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STATISTICAL ANALYSIS PLAN

Version 1.0, dated 2018-09-03


Study: VF-BAQ10/2018

Bioavailability Study of COQUN ORAL FORMULATION
(CoQ10) administered in Healthy Adults (CoQ10-01)

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LIST OF ABBREVIATIONS AND KEY TERMS

Abbreviations

Abbreviations	Description of abbreviations
AE	Adverse Events
AST	Aspartate aminotransferase/glutamic oxaloacetic transaminase/GOT
AUC	Area under the concentration-time curve
AUC _t	Area under the serum concentration versus time curve to the last measurable concentration (t)
AUC _∞	Area under the serum concentration versus time curve to infinity
C _{max}	Maximum measured serum concentration
C _{min}	Concentration at the end of a dosing interval
CFR	Code of Federal Regulations
°C	Degrees Celsius
CRO	Contract Research Organization
CSR	Clinical Study Report
CRF	Case Report Form
DRM	Data Review Meeting
DRR	Data Review Report
e.g.	Exempligratia, for example
EOS	End Of Study
GCP	Good Clinical Practice
ICH	International Conference on Harmonization
i.e.	Id est, that is
IEC	Independent Ethics Committee
IP	Investigational Product
IRB	Institutional Review Board
ITT	Intention-to-treat
kg	Kilogram
MedDRA	Medical Dictionary or Regulatory Activities
mg	Milligram
ug/ml	Microgram/Milliliter
PD	Pharmacodynamic
PK	Pharmacokinetic
QA	Quality assurance
QC	Quality control
PP	Per Protocol
PK	Pharmacokinetics
SAE	Serious Adverse Event
SAS	Statistical Analysis System (SAS®)
SD	Standard Deviation
SOP	Standard operating procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
t _{1/2}	Apparent terminal elimination half-life
t _{max}	Time of the maximum measured serum concentration
TLF	Table Listing Figure
TMF	Trial Master File

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2. STUDY OBJECTIVE(S) AND DESIGN

2.1 Study Objectives

Primary objective

The primary objective of this study is to evaluate the best dosage between 100mg OD or 100mg BID for COQUN ORAL FORMULATION in order to reach a level of plasma concentration which might assure its antioxidant effect if taken on a regular basis.

Secondary Objectives

Secondary objectives of this study are:

- To evaluate the safety and tolerability COQUN ORAL FORMULATION following single dose of 100mg
- To evaluate the safety and tolerability of COQUN ORAL FORMULATION during the 1 month daily dose

2.2 Overall Study Design

This is an interventional, single-center, single- and multi-dose bioavailability study of COQUN ORAL FORMULATION in healthy adults.

The study will include 24 healthy subjects who will test the CoQ10 formulation. All 24 subjects will test a single dose of 100mg CoQ10 in 1 day to assess bioavailability, which will be followed by a one-week wash-out period and then by a 4-week period of continuous administration of COQUN ORAL FORMULATION in parallel groups (1:1): patients will be divided in the continuous treatment period into two groups, one group of 12 patients with intake of 100mg OD, the other group of 12 patients with intake of 100mg BID, in order to assess multiple-dose profile of COQUN ORAL FORMULATION.

2.3 Randomization

After the screening visit, subjects will have one week of wash-out period, then will be requested to return to the site for V2, during which subjects will be randomly assigned to one of the two groups:

- group A: 12 adult healthy subjects will be given OD 100mg of COQUN ORAL FORMULATION, to be taken after dinner
- group B: 12 adult healthy subjects will be given BID a dose of 100 mg of COQUN ORAL FORMULATION, to be taken after lunch and after dinner

2.4 Treatments


In this bioavailability study, the investigational product (IP) is COQUN ORAL FORMULATION (Coenzyme Q10 Miniactive Retard 100mg capsules). COQUN ORAL FORMULATION is a food supplement based on Coenzyme Q10 MINIACTIVESR. The IP capsules will be administered orally, always after food intake and at specific moments during the day, according to the OD or BID intake:

- group A: 100mg OD, after dinner
- group B: 100mg BID after lunch and after dinner

All 24 subjects will test a single dose of 100mg CoQ10 in 1 day to assess bioavailability, which will be followed by a one-week wash-out period and then by a 4-week period of continuous administration of COQUN ORAL FORMULATION in the above-mentioned parallel groups (allocation ratio 1:1).

2.5 Sample Size

The simple size for this study is not based on any power calculation.

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24 subjects (12 for each arm) have been considered sufficient to obtain reliable results for the exploratory purposes of the study.

2.6 Blinding

Not applicable in this study.

3. ANALYSIS SETS AND SUBGROUPS

3.1 Analysis sets

The following analysis sets will be considered in this study.

Safety Set

This set consists of all randomized subjects who sign informed consent and take at least one dose of study product.

Intention-to-treat Population

This set contains all randomized subjects.

Per Protocol Population

The per protocol population consists of all subjects who meet all inclusion/exclusion criteria and who do not have any major protocol deviation.

The primary endpoint will be evaluated on ITT and PP populations. Results obtained on the PP population will be considered as supportive of those obtained on the ITT set.


Secondary endpoints and safety assessment will be evaluated on the Safety set.

