xxx

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model					
Error					
Corrected Total					

R-Square	Coeff Var	Root MSE	VAR Mean
----------	-----------	----------	----------

Source	DF	Type I SS	Mean Square	F Value	Pr > F
SEQ					
PERIOD					
TRT					
SUBJECT (SEQ)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
SEQ					
PERIOD					
TRT					
SUBJECT (SEQ)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
SEQ					
PERIOD					
TRT					
SUBJECT (SEQ)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
SEQ					
PERIOD					
TRT					
SUBJECT (SEQ)					



Tests of Hypotheses Using the Type III MS for SUBJECT(SEQ) as an Error Term					
Source	DF	Type III SS	Mean Square	F Value	Pr > F
SEQ					

Level of				
TRT	N	Mean	Std Dev	
A				
B				

TRT	VAR	LSMEAN	Standard Error	Pr > t
A				
B				

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B					

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content)

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content)

Note 1: For each comparison, all ANOVA results for ln-transformed AUC_{0-t}, AUC_{0-inf}, C_{max}, Cl/F, Cl/F/kg, Vd/F, Vd/F/kg and untransformed, K_{el}, and T_{1/2 el} for plasma concentration will be presented in this listing.

Note 2: For B vs C comparison, PERIOD will not be included in the model.

Note: Similar layout will be used for listing 16.1.9-2. Please adapt title and footnotes accordingly.

Listing 16.1.9-3 Wilcoxon Signed-Rank Test for T_{max} for Treatment Comparison of Diazepam – PK Population

Comparison: A vs B

Difference	Statistic	Value
A – B	n	
	Mean	
	Median	
	SD	
Wilcoxon Signed-rank Test	S	
	p-value	

n: Number of subjects; SD: Standard Deviation.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content)

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content)

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content)

Note 1: For each comparison Wilcoxon Signed-Rank Test for T_{max} will be presented in this listing.

Note2: Similar layout will be used for listing 16.1.9-4. Please adapt title and footnotes accordingly.



Listing 16.2.1-1 Subjects Completion and Discontinuation Information

Subject Number	Treatment Sequence	Period	Last Treatment Received Prior to Discontinuation	Last Period Prior to Discontinuation	Completion/ Discontinuation Date and Time	Primary Reason for Discontinuation	Comment
	ABC	1	A	2	DD-MM-YYYY/HH:MM	XXX	XXX
		2	B	3			

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);
Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);
Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).



Listing 16.2.2-1 Protocol Deviations

Subject	Treatment Sequence	Period	Category	Deviation
---------	--------------------	--------	----------	-----------

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);
Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);
Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).



Listing 16.2.4-1 Demographics

Subject	Treatment Sequence	Age (years)	Gender	Race	Ethnicity	BMI (kg/m ²)	Height (cm)	Weight (kg)
	ABC							

BMI: Body Mass Index.

Last results (scheduled or unscheduled) obtained at screening were used to generate this table.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).



Listing 16.2.4-2 Medical History Findings at Screening

Subject	Treatment Sequence	Finding	MedDRA [®] Preferred Term	MedDRA [®] System Organ Class	Onset Date	Resolution Date (or Ongoing)
		FINDING 1	Preferred Term 1	SOC 1	YYYY-MM-DDTHH:MM	YYYY-MM-DDTHH:MM
		FINDING 2	Preferred Term 2	SOC 2	YYYY-MM-DDTHH:MM	ONGOING

Programming Notes:

- 1) SOC and Finding will be presented in uppercase. The Preferred Term will be presented in "propcase". The SAS coding "/~n" between terms will generate the break line.
- 2) The SAS coding "/~n" between dates will generate the break line.
- 3) If finding is ongoing, replace missing resolution date per ONGOING.
- 4) Sort events per Subject, Start Date, Stop Date, SOC and PT.
- 5) For incomplete date display, refer to CDISC SDTM Implementation Guide according to ISO 8601 format.

MedDRA[®]: Medical Dictionary for Regulatory Activities; MedDRA[®] Version 21.1.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).



Listing 16.2.4-3 Prior and Concomitant Medications

Subject	Treatment Sequence/ Treatment	Prior/ Concomitant	WHO DDE ATC / WHO DDE Preferred Term / Medication	Dose (unit)/ Frequency	Route	Onset Date and Time/ Resolution Date and Time (or Ongoing)	Indication (Condition or AE No.)
	ABC	Prior	ATC 1/ Preferred Term 1/ MEDICATION 1/	20 (mg) QID	ORAL	YYYY-MM-DDTHH:MM/ YYYY-MM-DDTHH:MM	
	BAC/ B	Concomitant	ATC 2/ Preferred Term 2/ MEDICATION 2/			YYYY-MM-DDTHH:MM/ ONGOING	

Programming Notes:

- 1) ATC and Medication will be presented in uppercase. The Preferred Term will be presented in "propcase". The SAS coding "/~n" between terms will generate the break line.
- 2) The SAS coding "/~n" will generate the break line between treatment sequence and treatment, dose with units and frequency. In the same way apply a break line between dates.
- 3) If medication is ongoing, replace missing resolution date per ONGOING.
- 4) Sort events per Subject, Onset Date, Resolution Date, ATC and PT.
- 5) For incomplete date display, refer to CDISC SDTM Implementation Guide according to ISO 8601 format.

ATC: Anatomic Therapeutic Chemical; WHO DDE: World Health Organization Drug Dictionary Enhanced Version Sep2018, format B.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat® AcuDial™ rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).



Listing 16.2.4-4 Study Drug Administration

Subject	Treatment Sequence	Period	Treatment	Total Dose	Units	Start Date and Time	End Date and Time
---------	--------------------	--------	-----------	------------	-------	---------------------	-------------------

YYYY-MM-DDTHH:MM:SS YYYY-MM-DDTHH:MM:SS

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);
Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);
Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).



Listing 16.2.4-5 Assignment to Analysis Populations

Subject	Included in	
	Safety Population	Pharmacokinetic Population
101	Y	N

Y: Yes; N: No



Listing 16.2.6-1 Listing of Individual Actual Sampling Times and Pharmacokinetic Concentrations

Analyte	Subject	Period	Treatment	Nominal Time	Time Unit	Actual Time	Concentration	Concentration Unit	Excluded flag	Reason	Dose Date and Time	PK Sampling Date and Time	
Diazepam	001	01	A	0.500	h	0.450	ng/mL		N		DDMMYYYY/HH:MM:SS	DDMMYYYY/HH:MM:SS	
				1.00	h	1.00	ng /mL		N				
				2.00	h	2.01	ng /mL	Y	inconclusive				
										
	001	02	B	0.500	h	0.450	ng /mL		N				
				1.00	h	1.00	ng /mL		N				
				2.00	h	2.01	ng /mL	Y	inconclusive				
										
	002	02	B	0.500	h	0.450	ng /mL						
				1.00	h	1.00	ng /mL						
				2.00	h	2.01	ng /mL						
										

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);
 Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);
 Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).



Listing 16.2.6-2 Listing of Individual Pharmacokinetic Parameters

Analyte	Subject	Period	Treatment	Parameter	Results	Unit	Excluding flag	Reason	
Diazepam	001	01	A	AUC _{0-t}			N		
				AUC _{0-inf}			N		
				C _{max}			Y	Not Estimable	
				Residual area			Y	Not Estimable	
				...					
		02		B	AUC _{0-t}			N	
					AUC _{0-inf}			N	
					C _{max}			Y	Not Estimable
					Residual area			Y	Not Estimable
					...				

...

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);
 Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);
 Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).



Listing 16.2.6-3 Listing of Individual Ratios or Differences between Treatment for Pharmacokinetic Parameters

Analyte	Subject	Parameter (unit)	Treatment A	Treatment B	Treatment C	A/B	C/B	Unit
Diazepam	001	AUC _{0-t} (h*ng/mL)						%
		AUC _{0-inf} (h*ng/mL)						%
		Residual Area(%)						%
		C _{max} (ng/mL)						%
		T _{max} (h)						h
		T _{½ el} (h)						%
		K _{el} (/h)						%

...

Differences are presented for Residual area and T_{max}.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).



Listing 16.2.7-1 Non-Treatment-Emergent Adverse Events

Subject	AE Number	MedDRA [®] System Organ Class/ MedDRA [®] Preferred Term/ Adverse Event Description	Onset Date and Time/ Resolution Date and Time (or Ongoing)	Severity/ Relationship	Serious (Yes/No)	Action taken		
						Study Drug	Other	Outcome
		SOC 1/ Preferred Term 1/ DESCRIPTION 1	YYYY-MM-DDTHH:MM/ YYYY-MM-DDTHH:MM	Severe/ Unrelated	Yes			
		SOC 2/ Preferred Term 2/ DESCRIPTION 2	YYYY-MM-DDTHH:MM/ ONGOING	Mild/	No			

Programming Notes:

- 1) SOC and AE Description will be presented in uppercase. The Preferred Term will be presented in "procase". The SAS coding "/-n" between terms will generate the break line.
- 2) The SAS coding "/-n" will generate the break line between dates and between Severity and Relationship.
- 3) If needed, hardcode OUTCOME and ACTIONS in order to introduce break line (~n) between answer elements.
- 4) If medication is ongoing, replace missing resolution date per ONGOING.
- 5) Sort events per Subject, Onset Date/time, Resolution Date/time, SOC and PT.
- 6) For incomplete date display, refer to CDISC SDTM Implementation Guide according to ISO 8601 format.
- 7) Please update 'MedDRA[®] System Organ Class' footnote by keeping only those SOC terms referred in table.

MedDRA[®]: Medical Dictionary for Regulatory Activities (MedDRA[®]); MedDRA[®] Version 21.1.

MedDRA[®] System Organ Class (SOC): Cardiac disorders (Card); Eye disorders (Eye); Gastrointestinal disorders (Gastr); General disorders and administration site conditions (Genrl); Infections and infestations (Infec); Injury, poisoning and procedural complications (Inj&P); Investigations (Inv); Musculoskeletal and connective tissue disorders (Musc); Nervous system disorders (Nerv); Psychiatric disorders (Psych); Respiratory, thoracic and mediastinal disorders (Resp); Skin and subcutaneous tissue disorders (Skin) Vascular disorders (Vasc).

Note: The list of MedDRA[®] SOC will be updated according to the AEs observed for the study.



Listing 16.2.7-2 Treatment-Emergent Adverse Events

Subject	Treatment	AE Number	MedDRA [®] System Organ Class/ MedDRA [®] Preferred Term/ Adverse Event Description	Onset Date and Time/ Resolution Date and Time (or Ongoing)	Severity/ Relationship	Serious (Yes/No)	Action taken		
							Study Drug	Other	Outcome
001			SOC 1/ Preferred Term 1/ DESCRIPTION 1	YYYY-MM-DDTHH:MM/ YYYY-MM-DDTHH:MM	Severe/ Unrelated	Yes			
			SOC 2/ Preferred Term 2/ DESCRIPTION 2	YYYY-MM-DDTHH:MM/ ONGOING	Mild/	No			

Programming Notes:

- 1) SOC and AE Description will be presented in uppercase. The Preferred Term will be presented in "propcase". The SAS coding "/~n" between terms will generate the break line.
- 2) The SAS coding "/~n" will generate the break line between dates and between Severity and Relationship.
- 3) If needed, hardcode OUTCOME and ACTIONS in order to introduce break line (~n) between answer elements.
- 4) If medication is ongoing, replace missing resolution date per ONGOING.
- 5) Sort events per Subject, Onset Date/time, Resolution Date/time, SOC and PT.
- 6) For incomplete date display, refer to CDISC SDTM Implementation Guide according to ISO 8601 format.
- 7) Please update 'MedDRA[®] System Organ Class' footnote by keeping only those SOC terms referred in table.

MedDRA[®]: Medical Dictionary for Regulatory Activities (MedDRA[®]); MedDRA[®] Version 21.1.

MedDRA[®] System Organ Class (SOC): Cardiac disorders (Card); Eye disorders (Eye); Gastrointestinal disorders (Gastr); General disorders and administration site conditions (Genrl); Infections and infestations (Infec); Injury, poisoning and procedural complications (Inj&P); Investigations (Inv); Musculoskeletal and connective tissue disorders (Musc); Nervous system disorders (Nerv); Psychiatric disorders (Psych); Respiratory, thoracic and mediastinal disorders (Resp); Skin and subcutaneous tissue disorders (Skin) Vascular disorders (Vasc).

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Note: The list of MedDRA[®] SOC will be updated according to the AEs observed for the study.

Note: Similar layout will be used for Listings 16.2.7-3 and 16.2.7-4, please adapt title and footnotes accordingly.



Listing 16.2.8-1 Clinical Laboratory - Biochemistry

Subject	Period	Treatment	Laboratory	Visit	Collection Date and Time	Parameter(unit)	Result	Flag	Normal Range
001					YYYY-MM-DDTHH:MM			H	XX.X-XX.X

Programming Notes:

- 1) Sort assessments per Subject, Timepoint/Date and parameters. Sorting for parameter should be as defined in Summary Descriptive Statistics Table.
- 2) For each parameter provide normal range of primary facility and, for gender specific parameters, use the same sorting of gender from demographic table.
- 3) If multiple laboratories involved, display standard and normalised results. Display the ranges in the same way. The SAS coding “/~n” between results or ranges will generate the break line.
Take care to use the same precision of both, standard and normalised results/ranges.
- 4) Adapt flag footnote for Urinalysis listing per
N: Normal result; A: Abnormal result; H: Above normal range; L: Below normal range.
- 5) Laboratory facilities could be abbreviated with appropriation description on footnote (iHC: inVentiv Health Clinical Laboratory; BML: Biron Medical Laboratory).

H: Above normal range; L: Below normal range; N: Normal Range.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat® AcuDial™ rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Note: Similar layout will be used for Listing 16.2.8-2 and 16.2.8-3. Please adapt title and footnotes accordingly.



Listing 16.2.8-4 Vital Signs Result

Subject	Period	Treatment	Time point	Measurement Date and Time	Parameter(unit)	Result
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YYYY-MM-DDTHH:MM

Programming Notes:

1) *Sort assessments per Subject, Timepoint/Date and parameter. Parameters for each subject to be sorted as defined in Summary Descriptive Statistics Table.*

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).



Listing 16.2.8-5 Electrocardiogram Result

Subject	Period	Treatment	Visit	Measurement Date and Time	Parameter(unit)	Result/ Interpretation*
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YYYY-MM-DDTHH:MM

Programming Notes:

- 1) *Sort assessments per Subject, timepoint/Date and parameter. Parameters for each subject to be sorted as defined in Summary Descriptive Statistics Table.*

*The medical judgement for abnormal ECG interpretation is also presented in this column as CS: Clinically significant or NCS: Not clinically significant.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).



Listing 16.2.8-6 DBF Application Site Visual Inspection

Subject	Time point	Inspection Date and Time	Result	Abnormality
		YYYY-MM-DDTHH:MM	Normal Abnormal	

DBF: Diazepam Buccal Film

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam – PK Population

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	27 101 201 202 203 204 205 301 302 303 304 402 404 406 407 408 409 410 411 412 413 414 501 502 503 505 507 508
sequence	2 AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	54
Number of Observations Used	54

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL)

The GLM Procedure

Dependent Variable: LN_AUCLST

R-Square	Coeff Var	Root MSE	LN_AUCLST Mean
0.695214	7.128689	0.625101	8.768809

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.03076554	0.03076554	0.08	0.7813
period	1	0.00220583	0.00220583	0.01	0.9407
trt	1	0.83747933	0.83747933	2.14	0.1557
subject(sequence)	25	21.41205990	0.85648240	2.19	0.0275

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.03076554	0.03076554	0.08	0.7813
period	1	0.00653318	0.00653318	0.02	0.8982
trt	1	0.83747933	0.83747933	2.14	0.1557
subject(sequence)	25	21.41205990	0.85648240	2.19	0.0275

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.03076554	0.03076554	0.08	0.7813
period	1	0.00653318	0.00653318	0.02	0.8982
trt	1	0.83747933	0.83747933	2.14	0.1557
subject(sequence)	25	21.41205990	0.85648240	2.19	0.0275

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.03076554	0.03076554	0.08	0.7813
period	1	0.00653318	0.00653318	0.02	0.8982
trt	1	0.83747933	0.83747933	2.14	0.1557
subject(sequence)	25	21.41205990	0.85648240	2.19	0.0275

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL)

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.030766	0.030766	0.04	0.8512
Error	25	21.412060	0.856482		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.002206	0.002206	0.01	0.9407
trt	1	0.837479	0.837479	2.14	0.1557
subject(sequence)	25	21.412060	0.856482	2.19	0.0275
Error: MS(Error)	25	9.768787	0.390751		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.030766	0.030766	0.04	0.8512
Error	25	21.412060	0.856482		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.006533	0.006533	0.02	0.8982
trt	1	0.837479	0.837479	2.14	0.1557
subject(sequence)	25	21.412060	0.856482	2.19	0.0275
Error: MS(Error)	25	9.768787	0.390751		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.030766	0.030766	0.04	0.8512
Error	25	21.412060	0.856482		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.006533	0.006533	0.02	0.8982
trt	1	0.837479	0.837479	2.14	0.1557
subject(sequence)	25	21.412060	0.856482	2.19	0.0275
Error: MS(Error)	25	9.768787	0.390751		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.030766	0.030766	0.04	0.8512
Error	25	21.412060	0.856482		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.006533	0.006533	0.02	0.8982
trt	1	0.837479	0.837479	2.14	0.1557
subject(sequence)	25	21.412060	0.856482	2.19	0.0275
Error: MS(Error)	25	9.768787	0.390751		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCLST	LSMEAN	Pr > t
A	8.89431407		0.1557
B	8.64507378		

trt	LN_AUCLST	LSMEAN	90% Confidence Limits	
A	8.894314	8.688682	9.099946	
B	8.645074	8.439442	8.850706	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.249240	-0.041567	0.540047

Dependent Variable: LN_AUCLST

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	0.24924028	0.17024780	1.46	0.1557	-0.04156692 0.54004749

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	27 101 201 202 203 204 205 301 302 303 304 402 404 406 407 408 409 410 411 412 413 414 501 502 503 505 507 508
sequence	2 AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	54
Number of Observations Used	54

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL)

The GLM Procedure

Dependent Variable: LN_AUCIFO

R-Square	Coeff Var	Root MSE	LN_AUCIFO Mean
0.845550	4.690616	0.419817	8.950149

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.16367800	0.16367800	0.93	0.3444
period	1	0.11005743	0.11005743	0.62	0.4368
trt	1	0.72158060	0.72158060	4.09	0.0538
subject(sequence)	25	23.12666887	0.92506675	5.25	<.0001

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.16367800	0.16367800	0.93	0.3444
period	1	0.09003600	0.09003600	0.51	0.4814
trt	1	0.72158060	0.72158060	4.09	0.0538
subject(sequence)	25	23.12666887	0.92506675	5.25	<.0001

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.16367800	0.16367800	0.93	0.3444
period	1	0.09003600	0.09003600	0.51	0.4814
trt	1	0.72158060	0.72158060	4.09	0.0538
subject(sequence)	25	23.12666887	0.92506675	5.25	<.0001

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.16367800	0.16367800	0.93	0.3444
period	1	0.09003600	0.09003600	0.51	0.4814
trt	1	0.72158060	0.72158060	4.09	0.0538
subject(sequence)	25	23.12666887	0.92506675	5.25	<.0001

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL)

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.163678	0.163678	0.18	0.6776
Error	25	23.126669	0.925067		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.110057	0.110057	0.62	0.4368
trt	1	0.721581	0.721581	4.09	0.0538
subject(sequence)	25	23.126669	0.925067	5.25	<.0001
Error: MS(Error)	25	4.406161	0.176246		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.163678	0.163678	0.18	0.6776
Error	25	23.126669	0.925067		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.090036	0.090036	0.51	0.4814
trt	1	0.721581	0.721581	4.09	0.0538
subject(sequence)	25	23.126669	0.925067	5.25	<.0001
Error: MS(Error)	25	4.406161	0.176246		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.163678	0.163678	0.18	0.6776
Error	25	23.126669	0.925067		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.090036	0.090036	0.51	0.4814
trt	1	0.721581	0.721581	4.09	0.0538
subject(sequence)	25	23.126669	0.925067	5.25	<.0001
Error: MS(Error)	25	4.406161	0.176246		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.163678	0.163678	0.18	0.6776
Error	25	23.126669	0.925067		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.090036	0.090036	0.51	0.4814
trt	1	0.721581	0.721581	4.09	0.0538
subject(sequence)	25	23.126669	0.925067	5.25	<.0001
Error: MS(Error)	25	4.406161	0.176246		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCIFO	LSMEAN	Pr > t
A	9.06786545		0.0538
B	8.83651326		

trt	LN_AUCIFO	LSMEAN	90% Confidence Limits	
A	9.067865		8.929763	9.205967
B	8.836513		8.698411	8.974615

Least Squares Means for Effect trt

Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.231352	0.036046	0.426658

Dependent Variable: LN_AUCIFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.23135219	0.11433820	2.02	0.05380	0.03604644	0.42665794

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: C_{\max} (ng/mL)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	28 101 201 202 203 204 205 301 302 303 304 402 404 406 407 408 409 410 411 412 413 414 501 502 503 505 506 507 508
sequence2	AB BA
period	1 2
trt	A B

Number of Observations Read	56
Number of Observations Used	56

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: C_{\max} (ng/mL)

The GLM Procedure

Dependent Variable: LN_CMAX

R-Square	Coeff Var	Root MSE	LN_CMAX Mean
0.507826	12.97276	0.692244	5.336136

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.04753083	0.04753083	0.10	0.7553
period	1	0.03349429	0.03349429	0.07	0.7936
trt	1	0.01574029	0.01574029	0.03	0.8576
subject(sequence)	26	12.75869056	0.49071887	1.02	0.4761

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.04753083	0.04753083	0.10	0.7553
period	1	0.03349429	0.03349429	0.07	0.7936
trt	1	0.01574029	0.01574029	0.03	0.8576
subject(sequence)	26	12.75869056	0.49071887	1.02	0.4761

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.04753083	0.04753083	0.10	0.7553
period	1	0.03349429	0.03349429	0.07	0.7936
trt	1	0.01574029	0.01574029	0.03	0.8576
subject(sequence)	26	12.75869056	0.49071887	1.02	0.4761

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.04753083	0.04753083	0.10	0.7553
period	1	0.03349429	0.03349429	0.07	0.7936
trt	1	0.01574029	0.01574029	0.03	0.8576
subject(sequence)	26	12.75869056	0.49071887	1.02	0.4761

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: C_{\max} (ng/mL)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.047531	0.047531	0.10	0.7581
Error	26	12.758691	0.490719		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	0.033494	0.033494	0.07	0.7936
trt	1	0.015740	0.015740	0.03	0.8576
subject(sequence)	26	12.758691	0.490719	1.02	0.4761
Error: MS(Error)	26	12.459242	0.479202		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.047531	0.047531	0.10	0.7581
Error	26	12.758691	0.490719		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.033494	0.033494	0.07	0.7936
trt	1	0.015740	0.015740	0.03	0.8576
subject(sequence)	26	12.758691	0.490719	1.02	0.4761
Error: MS(Error)	26	12.459242	0.479202		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: C_{\max} (ng/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.047531	0.047531	0.10	0.7581
Error	26	12.758691	0.490719		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.033494	0.033494	0.07	0.7936
trt	1	0.015740	0.015740	0.03	0.8576
subject(sequence)	26	12.758691	0.490719	1.02	0.4761
Error: MS(Error)	26	12.459242	0.479202		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.047531	0.047531	0.10	0.7581
Error	26	12.758691	0.490719		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.033494	0.033494	0.07	0.7936
trt	1	0.015740	0.015740	0.03	0.8576
subject(sequence)	26	12.758691	0.490719	1.02	0.4761
Error: MS(Error)	26	12.459242	0.479202		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_CMAX	LSMEAN	Pr > t
A	5.31937021		0.8576
B	5.35290089		

trt	LN_CMAX	LSMEAN	90% Confidence Limits	
A	5.319370		5.096238	5.542502
B	5.352901		5.129769	5.576033

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.033531	-0.349087	0.282026

Dependent Variable: LN_CMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.03353068	0.18500996	-0.18	0.8576	-0.34908699 0.28202562

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	28 101 201 202 203 204 205 301 302 303 304 402 404 406 407 408 409 410 411 412 413 414 501 502 503 505 506 507 508
sequence2	AB BA
period	1 2
trt	A B

Number of Observations Read	55
Number of Observations Used	55

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

The GLM Procedure

Dependent Variable: LN_CLFOW

R-Square	Coeff Var	Root MSE	LN_CLFOW Mean
0.855739	-11.79232	0.435284	-3.691249

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.40957690	0.40957690	2.16	0.1540
period	1	0.04998166	0.04998166	0.26	0.6120
trt	1	1.58691124	1.58691124	8.38	0.0078
subject(sequence)	26	26.05157410	1.00198362	5.29	<.0001

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.38456027	0.38456027	2.03	0.1666
period	1	0.07279375	0.07279375	0.38	0.5410
trt	1	1.38322100	1.38322100	7.30	0.0122
subject(sequence)	26	26.05157410	1.00198362	5.29	<.0001

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.47095872	0.47095872	2.49	0.1275
period	1	0.07279375	0.07279375	0.38	0.5410
trt	1	1.38322100	1.38322100	7.30	0.0122
subject(sequence)	26	26.05157410	1.00198362	5.29	<.0001

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.47095872	0.47095872	2.49	0.1275
period	1	0.07279375	0.07279375	0.38	0.5410
trt	1	1.38322100	1.38322100	7.30	0.0122
subject(sequence)	26	26.05157410	1.00198362	5.29	<.0001

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.409577	0.409577	0.41	0.5299
Error	25.903	26.164431	1.010105		

Error: 1.01*MS(subject(sequence)) - 0.01*MS(Error)
 * This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.049982	0.049982	0.25	0.6185
Error	27.469	5.411267	0.196998		

Error: 0.0093*MS(subject(sequence)) + 0.9907*MS(Error)
 * This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	1.586911	1.586911	8.04	0.0085
Error	27.564	5.438057	0.197288		

Error: 0.0096*MS(subject(sequence)) + 0.9904*MS(Error)

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	26	26.051574	1.001984	5.29	<.0001
Error: MS(Error)	25	4.736800	0.189472		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.384560	0.384560	0.38	0.5426
Error	25.903	26.164357	1.010100		
Error: 1.01*MS(subject(sequence)) - 0.01*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.072794	0.072794	0.38	0.5410
trt	1	1.383221	1.383221	7.30	0.0122
subject(sequence)	26	26.051574	1.001984	5.29	<.0001
Error: MS(Error)	25	4.736800	0.189472		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.470959	0.470959	0.48	0.4958
Error	26.182	25.847523	0.987232		
Error: 0.9818*MS(subject(sequence)) + 0.0182*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.072794	0.072794	0.38	0.5410
trt	1	1.383221	1.383221	7.30	0.0122
subject(sequence)	26	26.051574	1.001984	5.29	<.0001
Error: MS(Error)	25	4.736800	0.189472		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.470959	0.470959	0.48	0.4958
Error	26.182	25.847523	0.987232		
Error: 0.9818*MS(subject(sequence)) + 0.0182*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.072794	0.072794	0.38	0.5410
trt	1	1.383221	1.383221	7.30	0.0122
subject(sequence)	26	26.051574	1.001984	5.29	<.0001
Error: MS(Error)	25	4.736800	0.189472		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFOW	LSMEAN	Pr > t
A	-3.86011863		0.0122
B	-3.53980386		

trt	LN_CLFOW	LSMEAN	90% Confidence Limits	
A	-3.860119		-4.000632	-3.719605
B	-3.539804		-3.685621	-3.393986

Least Squares Means for Effect trt

Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.320315	-0.522816	-0.117814

Dependent Variable: LN_CLFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	-0.32031478	0.11855059	-2.70	0.0122	-0.52281587	-0.11781369

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	28 101 201 202 203 204 205 301 302 303 304 402 404 406 407 408 409 410 411 412 413 414 501 502 503 505 506 507 508
sequence2	AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	55
Number of Observations Used	55

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h)

The GLM Procedure

Dependent Variable: LN_CLFO

R-Square	Coeff Var	Root MSE	LN_CLFO Mean
0.853402	60.55102	0.435284	0.718871

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.10625215	0.10625215	0.56	0.4609
period	1	0.04807082	0.04807082	0.25	0.6189
trt	1	1.59800963	1.59800963	8.43	0.0076
subject(sequence)	26	25.82232211	0.99316624	5.24	<.0001

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.09367124	0.09367124	0.49	0.4885
period	1	0.07279375	0.07279375	0.38	0.5410
trt	1	1.38322100	1.38322100	7.30	0.0122
subject(sequence)	26	25.82232211	0.99316624	5.24	<.0001

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.14399810	0.14399810	0.76	0.3916
period	1	0.07279375	0.07279375	0.38	0.5410
trt	1	1.38322100	1.38322100	7.30	0.0122
subject(sequence)	26	25.82232211	0.99316624	5.24	<.0001

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.14399810	0.14399810	0.76	0.3916
period	1	0.07279375	0.07279375	0.38	0.5410
trt	1	1.38322100	1.38322100	7.30	0.0122
subject(sequence)	26	25.82232211	0.99316624	5.24	<.0001

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.106252	0.106252	0.11	0.7472
Error	25.902	25.932889	1.001199		

Error: 1.01*MS(subject(sequence)) - 0.01*MS(Error)

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.048071	0.048071	0.24	0.6252
Error	27.447	5.404762	0.196916		

Error: 0.0093*MS(subject(sequence)) + 0.9907*MS(Error)

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	1.598010	1.598010	8.10	0.0083
Error	27.542	5.431288	0.197203		

Error: 0.0096*MS(subject(sequence)) + 0.9904*MS(Error)

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	26	25.822322	0.993166	5.24	<.0001
Error: MS(Error)	25	4.736800	0.189472		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.093671	0.093671	0.09	0.7621
Error	25.902	25.932817	1.001194		
Error: 1.01*MS(subject(sequence)) - 0.01*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.072794	0.072794	0.38	0.5410
trt	1	1.383221	1.383221	7.30	0.0122
subject(sequence)	26	25.822322	0.993166	5.24	<.0001
Error: MS(Error)	25	4.736800	0.189472		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.143998	0.143998	0.15	0.7044
Error	26.183	25.622439	0.978575		
Error: 0.9818*MS(subject(sequence)) + 0.0182*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.072794	0.072794	0.38	0.5410
trt	1	1.383221	1.383221	7.30	0.0122
subject(sequence)	26	25.822322	0.993166	5.24	<.0001
Error: MS(Error)	25	4.736800	0.189472		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.143998	0.143998	0.15	0.7044
Error	26.183	25.622439	0.978575		
Error: 0.9818*MS(subject(sequence)) + 0.0182*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.072794	0.072794	0.38	0.5410
trt	1	1.383221	1.383221	7.30	0.0122
subject(sequence)	26	25.822322	0.993166	5.24	<.0001
Error: MS(Error)	25	4.736800	0.189472		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFO	LSMEAN	Pr > t
A	0.55019981		0.0122
B	0.87051459		

trt	LN_CLFO	LSMEAN	90% Confidence Limits	
A	0.550200	0.409687	0.690713	
B	0.870515	0.724697	1.016332	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.320315	-0.522816	-0.117814

Dependent Variable: LN_CLFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	-0.32031478	0.11855059	-2.70	0.0122	-0.52281587	-0.11781369

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	28 101 201 202 203 204 205 301 302 303 304 402 404 406 407 408 409 410 411 412 413 414 501 502 503 505 506 507 508
sequence2	AB BA
period	1 2
trt	A B

Number of Observations Read	55
Number of Observations Used	55

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

The GLM Procedure

Dependent Variable: LN_VZFOW

R-Square	Coeff Var	Root MSE	LN_VZFOW Mean
0.632660	86.92906	0.774751	0.891245

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.47432211	0.47432211	0.79	0.3825
period	1	0.06567700	0.06567700	0.11	0.7436
trt	1	1.61360452	1.61360452	2.69	0.1136
subject(sequence)	26	23.69080306	0.91118473	1.52	0.1502

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.51435042	0.51435042	0.86	0.3635
period	1	0.03845720	0.03845720	0.06	0.8022
trt	1	1.38527031	1.38527031	2.31	0.1413
subject(sequence)	26	23.69080306	0.91118473	1.52	0.1502

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.39567269	0.39567269	0.66	0.4245
period	1	0.03845720	0.03845720	0.06	0.8022
trt	1	1.38527031	1.38527031	2.31	0.1413
subject(sequence)	26	23.69080306	0.91118473	1.52	0.1502

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.39567269	0.39567269	0.66	0.4245
period	1	0.03845720	0.03845720	0.06	0.8022
trt	1	1.38527031	1.38527031	2.31	0.1413
subject(sequence)	26	23.69080306	0.91118473	1.52	0.1502

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFLOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.474322	0.474322	0.52	0.4779
Error	25.661	23.461639	0.914293		

Error: $1.01 \cdot MS(\text{subject}(\text{sequence})) - 0.01 \cdot MS(\text{Error})$
 * This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.065677	0.065677	0.11	0.7441
Error	25.71	15.505995	0.603119		

Error: $0.0093 \cdot MS(\text{subject}(\text{sequence})) + 0.9907 \cdot MS(\text{Error})$
 * This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	1.613605	1.613605	2.67	0.1141
Error	25.737	15.525466	0.603230		

Error: $0.0096 \cdot MS(\text{subject}(\text{sequence})) + 0.9904 \cdot MS(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	26	23.690803	0.911185	1.52	0.1502
Error: MS(Error)	25	15.005966	0.600239		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFLOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.514350	0.514350	0.56	0.4600
Error	25.661	23.461786	0.914291		
Error: 1.01*MS(subject(sequence)) - 0.01*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.038457	0.038457	0.06	0.8022
trt	1	1.385270	1.385270	2.31	0.1413
subject(sequence)	26	23.690803	0.911185	1.52	0.1502
Error: MS(Error)	25	15.005966	0.600239		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFLOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.395673	0.395673	0.44	0.5143
Error	26.633	24.117372	0.905539		
Error: 0.9818*MS(subject(sequence)) + 0.0182*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.038457	0.038457	0.06	0.8022
trt	1	1.385270	1.385270	2.31	0.1413
subject(sequence)	26	23.690803	0.911185	1.52	0.1502
Error: MS(Error)	25	15.005966	0.600239		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.395673	0.395673	0.44	0.5143
Error	26.633	24.117372	0.905539		
Error: 0.9818*MS(subject(sequence)) + 0.0182*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.038457	0.038457	0.06	0.8022
trt	1	1.385270	1.385270	2.31	0.1413
subject(sequence)	26	23.690803	0.911185	1.52	0.1502
Error: MS(Error)	25	15.005966	0.600239		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_VZFOW	LSMEAN	Pr > t
A	0.72543476		0.1413
B	1.04598673		

trt	LN_VZFOW	LSMEAN	90% Confidence Limits	
A	0.725435		0.475339	0.975531
B	1.045987		0.786450	1.305524

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.320552	-0.680979	0.039875

Dependent Variable: LN_VZFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.32055197	0.21100520	-1.52	0.1413	-0.68097856 0.03987461

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	28 101 201 202 203 204 205 301 302 303 304 402 404 406 407 408 409 410 411 412 413 414 501 502 503 505 506 507 508
sequence2	AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	55
Number of Observations Used	55

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L)

The GLM Procedure

Dependent Variable: LN_VZFO

R-Square	Coeff Var	Root MSE	LN_VZFO Mean
0.717804	14.61417	0.774751	5.301365

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.00546546	1.00546546	1.68	0.2074
period	1	0.06790738	0.06790738	0.11	0.7394
trt	1	1.62479570	1.62479570	2.71	0.1124
subject(sequence)	26	35.47146425	1.36428709	2.27	0.0218

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.06348469	1.06348469	1.77	0.1952
period	1	0.03845720	0.03845720	0.06	0.8022
trt	1	1.38527031	1.38527031	2.31	0.1413
subject(sequence)	26	35.47146425	1.36428709	2.27	0.0218

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.87575663	0.87575663	1.46	0.2384
period	1	0.03845720	0.03845720	0.06	0.8022
trt	1	1.38527031	1.38527031	2.31	0.1413
subject(sequence)	26	35.47146425	1.36428709	2.27	0.0218

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.87575663	0.87575663	1.46	0.2384
period	1	0.03845720	0.03845720	0.06	0.8022
trt	1	1.38527031	1.38527031	2.31	0.1413
subject(sequence)	26	35.47146425	1.36428709	2.27	0.0218

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L)

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	1.005465	1.005465	0.73	0.3998
Error	25.774	35.359383	1.371924		

Error: $1.01 \cdot \text{MS}(\text{subject}(\text{sequence})) - 0.01 \cdot \text{MS}(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.067907	0.067907	0.11	0.7408
Error	26.062	15.828153	0.607316		

Error: $0.0093 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.9907 \cdot \text{MS}(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	1.624796	1.624796	2.67	0.1140
Error	26.104	15.860304	0.607588		

Error: $0.0096 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.9904 \cdot \text{MS}(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	26	35.471464	1.364287	2.27	0.0218
Error: MS(Error)	25	15.005966	0.600239		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.063485	1.063485	0.78	0.3868
Error	25.774	35.359454	1.371919		
Error: 1.01*MS(subject(sequence)) - 0.01*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.038457	0.038457	0.06	0.8022
trt	1	1.385270	1.385270	2.31	0.1413
subject(sequence)	26	35.471464	1.364287	2.27	0.0218
Error: MS(Error)	25	15.005966	0.600239		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.875757	0.875757	0.65	0.4278
Error	26.423	35.681954	1.350415		
Error: 0.9818*MS(subject(sequence)) + 0.0182*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.038457	0.038457	0.06	0.8022
trt	1	1.385270	1.385270	2.31	0.1413
subject(sequence)	26	35.471464	1.364287	2.27	0.0218
Error: MS(Error)	25	15.005966	0.600239		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.875757	0.875757	0.65	0.4278
Error	26.423	35.681954	1.350415		
Error: 0.9818*MS(subject(sequence)) + 0.0182*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.038457	0.038457	0.06	0.8022
trt	1	1.385270	1.385270	2.31	0.1413
subject(sequence)	26	35.471464	1.364287	2.27	0.0218
Error: MS(Error)	25	15.005966	0.600239		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_VZFO	LSMEAN	Pr > t
A	5.13575320		0.1413
B	5.45630517		

trt	LN_VZFO	LSMEAN	90% Confidence Limits	
A	5.135753		4.885657	5.385849
B	5.456305		5.196768	5.715842

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.320552	-0.680979	0.039875

Dependent Variable: LN_VZFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.32055197	0.21100520	-1.52	0.1413	-0.68097856 0.03987461

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	28 101 201 202 203 204 205 301 302 303 304 402 404 406 407 408 409 410 411 412 413 414 501 502 503 505 506 507 508
sequence2	AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	56
Number of Observations Used	56

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: T_{max} (h)

The GLM Procedure

Dependent Variable: TMAX

R-Square	Coeff Var	Root MSE	TMAX Mean
0.501084	86.12793	0.961541	1.116411

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.04855716	0.04855716	0.05	0.8205
period	1	0.16973016	0.16973016	0.18	0.6718
trt	1	7.32326787	7.32326787	7.92	0.0092
subject(sequence)	26	16.60152389	0.63852015	0.69	0.8244

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.04855716	0.04855716	0.05	0.8205
period	1	0.16973016	0.16973016	0.18	0.6718
trt	1	7.32326787	7.32326787	7.92	0.0092
subject(sequence)	26	16.60152389	0.63852015	0.69	0.8244

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.04855716	0.04855716	0.05	0.8205
period	1	0.16973016	0.16973016	0.18	0.6718
trt	1	7.32326787	7.32326787	7.92	0.0092
subject(sequence)	26	16.60152389	0.63852015	0.69	0.8244

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.04855716	0.04855716	0.05	0.8205
period	1	0.16973016	0.16973016	0.18	0.6718
trt	1	7.32326787	7.32326787	7.92	0.0092
subject(sequence)	26	16.60152389	0.63852015	0.69	0.8244

