Statistical Analysis Plan I6T-MC-AMAQ

A Safety, Tolerability, and Pharmacokinetic Study of 1- and 2-mL Injections of LY3074828 Solution Using Investigational Pre-filled Syringes and Investigational Autoinjectors in Healthy Subjects

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STATISTICAL ANALYSIS PLAN

A Safety, Tolerability, and Pharmacokinetic Study of 1- and 2-mL Injections of LY3074828 Solution Using Investigational Pre-filled Syringes and Investigational Autoinjectors in Healthy Subjects

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2. ABBREVIATIONS

Abbreviations pertain to the Statistical Analysis Plan (SAP) only (not the tables, figures and listings [TFLs]).

ADA	Anti-drug antibody
AE	Adverse event
AI	Autoinjector
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
AUC	Area under the concentration versus time curve
$AUC(0-\infty)$	Area under the concentration versus time curve from zero to infinity
$AUC(0-t_{last})$	Area under the concentration versus time curve from time zero to time t, where t is the last time point with a measurable concentration
$\%AUC(t_{last}-\infty)$	Percentage of $AUC(0-\infty)$ extrapolated
BQL	Below the quantifiable lower limit of the assay
C_{last}	Last quantifiable drug concentration
C_{max}	Maximum observed drug concentration
CI	Confidence interval
CL/F	Apparent total body clearance of drug calculated after extra-vascular administration
CRF	Case Report Form
CRU	Clinical Research Unit
CSR	Clinical Study Report
CV	Coefficient of variation
EC	Early Clinical
ECG	Electrocardiogram
e.g.	For example (Latin: *exempli gratia*)
ICH	International Council on Harmonisation
LLOQ	Lower limit of quantification
MedDRA	Medical Dictionary for Regulatory Activities
MRE	Magnetic resonance elastography
PFS	Pre-filled syringe
PK	Pharmacokinetic

SAP	Statistical Analysis Plan
SC	Subcutaneous
SD	Standard deviation
SF-MPQ	Short Form-McGill Pain Questionnaire
TBL	Total bilirubin
TFLs	Tables, Figures, and Listings
$t_{1/2}$	Half-life associated with the terminal rate constant (λ_z) in non-compartmental analysis
t_{max}	Time of maximum observed drug concentration
ULN	Upper limit of normal
VAS	Visual analog scale
V_{ss}/F	Apparent volume of distribution at steady state after extra vascular administration
V_z/F	Apparent volume of distribution during the terminal phase after extra-vascular administration
WHO	World Health Organization

3. INTRODUCTION

This SAP has been developed after review of the Clinical Study Protocol (final version dated 13 December 2017) and Protocol Amendment (a) (final version dated 12 March 2018).

This SAP describes the planned analysis of the safety, tolerability and pharmacokinetic (PK) data from this study. A detailed description of the planned TFLs to be presented in the clinical study report (CSR) is provided in the accompanying TFL shell document.

The intent of this document is to provide guidance for the statistical and PK analyses of data. In general, the analyses are based on information from the protocol, unless they have been modified by agreement between Eli Lilly and Company and Covance Early Clinical (EC) Biometrics. A limited amount of information concerning this study (e.g., objectives, study design) is given to help the reader's interpretation. This SAP must be signed off prior to first subject administration for this study. When the SAP and TFL shells are agreed upon and finalized, they will serve as the template for this study's CSR.

This SAP supersedes the statistical considerations identified in the protocol; where considerations are substantially different, they will be so identified. If additional analyses are required to supplement the planned analyses described in this SAP, they may be performed and will be identified in the CSR. Any substantial deviations from this SAP will be agreed upon between Eli Lilly and Company and Covance EC Biometrics and identified in the CSR. Any minor deviations from the TFLs may not be documented in the CSR.

This SAP is written with consideration of the recommendations outlined in the International Council on Harmonisation (ICH) E9 Guideline entitled Guidance for Industry: Statistical Principles for Clinical Trials[1] and the ICH E3 Guideline entitled Guidance for Industry: Structure and Content of Clinical Study Reports[2].

4. STUDY OBJECTIVES

4.1 Primary Objectives

Part A

- To evaluate the PK of LY3074828 solution formulation after administration of 250-mg doses using 2 x 1-mL and 1 x 2-mL pre-filled syringe (PFS) injections in healthy subjects.

- To assess the safety and tolerability of, and pain associated with, LY3074828 PFS administrations in healthy subjects.