3.2 Subgroups

No subgroup analysis has been planned in this study.

3.3 Data Review

No data review has been planned in this study.

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4. GENERAL DEFINITIONS AND NAMING CONVENTIONS

In order to avoid ambiguity during the analysis, a number of definitions and conventions for data handling are described here.

4.1 General Methodology and Presentation of the Results

The default summary statistics for quantitative variables will be the number of observations (n), mean, standard deviation (SD), median, interquartile range, minimum (min) and maximum (max), for those subjects with data.

For qualitative variables, the number (n) and percentage (%) of subjects with non-missing data per category will be the default summary presentation, and where appropriate and present, the number of missing values as a “Missing” category.

Percentages will be calculated using a denominator of all subjects in a specified population or treatment group, unless specified otherwise. The denominator will be specified in a footnote to the tables for clarification if necessary.

Statistical Output Layout

Tables and listings exceeding one page should indicate “Page x of y” at the bottom of each page. The definition of baseline and endpoint value will be described in a footnote in every TLF where applicable.

All listings contain columns for subject screening number and treatment group.

The format for presentation of time variables will be hh:mm. The format for presentation of date variables will be dd/mm/yyyy.


Dates that are missing because they are not applicable for the subject will be presented as “N/A”, unless otherwise specified. Missing data will be represented on subject listings as “/” fields.

Listings will be sorted by subject screening number unless specified otherwise.

4.2 Treatment Group Names and Labels

Statistical output will be presented by treatment group and the treatment labels to be used in the tables, listings and figures are defined in the table below.

Treatment Code Number	Treatment Group Description	Treatment Group Label, which will appear in the TLFs
Treatment A	100mg OD of COQUN ORAL FORMULATION	Group A
Treatment B	100mg BID of COQUN ORAL FORMULATION	Group B

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4.3 Visit Names and Labels

The names to be used in the analysis datasets and the labels to be used in the tables, listings and figures for the different study visits are defined below.

Visit number	Visit name	Visit label, which appear in TLFs
V1-H0	Visit 1: assessment moment 0 (before COQUN intake)	Visit 1 – Hour 0
V1-H1	Visit 1: assessment hour 1	Visit 1 – Hour 1
V1-H2	Visit 1: assessment hour 2	Visit 1 – Hour 2
V1-H4	Visit 1: assessment hour 4	Visit 1 – Hour 4
V1-H8	Visit 1: assessment hour 8	Visit 1 – Hour 8
V1-H12	Visit 1: assessment hour 12	Visit 1 – Hour 12
V2	Visit 2 - Day 0	Visit 2
V3	Visit 3 - Day 7	Visit 3
V4	Visit 4 - Day 14	Visit 4
V5	Visit 5 - Day 28 (EOS)	Visit 5

4.4 Study periods, Baseline and Endpoint Values

- First date of medication administration

Day 1 date (collected in patients' V2-V5 diary) will be treated as first intake of study medication.

- Last date of medication administration

Day 28 date (collected in patients' V2-V5 diary) will be treated as last intake of study medication (if the subject completes the study this date should coincide with the date of last investigational product intake).

If the date of last intake of study medication is not available, due to premature termination or other reasons, date of last investigational product intake (collected in the end of study form of the CRF) will be imputed.

- Duration of study medication treatment


Duration (days) = Date of last medication administration - Date of first medication administration + 1

- Baseline value

The baseline value for a variable is defined as the last non-missing value collected before first study medication administration. In the single dose phase, the moment 0 (visit 1- hour 0) will be considered as baseline value while in the multidose phase, baseline will be visit 2 (day 0) if not specified otherwise.

4.5 Visit Windows

Visit 1 is the screening visit: once the subjects are considered eligible for the study, all 24 adult healthy subjects will enter the single dose treatment phase and will be given a dose of 100 mg of COQUN ORAL FORMULATION and plasma coenzyme Q10 will be measured over the next 12 hours: at 1, 2, 4, 8 and 12 hours after intake.

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After 7 days (Visit 2 – Day 0), subjects will return at site for entering the multidose phase and will be randomly divided into two groups of treatment.

After 7, 14, and 28 days Visit 3, Visit 4, Visit 5 (EOS) will be performed respectively.

4.6 Coding Systems and Conventions

4.6.1 Coding of adverse events and medical history

Adverse event and medical history investigator terms will be presented in TLF as recorded in CRF. Any coding will be used upon request.

4.6.2 Coding of medications


Medications will be presented in TLF as recorded in CRF. Any coding will be used upon request.

4.7 Handling of Missing Data

Handling of missing data, if applicable, is discussed in the relevant sub-sections of Section 5 (STATISTICAL ANALYSIS: DEFINITIONS, DERIVATIONS, CALCULATIONS AND METHODOLOGY).

4.8 Multiple testing

Not applicable in this study.