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.048557	0.048557	0.08	0.7849
Error	26	16.601524	0.638520		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	0.169730	0.169730	0.18	0.6718
trt	1	7.323268	7.323268	7.92	0.0092
subject(sequence)	26	16.601524	0.638520	0.69	0.8244
Error: MS(Error)	26	24.038608	0.924562		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.048557	0.048557	0.08	0.7849
Error	26	16.601524	0.638520		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.169730	0.169730	0.18	0.6718
trt	1	7.323268	7.323268	7.92	0.0092
subject(sequence)	26	16.601524	0.638520	0.69	0.8244
Error: MS(Error)	26	24.038608	0.924562		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.048557	0.048557	0.08	0.7849
Error	26	16.601524	0.638520		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.169730	0.169730	0.18	0.6718
trt	1	7.323268	7.323268	7.92	0.0092
subject(sequence)	26	16.601524	0.638520	0.69	0.8244
Error: MS(Error)	26	24.038608	0.924562		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.048557	0.048557	0.08	0.7849
Error	26	16.601524	0.638520		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.169730	0.169730	0.18	0.6718
trt	1	7.323268	7.323268	7.92	0.0092
subject(sequence)	26	16.601524	0.638520	0.69	0.8244
Error: MS(Error)	26	24.038608	0.924562		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h)

Least Squares Means

		H0:LSMean1=LSMean2	
trt	TMAX LSMEAN		Pr > t
A	1.47803571		0.0092
B	0.75478571		

trt	TMAX LSMEAN	90% Confidence Limits	
A	1.478036	1.168101	1.787971
B	0.754786	0.444851	1.064721

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.723250	0.284936	1.161564

Dependent Variable: TMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.72325000	0.25698275	2.81	0.00920	0.28493562	1.16156438

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	28 101 201 202 203 204 205 301 302 303 304 402 404 406 407 408 409 410 411 412 413 414 501 502 503 505 506 507 508
sequence2	AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	55
Number of Observations Used	55

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h)

The GLM Procedure

Dependent Variable: LAMZ

R-Square	Coeff Var	Root MSE	LAMZ Mean
0.946551	25.74042	0.003426	0.013309

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00056954	0.00056954	48.53	<.0001
period	1	0.00000351	0.00000351	0.30	0.5896
trt	1	0.00000846	0.00000846	0.72	0.4039
subject(sequence)	26	0.00461412	0.00017747	15.12	<.0001

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00057011	0.00057011	48.58	<.0001
period	1	0.00000301	0.00000301	0.26	0.6167
trt	1	0.00000867	0.00000867	0.74	0.3981
subject(sequence)	26	0.00461412	0.00017747	15.12	<.0001

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00056257	0.00056257	47.94	<.0001
period	1	0.00000301	0.00000301	0.26	0.6167
trt	1	0.00000867	0.00000867	0.74	0.3981
subject(sequence)	26	0.00461412	0.00017747	15.12	<.0001

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00056257	0.00056257	47.94	<.0001
period	1	0.00000301	0.00000301	0.26	0.6167
trt	1	0.00000867	0.00000867	0.74	0.3981
subject(sequence)	26	0.00461412	0.00017747	15.12	<.0001

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.000570	0.000570	3.18	0.0863
Error	25.966	0.004651	0.000179		

Error: $1.01 \cdot MS(\text{subject}(\text{sequence})) - 0.01 \cdot MS(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.000003505	0.000003505	0.26	0.6108
Error	31.955	0.000424	0.000013270		

Error: $0.0093 \cdot MS(\text{subject}(\text{sequence})) + 0.9907 \cdot MS(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.000008459	0.000008459	0.63	0.4315
Error	32.215	0.000429	0.000013329		

Error: $0.0096 \cdot MS(\text{subject}(\text{sequence})) + 0.9904 \cdot MS(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	26	0.004614	0.000177	15.12	<.0001
Error: MS(Error)	25	0.000293	0.000011735		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.000570	0.000570	3.18	0.0861
Error	25.966	0.004651	0.000179		
Error: $1.01 * MS(\text{subject}(\text{sequence})) - 0.01 * MS(\text{Error})$					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.000003015	0.000003015	0.26	0.6167
trt	1	0.000008674	0.000008674	0.74	0.3981
subject(sequence)	26	0.004614	0.000177	15.12	<.0001
Error: MS(Error)	25	0.000293	0.000011735		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.000563	0.000563	3.22	0.0841
Error	26.064	0.004547	0.000174		
Error: $0.9818 * MS(\text{subject}(\text{sequence})) + 0.0182 * MS(\text{Error})$					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.000003015	0.000003015	0.26	0.6167
trt	1	0.000008674	0.000008674	0.74	0.3981
subject(sequence)	26	0.004614	0.000177	15.12	<.0001
Error: MS(Error)	25	0.000293	0.000011735		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.000563	0.000563	3.22	0.0841
Error	26.064	0.004547	0.000174		
Error: 0.9818*MS(subject(sequence)) + 0.0182*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.000003015	0.000003015	0.26	0.6167
trt	1	0.000008674	0.000008674	0.74	0.3981
subject(sequence)	26	0.004614	0.000177	15.12	<.0001
Error: MS(Error)	25	0.000293	0.000011735		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h)

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LAMZ LSMEAN		Pr > t
A	0.01363966		0.3981
B	0.01283753		

trt	LAMZ LSMEAN	90% Confidence Limits	
A	0.013640	0.012534	0.014745
B	0.012838	0.011690	0.013985

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.000802	-0.000792	0.002396

Dependent Variable: LAMZ

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	0.00080213	0.00093299	0.86	0.3981	-0.00079154 0.00239581

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	28 101 201 202 203 204 205 301 302 303 304 402 404 406 407 408 409 410 411 412 413 414 501 502 503 505 506 507 508
sequence2	AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	55
Number of Observations Used	55

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

The GLM Procedure

Dependent Variable: LAMZHL

R-Square	Coeff Var	Root MSE	LAMZHL Mean
0.606732	108.1335	103.9234	96.10660

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	4800.1835	4800.1835	0.44	0.5111
period	1	25036.9728	25036.9728	2.32	0.1404
trt	1	15.8745	15.8745	0.00	0.9697
subject(sequence)	26	386704.1776	14873.2376	1.38	0.2134

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	5200.3781	5200.3781	0.48	0.4941
period	1	23912.6921	23912.6921	2.21	0.1493
trt	1	35.5975	35.5975	0.00	0.9547
subject(sequence)	26	386704.1776	14873.2376	1.38	0.2134

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	4819.6458	4819.6458	0.45	0.5102
period	1	23912.6921	23912.6921	2.21	0.1493
trt	1	35.5975	35.5975	0.00	0.9547
subject(sequence)	26	386704.1776	14873.2376	1.38	0.2134

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	4819.6458	4819.6458	0.45	0.5102
period	1	23912.6921	23912.6921	2.21	0.1493
trt	1	35.5975	35.5975	0.00	0.9547
subject(sequence)	26	386704.1776	14873.2376	1.38	0.2134

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	4800.183539	4800.183539	0.32	0.5754
Error	25.626	382189	14914		

Error: $1.01 \cdot \text{MS}(\text{subject}(\text{sequence})) - 0.01 \cdot \text{MS}(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	25037	25037	2.31	0.1408
Error	25.644	277923	10838		

Error: $0.0093 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.9907 \cdot \text{MS}(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	15.874529	15.874529	0.00	0.9698
Error	25.669	278231	10839		

Error: $0.0096 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.9904 \cdot \text{MS}(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	26	386704	14873	1.38	0.2134
Error: MS(Error)	25	270002	10800		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	5200.378088	5200.378088	0.35	0.5600
Error	25.627	382192	14914		
Error: 1.01*MS(subject(sequence)) - 0.01*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	23913	23913	2.21	0.1493
trt	1	35.597453	35.597453	0.00	0.9547
subject(sequence)	26	386704	14873	1.38	0.2134
Error: MS(Error)	25	270002	10800		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	4819.645818	4819.645818	0.33	0.5730
Error	26.698	395110	14799		
Error: 0.9818*MS(subject(sequence)) + 0.0182*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	23913	23913	2.21	0.1493
trt	1	35.597453	35.597453	0.00	0.9547
subject(sequence)	26	386704	14873	1.38	0.2134
Error: MS(Error)	25	270002	10800		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	4819.645818	4819.645818	0.33	0.5730
Error	26.698	395110	14799		
Error: 0.9818*MS(subject(sequence)) + 0.0182*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	23913	23913	2.21	0.1493
trt	1	35.597453	35.597453	0.00	0.9547
subject(sequence)	26	386704	14873	1.38	0.2134
Error: MS(Error)	25	270002	10800		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LAMZHL	LSMEAN	Pr > t
A		97.1991044	0.9547
B		95.5741519	

trt	LAMZHL	LSMEAN	90% Confidence Limits	
A		97.199104	63.651764	130.746444
B		95.574152	60.760432	130.387872

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	1.624952	-46.721910	49.971815

Dependent Variable: LAMZHL

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	1.62495244	28.3037931	0.06	0.9547	-46.72191032 49.97181521

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	9	101 201 202 203 204 301 402 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	18
Number of Observations Used	18

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL)

The GLM Procedure

Dependent Variable: LN_AUCLST

R-Square	Coeff Var	Root MSE	LN_AUCLST Mean
0.756552	3.539328	0.317973	8.983989

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00053007	0.00053007	0.01	0.9441
trt	1	0.02765765	0.02765765	0.27	0.6151
subject(sequence)	7	2.48544900	0.35506414	3.51	0.0496

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00053007	0.00053007	0.01	0.9441
trt	1	0.02765765	0.02765765	0.27	0.6151
subject(sequence)	7	2.48544900	0.35506414	3.51	0.0496

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00053007	0.00053007	0.01	0.9441
trt	1	0.02765765	0.02765765	0.27	0.6151
subject(sequence)	7	2.48544900	0.35506414	3.51	0.0496

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00053007	0.00053007	0.01	0.9441
trt	1	0.02765765	0.02765765	0.27	0.6151
subject(sequence)	7	2.48544900	0.35506414	3.51	0.0496

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL)

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.000530	0.000530	0.00	0.9703
Error	7	2.485449	0.355064		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.027658	0.027658	0.27	0.6151
subject(sequence)	7	2.485449	0.355064	3.51	0.0496
Error: MS(Error)	8	0.808854	0.101107		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.000530	0.000530	0.00	0.9703
Error	7	2.485449	0.355064		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.027658	0.027658	0.27	0.6151
subject(sequence)	7	2.485449	0.355064	3.51	0.0496
Error: MS(Error)	8	0.808854	0.101107		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.000530	0.000530	0.00	0.9703
Error	7	2.485449	0.355064		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.027658	0.027658	0.27	0.6151
subject(sequence)	7	2.485449	0.355064	3.51	0.0496
Error: MS(Error)	8	0.808854	0.101107		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.000530	0.000530	0.00	0.9703
Error	7	2.485449	0.355064		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.027658	0.027658	0.27	0.6151
subject(sequence)	7	2.485449	0.355064	3.51	0.0496
Error: MS(Error)	8	0.808854	0.101107		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCLST	LSMEAN	Pr > t
B	8.94418393		0.6151
C	9.02258127		

trt	LN_AUCLST	LSMEAN	90% Confidence Limits	
B	8.944184	8.746474	9.141894	
C	9.022581	8.824871	9.220291	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.078397	-0.357132	0.200337

Dependent Variable: LN_AUCLST

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	0.07839735	0.14989384	0.52	0.6151	-0.20033744	0.35713214

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: $AUC_{0-\infty}$ (h*ng/mL)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	9	101 201 202 203 204 301 402 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	18
Number of Observations Used	18

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL)

The GLM Procedure

Dependent Variable: LN_AUCIFO

R-Square	Coeff Var	Root MSE	LN_AUCIFO Mean
0.808882	3.355740	0.305435	9.101874

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.01021615	0.01021615	0.11	0.7492
trt	1	0.06391088	0.06391088	0.69	0.4318
subject(sequence)	7	3.08458984	0.44065569	4.72	0.0222

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.01021615	0.01021615	0.11	0.7492
trt	1	0.06391088	0.06391088	0.69	0.4318
subject(sequence)	7	3.08458984	0.44065569	4.72	0.0222

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.01021615	0.01021615	0.11	0.7492
trt	1	0.06391088	0.06391088	0.69	0.4318
subject(sequence)	7	3.08458984	0.44065569	4.72	0.0222

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.01021615	0.01021615	0.11	0.7492
trt	1	0.06391088	0.06391088	0.69	0.4318
subject(sequence)	7	3.08458984	0.44065569	4.72	0.0222

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL)

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.010216	0.010216	0.02	0.8833
Error	7	3.084590	0.440656		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.063911	0.063911	0.69	0.4318
subject(sequence)	7	3.084590	0.440656	4.72	0.0222
Error: MS(Error)	8	0.746325	0.093291		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.010216	0.010216	0.02	0.8833
Error	7	3.084590	0.440656		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.063911	0.063911	0.69	0.4318
subject(sequence)	7	3.084590	0.440656	4.72	0.0222
Error: MS(Error)	8	0.746325	0.093291		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.010216	0.010216	0.02	0.8833
Error	7	3.084590	0.440656		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.063911	0.063911	0.69	0.4318
subject(sequence)	7	3.084590	0.440656	4.72	0.0222
Error: MS(Error)	8	0.746325	0.093291		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.010216	0.010216	0.02	0.8833
Error	7	3.084590	0.440656		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.063911	0.063911	0.69	0.4318
subject(sequence)	7	3.084590	0.440656	4.72	0.0222
Error: MS(Error)	8	0.746325	0.093291		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCIFO	LSMEAN	Pr > t
B	9.03962326		0.4318
C	9.15879716		

trt	LN_AUCIFO	LSMEAN	90% Confidence Limits	
B	9.039623		8.849709	9.229538
C	9.158797		8.968883	9.348712

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.119174	-0.386918	0.148570

Dependent Variable: LN_AUCIFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	0.11917390	0.14398354	0.83	0.4318	-0.14857041 0.38691820

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: C_{\max} (ng/mL)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	9	101 201 202 203 204 301 402 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	18
Number of Observations Used	18

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: C_{\max} (ng/mL)

The GLM Procedure

Dependent Variable: LN_CMAX

R-Square	Coeff Var	Root MSE	LN_CMAX Mean
0.611429	8.546452	0.452382	5.293215

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.02048684	0.02048684	0.10	0.7598
trt	1	0.16288431	0.16288431	0.80	0.3984
subject(sequence)	7	2.39281131	0.34183019	1.67	0.2436

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.02048684	0.02048684	0.10	0.7598
trt	1	0.16288431	0.16288431	0.80	0.3984
subject(sequence)	7	2.39281131	0.34183019	1.67	0.2436

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.02048684	0.02048684	0.10	0.7598
trt	1	0.16288431	0.16288431	0.80	0.3984
subject(sequence)	7	2.39281131	0.34183019	1.67	0.2436

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.02048684	0.02048684	0.10	0.7598
trt	1	0.16288431	0.16288431	0.80	0.3984
subject(sequence)	7	2.39281131	0.34183019	1.67	0.2436

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: C_{\max} (ng/mL)

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.020487	0.020487	0.06	0.8136
Error	7	2.392811	0.341830		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.162884	0.162884	0.80	0.3984
subject(sequence)	7	2.392811	0.341830	1.67	0.2436
Error: MS(Error)	8	1.637197	0.204650		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.020487	0.020487	0.06	0.8136
Error	7	2.392811	0.341830		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.162884	0.162884	0.80	0.3984
subject(sequence)	7	2.392811	0.341830	1.67	0.2436
Error: MS(Error)	8	1.637197	0.204650		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: C_{\max} (ng/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.020487	0.020487	0.06	0.8136
Error	7	2.392811	0.341830		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.162884	0.162884	0.80	0.3984
subject(sequence)	7	2.392811	0.341830	1.67	0.2436
Error: MS(Error)	8	1.637197	0.204650		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.020487	0.020487	0.06	0.8136
Error	7	2.392811	0.341830		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.162884	0.162884	0.80	0.3984
subject(sequence)	7	2.392811	0.341830	1.67	0.2436
Error: MS(Error)	8	1.637197	0.204650		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: C_{max} (ng/mL)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_CMAX	LSMEAN	Pr > t
B	5.39211392		0.3984
C	5.20186011		

trt	LN_CMAX	LSMEAN	90% Confidence Limits	
B	5.392114		5.110830	5.673398
C	5.201860		4.920576	5.483144

Least Squares Means for Effect trt

Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.190254	-0.206304	0.586812

Dependent Variable: LN_CMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.19025381	0.21325497	-0.89	0.3984	-0.58681167 0.20630405

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	9	101 201 202 203 204 301 402 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	18
Number of Observations Used	18

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

The GLM Procedure

Dependent Variable: LN_CLFOW

R-Square	Coeff Var	Root MSE	LN_CLFOW Mean
0.830934	-8.026668	0.309145	-3.851478

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.10324202	0.10324202	1.08	0.3290
trt	1	0.20373302	0.20373302	2.13	0.1824
subject(sequence)	7	3.45075985	0.49296569	5.16	0.0172

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.10324202	0.10324202	1.08	0.3290
trt	1	0.20373302	0.20373302	2.13	0.1824
subject(sequence)	7	3.45075985	0.49296569	5.16	0.0172

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.10324202	0.10324202	1.08	0.3290
trt	1	0.20373302	0.20373302	2.13	0.1824
subject(sequence)	7	3.45075985	0.49296569	5.16	0.0172

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.10324202	0.10324202	1.08	0.3290
trt	1	0.20373302	0.20373302	2.13	0.1824
subject(sequence)	7	3.45075985	0.49296569	5.16	0.0172

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.103242	0.103242	0.21	0.6611
Error	7	3.450760	0.492966		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.203733	0.203733	2.13	0.1824
subject(sequence)	7	3.450760	0.492966	5.16	0.0172
Error: MS(Error)	8	0.764567	0.095571		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.103242	0.103242	0.21	0.6611
Error	7	3.450760	0.492966		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.203733	0.203733	2.13	0.1824
subject(sequence)	7	3.450760	0.492966	5.16	0.0172
Error: MS(Error)	8	0.764567	0.095571		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.103242	0.103242	0.21	0.6611
Error	7	3.450760	0.492966		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.203733	0.203733	2.13	0.1824
subject(sequence)	7	3.450760	0.492966	5.16	0.0172
Error: MS(Error)	8	0.764567	0.095571		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.103242	0.103242	0.21	0.6611
Error	7	3.450760	0.492966		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.203733	0.203733	2.13	0.1824
subject(sequence)	7	3.450760	0.492966	5.16	0.0172
Error: MS(Error)	8	0.764567	0.095571		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFOW	LSMEAN	Pr > t
B	-3.73662235		0.1824
C	-3.94939924		

trt	LN_CLFOW	LSMEAN	90% Confidence Limits	
B	-3.736622		-3.928844	-3.544401
C	-3.949399		-4.141621	-3.757178

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.212777	-0.058220	0.483774

Dependent Variable: LN_CLFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.21277689	0.14573253	-1.46	0.1824	-0.48377353 0.05821975

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	9	101 201 202 203 204 301 402 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	18
Number of Observations Used	18

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h)

The GLM Procedure

Dependent Variable: LN_CLFO

R-Square	Coeff Var	Root MSE	LN_CLFO Mean
0.836327	52.51067	0.309145	0.588729

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.06051145	0.06051145	0.63	0.4492
trt	1	0.20373302	0.20373302	2.13	0.1824
subject(sequence)	7	3.64249195	0.52035599	5.44	0.0147

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.06051145	0.06051145	0.63	0.4492
trt	1	0.20373302	0.20373302	2.13	0.1824
subject(sequence)	7	3.64249195	0.52035599	5.44	0.0147

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.06051145	0.06051145	0.63	0.4492
trt	1	0.20373302	0.20373302	2.13	0.1824
subject(sequence)	7	3.64249195	0.52035599	5.44	0.0147

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.06051145	0.06051145	0.63	0.4492
trt	1	0.20373302	0.20373302	2.13	0.1824
subject(sequence)	7	3.64249195	0.52035599	5.44	0.0147

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.060511	0.060511	0.12	0.7431
Error	7	3.642492	0.520356		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.203733	0.203733	2.13	0.1824
subject(sequence)	7	3.642492	0.520356	5.44	0.0147
Error: MS(Error)	8	0.764567	0.095571		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.060511	0.060511	0.12	0.7431
Error	7	3.642492	0.520356		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.203733	0.203733	2.13	0.1824
subject(sequence)	7	3.642492	0.520356	5.44	0.0147
Error: MS(Error)	8	0.764567	0.095571		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.060511	0.060511	0.12	0.7431
Error	7	3.642492	0.520356		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.203733	0.203733	2.13	0.1824
subject(sequence)	7	3.642492	0.520356	5.44	0.0147
Error: MS(Error)	8	0.764567	0.095571		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.060511	0.060511	0.12	0.7431
Error	7	3.642492	0.520356		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.203733	0.203733	2.13	0.1824
subject(sequence)	7	3.642492	0.520356	5.44	0.0147
Error: MS(Error)	8	0.764567	0.095571		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFO	LSMEAN	Pr > t
B	0.68863474		0.1824
C	0.47585785		

trt	LN_CLFO	LSMEAN	90% Confidence Limits	
B	0.688635	0.496413	0.880856	
C	0.475858	0.283636	0.668079	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.212777	-0.058220	0.483774

Dependent Variable: LN_CLFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.21277689	0.14573253	-1.46	0.1824	-0.48377353 0.05821975

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	9	101 201 202 203 204 301 402 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	18
Number of Observations Used	18

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

The GLM Procedure

Dependent Variable: LN_VZFOW

R-Square	Coeff Var	Root MSE	LN_VZFOW Mean
0.476731	65.76292	0.488595	0.742964

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.29614945	0.29614945	1.24	0.2977
trt	1	0.00000581	0.00000581	0.00	0.9962
subject(sequence)	7	1.44379145	0.20625592	0.86	0.5700

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.29614945	0.29614945	1.24	0.2977
trt	1	0.00000581	0.00000581	0.00	0.9962
subject(sequence)	7	1.44379145	0.20625592	0.86	0.5700

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.29614945	0.29614945	1.24	0.2977
trt	1	0.00000581	0.00000581	0.00	0.9962
subject(sequence)	7	1.44379145	0.20625592	0.86	0.5700

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.29614945	0.29614945	1.24	0.2977
trt	1	0.00000581	0.00000581	0.00	0.9962
subject(sequence)	7	1.44379145	0.20625592	0.86	0.5700

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.296149	0.296149	1.44	0.2698
Error	7	1.443791	0.206256		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.000005808	0.000005808	0.00	0.9962
subject(sequence)	7	1.443791	0.206256	0.86	0.5700
Error: MS(Error)	8	1.909799	0.238725		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.296149	0.296149	1.44	0.2698
Error	7	1.443791	0.206256		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.000005808	0.000005808	0.00	0.9962
subject(sequence)	7	1.443791	0.206256	0.86	0.5700
Error: MS(Error)	8	1.909799	0.238725		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.296149	0.296149	1.44	0.2698
Error	7	1.443791	0.206256		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.000005808	0.000005808	0.00	0.9962
subject(sequence)	7	1.443791	0.206256	0.86	0.5700
Error: MS(Error)	8	1.909799	0.238725		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.296149	0.296149	1.44	0.2698
Error	7	1.443791	0.206256		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.000005808	0.000005808	0.00	0.9962
subject(sequence)	7	1.443791	0.206256	0.86	0.5700
Error: MS(Error)	8	1.909799	0.238725		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_VZFOW	LSMEAN	Pr > t
B	0.72919115		0.9962
C	0.72805507		

trt	LN_VZFOW	LSMEAN	90% Confidence Limits	
B	0.729191		0.425391	1.032991
C	0.728055		0.424255	1.031855

Least Squares Means for Effect trt

Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.001136	-0.427166	0.429438

Dependent Variable: LN_VZFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	-0.00113608	0.23032577	-0.00	0.9962	-0.42943792	0.42716576

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	9	101 201 202 203 204 301 402 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	18
Number of Observations Used	18

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L)

The GLM Procedure

Dependent Variable: LN_VZFO

R-Square	Coeff Var	Root MSE	LN_VZFO Mean
0.671281	9.426561	0.488595	5.183171

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.23543199	1.23543199	5.18	0.0525
trt	1	0.00000581	0.00000581	0.00	0.9962
subject(sequence)	7	2.66458657	0.38065522	1.59	0.2632

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.23543199	1.23543199	5.18	0.0525
trt	1	0.00000581	0.00000581	0.00	0.9962
subject(sequence)	7	2.66458657	0.38065522	1.59	0.2632

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.23543199	1.23543199	5.18	0.0525
trt	1	0.00000581	0.00000581	0.00	0.9962
subject(sequence)	7	2.66458657	0.38065522	1.59	0.2632

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.23543199	1.23543199	5.18	0.0525
trt	1	0.00000581	0.00000581	0.00	0.9962
subject(sequence)	7	2.66458657	0.38065522	1.59	0.2632

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.235432	1.235432	3.25	0.1146
Error	7	2.664587	0.380655		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.000005808	0.000005808	0.00	0.9962
subject(sequence)	7	2.664587	0.380655	1.59	0.2632
Error: MS(Error)	8	1.909799	0.238725		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.235432	1.235432	3.25	0.1146
Error	7	2.664587	0.380655		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.000005808	0.000005808	0.00	0.9962
subject(sequence)	7	2.664587	0.380655	1.59	0.2632
Error: MS(Error)	8	1.909799	0.238725		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.235432	1.235432	3.25	0.1146
Error	7	2.664587	0.380655		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.000005808	0.000005808	0.00	0.9962
subject(sequence)	7	2.664587	0.380655	1.59	0.2632
Error: MS(Error)	8	1.909799	0.238725		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.235432	1.235432	3.25	0.1146
Error	7	2.664587	0.380655		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.000005808	0.000005808	0.00	0.9962
subject(sequence)	7	2.664587	0.380655	1.59	0.2632
Error: MS(Error)	8	1.909799	0.238725		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_VZFO	LSMEAN	Pr > t
B	5.15444823		0.9962
C	5.15331216		

trt	LN_VZFO	LSMEAN	90% Confidence Limits	
B	5.154448	4.850648	5.458248	
C	5.153312	4.849512	5.457112	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.001136	-0.427166	0.429438

Dependent Variable: LN_VZFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	-0.00113608	0.23032577	-0.00	0.9962	-0.42943792	0.42716576

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population
Comparison: C vs B
Dependent Variable: T_{\max} (h)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	9	101 201 202 203 204 301 402 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	18
Number of Observations Used	18

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h)

The GLM Procedure

Dependent Variable: TMAX

R-Square	Coeff Var	Root MSE	TMAX Mean
0.631705	72.78556	0.933434	1.282444

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.35576247	0.35576247	0.41	0.5407
trt	1	7.32679200	7.32679200	8.41	0.0199
subject(sequence)	7	4.27317898	0.61045414	0.70	0.6739

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.35576247	0.35576247	0.41	0.5407
trt	1	7.32679200	7.32679200	8.41	0.0199
subject(sequence)	7	4.27317898	0.61045414	0.70	0.6739

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.35576247	0.35576247	0.41	0.5407
trt	1	7.32679200	7.32679200	8.41	0.0199
subject(sequence)	7	4.27317898	0.61045414	0.70	0.6739

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.35576247	0.35576247	0.41	0.5407
trt	1	7.32679200	7.32679200	8.41	0.0199
subject(sequence)	7	4.27317898	0.61045414	0.70	0.6739

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.355762	0.355762	0.58	0.4702
Error	7	4.273179	0.610454		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	7.326792	7.326792	8.41	0.0199
subject(sequence)	7	4.273179	0.610454	0.70	0.6739
Error: MS(Error)	8	6.970397	0.871300		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.355762	0.355762	0.58	0.4702
Error	7	4.273179	0.610454		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	7.326792	7.326792	8.41	0.0199
subject(sequence)	7	4.273179	0.610454	0.70	0.6739
Error: MS(Error)	8	6.970397	0.871300		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.355762	0.355762	0.58	0.4702
Error	7	4.273179	0.610454		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	7.326792	7.326792	8.41	0.0199
subject(sequence)	7	4.273179	0.610454	0.70	0.6739
Error: MS(Error)	8	6.970397	0.871300		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.355762	0.355762	0.58	0.4702
Error	7	4.273179	0.610454		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	7.326792	7.326792	8.41	0.0199
subject(sequence)	7	4.273179	0.610454	0.70	0.6739
Error: MS(Error)	8	6.970397	0.871300		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: T_{max} (h)

Least Squares Means

		H0:LSMean1=LSMean2	
trt	TMAX LSMEAN		Pr > t
B	0.66016250		0.0199
C	1.93616250		

trt	TMAX LSMEAN	90% Confidence Limits	
B	0.660162	0.079769	1.240556
C	1.936163	1.355769	2.516556

Least Squares Means for Effect trt

		Difference Between		
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-1.276000	-2.094248	-0.457752

Dependent Variable: TMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	1.27600000	0.44002516	2.90	0.01990	0.45775208 2.09424792

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population
 Comparison: C vs B
 Dependent Variable: K_{el} (/h)

The GLM Procedure

Class Level Information										
Class	Levels	Values								
subject	9	101	201	202	203	204	301	402	404	406
sequence	2	ABC	BAC							
trt	2	B C								

Number of Observations Read	18
Number of Observations Used	18

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h)

The GLM Procedure

Dependent Variable: LAMZ

R-Square	Coeff Var	Root MSE	LAMZ Mean
0.964128	21.79042	0.002662	0.012217

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00024799	0.00024799	34.99	0.0004
trt	1	0.00001316	0.00001316	1.86	0.2100
subject(sequence)	7	0.00126274	0.00018039	25.45	<.0001

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00024799	0.00024799	34.99	0.0004
trt	1	0.00001316	0.00001316	1.86	0.2100
subject(sequence)	7	0.00126274	0.00018039	25.45	<.0001

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00024799	0.00024799	34.99	0.0004
trt	1	0.00001316	0.00001316	1.86	0.2100
subject(sequence)	7	0.00126274	0.00018039	25.45	<.0001

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00024799	0.00024799	34.99	0.0004
trt	1	0.00001316	0.00001316	1.86	0.2100
subject(sequence)	7	0.00126274	0.00018039	25.45	<.0001

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.000248	0.000248	1.37	0.2793
Error	7	0.001263	0.000180		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.000013165	0.000013165	1.86	0.2100
subject(sequence)	7	0.001263	0.000180	25.45	<.0001
Error: MS(Error)	8	0.000056699	0.000007087		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.000248	0.000248	1.37	0.2793
Error	7	0.001263	0.000180		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.000013165	0.000013165	1.86	0.2100
subject(sequence)	7	0.001263	0.000180	25.45	<.0001
Error: MS(Error)	8	0.000056699	0.000007087		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.000248	0.000248	1.37	0.2793
Error	7	0.001263	0.000180		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.000013165	0.000013165	1.86	0.2100
subject(sequence)	7	0.001263	0.000180	25.45	<.0001
Error: MS(Error)	8	0.000056699	0.000007087		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.000248	0.000248	1.37	0.2793
Error	7	0.001263	0.000180		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.000013165	0.000013165	1.86	0.2100
subject(sequence)	7	0.001263	0.000180	25.45	<.0001
Error: MS(Error)	8	0.000056699	0.000007087		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LAMZ	LSMEAN	Pr > t
B	0.01348751		0.2100
C	0.01177711		

trt	LAMZ	LSMEAN	90% Confidence Limits	
B	0.013488		0.011832	0.015143
C	0.011777		0.010122	0.013432

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.001710	-0.000623	0.004044

Dependent Variable: LAMZ

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.00171041	0.00125498	-1.36	0.2100	-0.00404409 0.00062328

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

The GLM Procedure

Class Level Information										
Class	Levels	Values								
subject	9	101	201	202	203	204	301	402	404	406
sequence	2	ABC		BAC						
trt	2	B		C						

Number of Observations Read	18
Number of Observations Used	18

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

The GLM Procedure

Dependent Variable: LAMZHL

R-Square	Coeff Var	Root MSE	LAMZHL Mean
0.678170	39.06391	30.52961	78.15299

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1843.72360	1843.72360	1.98	0.1972
trt	1	1955.28434	1955.28434	2.10	0.1855
subject(sequence)	7	11913.47712	1701.92530	1.83	0.2085

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1843.72360	1843.72360	1.98	0.1972
trt	1	1955.28434	1955.28434	2.10	0.1855
subject(sequence)	7	11913.47712	1701.92530	1.83	0.2085

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1843.72360	1843.72360	1.98	0.1972
trt	1	1955.28434	1955.28434	2.10	0.1855
subject(sequence)	7	11913.47712	1701.92530	1.83	0.2085

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1843.72360	1843.72360	1.98	0.1972
trt	1	1955.28434	1955.28434	2.10	0.1855
subject(sequence)	7	11913.47712	1701.92530	1.83	0.2085

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1843.723597	1843.723597	1.08	0.3326
Error	7	11913	1701.925303		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	1955.284335	1955.284335	2.10	0.1855
subject(sequence)	7	11913	1701.925303	1.83	0.2085
Error: MS(Error)	8	7456.458594	932.057324		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1843.723597	1843.723597	1.08	0.3326
Error	7	11913	1701.925303		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	1955.284335	1955.284335	2.10	0.1855
subject(sequence)	7	11913	1701.925303	1.83	0.2085
Error: MS(Error)	8	7456.458594	932.057324		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1843.723597	1843.723597	1.08	0.3326
Error	7	11913	1701.925303		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	1955.284335	1955.284335	2.10	0.1855
subject(sequence)	7	11913	1701.925303	1.83	0.2085
Error: MS(Error)	8	7456.458594	932.057324		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1843.723597	1843.723597	1.08	0.3326
Error	7	11913	1701.925303		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	1955.284335	1955.284335	2.10	0.1855
subject(sequence)	7	11913	1701.925303	1.83	0.2085
Error: MS(Error)	8	7456.458594	932.057324		

Listing 16.1.9-1 ANOVA for Treatment Comparison of Diazepam - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LAMZHL	LSMEAN	Pr > t
B		66.5990342	0.1855
C		87.4438808	

trt	LAMZHL	LSMEAN	90% Confidence Limits	
B		66.599034	47.616228	85.581840
C		87.443881	68.461075	106.426687

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-20.844847	-47.607086	5.917393

Dependent Variable: LAMZHL

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	20.8448466	14.3917980	1.45	0.1855	-5.9173931 47.6070863

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam – PK Population

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*pg/mL)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	27 101 201 202 203 204 205 301 302 303 304 402 404 406 407 408 409 410 411 412 413 414 501 502 503 505 507 508
sequence	2 AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	54
Number of Observations Used	54

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*pg/mL)

The GLM Procedure

Dependent Variable: LN_AUCLST

R-Square	Coeff Var	Root MSE	LN_AUCLST Mean
0.598953	3.509791	0.548042	15.61468

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.19341151	0.19341151	0.64	0.4298
period	1	0.10547371	0.10547371	0.35	0.5588
trt	1	0.58421444	0.58421444	1.95	0.1754
subject(sequence)	25	10.33106002	0.41324240	1.38	0.2153

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.19341151	0.19341151	0.64	0.4298
period	1	0.12450538	0.12450538	0.41	0.5255
trt	1	0.58421444	0.58421444	1.95	0.1754
subject(sequence)	25	10.33106002	0.41324240	1.38	0.2153

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.19341151	0.19341151	0.64	0.4298
period	1	0.12450538	0.12450538	0.41	0.5255
trt	1	0.58421444	0.58421444	1.95	0.1754
subject(sequence)	25	10.33106002	0.41324240	1.38	0.2153

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.19341151	0.19341151	0.64	0.4298
period	1	0.12450538	0.12450538	0.41	0.5255
trt	1	0.58421444	0.58421444	1.95	0.1754
subject(sequence)	25	10.33106002	0.41324240	1.38	0.2153

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*pg/mL)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.193412	0.193412	0.47	0.5002
Error	25	10.331060	0.413242		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.105474	0.105474	0.35	0.5588
trt	1	0.584214	0.584214	1.95	0.1754
subject(sequence)	25	10.331060	0.413242	1.38	0.2153
Error: MS(Error)	25	7.508763	0.300351		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.193412	0.193412	0.47	0.5002
Error	25	10.331060	0.413242		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.124505	0.124505	0.41	0.5255
trt	1	0.584214	0.584214	1.95	0.1754
subject(sequence)	25	10.331060	0.413242	1.38	0.2153
Error: MS(Error)	25	7.508763	0.300351		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*pg/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.193412	0.193412	0.47	0.5002
Error	25	10.331060	0.413242		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.124505	0.124505	0.41	0.5255
trt	1	0.584214	0.584214	1.95	0.1754
subject(sequence)	25	10.331060	0.413242	1.38	0.2153
Error: MS(Error)	25	7.508763	0.300351		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.193412	0.193412	0.47	0.5002
Error	25	10.331060	0.413242		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.124505	0.124505	0.41	0.5255
trt	1	0.584214	0.584214	1.95	0.1754
subject(sequence)	25	10.331060	0.413242	1.38	0.2153
Error: MS(Error)	25	7.508763	0.300351		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*pg/mL)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCLST	LSMEAN	Pr > t
A	15.7165433		0.1754
B	15.5083737		

trt	LN_AUCLST	LSMEAN	90% Confidence Limits	
A	15.716543	15.536261	15.896826	
B	15.508374	15.328091	15.688656	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.208170	-0.046789	0.463128

Dependent Variable: LN_AUCLST

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	0.20816961	0.14926067	1.39	0.1754	-0.04678862 0.46312785

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*pg/mL)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	23 101 201 202 203 204 205 301 302 303 304 404 407 408 410 411 412 413 414 501 502 503 505 507
sequence2	AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	38
Number of Observations Used	38

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*pg/mL)

The GLM Procedure

Dependent Variable: LN_AUCIFO

R-Square	Coeff Var	Root MSE	LN_AUCIFO Mean
0.798291	2.274302	0.367814	16.17260

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.03357891	0.03357891	0.25	0.6267
period	1	0.07277073	0.07277073	0.54	0.4763
trt	1	0.27876163	0.27876163	2.06	0.1748
subject(sequence)	21	6.57528343	0.31310873	2.31	0.0612

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.01837981	0.01837981	0.14	0.7184
period	1	0.18098559	0.18098559	1.34	0.2682
trt	1	0.14121341	0.14121341	1.04	0.3256
subject(sequence)	21	6.57528343	0.31310873	2.31	0.0612

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.02101493	0.02101493	0.16	0.6999
period	1	0.18098559	0.18098559	1.34	0.2682
trt	1	0.14121341	0.14121341	1.04	0.3256
subject(sequence)	21	6.57528343	0.31310873	2.31	0.0612

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.02101493	0.02101493	0.16	0.6999
period	1	0.18098559	0.18098559	1.34	0.2682
trt	1	0.14121341	0.14121341	1.04	0.3256
subject(sequence)	21	6.57528343	0.31310873	2.31	0.0612

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*pg/mL)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.033579	0.033579	0.10	0.7532
Error	19.404	6.404979	0.330078		

Error: $1.0954 * MS(\text{subject}(\text{sequence})) - 0.0954 * MS(\text{Error})$
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.072771	0.072771	0.46	0.5049
Error	21.876	3.462747	0.158289		

Error: $0.1294 * MS(\text{subject}(\text{sequence})) + 0.8706 * MS(\text{Error})$
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.278762	0.278762	1.74	0.2004
Error	22.69	3.636742	0.160278		