Part B

- To compare the safety and tolerability of, and pain associated with, LY3074828 solution formulation after administration of 125- and 250-mg doses using 1-mL autoinjector (AI)

and 2-mL AI subcutaneous (SC) injections with different injection speeds (slow and fast) in healthy subjects.

5. STUDY DESIGN

Study I6T-MC-AMAQ (AMAQ) is a single-center, randomized, parallel-treatment, open-label, Phase 1 single-dose study of LY3074828 solution formulation in healthy subjects. In Part A, PK, safety and tolerability of, and pain associated with, SC doses administered using 1- and 2-mL PFS injections will be evaluated. In Part B, safety and tolerability of, and pain associated with, single AI injections of 1- and 2-mL that will be administered with 2 different injection speeds will be evaluated.

A total of approximately 72 subjects (approximately 36 subjects per study Parts A and B) who fulfil the eligibility criteria will be randomized to 1 of 2 dosing regimen arms within their assigned study part, with 18 subjects randomized to each arm in order to ensure completion of 16 subjects in each:

Part A
- Reference: 250 mg LY3074828 solution formulation, 2 x 1-mL 125-mg/mL PFS injections using an investigational PFS targeting 5- to 10-second injection time for each injection

- Test 1: 250 mg LY3074828 solution formulation, 1 x 2-mL 125-mg/mL PFS injection using an investigational PFS targeting 5- to 15-second injection time

Part B
- Tests 2 and 3: 250 mg LY3074828 solution formulation, 1 x 2-mL 125-mg/mL AI slow injection (Test 2; targeting approximately 13-second injection time) and fast injection (Test 3; targeting approximately 5-second injection time) using an investigational 2-mL AI

- Tests 4 and 5: 125 mg LY3074828 solution formulation, 1 x 1-mL 125 mg/mL AI slow injection (Test 4; targeting approximately 7-second injection time) and fast injection (Test 5; targeting approximately 4.5-second injection time) using an investigational 1-mL AI

For Part A, subjects will report to the clinical research unit (CRU) on Day -1 and will remain at the CRU until the scheduled procedures have been completed on Day 2. After randomization to either a 2 x 1-mL or a 1 x 2-mL 125-mg/mL PFS dose regimen, study drug will be administered by investigative site staff by SC injection in the abdomen in the morning of Day 1 after an overnight fast.

For Part B, subjects will report to the CRU on Day -1 and will remain at the CRU until the scheduled procedures have been completed on Day 3. Subjects will be randomized to receive, on Days 1 and 2, either a 1 x 1-mL or a 1 x 2-mL 125-mg/mL AI dose regimen. The allocated AI dose regimen will be self-administered by slow and fast SC injection(s) on consecutive days (sequence randomized) in the abdomen after an overnight fast.

Safety and tolerability will be explored by clinical laboratory tests, vital sign measurements, 12-lead electrocardiograms (ECGs), recording of adverse events (AEs) and product complaints, physical examinations/medical assessments, immunogenicity, and injection-site assessments. Pain assessments will be made using the Short Form McGill Pain Questionnaire (SF-MPQ), which includes a subject-assessed injection-site pain visual analog scale (VAS).

6. TREATMENTS

The following is a list of the study treatment abbreviations that will be used in the TFLs.

Part	Study Treatment Name	Abbreviation	Treatment order in TFL
A	250 mg LY3074828 PFS (2 x 1 mL)	Reference	1
	250 mg LY3074828 PFS (1 x 2 mL)	Test 1	2
B	250 mg LY3074828 AI (1 x 2 mL) [Slow]	Test 2	3
	250 mg LY3074828 AI (1 x 2 mL) [Fast]	Test 3	4
	125 mg LY3074828 AI (1 x 1 mL) [Slow]	Test 4	5
	125 mg LY3074828 AI (1 x 1 mL) [Fast]	Test 5	6