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5. STATISTICAL ANALYSIS: DEFINITIONS, DERIVATIONS, CALCULATIONS AND METHODOLOGY

5.1 Baseline Characteristics

5.1.1 Disposition of Subjects

Collected Variables:

- Treatment group assigned (categories: treatment 1/treatment 2) [CRF – Visit 2]
- Has the subject completed the study (yes, no) [CRF - EOS]
- Primary reason for the premature termination (free text) [CRF - EOS]
- Date of informed consent [CRF – Visit 1]
- Is the subject eligible for entering the study (yes, no) [CRF – Visit 1]
- Inclusion/exclusion criteria (yes, no) [CRF – Visit 1]
- Was the investigational product taken correctly? (yes, no) [CRF – Visit 3, 4, 5]

Derived Variables:

- whether the subject belongs to the :
 - safety set (subjects must have signed the informed consent and they must have taken at least one dose i.e. the answer to the question “Was the investigational product taken correctly” must be “yes” at least once)
 - ITT set (subjects must have been randomized)
 - PP set (subjects must have been randomized and they do not have major deviations)


Imputations for missing values:

If the date of last intake of study medication is not available, due to premature termination or other reasons, date of last investigational product intake (collected in the end of study form of the CRF) will be imputed.

Analysis Sets to be used for:	Tables	Table1: All subjects Tables 2,3, 4: ITT analysis set
	Listings	Listing 1: All subjects Listings 2, 3, 4: ITT analysis set
	Figures	Figure 1: All subjects Figure 2: ITT analysis set

Subject disposition will be summarized by treatment group as follows:

Table 1. Number of Subjects and Subjects Disposition (Total set)	Total number of subjects screened, randomized and number of subjects in analysis sets will be presented by treatment group. The percentage of subjects will be calculated relative to the number of all randomized subjects.
Table 2. Reasons for premature study termination (All Randomized Subjects)	For study termination and for premature discontinuation reason, a default frequency tabulation will be provided. The percentage of subjects will be calculated relative to the number of subjects who were randomized.
Table 3. Analysis Sets (All Randomized Subjects)	Subject analyses set status will be summarized for each treatment group, together with the reason(s) for exclusion from the Safety, ITT and PP

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analysis sets. Percentages will be calculated relative to the number of subjects who were randomized.

Table 4. Study Status by Visit (All Randomized Subjects)

Study Status by visit identifying number of subjects who continue the study will be presented.

Subjects data listings will include:

- Listing 1. Subjects Who Prematurely Terminated the Study Prior to Randomization** A listing of subjects who prematurely discontinued their participation in the study prior to randomization.
- Listing 2. Randomized Subjects Who Prematurely Terminated the Study** A listing of subjects who discontinued participation after randomization.
- Listing 3. Visit Dates and Informed Consent Dates** Listing of visit dates and informed consent dates
- Listing 4. Analysis Sets** Inclusion/Exclusion from each analysis sets together with the reason(s) for exclusion will be presented. This listing will include all possible reasons for exclusion per subject.

In addition to the tables and listings described above, two figures will present subjects disposition in the form of a flowchart:

- Figure 1. Flow Chart of Subjects Disposition** The number of subjects who provided written informed consent, were randomized and the number of subjects per treatment group who completed the study or prematurely discontinued participation in the study will be presented in the form of a flowchart.
- Figure 2. Flow Chart of Analysis Sets** The number of subjects considered valid for the Safety, ITT, and PP analyses set per treatment group will be presented in the form of a flowchart.

5.1.2 Demographic and Other Baseline Characteristics


Collected Variables:

- Age (years) [CRF – Visit 1]
- Gender (male, female) [CRF – Visit 1]
- Ethnic group (caucasian, black, asian, other) [CRF – Visit 1]
- Height (cm) [CRF – Visit 1]
- Weight (kg) [CRF – Visit 1]
- BMI (kg/m²) [CRF – Visit 1]

Derived Variables: Not applicable

Imputations for missing values: No imputation of missing data will be performed

Analysis Sets to be used for:	Tables	Safety analysis set
	Listings	All subjects
	Figures	Not applicable

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Demography will be summarized by treatment group as follows:

Table 5. Demographics (Safety set) Default descriptive statistics for age, height, weight and BMI will be presented. Frequency tabulations for sex, ethnicity will be presented.

Subject data listings will include:

Listing 5. Demographics All demographic data will be presented.

5.1.3 Protocol Violations

Protocol violations are major deviations from the procedures outlined in the protocol like for example missed evaluations, incorrect timing of evaluations, non-compliance with study medications and intake of medications not allowed or any non-adherence to the protocol that impacts subject's rights, safety or welfare.

Protocol violations are defined as any deviations that may affect the efficacy outcome or the treatment of the subjects. All potential protocol violations will be discussed and reviewed on a case-by-case basis. A decision will be made as to the effect of the possible violations to determine if it is considered major or minor. The status, major or minor, of each potential protocol violation will be tabulated. A subject may have one or more major protocol violations resulting in the exclusion of that subject from the per protocol analysis set.

Collected Variables: Not applicable

Derived Variables:

- protocol violation category
- type of violation (descriptive free text)
- details of violation (descriptive free text)

Imputations for missing values: Not applicable


Analysis Sets to be used for:	Tables	ITT analysis set
	Listings	ITT analysis set
	Figures	Not applicable

Protocol violations will be summarized by treatment group as follows:

Table 8. Major/Minor Protocol Violations (ITT set) The number of all subjects with at least one major or minor protocol violation, will be presented by treatment group. For all categories of major and minor protocol violations, default frequency tabulation will be presented. Subjects may have more than one major/minor protocol violation.