Error: $0.1405 * MS(\text{subject}(\text{sequence})) + 0.8595 * MS(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	21	6.575283	0.313109	2.31	0.0612
Error: MS(Error)	13	1.758730	0.135287		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*pg/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.018380	0.018380	0.06	0.8159
Error	19.415	6.406079	0.329958		
Error: $1.0948 * MS(\text{subject}(\text{sequence})) - 0.0948 * MS(\text{Error})$					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.180986	0.180986	1.34	0.2682
trt	1	0.141213	0.141213	1.04	0.3256
subject(sequence)	21	6.575283	0.313109	2.31	0.0612
Error: MS(Error)	13	1.758730	0.135287		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.021015	0.021015	0.07	0.7896
Error	23.811	6.873102	0.288651		
Error: $0.8625 * MS(\text{subject}(\text{sequence})) + 0.1375 * MS(\text{Error})$					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.180986	0.180986	1.34	0.2682
trt	1	0.141213	0.141213	1.04	0.3256
subject(sequence)	21	6.575283	0.313109	2.31	0.0612
Error: MS(Error)	13	1.758730	0.135287		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*pg/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.021015	0.021015	0.07	0.7896
Error	23.811	6.873102	0.288651		
Error: $0.8625*MS(\text{subject}(\text{sequence})) + 0.1375*MS(\text{Error})$					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.180986	0.180986	1.34	0.2682
trt	1	0.141213	0.141213	1.04	0.3256
subject(sequence)	21	6.575283	0.313109	2.31	0.0612
Error: MS(Error)	13	1.758730	0.135287		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*pg/mL)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCIFO	LSMEAN	Pr > t
A	16.3376718		0.3256
B	16.1976255		

trt	LN_AUCIFO	LSMEAN	90% Confidence Limits	
A	16.337672		16.182337	16.493007
B	16.197625		16.019279	16.375972

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.140046	-0.102706	0.382799

Dependent Variable: LN_AUCIFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	0.14004633	0.13707607	1.02	0.3256	-0.10270627 0.38279892

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: C_{\max} (pg/mL)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	28 101 201 202 203 204 205 301 302 303 304 402 404 406 407 408 409 410 411 412 413 414 501 502 503 505 506 507 508
sequence2	AB BA
period	1 2
trt	A B

Number of Observations Read	56
Number of Observations Used	56

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (pg/mL)

The GLM Procedure

Dependent Variable: LN_CMAX

R-Square	Coeff Var	Root MSE	LN_CMAX Mean
0.652247	5.248044	0.551299	10.50485

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.00601538	1.00601538	3.31	0.0804
period	1	0.05642288	0.05642288	0.19	0.6701
trt	1	0.63660316	0.63660316	2.09	0.1598
subject(sequence)	26	13.12238367	0.50470706	1.66	0.1013

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.00601538	1.00601538	3.31	0.0804
period	1	0.05642288	0.05642288	0.19	0.6701
trt	1	0.63660316	0.63660316	2.09	0.1598
subject(sequence)	26	13.12238367	0.50470706	1.66	0.1013

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.00601538	1.00601538	3.31	0.0804
period	1	0.05642288	0.05642288	0.19	0.6701
trt	1	0.63660316	0.63660316	2.09	0.1598
subject(sequence)	26	13.12238367	0.50470706	1.66	0.1013

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.00601538	1.00601538	3.31	0.0804
period	1	0.05642288	0.05642288	0.19	0.6701
trt	1	0.63660316	0.63660316	2.09	0.1598
subject(sequence)	26	13.12238367	0.50470706	1.66	0.1013

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (pg/mL)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.006015	1.006015	1.99	0.1699
Error	26	13.122384	0.504707		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	0.056423	0.056423	0.19	0.6701
trt	1	0.636603	0.636603	2.09	0.1598
subject(sequence)	26	13.122384	0.504707	1.66	0.1013
Error: MS(Error)	26	7.902201	0.303931		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.006015	1.006015	1.99	0.1699
Error	26	13.122384	0.504707		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.056423	0.056423	0.19	0.6701
trt	1	0.636603	0.636603	2.09	0.1598
subject(sequence)	26	13.122384	0.504707	1.66	0.1013
Error: MS(Error)	26	7.902201	0.303931		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: C_{\max} (pg/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.006015	1.006015	1.99	0.1699
Error	26	13.122384	0.504707		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.056423	0.056423	0.19	0.6701
trt	1	0.636603	0.636603	2.09	0.1598
subject(sequence)	26	13.122384	0.504707	1.66	0.1013
Error: MS(Error)	26	7.902201	0.303931		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.006015	1.006015	1.99	0.1699
Error	26	13.122384	0.504707		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.056423	0.056423	0.19	0.6701
trt	1	0.636603	0.636603	2.09	0.1598
subject(sequence)	26	13.122384	0.504707	1.66	0.1013
Error: MS(Error)	26	7.902201	0.303931		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (pg/mL)

Least Squares Means

			H0:LSMean1=LSMean2	
trt	LN_CMAX	LSMEAN		Pr > t
A	10.6114713			0.1598
B	10.3982305			

trt	LN_CMAX	LSMEAN	90% Confidence Limits	
A	10.611471		10.433770	10.789172
B	10.398230		10.220529	10.575932

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.213241	-0.038066	0.464548

Dependent Variable: LN_CMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	0.21324084	0.14734091	1.45	0.1598	-0.03806646 0.46454814

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	23 101 201 202 203 204 205 301 302 303 304 404 407 408 410 411 412 413 414 501 502 503 505 507
sequence2	AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	38
Number of Observations Used	38

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

The GLM Procedure

Dependent Variable: LN_CLFOW

R-Square	Coeff Var	Root MSE	LN_CLFOW Mean
0.809488	-9.734415	0.385756	-3.962809

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.08291686	0.08291686	0.56	0.4687
period	1	0.03561332	0.03561332	0.24	0.6328
trt	1	0.70236923	0.70236923	4.72	0.0489
subject(sequence)	21	7.39881399	0.35232448	2.37	0.0564

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.03880462	0.03880462	0.26	0.6182
period	1	0.16754588	0.16754588	1.13	0.3080
trt	1	0.31055767	0.31055767	2.09	0.1722
subject(sequence)	21	7.39881399	0.35232448	2.37	0.0564

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.05903403	0.05903403	0.40	0.5397
period	1	0.16754588	0.16754588	1.13	0.3080
trt	1	0.31055767	0.31055767	2.09	0.1722
subject(sequence)	21	7.39881399	0.35232448	2.37	0.0564

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.05903403	0.05903403	0.40	0.5397
period	1	0.16754588	0.16754588	1.13	0.3080
trt	1	0.31055767	0.31055767	2.09	0.1722
subject(sequence)	21	7.39881399	0.35232448	2.37	0.0564

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.082917	0.082917	0.22	0.6420
Error	19.441	7.226947	0.371746		

Error: 1.0954*MS(subject(sequence)) - 0.0954*MS(Error)
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.035613	0.035613	0.20	0.6564
Error	22.064	3.864214	0.175134		

Error: 0.1294*MS(subject(sequence)) + 0.8706*MS(Error)
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.702369	0.702369	3.96	0.0587
Error	22.891	4.061091	0.177411		

Error: 0.1405*MS(subject(sequence)) + 0.8595*MS(Error)

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	21	7.398814	0.352324	2.37	0.0564
Error: MS(Error)	13	1.934503	0.148808		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.038805	0.038805	0.10	0.7500
Error	19.451	7.228050	0.371608		
Error: 1.0948*MS(subject(sequence)) - 0.0948*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.167546	0.167546	1.13	0.3080
trt	1	0.310558	0.310558	2.09	0.1722
subject(sequence)	21	7.398814	0.352324	2.37	0.0564
Error: MS(Error)	13	1.934503	0.148808		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.059034	0.059034	0.18	0.6735
Error	23.75	7.702956	0.324333		
Error: 0.8625*MS(subject(sequence)) + 0.1375*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.167546	0.167546	1.13	0.3080
trt	1	0.310558	0.310558	2.09	0.1722
subject(sequence)	21	7.398814	0.352324	2.37	0.0564
Error: MS(Error)	13	1.934503	0.148808		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.059034	0.059034	0.18	0.6735
Error	23.75	7.702956	0.324333		
Error: 0.8625*MS(subject(sequence)) + 0.1375*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.167546	0.167546	1.13	0.3080
trt	1	0.310558	0.310558	2.09	0.1722
subject(sequence)	21	7.398814	0.352324	2.37	0.0564
Error: MS(Error)	13	1.934503	0.148808		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_CLFOW	LSMEAN	Pr > t
A	-4.17286608		0.1722
B	-3.96518120		

trt	LN_CLFOW	LSMEAN	90% Confidence Limits	
A	-4.172866		-4.335778	-4.009954
B	-3.965181		-4.152228	-3.778135

Least Squares Means for Effect trt

Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.207685	-0.462279	0.046910

Dependent Variable: LN_CLFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	-0.20768488	0.14376288	-1.44	0.1722	-0.46227937	0.04690961

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	23 101 201 202 203 204 205 301 302 303 304 404 407 408 410 411 412 413 414 501 502 503 505 507
sequence2	AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	38
Number of Observations Used	38

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h)

The GLM Procedure

Dependent Variable: LN_CLFO

R-Square	Coeff Var	Root MSE	LN_CLFO Mean
0.772445	101.1422	0.385756	0.381400

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.01820094	0.01820094	0.12	0.7321
period	1	0.15040156	0.15040156	1.01	0.3331
trt	1	0.36542174	0.36542174	2.46	0.1411
subject(sequence)	21	6.03273972	0.28727332	1.93	0.1119

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00740836	0.00740836	0.05	0.8269
period	1	0.16754588	0.16754588	1.13	0.3080
trt	1	0.31055767	0.31055767	2.09	0.1722
subject(sequence)	21	6.03273972	0.28727332	1.93	0.1119

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00335522	0.00335522	0.02	0.8829
period	1	0.16754588	0.16754588	1.13	0.3080
trt	1	0.31055767	0.31055767	2.09	0.1722
subject(sequence)	21	6.03273972	0.28727332	1.93	0.1119

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00335522	0.00335522	0.02	0.8829
period	1	0.16754588	0.16754588	1.13	0.3080
trt	1	0.31055767	0.31055767	2.09	0.1722
subject(sequence)	21	6.03273972	0.28727332	1.93	0.1119

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.018201	0.018201	0.06	0.8082
Error	19.085	5.734701	0.300487		

Error: 1.0954*MS(subject(sequence)) - 0.0954*MS(Error)
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.150402	0.150402	0.90	0.3533
Error	20.484	3.414999	0.166719		

Error: 0.1294*MS(subject(sequence)) + 0.8706*MS(Error)
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.365422	0.365422	2.17	0.1553
Error	21.196	3.566563	0.168268		

Error: 0.1405*MS(subject(sequence)) + 0.8595*MS(Error)

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	21	6.032740	0.287273	1.93	0.1119
Error: MS(Error)	13	1.934503	0.148808		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.007408	0.007408	0.02	0.8769
Error	19.097	5.736667	0.300393		
Error: 1.0948*MS(subject(sequence)) - 0.0948*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.167546	0.167546	1.13	0.3080
trt	1	0.310558	0.310558	2.09	0.1722
subject(sequence)	21	6.032740	0.287273	1.93	0.1119
Error: MS(Error)	13	1.934503	0.148808		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.003355	0.003355	0.01	0.9119
Error	24.345	6.529893	0.268229		
Error: 0.8625*MS(subject(sequence)) + 0.1375*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.167546	0.167546	1.13	0.3080
trt	1	0.310558	0.310558	2.09	0.1722
subject(sequence)	21	6.032740	0.287273	1.93	0.1119
Error: MS(Error)	13	1.934503	0.148808		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.003355	0.003355	0.01	0.9119
Error	24.345	6.529893	0.268229		
Error: 0.8625*MS(subject(sequence)) + 0.1375*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.167546	0.167546	1.13	0.3080
trt	1	0.310558	0.310558	2.09	0.1722
subject(sequence)	21	6.032740	0.287273	1.93	0.1119
Error: MS(Error)	13	1.934503	0.148808		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFO	LSMEAN	Pr > t
A	0.18972659		0.1722
B	0.39741148		

trt	LN_CLFO	LSMEAN	90% Confidence Limits	
A	0.189727	0.026814	0.352639	
B	0.397411	0.210365	0.584458	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.207685	-0.462279	0.046910

Dependent Variable: LN_CLFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.20768488	0.14376288	-1.44	0.1722	-0.46227937 0.04690961

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	23 101 201 202 203 204 205 301 302 303 304 404 407 408 410 411 412 413 414 501 502 503 505 507
sequence2	AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	38
Number of Observations Used	38

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

The GLM Procedure

Dependent Variable: LN_VZFOW

R-Square	Coeff Var	Root MSE	LN_VZFOW Mean
0.868076	29.95886	0.380787	1.271034

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.17703292	0.17703292	1.22	0.2892
period	1	0.35833365	0.35833365	2.47	0.1400
trt	1	0.53284924	0.53284924	3.67	0.0775
subject(sequence)	21	11.33526148	0.53977436	3.72	0.0091

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.21714612	0.21714612	1.50	0.2428
period	1	0.10125275	0.10125275	0.70	0.4184
trt	1	0.23872722	0.23872722	1.65	0.2219
subject(sequence)	21	11.33526148	0.53977436	3.72	0.0091

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.01415919	0.01415919	0.10	0.7596
period	1	0.10125275	0.10125275	0.70	0.4184
trt	1	0.23872722	0.23872722	1.65	0.2219
subject(sequence)	21	11.33526148	0.53977436	3.72	0.0091

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.01415919	0.01415919	0.10	0.7596
period	1	0.10125275	0.10125275	0.70	0.4184
trt	1	0.23872722	0.23872722	1.65	0.2219
subject(sequence)	21	11.33526148	0.53977436	3.72	0.0091

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFLOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.177033	0.177033	0.31	0.5859
Error	20.011	11.555255	0.577447		

Error: $1.0954 \cdot MS(\text{subject}(\text{sequence})) - 0.0954 \cdot MS(\text{Error})$
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.358334	0.358334	1.83	0.1879
Error	26.364	5.169085	0.196065		

Error: $0.1294 \cdot MS(\text{subject}(\text{sequence})) + 0.8706 \cdot MS(\text{Error})$
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.532849	0.532849	2.66	0.1145
Error	27.367	5.486520	0.200482		

Error: $0.1405 \cdot MS(\text{subject}(\text{sequence})) + 0.8595 \cdot MS(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	21	11.335261	0.539774	3.72	0.0091
Error: MS(Error)	13	1.884985	0.144999		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFLOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.217146	0.217146	0.38	0.5465
Error	20.017	11.553626	0.577180		
Error: $1.0948 * MS(\text{subject}(\text{sequence})) - 0.0948 * MS(\text{Error})$					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.101253	0.101253	0.70	0.4184
trt	1	0.238727	0.238727	1.65	0.2219
subject(sequence)	21	11.335261	0.539774	3.72	0.0091
Error: MS(Error)	13	1.884985	0.144999		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFLOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.014159	0.014159	0.03	0.8659
Error	22.77	11.054446	0.485476		
Error: $0.8625 * MS(\text{subject}(\text{sequence})) + 0.1375 * MS(\text{Error})$					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.101253	0.101253	0.70	0.4184
trt	1	0.238727	0.238727	1.65	0.2219
subject(sequence)	21	11.335261	0.539774	3.72	0.0091
Error: MS(Error)	13	1.884985	0.144999		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.014159	0.014159	0.03	0.8659
Error	22.77	11.054446	0.485476		
Error: 0.8625*MS(subject(sequence)) + 0.1375*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.101253	0.101253	0.70	0.4184
trt	1	0.238727	0.238727	1.65	0.2219
subject(sequence)	21	11.335261	0.539774	3.72	0.0091
Error: MS(Error)	13	1.884985	0.144999		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_VZFOW	LSMEAN	Pr > t
A	1.20517079		0.2219
B	1.38726022		

trt	LN_VZFOW	LSMEAN	90% Confidence Limits	
A	1.205171		1.044357	1.365984
B	1.387260		1.202623	1.571897

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.182089	-0.433404	0.069225

Dependent Variable: LN_VZFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.18208942	0.14191099	-1.28	0.2219	-0.43340434 0.06922549

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	23 101 201 202 203 204 205 301 302 303 304 404 407 408 410 411 412 413 414 501 502 503 505 507
sequence2	AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	38
Number of Observations Used	38

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L)

The GLM Procedure

Dependent Variable: LN_VZFO

R-Square	Coeff Var	Root MSE	LN_VZFO Mean
0.913813	6.781312	0.380787	5.615243

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.32924050	0.32924050	2.27	0.1558
period	1	0.63634324	0.63634324	4.39	0.0563
trt	1	0.24640477	0.24640477	1.70	0.2150
subject(sequence)	21	18.77380507	0.89399072	6.17	0.0008

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.33282108	0.33282108	2.30	0.1537
period	1	0.10125275	0.10125275	0.70	0.4184
trt	1	0.23872722	0.23872722	1.65	0.2219
subject(sequence)	21	18.77380507	0.89399072	6.17	0.0008

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.09243872	0.09243872	0.64	0.4390
period	1	0.10125275	0.10125275	0.70	0.4184
trt	1	0.23872722	0.23872722	1.65	0.2219
subject(sequence)	21	18.77380507	0.89399072	6.17	0.0008

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.09243872	0.09243872	0.64	0.4390
period	1	0.10125275	0.10125275	0.70	0.4184
trt	1	0.23872722	0.23872722	1.65	0.2219
subject(sequence)	21	18.77380507	0.89399072	6.17	0.0008

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.329240	0.329240	0.34	0.5656
Error	20.404	19.699538	0.965466		

Error: $1.0954 \cdot \text{MS}(\text{subject}(\text{sequence})) - 0.0954 \cdot \text{MS}(\text{Error})$
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.636343	0.636343	2.63	0.1148
Error	31.409	7.597440	0.241884		

Error: $0.1294 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.8706 \cdot \text{MS}(\text{Error})$
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.246405	0.246405	0.98	0.3285
Error	32.179	8.053252	0.250264		

Error: $0.1405 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.8595 \cdot \text{MS}(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	21	18.773805	0.893991	6.17	0.0008
Error: MS(Error)	13	1.884985	0.144999		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.332821	0.332821	0.34	0.5635
Error	20.408	19.692930	0.964959		
Error: $1.0948 \cdot \text{MS}(\text{subject}(\text{sequence})) - 0.0948 \cdot \text{MS}(\text{Error})$					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.101253	0.101253	0.70	0.4184
trt	1	0.238727	0.238727	1.65	0.2219
subject(sequence)	21	18.773805	0.893991	6.17	0.0008
Error: MS(Error)	13	1.884985	0.144999		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.092439	0.092439	0.12	0.7357
Error	22.077	17.461966	0.790973		
Error: $0.8625 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.1375 \cdot \text{MS}(\text{Error})$					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.101253	0.101253	0.70	0.4184
trt	1	0.238727	0.238727	1.65	0.2219
subject(sequence)	21	18.773805	0.893991	6.17	0.0008
Error: MS(Error)	13	1.884985	0.144999		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.092439	0.092439	0.12	0.7357
Error	22.077	17.461966	0.790973		
Error: 0.8625*MS(subject(sequence)) + 0.1375*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.101253	0.101253	0.70	0.4184
trt	1	0.238727	0.238727	1.65	0.2219
subject(sequence)	21	18.773805	0.893991	6.17	0.0008
Error: MS(Error)	13	1.884985	0.144999		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L)

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LN_VZFO LSMEAN		Pr > t
A	5.56776347		0.2219
B	5.74985289		

trt	LN_VZFO LSMEAN	90% Confidence Limits	
A	5.567763	5.406950	5.728577
B	5.749853	5.565216	5.934490

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.182089	-0.433404	0.069225

Dependent Variable: LN_VZFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.18208942	0.14191099	-1.28	0.2219	-0.43340434 0.06922549

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	28 101 201 202 203 204 205 301 302 303 304 402 404 406 407 408 409 410 411 412 413 414 501 502 503 505 506 507 508
sequence2	AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	56
Number of Observations Used	56

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: T_{max} (h)

The GLM Procedure

Dependent Variable: TMAX

R-Square	Coeff Var	Root MSE	TMAX Mean
0.862069	30.47680	34.15705	112.0756

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	17217.7568	17217.7568	14.76	0.0007
period	1	1236.4385	1236.4385	1.06	0.3127
trt	1	679.7005	679.7005	0.58	0.4522
subject(sequence)	26	170454.9347	6555.9590	5.62	<.0001

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	17217.7568	17217.7568	14.76	0.0007
period	1	1236.4385	1236.4385	1.06	0.3127
trt	1	679.7005	679.7005	0.58	0.4522
subject(sequence)	26	170454.9347	6555.9590	5.62	<.0001

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	17217.7568	17217.7568	14.76	0.0007
period	1	1236.4385	1236.4385	1.06	0.3127
trt	1	679.7005	679.7005	0.58	0.4522
subject(sequence)	26	170454.9347	6555.9590	5.62	<.0001

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	17217.7568	17217.7568	14.76	0.0007
period	1	1236.4385	1236.4385	1.06	0.3127
trt	1	679.7005	679.7005	0.58	0.4522
subject(sequence)	26	170454.9347	6555.9590	5.62	<.0001

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	17218	17218	2.63	0.1172
Error	26	170455	6555.959028		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	1236.438473	1236.438473	1.06	0.3127
trt	1	679.700529	679.700529	0.58	0.4522
subject(sequence)	26	170455	6555.959028	5.62	<.0001
Error: MS(Error)	26	30334	1166.704165		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	17218	17218	2.63	0.1172
Error	26	170455	6555.959028		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	1236.438473	1236.438473	1.06	0.3127
trt	1	679.700529	679.700529	0.58	0.4522
subject(sequence)	26	170455	6555.959028	5.62	<.0001
Error: MS(Error)	26	30334	1166.704165		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: T_{max} (h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	17218	17218	2.63	0.1172
Error	26	170455	6555.959028		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	1236.438473	1236.438473	1.06	0.3127
trt	1	679.700529	679.700529	0.58	0.4522
subject(sequence)	26	170455	6555.959028	5.62	<.0001
Error: MS(Error)	26	30334	1166.704165		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	17218	17218	2.63	0.1172
Error	26	170455	6555.959028		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	1236.438473	1236.438473	1.06	0.3127
trt	1	679.700529	679.700529	0.58	0.4522
subject(sequence)	26	170455	6555.959028	5.62	<.0001
Error: MS(Error)	26	30334	1166.704165		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: T_{max} (h)

Least Squares Means

		H0:LSMean1=LSMean2	
trt	TMAX LSMEAN		Pr > t
A	115.559464		0.4522
B	108.591679		

trt	TMAX LSMEAN	90% Confidence Limits	
A	115.559464	104.549571	126.569358
B	108.591679	97.581785	119.601572

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	6.967786	-8.602555	22.538126

Dependent Variable: TMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	6.96778571	9.12885599	0.76	0.4522	-8.60255466 22.53812609

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	23 101 201 202 203 204 205 301 302 303 304 404 407 408 410 411 412 413 414 501 502 503 505 507
sequence2	AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	38
Number of Observations Used	38

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h)

The GLM Procedure

Dependent Variable: LAMZ

R-Square	Coeff Var	Root MSE	LAMZ Mean
0.982877	17.62657	0.001282	0.007272

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00012625	0.00012625	76.83	<.0001
period	1	0.00000679	0.00000679	4.13	0.0631
trt	1	0.00000006	0.00000006	0.04	0.8537
subject(sequence)	21	0.00109304	0.00005205	31.68	<.0001

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00011961	0.00011961	72.79	<.0001
period	1	0.00000016	0.00000016	0.10	0.7608
trt	1	0.00000000	0.00000000	0.00	0.9849
subject(sequence)	21	0.00109304	0.00005205	31.68	<.0001

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00007798	0.00007798	47.46	<.0001
period	1	0.00000016	0.00000016	0.10	0.7608
trt	1	0.00000000	0.00000000	0.00	0.9849
subject(sequence)	21	0.00109304	0.00005205	31.68	<.0001

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00007798	0.00007798	47.46	<.0001
period	1	0.00000016	0.00000016	0.10	0.7608
trt	1	0.00000000	0.00000000	0.00	0.9849
subject(sequence)	21	0.00109304	0.00005205	31.68	<.0001

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.000126	0.000126	2.22	0.1511
Error	20.884	0.001187	0.000056860		

Error: $1.0954 \cdot \text{MS}(\text{subject}(\text{sequence})) - 0.0954 \cdot \text{MS}(\text{Error})$
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.000006786	0.000006786	0.83	0.3695
Error	28.774	0.000235	0.000008163		

Error: $0.1294 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.8706 \cdot \text{MS}(\text{Error})$
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	5.810284E-8	5.810284E-8	0.01	0.9355
Error	28.194	0.000246	0.000008727		

Error: $0.1405 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.8595 \cdot \text{MS}(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	21	0.001093	0.000052050	31.68	<.0001
Error: MS(Error)	13	0.000021361	0.000001643		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.000120	0.000120	2.10	0.1617
Error	20.885	0.001187	0.000056826		
Error: 1.0948*MS(subject(sequence)) - 0.0948*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.000000159	0.000000159	0.10	0.7608
trt	1	6.101771E-10	6.101771E-10	0.00	0.9849
subject(sequence)	21	0.001093	0.000052050	31.68	<.0001
Error: MS(Error)	13	0.000021361	0.000001643		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.000077983	0.000077983	1.73	0.2026
Error	21.211	0.000957	0.000045117		
Error: 0.8625*MS(subject(sequence)) + 0.1375*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.000000159	0.000000159	0.10	0.7608
trt	1	6.101771E-10	6.101771E-10	0.00	0.9849
subject(sequence)	21	0.001093	0.000052050	31.68	<.0001
Error: MS(Error)	13	0.000021361	0.000001643		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.000077983	0.000077983	1.73	0.2026
Error	21.211	0.000957	0.000045117		
Error: 0.8625*MS(subject(sequence)) + 0.1375*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.000000159	0.000000159	0.10	0.7608
trt	1	6.101771E-10	6.101771E-10	0.00	0.9849
subject(sequence)	21	0.001093	0.000052050	31.68	<.0001
Error: MS(Error)	13	0.000021361	0.000001643		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h)

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LAMZ LSMEAN		Pr > t
A	0.00646826		0.9849
B	0.00647746		

trt	LAMZ LSMEAN	90% Confidence Limits	
A	0.006468	0.005927	0.007010
B	0.006477	0.005856	0.007099

Least Squares Means for Effect trt			
i	j	Difference Between Means	90% Confidence Limits for LSMean(i)-LSMean(j)
1	2	-0.000009206	-0.000855 0.000837

Dependent Variable: LAMZ

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-9.205803E-6	0.00047772	-0.02	0.9849	-0.000855215 0.0008368035

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

The GLM Procedure

Class Level Information	
Class	Levels Values
subject	23 101 201 202 203 204 205 301 302 303 304 404 407 408 410 411 412 413 414 501 502 503 505 507
sequence2	AB BA
period	2 1 2
trt	2 A B

Number of Observations Read	38
Number of Observations Used	38

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

The GLM Procedure

Dependent Variable: LAMZHL

R-Square	Coeff Var	Root MSE	LAMZHL Mean
0.824637	77.23745	146.9343	190.2371

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	14942.202	14942.202	0.69	0.4205
period	1	3473.904	3473.904	0.16	0.6948
trt	1	29.534	29.534	0.00	0.9711
subject(sequence)	21	1301373.296	61970.157	2.87	0.0272

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	15431.968	15431.968	0.71	0.4132
period	1	7687.035	7687.035	0.36	0.5610
trt	1	1577.042	1577.042	0.07	0.7912
subject(sequence)	21	1301373.296	61970.157	2.87	0.0272

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	42212.895	42212.895	1.96	0.1854
period	1	7687.035	7687.035	0.36	0.5610
trt	1	1577.042	1577.042	0.07	0.7912
subject(sequence)	21	1301373.296	61970.157	2.87	0.0272

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	42212.895	42212.895	1.96	0.1854
period	1	7687.035	7687.035	0.36	0.5610
trt	1	1577.042	1577.042	0.07	0.7912
subject(sequence)	21	1301373.296	61970.157	2.87	0.0272

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	14942	14942	0.23	0.6390
Error	19.715	1297733	65824		

Error: $1.0954 \cdot \text{MS}(\text{subject}(\text{sequence})) - 0.0954 \cdot \text{MS}(\text{Error})$
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	3473.903776	3473.903776	0.13	0.7221
Error	23.775	637490	26813		

Error: $0.1294 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.8706 \cdot \text{MS}(\text{Error})$
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	29.534427	29.534427	0.00	0.9740
Error	24.699	673421	27265		

Error: $0.1405 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.8595 \cdot \text{MS}(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	21	1301373	61970	2.87	0.0272
Error: MS(Error)	13	280666	21590		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	15432	15432	0.23	0.6335
Error	19.724	1297745	65796		
Error: 1.0948*MS(subject(sequence)) - 0.0948*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	7687.035147	7687.035147	0.36	0.5610
trt	1	1577.042328	1577.042328	0.07	0.7912
subject(sequence)	21	1301373	61970	2.87	0.0272
Error: MS(Error)	13	280666	21590		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	42213	42213	0.75	0.3959
Error	23.282	1313494	56416		
Error: 0.8625*MS(subject(sequence)) + 0.1375*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	7687.035147	7687.035147	0.36	0.5610
trt	1	1577.042328	1577.042328	0.07	0.7912
subject(sequence)	21	1301373	61970	2.87	0.0272
Error: MS(Error)	13	280666	21590		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	42213	42213	0.75	0.3959
Error	23.282	1313494	56416		
Error: $0.8625 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.1375 \cdot \text{MS}(\text{Error})$					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	7687.035147	7687.035147	0.36	0.5610
trt	1	1577.042328	1577.042328	0.07	0.7912
subject(sequence)	21	1301373	61970	2.87	0.0272
Error: MS(Error)	13	280666	21590		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LAMZHL	LSMEAN	Pr > t
A		223.656359	0.7912
B		208.856574	

trt	LAMZHL	LSMEAN	90% Confidence Limits	
A		223.656359	161.603193	285.709526
B		208.856574	137.610653	280.102495

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	14.799786	-82.175073	111.774644

Dependent Variable: LAMZHL

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	14.7997857	54.7591787	0.27	0.7912	-82.1750725 111.7746439

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*pg/mL)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	9	101 201 202 203 204 301 402 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	18
Number of Observations Used	18

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*pg/mL)

The GLM Procedure

Dependent Variable: LN_AUCLST

R-Square	Coeff Var	Root MSE	LN_AUCLST Mean
0.724163	2.081304	0.328591	15.78774

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.05754936	0.05754936	0.53	0.4862
trt	1	0.17097803	0.17097803	1.58	0.2437
subject(sequence)	7	2.03916611	0.29130944	2.70	0.0939

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.05754936	0.05754936	0.53	0.4862
trt	1	0.17097803	0.17097803	1.58	0.2437
subject(sequence)	7	2.03916611	0.29130944	2.70	0.0939

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.05754936	0.05754936	0.53	0.4862
trt	1	0.17097803	0.17097803	1.58	0.2437
subject(sequence)	7	2.03916611	0.29130944	2.70	0.0939

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.05754936	0.05754936	0.53	0.4862
trt	1	0.17097803	0.17097803	1.58	0.2437
subject(sequence)	7	2.03916611	0.29130944	2.70	0.0939

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*pg/mL)

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.057549	0.057549	0.20	0.6701
Error	7	2.039166	0.291309		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.170978	0.170978	1.58	0.2437
subject(sequence)	7	2.039166	0.291309	2.70	0.0939
Error: MS(Error)	8	0.863775	0.107972		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.057549	0.057549	0.20	0.6701
Error	7	2.039166	0.291309		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.170978	0.170978	1.58	0.2437
subject(sequence)	7	2.039166	0.291309	2.70	0.0939
Error: MS(Error)	8	0.863775	0.107972		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*pg/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.057549	0.057549	0.20	0.6701
Error	7	2.039166	0.291309		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.170978	0.170978	1.58	0.2437
subject(sequence)	7	2.039166	0.291309	2.70	0.0939
Error: MS(Error)	8	0.863775	0.107972		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.057549	0.057549	0.20	0.6701
Error	7	2.039166	0.291309		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.170978	0.170978	1.58	0.2437
subject(sequence)	7	2.039166	0.291309	2.70	0.0939
Error: MS(Error)	8	0.863775	0.107972		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*pg/mL)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCLST	LSMEAN	Pr > t
B	15.6965982		0.2437
C	15.8915216		

trt	LN_AUCLST	LSMEAN	90% Confidence Limits	
B	15.696598	15.492286	15.900911	
C	15.891522	15.687209	16.095834	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.194923	-0.482966	0.093119

Dependent Variable: LN_AUCLST

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	0.19492337	0.15489919	1.26	0.2437	-0.09311913 0.48296586

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*pg/mL)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	8	101 201 202 203 204 301 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	11
Number of Observations Used	11

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*pg/mL)

The GLM Procedure

Dependent Variable: LN_AUCIFO

R-Square	Coeff Var	Root MSE	LN_AUCIFO Mean
0.904625	2.451480	0.399149	16.28198

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.07415386	0.07415386	0.47	0.5655
trt	1	0.36277910	0.36277910	2.28	0.2704
subject(sequence)	6	2.58535267	0.43089211	2.70	0.2944

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.04440121	0.04440121	0.28	0.6503
trt	1	0.35468757	0.35468757	2.23	0.2742
subject(sequence)	6	2.58535267	0.43089211	2.70	0.2944

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.02708903	0.02708903	0.17	0.7201
trt	1	0.35468757	0.35468757	2.23	0.2742
subject(sequence)	6	2.58535267	0.43089211	2.70	0.2944

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.02708903	0.02708903	0.17	0.7201
trt	1	0.35468757	0.35468757	2.23	0.2742
subject(sequence)	6	2.58535267	0.43089211	2.70	0.2944

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*pg/mL)

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.074154	0.074154	0.15	0.7130
Error	5.1578	2.530606	0.490633		

Error: $1.22*MS(\text{subject}(\text{sequence})) - 0.22*MS(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.362779	0.362779	1.41	0.2731
Error	7.2018	1.856133	0.257731		

Error: $0.3624*MS(\text{subject}(\text{sequence})) + 0.6376*MS(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	6	2.585353	0.430892	2.70	0.2944
Error: MS(Error)	2	0.318641	0.159320		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*pg/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.044401	0.044401	0.09	0.7752
Error	5.1649	2.531028	0.490046		
Error: $1.2178 * MS(\text{subject}(\text{sequence})) - 0.2178 * MS(\text{Error})$					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.354688	0.354688	2.23	0.2742
subject(sequence)	6	2.585353	0.430892	2.70	0.2944
Error: MS(Error)	2	0.318641	0.159320		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.027089	0.027089	0.06	0.8079
Error	6.1708	2.595918	0.420675		
Error: $0.9624 * MS(\text{subject}(\text{sequence})) + 0.0376 * MS(\text{Error})$					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.354688	0.354688	2.23	0.2742
subject(sequence)	6	2.585353	0.430892	2.70	0.2944
Error: MS(Error)	2	0.318641	0.159320		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*pg/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.027089	0.027089	0.06	0.8079
Error	6.1708	2.595918	0.420675		
Error: $0.9624*MS(\text{subject}(\text{sequence})) + 0.0376*MS(\text{Error})$					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.354688	0.354688	2.23	0.2742
subject(sequence)	6	2.585353	0.430892	2.70	0.2944
Error: MS(Error)	2	0.318641	0.159320		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*pg/mL)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCIFO	LSMEAN	Pr > t
B	16.1264488		0.2742
C	16.6127187		

trt	LN_AUCIFO	LSMEAN	90% Confidence Limits	
B	16.126449		15.474909	16.777989
C	16.612719		16.054773	17.170664

Least Squares Means for Effect trt

Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.486270	-1.437905	0.465366

Dependent Variable: LN_AUCIFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	0.48626987	0.32590416	1.49	0.2742	-0.46536558	1.43790531

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: C_{\max} (pg/mL)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	9	101 201 202 203 204 301 402 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	18
Number of Observations Used	18

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: C_{max} (pg/mL)

The GLM Procedure

Dependent Variable: LN_CMAX

R-Square	Coeff Var	Root MSE	LN_CMAX Mean
0.742680	3.444682	0.366647	10.64385

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.19249555	0.19249555	1.43	0.2657
trt	1	0.14829852	0.14829852	1.10	0.3243
subject(sequence)	7	2.76314852	0.39473550	2.94	0.0771

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.19249555	0.19249555	1.43	0.2657
trt	1	0.14829852	0.14829852	1.10	0.3243
subject(sequence)	7	2.76314852	0.39473550	2.94	0.0771

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.19249555	0.19249555	1.43	0.2657
trt	1	0.14829852	0.14829852	1.10	0.3243
subject(sequence)	7	2.76314852	0.39473550	2.94	0.0771

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.19249555	0.19249555	1.43	0.2657
trt	1	0.14829852	0.14829852	1.10	0.3243
subject(sequence)	7	2.76314852	0.39473550	2.94	0.0771

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: C_{\max} (pg/mL)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.192496	0.192496	0.49	0.5075
Error	7	2.763149	0.394736		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.148299	0.148299	1.10	0.3243
subject(sequence)	7	2.763149	0.394736	2.94	0.0771
Error: MS(Error)	8	1.075439	0.134430		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.192496	0.192496	0.49	0.5075
Error	7	2.763149	0.394736		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.148299	0.148299	1.10	0.3243
subject(sequence)	7	2.763149	0.394736	2.94	0.0771
Error: MS(Error)	8	1.075439	0.134430		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: C_{\max} (pg/mL)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.192496	0.192496	0.49	0.5075
Error	7	2.763149	0.394736		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.148299	0.148299	1.10	0.3243
subject(sequence)	7	2.763149	0.394736	2.94	0.0771
Error: MS(Error)	8	1.075439	0.134430		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.192496	0.192496	0.49	0.5075
Error	7	2.763149	0.394736		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.148299	0.148299	1.10	0.3243
subject(sequence)	7	2.763149	0.394736	2.94	0.0771
Error: MS(Error)	8	1.075439	0.134430		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: C_{max} (pg/mL)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_CMAX	LSMEAN	Pr > t
B	10.5646446		0.3243
C	10.7461803		

trt	LN_CMAX	LSMEAN	90% Confidence Limits	
B	10.564645		10.336670	10.792619
C	10.746180		10.518205	10.974155

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.181536	-0.502938	0.139867

Dependent Variable: LN_CMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	0.18153574	0.17283895	1.05	0.3243	-0.13986659 0.50293808

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	8	101 201 202 203 204 301 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	11
Number of Observations Used	11

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

The GLM Procedure

Dependent Variable: LN_CLFOW

R-Square	Coeff Var	Root MSE	LN_CLFOW Mean
0.902109	-10.77248	0.443098	-4.113246

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.16198223	0.16198223	0.83	0.4596
trt	1	0.73224034	0.73224034	3.73	0.1932
subject(sequence)	6	2.72441644	0.45406941	2.31	0.3323

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.09915049	0.09915049	0.51	0.5510
trt	1	0.50837219	0.50837219	2.59	0.2489
subject(sequence)	6	2.72441644	0.45406941	2.31	0.3323

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00445321	0.00445321	0.02	0.8941
trt	1	0.50837219	0.50837219	2.59	0.2489
subject(sequence)	6	2.72441644	0.45406941	2.31	0.3323

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00445321	0.00445321	0.02	0.8941
trt	1	0.50837219	0.50837219	2.59	0.2489
subject(sequence)	6	2.72441644	0.45406941	2.31	0.3323

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.161982	0.161982	0.32	0.5976
Error	5.0095	2.558688	0.510766		

Error: 1.22*MS(subject(sequence)) - 0.22*MS(Error)

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.732240	0.732240	2.53	0.1572
Error	6.798	1.969591	0.289733		

Error: 0.3624*MS(subject(sequence)) + 0.6376*MS(Error)

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	6	2.724416	0.454069	2.31	0.3323
Error: MS(Error)	2	0.392672	0.196336		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.099150	0.099150	0.19	0.6777
Error	5.0178	2.560122	0.510209		
Error: 1.2178*MS(subject(sequence)) - 0.2178*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.508372	0.508372	2.59	0.2489
subject(sequence)	6	2.724416	0.454069	2.31	0.3323
Error: MS(Error)	2	0.392672	0.196336		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.004453	0.004453	0.01	0.9234
Error	6.1993	2.754777	0.444373		
Error: 0.9624*MS(subject(sequence)) + 0.0376*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.508372	0.508372	2.59	0.2489
subject(sequence)	6	2.724416	0.454069	2.31	0.3323
Error: MS(Error)	2	0.392672	0.196336		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.004453	0.004453	0.01	0.9234
Error	6.1993	2.754777	0.444373		
Error: 0.9624*MS(subject(sequence)) + 0.0376*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.508372	0.508372	2.59	0.2489
subject(sequence)	6	2.724416	0.454069	2.31	0.3323
Error: MS(Error)	2	0.392672	0.196336		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_CLFOW	LSMEAN	Pr > t
B	-3.91316447		0.2489
C	-4.49532836		

trt	LN_CLFOW	LSMEAN	90% Confidence Limits	
B	-3.913164		-4.636444	-3.189885
C	-4.495328		-5.114708	-3.875949