7. SAMPLE SIZE JUSTIFICATION

A total of approximately 72 subjects (approximately 36 subjects per study Parts A and B) who fulfil the eligibility criteria will be randomized to 1 of 2 dosing regimen arms within their assigned study part, with 18 subjects randomized to each arm in order to ensure completion of 16 subjects in each. The estimated total variability (coefficient of variation) in the area under the concentration-time curve (AUC) from time zero to infinity AUC($0-\infty$), AUC from time zero to time t, where t is the last sample with a measurable concentration (AUC[$0-t_{last}$]), and maximum observed drug concentration (C_{max}) was 49%, 49%, and 23%, respectively, in Study AMAA following a single SC dose of 120 mg LY3074828. The coefficient of variation of 49% was used for precision estimates and is assumed for all dosing regimen arms. A sample size of 64 subjects will provide a precision, in log scale, of approximately 0.28 for the geometric means ratio in AUC($0-\infty$), AUC($0-t_{last}$), and C_{max} of 1- to 2-mL solution formulation injection. That is, there is a 90% probability that the half-length of the 90% confidence interval (CI) of the geometric means ratio in log scale is not larger than 0.28. Subjects who are randomized but not administered treatment, or subjects that are administered treatment but do not have PK and anti-drug antibody (ADA) samples collected up to and including Day 57, may be replaced (maximum of 4 per arm per study part) to ensure that approximately 16 subjects from each dosing regimen arm complete the study.

8. DEFINITION OF ANALYSIS POPULATIONS

The "Safety" population will consist of all subjects who received a dose of LY3074828 whether or not they completed all protocol requirements.

The "Pharmacokinetic" population will consist of all randomized subjects who received at least one dose of LY3074828 and have evaluable PK data in Part A.

All protocol deviations that occur during the study will be considered for their severity/impact and will be taken into consideration when subjects are assigned to analysis populations.

9. STATISTICAL METHODOLOGY

9.1 General

Data listings will be provided for all data that is databased. Summary statistics and statistical analysis will only be presented for data where detailed in this SAP. For continuous data, summary statistics will include the arithmetic mean, arithmetic standard deviation (SD), median, minimum, maximum, and N. For log-normal data (e.g. the PK parameters: AUCs and C_{max}) the geometric mean and geometric coefficient of variation (CV%) will also be presented. For categorical data, frequency count and percentages will be presented. Data listings will be provided for all subjects up to the point of withdrawal, with any subjects excluded from the relevant population highlighted. Summary statistics and statistical analyses will generally only be performed for subjects included in the relevant analysis population. For the calculation of summary statistics and statistical analysis, unrounded data will be used.

Mean change from baseline is the mean of all individual subjects' change from baseline values. Each individual change from baseline will be calculated by subtracting the individual subject's baseline value from the value at the timepoint. The individual subject's change from baseline values will be used to calculate the mean change from baseline using a SAS procedure such as Proc Univariate.

Data analysis will be performed using SAS® Version 9.4 or greater.

9.2   Demographics and Subject Disposition

Subject disposition will be listed. The demographic variables age, sex, race, ethnicity, body weight, height and body mass index will be summarized and listed. All other demographic variables will be listed only.

9.3   Pharmacokinetic Assessment

9.3.1   Pharmacokinetic Analysis

The PK parameter estimates will be determined for Part A using non-compartmental procedures in a validated software program (Phoenix WinNonlin Version 6.4 or later). Samples from Part B

will be stored and will only be sent for bioanalysis at a later date based on immunogenicity or safety results from Part B of the study.

Serum concentrations of LY3074828 will be used to determine the following PK parameters, when possible:

Parameter	Units	Definition
AUC(0-t_{last})	day*µg/mL	area under the concentration versus time curve from time zero to time t, where t is the last time point with a measurable concentration
AUC(0-∞)	day*µg/mL	area under the concentration versus time curve from time zero to infinity
%AUC(t_{last}-∞)	%	percentage of AUC(0-∞) extrapolated
C_{max}	µg/mL	maximum observed drug concentration
t_{max}	day	time of maximum observed drug concentration
$t_{1/2}$	day	half-life associated with the terminal rate constant (λz) in non-compartmental analysis
CL/F	L/day	apparent total body clearance of drug calculated after extra-vascular administration
V_Z/F	L	apparent volume of distribution during the terminal phase after extra-vascular administration
V_{SS}/F	L	apparent volume of distribution at steady state after extra-vascular administration

Additional PK parameters may be calculated, as appropriate. The software and version used for the final analyses will be specified in the CSR. Any exceptions or special handling of data will be clearly documented within the final study report.

Formatting of tables, figures and abbreviations will follow the Eli Lilly Global PK/PD/TS Tool: NON-COMPARTMENTAL PHARMACOKINETIC STYLE GUIDE. The version of the tool effective at the time of PK analysis will be followed.