Subjects data listings will include:

Listing 6. Minor and Major Protocol Violations A by-subject listing of all subjects with their minor and major protocol violations will be presented.

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5.1.4 Compliance to Study Treatment and Procedures

Collected Variables

Compliance to the treatment:

- Was the investigational product delivered to the subject? [CRF - Visit 2] (yes/no)
- Was the investigational product taken correctly? [CRF - Visit 3, 4, 5] (yes/no)

Compliance to the study procedures:

- Was the subject fasting for at least 10 hours before IP intake? [CRF - Visit 1] (yes/no)
- Was the investigational device taken by the subject? [CRF - Visit 1] (yes/no)
- Was the blood sampling taken? [CRF - Visit 1, 2, 3, 4, 5] (yes/no)
- Was the V1-V2 DIARY given to the subject? [CRF - Visit 1] (yes/no)
- Was the V1-V2 DIARY checked and retrieved from subject? [CRF - Visit 2] (yes/no)
- Was the V2-V5 given to the subject? [CRF - Visit 2] (yes/no)
- Was the V2-V5 given back to the subject? [CRF - Visit 3, 4] (yes/no)
- Was the V2-V5 DIARY checked? [CRF - Visit 3, 4, 5] (yes/no)
- Was the investigational product retrieved from subject? [CRF - Visit 5] (yes/no)
- Was the V2-V5 retrieved from subject? [CRF - Visit 5] (yes/no)

Derived Variables: Not applicable

Imputations for missing values: Not applicable

Analysis Sets to be used for:	Tables	Safety analysis set
	Listings	Safety analysis set
	Figures	Not applicable

Compliance will be summarized as follows:

Table 6. Compliance to Investigational Product (Safety set)

Compliance to the treatment will be presented by treatment group using default frequency statistics. The percentage of subjects will be calculated relative to the total number of subjects in Safety analysis set. Subjects with missing data will be presented as part of a "Missing" category.

Table 7. Compliance to The Study Procedures (Safety set)

Compliance to the study procedures will be presented by treatment group using default frequency statistics. The percentage of subjects will be calculated relative to the total number of subjects in Safety analysis set. Subjects with missing data will be presented as part of a "Missing" category.

Compliance variables will be presented in subjects data listings as follows:


Listing 7. Treatment Compliance

Treatment compliance data from CRF will be presented as a subject data listing.

Listing 8. Compliance to study procedures [1]

Listing 9. Compliance to study procedures [2]

Compliance to study procedures will be presented as a subject data listing.

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Inclusion/Exclusion criteria

Collected Variables:

The study specific Inclusion/Exclusion Criteria are presented in Section 8.2 and 8.3 of the *Study Protocol Version Final – March 03, 2018*. For those criteria, as appropriate, a response of “Yes/No” is to be obtained at the screening visit and checked prior to allocated to treatment, at Visit 2.

Derived Variables: Not applicable

Imputations for missing values: Not applicable

Analysis Sets to be used for:	Tables	Not applicable
	Listings	All subjects
	Figures	Not applicable

If a subject fulfills all Inclusion/Exclusion criteria its eligibility will be considered as “Yes”. The response per subject to the study specific Inclusion/Exclusion Criteria, will be presented as a subject data listing as follows:

Listing 14. Inclusion Criteria	Listing of all Inclusion Criteria including the response as either “Yes” or “No” for the eligibility of all subjects.
Listing 15. Exclusion Criteria	Listing of all Exclusion Criteria including the response as either “Yes” or “No” for the eligibility of all subjects.

5.1.5 Physical Examination Findings

Physical Examination in this study is performed at Visit 1.

Collected Variables:

- General appearance of the system (categories: skin, eyes, ears-nose-throat, breast, head&neck, lungs, heart, abdomen, extremities, limphonodes, musculoskeletal, peripheral vascular, genitourinary, other) [CRF – Visit 1]
- normal/abnormal/not assessed statement [CRF – Visit 1]
- abnormalities (text) [CRF – Visit 1]

Derived Variables: Not applicable

Imputations for missing values: Not applicable

Analysis Sets to be used for:	Tables	Safety set
	Listings	Safety set
	Figures	Not applicable

Physical Examination Findings will be summarized as follows:


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Table 9. Physical Examination Findings by Body System (Safety set)

Number and percent of subjects with abnormal findings for each body system of physical examination will be tabulated at visit 1 by treatment group.

In addition, physical examination data will be presented as follows:

Listing 10. Physical Examination

Physical examination findings will be presented by subject.

5.1.6 Pregnancy

Pregnancy data in this study is recorded at Visit 1.

Collected Variables:

- Pregnancy test performed (categories: Done, Not Done, Not Applicable) [CRF – Visit 1]
- Pregnancy test result (categories: Positive, Negative) [CRF – Visit 1]

Derived Variables: Not applicable

Imputations for missing values: Not applicable

Analysis Sets to be used for:	Tables	Safety set
	Listings	Safety set
	Figures	Not applicable

Pregnancy data will be summarized as follows:

Table 10. Pregnancy test (Safety set)

Number and percent of subjects with a positive result in the pregnancy test will be tabulated at visit 1 by treatment group.