Least Squares Means for Effect trt

Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.582164	-0.474253	1.638581

Dependent Variable: LN_CLFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	-0.58216389	0.36178831	-1.61	0.2489	-1.63858054	0.47425276

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	8	101 201 202 203 204 301 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	11
Number of Observations Used	11

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h)

The GLM Procedure

Dependent Variable: LN_CLFO

R-Square	Coeff Var	Root MSE	LN_CLFO Mean
0.911563	161.6764	0.443098	0.274065

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00821426	0.00821426	0.04	0.8569
trt	1	0.32342250	0.32342250	1.65	0.3280
subject(sequence)	6	3.71584302	0.61930717	3.15	0.2602

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00110942	0.00110942	0.01	0.9469
trt	1	0.50837219	0.50837219	2.59	0.2489
subject(sequence)	6	3.71584302	0.61930717	3.15	0.2602

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.15060463	0.15060463	0.77	0.4735
trt	1	0.50837219	0.50837219	2.59	0.2489
subject(sequence)	6	3.71584302	0.61930717	3.15	0.2602

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.15060463	0.15060463	0.77	0.4735
trt	1	0.50837219	0.50837219	2.59	0.2489
subject(sequence)	6	3.71584302	0.61930717	3.15	0.2602

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.008214	0.008214	0.01	0.9184
Error	5.2819	3.762543	0.712353		

Error: 1.22*MS(subject(sequence)) - 0.22*MS(Error)

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.323422	0.323422	0.93	0.3660
Error	7.5308	2.632859	0.349611		

Error: 0.3624*MS(subject(sequence)) + 0.6376*MS(Error)

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	6	3.715843	0.619307	3.15	0.2602
Error: MS(Error)	2	0.392672	0.196336		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.001109	0.001109	0.00	0.9699
Error	5.2878	3.761979	0.711439		
Error: 1.2178*MS(subject(sequence)) - 0.2178*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.508372	0.508372	2.59	0.2489
subject(sequence)	6	3.715843	0.619307	3.15	0.2602
Error: MS(Error)	2	0.392672	0.196336		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.150605	0.150605	0.25	0.6347
Error	6.1468	3.708949	0.603393		
Error: 0.9624*MS(subject(sequence)) + 0.0376*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.508372	0.508372	2.59	0.2489
subject(sequence)	6	3.715843	0.619307	3.15	0.2602
Error: MS(Error)	2	0.392672	0.196336		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.150605	0.150605	0.25	0.6347
Error	6.1468	3.708949	0.603393		
Error: 0.9624*MS(subject(sequence)) + 0.0376*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.508372	0.508372	2.59	0.2489
subject(sequence)	6	3.715843	0.619307	3.15	0.2602
Error: MS(Error)	2	0.392672	0.196336		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFO	LSMEAN	Pr > t
B	0.48125860		0.2489
C	-0.10090529		

trt	LN_CLFO	LSMEAN	90% Confidence Limits	
B	0.481259		-0.242020	1.204538
C	-0.100905		-0.720284	0.518474

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.582164	-0.474253	1.638581

Dependent Variable: LN_CLFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.58216389	0.36178831	-1.61	0.2489	-1.63858054 0.47425276

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	8	101 201 202 203 204 301 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	11
Number of Observations Used	11

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

The GLM Procedure

Dependent Variable: LN_VZFOW

R-Square	Coeff Var	Root MSE	LN_VZFOW Mean
0.770703	58.09245	0.685302	1.179674

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00961309	0.00961309	0.02	0.8993
trt	1	0.23838114	0.23838114	0.51	0.5501
subject(sequence)	6	2.90905346	0.48484224	1.03	0.5680

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.02142687	0.02142687	0.05	0.8507
trt	1	0.46004136	0.46004136	0.98	0.4266
subject(sequence)	6	2.90905346	0.48484224	1.03	0.5680

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.04288477	0.04288477	0.09	0.7910
trt	1	0.46004136	0.46004136	0.98	0.4266
subject(sequence)	6	2.90905346	0.48484224	1.03	0.5680

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.04288477	0.04288477	0.09	0.7910
trt	1	0.46004136	0.46004136	0.98	0.4266
subject(sequence)	6	2.90905346	0.48484224	1.03	0.5680

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.009613	0.009613	0.02	0.8956
Error	3.7444	1.827974	0.488187		

Error: $1.22 * MS(\text{subject}(\text{sequence})) - 0.22 * MS(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.238381	0.238381	0.50	0.5136
Error	4.5171	2.146267	0.475148		

Error: $0.3624 * MS(\text{subject}(\text{sequence})) + 0.6376 * MS(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	6	2.909053	0.484842	1.03	0.5680
Error: MS(Error)	2	0.939277	0.469638		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.021427	0.021427	0.04	0.8449
Error	3.7623	1.836568	0.488154		
Error: 1.2178*MS(subject(sequence)) - 0.2178*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.460041	0.460041	0.98	0.4266
subject(sequence)	6	2.909053	0.484842	1.03	0.5680
Error: MS(Error)	2	0.939277	0.469638		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.042885	0.042885	0.09	0.7754
Error	6.4353	3.116445	0.484270		
Error: 0.9624*MS(subject(sequence)) + 0.0376*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.460041	0.460041	0.98	0.4266
subject(sequence)	6	2.909053	0.484842	1.03	0.5680
Error: MS(Error)	2	0.939277	0.469638		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.042885	0.042885	0.09	0.7754
Error	6.4353	3.116445	0.484270		
Error: 0.9624*MS(subject(sequence)) + 0.0376*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.460041	0.460041	0.98	0.4266
subject(sequence)	6	2.909053	0.484842	1.03	0.5680
Error: MS(Error)	2	0.939277	0.469638		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_VZFOW	LSMEAN	Pr > t
B	1.48139692		0.4266
C	0.92759710		

trt	LN_VZFOW	LSMEAN	90% Confidence Limits	
B	1.481397		0.362764	2.600030
C	0.927597		-0.030343	1.885537

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.553800	-1.080068	2.187667

Dependent Variable: LN_VZFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.55379982	0.55954645	-0.99	0.4266	-2.18766737 1.08006773

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	8	101 201 202 203 204 301 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	11
Number of Observations Used	11

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L)

The GLM Procedure

Dependent Variable: LN_VZFO

R-Square	Coeff Var	Root MSE	LN_VZFO Mean
0.855335	12.31010	0.685302	5.566985

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.16800486	0.16800486	0.36	0.6105
trt	1	0.04049550	0.04049550	0.09	0.7967
subject(sequence)	6	5.34497302	0.89082884	1.90	0.3847

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.18314367	0.18314367	0.39	0.5961
trt	1	0.46004136	0.46004136	0.98	0.4266
subject(sequence)	6	5.34497302	0.89082884	1.90	0.3847

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.27924049	0.27924049	0.59	0.5213
trt	1	0.46004136	0.46004136	0.98	0.4266
subject(sequence)	6	5.34497302	0.89082884	1.90	0.3847

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.27924049	0.27924049	0.59	0.5213
trt	1	0.46004136	0.46004136	0.98	0.4266
subject(sequence)	6	5.34497302	0.89082884	1.90	0.3847

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.168005	0.168005	0.17	0.6972
Error	4.7838	4.704785	0.983483		

Error: 1.22*MS(subject(sequence)) - 0.22*MS(Error)

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.040496	0.040496	0.07	0.8069
Error	6.2249	3.873577	0.622268		

Error: 0.3624*MS(subject(sequence)) + 0.6376*MS(Error)

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	6	5.344973	0.890829	1.90	0.3847
Error: MS(Error)	2	0.939277	0.469638		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.183144	0.183144	0.19	0.6847
Error	4.7939	4.710396	0.982573		
Error: 1.2178*MS(subject(sequence)) - 0.2178*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.460041	0.460041	0.98	0.4266
subject(sequence)	6	5.344973	0.890829	1.90	0.3847
Error: MS(Error)	2	0.939277	0.469638		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.279240	0.279240	0.32	0.5918
Error	6.2419	5.461567	0.874982		
Error: 0.9624*MS(subject(sequence)) + 0.0376*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.460041	0.460041	0.98	0.4266
subject(sequence)	6	5.344973	0.890829	1.90	0.3847
Error: MS(Error)	2	0.939277	0.469638		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.279240	0.279240	0.32	0.5918
Error	6.2419	5.461567	0.874982		
Error: 0.9624*MS(subject(sequence)) + 0.0376*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.460041	0.460041	0.98	0.4266
subject(sequence)	6	5.344973	0.890829	1.90	0.3847
Error: MS(Error)	2	0.939277	0.469638		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L)

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_VZFO	LSMEAN	Pr > t
B	5.87582000		0.4266
C	5.32202018		

trt	LN_VZFO	LSMEAN	90% Confidence Limits	
B	5.875820		4.757187	6.994453
C	5.322020		4.364080	6.279960

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.553800	-1.080068	2.187667

Dependent Variable: LN_VZFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.55379982	0.55954645	-0.99	0.4266	-2.18766737 1.08006773

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	9	101 201 202 203 204 301 402 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	18
Number of Observations Used	18

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: T_{max} (h)

The GLM Procedure

Dependent Variable: TMAX

R-Square	Coeff Var	Root MSE	TMAX Mean
0.709476	32.06432	33.76521	105.3046

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1284.96583	1284.96583	1.13	0.3194
trt	1	1546.58827	1546.58827	1.36	0.2777
subject(sequence)	7	19441.71556	2777.38794	2.44	0.1178

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1284.96583	1284.96583	1.13	0.3194
trt	1	1546.58827	1546.58827	1.36	0.2777
subject(sequence)	7	19441.71556	2777.38794	2.44	0.1178

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1284.96583	1284.96583	1.13	0.3194
trt	1	1546.58827	1546.58827	1.36	0.2777
subject(sequence)	7	19441.71556	2777.38794	2.44	0.1178

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1284.96583	1284.96583	1.13	0.3194
trt	1	1546.58827	1546.58827	1.36	0.2777
subject(sequence)	7	19441.71556	2777.38794	2.44	0.1178

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1284.965831	1284.965831	0.46	0.5182
Error	7	19442	2777.387937		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	1546.588267	1546.588267	1.36	0.2777
subject(sequence)	7	19442	2777.387937	2.44	0.1178
Error: MS(Error)	8	9120.713962	1140.089245		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1284.965831	1284.965831	0.46	0.5182
Error	7	19442	2777.387937		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	1546.588267	1546.588267	1.36	0.2777
subject(sequence)	7	19442	2777.387937	2.44	0.1178
Error: MS(Error)	8	9120.713962	1140.089245		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: T_{max} (h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1284.965831	1284.965831	0.46	0.5182
Error	7	19442	2777.387937		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	1546.588267	1546.588267	1.36	0.2777
subject(sequence)	7	19442	2777.387937	2.44	0.1178
Error: MS(Error)	8	9120.713962	1140.089245		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1284.965831	1284.965831	0.46	0.5182
Error	7	19442	2777.387937		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	1546.588267	1546.588267	1.36	0.2777
subject(sequence)	7	19442	2777.387937	2.44	0.1178
Error: MS(Error)	8	9120.713962	1140.089245		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: T_{max} (h)

Least Squares Means

		H0:LSMean1=LSMean2	
trt	TMAX LSMEAN		Pr > t
B	113.629364		0.2777
C	95.090586		

trt	TMAX LSMEAN	90% Confidence Limits	
B	113.629364	92.634720	134.624008
C	95.090586	74.095942	116.085230

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	18.538778	-11.059781	48.137337

Dependent Variable: TMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-18.538778	15.9170715	-1.16	0.2777	-48.1373369 11.0597813

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	8	101 201 202 203 204 301 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	11
Number of Observations Used	11

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h)

The GLM Procedure

Dependent Variable: LAMZ

R-Square	Coeff Var	Root MSE	LAMZ Mean
0.979044	25.02204	0.001571	0.006279

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00002833	0.00002833	11.48	0.0772
trt	1	0.00000170	0.00000170	0.69	0.4941
subject(sequence)	6	0.00020060	0.00003343	13.55	0.0703

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00002668	0.00002668	10.81	0.0814
trt	1	0.00000001	0.00000001	0.01	0.9482
subject(sequence)	6	0.00020060	0.00003343	13.55	0.0703

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00000850	0.00000850	3.44	0.2046
trt	1	0.00000001	0.00000001	0.01	0.9482
subject(sequence)	6	0.00020060	0.00003343	13.55	0.0703

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00000850	0.00000850	3.44	0.2046
trt	1	0.00000001	0.00000001	0.01	0.9482
subject(sequence)	6	0.00020060	0.00003343	13.55	0.0703

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.00028326	0.00028326	0.70	0.4345
Error	5.8382	0.000235	0.000040245		

Error: $1.22 * MS(\text{subject}(\text{sequence})) - 0.22 * MS(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.00001698	0.00001698	0.12	0.7347
Error	7.2909	0.00099806	0.00013689		

Error: $0.3624 * MS(\text{subject}(\text{sequence})) + 0.6376 * MS(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	6	0.000201	0.000033433	13.55	0.0703
Error: MS(Error)	2	0.00004936	0.00002468		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.000026680	0.000026680	0.66	0.4471
Error	5.8395	0.000235	0.000040178		
Error: 1.2178*MS(subject(sequence)) - 0.2178*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	1.3259677E-8	1.3259677E-8	0.01	0.9482
subject(sequence)	6	0.000201	0.000033433	13.55	0.0703
Error: MS(Error)	2	0.000004936	0.000002468		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.000008502	0.000008502	0.26	0.6260
Error	6.0345	0.000195	0.000032268		
Error: 0.9624*MS(subject(sequence)) + 0.0376*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	1.3259677E-8	1.3259677E-8	0.01	0.9482
subject(sequence)	6	0.000201	0.000033433	13.55	0.0703
Error: MS(Error)	2	0.000004936	0.000002468		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.000008502	0.000008502	0.26	0.6260
Error	6.0345	0.000195	0.000032268		
Error: 0.9624*MS(subject(sequence)) + 0.0376*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	1.3259677E-8	1.3259677E-8	0.01	0.9482
subject(sequence)	6	0.000201	0.000033433	13.55	0.0703
Error: MS(Error)	2	0.000004936	0.000002468		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LAMZ	LSMEAN	Pr > t
B	0.00555261		0.9482
C	0.00545859		

trt	LAMZ	LSMEAN	90% Confidence Limits	
B	0.005553		0.002988	0.008117
C	0.005459		0.003263	0.007655

Least Squares Means for Effect trt				
i	j	Difference Between Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.000094020	-0.003652	0.003840

Dependent Variable: LAMZ

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.00009402	0.00128273	-0.07	0.9482	-0.00383959 0.00365155

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	8	101 201 202 203 204 301 404 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	11
Number of Observations Used	11

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

The GLM Procedure

Dependent Variable: LAMZHL

R-Square	Coeff Var	Root MSE	LAMZHL Mean
0.936339	32.11823	52.93033	164.7984

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	781.19473	781.19473	0.28	0.6502
trt	1	6489.38122	6489.38122	2.32	0.2674
subject(sequence)	6	75143.68682	12523.94780	4.47	0.1941

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	390.22411	390.22411	0.14	0.7448
trt	1	78.94660	78.94660	0.03	0.8821
subject(sequence)	6	75143.68682	12523.94780	4.47	0.1941

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	455.07734	455.07734	0.16	0.7259
trt	1	78.94660	78.94660	0.03	0.8821
subject(sequence)	6	75143.68682	12523.94780	4.47	0.1941

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	455.07734	455.07734	0.16	0.7259
trt	1	78.94660	78.94660	0.03	0.8821
subject(sequence)	6	75143.68682	12523.94780	4.47	0.1941

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	781.194725	781.194725	0.05	0.8258
Error	5.4989	80628	14663		

Error: $1.22 \cdot \text{MS}(\text{subject}(\text{sequence})) - 0.22 \cdot \text{MS}(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	6489.381224	6489.381224	1.03	0.3409
Error	7.9553	50316	6324.760478		

Error: $0.3624 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.6376 \cdot \text{MS}(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	6	75144	12524	4.47	0.1941
Error: MS(Error)	2	5603.239711	2801.619856		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	390.224108	390.224108	0.03	0.8761
Error	5.503	80574	14642		
Error: 1.2178*MS(subject(sequence)) - 0.2178*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	78.946602	78.946602	0.03	0.8821
subject(sequence)	6	75144	12524	4.47	0.1941
Error: MS(Error)	2	5603.239711	2801.619856		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	455.077342	455.077342	0.04	0.8529
Error	6.104	74213	12158		
Error: 0.9624*MS(subject(sequence)) + 0.0376*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	78.946602	78.946602	0.03	0.8821
subject(sequence)	6	75144	12524	4.47	0.1941
Error: MS(Error)	2	5603.239711	2801.619856		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	455.077342	455.077342	0.04	0.8529
Error	6.104	74213	12158		
Error: $0.9624 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.0376 \cdot \text{MS}(\text{Error})$					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	78.946602	78.946602	0.03	0.8821
subject(sequence)	6	75144	12524	4.47	0.1941
Error: MS(Error)	2	5603.239711	2801.619856		

Listing 16.1.9-2 ANOVA for Treatment Comparison of Nordiazepam - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h)

Least Squares Means

			H0:LSMean1=LSMean2
trt	LAMZHL	LSMEAN	Pr > t
B		177.749549	0.8821
C		185.004276	

trt	LAMZHL	LSMEAN	90% Confidence Limits	
B		177.749549	91.350230	264.148869
C		185.004276	111.016320	258.992233

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-7.254727	-133.449010	118.939556

Dependent Variable: LAMZHL

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	7.25472729	43.2174336	0.17	0.8821	-118.9395558 133.44901033

Listing 16.1.9-3 Wilcoxon Signed-Rank Test for T_{\max} for Treatment Comparison of Diazepam – PK Population

Listing 16.1.9-3 Wilcoxon Signed-Rank Test for T_{max} for Treatment Comparison of Diazepam - PK Population

Difference	Statistic	Value
A - B	n	28
	Mean	0.723
	Median	0.367
	SD	1.339
Wilcoxon Signed-rank Test	S	116.5
	p-value	0.0015
C - B	n	9
	Mean	1.276
	Median	1.017
	SD	1.320
Wilcoxon Signed-rank Test	S	16
	p-value	0.0234

n: Number of subjects; SD: Standard Deviation.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Listing 16.1.9-4 Wilcoxon Signed-Rank Test for T_{\max} for Treatment Comparison of Nordiazepam – PK Population

Listing 16.1.9-4 Wilcoxon Signed-Rank Test for T_{max} for Treatment Comparison of Nordiazepam - PK Population

Difference	Statistic	Value
A - B	n	28
	Mean	6.968
	Median	0.192
	SD	48.359
Wilcoxon Signed-rank Test	S	36
	p-value	0.4223
C - B	n	9
	Mean	-18.539
	Median	-23.083
	SD	47.751
Wilcoxon Signed-rank Test	S	-7.5
	p-value	0.4258

n: Number of subjects; SD: Standard Deviation.

Treatment A: Diazepam Buccal Film under fed conditions (breakfast with moderate fat content);

Treatment B: Diastat[®] AcuDial[™] rectal gel under fed conditions (breakfast with moderate fat content);

Treatment C: Diazepam Buccal Film under fed conditions (breakfast with high fat content).

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	6	101 201 302 412 414 503
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	12
Number of Observations Used	12

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LN_AUCLST

R-Square	Coeff Var	Root MSE	LN_AUCLST Mean
0.989131	1.149609	0.104716	9.108814

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.87353230	0.87353230	79.66	0.0009
period	1	0.02943586	0.02943586	2.68	0.1767
trt	1	0.00942171	0.00942171	0.86	0.4064
subject(sequence)	4	3.07934290	0.76983573	70.21	0.0006

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.87353230	0.87353230	79.66	0.0009
period	1	0.03767939	0.03767939	3.44	0.1374
trt	1	0.00942171	0.00942171	0.86	0.4064
subject(sequence)	4	3.07934290	0.76983573	70.21	0.0006

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.87353230	0.87353230	79.66	0.0009
period	1	0.03767939	0.03767939	3.44	0.1374
trt	1	0.00942171	0.00942171	0.86	0.4064
subject(sequence)	4	3.07934290	0.76983573	70.21	0.0006

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.87353230	0.87353230	79.66	0.0009
period	1	0.03767939	0.03767939	3.44	0.1374
trt	1	0.00942171	0.00942171	0.86	0.4064
subject(sequence)	4	3.07934290	0.76983573	70.21	0.0006

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 51-62

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.873532	0.873532	1.13	0.3468
Error	4	3.079343	0.769836		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.029436	0.029436	2.68	0.1767
trt	1	0.009422	0.009422	0.86	0.4064
subject(sequence)	4	3.079343	0.769836	70.21	0.0006
Error: MS(Error)	4	0.043862	0.010965		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.873532	0.873532	1.13	0.3468
Error	4	3.079343	0.769836		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.037679	0.037679	3.44	0.1374
trt	1	0.009422	0.009422	0.86	0.4064
subject(sequence)	4	3.079343	0.769836	70.21	0.0006
Error: MS(Error)	4	0.043862	0.010965		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 51-62

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.873532	0.873532	1.13	0.3468
Error	4	3.079343	0.769836		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.037679	0.037679	3.44	0.1374
trt	1	0.009422	0.009422	0.86	0.4064
subject(sequence)	4	3.079343	0.769836	70.21	0.0006
Error: MS(Error)	4	0.043862	0.010965		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.873532	0.873532	1.13	0.3468
Error	4	3.079343	0.769836		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.037679	0.037679	3.44	0.1374
trt	1	0.009422	0.009422	0.86	0.4064
subject(sequence)	4	3.079343	0.769836	70.21	0.0006
Error: MS(Error)	4	0.043862	0.010965		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 51-62

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCLST	LSMEAN	Pr > t
A	9.23392481		0.4064
B	9.17448459		

trt	LN_AUCLST	LSMEAN	90% Confidence Limits	
A	9.233925	9.137260	9.330590	
B	9.174485	9.077820	9.271149	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.059440	-0.077265	0.196145

Dependent Variable: LN_AUCLST

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.05944022	0.06412503	0.93	0.4064	-0.07726452	0.19614497

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	6	101 201 302 412 414 503
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	12
Number of Observations Used	12

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LN_AUCIFO

R-Square	Coeff Var	Root MSE	LN_AUCIFO Mean
0.995963	0.748004	0.068472	9.154019

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.05980441	1.05980441	226.04	0.0001
period	1	0.04650127	0.04650127	9.92	0.0345
trt	1	0.02448664	0.02448664	5.22	0.0843
subject(sequence)	4	3.49588930	0.87397232	186.41	<.0001

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.05980441	1.05980441	226.04	0.0001
period	1	0.06526465	0.06526465	13.92	0.0203
trt	1	0.02448664	0.02448664	5.22	0.0843
subject(sequence)	4	3.49588930	0.87397232	186.41	<.0001

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.05980441	1.05980441	226.04	0.0001
period	1	0.06526465	0.06526465	13.92	0.0203
trt	1	0.02448664	0.02448664	5.22	0.0843
subject(sequence)	4	3.49588930	0.87397232	186.41	<.0001

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.05980441	1.05980441	226.04	0.0001
period	1	0.06526465	0.06526465	13.92	0.0203
trt	1	0.02448664	0.02448664	5.22	0.0843
subject(sequence)	4	3.49588930	0.87397232	186.41	<.0001

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 51-62

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.059804	1.059804	1.21	0.3326
Error	4	3.495889	0.873972		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.046501	0.046501	9.92	0.0345
trt	1	0.024487	0.024487	5.22	0.0843
subject(sequence)	4	3.495889	0.873972	186.41	<.0001
Error: MS(Error)	4	0.018754	0.004688		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.059804	1.059804	1.21	0.3326
Error	4	3.495889	0.873972		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.065265	0.065265	13.92	0.0203
trt	1	0.024487	0.024487	5.22	0.0843
subject(sequence)	4	3.495889	0.873972	186.41	<.0001
Error: MS(Error)	4	0.018754	0.004688		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 51-62

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.059804	1.059804	1.21	0.3326
Error	4	3.495889	0.873972		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.065265	0.065265	13.92	0.0203
trt	1	0.024487	0.024487	5.22	0.0843
subject(sequence)	4	3.495889	0.873972	186.41	<.0001
Error: MS(Error)	4	0.018754	0.004688		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.059804	1.059804	1.21	0.3326
Error	4	3.495889	0.873972		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.065265	0.065265	13.92	0.0203
trt	1	0.024487	0.024487	5.22	0.0843
subject(sequence)	4	3.495889	0.873972	186.41	<.0001
Error: MS(Error)	4	0.018754	0.004688		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 51-62

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCIFO	LSMEAN	Pr > t
A	9.30700089		0.0843
B	9.21117558		

trt	LN_AUCIFO	LSMEAN	90% Confidence Limits	
A	9.307001	9.243793	9.370209	
B	9.211176	9.147968	9.274384	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.095825	0.006436	0.185215

Dependent Variable: LN_AUCIFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	0.09582531	0.04193065	2.29	0.08430	0.00643560 0.18521503

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{\max} (ng/mL) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	6	101 201 302 412 414 503
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	12
Number of Observations Used	12

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LN_CMAX

R-Square	Coeff Var	Root MSE	LN_CMAX Mean
0.825032	4.588682	0.263298	5.737989

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.04000138	0.04000138	0.58	0.4898
period	1	0.20877172	0.20877172	3.01	0.1577
trt	1	0.28386147	0.28386147	4.09	0.1130
subject(sequence)	4	0.77494679	0.19373670	2.79	0.1717

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.04000138	0.04000138	0.58	0.4898
period	1	0.06410442	0.06410442	0.92	0.3907
trt	1	0.28386147	0.28386147	4.09	0.1130
subject(sequence)	4	0.77494679	0.19373670	2.79	0.1717

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.04000138	0.04000138	0.58	0.4898
period	1	0.06410442	0.06410442	0.92	0.3907
trt	1	0.28386147	0.28386147	4.09	0.1130
subject(sequence)	4	0.77494679	0.19373670	2.79	0.1717

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.04000138	0.04000138	0.58	0.4898
period	1	0.06410442	0.06410442	0.92	0.3907
trt	1	0.28386147	0.28386147	4.09	0.1130
subject(sequence)	4	0.77494679	0.19373670	2.79	0.1717

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 51-62

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.040001	0.040001	0.21	0.6731
Error	4	0.774947	0.193737		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.208772	0.208772	3.01	0.1577
trt	1	0.283861	0.283861	4.09	0.1130
subject(sequence)	4	0.774947	0.193737	2.79	0.1717
Error: MS(Error)	4	0.277304	0.069326		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.040001	0.040001	0.21	0.6731
Error	4	0.774947	0.193737		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.064104	0.064104	0.92	0.3907
trt	1	0.283861	0.283861	4.09	0.1130
subject(sequence)	4	0.774947	0.193737	2.79	0.1717
Error: MS(Error)	4	0.277304	0.069326		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 51-62

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.040001	0.040001	0.21	0.6731
Error	4	0.774947	0.193737		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.064104	0.064104	0.92	0.3907
trt	1	0.283861	0.283861	4.09	0.1130
subject(sequence)	4	0.774947	0.193737	2.79	0.1717
Error: MS(Error)	4	0.277304	0.069326		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.040001	0.040001	0.21	0.6731
Error	4	0.774947	0.193737		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.064104	0.064104	0.92	0.3907
trt	1	0.283861	0.283861	4.09	0.1130
subject(sequence)	4	0.774947	0.193737	2.79	0.1717
Error: MS(Error)	4	0.277304	0.069326		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 51-62

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LN_CMAX LSMEAN		Pr > t
A	5.55444448		0.1130
B	5.88070825		

trt	LN_CMAX LSMEAN	90% Confidence Limits	
A	5.554444	5.311390	5.797499
B	5.880708	5.637653	6.123763

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.326264	-0.669995	0.017468

Dependent Variable: LN_CMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.32626377	0.16123650	-2.02	0.1130	-0.66999529 0.01746774

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	6	101 201 302 412 414 503
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	12
Number of Observations Used	12

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LN_CLFOW

R-Square	Coeff Var	Root MSE	LN_CLFOW Mean
0.995684	-1.805055	0.068472	-3.793372

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.82529228	0.82529228	176.03	0.0002
period	1	0.04650127	0.04650127	9.92	0.0345
trt	1	0.02448664	0.02448664	5.22	0.0843
subject(sequence)	4	3.42986729	0.85746682	182.89	<.0001

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.82529228	0.82529228	176.03	0.0002
period	1	0.06526465	0.06526465	13.92	0.0203
trt	1	0.02448664	0.02448664	5.22	0.0843
subject(sequence)	4	3.42986729	0.85746682	182.89	<.0001

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.82529228	0.82529228	176.03	0.0002
period	1	0.06526465	0.06526465	13.92	0.0203
trt	1	0.02448664	0.02448664	5.22	0.0843
subject(sequence)	4	3.42986729	0.85746682	182.89	<.0001

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.82529228	0.82529228	176.03	0.0002
period	1	0.06526465	0.06526465	13.92	0.0203
trt	1	0.02448664	0.02448664	5.22	0.0843
subject(sequence)	4	3.42986729	0.85746682	182.89	<.0001

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 51-62

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.825292	0.825292	0.96	0.3821
Error	4	3.429867	0.857467		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.046501	0.046501	9.92	0.0345
trt	1	0.024487	0.024487	5.22	0.0843
subject(sequence)	4	3.429867	0.857467	182.89	<.0001
Error: MS(Error)	4	0.018754	0.004688		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.825292	0.825292	0.96	0.3821
Error	4	3.429867	0.857467		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.065265	0.065265	13.92	0.0203
trt	1	0.024487	0.024487	5.22	0.0843
subject(sequence)	4	3.429867	0.857467	182.89	<.0001
Error: MS(Error)	4	0.018754	0.004688		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 51-62

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.825292	0.825292	0.96	0.3821
Error	4	3.429867	0.857467		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.065265	0.065265	13.92	0.0203
trt	1	0.024487	0.024487	5.22	0.0843
subject(sequence)	4	3.429867	0.857467	182.89	<.0001
Error: MS(Error)	4	0.018754	0.004688		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.825292	0.825292	0.96	0.3821
Error	4	3.429867	0.857467		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.065265	0.065265	13.92	0.0203
trt	1	0.024487	0.024487	5.22	0.0843
subject(sequence)	4	3.429867	0.857467	182.89	<.0001
Error: MS(Error)	4	0.018754	0.004688		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 51-62

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_CLFOW	LSMEAN	Pr > t
A	-3.93400394		0.0843
B	-3.83817863		

trt	LN_CLFOW	LSMEAN	90% Confidence Limits	
A	-3.934004		-3.997212	-3.870796
B	-3.838179		-3.901387	-3.774971

Least Squares Means for Effect trt

Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.095825	-0.185215	-0.006436

Dependent Variable: LN_CLFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	-0.09582531	0.04193065	-2.29	0.0843	-0.18521503	-0.00643560

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	6	101 201 302 412 414 503
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	12
Number of Observations Used	12

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LN_CLFO

R-Square	Coeff Var	Root MSE	LN_CLFO Mean
0.995963	24.50124	0.068472	0.279465

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.05980441	1.05980441	226.04	0.0001
period	1	0.04650127	0.04650127	9.92	0.0345
trt	1	0.02448664	0.02448664	5.22	0.0843
subject(sequence)	4	3.49588930	0.87397232	186.41	<.0001

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.05980441	1.05980441	226.04	0.0001
period	1	0.06526465	0.06526465	13.92	0.0203
trt	1	0.02448664	0.02448664	5.22	0.0843
subject(sequence)	4	3.49588930	0.87397232	186.41	<.0001

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.05980441	1.05980441	226.04	0.0001
period	1	0.06526465	0.06526465	13.92	0.0203
trt	1	0.02448664	0.02448664	5.22	0.0843
subject(sequence)	4	3.49588930	0.87397232	186.41	<.0001

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.05980441	1.05980441	226.04	0.0001
period	1	0.06526465	0.06526465	13.92	0.0203
trt	1	0.02448664	0.02448664	5.22	0.0843
subject(sequence)	4	3.49588930	0.87397232	186.41	<.0001

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 51-62

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.059804	1.059804	1.21	0.3326
Error	4	3.495889	0.873972		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.046501	0.046501	9.92	0.0345
trt	1	0.024487	0.024487	5.22	0.0843
subject(sequence)	4	3.495889	0.873972	186.41	<.0001
Error: MS(Error)	4	0.018754	0.004688		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.059804	1.059804	1.21	0.3326
Error	4	3.495889	0.873972		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.065265	0.065265	13.92	0.0203
trt	1	0.024487	0.024487	5.22	0.0843
subject(sequence)	4	3.495889	0.873972	186.41	<.0001
Error: MS(Error)	4	0.018754	0.004688		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 51-62

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.059804	1.059804	1.21	0.3326
Error	4	3.495889	0.873972		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.065265	0.065265	13.92	0.0203
trt	1	0.024487	0.024487	5.22	0.0843
subject(sequence)	4	3.495889	0.873972	186.41	<.0001
Error: MS(Error)	4	0.018754	0.004688		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.059804	1.059804	1.21	0.3326
Error	4	3.495889	0.873972		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.065265	0.065265	13.92	0.0203
trt	1	0.024487	0.024487	5.22	0.0843
subject(sequence)	4	3.495889	0.873972	186.41	<.0001
Error: MS(Error)	4	0.018754	0.004688		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 51-62

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFO	LSMEAN	Pr > t
A	0.12648303		0.0843
B	0.22230834		

trt	LN_CLFO	LSMEAN	90% Confidence Limits	
A	0.126483		0.063275	0.189691
B	0.222308		0.159100	0.285516

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.095825	-0.185215	-0.006436

Dependent Variable: LN_CLFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	-0.09582531	0.04193065	-2.29	0.0843	-0.18521503	-0.00643560

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	6	101 201 302 412 414 503
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	12
Number of Observations Used	12

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LN_VZFOW

R-Square	Coeff Var	Root MSE	LN_VZFOW Mean
0.850422	149.0144	0.249852	0.167670

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.06679525	0.06679525	1.07	0.3594
period	1	0.00364857	0.00364857	0.06	0.8209
trt	1	0.00056004	0.00056004	0.01	0.9291
subject(sequence)	4	1.34868165	0.33717041	5.40	0.0656

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.06679525	0.06679525	1.07	0.3594
period	1	0.00420387	0.00420387	0.07	0.8081
trt	1	0.00056004	0.00056004	0.01	0.9291
subject(sequence)	4	1.34868165	0.33717041	5.40	0.0656

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.06679525	0.06679525	1.07	0.3594
period	1	0.00420387	0.00420387	0.07	0.8081
trt	1	0.00056004	0.00056004	0.01	0.9291
subject(sequence)	4	1.34868165	0.33717041	5.40	0.0656

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.06679525	0.06679525	1.07	0.3594
period	1	0.00420387	0.00420387	0.07	0.8081
trt	1	0.00056004	0.00056004	0.01	0.9291
subject(sequence)	4	1.34868165	0.33717041	5.40	0.0656

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 51-62

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.066795	0.066795	0.20	0.6793
Error	4	1.348682	0.337170		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.003649	0.003649	0.06	0.8209
trt	1	0.000560	0.000560	0.01	0.9291
subject(sequence)	4	1.348682	0.337170	5.40	0.0656
Error: MS(Error)	4	0.249704	0.062426		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.066795	0.066795	0.20	0.6793
Error	4	1.348682	0.337170		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.004204	0.004204	0.07	0.8081
trt	1	0.000560	0.000560	0.01	0.9291
subject(sequence)	4	1.348682	0.337170	5.40	0.0656
Error: MS(Error)	4	0.249704	0.062426		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 51-62

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.066795	0.066795	0.20	0.6793
Error	4	1.348682	0.337170		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.004204	0.004204	0.07	0.8081
trt	1	0.000560	0.000560	0.01	0.9291
subject(sequence)	4	1.348682	0.337170	5.40	0.0656
Error: MS(Error)	4	0.249704	0.062426		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.066795	0.066795	0.20	0.6793
Error	4	1.348682	0.337170		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.004204	0.004204	0.07	0.8081
trt	1	0.000560	0.000560	0.01	0.9291
subject(sequence)	4	1.348682	0.337170	5.40	0.0656
Error: MS(Error)	4	0.249704	0.062426		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 51-62

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_VZFOW	LSMEAN	Pr > t
A	0.20129341		0.9291
B	0.18680157		

trt	LN_VZFOW	LSMEAN	90% Confidence Limits	
A	0.201293		-0.029349	0.431936
B	0.186802		-0.043841	0.417444

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.014492	-0.311686	0.340670

Dependent Variable: LN_VZFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.01449185	0.15300260	0.09	0.9291	-0.31168624	0.34066994

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	6	101 201 302 412 414 503
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	12
Number of Observations Used	12

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LN_VZFO

R-Square	Coeff Var	Root MSE	LN_VZFO Mean
0.847614	5.892035	0.249852	4.240507

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.01888858	0.01888858	0.30	0.6115
period	1	0.00364857	0.00364857	0.06	0.8209
trt	1	0.00056004	0.00056004	0.01	0.9291
subject(sequence)	4	1.36582781	0.34145695	5.47	0.0643

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.01888858	0.01888858	0.30	0.6115
period	1	0.00420387	0.00420387	0.07	0.8081
trt	1	0.00056004	0.00056004	0.01	0.9291
subject(sequence)	4	1.36582781	0.34145695	5.47	0.0643

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.01888858	0.01888858	0.30	0.6115
period	1	0.00420387	0.00420387	0.07	0.8081
trt	1	0.00056004	0.00056004	0.01	0.9291
subject(sequence)	4	1.36582781	0.34145695	5.47	0.0643

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.01888858	0.01888858	0.30	0.6115
period	1	0.00420387	0.00420387	0.07	0.8081
trt	1	0.00056004	0.00056004	0.01	0.9291
subject(sequence)	4	1.36582781	0.34145695	5.47	0.0643

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 51-62

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.018889	0.018889	0.06	0.8256
Error	4	1.365828	0.341457		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.003649	0.003649	0.06	0.8209
trt	1	0.000560	0.000560	0.01	0.9291
subject(sequence)	4	1.365828	0.341457	5.47	0.0643
Error: MS(Error)	4	0.249704	0.062426		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.018889	0.018889	0.06	0.8256
Error	4	1.365828	0.341457		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.004204	0.004204	0.07	0.8081
trt	1	0.000560	0.000560	0.01	0.9291
subject(sequence)	4	1.365828	0.341457	5.47	0.0643
Error: MS(Error)	4	0.249704	0.062426		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 51-62

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.018889	0.018889	0.06	0.8256
Error	4	1.365828	0.341457		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.004204	0.004204	0.07	0.8081
trt	1	0.000560	0.000560	0.01	0.9291
subject(sequence)	4	1.365828	0.341457	5.47	0.0643
Error: MS(Error)	4	0.249704	0.062426		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.018889	0.018889	0.06	0.8256
Error	4	1.365828	0.341457		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.004204	0.004204	0.07	0.8081
trt	1	0.000560	0.000560	0.01	0.9291
subject(sequence)	4	1.365828	0.341457	5.47	0.0643
Error: MS(Error)	4	0.249704	0.062426		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 51-62

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_VZFO	LSMEAN	Pr > t
A	4.26178039		0.9291
B	4.24728854		

trt	LN_VZFO	LSMEAN	90% Confidence Limits	
A	4.261780	4.031138	4.492423	
B	4.247289	4.016646	4.477931	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.014492	-0.311686	0.340670

Dependent Variable: LN_VZFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.01449185	0.15300260	0.09	0.9291	-0.31168624	0.34066994

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	6	101 201 302 412 414 503
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	12
Number of Observations Used	12

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{max} (h) Weight Group: 51-62