General PK Parameter Rules

- Actual sampling times will be used in the final analyses of individual PK parameters, except for non-bolus pre-dose sampling times which will be set to zero.

- C_{max} and t_{max} will be reported from observed values. If C_{max} occurs at more than one time point, t_{max} will be assigned to the first occurrence of C_{max}.

- AUC parameters will be calculated using a combination of the linear and logarithmic trapezoidal methods (linear-log trapezoidal rule). The linear trapezoidal method will be applied up to t_{max} and then the logarithmic trapezoidal method will be used after t_{max}. The minimum requirement for the calculation of AUC will be the inclusion of at least three

consecutive concentrations above the lower limit of quantification (LLOQ), with at least one of these concentrations following C_{max}.

- AUC(0-∞) values where the percentage of the total area extrapolated is more than 20% will be flagged. Any AUC(0-∞) value excluded from summary statistics will be noted in the footnote of the summary table.

- Half-life ($t_{1/2}$) will be calculated, when appropriate, based on the apparent terminal log-linear portion of the concentration-time curve. The start of the terminal elimination phase for each subject will be defined by visual inspection and generally will be the first point at which there is no systematic deviation from the log-linear decline in serum concentrations. $t_{1/2}$ will only be calculated when a reliable estimate for this parameter can be obtained comprising of at least 3 data points. If $t_{1/2}$ is estimated over a time window of less than 2 half-lives, the values will be flagged in the data listings. Any $t_{1/2}$ value excluded from summary statistics will be documented in the footnote of the summary table.

- A uniform weighting scheme will be used in the regression analysis of the terminal log-linear portion of the concentration-time curve.

- The parameters based on the observed last quantifiable drug concentration (C_{last}) will be reported.

Individual PK Parameter Rules

- Only quantifiable concentrations will be used to calculate PK parameters with the exception of special handling of certain concentrations reported below the lower limit of quantitation (BQL). Serum concentrations reported as BQL will be set to a value of zero when all of the following conditions are met:

    - The compound is non-endogenous.

    - The samples are from the initial dose period for a subject or from a subsequent dose period following a suitable wash-out period.

    - The time points occur before the first quantifiable concentration.

- All other BQL concentrations that do not meet the above criteria will be set to missing.

- Also, where two or more consecutive concentrations are BQL towards the end of a profile, the profile will be deemed to have terminated and therefore any further quantifiable concentrations will be set to missing for the calculation of the PK parameters unless it is considered to be a true characteristic of the profile of the drug.

Individual Concentration vs. Time Profiles

- Individual concentrations will be plotted utilizing actual sampling times.

- The terminal point selections will be indicated on a semi-logarithmic plot.

Average Concentration vs. Time Profiles

- The average concentration profiles will be graphed using scheduled (nominal) sampling times.

- The average concentration profiles will be graphed using arithmetic average concentrations.

- The pre-dose average concentration for single-dose data from non-endogenous compounds will be set to zero. Otherwise, only quantifiable concentrations will be used to calculate average concentrations.

- Concentrations at a sampling time exceeding the sampling time window specified in the protocol, or ± 10%, will be excluded from the average concentration profiles.

- Concentrations excluded from the mean calculation will be documented in the final study report.

- A concentration average will be plotted for a given sampling time only if 2/3 of the individual data at the time point have quantifiable measurements that are within the sampling time window specified in the protocol or ± 10%. An average concentration estimated with less than 2/3 but more than 3 data points may be displayed on the mean concentration plot if determined to be appropriate and will be documented within the final study report.

Treatment of Outliers during Pharmacokinetic Analysis

Application of this procedure to all PK analyses is not a requirement. Rather, this procedure provides justification for exclusion of data when scientifically appropriate. This procedure describes the methodology for identifying an individual value as an outlier for potential exclusion, but does not require that the value be excluded from analysis. The following methodology will not be used to exclude complete profiles from analysis.

Data within an Individual Profile

A value within an individual profile may be excluded from analysis if any of the following criteria are met:

- For PK profiles during single dosing of non-endogenous compounds, the concentration in a pre-dose sample is quantifiable.

- For any questionable datum that does not satisfy the above criteria, the profile will be evaluated and results reported with and without the suspected datum.

Data between Individual Profiles

1. If n<6, then the dataset is too small to conduct a reliable range test. Data will be analyzed with and without the atypical value, and both sets of results will be reported.