In addition, physical examination data will be presented as follows:

Listing 11. Pregnancy

Pregnancy data will be presented by subject.


5.1.7 Medical History and Trial Specific Diseases

5.1.7.1 Medical History

Medical history is defined as any condition, except for the study indication, that the subject may have had prior to enrollment in the study, including any chronic conditions diagnosed prior to entry in the study, for example, diabetes. Medical history will be reported on a by-subject basis. Medical history findings will be presented in disorder categories as reported in the CRF.

Collected Variables:

- Disorder (categories: infections and infestations, neoplasms, blood and lymphatic system, immune system disease, endocrine disorders, metabolism and nutrition disorders, nervous system disorders, ear and labyrinth disorders, cardiac disorders, vascular disorders, respiratory, thoracic and mediastinal disorders, gastrointestinal

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- disorders, hepatobiliary disorders, skin and cutaneous tissue disorders, musculoskeletal and connective tissue disorders, renal and urinary disorders, reproductive system disorders, injury, poisoning and procedural complications, surgical procedures, other)
- Has the patient experienced the disorder (yes, no) [CRF – Visit 1]
 - Details (free text) [CRF – Visit 1]
 - Start date of event [CRF – Visit 1]
 - Stop date of event [CRF – Visit 1]
 - Event ongoing (yes, no) [CRF – Visit 1]

Derived Variables: Not applicable

Imputations for missing values:

Missing or partial dates for medical history will not be completed, for example, if only a month and year are available as --FEB2005, the day will not be imputed in order to complete the date. If “End Date” information is not available, it will be assumed that the finding is “Ongoing” at the time of enrollment in the study.

Analysis Sets to be used for:	Tables	Safety analysis set
	Listings	Safety analysis set
	Figures	Not applicable

Medical history findings will be summarized by treatment group as follows:

Table 11. Medical History (safety set)	The number of subjects with at least one medical history finding will be presented by default summary statistics, where the percentage of subjects is calculated relative to the total number of subjects in the safety analysis set.
---	---

All medical history will be presented in subjects data listings as follows:

Listing 13. Medical History	Medical history findings will be presented by-subject and within subjects by disease category of each medical history finding as a subject data listing.
------------------------------------	--

5.1.7.2 Trial Specific Diseases


Not applicable

5.1.8 Prior and Concomitant Medication

Medications will be reported as recorded in CRF.

Collected Variables:

- Medication generic name (text) [CRF – Cumulative Concomitant Medication Form]
- Dose administered [CRF – Cumulative Concomitant Medication Form]
- Unit (standard dosage units, e.g., mg, mcg, cc, mL, IU, etc.) [CRF – Cumulative Concomitant Medication Form]
- Frequency (categories: od=once daily / bid=twice daily / tid=3 times daily /qid=4 times daily / 5/day=5 times daily /prn= as required; etc) [CRF – Cumulative Concomitant Medication Form]
- Dosage form (categories: tab= tablet; cap = capsule, oint = ointment, supp = suppository, aer = aerosol, susp = suspension, spray, patch, syrups, drops, vials, gel, cream, etc.) [CRF – Cumulative Concomitant Medication Form]

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- Route of administration (categories: os= oral / iv= intravenous / sc= subcutaneous / im= intramuscular / inh= inhalation / top= topical/ sl= sublingual/ oth= other) [CRF – Cumulative Concomitant Medication Form]
- Indication [CRF – Cumulative Concomitant Medication Form]
- Start date of medication [CRF – Cumulative Concomitant Medication Form]
- Stop date of medication [CRF – Cumulative Concomitant Medication Form]
- Medication ongoing (yes, no) [CRF – Cumulative Concomitant Medication Form]

Derived Variables:

- **Prior medications** are defined as those starting and ending prior to the first administration of investigational study medication.
- **Concomitant medications** are defined as medications started at or after first administration of investigational study medication and include medications started prior to the first administration of investigational study medication but continued during the study.

Imputations for missing values: Not applicable

Analysis Sets to be used for:	Tables	Safety analysis set
	Listings	Safety analysis set
	Figures	Not applicable

Concomitant and prior medication will be summarized by treatment group as follows:

Table 12. Concomitant and Prior Medication (Safety set)	The number of subjects with at least one concomitant/prior medication will be presented by default summary statistics, where the percentage of subjects is calculated relative to the total number of subjects considered valid for the safety analysis set.
--	--

All medications entered on the “Cumulative Concomitant Medication” CRF form will be presented in subject data listings as follows:

Listing 12. Prior and Concomitant Medications	By-subject and within-subject by ascending start date of medication use will be presented for those subjects who were allocated to treatment and received at least one dose of investigational study medication.
--	--

5.2 Efficacy Analysis

5.2.1 Primary Efficacy Analysis


The primary objective of this study is to evaluate the best dosage between 100mg once daily or 100mg twice daily for COQUN ORAL FORMULATION in order to reach a level of plasma concentration which might assure its antioxidant effect if taken on a regular basis.