The GLM Procedure

Dependent Variable: TMAX

R-Square	Coeff Var	Root MSE	TMAX Mean
0.730498	75.37925	0.965357	1.280667

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.25317604	0.25317604	0.27	0.6297
period	1	1.54083333	1.54083333	1.65	0.2679
trt	1	3.84080004	3.84080004	4.12	0.1122
subject(sequence)	4	4.46918363	1.11729591	1.20	0.4323

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.25317604	0.25317604	0.27	0.6297
period	1	0.26733704	0.26733704	0.29	0.6206
trt	1	3.84080004	3.84080004	4.12	0.1122
subject(sequence)	4	4.46918363	1.11729591	1.20	0.4323

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.25317604	0.25317604	0.27	0.6297
period	1	0.26733704	0.26733704	0.29	0.6206
trt	1	3.84080004	3.84080004	4.12	0.1122
subject(sequence)	4	4.46918363	1.11729591	1.20	0.4323

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.25317604	0.25317604	0.27	0.6297
period	1	0.26733704	0.26733704	0.29	0.6206
trt	1	3.84080004	3.84080004	4.12	0.1122
subject(sequence)	4	4.46918363	1.11729591	1.20	0.4323

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 51-62

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.253176	0.253176	0.23	0.6589
Error	4	4.469184	1.117296		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	1.540833	1.540833	1.65	0.2679
trt	1	3.840800	3.840800	4.12	0.1122
subject(sequence)	4	4.469184	1.117296	1.20	0.4323
Error: MS(Error)	4	3.727656	0.931914		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.253176	0.253176	0.23	0.6589
Error	4	4.469184	1.117296		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.267337	0.267337	0.29	0.6206
trt	1	3.840800	3.840800	4.12	0.1122
subject(sequence)	4	4.469184	1.117296	1.20	0.4323
Error: MS(Error)	4	3.727656	0.931914		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{max} (h) Weight Group: 51-62

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.253176	0.253176	0.23	0.6589
Error	4	4.469184	1.117296		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.267337	0.267337	0.29	0.6206
trt	1	3.840800	3.840800	4.12	0.1122
subject(sequence)	4	4.469184	1.117296	1.20	0.4323
Error: MS(Error)	4	3.727656	0.931914		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.253176	0.253176	0.23	0.6589
Error	4	4.469184	1.117296		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.267337	0.267337	0.29	0.6206
trt	1	3.840800	3.840800	4.12	0.1122
subject(sequence)	4	4.469184	1.117296	1.20	0.4323
Error: MS(Error)	4	3.727656	0.931914		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 51-62

Least Squares Means

		H0:LSMean1=LSMean2	
trt	TMAX LSMEAN		Pr > t
A	1.82937500		0.1122
B	0.62925000		

trt	TMAX LSMEAN	90% Confidence Limits	
A	1.829375	0.938238	2.720512
B	0.629250	-0.261887	1.520387

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	1.200125	-0.060133	2.460383

Dependent Variable: TMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	1.20012500	0.59115794	2.03	0.1122	-0.06013316 2.46038316

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	6	101 201 302 412 414 503
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	12
Number of Observations Used	12

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LAMZ

R-Square	Coeff Var	Root MSE	LAMZ Mean
0.984784	11.99520	0.002714	0.022627

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00062156	0.00062156	84.37	0.0008
period	1	0.00002840	0.00002840	3.86	0.1211
trt	1	0.00000016	0.00000016	0.02	0.8885
subject(sequence)	4	0.00125697	0.00031424	42.66	0.0016

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00062156	0.00062156	84.37	0.0008
period	1	0.00002391	0.00002391	3.25	0.1460
trt	1	0.00000016	0.00000016	0.02	0.8885
subject(sequence)	4	0.00125697	0.00031424	42.66	0.0016

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00062156	0.00062156	84.37	0.0008
period	1	0.00002391	0.00002391	3.25	0.1460
trt	1	0.00000016	0.00000016	0.02	0.8885
subject(sequence)	4	0.00125697	0.00031424	42.66	0.0016

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00062156	0.00062156	84.37	0.0008
period	1	0.00002391	0.00002391	3.25	0.1460
trt	1	0.00000016	0.00000016	0.02	0.8885
subject(sequence)	4	0.00125697	0.00031424	42.66	0.0016

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 51-62

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.000622	0.000622	1.98	0.2323
Error	4	0.001257	0.000314		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.000028401	0.000028401	3.86	0.1211
trt	1	0.000000164	0.000000164	0.02	0.8885
subject(sequence)	4	0.001257	0.000314	42.66	0.0016
Error: MS(Error)	4	0.000029467	0.000007367		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.000622	0.000622	1.98	0.2323
Error	4	0.001257	0.000314		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.000023907	0.000023907	3.25	0.1460
trt	1	0.000000164	0.000000164	0.02	0.8885
subject(sequence)	4	0.001257	0.000314	42.66	0.0016
Error: MS(Error)	4	0.000029467	0.000007367		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 51-62

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.000622	0.000622	1.98	0.2323
Error	4	0.001257	0.000314		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.000023907	0.000023907	3.25	0.1460
trt	1	0.000000164	0.000000164	0.02	0.8885
subject(sequence)	4	0.001257	0.000314	42.66	0.0016
Error: MS(Error)	4	0.000029467	0.000007367		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.000622	0.000622	1.98	0.2323
Error	4	0.001257	0.000314		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.000023907	0.000023907	3.25	0.1460
trt	1	0.000000164	0.000000164	0.02	0.8885
subject(sequence)	4	0.001257	0.000314	42.66	0.0016
Error: MS(Error)	4	0.000029467	0.000007367		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 51-62

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LAMZ LSMEAN		Pr > t
A	0.02020687		0.8885
B	0.01995872		

trt	LAMZ LSMEAN	90% Confidence Limits	
A	0.020207	0.017701	0.022712
B	0.019959	0.017453	0.022464

Least Squares Means for Effect trt

		Difference Between		
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.000248	-0.003295	0.003791

Dependent Variable: LAMZ

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.00024814	0.00166210	0.15	0.8885	-0.00329519	0.00379148

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	6	101 201 302 412 414 503
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	12
Number of Observations Used	12

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LAMZHL

R-Square	Coeff Var	Root MSE	LAMZHL Mean
0.912041	30.75229	13.38035	43.51010

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	2163.641142	2163.641142	12.09	0.0254
period	1	231.387288	231.387288	1.29	0.3191
trt	1	354.611103	354.611103	1.98	0.2321
subject(sequence)	4	4675.957475	1168.989369	6.53	0.0482

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	2163.641142	2163.641142	12.09	0.0254
period	1	425.122715	425.122715	2.37	0.1982
trt	1	354.611103	354.611103	1.98	0.2321
subject(sequence)	4	4675.957475	1168.989369	6.53	0.0482

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	2163.641142	2163.641142	12.09	0.0254
period	1	425.122715	425.122715	2.37	0.1982
trt	1	354.611103	354.611103	1.98	0.2321
subject(sequence)	4	4675.957475	1168.989369	6.53	0.0482

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	2163.641142	2163.641142	12.09	0.0254
period	1	425.122715	425.122715	2.37	0.1982
trt	1	354.611103	354.611103	1.98	0.2321
subject(sequence)	4	4675.957475	1168.989369	6.53	0.0482

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 51-62

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	2163.641142	2163.641142	1.85	0.2453
Error	4	4675.957475	1168.989369		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	231.387288	231.387288	1.29	0.3191
trt	1	354.611103	354.611103	1.98	0.2321
subject(sequence)	4	4675.957475	1168.989369	6.53	0.0482
Error: MS(Error)	4	716.135395	179.033849		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	2163.641142	2163.641142	1.85	0.2453
Error	4	4675.957475	1168.989369		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	425.122715	425.122715	2.37	0.1982
trt	1	354.611103	354.611103	1.98	0.2321
subject(sequence)	4	4675.957475	1168.989369	6.53	0.0482
Error: MS(Error)	4	716.135395	179.033849		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 51-62

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	2163.641142	2163.641142	1.85	0.2453
Error	4	4675.957475	1168.989369		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	425.122715	425.122715	2.37	0.1982
trt	1	354.611103	354.611103	1.98	0.2321
subject(sequence)	4	4675.957475	1168.989369	6.53	0.0482
Error: MS(Error)	4	716.135395	179.033849		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	2163.641142	2163.641142	1.85	0.2453
Error	4	4675.957475	1168.989369		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	425.122715	425.122715	2.37	0.1982
trt	1	354.611103	354.611103	1.98	0.2321
subject(sequence)	4	4675.957475	1168.989369	6.53	0.0482
Error: MS(Error)	4	716.135395	179.033849		

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 51-62

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LAMZHL LSMEAN		Pr > t
A	54.0233424		0.2321
B	42.4916832		

trt	LAMZHL LSMEAN	90% Confidence Limits	
A	54.023342	41.671714	66.374970
B	42.491683	30.140055	54.843311

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	11.531659	-5.936180	28.999499

Dependent Variable: LAMZHL

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	11.5316592	8.19375941	1.41	0.2321	-5.9361805 28.9994989

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	101 201
sequence	1	ABC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LN_AUCLST

R-Square	Coeff Var	Root MSE	LN_AUCLST Mean
0.995425	0.993048	0.089625	9.025241

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.00308741	0.00308741	0.38	0.6467
subject(sequence)	1	1.74458843	1.74458843	217.19	0.0431

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.00308741	0.00308741	0.38	0.6467
subject(sequence)	1	1.74458843	1.74458843	217.19	0.0431

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.00308741	0.00308741	0.38	0.6467
subject(sequence)	1	1.74458843	1.74458843	217.19	0.0431

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.00308741	0.00308741	0.38	0.6467
subject(sequence)	1	1.74458843	1.74458843	217.19	0.0431

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 51-62

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCLST	LSMEAN	Pr > t
B	9.05302332		0.6467
C	8.99745888		

trt	LN_AUCLST	LSMEAN	90% Confidence Limits	
B	9.053023		8.652893	9.453154
C	8.997459		8.597329	9.397589

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.055564	-0.510305	0.621434

The GLM Procedure

Dependent Variable: LN_AUCLST

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	-0.05556445	0.08962497	-0.62	0.6467	-0.62143424	0.51030535

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	101 201
sequence	1	ABC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LN_AUCIFO

R-Square	Coeff Var	Root MSE	LN_AUCIFO Mean
0.999287	0.422185	0.038401	9.095817

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00001005	0.00001005	0.01	0.9476
subject(sequence)	1	2.06771611	2.06771611	1402.17	0.0170

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00001005	0.00001005	0.01	0.9476
subject(sequence)	1	2.06771611	2.06771611	1402.17	0.0170

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00001005	0.00001005	0.01	0.9476
subject(sequence)	1	2.06771611	2.06771611	1402.17	0.0170

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00001005	0.00001005	0.01	0.9476
subject(sequence)	1	2.06771611	2.06771611	1402.17	0.0170

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 51-62

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCIFO	LSMEAN	Pr > t
B	9.09740260		0.9476
C	9.09423224		

trt	LN_AUCIFO	LSMEAN	90% Confidence Limits	
B	9.097403		8.925960	9.268845
C	9.094232		8.922790	9.265674

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.003170	-0.239285	0.245626

The GLM Procedure

Dependent Variable: LN_AUCIFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	-0.00317035	0.03840122	-0.08	0.9476	-0.24562613	0.23928542

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: C_{\max} (ng/mL) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	101 201
sequence	1	ABC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LN_CMAX

R-Square	Coeff Var	Root MSE	LN_CMAX Mean
0.996701	1.022835	0.056591	5.532719

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.27556715	0.27556715	86.05	0.0684
subject(sequence)	1	0.69186372	0.69186372	216.04	0.0432

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.27556715	0.27556715	86.05	0.0684
subject(sequence)	1	0.69186372	0.69186372	216.04	0.0432

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.27556715	0.27556715	86.05	0.0684
subject(sequence)	1	0.69186372	0.69186372	216.04	0.0432

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.27556715	0.27556715	86.05	0.0684
subject(sequence)	1	0.69186372	0.69186372	216.04	0.0432

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 51-62

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CMAX	LSMEAN	Pr > t
B	5.79519172		0.0684
C	5.27024682		

trt	LN_CMAX	LSMEAN	90% Confidence Limits	
B	5.795192		5.542543	6.047840
C	5.270247		5.017598	5.522895

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.524945	0.167646	0.882244

The GLM Procedure

Dependent Variable: LN_CMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	-0.52494490	0.05659061	-9.28	0.0684	-0.88224396	-0.16764585

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	101 201
sequence	1	ABC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LN_CLFOW

R-Square	Coeff Var	Root MSE	LN_CLFOW Mean
0.999296	-1.025649	0.038401	-3.744090

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00001005	0.00001005	0.01	0.9476
subject(sequence)	1	2.09205676	2.09205676	1418.68	0.0169

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00001005	0.00001005	0.01	0.9476
subject(sequence)	1	2.09205676	2.09205676	1418.68	0.0169

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00001005	0.00001005	0.01	0.9476
subject(sequence)	1	2.09205676	2.09205676	1418.68	0.0169

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00001005	0.00001005	0.01	0.9476
subject(sequence)	1	2.09205676	2.09205676	1418.68	0.0169

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 51-62

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFOW	LSMEAN	Pr > t
B	-3.74567555		0.9476
C	-3.74250520		

trt	LN_CLFOW	LSMEAN	90% Confidence Limits	
B	-3.745676		-3.917118	-3.574233
C	-3.742505		-3.913947	-3.571063

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.003170	-0.245626	0.239285

The GLM Procedure

Dependent Variable: LN_CLFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	0.00317035	0.03840122	0.08	0.9476	-0.23928542	0.24562613

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	101 201
sequence	1	ABC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LN_CLFO

R-Square	Coeff Var	Root MSE	LN_CLFO Mean
0.999287	11.37253	0.038401	0.337667

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00001005	0.00001005	0.01	0.9476
subject(sequence)	1	2.06771611	2.06771611	1402.17	0.0170

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00001005	0.00001005	0.01	0.9476
subject(sequence)	1	2.06771611	2.06771611	1402.17	0.0170

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00001005	0.00001005	0.01	0.9476
subject(sequence)	1	2.06771611	2.06771611	1402.17	0.0170

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00001005	0.00001005	0.01	0.9476
subject(sequence)	1	2.06771611	2.06771611	1402.17	0.0170

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h) Weight Group: 51-62

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFO	LSMEAN	Pr > t
B	0.33608132		0.9476
C	0.33925168		

trt	LN_CLFO	LSMEAN	90% Confidence Limits	
B	0.336081		0.164639	0.507523
C	0.339252		0.167810	0.510694

Least Squares Means for Effect trt

Difference Between

i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.003170	-0.245626	0.239285

The GLM Procedure

Dependent Variable: LN_CLFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	0.00317035	0.03840122	0.08	0.9476	-0.23928542 0.24562613

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	101 201
sequence	1	ABC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LN_VZFOW

R-Square	Coeff Var	Root MSE	LN_VZFOW Mean
0.507929	87.10023	0.257878	0.296071

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.06357519	0.06357519	0.96	0.5072
subject(sequence)	1	0.00506924	0.00506924	0.08	0.8285

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.06357519	0.06357519	0.96	0.5072
subject(sequence)	1	0.00506924	0.00506924	0.08	0.8285

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.06357519	0.06357519	0.96	0.5072
subject(sequence)	1	0.00506924	0.00506924	0.08	0.8285

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.06357519	0.06357519	0.96	0.5072
subject(sequence)	1	0.00506924	0.00506924	0.08	0.8285

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 51-62

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_VZFOW	LSMEAN	Pr > t
B	0.1700011		0.5072
C	0.42214132		

trt	LN_VZFOW	LSMEAN	90% Confidence Limits	
B	0.170000		-0.981296	1.321297
C	0.422141		-0.729155	1.573438

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.252141	-1.880320	1.376038

The GLM Procedure

Dependent Variable: LN_VZFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	0.25214122	0.25787826	0.98	0.5072	-1.37603804	1.88032048

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	101 201
sequence	1	ABC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LN_VZFO

R-Square	Coeff Var	Root MSE	LN_VZFO Mean
0.512521	5.890553	0.257878	4.377828

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.06357519	0.06357519	0.96	0.5072
subject(sequence)	1	0.00634213	0.00634213	0.10	0.8093

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.06357519	0.06357519	0.96	0.5072
subject(sequence)	1	0.00634213	0.00634213	0.10	0.8093

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.06357519	0.06357519	0.96	0.5072
subject(sequence)	1	0.00634213	0.00634213	0.10	0.8093

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	0.06357519	0.06357519	0.96	0.5072
subject(sequence)	1	0.00634213	0.00634213	0.10	0.8093

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L) Weight Group: 51-62

The GLM Procedure
Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_VZFO	LSMEAN	Pr > t
B	4.25175698		0.5072
C	4.50389820		

trt	LN_VZFO	LSMEAN	90% Confidence Limits	
B	4.251757		3.100460	5.403054
C	4.503898		3.352602	5.655195

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.252141	-1.880320	1.376038

The GLM Procedure

Dependent Variable: LN_VZFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	0.25214122	0.25787826	0.98	0.5072	-1.37603804	1.88032048

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	101 201
sequence	1	ABC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h) Weight Group: 51-62

The GLM Procedure

Dependent Variable: TMAX

R-Square	Coeff Var	Root MSE	TMAX Mean
0.470588	120.0000	1.500000	1.250000

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	1.0000000	1.0000000	0.44	0.6257
subject(sequence)	1	1.0000000	1.0000000	0.44	0.6257

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	1.0000000	1.0000000	0.44	0.6257
subject(sequence)	1	1.0000000	1.0000000	0.44	0.6257

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	1.0000000	1.0000000	0.44	0.6257
subject(sequence)	1	1.0000000	1.0000000	0.44	0.6257

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.0000000			
trt	1	1.0000000	1.0000000	0.44	0.6257
subject(sequence)	1	1.0000000	1.0000000	0.44	0.6257

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h) Weight Group: 51-62

The GLM Procedure
Least Squares Means

		H0:LSMean1=LSMean2	
trt	TMAX LSMEAN		Pr > t
B	0.7500000		0.6257
C	1.7500000		

trt	TMAX LSMEAN	90% Confidence Limits	
B	0.750000	-5.946745	7.446745
C	1.750000	-4.946745	8.446745

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-1.000000	-10.470627	8.470627

The GLM Procedure

Dependent Variable: TMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	1.0000000	1.5000000	0.67	0.6257	-8.47062727 10.47062727

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	101 201
sequence	1	ABC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LAMZ

R-Square	Coeff Var	Root MSE	LAMZ Mean
0.997732	6.051039	0.001393	0.023023

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00000626	0.00000626	3.22	0.3235
subject(sequence)	1	0.00084772	0.00084772	436.78	0.0304

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00000626	0.00000626	3.22	0.3235
subject(sequence)	1	0.00084772	0.00084772	436.78	0.0304

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00000626	0.00000626	3.22	0.3235
subject(sequence)	1	0.00084772	0.00084772	436.78	0.0304

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00000626	0.00000626	3.22	0.3235
subject(sequence)	1	0.00084772	0.00084772	436.78	0.0304

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h) Weight Group: 51-62

The GLM Procedure
Least Squares Means

			H0:LSMean1=LSMean2
trt	LAMZ LSMEAN		Pr > t
B	0.02427392		0.3235
C	0.02177245		

trt	LAMZ LSMEAN	90% Confidence Limits	
B	0.024274	0.018054	0.030494
C	0.021772	0.015553	0.027992

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.002501	-0.006294	0.011297

The GLM Procedure

Dependent Variable: LAMZ

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.00250147	0.00139314	-1.80	0.3235	-0.01129742 0.00629448

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 51-62

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	101 201
sequence	1	ABC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 51-62

The GLM Procedure

Dependent Variable: LAMZHL

R-Square	Coeff Var	Root MSE	LAMZHL Mean
0.928959	37.39729	19.61552	52.45171

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.000000			
trt	1	406.408780	406.408780	1.06	0.4913
subject(sequence)	1	4624.986296	4624.986296	12.02	0.1788

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.000000			
trt	1	406.408780	406.408780	1.06	0.4913
subject(sequence)	1	4624.986296	4624.986296	12.02	0.1788

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.000000			
trt	1	406.408780	406.408780	1.06	0.4913
subject(sequence)	1	4624.986296	4624.986296	12.02	0.1788

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.000000			
trt	1	406.408780	406.408780	1.06	0.4913
subject(sequence)	1	4624.986296	4624.986296	12.02	0.1788

Listing 16.1.9-5 ANOVA for Treatment Comparison of Diazepam for Weight Group 51-62 kg - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 51-62

The GLM Procedure
Least Squares Means

			H0:LSMean1=LSMean2
trt	LAMZHL LSMEAN		Pr > t
B	42.3719162		0.4913
C	62.5314991		

trt	LAMZHL LSMEAN	90% Confidence Limits	
B	42.371916	-45.201494	129.945327
C	62.531499	-25.041912	150.104910

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-20.159583	-144.007088	103.687922

The GLM Procedure

Dependent Variable: LAMZHL

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	20.1595828	19.6155178	1.03	0.4913	-103.6879223 144.0070879

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	202 303 408 413
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LN_AUCLST

R-Square	Coeff Var	Root MSE	LN_AUCLST Mean
0.998187	0.385829	0.032800	8.501081

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.09031713	0.09031713	83.95	0.0117
period	1	0.02145914	0.02145914	19.95	0.0467
trt	1	0.00001757	0.00001757	0.02	0.9100
subject(sequence)	2	1.07303798	0.53651899	498.71	0.0020

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.09031713	0.09031713	83.95	0.0117
period	1	0.02145914	0.02145914	19.95	0.0467
trt	1	0.00001757	0.00001757	0.02	0.9100
subject(sequence)	2	1.07303798	0.53651899	498.71	0.0020

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.09031713	0.09031713	83.95	0.0117
period	1	0.02145914	0.02145914	19.95	0.0467
trt	1	0.00001757	0.00001757	0.02	0.9100
subject(sequence)	2	1.07303798	0.53651899	498.71	0.0020

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.09031713	0.09031713	83.95	0.0117
period	1	0.02145914	0.02145914	19.95	0.0467
trt	1	0.00001757	0.00001757	0.02	0.9100
subject(sequence)	2	1.07303798	0.53651899	498.71	0.0020

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 63-75

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.090317	0.090317	0.17	0.7214
Error	2	1.073038	0.536519		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	0.021459	0.021459	19.95	0.0467
trt	1	0.000017570	0.000017570	0.02	0.9100
subject(sequence)	2	1.073038	0.536519	498.71	0.0020
Error: MS(Error)	2	0.002152	0.001076		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.090317	0.090317	0.17	0.7214
Error	2	1.073038	0.536519		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.021459	0.021459	19.95	0.0467
trt	1	0.000017570	0.000017570	0.02	0.9100
subject(sequence)	2	1.073038	0.536519	498.71	0.0020
Error: MS(Error)	2	0.002152	0.001076		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 63-75

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.090317	0.090317	0.17	0.7214
Error	2	1.073038	0.536519		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.021459	0.021459	19.95	0.0467
trt	1	0.000017570	0.000017570	0.02	0.9100
subject(sequence)	2	1.073038	0.536519	498.71	0.0020
Error: MS(Error)	2	0.002152	0.001076		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.090317	0.090317	0.17	0.7214
Error	2	1.073038	0.536519		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.021459	0.021459	19.95	0.0467
trt	1	0.000017570	0.000017570	0.02	0.9100
subject(sequence)	2	1.073038	0.536519	498.71	0.0020
Error: MS(Error)	2	0.002152	0.001076		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 63-75

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCLST	LSMEAN	Pr > t
A	8.50256332		0.9100
B	8.49959937		

trt	LN_AUCLST	LSMEAN	90% Confidence Limits	
A	8.502563	8.454676	8.550451	
B	8.499599	8.451712	8.547487	

Least Squares Means for Effect trt

Difference Between

i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.002964	-0.064759	0.070687

Dependent Variable: LN_AUCLST

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	0.00296395	0.02319284	0.13	0.9100	-0.06475879 0.07068670

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: $AUC_{0-\infty}$ (h*ng/mL) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	202 303 408 413
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LN_AUCIFO

R-Square	Coeff Var	Root MSE	LN_AUCIFO Mean
0.998102	0.409031	0.034910	8.534749

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.10836268	0.10836268	88.92	0.0111
period	1	0.01560178	0.01560178	12.80	0.0700
trt	1	0.00019420	0.00019420	0.16	0.7283
subject(sequence)	2	1.15775241	0.57887620	475.00	0.0021

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.10836268	0.10836268	88.92	0.0111
period	1	0.01560178	0.01560178	12.80	0.0700
trt	1	0.00019420	0.00019420	0.16	0.7283
subject(sequence)	2	1.15775241	0.57887620	475.00	0.0021

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.10836268	0.10836268	88.92	0.0111
period	1	0.01560178	0.01560178	12.80	0.0700
trt	1	0.00019420	0.00019420	0.16	0.7283
subject(sequence)	2	1.15775241	0.57887620	475.00	0.0021

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.10836268	0.10836268	88.92	0.0111
period	1	0.01560178	0.01560178	12.80	0.0700
trt	1	0.00019420	0.00019420	0.16	0.7283
subject(sequence)	2	1.15775241	0.57887620	475.00	0.0021

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 63-75

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.108363	0.108363	0.19	0.7074
Error	2	1.157752	0.578876		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	0.015602	0.015602	12.80	0.0700
trt	1	0.000194	0.000194	0.16	0.7283
subject(sequence)	2	1.157752	0.578876	475.00	0.0021
Error: MS(Error)	2	0.002437	0.001219		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.108363	0.108363	0.19	0.7074
Error	2	1.157752	0.578876		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.015602	0.015602	12.80	0.0700
trt	1	0.000194	0.000194	0.16	0.7283
subject(sequence)	2	1.157752	0.578876	475.00	0.0021
Error: MS(Error)	2	0.002437	0.001219		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 63-75

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.108363	0.108363	0.19	0.7074
Error	2	1.157752	0.578876		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.015602	0.015602	12.80	0.0700
trt	1	0.000194	0.000194	0.16	0.7283
subject(sequence)	2	1.157752	0.578876	475.00	0.0021
Error: MS(Error)	2	0.002437	0.001219		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.108363	0.108363	0.19	0.7074
Error	2	1.157752	0.578876		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.015602	0.015602	12.80	0.0700
trt	1	0.000194	0.000194	0.16	0.7283
subject(sequence)	2	1.157752	0.578876	475.00	0.0021
Error: MS(Error)	2	0.002437	0.001219		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 63-75

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCIFO	LSMEAN	Pr > t
A	8.53967571		0.7283
B	8.52982180		

trt	LN_AUCIFO	LSMEAN	90% Confidence Limits	
A	8.539676	8.488708	8.590644	
B	8.529822	8.478854	8.580790	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.009854	-0.062226	0.081933

Dependent Variable: LN_AUCIFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.00985391	0.02468491	0.40	0.7283	-0.06222566	0.08193349

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{\max} (ng/mL) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	202 303 408 413
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LN_CMAX

R-Square	Coeff Var	Root MSE	LN_CMAX Mean
0.395997	10.38897	0.572102	5.506819

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.24870956	0.24870956	0.76	0.4753
period	1	0.00507523	0.00507523	0.02	0.9123
trt	1	0.01964743	0.01964743	0.06	0.8293
subject(sequence)	2	0.15573658	0.07786829	0.24	0.8078

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.24870956	0.24870956	0.76	0.4753
period	1	0.00507523	0.00507523	0.02	0.9123
trt	1	0.01964743	0.01964743	0.06	0.8293
subject(sequence)	2	0.15573658	0.07786829	0.24	0.8078

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.24870956	0.24870956	0.76	0.4753
period	1	0.00507523	0.00507523	0.02	0.9123
trt	1	0.01964743	0.01964743	0.06	0.8293
subject(sequence)	2	0.15573658	0.07786829	0.24	0.8078

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.24870956	0.24870956	0.76	0.4753
period	1	0.00507523	0.00507523	0.02	0.9123
trt	1	0.01964743	0.01964743	0.06	0.8293
subject(sequence)	2	0.15573658	0.07786829	0.24	0.8078

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 63-75

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.248710	0.248710	3.19	0.2158
Error	2	0.155737	0.077868		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	0.005075	0.005075	0.02	0.9123
trt	1	0.019647	0.019647	0.06	0.8293
subject(sequence)	2	0.155737	0.077868	0.24	0.8078
Error: MS(Error)	2	0.654600	0.327300		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.248710	0.248710	3.19	0.2158
Error	2	0.155737	0.077868		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.005075	0.005075	0.02	0.9123
trt	1	0.019647	0.019647	0.06	0.8293
subject(sequence)	2	0.155737	0.077868	0.24	0.8078
Error: MS(Error)	2	0.654600	0.327300		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 63-75

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.248710	0.248710	3.19	0.2158
Error	2	0.155737	0.077868		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.005075	0.005075	0.02	0.9123
trt	1	0.019647	0.019647	0.06	0.8293
subject(sequence)	2	0.155737	0.077868	0.24	0.8078
Error: MS(Error)	2	0.654600	0.327300		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.248710	0.248710	3.19	0.2158
Error	2	0.155737	0.077868		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.005075	0.005075	0.02	0.9123
trt	1	0.019647	0.019647	0.06	0.8293
subject(sequence)	2	0.155737	0.077868	0.24	0.8078
Error: MS(Error)	2	0.654600	0.327300		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 63-75

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LN_CMAX LSMEAN		Pr > t
A	5.45726168		0.8293
B	5.55637635		

trt	LN_CMAX LSMEAN	90% Confidence Limits	
A	5.457262	4.621998	6.292526
B	5.556376	4.721112	6.391640

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.099115	-1.280356	1.082127

Dependent Variable: LN_CMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.09911467	0.40453685	-0.25	0.8293	-1.28035645 1.08212712

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	202 303 408 413
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LN_CLFOW

R-Square	Coeff Var	Root MSE	LN_CLFOW Mean
0.998313	-1.114725	0.034910	-3.131690

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.13920778	0.13920778	114.23	0.0086
period	1	0.01560178	0.01560178	12.80	0.0700
trt	1	0.00019420	0.00019420	0.16	0.7283
subject(sequence)	2	1.28746738	0.64373369	528.22	0.0019

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.13920778	0.13920778	114.23	0.0086
period	1	0.01560178	0.01560178	12.80	0.0700
trt	1	0.00019420	0.00019420	0.16	0.7283
subject(sequence)	2	1.28746738	0.64373369	528.22	0.0019

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.13920778	0.13920778	114.23	0.0086
period	1	0.01560178	0.01560178	12.80	0.0700
trt	1	0.00019420	0.00019420	0.16	0.7283
subject(sequence)	2	1.28746738	0.64373369	528.22	0.0019

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.13920778	0.13920778	114.23	0.0086
period	1	0.01560178	0.01560178	12.80	0.0700
trt	1	0.00019420	0.00019420	0.16	0.7283
subject(sequence)	2	1.28746738	0.64373369	528.22	0.0019

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 63-75

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.139208	0.139208	0.22	0.6876
Error	2	1.287467	0.643734		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	0.015602	0.015602	12.80	0.0700
trt	1	0.000194	0.000194	0.16	0.7283
subject(sequence)	2	1.287467	0.643734	528.22	0.0019
Error: MS(Error)	2	0.002437	0.001219		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.139208	0.139208	0.22	0.6876
Error	2	1.287467	0.643734		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.015602	0.015602	12.80	0.0700
trt	1	0.000194	0.000194	0.16	0.7283
subject(sequence)	2	1.287467	0.643734	528.22	0.0019
Error: MS(Error)	2	0.002437	0.001219		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 63-75

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.139208	0.139208	0.22	0.6876
Error	2	1.287467	0.643734		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.015602	0.015602	12.80	0.0700
trt	1	0.000194	0.000194	0.16	0.7283
subject(sequence)	2	1.287467	0.643734	528.22	0.0019
Error: MS(Error)	2	0.002437	0.001219		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.139208	0.139208	0.22	0.6876
Error	2	1.287467	0.643734		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.015602	0.015602	12.80	0.0700
trt	1	0.000194	0.000194	0.16	0.7283
subject(sequence)	2	1.287467	0.643734	528.22	0.0019
Error: MS(Error)	2	0.002437	0.001219		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 63-75

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_CLFOW	LSMEAN	Pr > t
A	-3.13661745		0.7283
B	-3.12676354		

trt	LN_CLFOW	LSMEAN	90% Confidence Limits	
A	-3.136617		-3.187585	-3.085649
B	-3.126764		-3.177731	-3.075796

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.009854	-0.081933	0.062226

Dependent Variable: LN_CLFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.00985391	0.02468491	-0.40	0.7283	-0.08193349 0.06222566

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	202 303 408 413
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LN_CLFO

R-Square	Coeff Var	Root MSE	LN_CLFO Mean
0.998102	3.229223	0.034910	1.081057

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.10836268	0.10836268	88.92	0.0111
period	1	0.01560178	0.01560178	12.80	0.0700
trt	1	0.00019420	0.00019420	0.16	0.7283
subject(sequence)	2	1.15775241	0.57887620	475.00	0.0021

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.10836268	0.10836268	88.92	0.0111
period	1	0.01560178	0.01560178	12.80	0.0700
trt	1	0.00019420	0.00019420	0.16	0.7283
subject(sequence)	2	1.15775241	0.57887620	475.00	0.0021

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.10836268	0.10836268	88.92	0.0111
period	1	0.01560178	0.01560178	12.80	0.0700
trt	1	0.00019420	0.00019420	0.16	0.7283
subject(sequence)	2	1.15775241	0.57887620	475.00	0.0021

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.10836268	0.10836268	88.92	0.0111
period	1	0.01560178	0.01560178	12.80	0.0700
trt	1	0.00019420	0.00019420	0.16	0.7283
subject(sequence)	2	1.15775241	0.57887620	475.00	0.0021

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 63-75

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.108363	0.108363	0.19	0.7074
Error	2	1.157752	0.578876		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	0.015602	0.015602	12.80	0.0700
trt	1	0.000194	0.000194	0.16	0.7283
subject(sequence)	2	1.157752	0.578876	475.00	0.0021
Error: MS(Error)	2	0.002437	0.001219		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.108363	0.108363	0.19	0.7074
Error	2	1.157752	0.578876		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.015602	0.015602	12.80	0.0700
trt	1	0.000194	0.000194	0.16	0.7283
subject(sequence)	2	1.157752	0.578876	475.00	0.0021
Error: MS(Error)	2	0.002437	0.001219		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 63-75

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.108363	0.108363	0.19	0.7074
Error	2	1.157752	0.578876		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.015602	0.015602	12.80	0.0700
trt	1	0.000194	0.000194	0.16	0.7283
subject(sequence)	2	1.157752	0.578876	475.00	0.0021
Error: MS(Error)	2	0.002437	0.001219		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.108363	0.108363	0.19	0.7074
Error	2	1.157752	0.578876		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.015602	0.015602	12.80	0.0700
trt	1	0.000194	0.000194	0.16	0.7283
subject(sequence)	2	1.157752	0.578876	475.00	0.0021
Error: MS(Error)	2	0.002437	0.001219		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 63-75

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFO	LSMEAN	Pr > t
A	1.07612977		0.7283
B	1.08598368		

trt	LN_CLFO	LSMEAN	90% Confidence Limits	
A	1.076130	1.025162	1.127098	
B	1.085984	1.035016	1.136952	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.009854	-0.081933	0.062226

Dependent Variable: LN_CLFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.00985391	0.02468491	-0.40	0.7283	-0.08193349 0.06222566

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	202 303 408 413
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LN_VZFOW

R-Square	Coeff Var	Root MSE	LN_VZFOW Mean
0.943812	10.17324	0.088331	0.868266

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.01194838	0.01194838	1.53	0.3415
period	1	0.10103255	0.10103255	12.95	0.0693
trt	1	0.05015616	0.05015616	6.43	0.1267
subject(sequence)	2	0.09897914	0.04948957	6.34	0.1362

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.01194838	0.01194838	1.53	0.3415
period	1	0.10103255	0.10103255	12.95	0.0693
trt	1	0.05015616	0.05015616	6.43	0.1267
subject(sequence)	2	0.09897914	0.04948957	6.34	0.1362

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.01194838	0.01194838	1.53	0.3415
period	1	0.10103255	0.10103255	12.95	0.0693
trt	1	0.05015616	0.05015616	6.43	0.1267
subject(sequence)	2	0.09897914	0.04948957	6.34	0.1362

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.01194838	0.01194838	1.53	0.3415
period	1	0.10103255	0.10103255	12.95	0.0693
trt	1	0.05015616	0.05015616	6.43	0.1267
subject(sequence)	2	0.09897914	0.04948957	6.34	0.1362

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 63-75

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.011948	0.011948	0.24	0.6718
Error	2	0.098979	0.049490		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	0.101033	0.101033	12.95	0.0693
trt	1	0.050156	0.050156	6.43	0.1267
subject(sequence)	2	0.098979	0.049490	6.34	0.1362
Error: MS(Error)	2	0.015605	0.007802		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.011948	0.011948	0.24	0.6718
Error	2	0.098979	0.049490		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.101033	0.101033	12.95	0.0693
trt	1	0.050156	0.050156	6.43	0.1267
subject(sequence)	2	0.098979	0.049490	6.34	0.1362
Error: MS(Error)	2	0.015605	0.007802		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 63-75

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.011948	0.011948	0.24	0.6718
Error	2	0.098979	0.049490		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.101033	0.101033	12.95	0.0693
trt	1	0.050156	0.050156	6.43	0.1267
subject(sequence)	2	0.098979	0.049490	6.34	0.1362
Error: MS(Error)	2	0.015605	0.007802		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.011948	0.011948	0.24	0.6718
Error	2	0.098979	0.049490		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.101033	0.101033	12.95	0.0693
trt	1	0.050156	0.050156	6.43	0.1267
subject(sequence)	2	0.098979	0.049490	6.34	0.1362
Error: MS(Error)	2	0.015605	0.007802		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 63-75

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_VZFOW	LSMEAN	Pr > t
A	0.78908533		0.1267
B	0.94744593		

trt	LN_VZFOW	LSMEAN	90% Confidence Limits	
A	0.789085		0.660123	0.918048
B	0.947446		0.818484	1.076408

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.158361	-0.340741	0.024020

Dependent Variable: LN_VZFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.15836060	0.06245926	-2.54	0.1267	-0.34074073 0.02401953

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	202 303 408 413
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LN_VZFO

R-Square	Coeff Var	Root MSE	LN_VZFO Mean
0.940999	1.738447	0.088331	5.081013

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.02347924	0.02347924	3.01	0.2249
period	1	0.10103255	0.10103255	12.95	0.0693
trt	1	0.05015616	0.05015616	6.43	0.1267
subject(sequence)	2	0.07420835	0.03710417	4.76	0.1737

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.02347924	0.02347924	3.01	0.2249
period	1	0.10103255	0.10103255	12.95	0.0693
trt	1	0.05015616	0.05015616	6.43	0.1267
subject(sequence)	2	0.07420835	0.03710417	4.76	0.1737

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.02347924	0.02347924	3.01	0.2249
period	1	0.10103255	0.10103255	12.95	0.0693
trt	1	0.05015616	0.05015616	6.43	0.1267
subject(sequence)	2	0.07420835	0.03710417	4.76	0.1737

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.02347924	0.02347924	3.01	0.2249
period	1	0.10103255	0.10103255	12.95	0.0693
trt	1	0.05015616	0.05015616	6.43	0.1267
subject(sequence)	2	0.07420835	0.03710417	4.76	0.1737

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 63-75

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.023479	0.023479	0.63	0.5097
Error	2	0.074208	0.037104		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	0.101033	0.101033	12.95	0.0693
trt	1	0.050156	0.050156	6.43	0.1267
subject(sequence)	2	0.074208	0.037104	4.76	0.1737
Error: MS(Error)	2	0.015605	0.007802		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.023479	0.023479	0.63	0.5097
Error	2	0.074208	0.037104		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.101033	0.101033	12.95	0.0693
trt	1	0.050156	0.050156	6.43	0.1267
subject(sequence)	2	0.074208	0.037104	4.76	0.1737
Error: MS(Error)	2	0.015605	0.007802		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 63-75