2. If n≥6, then an objective outlier test will be used to compare the atypical value to other values included in that calculation:

    a. Transform all values in the calculation to the logarithmic domain.

    b. Find the most extreme value from the arithmetic mean of the log transformed values and exclude that value from the dataset.

    c. Calculate the lower and upper bounds of the range defined by the arithmetic mean ±3*SD of the remaining log-transformed values.

    d. If the extreme value is within the range of arithmetic mean ±3*SD, then it is not an outlier and will be retained in the dataset.

    e. If the extreme value is outside the range of arithmetic mean ±3*SD, then it is an outlier and will be excluded from analysis.

If the remaining dataset contains another atypical datum suspected to be an outlier and $n \geq 6$ following the exclusion, then repeat step 2 above. This evaluation may be repeated as many times as necessary, excluding only one suspected outlier in each iteration, until all data remaining in the dataset fall within the range of arithmetic mean ±3*SD of the log-transformed values.

Reporting of Excluded Values

Individual values excluded as outliers will be documented in the final report. Approval of the final report will connote approval of the exclusion.

9.3.2 Pharmacokinetic Statistical Methodology

For Part A, the AUC(0-∞), AUC(0-t_{last}), and C_{max} will be log-transformed and analyzed using a linear fixed-effects model. The model will include dosing regimen arm as a fixed effect. The dosing regimen differences between the Test 1 arm and the Reference arm will be back-transformed to present the ratios of geometric least squares means and the corresponding 90% CI.

Example SAS code:

```
proc mixed data=xxx;
    by parameter;
    class arm;
    model log_pk = arm / residual;
    lsmeans arm / alpha=0.1 cl pdiff;
    ods output lsmeans=lsmeans;
    ods output diffs=diffs;
```

```
run;
```

The t_{max} of LY3074828 between the 1 x 2-mL PFS (Test 1) and the 2 x 1-mL PFS (Reference) will be analyzed using a Wilcoxon rank sum test for Part A. Estimates of the median difference, 90% CIs, and p-values from the Wilcoxon rank sum test will be calculated.

Additional PK analyses may be conducted for Part A if deemed appropriate.

9.4   Safety and Tolerability Assessments

9.4.1   Adverse events

Where changes in severity are recorded in the Case Report Form (CRF), each separate severity of the AE will be reported in the listings, only the most severe will be used in the summary tables. A pre-existing condition is defined as an AE that starts before the subject has provided written informed consent and is ongoing at consent. A non-treatment emergent AE is defined as an AE which starts after informed consent but prior to dosing. A treatment-emergent AE is defined as an AE which occurs postdose or which is present prior to dosing and becomes more severe postdose.

All AEs will be listed. Treatment-emergent AEs will be summarized by treatment, severity and relationship to the study drug. The frequency (the number of AEs, the number of subjects experiencing an AE and the percentage of subjects experiencing an AE) of treatment-emergent AEs will be summarized by treatment, Medical Dictionary for Regulatory Activities (MedDRA) version 20.1 system organ class and preferred term. The summary and frequency AE tables will be presented for all causalities and those considered related to the study drug. Any serious AEs will be tabulated.

9.4.2   Concomitant medication

Concomitant medication will be coded using the WHO drug dictionary (Version September 2017). Concomitant medication will be listed.

9.4.3   Clinical laboratory parameters

All clinical chemistry and hematology data will be summarized by parameter and treatment, and listed. Urinalysis data will be listed. Additionally clinical chemistry, hematology and urinalysis data outside the reference ranges will be listed.

Values for any clinical chemistry, hematology and urinalysis values outside the reference ranges will be flagged on the individual subject data listings.

9.4.4   Vital signs

Vital signs data will be summarized by treatment together with changes from baseline, where baseline is defined as Day 1 predose.

Furthermore, values for individual subjects will be listed.

9.4.5   Electrocardiogram (ECG)

ECGs will be performed for safety monitoring purposes only and will not be presented.

9.4.6   Hepatic Monitoring

If a subject experiences elevated alanine aminotransferase (ALT) $\geq 3\times$ upper limit of normal (ULN), alkaline phosphatase (ALP) $\geq 2\times$ ULN, or elevated total bilirubin (TBL) $\geq 2\times$ ULN, liver tests will be performed to confirm the abnormality.

The subjects' liver disease history and associated person liver disease history data will be listed. Any concomitant medication of acetaminophen/paracetamol will be listed. Results from any hepatic monitoring procedures, such as a magnetic resonance elastography (MRE) scan, and a biopsy assessment will be listed, if performed.