The following pharmacokinetic properties will be evaluated:

- Area under the curve (microg/ml x h)
- C_{max}
- T_{max}
- Elimination half-life ($t_{1/2}$)

Collected Variables

- Plasma concentration of coenzyme Q10 [CRF – Visit 2, 3, 4, 5]

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Derived Variables

Derived variables are shown in Image 1 and are the following^[2,3]:

- AUC_t
The area under the plasma concentration curve to the last quantifiable concentration (C_t) at time t (AUC_t) will be determined by linear trapezoidal rule. The trapezoidal rule is a method used to numerically approximate the area under the concentration by time curve obtained by summing the area of all trapezoids constructed under the curve. Each trapezoid's area is obtained as:

$$\frac{(C_i + C_{i+1}) * (T_{i+1} - T_i)}{2}$$

where C_i is the concentration at time i (where i is any timepoint before the last observed timepoint T_t), C_{i+1} is the concentration at the following timepoint, T_i is the timepoint i and T_{i+1} is the following timepoint.

- C_{max}
Maximum concentration in the plasma (C_{max}) is obtained directly from the data being the highest plasma concentration value.
- T_{max}
 T_{max} is the collection time in which the maximum concentration is observed and is related to the drug absorption speed.

- $t_{\frac{1}{2}}$
The terminal half-life is defined as the time required for the plasma concentration of a drug to decrease 50% in the final stage of its elimination; this parameter is computed with the formula^[2]:

$$t_{\frac{1}{2}} = \frac{\ln 2}{\lambda_z}$$

where λ_z is the smallest elimination rate constant observed which is obtained as the ratio of clearance and volume of distribution. Clearance is calculated as the ratio of dose and AUC while volume of distribution is obtained as dose divided by concentration at time 0 that is the concentration registered after the first intake of coenzyme (in the single dose time 0 is hour 1, in the multidose phase time 0 is visit 2).

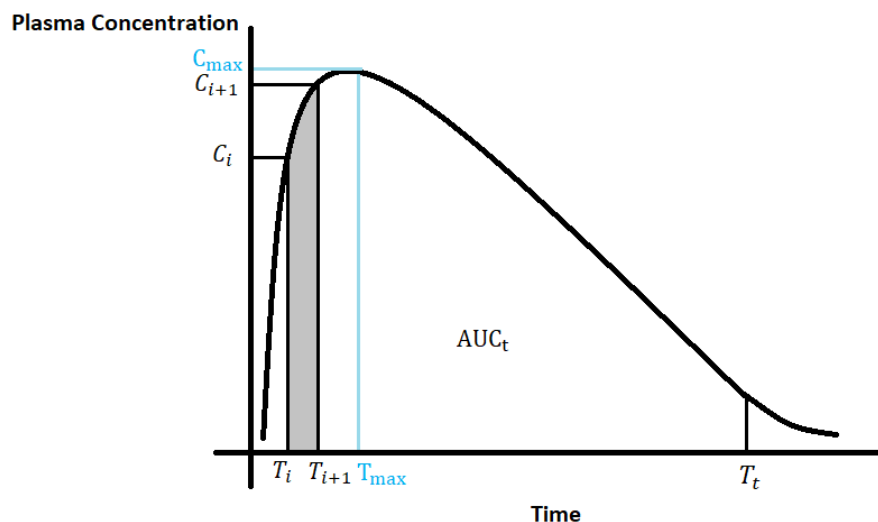



Image 1. Pharmacokinetic parameters

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Analysis of Primary Efficacy variable:

Descriptive statistics such as mean \pm standard deviation, median with interquartile range, minimum, maximum and coefficient of variation will be presented for the plasma concentration of coenzyme Q10 at each time point in the entire sample of subjects. 95% confidence interval will be provided as well.

An explorative analysis on gender will be performed showing descriptive statistics for plasma concentration of coenzyme Q10 by gender. The effect of gender will be explored by means of a mixed model for repeated measures with covariates *gender*, time and the interaction term *gender*time*.

Descriptive statistics will be also provided for the plasma concentration of coenzyme Q10 at each time point by treatment group.

Change of plasma concentration versus baseline (i.e. change versus visit 2 values) will be computed for each study visit both for the whole sample and by treatment group.

Change will be computed in the following way:

$$\text{Change (\%)} = \frac{\text{Value at Visit X} - \text{Baseline Value}}{\text{Baseline Value}} \times 100$$

Area under the curve, maximum concentration in the plasma, time of maximum concentration and terminal half-life will be presented descriptively on the original scale.

95% confidence interval will be provided for the means of 100mg OD and 100mg BID for COQUN ORAL FORMULATION for the parameters AUC_t , C_{max} , T_{max} and terminal half-life.

A Student t-test for unpaired data will be performed in order to detect differences between the two groups in the pharmacokinetics parameters.

A concentration by time graph will be presented for the multidose phase by treatment group in order to have a graphical visualization of the pharmacokinetics properties over time.


Line graphs will be provided for the concentration of coenzyme Q10 in the whole sample and by gender.

In performing statistical analysis, it is important to assess the statistical outliers. In fact, inclusion or exclusion of outlying subjects may lead to a different conclusion in assessment of differences in bioavailability between two formulations. It is therefore important to identify these outliers and study their effects.