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.023479	0.023479	0.63	0.5097
Error	2	0.074208	0.037104		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.101033	0.101033	12.95	0.0693
trt	1	0.050156	0.050156	6.43	0.1267
subject(sequence)	2	0.074208	0.037104	4.76	0.1737
Error: MS(Error)	2	0.015605	0.007802		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.023479	0.023479	0.63	0.5097
Error	2	0.074208	0.037104		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.101033	0.101033	12.95	0.0693
trt	1	0.050156	0.050156	6.43	0.1267
subject(sequence)	2	0.074208	0.037104	4.76	0.1737
Error: MS(Error)	2	0.015605	0.007802		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 63-75

Least Squares Means

			H0:LSMean1=LSMean2	
trt	LN_VZFO	LSMEAN		Pr > t
A	5.00183256			0.1267
B	5.16019315			

trt	LN_VZFO	LSMEAN	90% Confidence Limits	
A	5.001833		4.872870	5.130795
B	5.160193		5.031231	5.289155

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.158361	-0.340741	0.024020

Dependent Variable: LN_VZFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.15836060	0.06245926	-2.54	0.1267	-0.34074073 0.02401953

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	202 303 408 413
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 63-75

The GLM Procedure

Dependent Variable: TMAX

R-Square	Coeff Var	Root MSE	TMAX Mean
0.688311	116.3511	1.243502	1.068750

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.51728200	1.51728200	0.98	0.4263
period	1	1.54528200	1.54528200	1.00	0.4228
trt	1	1.48781250	1.48781250	0.96	0.4301
subject(sequence)	2	2.27909450	1.13954725	0.74	0.5757

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.51728200	1.51728200	0.98	0.4263
period	1	1.54528200	1.54528200	1.00	0.4228
trt	1	1.48781250	1.48781250	0.96	0.4301
subject(sequence)	2	2.27909450	1.13954725	0.74	0.5757

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.51728200	1.51728200	0.98	0.4263
period	1	1.54528200	1.54528200	1.00	0.4228
trt	1	1.48781250	1.48781250	0.96	0.4301
subject(sequence)	2	2.27909450	1.13954725	0.74	0.5757

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.51728200	1.51728200	0.98	0.4263
period	1	1.54528200	1.54528200	1.00	0.4228
trt	1	1.48781250	1.48781250	0.96	0.4301
subject(sequence)	2	2.27909450	1.13954725	0.74	0.5757

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 63-75

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.517282	1.517282	1.33	0.3678
Error	2	2.279094	1.139547		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	1.545282	1.545282	1.00	0.4228
trt	1	1.487813	1.487813	0.96	0.4301
subject(sequence)	2	2.279095	1.139547	0.74	0.5757
Error: MS(Error)	2	3.092595	1.546297		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.517282	1.517282	1.33	0.3678
Error	2	2.279094	1.139547		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	1.545282	1.545282	1.00	0.4228
trt	1	1.487813	1.487813	0.96	0.4301
subject(sequence)	2	2.279095	1.139547	0.74	0.5757
Error: MS(Error)	2	3.092595	1.546297		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 63-75

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.517282	1.517282	1.33	0.3678
Error	2	2.279094	1.139547		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	1.545282	1.545282	1.00	0.4228
trt	1	1.487813	1.487813	0.96	0.4301
subject(sequence)	2	2.279095	1.139547	0.74	0.5757
Error: MS(Error)	2	3.092595	1.546297		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.517282	1.517282	1.33	0.3678
Error	2	2.279094	1.139547		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	1.545282	1.545282	1.00	0.4228
trt	1	1.487813	1.487813	0.96	0.4301
subject(sequence)	2	2.279095	1.139547	0.74	0.5757
Error: MS(Error)	2	3.092595	1.546297		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{max} (h) Weight Group: 63-75

Least Squares Means

		H0:LSMean1=LSMean2	
trt	TMAX LSMEAN		Pr > t
A	1.5000000		0.4301
B	0.6375000		

trt	TMAX LSMEAN	90% Confidence Limits	
A	1.500000	-0.315504	3.315504
B	0.637500	-1.178004	2.453004

Least Squares Means for Effect trt

		Difference Between		90% Confidence Limits for LSMean(i)-LSMean(j)	
i	j	Means			
1	2	0.862500	-1.705010	3.430010	

Dependent Variable: TMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.8625000	0.87928870	0.98	0.4301	-1.70501034	3.43001034

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	202 303 408 413
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LAMZ

R-Square	Coeff Var	Root MSE	LAMZ Mean
0.948689	21.40862	0.004371	0.020416

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00009919	0.00009919	5.19	0.1503
period	1	0.00002579	0.00002579	1.35	0.3652
trt	1	0.00003954	0.00003954	2.07	0.2868
subject(sequence)	2	0.00054187	0.00027093	14.18	0.0659

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00009919	0.00009919	5.19	0.1503
period	1	0.00002579	0.00002579	1.35	0.3652
trt	1	0.00003954	0.00003954	2.07	0.2868
subject(sequence)	2	0.00054187	0.00027093	14.18	0.0659

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00009919	0.00009919	5.19	0.1503
period	1	0.00002579	0.00002579	1.35	0.3652
trt	1	0.00003954	0.00003954	2.07	0.2868
subject(sequence)	2	0.00054187	0.00027093	14.18	0.0659

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00009919	0.00009919	5.19	0.1503
period	1	0.00002579	0.00002579	1.35	0.3652
trt	1	0.00003954	0.00003954	2.07	0.2868
subject(sequence)	2	0.00054187	0.00027093	14.18	0.0659

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 63-75

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.000099193	0.000099193	0.37	0.6066
Error	2	0.000542	0.000271		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	0.000025787	0.000025787	1.35	0.3652
trt	1	0.000039543	0.000039543	2.07	0.2868
subject(sequence)	2	0.000542	0.000271	14.18	0.0659
Error: MS(Error)	2	0.000038206	0.000019103		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.000099193	0.000099193	0.37	0.6066
Error	2	0.000542	0.000271		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.000025787	0.000025787	1.35	0.3652
trt	1	0.000039543	0.000039543	2.07	0.2868
subject(sequence)	2	0.000542	0.000271	14.18	0.0659
Error: MS(Error)	2	0.000038206	0.000019103		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 63-75

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.000099193	0.000099193	0.37	0.6066
Error	2	0.000542	0.000271		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.000025787	0.000025787	1.35	0.3652
trt	1	0.000039543	0.000039543	2.07	0.2868
subject(sequence)	2	0.000542	0.000271	14.18	0.0659
Error: MS(Error)	2	0.000038206	0.000019103		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.000099193	0.000099193	0.37	0.6066
Error	2	0.000542	0.000271		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.000025787	0.000025787	1.35	0.3652
trt	1	0.000039543	0.000039543	2.07	0.2868
subject(sequence)	2	0.000542	0.000271	14.18	0.0659
Error: MS(Error)	2	0.000038206	0.000019103		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 63-75

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LAMZ LSMEAN		Pr > t
A	0.02263887		0.2868
B	0.01819235		

trt	LAMZ LSMEAN	90% Confidence Limits	
A	0.022639	0.016258	0.029020
B	0.018192	0.011811	0.024574

Least Squares Means for Effect trt

Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.004447	-0.004578	0.013471

Dependent Variable: LAMZ

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	0.00444652	0.00309055	1.44	0.2868	-0.00457784 0.01347089

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	202 303 408 413
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LAMZHL

R-Square	Coeff Var	Root MSE	LAMZHL Mean
0.992313	7.735473	3.247983	41.98816

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	402.676341	402.676341	38.17	0.0252
period	1	43.461721	43.461721	4.12	0.1795
trt	1	22.577445	22.577445	2.14	0.2810
subject(sequence)	2	2254.889672	1127.444836	106.87	0.0093

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	402.676341	402.676341	38.17	0.0252
period	1	43.461721	43.461721	4.12	0.1795
trt	1	22.577445	22.577445	2.14	0.2810
subject(sequence)	2	2254.889672	1127.444836	106.87	0.0093

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	402.676341	402.676341	38.17	0.0252
period	1	43.461721	43.461721	4.12	0.1795
trt	1	22.577445	22.577445	2.14	0.2810
subject(sequence)	2	2254.889672	1127.444836	106.87	0.0093

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	402.676341	402.676341	38.17	0.0252
period	1	43.461721	43.461721	4.12	0.1795
trt	1	22.577445	22.577445	2.14	0.2810
subject(sequence)	2	2254.889672	1127.444836	106.87	0.0093

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 63-75

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	402.676341	402.676341	0.36	0.6107
Error	2	2254.889672	1127.444836		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	43.461721	43.461721	4.12	0.1795
trt	1	22.577445	22.577445	2.14	0.2810
subject(sequence)	2	2254.889672	1127.444836	106.87	0.0093
Error: MS(Error)	2	21.098782	10.549391		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	402.676341	402.676341	0.36	0.6107
Error	2	2254.889672	1127.444836		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	43.461721	43.461721	4.12	0.1795
trt	1	22.577445	22.577445	2.14	0.2810
subject(sequence)	2	2254.889672	1127.444836	106.87	0.0093
Error: MS(Error)	2	21.098782	10.549391		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 63-75

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	402.676341	402.676341	0.36	0.6107
Error	2	2254.889672	1127.444836		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	43.461721	43.461721	4.12	0.1795
trt	1	22.577445	22.577445	2.14	0.2810
subject(sequence)	2	2254.889672	1127.444836	106.87	0.0093
Error: MS(Error)	2	21.098782	10.549391		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	402.676341	402.676341	0.36	0.6107
Error	2	2254.889672	1127.444836		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	43.461721	43.461721	4.12	0.1795
trt	1	22.577445	22.577445	2.14	0.2810
subject(sequence)	2	2254.889672	1127.444836	106.87	0.0093
Error: MS(Error)	2	21.098782	10.549391		

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 63-75

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LAMZHL LSMEAN		Pr > t
A	40.3082215		0.2810
B	43.6680910		

trt	LAMZHL LSMEAN	90% Confidence Limits	
A	40.308222	35.566190	45.050253
B	43.668091	38.926060	48.410122

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-3.359869	-10.066114	3.346375

Dependent Variable: LAMZHL

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-3.35986944	2.29667055	-1.46	0.2810	-10.06611433 3.34637545

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	1	202
sequence	1	BAC
trt	2	B C

Number of Observations Read	2
Number of Observations Used	2

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LN_AUCLST

R-Square	Coeff Var	Root MSE	LN_AUCLST Mean
1.000000			8.989924

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00749245	0.00749245		
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00749245	0.00749245		
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00749245	0.00749245		
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00749245	0.00749245		
subject(sequence)	0	0.00000000			

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 63-75

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCLST	LSMEAN	Pr > t
B	8.92871712		
C	9.05112994		

trt	LN_AUCLST	LSMEAN	90% Confidence Limits
B	8.928717		
C	9.051130		

Least Squares Means for Effect trt			
Difference Between			
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)
1	2	-0.122413	

The GLM Procedure

Dependent Variable: LN_AUCLST

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	0.12241283			0.00000000	0.00000000

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	1	202
sequence	1	BAC
trt	2	B C

Number of Observations Read	2
Number of Observations Used	2

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LN_AUCIFO

R-Square	Coeff Var	Root MSE	LN_AUCIFO Mean
1.000000			9.152155

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.05815112	0.05815112		
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.05815112	0.05815112		
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.05815112	0.05815112		
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.05815112	0.05815112		
subject(sequence)	0	0.00000000			

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 63-75

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCIFO	LSMEAN	Pr > t
B	8.98163980		
C	9.32267095		

trt	LN_AUCIFO	LSMEAN	90% Confidence Limits
B	8.981640		
C	9.322671		

Least Squares Means for Effect trt			
Difference Between			
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)
1	2	-0.341031	

The GLM Procedure

Dependent Variable: LN_AUCIFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	0.34103116			0.00000000	0.00000000

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: C_{\max} (ng/mL) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	1	202
sequence	1	BAC
trt	2	B C

Number of Observations Read	2
Number of Observations Used	2

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LN_CMAX

R-Square	Coeff Var	Root MSE	LN_CMAX Mean
1.000000			5.618963

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.36116740	0.36116740		
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.36116740	0.36116740		
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.36116740	0.36116740		
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.36116740	0.36116740		
subject(sequence)	0	0.00000000			

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 63-75

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CMAX	LSMEAN	Pr > t
B	6.04391467		
C	5.19401185		

trt	LN_CMAX	LSMEAN	90% Confidence Limits
B	6.043915		
C	5.194012		

Least Squares Means for Effect trt			
Difference Between			
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)
1	2	0.849903	

The GLM Procedure

Dependent Variable: LN_CMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.84990282			0.00000000	0.00000000

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	1	202
sequence	1	BAC
trt	2	B C

Number of Observations Read	2
Number of Observations Used	2

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LN_CLFOW

R-Square	Coeff Var	Root MSE	LN_CLFOW Mean
1.000000			-3.758794

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.05815112	0.05815112		
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.05815112	0.05815112		
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.05815112	0.05815112		
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.05815112	0.05815112		
subject(sequence)	0	0.00000000			

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 63-75

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFOW	LSMEAN	Pr > t
B	-3.58827888		
C	-3.92931004		

trt	LN_CLFOW	LSMEAN	90% Confidence Limits
B	-3.588279		
C	-3.929310		

Least Squares Means for Effect trt			
Difference Between			
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)
1	2	0.341031	

The GLM Procedure

Dependent Variable: LN_CLFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.34103116			0.00000000	0.00000000

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	1	202
sequence	1	BAC
trt	2	B C

Number of Observations Read	2
Number of Observations Used	2

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LN_CLFO

R-Square	Coeff Var	Root MSE	LN_CLFO Mean
1.000000			0.463650

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.05815112	0.05815112		
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.05815112	0.05815112		
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.05815112	0.05815112		
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.05815112	0.05815112		
subject(sequence)	0	0.00000000			

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h) Weight Group: 63-75

The GLM Procedure
Least Squares Means

			H0:LSMean1=LSMean2	
trt	LN_CLFO	LSMEAN		Pr > t
B	0.63416568			
C	0.29313453			

trt	LN_CLFO	LSMEAN	90% Confidence Limits
B	0.634166		
C	0.293135		

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.341031		

The GLM Procedure

Dependent Variable: LN_CLFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.34103116			0.00000000	0.00000000

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	1	202
sequence	1	BAC
trt	2	B C

Number of Observations Read	2
Number of Observations Used	2

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LN_VZFOW

R-Square	Coeff Var	Root MSE	LN_VZFOW Mean
1.000000			1.259065

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.17042279	0.17042279		
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.17042279	0.17042279		
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.17042279	0.17042279		
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.17042279	0.17042279		
subject(sequence)	0	0.00000000			

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 63-75

The GLM Procedure
Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_VZFOW	LSMEAN	Pr > t
B	0.96715507		
C	1.55097489		

trt	LN_VZFOW	LSMEAN	90% Confidence Limits
B	0.967155		
C	1.550975		

Least Squares Means for Effect trt			
Difference Between			
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)
1	2	-0.583820	

The GLM Procedure

Dependent Variable: LN_VZFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	0.58381983			0.00000000	0.00000000

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	1	202
sequence	1	BAC
trt	2	B C

Number of Observations Read	2
Number of Observations Used	2

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LN_VZFO

R-Square	Coeff Var	Root MSE	LN_VZFO Mean
1.000000			5.481510

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.17042279	0.17042279		
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.17042279	0.17042279		
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.17042279	0.17042279		
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.17042279	0.17042279		
subject(sequence)	0	0.00000000			

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L) Weight Group: 63-75

The GLM Procedure
Least Squares Means

		H0:LSMean1=LSMean2	Pr > t
trt	LN_VZFO LSMEAN		
B	5.1895963		
C	5.77341946		

trt	LN_VZFO LSMEAN	90% Confidence Limits
B	5.189600	
C	5.773419	

Least Squares Means for Effect trt			Difference Between	
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.583820		

The GLM Procedure

Dependent Variable: LN_VZFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	0.58381983			0.00000000	0.00000000

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	1	202
sequence	1	BAC
trt	2	B C

Number of Observations Read	2
Number of Observations Used	2

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h) Weight Group: 63-75

The GLM Procedure

Dependent Variable: TMAX

R-Square	Coeff Var	Root MSE	TMAX Mean
1.000000			1.375000

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.78125000	0.78125000		
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.78125000	0.78125000		
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.78125000	0.78125000		
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.78125000	0.78125000		
subject(sequence)	0	0.00000000			

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h) Weight Group: 63-75

The GLM Procedure
Least Squares Means

		H0:LSMean1=LSMean2	Pr > t
trt	TMAX LSMEAN		
B	0.7500000		
C	2.0000000		

trt	TMAX LSMEAN	90% Confidence Limits
B	0.750000	
C	2.000000	

Least Squares Means for Effect trt			90% Confidence Limits for LSMean(i)-LSMean(j)	
Difference Between				
i	j	Means		
1	2	-1.250000		

The GLM Procedure

Dependent Variable: TMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	1.2500000			0.0000000	0.0000000

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	1	202
sequence	1	BAC
trt	2	B C

Number of Observations Read	2
Number of Observations Used	2

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LAMZ

R-Square	Coeff Var	Root MSE	LAMZ Mean
1.000000			0.007339

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00002011	0.00002011		
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00002011	0.00002011		
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00002011	0.00002011		
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.00000000			
trt	1	0.00002011	0.00002011		
subject(sequence)	0	0.00000000			

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h) Weight Group: 63-75

The GLM Procedure
Least Squares Means

		H0:LSMean1=LSMean2	Pr > t
trt	LAMZ LSMEAN		
B	0.01050994		
C	0.00416814		

trt	LAMZ LSMEAN	90% Confidence Limits
B	0.010510	
C	0.004168	

Least Squares Means for Effect trt			
Difference Between			
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)
1	2	0.006342	

The GLM Procedure

Dependent Variable: LAMZ

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.00634180			0.00000000	0.00000000

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 63-75

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	1	202
sequence	1	BAC
trt	2	B C

Number of Observations Read	2
Number of Observations Used	2

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 63-75

The GLM Procedure

Dependent Variable: LAMZHL

R-Square	Coeff Var	Root MSE	LAMZHL Mean
1.000000			116.1240

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	0	0.000000			
trt	1	5034.544709	5034.544709		
subject(sequence)	0	0.000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	0	0.000000			
trt	1	5034.544709	5034.544709		
subject(sequence)	0	0.000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	0	0.000000			
trt	1	5034.544709	5034.544709		
subject(sequence)	0	0.000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	0	0.000000			
trt	1	5034.544709	5034.544709		
subject(sequence)	0	0.000000			

Listing 16.1.9-6 ANOVA for Treatment Comparison of Diazepam for Weight Group 63-75 kg - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 63-75

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2		
trt	LAMZHL LSMEAN	Pr > t
B	65.951593	
C	166.296445	

trt	LAMZHL LSMEAN	90% Confidence Limits
B	65.951593	
C	166.296445	

Least Squares Means for Effect trt			
i	j	Difference Between Means	90% Confidence Limits for LSMean(i)-LSMean(j)
1	2	-100.344852	

The GLM Procedure

Dependent Variable: LAMZHL

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	100.344852			0.000000	0.000000

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	6	205 301 406 410 411 501
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	12
Number of Observations Used	12

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LN_AUCLST

R-Square	Coeff Var	Root MSE	LN_AUCLST Mean
0.964977	1.738422	0.154632	8.894970

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.12739488	1.12739488	47.15	0.0024
period	1	0.02008228	0.02008228	0.84	0.4113
trt	1	0.02193858	0.02193858	0.92	0.3924
subject(sequence)	4	1.46581263	0.36645316	15.33	0.0108

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.12739488	1.12739488	47.15	0.0024
period	1	0.02008228	0.02008228	0.84	0.4113
trt	1	0.02193858	0.02193858	0.92	0.3924
subject(sequence)	4	1.46581263	0.36645316	15.33	0.0108

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.12739488	1.12739488	47.15	0.0024
period	1	0.02008228	0.02008228	0.84	0.4113
trt	1	0.02193858	0.02193858	0.92	0.3924
subject(sequence)	4	1.46581263	0.36645316	15.33	0.0108

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.12739488	1.12739488	47.15	0.0024
period	1	0.02008228	0.02008228	0.84	0.4113
trt	1	0.02193858	0.02193858	0.92	0.3924
subject(sequence)	4	1.46581263	0.36645316	15.33	0.0108

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 76-87

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.127395	1.127395	3.08	0.1543
Error	4	1.465813	0.366453		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	0.020082	0.020082	0.84	0.4113
trt	1	0.021939	0.021939	0.92	0.3924
subject(sequence)	4	1.465813	0.366453	15.33	0.0108
Error: MS(Error)	4	0.095644	0.023911		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.127395	1.127395	3.08	0.1543
Error	4	1.465813	0.366453		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.020082	0.020082	0.84	0.4113
trt	1	0.021939	0.021939	0.92	0.3924
subject(sequence)	4	1.465813	0.366453	15.33	0.0108
Error: MS(Error)	4	0.095644	0.023911		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.127395	1.127395	3.08	0.1543
Error	4	1.465813	0.366453		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.020082	0.020082	0.84	0.4113
trt	1	0.021939	0.021939	0.92	0.3924
subject(sequence)	4	1.465813	0.366453	15.33	0.0108
Error: MS(Error)	4	0.095644	0.023911		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.127395	1.127395	3.08	0.1543
Error	4	1.465813	0.366453		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.020082	0.020082	0.84	0.4113
trt	1	0.021939	0.021939	0.92	0.3924
subject(sequence)	4	1.465813	0.366453	15.33	0.0108
Error: MS(Error)	4	0.095644	0.023911		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 76-87

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCLST	LSMEAN	Pr > t
A	8.85221198		0.3924
B	8.93772725		

trt	LN_AUCLST	LSMEAN	90% Confidence Limits	
A	8.852212	8.717632	8.986792	
B	8.937727	8.803147	9.072307	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.085515	-0.275840	0.104809

Dependent Variable: LN_AUCLST

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.08551527	0.08927691	-0.96	0.3924	-0.27583996 0.10480942

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	6	205 301 406 410 411 501
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	12
Number of Observations Used	12

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LN_AUCIFO

R-Square	Coeff Var	Root MSE	LN_AUCIFO Mean
0.963280	2.122888	0.192833	9.083543

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.57345243	1.57345243	42.31	0.0029
period	1	0.02783629	0.02783629	0.75	0.4357
trt	1	0.00812175	0.00812175	0.22	0.6646
subject(sequence)	4	2.29244990	0.57311247	15.41	0.0107

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.57345243	1.57345243	42.31	0.0029
period	1	0.02783629	0.02783629	0.75	0.4357
trt	1	0.00812175	0.00812175	0.22	0.6646
subject(sequence)	4	2.29244990	0.57311247	15.41	0.0107

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.57345243	1.57345243	42.31	0.0029
period	1	0.02783629	0.02783629	0.75	0.4357
trt	1	0.00812175	0.00812175	0.22	0.6646
subject(sequence)	4	2.29244990	0.57311247	15.41	0.0107

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.57345243	1.57345243	42.31	0.0029
period	1	0.02783629	0.02783629	0.75	0.4357
trt	1	0.00812175	0.00812175	0.22	0.6646
subject(sequence)	4	2.29244990	0.57311247	15.41	0.0107

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 76-87

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.573452	1.573452	2.75	0.1729
Error	4	2.292450	0.573112		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
period	1	0.027836	0.027836	0.75	0.4357
trt	1	0.008122	0.008122	0.22	0.6646
subject(sequence)	4	2.292450	0.573112	15.41	0.0107
Error: MS(Error)	4	0.148739	0.037185		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.573452	1.573452	2.75	0.1729
Error	4	2.292450	0.573112		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.027836	0.027836	0.75	0.4357
trt	1	0.008122	0.008122	0.22	0.6646
subject(sequence)	4	2.292450	0.573112	15.41	0.0107
Error: MS(Error)	4	0.148739	0.037185		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.573452	1.573452	2.75	0.1729
Error	4	2.292450	0.573112		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.027836	0.027836	0.75	0.4357
trt	1	0.008122	0.008122	0.22	0.6646
subject(sequence)	4	2.292450	0.573112	15.41	0.0107
Error: MS(Error)	4	0.148739	0.037185		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.573452	1.573452	2.75	0.1729
Error	4	2.292450	0.573112		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.027836	0.027836	0.75	0.4357
trt	1	0.008122	0.008122	0.22	0.6646
subject(sequence)	4	2.292450	0.573112	15.41	0.0107
Error: MS(Error)	4	0.148739	0.037185		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 76-87

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCIFO	LSMEAN	Pr > t
A	9.10955867		0.6646
B	9.05752745		

trt	LN_AUCIFO	LSMEAN	90% Confidence Limits	
A	9.109559	8.941731	9.277386	
B	9.057527	8.889700	9.225355	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.052031	-0.185312	0.289375

Dependent Variable: LN_AUCIFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.05203123	0.11133243	0.47	0.6646	-0.18531246	0.28937491

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{\max} (ng/mL) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	7	205 301 406 410 411 501 506
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	14
Number of Observations Used	14

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LN_CMAX

R-Square	Coeff Var	Root MSE	LN_CMAX Mean
0.663147	6.456680	0.353705	5.478128

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.14298687	0.14298687	1.14	0.3339
period	1	0.05353200	0.05353200	0.43	0.5419
trt	1	0.48189892	0.48189892	3.85	0.1069
subject(sequence)	5	0.55304583	0.11060917	0.88	0.5521

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.14298687	0.14298687	1.14	0.3339
period	1	0.10769335	0.10769335	0.86	0.3961
trt	1	0.48189892	0.48189892	3.85	0.1069
subject(sequence)	5	0.55304583	0.11060917	0.88	0.5521

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.14298687	0.14298687	1.14	0.3339
period	1	0.10769335	0.10769335	0.86	0.3961
trt	1	0.48189892	0.48189892	3.85	0.1069
subject(sequence)	5	0.55304583	0.11060917	0.88	0.5521

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.14298687	0.14298687	1.14	0.3339
period	1	0.10769335	0.10769335	0.86	0.3961
trt	1	0.48189892	0.48189892	3.85	0.1069
subject(sequence)	5	0.55304583	0.11060917	0.88	0.5521

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 76-87

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.142987	0.142987	1.29	0.3071
Error	5	0.553046	0.110609		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.053532	0.053532	0.43	0.5419
trt	1	0.481899	0.481899	3.85	0.1069
subject(sequence)	5	0.553046	0.110609	0.88	0.5521
Error: MS(Error)	5	0.625537	0.125107		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.142987	0.142987	1.29	0.3071
Error	5	0.553046	0.110609		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.107693	0.107693	0.86	0.3961
trt	1	0.481899	0.481899	3.85	0.1069
subject(sequence)	5	0.553046	0.110609	0.88	0.5521
Error: MS(Error)	5	0.625537	0.125107		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.142987	0.142987	1.29	0.3071
Error	5	0.553046	0.110609		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.107693	0.107693	0.86	0.3961
trt	1	0.481899	0.481899	3.85	0.1069
subject(sequence)	5	0.553046	0.110609	0.88	0.5521
Error: MS(Error)	5	0.625537	0.125107		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.142987	0.142987	1.29	0.3071
Error	5	0.553046	0.110609		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.107693	0.107693	0.86	0.3961
trt	1	0.481899	0.481899	3.85	0.1069
subject(sequence)	5	0.553046	0.110609	0.88	0.5521
Error: MS(Error)	5	0.625537	0.125107		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 76-87

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LN_CMAX LSMEAN		Pr > t
A	5.30526255		0.1069
B	5.68016767		

trt	LN_CMAX LSMEAN	90% Confidence Limits	
A	5.305263	5.033083	5.577442
B	5.680168	5.407988	5.952347

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.374905	-0.759825	0.010015

Dependent Variable: LN_CMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.37490513	0.19102264	-1.96	0.1069	-0.75982499 0.01001474

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	7	205 301 406 410 411 501 506
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	13
Number of Observations Used	13

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LN_CLFOW

R-Square	Coeff Var	Root MSE	LN_CLFOW Mean
0.966101	-4.963592	0.192833	-3.884957

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.04930375	1.04930375	28.22	0.0060
period	1	0.00397640	0.00397640	0.11	0.7601
trt	1	0.32070448	0.32070448	8.62	0.0425
subject(sequence)	5	2.86497841	0.57299568	15.41	0.0101

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.12723610	1.12723610	30.31	0.0053
period	1	0.02783629	0.02783629	0.75	0.4357
trt	1	0.12753294	0.12753294	3.43	0.1377
subject(sequence)	5	2.86497841	0.57299568	15.41	0.0101

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.70022141	0.70022141	18.83	0.0123
period	1	0.02783629	0.02783629	0.75	0.4357
trt	1	0.12753294	0.12753294	3.43	0.1377
subject(sequence)	5	2.86497841	0.57299568	15.41	0.0101

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.70022141	0.70022141	18.83	0.0123
period	1	0.02783629	0.02783629	0.75	0.4357
trt	1	0.12753294	0.12753294	3.43	0.1377
subject(sequence)	5	2.86497841	0.57299568	15.41	0.0101

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 76-87

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	1.049304	1.049304	1.71	0.2481
Error	4.955	3.036931	0.612903		

Error: 1.0745*MS(subject(sequence)) - 0.0745*MS(Error)
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.003976	0.003976	0.07	0.8029
Error	8.2446	0.493559	0.059865		

Error: 0.0423*MS(subject(sequence)) + 0.9577*MS(Error)
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.320704	0.320704	5.62	0.0455
Error	7.9206	0.451711	0.057030		

Error: 0.037*MS(subject(sequence)) + 0.963*MS(Error)

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	5	2.864978	0.572996	15.41	0.0101
Error: MS(Error)	4	0.148739	0.037185		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.127236	1.127236	1.84	0.2335
Error	4.9552	3.035991	0.612685		
Error: 1.0741*MS(subject(sequence)) - 0.0741*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.027836	0.027836	0.75	0.4357
trt	1	0.127533	0.127533	3.43	0.1377
subject(sequence)	5	2.864978	0.572996	15.41	0.0101
Error: MS(Error)	4	0.148739	0.037185		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.700221	0.700221	1.25	0.3134
Error	5.0185	2.800906	0.558112		
Error: 0.9722*MS(subject(sequence)) + 0.0278*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.027836	0.027836	0.75	0.4357
trt	1	0.127533	0.127533	3.43	0.1377
subject(sequence)	5	2.864978	0.572996	15.41	0.0101
Error: MS(Error)	4	0.148739	0.037185		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.700221	0.700221	1.25	0.3134
Error	5.0185	2.800906	0.558112		
Error: 0.9722*MS(subject(sequence)) + 0.0278*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.027836	0.027836	0.75	0.4357
trt	1	0.127533	0.127533	3.43	0.1377
subject(sequence)	5	2.864978	0.572996	15.41	0.0101
Error: MS(Error)	4	0.148739	0.037185		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 76-87

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_CLFOW	LSMEAN	Pr > t
A	-4.05335533		0.1377
B	-3.84717342		

trt	LN_CLFOW	LSMEAN	90% Confidence Limits	
A	-4.053355		-4.210343	-3.896367
B	-3.847173		-4.025181	-3.669166

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.206182	-0.443526	0.031162

Dependent Variable: LN_CLFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	-0.20618191	0.11133243	-1.85	0.1377	-0.44352559	0.03116178

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	7	205 301 406 410 411 501 506
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	13
Number of Observations Used	13

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LN_CLFO

R-Square	Coeff Var	Root MSE	LN_CLFO Mean
0.967079	34.30586	0.192833	0.562101

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.10473169	1.10473169	29.71	0.0055
period	1	0.00520841	0.00520841	0.14	0.7272
trt	1	0.33042950	0.33042950	8.89	0.0407
subject(sequence)	5	2.92899343	0.58579869	15.75	0.0097

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.18703340	1.18703340	31.92	0.0048
period	1	0.02783629	0.02783629	0.75	0.4357
trt	1	0.12753294	0.12753294	3.43	0.1377
subject(sequence)	5	2.92899343	0.58579869	15.75	0.0097

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.73180313	0.73180313	19.68	0.0114
period	1	0.02783629	0.02783629	0.75	0.4357
trt	1	0.12753294	0.12753294	3.43	0.1377
subject(sequence)	5	2.92899343	0.58579869	15.75	0.0097

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.73180313	0.73180313	19.68	0.0114
period	1	0.02783629	0.02783629	0.75	0.4357
trt	1	0.12753294	0.12753294	3.43	0.1377
subject(sequence)	5	2.92899343	0.58579869	15.75	0.0097

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 76-87

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	1.104732	1.104732	1.76	0.2421
Error	4.956	3.105712	0.626660		

Error: 1.0745*MS(subject(sequence)) - 0.0745*MS(Error)
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.005208	0.005208	0.09	0.7763
Error	8.2931	0.500957	0.060406		

Error: 0.0423*MS(subject(sequence)) + 0.9577*MS(Error)
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.330430	0.330430	5.75	0.0435
Error	7.9739	0.458527	0.057504		

Error: 0.037*MS(subject(sequence)) + 0.963*MS(Error)

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	5	2.928993	0.585799	15.75	0.0097
Error: MS(Error)	4	0.148739	0.037185		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.187033	1.187033	1.89	0.2276
Error	4.9562	3.104746	0.626437		
Error: 1.0741*MS(subject(sequence)) - 0.0741*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.027836	0.027836	0.75	0.4357
trt	1	0.127533	0.127533	3.43	0.1377
subject(sequence)	5	2.928993	0.585799	15.75	0.0097
Error: MS(Error)	4	0.148739	0.037185		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.731803	0.731803	1.28	0.3086
Error	5.0181	2.863142	0.570559		
Error: 0.9722*MS(subject(sequence)) + 0.0278*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.027836	0.027836	0.75	0.4357
trt	1	0.127533	0.127533	3.43	0.1377
subject(sequence)	5	2.928993	0.585799	15.75	0.0097
Error: MS(Error)	4	0.148739	0.037185		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.731803	0.731803	1.28	0.3086
Error	5.0181	2.863142	0.570559		
Error: 0.9722*MS(subject(sequence)) + 0.0278*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.027836	0.027836	0.75	0.4357
trt	1	0.127533	0.127533	3.43	0.1377
subject(sequence)	5	2.928993	0.585799	15.75	0.0097
Error: MS(Error)	4	0.148739	0.037185		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 76-87

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFO	LSMEAN	Pr > t
A	0.39108899		0.1377
B	0.59727089		

trt	LN_CLFO	LSMEAN	90% Confidence Limits	
A	0.391089		0.234101	0.548077
B	0.597271		0.419263	0.775279

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.206182	-0.443526	0.031162

Dependent Variable: LN_CLFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	-0.20618191	0.11133243	-1.85	0.1377	-0.44352559	0.03116178

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	7	205 301 406 410 411 501 506
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	13
Number of Observations Used	13

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LN_VZFOW

R-Square	Coeff Var	Root MSE	LN_VZFOW Mean
0.827623	54.35284	0.457834	0.842336

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.55584599	0.55584599	2.65	0.1788
period	1	0.47525416	0.47525416	2.27	0.2066
trt	1	0.01535182	0.01535182	0.07	0.8001
subject(sequence)	5	2.97913450	0.59582690	2.84	0.1667

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.61287645	0.61287645	2.92	0.1625
period	1	0.22564597	0.22564597	1.08	0.3581
trt	1	0.10173215	0.10173215	0.49	0.5244
subject(sequence)	5	2.97913450	0.59582690	2.84	0.1667

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.31250150	0.31250150	1.49	0.2891
period	1	0.22564597	0.22564597	1.08	0.3581
trt	1	0.10173215	0.10173215	0.49	0.5244
subject(sequence)	5	2.97913450	0.59582690	2.84	0.1667

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.31250150	0.31250150	1.49	0.2891
period	1	0.22564597	0.22564597	1.08	0.3581
trt	1	0.10173215	0.10173215	0.49	0.5244
subject(sequence)	5	2.97913450	0.59582690	2.84	0.1667

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 76-87

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFLOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.555846	0.555846	0.89	0.3909
Error	4.7556	2.970298	0.624593		

Error: $1.0745 \cdot MS(\text{subject}(\text{sequence})) - 0.0745 \cdot MS(\text{Error})$
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.475254	0.475254	2.10	0.2066
Error	5.005	1.130933	0.225959		

Error: $0.0423 \cdot MS(\text{subject}(\text{sequence})) + 0.9577 \cdot MS(\text{Error})$
* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.015352	0.015352	0.07	0.8041
Error	4.8758	1.091772	0.223916		

Error: $0.037 \cdot MS(\text{subject}(\text{sequence})) + 0.963 \cdot MS(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	5	2.979134	0.595827	2.84	0.1667
Error: MS(Error)	4	0.838447	0.209612		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.612876	0.612876	0.98	0.3695
Error	4.7568	2.970329	0.624435		
Error: $1.0741 * MS(\text{subject}(\text{sequence})) - 0.0741 * MS(\text{Error})$					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.225646	0.225646	1.08	0.3581
trt	1	0.101732	0.101732	0.49	0.5244
subject(sequence)	5	2.979134	0.595827	2.84	0.1667
Error: MS(Error)	4	0.838447	0.209612		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.312501	0.312501	0.53	0.4971
Error	5.1004	2.984223	0.585099		
Error: $0.9722 * MS(\text{subject}(\text{sequence})) + 0.0278 * MS(\text{Error})$					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.225646	0.225646	1.08	0.3581
trt	1	0.101732	0.101732	0.49	0.5244
subject(sequence)	5	2.979134	0.595827	2.84	0.1667
Error: MS(Error)	4	0.838447	0.209612		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.312501	0.312501	0.53	0.4971
Error	5.1004	2.984223	0.585099		
Error: 0.9722*MS(subject(sequence)) + 0.0278*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.225646	0.225646	1.08	0.3581
trt	1	0.101732	0.101732	0.49	0.5244
subject(sequence)	5	2.979134	0.595827	2.84	0.1667
Error: MS(Error)	4	0.838447	0.209612		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 76-87

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_VZFOW	LSMEAN	Pr > t
A	0.87243886		0.5244
B	0.68829023		

trt	LN_VZFOW	LSMEAN	90% Confidence Limits	
A	0.872439		0.499711	1.245167
B	0.688290		0.265656	1.110924

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.184149	-0.379363	0.747661

Dependent Variable: LN_VZFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.18414862	0.26433041	0.70	0.5244	-0.37936331	0.74766056

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	7	205 301 406 410 411 501 506
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	13
Number of Observations Used	13

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LN_VZFO

R-Square	Coeff Var	Root MSE	LN_VZFO Mean
0.829814	8.655693	0.457834	5.289394

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.59638193	0.59638193	2.85	0.1669
period	1	0.48789867	0.48789867	2.33	0.2018
trt	1	0.01331260	0.01331260	0.06	0.8134
subject(sequence)	5	2.99060271	0.59812054	2.85	0.1658

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.65717146	0.65717146	3.14	0.1513
period	1	0.22564597	0.22564597	1.08	0.3581
trt	1	0.10173215	0.10173215	0.49	0.5244
subject(sequence)	5	2.99060271	0.59812054	2.85	0.1658

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.33371526	0.33371526	1.59	0.2756
period	1	0.22564597	0.22564597	1.08	0.3581
trt	1	0.10173215	0.10173215	0.49	0.5244
subject(sequence)	5	2.99060271	0.59812054	2.85	0.1658

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.33371526	0.33371526	1.59	0.2756
period	1	0.22564597	0.22564597	1.08	0.3581
trt	1	0.10173215	0.10173215	0.49	0.5244
subject(sequence)	5	2.99060271	0.59812054	2.85	0.1658

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 76-87

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	0.596382	0.596382	0.95	0.3764
Error	4.7565	2.982607	0.627057		

Error: $1.0745 \cdot \text{MS}(\text{subject}(\text{sequence})) - 0.0745 \cdot \text{MS}(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.487899	0.487899	2.16	0.2016
Error	5.0088	1.132283	0.226057		

Error: $0.0423 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.9577 \cdot \text{MS}(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.013313	0.013313	0.06	0.8173
Error	4.8792	1.092935	0.224001		