Hepatic risk factor assessment data will be listed. Liver related signs and symptoms data will be summarized by treatment and listed. Alcohol and recreational drug use data will also be listed.

All hepatic chemistry, hematology, coagulation, and serology data will be listed. Values outside the reference ranges will be flagged on the individual subject data listings.

9.4.7   Injection Site Assessment

Injection site assessment data (erythema, induration, categorical pain, pruritus and edema) will be listed and summarized in frequency tables. Whether bleeding occurred will also be listed.

9.4.8   Pain Assessment

Pain will be assessed by the SF-MPQ and will be quantified using the 100-mm validated VAS where 0 mm represents "no pain" and 100 mm represents "worst possible pain". Assessments will be performed at 0, 15, 30, 60, 120, and 240 minutes post injection; however, the primary endpoint will be the 0-hour assessment.

The data will be summarized by treatment and timepoint and listed for individual subjects. Individual profiles will be presented over time. Furthermore, scatter plots of the 0, 15 and 30 minutes post injection pain scores will be presented by treatment.

In Part A, a linear fixed-effects model will be used to analyze the 0-hour (post-injection) pain VAS score and SF-MPQ total score. The model will include treatment (Reference or Test 1) as a fixed effect. The least squares means and differences in least squares means (between Test 1 and Reference) will be presented along with the corresponding 90% CI. Similar SAS code to the PK statistical analysis will be used.

The distribution of the data will be explored prior to analysis to determine whether data transformation is required. It is possible that the pain scores will be 0 so if the distribution of the data implies that a log-transformation is required then the score may be updated to log(VAS+1) to allow for the inclusion of the 0 values in the analysis.

A similar model will be used to analyze the 0-hour (post-injection) pain VAS score and SF-MPQ total score in Part B.

The following comparisons will be performed in Part B:

- Test 2 versus Test 3 (slow versus fast injection for 2-mL AI)

- Test 4 versus Test 5 (slow versus fast injection for 1-mL AI)

9.4.9 Duration of Injection

The duration of the injection (measured in seconds) will be summarized by treatment, and listed.

9.4.10 Autoinjector Use Assessment Questionnaire (Part B only)

The AI use assessment questionnaire data will be summarized in a frequency table by treatment, and listed.

9.4.11 Immunogenicity

Immunogenicity data will be listed and frequency tables will be presented. The frequency of treatment-emergent ADAs will also be calculated. Treatment-emergent ADAs are those that are induced or boosted by exposure to study drug, with a 4-fold increase in titer compared to baseline if ADAs were detected at baseline or a titer 2-fold greater than the minimum required dilution (1:10) if no ADAs were detected at baseline.

To show the association of treatment-emergent ADAs with AEs, the frequency of treatment-emergent ADAs will be presented by MedDRA preferred term. Relationship between the presence of antibodies and the PK parameters of LY3074828 may be assessed graphically.

9.4.12 Other assessments

All other safety assessments not detailed in this section will be listed but not summarized or statistically analyzed.

9.4.13 Safety and Tolerability Statistical Methodology

No inferential statistical analyses are planned.

10.   INTERIM ANALYSES

No interim statistical analyses are planned.

11.   CHANGES FROM THE PROTOCOL SPECIFIED STATISTICAL ANALYSES

There were no changes from the protocol specified statistical analyses.

12.   REFERENCES

1. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH Harmonized Tripartite Guideline, Statistical Principles for Clinical Trials (E9), 5 February 1998.

2. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH Harmonized Tripartite Guideline, Structure and Content of Clinical Study Reports (E3), 30 November 1995.

13.   DATA PRESENTATION

13.1   Derived Parameters

Individual derived parameters (e.g. PK parameters) and appropriate summary statistics will be reported to three significant figures. Observed concentration data, e.g. C_{max}, should be reported as received. Observed time data, e.g. t_{max}, should be reported as received. N and percentage values should be reported as whole numbers. Median values should be treated as an observed parameter and reported to the same number of decimal places as minimum and maximum values.

13.2   Missing Data

Missing data will not be displayed in listings.

13.3   Insufficient Data for Presentation

Some of the TFLs may not have sufficient numbers of subjects or data for presentation. If this occurs, the blank TFL shell will be presented with a message printed in the centre of the table, such as, "No serious adverse events occurred for this study."

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