Primary endpoint will be evaluated on the ITT population and analysis will be replied on the PP population. Results obtained on the PP population will be considered as supportive of those obtained on the ITT set.

Imputations for missing values: No imputation of missing data will be performed

Analysis Sets to be used for:	Tables	ITT and PP analysis set
	Listings	ITT analysis set
	Figures	ITT and PP analysis set

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Primary efficacy variable will be summarized by treatment group as follows:

Table 13. Primary Efficacy Variable at Each Study Visit (ITT Analysis Set)

Default summary statistics per treatment group for the primary efficacy variable (Plasma concentration of Coenzyme Q10) at each study visit will be presented for the ITT analysis set. This table will be replied on the PP analysis set.

Table 14. Plasma concentration of coenzyme Q10 by gender (ITT Analysis Set)

Default summary statistics per gender for the primary efficacy variable (Plasma concentration of Coenzyme Q10) at each study visit will be presented for the ITT analysis set. This table will be replied on the PP analysis set.

Table 15. Change versus baseline by Treatment (ITT Analysis Set)

Default summary statistics per treatment group for the change versus baseline at each study visit will be presented for the ITT analysis set. This table will be replied on the PP analysis set.

Table 16. Pharmacokinetic Parameters by Treatment (ITT Analysis Set)

Default summary statistics per treatment group for each pharmacokinetic parameter will be presented for the ITT analysis set. This table will be replied on the PP analysis set.

Table 17. Confidence Interval and Results of T-test for Primary Efficacy Variable (ITT Analysis Set)

Confidence interval at 95% will be presented for the means of the pharmacokinetics parameters in the two groups in the ITT analysis set. The table also contains the result of the Student t-test detecting the differences between the two groups. This table will be replied on the PP analysis set.

A Primary efficacy variable will be presented in subject data listings as follows:

Listing 16. Listing of Primary Efficacy Variable

A listing of the values for the primary efficacy variable (Plasma concentration of Coenzyme Q10) as used in the primary analysis, sorted by screening number and within subjects by time point will be presented.

Listing 17. Listing of Pharmacokinetic parameters

A listing of the values for the pharmacokinetic parameters as used in the primary analysis, sorted by screening number will be presented.

The primary endpoint will be presented in a graph as follows:

Figure 3. Concentration by time plot (ITT Analysis Set)

A concentration by time graph will be presented for the multidose phase in the ITT analysis set. This plot will be replied in the PP analysis set.


Figure 4. Concentration by time plot by treatment group (ITT Analysis Set)

A concentration by time graph by treatment group will be presented for the multidose phase in the ITT analysis set. This plot will be replied in the PP analysis set.

Figure 5. Concentration by time plot by gender (ITT Analysis Set)

A concentration by time graph by gender will be presented for the multidose phase in the ITT analysis set. This plot will be replied in the PP analysis set.

5.2.2 Analysis of Secondary Variables

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Secondary objectives of this study are:

- To evaluate the safety and tolerability COQUN ORAL FORMULATION following single dose of 100mg
- To evaluate the safety and tolerability of COQUN ORAL FORMULATION during the 1 month daily dose

The secondary variables are the ones regarding safety which will be monitored through:

- Vital signs
- Adverse events

Special interest will be paid on symptoms and signs like mild insomnia, elevated levels of liver enzymes, rash, nausea, upper abdominal pain, dizziness, sensitivity to light, irritability, headache, heartburn, and fatigue.

Analysis of safety will be performed on the safety analysis set.


5.2.2.1 Adverse Events

Collected Variables:

- Event, i.e. diagnosis or signs/symptoms (text) [CRF – Cumulative adverse event form]
- The start and stop date of the event [CRF – Cumulative adverse event form]
- Outcome of event (categories: recovered/resolved, recovered/resolved with residual effects, recovering/resolving, not recovered/ not resolved, fatal, unknown) [CRF – Cumulative adverse event form]
- Severity (categories: mild, moderate, severe, life threatening or disabling) [CRF – Cumulative adverse event form]
- Treatment (categories: none, specific drug treatment, specific non drug treatment) [CRF – Cumulative adverse event form]
- Relationship with study device (categories: definitive, probable, possible, unlikely, none) [CRF – Cumulative adverse event form]
- Action taken with study device (categories: none, dose reduction temporarily, dose reduced, discontinued temporarily, discontinued) [CRF – Cumulative adverse event form]
- Pattern (categories: every study drug administration, intermittent, continuous, other) [CRF – Cumulative adverse event form]
- Seriousness (yes, no) [CRF – Cumulative adverse event form]

Derived Variables:

- Adverse Events (AEs): an adverse event is any untoward medical occurrence in a subject or clinical study subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign, symptom, or disease temporarily associated with the use of a medicinal product, whether or not considered related to the medicinal product. The definition covers the entire study period, independent of whether IP was administered or not.
- Serious adverse event (SAEs): Any untoward medical occurrence or response to a medicinal product that at any dose: results in death, is life threatening, results in in-subject hospitalization or prolongation of existing hospitalization, results in a persistent or significant disability/incapacity, is a congenital anomaly/birth defect or, important AEs that are not immediately life-threatening or do not result in death or hospitalization but may jeopardize the subject or may require intervention to prevent one of the other outcomes listed.