Error: $0.037 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.963 \cdot \text{MS}(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	5	2.990603	0.598121	2.85	0.1658
Error: MS(Error)	4	0.838447	0.209612		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.657171	0.657171	1.05	0.3551
Error	4.7578	2.982633	0.626899		
Error: $1.0741 * MS(\text{subject}(\text{sequence})) - 0.0741 * MS(\text{Error})$					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.225646	0.225646	1.08	0.3581
trt	1	0.101732	0.101732	0.49	0.5244
subject(sequence)	5	2.990603	0.598121	2.85	0.1658
Error: MS(Error)	4	0.838447	0.209612		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.333715	0.333715	0.57	0.4843
Error	5.1	2.995371	0.587329		
Error: $0.9722 * MS(\text{subject}(\text{sequence})) + 0.0278 * MS(\text{Error})$					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.225646	0.225646	1.08	0.3581
trt	1	0.101732	0.101732	0.49	0.5244
subject(sequence)	5	2.990603	0.598121	2.85	0.1658
Error: MS(Error)	4	0.838447	0.209612		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.333715	0.333715	0.57	0.4843
Error	5.1	2.995371	0.587329		
Error: 0.9722*MS(subject(sequence)) + 0.0278*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.225646	0.225646	1.08	0.3581
trt	1	0.101732	0.101732	0.49	0.5244
subject(sequence)	5	2.990603	0.598121	2.85	0.1658
Error: MS(Error)	4	0.838447	0.209612		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 76-87

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LN_VZFO LSMEAN		Pr > t
A	5.31688317		0.5244
B	5.13273455		

trt	LN_VZFO LSMEAN	90% Confidence Limits	
A	5.316883	4.944155	5.689611
B	5.132735	4.710101	5.555368

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.184149	-0.379363	0.747661

Dependent Variable: LN_VZFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.18414862	0.26433041	0.70	0.5244	-0.37936331	0.74766056

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	7	205 301 406 410 411 501 506
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	14
Number of Observations Used	14

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 76-87

The GLM Procedure

Dependent Variable: TMAX

R-Square	Coeff Var	Root MSE	TMAX Mean
0.547486	51.70082	0.529380	1.023929

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.04136010	0.04136010	0.15	0.7166
period	1	0.03837779	0.03837779	0.14	0.7265
trt	1	0.58717038	0.58717038	2.10	0.2074
subject(sequence)	5	1.02838533	0.20567707	0.73	0.6287

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.04136010	0.04136010	0.15	0.7166
period	1	0.09202752	0.09202752	0.33	0.5914
trt	1	0.58717038	0.58717038	2.10	0.2074
subject(sequence)	5	1.02838533	0.20567707	0.73	0.6287

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.04136010	0.04136010	0.15	0.7166
period	1	0.09202752	0.09202752	0.33	0.5914
trt	1	0.58717038	0.58717038	2.10	0.2074
subject(sequence)	5	1.02838533	0.20567707	0.73	0.6287

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.04136010	0.04136010	0.15	0.7166
period	1	0.09202752	0.09202752	0.33	0.5914
trt	1	0.58717038	0.58717038	2.10	0.2074
subject(sequence)	5	1.02838533	0.20567707	0.73	0.6287

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 76-87

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.041360	0.041360	0.20	0.6726
Error	5	1.028385	0.205677		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.038378	0.038378	0.14	0.7265
trt	1	0.587170	0.587170	2.10	0.2074
subject(sequence)	5	1.028385	0.205677	0.73	0.6287
Error: MS(Error)	5	1.401213	0.280243		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.041360	0.041360	0.20	0.6726
Error	5	1.028385	0.205677		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.092028	0.092028	0.33	0.5914
trt	1	0.587170	0.587170	2.10	0.2074
subject(sequence)	5	1.028385	0.205677	0.73	0.6287
Error: MS(Error)	5	1.401213	0.280243		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.041360	0.041360	0.20	0.6726
Error	5	1.028385	0.205677		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.092028	0.092028	0.33	0.5914
trt	1	0.587170	0.587170	2.10	0.2074
subject(sequence)	5	1.028385	0.205677	0.73	0.6287
Error: MS(Error)	5	1.401213	0.280243		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.041360	0.041360	0.20	0.6726
Error	5	1.028385	0.205677		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.092028	0.092028	0.33	0.5914
trt	1	0.587170	0.587170	2.10	0.2074
subject(sequence)	5	1.028385	0.205677	0.73	0.6287
Error: MS(Error)	5	1.401213	0.280243		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 76-87

Least Squares Means

		H0:LSMean1=LSMean2	
trt	TMAX LSMEAN		Pr > t
A	1.22300000		0.2074
B	0.80916667		

trt	TMAX LSMEAN	90% Confidence Limits	
A	1.223000	0.815638	1.630362
B	0.809167	0.401804	1.216529

Least Squares Means for Effect trt

		Difference Between		
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.413833	-0.162264	0.989931

Dependent Variable: TMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.41383333	0.28589761	1.45	0.2074	-0.16226418	0.98993085

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	7	205 301 406 410 411 501 506
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	13
Number of Observations Used	13

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LAMZ

R-Square	Coeff Var	Root MSE	LAMZ Mean
0.873885	28.10434	0.002893	0.010293

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00000004	0.00000004	0.01	0.9469
period	1	0.00000565	0.00000565	0.67	0.4575
trt	1	0.00002119	0.00002119	2.53	0.1868
subject(sequence)	5	0.00020508	0.00004102	4.90	0.0744

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00000000	0.00000000	0.00	0.9827
period	1	0.00000681	0.00000681	0.81	0.4181
trt	1	0.00001972	0.00001972	2.36	0.1996
subject(sequence)	5	0.00020508	0.00004102	4.90	0.0744

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00000001	0.00000001	0.00	0.9790
period	1	0.00000681	0.00000681	0.81	0.4181
trt	1	0.00001972	0.00001972	2.36	0.1996
subject(sequence)	5	0.00020508	0.00004102	4.90	0.0744

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00000001	0.00000001	0.00	0.9790
period	1	0.00000681	0.00000681	0.81	0.4181
trt	1	0.00001972	0.00001972	2.36	0.1996
subject(sequence)	5	0.00020508	0.00004102	4.90	0.0744

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 76-87

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	4.2090894E-8	4.2090894E-8	0.00	0.9764
Error	4.8584	0.000211	0.000043447		

Error: $1.0745 \cdot MS(\text{subject}(\text{sequence})) - 0.0745 \cdot MS(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.000005647	0.000005647	0.58	0.4769
Error	5.7064	0.000055641	0.000009751		

Error: $0.0423 \cdot MS(\text{subject}(\text{sequence})) + 0.9577 \cdot MS(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.000021191	0.000021191	2.21	0.1919
Error	5.494	0.000052620	0.000009578		

Error: $0.037 \cdot MS(\text{subject}(\text{sequence})) + 0.963 \cdot MS(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	5	0.000205	0.000041015	4.90	0.0744
Error: MS(Error)	4	0.000033475	0.000008369		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	4.4420302E-9	4.4420302E-9	0.00	0.9923
Error	4.8591	0.000211	0.000043433		
Error: 1.0741*MS(subject(sequence)) - 0.0741*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.000006809	0.000006809	0.81	0.4181
trt	1	0.000019719	0.000019719	2.36	0.1996
subject(sequence)	5	0.000205	0.000041015	4.90	0.0744
Error: MS(Error)	4	0.000033475	0.000008369		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	6.5762621E-9	6.5762621E-9	0.00	0.9903
Error	5.0583	0.000203	0.000040108		
Error: 0.9722*MS(subject(sequence)) + 0.0278*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.000006809	0.000006809	0.81	0.4181
trt	1	0.000019719	0.000019719	2.36	0.1996
subject(sequence)	5	0.000205	0.000041015	4.90	0.0744
Error: MS(Error)	4	0.000033475	0.000008369		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	6.5762621E-9	6.5762621E-9	0.00	0.9903
Error	5.0583	0.000203	0.000040108		
Error: 0.9722*MS(subject(sequence)) + 0.0278*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.000006809	0.000006809	0.81	0.4181
trt	1	0.000019719	0.000019719	2.36	0.1996
subject(sequence)	5	0.000205	0.000041015	4.90	0.0744
Error: MS(Error)	4	0.000033475	0.000008369		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 76-87

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LAMZ LSMEAN		Pr > t
A	0.00904945		0.1996
B	0.01161324		

trt	LAMZ LSMEAN	90% Confidence Limits	
A	0.009049	0.006694	0.011405
B	0.011613	0.008943	0.014284

Least Squares Means for Effect trt

Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.002564	-0.006124	0.000997

Dependent Variable: LAMZ

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.00256379	0.00167020	-1.54	0.1996	-0.00612439 0.00099681

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	7	205 301 406 410 411 501 506
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	13
Number of Observations Used	13

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LAMZHL

R-Square	Coeff Var	Root MSE	LAMZHL Mean
0.658688	115.2892	120.4972	104.5173

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	9566.77716	9566.77716	0.66	0.4625
period	1	17411.68113	17411.68113	1.20	0.3350
trt	1	15198.84251	15198.84251	1.05	0.3641
subject(sequence)	5	69906.18556	13981.23711	0.96	0.5294

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	9246.29628	9246.29628	0.64	0.4696
period	1	18021.71774	18021.71774	1.24	0.3277
trt	1	14534.90061	14534.90061	1.00	0.3737
subject(sequence)	5	69906.18556	13981.23711	0.96	0.5294

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	8891.77606	8891.77606	0.61	0.4776
period	1	18021.71774	18021.71774	1.24	0.3277
trt	1	14534.90061	14534.90061	1.00	0.3737
subject(sequence)	5	69906.18556	13981.23711	0.96	0.5294

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	8891.77606	8891.77606	0.61	0.4776
period	1	18021.71774	18021.71774	1.24	0.3277
trt	1	14534.90061	14534.90061	1.00	0.3737
subject(sequence)	5	69906.18556	13981.23711	0.96	0.5294

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 76-87

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*sequence	1	9566.777155	9566.777155	0.69	0.4512
Error	4.2783	59645	13941		

Error: $1.0745 \cdot \text{MS}(\text{subject}(\text{sequence})) - 0.0745 \cdot \text{MS}(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	17412	17412	1.20	0.3301
Error	4.3414	62937	14497		

Error: $0.0423 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.9577 \cdot \text{MS}(\text{Error})$

* This test assumes one or more other fixed effects are zero.

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	15199	15199	1.05	0.3601
Error	4.2971	62306	14500		

Error: $0.037 \cdot \text{MS}(\text{subject}(\text{sequence})) + 0.963 \cdot \text{MS}(\text{Error})$

Source	DF	Type I SS	Mean Square	F Value	Pr > F
subject(sequence)	5	69906	13981	0.96	0.5294
Error: MS(Error)	4	58078	14520		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	9246.296277	9246.296277	0.66	0.4583
Error	4.282	59697	13941		
Error: 1.0741*MS(subject(sequence)) - 0.0741*MS(Error)					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	18022	18022	1.24	0.3277
trt	1	14535	14535	1.00	0.3737
subject(sequence)	5	69906	13981	0.96	0.5294
Error: MS(Error)	4	58078	14520		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	8891.776063	8891.776063	0.64	0.4597
Error	5.2953	74114	13996		
Error: 0.9722*MS(subject(sequence)) + 0.0278*MS(Error)					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	18022	18022	1.24	0.3277
trt	1	14535	14535	1.00	0.3737
subject(sequence)	5	69906	13981	0.96	0.5294
Error: MS(Error)	4	58078	14520		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 76-87

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	8891.776063	8891.776063	0.64	0.4597
Error	5.2953	74114	13996		
Error: 0.9722*MS(subject(sequence)) + 0.0278*MS(Error)					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	18022	18022	1.24	0.3277
trt	1	14535	14535	1.00	0.3737
subject(sequence)	5	69906	13981	0.96	0.5294
Error: MS(Error)	4	58078	14520		

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 76-87

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LAMZHL LSMEAN		Pr > t
A	141.400412		0.3737
B	71.794615		

trt	LAMZHL LSMEAN	90% Confidence Limits	
A	141.400412	43.302149	239.498674
B	71.794615	-39.438359	183.027590

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	69.605796	-78.704837	217.916429

Dependent Variable: LAMZHL

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	69.6057962	69.5690862	1.00	0.3737	-78.7048366 217.9164290

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	301 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LN_AUCLST

R-Square	Coeff Var	Root MSE	LN_AUCLST Mean
0.814181	2.448131	0.222785	9.100215

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.20699244	0.20699244	4.17	0.2899
trt	1	0.01047938	0.01047938	0.21	0.7258
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.20699244	0.20699244	4.17	0.2899
trt	1	0.01047938	0.01047938	0.21	0.7258
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.20699244	0.20699244	4.17	0.2899
trt	1	0.01047938	0.01047938	0.21	0.7258
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.20699244	0.20699244	4.17	0.2899
trt	1	0.01047938	0.01047938	0.21	0.7258
subject(sequence)	0	0.00000000			

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 76-87

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCLST	LSMEAN	Pr > t
B	9.15139922		0.7258
C	9.04903038		

trt	LN_AUCLST	LSMEAN	90% Confidence Limits	
B	9.151399		8.156775	10.146023
C	9.049030		8.054407	10.043654

Least Squares Means for Effect trt

Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.102369	-1.304242	1.508979

The GLM Procedure

Dependent Variable: LN_AUCLST

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	-0.10236884	0.22278522	-0.46	0.7258	-1.50897936	1.30424169

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: $AUC_{0-\infty}$ (h*ng/mL) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	301 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LN_AUCIFO

R-Square	Coeff Var	Root MSE	LN_AUCIFO Mean
0.932143	1.708233	0.157513	9.220795

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.34080541	0.34080541	13.74	0.1678
trt	1	0.00000719	0.00000719	0.00	0.9892
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.34080541	0.34080541	13.74	0.1678
trt	1	0.00000719	0.00000719	0.00	0.9892
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.34080541	0.34080541	13.74	0.1678
trt	1	0.00000719	0.00000719	0.00	0.9892
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.34080541	0.34080541	13.74	0.1678
trt	1	0.00000719	0.00000719	0.00	0.9892
subject(sequence)	0	0.00000000			

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 76-87

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCIFO	LSMEAN	Pr > t
B	9.21945385		0.9892
C	9.22213570		

trt	LN_AUCIFO	LSMEAN	90% Confidence Limits	
B	9.219454		8.516239	9.922668
C	9.222136		8.518921	9.925350

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.002682	-0.997177	0.991814

The GLM Procedure

Dependent Variable: LN_AUCIFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	0.00268185	0.15751262	0.02	0.9892	-0.99181367	0.99717736

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: C_{\max} (ng/mL) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	301 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LN_CMAX

R-Square	Coeff Var	Root MSE	LN_CMAX Mean
0.263645	10.67177	0.587305	5.503351

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00664457	0.00664457	0.02	0.9122
trt	1	0.11685348	0.11685348	0.34	0.6644
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00664457	0.00664457	0.02	0.9122
trt	1	0.11685348	0.11685348	0.34	0.6644
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00664457	0.00664457	0.02	0.9122
trt	1	0.11685348	0.11685348	0.34	0.6644
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00664457	0.00664457	0.02	0.9122
trt	1	0.11685348	0.11685348	0.34	0.6644
subject(sequence)	0	0.00000000			

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 76-87

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CMAX	LSMEAN	Pr > t
B	5.67427068		0.6644
C	5.33243229		

trt	LN_CMAX	LSMEAN	90% Confidence Limits	
B	5.674271		3.052250	8.296291
C	5.332432		2.710412	7.954453

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.341838	-3.366259	4.049935

The GLM Procedure

Dependent Variable: LN_CMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	-0.34183838	0.58730486	-0.58	0.6644	-4.04993531	3.36625855

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	301 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LN_CLFOW

R-Square	Coeff Var	Root MSE	LN_CLFOW Mean
0.930720	-3.964760	0.157513	-3.972816

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.30870751	0.30870751	12.44	0.1759
trt	1	0.02459644	0.02459644	0.99	0.5014
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.30870751	0.30870751	12.44	0.1759
trt	1	0.02459644	0.02459644	0.99	0.5014
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.30870751	0.30870751	12.44	0.1759
trt	1	0.02459644	0.02459644	0.99	0.5014
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.30870751	0.30870751	12.44	0.1759
trt	1	0.02459644	0.02459644	0.99	0.5014
subject(sequence)	0	0.00000000			

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 76-87

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFOW	LSMEAN	Pr > t
B	-3.89439993		0.5014
C	-4.05123246		

trt	LN_CLFOW	LSMEAN	90% Confidence Limits	
B	-3.894400		-4.597614	-3.191185
C	-4.051232		-4.754447	-3.348018

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.156833	-0.837663	1.151328

The GLM Procedure

Dependent Variable: LN_CLFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	-0.15683253	0.15751262	-1.00	0.5014	-1.15132804	0.83766299

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	301 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LN_CLFO

R-Square	Coeff Var	Root MSE	LN_CLFO Mean
0.936419	33.36523	0.157513	0.472086

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.34080541	0.34080541	13.74	0.1678
trt	1	0.02459644	0.02459644	0.99	0.5014
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.34080541	0.34080541	13.74	0.1678
trt	1	0.02459644	0.02459644	0.99	0.5014
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.34080541	0.34080541	13.74	0.1678
trt	1	0.02459644	0.02459644	0.99	0.5014
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.34080541	0.34080541	13.74	0.1678
trt	1	0.02459644	0.02459644	0.99	0.5014
subject(sequence)	0	0.00000000			

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h) Weight Group: 76-87

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFO	LSMEAN	Pr > t
B	0.55050231		0.5014
C	0.39366978		

trt	LN_CLFO	LSMEAN	90% Confidence Limits	
B	0.550502		-0.152712	1.253717
C	0.393670		-0.309545	1.096884

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.156833	-0.837663	1.151328

The GLM Procedure

Dependent Variable: LN_CLFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.15683253	0.15751262	-1.00	0.5014	-1.15132804 0.83766299

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	301 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LN_VZFOW

R-Square	Coeff Var	Root MSE	LN_VZFOW Mean
0.677827	40.68762	0.281952	0.692967

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00005645	0.00005645	0.00	0.9830
trt	1	0.16719912	0.16719912	2.10	0.3843
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00005645	0.00005645	0.00	0.9830
trt	1	0.16719912	0.16719912	2.10	0.3843
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00005645	0.00005645	0.00	0.9830
trt	1	0.16719912	0.16719912	2.10	0.3843
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00005645	0.00005645	0.00	0.9830
trt	1	0.16719912	0.16719912	2.10	0.3843
subject(sequence)	0	0.00000000			

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 76-87

The GLM Procedure
Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_VZFOW	LSMEAN	Pr > t
B	0.48851732		0.3843
C	0.89741721		

trt	LN_VZFOW	LSMEAN	90% Confidence Limits	
B	0.488517		-0.770256	1.747291
C	0.897417		-0.361356	2.156191

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.408900	-2.189074	1.371274

The GLM Procedure

Dependent Variable: LN_VZFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	0.40889990	0.28195191	1.45	0.3843	-1.37127442 2.18907421

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	301 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LN_VZFO

R-Square	Coeff Var	Root MSE	LN_VZFO Mean
0.678310	5.487720	0.281952	5.137870

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00042674	0.00042674	0.01	0.9534
trt	1	0.16719912	0.16719912	2.10	0.3843
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00042674	0.00042674	0.01	0.9534
trt	1	0.16719912	0.16719912	2.10	0.3843
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00042674	0.00042674	0.01	0.9534
trt	1	0.16719912	0.16719912	2.10	0.3843
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00042674	0.00042674	0.01	0.9534
trt	1	0.16719912	0.16719912	2.10	0.3843
subject(sequence)	0	0.00000000			

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L) Weight Group: 76-87

The GLM Procedure
Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_VZFO	LSMEAN	Pr > t
B	4.93341956		0.3843
C	5.34231945		

trt	LN_VZFO	LSMEAN	90% Confidence Limits	
B	4.933420		3.674646	6.192193
C	5.342319		4.083546	6.601093

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.408900	-2.189074	1.371274

The GLM Procedure

Dependent Variable: LN_VZFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	0.40889990	0.28195191	1.45	0.3843	-1.37127442 2.18907421

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	301 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h) Weight Group: 76-87

The GLM Procedure

Dependent Variable: TMAX

R-Square	Coeff Var	Root MSE	TMAX Mean
0.500070	50.63480	0.508500	1.004250

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00007225	0.00007225	0.00	0.9894
trt	1	0.25857225	0.25857225	1.00	0.5000
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00007225	0.00007225	0.00	0.9894
trt	1	0.25857225	0.25857225	1.00	0.5000
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00007225	0.00007225	0.00	0.9894
trt	1	0.25857225	0.25857225	1.00	0.5000
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00007225	0.00007225	0.00	0.9894
trt	1	0.25857225	0.25857225	1.00	0.5000
subject(sequence)	0	0.00000000			

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h) Weight Group: 76-87

The GLM Procedure
Least Squares Means

		H0:LSMean1=LSMean2	
trt	TMAX LSMEAN		Pr > t
B	0.7500000		0.5000
C	1.2585000		

trt	TMAX LSMEAN	90% Confidence Limits	
B	0.750000	-1.520196	3.020196
C	1.258500	-1.011696	3.528696

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.508500	-3.719043	2.702043

The GLM Procedure

Dependent Variable: TMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	0.50850000	0.50850000	1.00	0.5000	-2.70204265 3.71904265

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	301 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LAMZ

R-Square	Coeff Var	Root MSE	LAMZ Mean
0.998640	2.704657	0.000275	0.010153

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00002754	0.00002754	365.23	0.0333
trt	1	0.00002782	0.00002782	368.87	0.0331
subject(sequence)	0	0.00000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00002754	0.00002754	365.23	0.0333
trt	1	0.00002782	0.00002782	368.87	0.0331
subject(sequence)	0	0.00000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00002754	0.00002754	365.23	0.0333
trt	1	0.00002782	0.00002782	368.87	0.0331
subject(sequence)	0	0.00000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00002754	0.00002754	365.23	0.0333
trt	1	0.00002782	0.00002782	368.87	0.0331
subject(sequence)	0	0.00000000			

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h) Weight Group: 76-87

The GLM Procedure
Least Squares Means

		H0:LSMean1=LSMean2	
trt	LAMZ LSMEAN		Pr > t
B	0.01279051		0.0331
C	0.00751627		

trt	LAMZ LSMEAN	90% Confidence Limits	
B	0.012791	0.011564	0.014017
C	0.007516	0.006290	0.008742

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.005274	0.003540	0.007008

The GLM Procedure

Dependent Variable: LAMZ

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	-0.00527424	0.00027461	-19.21	0.0331	-0.00700808	-0.00354039

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 76-87

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	2	301 406
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	4
Number of Observations Used	4

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 76-87

The GLM Procedure

Dependent Variable: LAMZHL

R-Square	Coeff Var	Root MSE	LAMZHL Mean
0.899909	27.41894	21.98952	80.19828

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	2165.315655	2165.315655	4.48	0.2810
trt	1	2182.123274	2182.123274	4.51	0.2801
subject(sequence)	0	0.000000			

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	2165.315655	2165.315655	4.48	0.2810
trt	1	2182.123274	2182.123274	4.51	0.2801
subject(sequence)	0	0.000000			

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	2165.315655	2165.315655	4.48	0.2810
trt	1	2182.123274	2182.123274	4.51	0.2801
subject(sequence)	0	0.000000			

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	2165.315655	2165.315655	4.48	0.2810
trt	1	2182.123274	2182.123274	4.51	0.2801
subject(sequence)	0	0.000000			

Listing 16.1.9-7 ANOVA for Treatment Comparison of Diazepam for Weight Group 76-87 kg - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 76-87

The GLM Procedure
Least Squares Means

			H0:LSMean1=LSMean2
trt	LAMZHL	LSMEAN	Pr > t
B	56.841678		0.2801
C	103.554880		

trt	LAMZHL	LSMEAN	90% Confidence Limits	
B	56.841678		-41.330441	155.013796
C	103.554880		5.382761	201.726999

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-46.713202	-185.549544	92.123140

The GLM Procedure

Dependent Variable: LAMZHL

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	46.7132024	21.9895163	2.12	0.2801	-92.1231396	185.5495443

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	11	203 204 304 402 404 407 409 502 505 507 508
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	22
Number of Observations Used	22

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LN_AUCLST

R-Square	Coeff Var	Root MSE	LN_AUCLST Mean
0.624540	10.97272	0.944959	8.611893

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.34347906	0.34347906	0.38	0.5505
period	1	0.00482396	0.00482396	0.01	0.9430
trt	1	2.32311575	2.32311575	2.60	0.1412
subject(sequence)	9	10.69654172	1.18850464	1.33	0.3385

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.34347906	0.34347906	0.38	0.5505
period	1	0.04315122	0.04315122	0.05	0.8309
trt	1	2.32311575	2.32311575	2.60	0.1412
subject(sequence)	9	10.69654172	1.18850464	1.33	0.3385

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.34347906	0.34347906	0.38	0.5505
period	1	0.04315122	0.04315122	0.05	0.8309
trt	1	2.32311575	2.32311575	2.60	0.1412
subject(sequence)	9	10.69654172	1.18850464	1.33	0.3385

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.34347906	0.34347906	0.38	0.5505
period	1	0.04315122	0.04315122	0.05	0.8309
trt	1	2.32311575	2.32311575	2.60	0.1412
subject(sequence)	9	10.69654172	1.18850464	1.33	0.3385

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 88-111

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.343479	0.343479	0.29	0.6039
Error	9	10.696542	1.188505		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.004824	0.004824	0.01	0.9430
trt	1	2.323116	2.323116	2.60	0.1412
subject(sequence)	9	10.696542	1.188505	1.33	0.3385
Error: MS(Error)	9	8.036520	0.892947		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.343479	0.343479	0.29	0.6039
Error	9	10.696542	1.188505		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.043151	0.043151	0.05	0.8309
trt	1	2.323116	2.323116	2.60	0.1412
subject(sequence)	9	10.696542	1.188505	1.33	0.3385
Error: MS(Error)	9	8.036520	0.892947		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.343479	0.343479	0.29	0.6039
Error	9	10.696542	1.188505		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.043151	0.043151	0.05	0.8309
trt	1	2.323116	2.323116	2.60	0.1412
subject(sequence)	9	10.696542	1.188505	1.33	0.3385
Error: MS(Error)	9	8.036520	0.892947		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.343479	0.343479	0.29	0.6039
Error	9	10.696542	1.188505		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.043151	0.043151	0.05	0.8309
trt	1	2.323116	2.323116	2.60	0.1412
subject(sequence)	9	10.696542	1.188505	1.33	0.3385
Error: MS(Error)	9	8.036520	0.892947		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 88-111

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCLST	LSMEAN	Pr > t
A	8.92679321		0.1412
B	8.27417958		

trt	LN_AUCLST	LSMEAN	90% Confidence Limits	
A	8.926793	8.402339	9.451248	
B	8.274180	7.749725	8.798634	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.652614	-0.089077	1.394304

Dependent Variable: LN_AUCLST

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	0.65261363	0.40460708	1.61	0.1412	-0.08907684 1.39430410

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: $AUC_{0-\infty}$ (h*ng/mL) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	11	203 204 304 402 404 407 409 502 505 507 508
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	22
Number of Observations Used	22

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LN_AUCIFO

R-Square	Coeff Var	Root MSE	LN_AUCIFO Mean
0.810830	6.590357	0.587678	8.917241

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.69862990	0.69862990	2.02	0.1887
period	1	0.23085126	0.23085126	0.67	0.4347
trt	1	1.60598632	1.60598632	4.65	0.0594
subject(sequence)	9	10.78744135	1.19860459	3.47	0.0389

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.69862990	0.69862990	2.02	0.1887
period	1	0.35246442	0.35246442	1.02	0.3388
trt	1	1.60598632	1.60598632	4.65	0.0594
subject(sequence)	9	10.78744135	1.19860459	3.47	0.0389

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.69862990	0.69862990	2.02	0.1887
period	1	0.35246442	0.35246442	1.02	0.3388
trt	1	1.60598632	1.60598632	4.65	0.0594
subject(sequence)	9	10.78744135	1.19860459	3.47	0.0389

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.69862990	0.69862990	2.02	0.1887
period	1	0.35246442	0.35246442	1.02	0.3388
trt	1	1.60598632	1.60598632	4.65	0.0594
subject(sequence)	9	10.78744135	1.19860459	3.47	0.0389

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 88-111

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.698630	0.698630	0.58	0.4647
Error	9	10.787441	1.198605		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.230851	0.230851	0.67	0.4347
trt	1	1.605986	1.605986	4.65	0.0594
subject(sequence)	9	10.787441	1.198605	3.47	0.0389
Error: MS(Error)	9	3.108289	0.345365		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.698630	0.698630	0.58	0.4647
Error	9	10.787441	1.198605		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.352464	0.352464	1.02	0.3388
trt	1	1.605986	1.605986	4.65	0.0594
subject(sequence)	9	10.787441	1.198605	3.47	0.0389
Error: MS(Error)	9	3.108289	0.345365		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.698630	0.698630	0.58	0.4647
Error	9	10.787441	1.198605		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.352464	0.352464	1.02	0.3388
trt	1	1.605986	1.605986	4.65	0.0594
subject(sequence)	9	10.787441	1.198605	3.47	0.0389
Error: MS(Error)	9	3.108289	0.345365		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.698630	0.698630	0.58	0.4647
Error	9	10.787441	1.198605		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.352464	0.352464	1.02	0.3388
trt	1	1.605986	1.605986	4.65	0.0594
subject(sequence)	9	10.787441	1.198605	3.47	0.0389
Error: MS(Error)	9	3.108289	0.345365		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 88-111

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LN_AUCIFO LSMEAN		Pr > t
A	9.17228121		0.0594
B	8.62966640		

trt	LN_AUCIFO LSMEAN	90% Confidence Limits	
A	9.172281	8.846118	9.498444
B	8.629666	8.303504	8.955829

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.542615	0.081351	1.003879

Dependent Variable: LN_AUCIFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	0.54261480	0.25162870	2.16	0.05940	0.08135098 1.00387863

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{\max} (ng/mL) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	11	203 204 304 402 404 407 409 502 505 507 508
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	22
Number of Observations Used	22

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LN_CMAX

R-Square	Coeff Var	Root MSE	LN_CMAX Mean
0.462659	19.25038	0.955689	4.964517

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.05327995	0.05327995	0.06	0.8146
period	1	0.73440347	0.73440347	0.80	0.3932
trt	1	0.94378043	0.94378043	1.03	0.3359
subject(sequence)	9	5.34614197	0.59401577	0.65	0.7341

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.05327995	0.05327995	0.06	0.8146
period	1	0.88687719	0.88687719	0.97	0.3502
trt	1	0.94378043	0.94378043	1.03	0.3359
subject(sequence)	9	5.34614197	0.59401577	0.65	0.7341

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.05327995	0.05327995	0.06	0.8146
period	1	0.88687719	0.88687719	0.97	0.3502
trt	1	0.94378043	0.94378043	1.03	0.3359
subject(sequence)	9	5.34614197	0.59401577	0.65	0.7341

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.05327995	0.05327995	0.06	0.8146
period	1	0.88687719	0.88687719	0.97	0.3502
trt	1	0.94378043	0.94378043	1.03	0.3359
subject(sequence)	9	5.34614197	0.59401577	0.65	0.7341

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 88-111

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.053280	0.053280	0.09	0.7714
Error	9	5.346142	0.594016		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.734403	0.734403	0.80	0.3932
trt	1	0.943780	0.943780	1.03	0.3359
subject(sequence)	9	5.346142	0.594016	0.65	0.7341
Error: MS(Error)	9	8.220065	0.913341		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.053280	0.053280	0.09	0.7714
Error	9	5.346142	0.594016		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.886877	0.886877	0.97	0.3502
trt	1	0.943780	0.943780	1.03	0.3359
subject(sequence)	9	5.346142	0.594016	0.65	0.7341
Error: MS(Error)	9	8.220065	0.913341		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.053280	0.053280	0.09	0.7714
Error	9	5.346142	0.594016		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.886877	0.886877	0.97	0.3502
trt	1	0.943780	0.943780	1.03	0.3359
subject(sequence)	9	5.346142	0.594016	0.65	0.7341
Error: MS(Error)	9	8.220065	0.913341		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.053280	0.053280	0.09	0.7714
Error	9	5.346142	0.594016		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.886877	0.886877	0.97	0.3502
trt	1	0.943780	0.943780	1.03	0.3359
subject(sequence)	9	5.346142	0.594016	0.65	0.7341
Error: MS(Error)	9	8.220065	0.913341		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 88-111

Least Squares Means

			H0:LSMean1=LSMean2	
trt	LN_CMAX	LSMEAN		Pr > t
A	5.16800682			0.3359
B	4.75204239			

trt	LN_CMAX	LSMEAN	90% Confidence Limits	
A	5.168007		4.637597	5.698416
B	4.752042		4.221633	5.282452

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.415964	-0.334148	1.166077

Dependent Variable: LN_CMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.41596444	0.40920138	1.02	0.3359	-0.33414790	1.16607677

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	11	203 204 304 402 404 407 409 502 505 507 508
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	22
Number of Observations Used	22

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LN_CLFOW

R-Square	Coeff Var	Root MSE	LN_CLFOW Mean
0.840724	-15.77847	0.587678	-3.724556

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.95042330	0.95042330	2.75	0.1315
period	1	0.20430477	0.20430477	0.59	0.4615
trt	1	2.49367461	2.49367461	7.22	0.0249
subject(sequence)	9	12.75844172	1.41760464	4.10	0.0236

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.95042330	0.95042330	2.75	0.1315
period	1	0.35246442	0.35246442	1.02	0.3388
trt	1	2.49367461	2.49367461	7.22	0.0249
subject(sequence)	9	12.75844172	1.41760464	4.10	0.0236

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.95042330	0.95042330	2.75	0.1315
period	1	0.35246442	0.35246442	1.02	0.3388
trt	1	2.49367461	2.49367461	7.22	0.0249
subject(sequence)	9	12.75844172	1.41760464	4.10	0.0236

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.95042330	0.95042330	2.75	0.1315
period	1	0.35246442	0.35246442	1.02	0.3388
trt	1	2.49367461	2.49367461	7.22	0.0249
subject(sequence)	9	12.75844172	1.41760464	4.10	0.0236

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 88-111

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.950423	0.950423	0.67	0.4340
Error	9	12.758442	1.417605		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.204305	0.204305	0.59	0.4615
trt	1	2.493675	2.493675	7.22	0.0249
subject(sequence)	9	12.758442	1.417605	4.10	0.0236
Error: MS(Error)	9	3.108289	0.345365		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.950423	0.950423	0.67	0.4340
Error	9	12.758442	1.417605		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.352464	0.352464	1.02	0.3388
trt	1	2.493675	2.493675	7.22	0.0249
subject(sequence)	9	12.758442	1.417605	4.10	0.0236
Error: MS(Error)	9	3.108289	0.345365		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.950423	0.950423	0.67	0.4340
Error	9	12.758442	1.417605		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.352464	0.352464	1.02	0.3388
trt	1	2.493675	2.493675	7.22	0.0249
subject(sequence)	9	12.758442	1.417605	4.10	0.0236
Error: MS(Error)	9	3.108289	0.345365		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.950423	0.950423	0.67	0.4340
Error	9	12.758442	1.417605		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.352464	0.352464	1.02	0.3388
trt	1	2.493675	2.493675	7.22	0.0249
subject(sequence)	9	12.758442	1.417605	4.10	0.0236
Error: MS(Error)	9	3.108289	0.345365		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 88-111

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_CLFOW	LSMEAN	Pr > t
A	-4.0436537		0.0249
B	-3.36750918		

trt	LN_CLFOW	LSMEAN	90% Confidence Limits	
A	-4.043655		-4.369818	-3.717493
B	-3.367509		-3.693672	-3.041346

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.676146	-1.137410	-0.214882

Dependent Variable: LN_CLFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	-0.67614620	0.25162870	-2.69	0.0249	-1.13741002	-0.21488237

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	11	203 204 304 402 404 407 409 502 505 507 508
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	22
Number of Observations Used	22

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LN_CLFO

R-Square	Coeff Var	Root MSE	LN_CLFO Mean
0.820251	63.91414	0.587678	0.919481

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.69862990	0.69862990	2.02	0.1887
period	1	0.20430477	0.20430477	0.59	0.4615
trt	1	2.49367461	2.49367461	7.22	0.0249
subject(sequence)	9	10.78744135	1.19860459	3.47	0.0389

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.69862990	0.69862990	2.02	0.1887
period	1	0.35246442	0.35246442	1.02	0.3388
trt	1	2.49367461	2.49367461	7.22	0.0249
subject(sequence)	9	10.78744135	1.19860459	3.47	0.0389

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.69862990	0.69862990	2.02	0.1887
period	1	0.35246442	0.35246442	1.02	0.3388
trt	1	2.49367461	2.49367461	7.22	0.0249
subject(sequence)	9	10.78744135	1.19860459	3.47	0.0389

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.69862990	0.69862990	2.02	0.1887
period	1	0.35246442	0.35246442	1.02	0.3388
trt	1	2.49367461	2.49367461	7.22	0.0249
subject(sequence)	9	10.78744135	1.19860459	3.47	0.0389

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 88-111

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.698630	0.698630	0.58	0.4647
Error	9	10.787441	1.198605		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.204305	0.204305	0.59	0.4615
trt	1	2.493675	2.493675	7.22	0.0249
subject(sequence)	9	10.787441	1.198605	3.47	0.0389
Error: MS(Error)	9	3.108289	0.345365		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.698630	0.698630	0.58	0.4647
Error	9	10.787441	1.198605		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.352464	0.352464	1.02	0.3388
trt	1	2.493675	2.493675	7.22	0.0249
subject(sequence)	9	10.787441	1.198605	3.47	0.0389
Error: MS(Error)	9	3.108289	0.345365		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.698630	0.698630	0.58	0.4647
Error	9	10.787441	1.198605		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.352464	0.352464	1.02	0.3388
trt	1	2.493675	2.493675	7.22	0.0249
subject(sequence)	9	10.787441	1.198605	3.47	0.0389
Error: MS(Error)	9	3.108289	0.345365		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.698630	0.698630	0.58	0.4647
Error	9	10.787441	1.198605		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.352464	0.352464	1.02	0.3388
trt	1	2.493675	2.493675	7.22	0.0249
subject(sequence)	9	10.787441	1.198605	3.47	0.0389
Error: MS(Error)	9	3.108289	0.345365		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: Cl/F (L/h) Weight Group: 88-111

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFO	LSMEAN	Pr > t
A	0.59767495		0.0249
B	1.27382115		

trt	LN_CLFO	LSMEAN	90% Confidence Limits	
A	0.597675		0.271512	0.923838
B	1.273821		0.947658	1.599984

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.676146	-1.137410	-0.214882

Dependent Variable: LN_CLFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	-0.67614620	0.25162870	-2.69	0.0249	-1.13741002	-0.21488237

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	11	203 204 304 402 404 407 409 502 505 507 508
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	22
Number of Observations Used	22

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LN_VZFOW

R-Square	Coeff Var	Root MSE	LN_VZFOW Mean
0.530952	83.84526	1.109423	1.323179

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.27195823	0.27195823	0.22	0.6495
period	1	0.01551644	0.01551644	0.01	0.9131
trt	1	3.73511476	3.73511476	3.03	0.1155
subject(sequence)	9	8.51675186	0.94630576	0.77	0.6491

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.27195823	0.27195823	0.22	0.6495
period	1	0.00266729	0.00266729	0.00	0.9639
trt	1	3.73511476	3.73511476	3.03	0.1155
subject(sequence)	9	8.51675186	0.94630576	0.77	0.6491

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.27195823	0.27195823	0.22	0.6495
period	1	0.00266729	0.00266729	0.00	0.9639
trt	1	3.73511476	3.73511476	3.03	0.1155
subject(sequence)	9	8.51675186	0.94630576	0.77	0.6491

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.27195823	0.27195823	0.22	0.6495
period	1	0.00266729	0.00266729	0.00	0.9639
trt	1	3.73511476	3.73511476	3.03	0.1155
subject(sequence)	9	8.51675186	0.94630576	0.77	0.6491

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 88-111

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.271958	0.271958	0.29	0.6049
Error	9	8.516752	0.946306		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.015516	0.015516	0.01	0.9131
trt	1	3.735115	3.735115	3.03	0.1155
subject(sequence)	9	8.516752	0.946306	0.77	0.6491
Error: MS(Error)	9	11.077366	1.230818		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.271958	0.271958	0.29	0.6049
Error	9	8.516752	0.946306		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.002667	0.002667	0.00	0.9639
trt	1	3.735115	3.735115	3.03	0.1155
subject(sequence)	9	8.516752	0.946306	0.77	0.6491
Error: MS(Error)	9	11.077366	1.230818		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.271958	0.271958	0.29	0.6049
Error	9	8.516752	0.946306		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.002667	0.002667	0.00	0.9639
trt	1	3.735115	3.735115	3.03	0.1155
subject(sequence)	9	8.516752	0.946306	0.77	0.6491
Error: MS(Error)	9	11.077366	1.230818		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.271958	0.271958	0.29	0.6049
Error	9	8.516752	0.946306		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.002667	0.002667	0.00	0.9639
trt	1	3.735115	3.735115	3.03	0.1155
subject(sequence)	9	8.516752	0.946306	0.77	0.6491
Error: MS(Error)	9	11.077366	1.230818		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 88-111

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_VZFOW	LSMEAN	Pr > t
A	0.91957377		0.1155
B	1.74708271		

trt	LN_VZFOW	LSMEAN	90% Confidence Limits	
A	0.919574		0.303841	1.535306
B	1.747083		1.131350	2.362815

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.827509	-1.698286	0.043268

Dependent Variable: LN_VZFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.82750894	0.47502636	-1.74	0.1155	-1.69828590 0.04326803

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	11	203 204 304 402 404 407 409 502 505 507 508
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	22
Number of Observations Used	22

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LN_VZFO

R-Square	Coeff Var	Root MSE	LN_VZFO Mean
0.511939	18.59196	1.109423	5.967215

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.14626067	0.14626067	0.12	0.7382
period	1	0.01551644	0.01551644	0.01	0.9131
trt	1	3.73511476	3.73511476	3.03	0.1155
subject(sequence)	9	7.72241356	0.85804595	0.70	0.7002

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.14626067	0.14626067	0.12	0.7382
period	1	0.00266729	0.00266729	0.00	0.9639
trt	1	3.73511476	3.73511476	3.03	0.1155
subject(sequence)	9	7.72241356	0.85804595	0.70	0.7002

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.14626067	0.14626067	0.12	0.7382
period	1	0.00266729	0.00266729	0.00	0.9639
trt	1	3.73511476	3.73511476	3.03	0.1155
subject(sequence)	9	7.72241356	0.85804595	0.70	0.7002

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.14626067	0.14626067	0.12	0.7382
period	1	0.00266729	0.00266729	0.00	0.9639
trt	1	3.73511476	3.73511476	3.03	0.1155
subject(sequence)	9	7.72241356	0.85804595	0.70	0.7002

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 88-111

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.146261	0.146261	0.17	0.6894
Error	9	7.722414	0.858046		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.015516	0.015516	0.01	0.9131
trt	1	3.735115	3.735115	3.03	0.1155
subject(sequence)	9	7.722414	0.858046	0.70	0.7002
Error: MS(Error)	9	11.077366	1.230818		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.146261	0.146261	0.17	0.6894
Error	9	7.722414	0.858046		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.002667	0.002667	0.00	0.9639
trt	1	3.735115	3.735115	3.03	0.1155
subject(sequence)	9	7.722414	0.858046	0.70	0.7002
Error: MS(Error)	9	11.077366	1.230818		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.146261	0.146261	0.17	0.6894
Error	9	7.722414	0.858046		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.002667	0.002667	0.00	0.9639
trt	1	3.735115	3.735115	3.03	0.1155
subject(sequence)	9	7.722414	0.858046	0.70	0.7002
Error: MS(Error)	9	11.077366	1.230818		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.146261	0.146261	0.17	0.6894
Error	9	7.722414	0.858046		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.002667	0.002667	0.00	0.9639
trt	1	3.735115	3.735115	3.03	0.1155
subject(sequence)	9	7.722414	0.858046	0.70	0.7002
Error: MS(Error)	9	11.077366	1.230818		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: V_d/F (L) Weight Group: 88-111

Least Squares Means

			H0:LSMean1=LSMean2	
trt	LN_VZFO	LSMEAN		Pr > t
A	5.56090410			0.1155
B	6.38841304			

trt	LN_VZFO	LSMEAN	90% Confidence Limits	
A	5.560904	4.945172	6.176636	
B	6.388413	5.772681	7.004145	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.827509	-1.698286	0.043268

Dependent Variable: LN_VZFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-0.82750894	0.47502636	-1.74	0.1155	-1.69828590 0.04326803

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	11	203 204 304 402 404 407 409 502 505 507 508
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	22
Number of Observations Used	22

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{max} (h) Weight Group: 88-111

The GLM Procedure

Dependent Variable: TMAX

R-Square	Coeff Var	Root MSE	TMAX Mean
0.669722	79.33433	0.875058	1.103000

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.59202165	0.59202165	0.77	0.4021
period	1	6.15015564	6.15015564	8.03	0.0196
trt	1	1.22817855	1.22817855	1.60	0.2371
subject(sequence)	9	6.00394735	0.66710526	0.87	0.5797

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.59202165	0.59202165	0.77	0.4021
period	1	5.61184527	5.61184527	7.33	0.0241
trt	1	1.22817855	1.22817855	1.60	0.2371
subject(sequence)	9	6.00394735	0.66710526	0.87	0.5797

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.59202165	0.59202165	0.77	0.4021
period	1	5.61184527	5.61184527	7.33	0.0241
trt	1	1.22817855	1.22817855	1.60	0.2371
subject(sequence)	9	6.00394735	0.66710526	0.87	0.5797

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.59202165	0.59202165	0.77	0.4021
period	1	5.61184527	5.61184527	7.33	0.0241
trt	1	1.22817855	1.22817855	1.60	0.2371
subject(sequence)	9	6.00394735	0.66710526	0.87	0.5797

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 88-111

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.592022	0.592022	0.89	0.3708
Error	9	6.003947	0.667105		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	6.150156	6.150156	8.03	0.0196
trt	1	1.228179	1.228179	1.60	0.2371
subject(sequence)	9	6.003947	0.667105	0.87	0.5797
Error: MS(Error)	9	6.891533	0.765726		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.592022	0.592022	0.89	0.3708
Error	9	6.003947	0.667105		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	5.611845	5.611845	7.33	0.0241
trt	1	1.228179	1.228179	1.60	0.2371
subject(sequence)	9	6.003947	0.667105	0.87	0.5797
Error: MS(Error)	9	6.891533	0.765726		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{max} (h) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.592022	0.592022	0.89	0.3708
Error	9	6.003947	0.667105		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	5.611845	5.611845	7.33	0.0241
trt	1	1.228179	1.228179	1.60	0.2371
subject(sequence)	9	6.003947	0.667105	0.87	0.5797
Error: MS(Error)	9	6.891533	0.765726		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.592022	0.592022	0.89	0.3708
Error	9	6.003947	0.667105		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	5.611845	5.611845	7.33	0.0241
trt	1	1.228179	1.228179	1.60	0.2371
subject(sequence)	9	6.003947	0.667105	0.87	0.5797
Error: MS(Error)	9	6.891533	0.765726		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: T_{\max} (h) Weight Group: 88-111

Least Squares Means

		H0:LSMean1=LSMean2	
trt	TMAX LSMEAN		Pr > t
A	1.32528333		0.2371
B	0.85076667		

trt	TMAX LSMEAN	90% Confidence Limits	
A	1.325283	0.839624	1.810943
B	0.850767	0.365107	1.336426

Least Squares Means for Effect trt

		Difference Between		
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.474517	-0.212309	1.161342

Dependent Variable: TMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.47451667	0.37467730	1.27	0.2371	-0.21230913	1.16134246

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	11	203 204 304 402 404 407 409 502 505 507 508
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	22
Number of Observations Used	22

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LAMZ

R-Square	Coeff Var	Root MSE	LAMZ Mean
0.660697	38.44030	0.002853	0.007423

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00000972	0.00000972	1.19	0.3028
period	1	0.00000474	0.00000474	0.58	0.4649
trt	1	0.00000587	0.00000587	0.72	0.4177
subject(sequence)	9	0.00012234	0.00001359	1.67	0.2285

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00000972	0.00000972	1.19	0.3028
period	1	0.00000380	0.00000380	0.47	0.5119
trt	1	0.00000587	0.00000587	0.72	0.4177
subject(sequence)	9	0.00012234	0.00001359	1.67	0.2285

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00000972	0.00000972	1.19	0.3028
period	1	0.00000380	0.00000380	0.47	0.5119
trt	1	0.00000587	0.00000587	0.72	0.4177
subject(sequence)	9	0.00012234	0.00001359	1.67	0.2285

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00000972	0.00000972	1.19	0.3028
period	1	0.00000380	0.00000380	0.47	0.5119
trt	1	0.00000587	0.00000587	0.72	0.4177
subject(sequence)	9	0.00012234	0.00001359	1.67	0.2285

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 88-111

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.000009724	0.000009724	0.72	0.4196
Error	9	0.000122	0.000013594		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	0.000004743	0.000004743	0.58	0.4649
trt	1	0.000005875	0.000005875	0.72	0.4177
subject(sequence)	9	0.000122	0.000013594	1.67	0.2285
Error: MS(Error)	9	0.000073276	0.000008142		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.000009724	0.000009724	0.72	0.4196
Error	9	0.000122	0.000013594		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	0.000003796	0.000003796	0.47	0.5119
trt	1	0.000005875	0.000005875	0.72	0.4177
subject(sequence)	9	0.000122	0.000013594	1.67	0.2285
Error: MS(Error)	9	0.000073276	0.000008142		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.000009724	0.000009724	0.72	0.4196
Error	9	0.000122	0.000013594		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	0.000003796	0.000003796	0.47	0.5119
trt	1	0.000005875	0.000005875	0.72	0.4177
subject(sequence)	9	0.000122	0.000013594	1.67	0.2285
Error: MS(Error)	9	0.000073276	0.000008142		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.000009724	0.000009724	0.72	0.4196
Error	9	0.000122	0.000013594		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	0.000003796	0.000003796	0.47	0.5119
trt	1	0.000005875	0.000005875	0.72	0.4177
subject(sequence)	9	0.000122	0.000013594	1.67	0.2285
Error: MS(Error)	9	0.000073276	0.000008142		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: K_{el} (/h) Weight Group: 88-111

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LAMZ LSMEAN		Pr > t
A	0.00800245		0.4177
B	0.00696467		

trt	LAMZ LSMEAN	90% Confidence Limits	
A	0.008002	0.006419	0.009586
B	0.006965	0.005381	0.008548

Least Squares Means for Effect trt

		Difference Between		
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.001038	-0.001202	0.003277

Dependent Variable: LAMZ

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
A - B	0.00103779	0.00122174	0.85	0.4177	-0.00120180	0.00327738

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	11	203 204 304 402 404 407 409 502 505 507 508
sequence	2	AB BA
period	2	1 2
trt	2	A B

Number of Observations Read	22
Number of Observations Used	22

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LAMZHL

R-Square	Coeff Var	Root MSE	LAMZHL Mean
0.574882	99.33196	138.5731	139.5051

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	5649.2726	5649.2726	0.29	0.6007
period	1	25232.1129	25232.1129	1.31	0.2812
trt	1	3972.7356	3972.7356	0.21	0.6600
subject(sequence)	9	198852.1366	22094.6818	1.15	0.4189

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	5649.2726	5649.2726	0.29	0.6007
period	1	23243.5863	23243.5863	1.21	0.2998
trt	1	3972.7356	3972.7356	0.21	0.6600
subject(sequence)	9	198852.1366	22094.6818	1.15	0.4189

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	5649.2726	5649.2726	0.29	0.6007
period	1	23243.5863	23243.5863	1.21	0.2998
trt	1	3972.7356	3972.7356	0.21	0.6600
subject(sequence)	9	198852.1366	22094.6818	1.15	0.4189

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	5649.2726	5649.2726	0.29	0.6007
period	1	23243.5863	23243.5863	1.21	0.2998
trt	1	3972.7356	3972.7356	0.21	0.6600
subject(sequence)	9	198852.1366	22094.6818	1.15	0.4189

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 88-111

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	5649.272565	5649.272565	0.26	0.6253
Error	9	198852	22095		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
*period	1	25232	25232	1.31	0.2812
trt	1	3972.735582	3972.735582	0.21	0.6600
subject(sequence)	9	198852	22095	1.15	0.4189
Error: MS(Error)	9	172823	19203		

* This test assumes one or more other fixed effects are zero.

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	5649.272565	5649.272565	0.26	0.6253
Error	9	198852	22095		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
period	1	23244	23244	1.21	0.2998
trt	1	3972.735582	3972.735582	0.21	0.6600
subject(sequence)	9	198852	22095	1.15	0.4189
Error: MS(Error)	9	172823	19203		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	5649.272565	5649.272565	0.26	0.6253
Error	9	198852	22095		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
period	1	23244	23244	1.21	0.2998
trt	1	3972.735582	3972.735582	0.21	0.6600
subject(sequence)	9	198852	22095	1.15	0.4189
Error: MS(Error)	9	172823	19203		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	5649.272565	5649.272565	0.26	0.6253
Error	9	198852	22095		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
period	1	23244	23244	1.21	0.2998
trt	1	3972.735582	3972.735582	0.21	0.6600
subject(sequence)	9	198852	22095	1.15	0.4189
Error: MS(Error)	9	172823	19203		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: A vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 88-111

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LAMZHL LSMEAN		Pr > t
A	124.548382		0.6600
B	151.536062		

trt	LAMZHL LSMEAN	90% Confidence Limits	
A	124.548382	47.639963	201.456802
B	151.536062	74.627643	228.444482

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-26.987680	-135.752610	81.777250

Dependent Variable: LAMZHL

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
A - B	-26.9876797	59.3334584	-0.45	0.6600	-135.7526097 81.7772502

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	203 204 402 404
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LN_AUCLST

R-Square	Coeff Var	Root MSE	LN_AUCLST Mean
0.443329	5.254932	0.467887	8.903767

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.36557536	0.36557536	1.67	0.2868
trt	1	0.10103184	0.10103184	0.46	0.5456
subject(sequence)	2	0.05642733	0.02821366	0.13	0.8837

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.36557536	0.36557536	1.67	0.2868
trt	1	0.10103184	0.10103184	0.46	0.5456
subject(sequence)	2	0.05642733	0.02821366	0.13	0.8837

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.36557536	0.36557536	1.67	0.2868
trt	1	0.10103184	0.10103184	0.46	0.5456
subject(sequence)	2	0.05642733	0.02821366	0.13	0.8837

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.36557536	0.36557536	1.67	0.2868
trt	1	0.10103184	0.10103184	0.46	0.5456
subject(sequence)	2	0.05642733	0.02821366	0.13	0.8837

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 88-111

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.365575	0.365575	12.96	0.0693
Error	2	0.056427	0.028214		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.101032	0.101032	0.46	0.5456
subject(sequence)	2	0.056427	0.028214	0.13	0.8837
Error: MS(Error)	3	0.656755	0.218918		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.365575	0.365575	12.96	0.0693
Error	2	0.056427	0.028214		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.101032	0.101032	0.46	0.5456
subject(sequence)	2	0.056427	0.028214	0.13	0.8837
Error: MS(Error)	3	0.656755	0.218918		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.365575	0.365575	12.96	0.0693
Error	2	0.056427	0.028214		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.101032	0.101032	0.46	0.5456
subject(sequence)	2	0.056427	0.028214	0.13	0.8837
Error: MS(Error)	3	0.656755	0.218918		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCLST

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.365575	0.365575	12.96	0.0693
Error	2	0.056427	0.028214		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.101032	0.101032	0.46	0.5456
subject(sequence)	2	0.056427	0.028214	0.13	0.8837
Error: MS(Error)	3	0.656755	0.218918		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-t} (h*ng/mL) Weight Group: 88-111

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCLST	LSMEAN	Pr > t
B	8.66796917		0.5456
C	8.89272663		

trt	LN_AUCLST	LSMEAN	90% Confidence Limits	
B	8.667969	8.073303	9.262635	
C	8.892727	8.298060	9.487393	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.224757	-1.003358	0.553843

Dependent Variable: LN_AUCLST

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	0.22475747	0.33084602	0.68	0.5456	-0.55384345 1.00335839

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: $AUC_{0-\infty}$ (h*ng/mL) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	203 204 402 404
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LN_AUCIFO

R-Square	Coeff Var	Root MSE	LN_AUCIFO Mean
0.498012	5.187536	0.468583	9.032871

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.50748249	0.50748249	2.31	0.2258
trt	1	0.06707153	0.06707153	0.31	0.6190
subject(sequence)	2	0.07893896	0.03946948	0.18	0.8439

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.50748249	0.50748249	2.31	0.2258
trt	1	0.06707153	0.06707153	0.31	0.6190
subject(sequence)	2	0.07893896	0.03946948	0.18	0.8439

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.50748249	0.50748249	2.31	0.2258
trt	1	0.06707153	0.06707153	0.31	0.6190
subject(sequence)	2	0.07893896	0.03946948	0.18	0.8439

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.50748249	0.50748249	2.31	0.2258
trt	1	0.06707153	0.06707153	0.31	0.6190
subject(sequence)	2	0.07893896	0.03946948	0.18	0.8439

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 88-111

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.507482	0.507482	12.86	0.0697
Error	2	0.078939	0.039469		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.067072	0.067072	0.31	0.6190
subject(sequence)	2	0.078939	0.039469	0.18	0.8439
Error: MS(Error)	3	0.658711	0.219570		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.507482	0.507482	12.86	0.0697
Error	2	0.078939	0.039469		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.067072	0.067072	0.31	0.6190
subject(sequence)	2	0.078939	0.039469	0.18	0.8439
Error: MS(Error)	3	0.658711	0.219570		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.507482	0.507482	12.86	0.0697
Error	2	0.078939	0.039469		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.067072	0.067072	0.31	0.6190
subject(sequence)	2	0.078939	0.039469	0.18	0.8439
Error: MS(Error)	3	0.658711	0.219570		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_AUCIFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.507482	0.507482	12.86	0.0697
Error	2	0.078939	0.039469		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.067072	0.067072	0.31	0.6190
subject(sequence)	2	0.078939	0.039469	0.18	0.8439
Error: MS(Error)	3	0.658711	0.219570		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: AUC_{0-inf} (h*ng/mL) Weight Group: 88-111

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_AUCIFO	LSMEAN	Pr > t
B	8.79589362		0.6190
C	8.97902135		

trt	LN_AUCIFO	LSMEAN	90% Confidence Limits	
B	8.795894	8.200342	9.391445	
C	8.979021	8.383470	9.574573	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.183128	-0.962888	0.596632

Dependent Variable: LN_AUCIFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	0.18312773	0.33133856	0.55	0.6190	-0.59663231 0.96288777

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: C_{\max} (ng/mL) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	203 204 402 404
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LN_CMAX

R-Square	Coeff Var	Root MSE	LN_CMAX Mean
0.422220	8.993728	0.448513	4.986958

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.09754320	0.09754320	0.48	0.5363
trt	1	0.09487043	0.09487043	0.47	0.5416
subject(sequence)	2	0.24859694	0.12429847	0.62	0.5960

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.09754320	0.09754320	0.48	0.5363
trt	1	0.09487043	0.09487043	0.47	0.5416
subject(sequence)	2	0.24859694	0.12429847	0.62	0.5960

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.09754320	0.09754320	0.48	0.5363
trt	1	0.09487043	0.09487043	0.47	0.5416
subject(sequence)	2	0.24859694	0.12429847	0.62	0.5960

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.09754320	0.09754320	0.48	0.5363
trt	1	0.09487043	0.09487043	0.47	0.5416
subject(sequence)	2	0.24859694	0.12429847	0.62	0.5960

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 88-111

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.097543	0.097543	0.78	0.4691
Error	2	0.248597	0.124298		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.094870	0.094870	0.47	0.5416
subject(sequence)	2	0.248597	0.124298	0.62	0.5960
Error: MS(Error)	3	0.603493	0.201164		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.097543	0.097543	0.78	0.4691
Error	2	0.248597	0.124298		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.094870	0.094870	0.47	0.5416
subject(sequence)	2	0.248597	0.124298	0.62	0.5960
Error: MS(Error)	3	0.603493	0.201164		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.097543	0.097543	0.78	0.4691
Error	2	0.248597	0.124298		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.094870	0.094870	0.47	0.5416
subject(sequence)	2	0.248597	0.124298	0.62	0.5960
Error: MS(Error)	3	0.603493	0.201164		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.097543	0.097543	0.78	0.4691
Error	2	0.248597	0.124298		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.094870	0.094870	0.47	0.5416
subject(sequence)	2	0.248597	0.124298	0.62	0.5960
Error: MS(Error)	3	0.603493	0.201164		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: C_{max} (ng/mL) Weight Group: 88-111

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LN_CMAX LSMEAN		Pr > t
B	4.81430790		0.5416
C	5.03210417		

trt	LN_CMAX LSMEAN	90% Confidence Limits	
B	4.814308	4.244265	5.384351
C	5.032104	4.462061	5.602147

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.217796	-0.964158	0.528566

Dependent Variable: LN_CMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	0.21779627	0.31714689	0.69	0.5416	-0.52856563 0.96415818

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	203 204 402 404
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LN_CLFOW

R-Square	Coeff Var	Root MSE	LN_CLFOW Mean
0.651142	-12.11538	0.468583	-3.867674

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.77546793	0.77546793	3.53	0.1568
trt	1	0.20054600	0.20054600	0.91	0.4097
subject(sequence)	2	0.25347050	0.12673525	0.58	0.6136

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.77546793	0.77546793	3.53	0.1568
trt	1	0.20054600	0.20054600	0.91	0.4097
subject(sequence)	2	0.25347050	0.12673525	0.58	0.6136

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.77546793	0.77546793	3.53	0.1568
trt	1	0.20054600	0.20054600	0.91	0.4097
subject(sequence)	2	0.25347050	0.12673525	0.58	0.6136

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.77546793	0.77546793	3.53	0.1568
trt	1	0.20054600	0.20054600	0.91	0.4097
subject(sequence)	2	0.25347050	0.12673525	0.58	0.6136

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 88-111

The GLM Procedure

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.775468	0.775468	6.12	0.1319
Error	2	0.253471	0.126735		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.200546	0.200546	0.91	0.4097
subject(sequence)	2	0.253471	0.126735	0.58	0.6136
Error: MS(Error)	3	0.658711	0.219570		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.775468	0.775468	6.12	0.1319
Error	2	0.253471	0.126735		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.200546	0.200546	0.91	0.4097
subject(sequence)	2	0.253471	0.126735	0.58	0.6136
Error: MS(Error)	3	0.658711	0.219570		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.775468	0.775468	6.12	0.1319
Error	2	0.253471	0.126735		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.200546	0.200546	0.91	0.4097
subject(sequence)	2	0.253471	0.126735	0.58	0.6136
Error: MS(Error)	3	0.658711	0.219570		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.775468	0.775468	6.12	0.1319
Error	2	0.253471	0.126735		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.200546	0.200546	0.91	0.4097
subject(sequence)	2	0.253471	0.126735	0.58	0.6136
Error: MS(Error)	3	0.658711	0.219570		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F/kg ((L/h)/kg) Weight Group: 88-111

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_CLFOW	LSMEAN	Pr > t
B	-3.52959127		0.4097
C	-3.84625040		

trt	LN_CLFOW	LSMEAN	90% Confidence Limits	
B	-3.529591		-4.125143	-2.934040
C	-3.846250		-4.441802	-3.250699

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.316659	-0.463101	1.096419

Dependent Variable: LN_CLFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.31665913	0.33133856	-0.96	0.4097	-1.09641917 0.46310091

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	203 204 402 404
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LN_CLFO

R-Square	Coeff Var	Root MSE	LN_CLFO Mean
0.544358	58.29234	0.468583	0.803851

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.50748249	0.50748249	2.31	0.2258
trt	1	0.20054600	0.20054600	0.91	0.4097
subject(sequence)	2	0.07893896	0.03946948	0.18	0.8439

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.50748249	0.50748249	2.31	0.2258
trt	1	0.20054600	0.20054600	0.91	0.4097
subject(sequence)	2	0.07893896	0.03946948	0.18	0.8439

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.50748249	0.50748249	2.31	0.2258
trt	1	0.20054600	0.20054600	0.91	0.4097
subject(sequence)	2	0.07893896	0.03946948	0.18	0.8439

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.50748249	0.50748249	2.31	0.2258
trt	1	0.20054600	0.20054600	0.91	0.4097
subject(sequence)	2	0.07893896	0.03946948	0.18	0.8439

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h) Weight Group: 88-111

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.507482	0.507482	12.86	0.0697
Error	2	0.078939	0.039469		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.200546	0.200546	0.91	0.4097
subject(sequence)	2	0.078939	0.039469	0.18	0.8439
Error: MS(Error)	3	0.658711	0.219570		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.507482	0.507482	12.86	0.0697
Error	2	0.078939	0.039469		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.200546	0.200546	0.91	0.4097
subject(sequence)	2	0.078939	0.039469	0.18	0.8439
Error: MS(Error)	3	0.658711	0.219570		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.507482	0.507482	12.86	0.0697
Error	2	0.078939	0.039469		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.200546	0.200546	0.91	0.4097
subject(sequence)	2	0.078939	0.039469	0.18	0.8439
Error: MS(Error)	3	0.658711	0.219570		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_CLFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.507482	0.507482	12.86	0.0697
Error	2	0.078939	0.039469		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.200546	0.200546	0.91	0.4097
subject(sequence)	2	0.078939	0.039469	0.18	0.8439
Error: MS(Error)	3	0.658711	0.219570		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: Cl/F (L/h) Weight Group: 88-111

Least Squares Means

H0:LSMean1=LSMean2			
trt	LN_CLFO	LSMEAN	Pr > t
B	1.10759394		0.4097
C	0.79093481		

trt	LN_CLFO	LSMEAN	90% Confidence Limits	
B	1.107594	0.512042	1.703146	
C	0.790935	0.195383	1.386486	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.316659	-0.463101	1.096419

Dependent Variable: LN_CLFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.31665913	0.33133856	-0.96	0.4097	-1.09641917 0.46310091

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	203 204 402 404
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LN_VZFOW

R-Square	Coeff Var	Root MSE	LN_VZFOW Mean
0.449575	63.64188	0.548837	0.862384

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.16265602	0.16265602	0.54	0.5157
trt	1	0.45894271	0.45894271	1.52	0.3049
subject(sequence)	2	0.11649724	0.05824862	0.19	0.8337

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.16265602	0.16265602	0.54	0.5157
trt	1	0.45894271	0.45894271	1.52	0.3049
subject(sequence)	2	0.11649724	0.05824862	0.19	0.8337

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.16265602	0.16265602	0.54	0.5157
trt	1	0.45894271	0.45894271	1.52	0.3049
subject(sequence)	2	0.11649724	0.05824862	0.19	0.8337

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.16265602	0.16265602	0.54	0.5157
trt	1	0.45894271	0.45894271	1.52	0.3049
subject(sequence)	2	0.11649724	0.05824862	0.19	0.8337

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 88-111

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.162656	0.162656	2.79	0.2367
Error	2	0.116497	0.058249		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.458943	0.458943	1.52	0.3049
subject(sequence)	2	0.116497	0.058249	0.19	0.8337
Error: MS(Error)	3	0.903667	0.301222		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.162656	0.162656	2.79	0.2367
Error	2	0.116497	0.058249		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.458943	0.458943	1.52	0.3049
subject(sequence)	2	0.116497	0.058249	0.19	0.8337
Error: MS(Error)	3	0.903667	0.301222		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.162656	0.162656	2.79	0.2367
Error	2	0.116497	0.058249		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.458943	0.458943	1.52	0.3049
subject(sequence)	2	0.116497	0.058249	0.19	0.8337
Error: MS(Error)	3	0.903667	0.301222		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFOW

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.162656	0.162656	2.79	0.2367
Error	2	0.116497	0.058249		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.458943	0.458943	1.52	0.3049
subject(sequence)	2	0.116497	0.058249	0.19	0.8337
Error: MS(Error)	3	0.903667	0.301222		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: $V_d/F/kg$ (L/kg) Weight Group: 88-111

Least Squares Means

			H0:LSMean1=LSMean2
trt	LN_VZFOW	LSMEAN	Pr > t
B	1.18422404		0.3049
C	0.70519235		

trt	LN_VZFOW	LSMEAN	90% Confidence Limits	
B	1.184224		0.486673	1.881775
C	0.705192		0.007642	1.402743

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.479032	-0.434277	1.392340

Dependent Variable: LN_VZFOW

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.47903169	0.38808644	-1.23	0.3049	-1.39234013 0.43427676

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	203 204 402 404
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LN_VZFO

R-Square	Coeff Var	Root MSE	LN_VZFO Mean
0.393998	9.917712	0.548837	5.533908

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.05526159	0.05526159	0.18	0.6973
trt	1	0.45894271	0.45894271	1.52	0.3049
subject(sequence)	2	0.07332197	0.03666098	0.12	0.8896

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.05526159	0.05526159	0.18	0.6973
trt	1	0.45894271	0.45894271	1.52	0.3049
subject(sequence)	2	0.07332197	0.03666098	0.12	0.8896

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.05526159	0.05526159	0.18	0.6973
trt	1	0.45894271	0.45894271	1.52	0.3049
subject(sequence)	2	0.07332197	0.03666098	0.12	0.8896

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.05526159	0.05526159	0.18	0.6973
trt	1	0.45894271	0.45894271	1.52	0.3049
subject(sequence)	2	0.07332197	0.03666098	0.12	0.8896

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L) Weight Group: 88-111

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.055262	0.055262	1.51	0.3444
Error	2	0.073322	0.036661		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.458943	0.458943	1.52	0.3049
subject(sequence)	2	0.073322	0.036661	0.12	0.8896
Error: MS(Error)	3	0.903667	0.301222		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.055262	0.055262	1.51	0.3444
Error	2	0.073322	0.036661		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.458943	0.458943	1.52	0.3049
subject(sequence)	2	0.073322	0.036661	0.12	0.8896
Error: MS(Error)	3	0.903667	0.301222		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.055262	0.055262	1.51	0.3444
Error	2	0.073322	0.036661		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.458943	0.458943	1.52	0.3049
subject(sequence)	2	0.073322	0.036661	0.12	0.8896
Error: MS(Error)	3	0.903667	0.301222		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LN_VZFO

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.055262	0.055262	1.51	0.3444
Error	2	0.073322	0.036661		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.458943	0.458943	1.52	0.3049
subject(sequence)	2	0.073322	0.036661	0.12	0.8896
Error: MS(Error)	3	0.903667	0.301222		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: V_d/F (L) Weight Group: 88-111

Least Squares Means

			H0:LSMean1=LSMean2	
trt	LN_VZFO	LSMEAN		Pr > t
B	5.82140924			0.3049
C	5.34237756			

trt	LN_VZFO	LSMEAN	90% Confidence Limits	
B	5.821409	5.123858	6.518960	
C	5.342378	4.644827	6.039928	

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.479032	-0.434277	1.392340

Dependent Variable: LN_VZFO

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-0.47903169	0.38808644	-1.23	0.3049	-1.39234013 0.43427676

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	203 204 402 404
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: T_{max} (h) Weight Group: 88-111

The GLM Procedure

Dependent Variable: TMAX

R-Square	Coeff Var	Root MSE	TMAX Mean
0.749116	73.44244	1.038935	1.414625

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.86093704	1.86093704	1.72	0.2806
trt	1	6.51063613	6.51063613	6.03	0.0912
subject(sequence)	2	1.29724633	0.64862317	0.60	0.6033

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.86093704	1.86093704	1.72	0.2806
trt	1	6.51063613	6.51063613	6.03	0.0912
subject(sequence)	2	1.29724633	0.64862317	0.60	0.6033

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.86093704	1.86093704	1.72	0.2806
trt	1	6.51063613	6.51063613	6.03	0.0912
subject(sequence)	2	1.29724633	0.64862317	0.60	0.6033

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.86093704	1.86093704	1.72	0.2806
trt	1	6.51063613	6.51063613	6.03	0.0912
subject(sequence)	2	1.29724633	0.64862317	0.60	0.6033

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: T_{max} (h) Weight Group: 88-111

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1.860937	1.860937	2.87	0.2324
Error	2	1.297246	0.648623		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	6.510636	6.510636	6.03	0.0912
subject(sequence)	2	1.297246	0.648623	0.60	0.6033
Error: MS(Error)	3	3.238158	1.079386		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1.860937	1.860937	2.87	0.2324
Error	2	1.297246	0.648623		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	6.510636	6.510636	6.03	0.0912
subject(sequence)	2	1.297246	0.648623	0.60	0.6033
Error: MS(Error)	3	3.238158	1.079386		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1.860937	1.860937	2.87	0.2324
Error	2	1.297246	0.648623		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	6.510636	6.510636	6.03	0.0912
subject(sequence)	2	1.297246	0.648623	0.60	0.6033
Error: MS(Error)	3	3.238158	1.079386		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: TMAX

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1.860937	1.860937	2.87	0.2324
Error	2	1.297246	0.648623		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	6.510636	6.510636	6.03	0.0912
subject(sequence)	2	1.297246	0.648623	0.60	0.6033
Error: MS(Error)	3	3.238158	1.079386		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: T_{\max} (h) Weight Group: 88-111

Least Squares Means

		H0:LSMean1=LSMean2	
trt	TMAX LSMEAN		Pr > t
B	0.79095833		0.0912
C	2.59520833		

trt	TMAX LSMEAN	90% Confidence Limits	
B	0.790958	-0.529488	2.111405
C	2.595208	1.274762	3.915655

Least Squares Means for Effect trt

		Difference Between		
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-1.804250	-3.533120	-0.075380

Dependent Variable: TMAX

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	1.80425000	0.73463805	2.46	0.09120	0.7537968 3.53312032

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	203 204 402 404
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LAMZ

R-Square	Coeff Var	Root MSE	LAMZ Mean
0.779248	18.43795	0.001672	0.009066

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.00002132	0.00002132	7.63	0.0700
trt	1	0.00000528	0.00000528	1.89	0.2629
subject(sequence)	2	0.00000299	0.00000150	0.54	0.6325

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.00002132	0.00002132	7.63	0.0700
trt	1	0.00000528	0.00000528	1.89	0.2629
subject(sequence)	2	0.00000299	0.00000150	0.54	0.6325

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.00002132	0.00002132	7.63	0.0700
trt	1	0.00000528	0.00000528	1.89	0.2629
subject(sequence)	2	0.00000299	0.00000150	0.54	0.6325

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.00002132	0.00002132	7.63	0.0700
trt	1	0.00000528	0.00000528	1.89	0.2629
subject(sequence)	2	0.00000299	0.00000150	0.54	0.6325

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h) Weight Group: 88-111

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	0.000021316	0.000021316	14.24	0.0636
Error	2	0.000002993	0.000001497		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	0.000005281	0.000005281	1.89	0.2629
subject(sequence)	2	0.000002993	0.000001497	0.54	0.6325
Error: MS(Error)	3	0.000008382	0.000002794		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	0.000021316	0.000021316	14.24	0.0636
Error	2	0.000002993	0.000001497		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	0.000005281	0.000005281	1.89	0.2629
subject(sequence)	2	0.000002993	0.000001497	0.54	0.6325
Error: MS(Error)	3	0.000008382	0.000002794		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	0.000021316	0.000021316	14.24	0.0636
Error	2	0.000002993	0.000001497		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	0.000005281	0.000005281	1.89	0.2629
subject(sequence)	2	0.000002993	0.000001497	0.54	0.6325
Error: MS(Error)	3	0.000008382	0.000002794		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZ

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	0.000021316	0.000021316	14.24	0.0636
Error	2	0.000002993	0.000001497		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	0.000005281	0.000005281	1.89	0.2629
subject(sequence)	2	0.000002993	0.000001497	0.54	0.6325
Error: MS(Error)	3	0.000008382	0.000002794		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: K_{el} (/h) Weight Group: 88-111

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LAMZ LSMEAN		Pr > t
B	0.00919589		0.2629
C	0.01082078		

trt	LAMZ LSMEAN	90% Confidence Limits	
B	0.009196	0.007071	0.011320
C	0.010821	0.008696	0.012945

Least Squares Means for Effect trt

		Difference Between		
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.001625	-0.004407	0.001157

Dependent Variable: LAMZ

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits	
C - B	0.00162489	0.00118198	1.37	0.2629	-0.00115673	0.00440651

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 88-111

The GLM Procedure

Class Level Information		
Class	Levels	Values
subject	4	203 204 402 404
sequence	2	ABC BAC
trt	2	B C

Number of Observations Read	8
Number of Observations Used	8

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 88-111

The GLM Procedure

Dependent Variable: LAMZHL

R-Square	Coeff Var	Root MSE	LAMZHL Mean
0.717423	18.29114	14.72222	80.48823

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1233.320675	1233.320675	5.69	0.0971
trt	1	270.127861	270.127861	1.25	0.3456
subject(sequence)	2	147.396875	73.698437	0.34	0.7360

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1233.320675	1233.320675	5.69	0.0971
trt	1	270.127861	270.127861	1.25	0.3456
subject(sequence)	2	147.396875	73.698437	0.34	0.7360

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1233.320675	1233.320675	5.69	0.0971
trt	1	270.127861	270.127861	1.25	0.3456
subject(sequence)	2	147.396875	73.698437	0.34	0.7360

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1233.320675	1233.320675	5.69	0.0971
trt	1	270.127861	270.127861	1.25	0.3456
subject(sequence)	2	147.396875	73.698437	0.34	0.7360

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 88-111

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type I SS	Mean Square	F Value	Pr > F
sequence	1	1233.320675	1233.320675	16.73	0.0549
Error	2	147.396875	73.698437		
Error: MS(subject(sequence))					

Source	DF	Type I SS	Mean Square	F Value	Pr > F
trt	1	270.127861	270.127861	1.25	0.3456
subject(sequence)	2	147.396875	73.698437	0.34	0.7360
Error: MS(Error)	3	650.230939	216.743646		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type II SS	Mean Square	F Value	Pr > F
sequence	1	1233.320675	1233.320675	16.73	0.0549
Error	2	147.396875	73.698437		
Error: MS(subject(sequence))					

Source	DF	Type II SS	Mean Square	F Value	Pr > F
trt	1	270.127861	270.127861	1.25	0.3456
subject(sequence)	2	147.396875	73.698437	0.34	0.7360
Error: MS(Error)	3	650.230939	216.743646		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 88-111

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type III SS	Mean Square	F Value	Pr > F
sequence	1	1233.320675	1233.320675	16.73	0.0549
Error	2	147.396875	73.698437		
Error: MS(subject(sequence))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
trt	1	270.127861	270.127861	1.25	0.3456
subject(sequence)	2	147.396875	73.698437	0.34	0.7360
Error: MS(Error)	3	650.230939	216.743646		

Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: LAMZHL

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
sequence	1	1233.320675	1233.320675	16.73	0.0549
Error	2	147.396875	73.698437		
Error: MS(subject(sequence))					

Source	DF	Type IV SS	Mean Square	F Value	Pr > F
trt	1	270.127861	270.127861	1.25	0.3456
subject(sequence)	2	147.396875	73.698437	0.34	0.7360
Error: MS(Error)	3	650.230939	216.743646		

Listing 16.1.9-8 ANOVA for Treatment Comparison of Diazepam for Weight Group 88-111 kg - PK Population

Comparison: C vs B

Dependent Variable: $T_{1/2\text{el}}$ (h) Weight Group: 88-111

Least Squares Means

		H0:LSMean1=LSMean2	
trt	LAMZHL LSMEAN		Pr > t
B	79.1305102		0.3456
C	67.5088094		

trt	LAMZHL LSMEAN	90% Confidence Limits	
B	79.130510	60.419140	97.841880
C	67.508809	48.797439	86.220179

Least Squares Means for Effect trt				
Difference Between				
i	j	Means	90% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	11.621701	-12.877233	36.120635

Dependent Variable: LAMZHL

Parameter	Estimate	Standard Error	t Value	Pr > t	90% Confidence Limits
C - B	-11.6217008	10.4101788	-1.12	0.3456	-36.1206350 12.8772334