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In the analysis serious adverse events will be identified by the variables “Seriousness” (yes, no).

- Related AEs: in the analysis related AEs will be defined as AEs for which the relationship with study device is assessed as “definitive” or “probable” or “possible”
- Severe AEs: in the analysis severe AEs will be defined as AEs for which the severity is assessed as “severe” or “life threatening”
- Subjects who prematurely terminated the Study Due to AE: in the analysis subjects who prematurely terminated the study due to AE are defined as defined as those subjects with an adverse event for which the reason for early termination in the CRF end of study has been recorded as “adverse event”
- Death: death is defined as a fatal outcome of an AE.

Adverse events (AEs) will be reported on a per-subject basis. This implies that even if a subject reported the same event repeatedly, the event will be counted only once. In the latter case, the event will be assigned the worst severity and strongest relationship to the investigational study medication. The presentation of AEs is therefore restricted to the incidence per subject of AEs assigned to the Treatment Period.

Analysis Sets to be used for:	Tables	Safety analysis set
	Listings	Safety analysis set
	Figures	Not applicable

Adverse events will be summarized by default summary statistics by treatment group. Percentages will be calculated relative to the total number of subjects considered valid for the Safety analysis set.

Table 18. Summary of Adverse Events in the Single Dose Phase (Safety set)

- Overview of AEs in the single dose phase including the:
- number of subjects with at least one AE.
 - number of subjects with at least one device-related AE.
 - number of subjects with at least one serious AE.
 - number of subjects with at least one severe AE.
 - number of subjects who prematurely terminated the study.
 - Number of AEs
 - Number of serious AEs
 - Number of related AEs
 - Number of severe AEs
 - Number of deaths

Table 19. Summary of Adverse Events in the Multidose Phase (Safety set)

- Overview of AEs in the multidose phase including the:
- number of subjects with at least one AE.
 - number of subjects with at least one device-related AE.
 - number of subjects with at least one serious AE.
 - number of subjects with at least one severe AE.
 - number of subjects who prematurely terminated the study.
 - Number of AEs
 - Number of serious AEs
 - Number of related AEs
 - Number of severe AEs
 - Number of deaths


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Table 20. AEs of Special Interest in the Single Dose Phase (Safety set)

AEs of special interest are symptoms and signs like mild insomnia, elevated levels of liver enzymes, rash, nausea, upper abdominal pain, dizziness, sensitivity to light, irritability, headache, heartburn, and fatigue. A default frequency table will be presented for the AEs of special interest experienced in the single dose phase.

Table 21. AEs of Special Interest in the Multidose Phase (Safety set)

AEs of special interest are symptoms and signs like mild insomnia, elevated levels of liver enzymes, rash, nausea, upper abdominal pain, dizziness, sensitivity to light, irritability, headache, heartburn, and fatigue. A default frequency table will be presented for the AEs of special interest experienced in the multidose phase.

Table 22. AEs by Relationship (Safety set)

A default frequency table will be presented by treatment group for AEs by relationship separately in the two phases of the study.

Table 23. AEs by Severity (Safety set)

A default frequency table will be presented by treatment group for AEs by severity separately in the two phases of the study.

In addition, AE data will be listed as follows:

Listing 18. Listing of AEs: General

All AEs by-subject and within-subject by start date. If the AE is "Ongoing" it will be indicated as such in the field "end date" in the listing. The listing also includes the general demographic data for each subject who experienced an adverse event (gender, age, ethnicity).

Listing 19. Listing of Deaths

List of all deaths in the study; the table also includes the general demographic data for each subject who died (gender, age, ethnicity and race).

Listing 20. Listing of SAEs

Lists all subjects with at least one serious adverse event. The listing also includes the general demographic data for each subject who experienced an adverse event (gender, age, ethnicity).

Listing 21. Listing of AEs Leading to Study Termination

This listing will be presented for those subjects with at least one adverse event leading to study termination: The listing also includes the general demographic data for each subject who experienced an adverse event (gender, age, ethnicity).

5.2.2.2 Vital Signs

Vital signs have been recorded at Visit 1, Visit 2, Visit 3, Visit 4, Visit 5.


Collected Variables:

- Systolic blood pressure (mmHg) [CRF – Visit 1, 2, 3, 4, 5]
- Diastolic blood pressure (mmHg) [CRF – Visit 1, 2, 3, 4, 5]
- Heart rate (beats/min) [CRF – Visit 1, 2, 3, 4, 5]
- Respiratory rate (acts/min) [CRF – Visit 1, 2, 3, 4, 5]
- Temperature (°C) [CRF – Visit 1, 2, 3, 4, 5]

Derived Variables:

- Change from Baseline will be derived as follows:

$$\text{Absolute change (unit)} = \text{Value at Visit X} - \text{Baseline Value}$$

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$$\text{Relative change (\%)} = \frac{\text{Value at Visit X} - \text{Baseline Value}}{\text{Baseline Value}} \times 100$$

Analysis Sets to be used for:	Tables	Safety analysis set
	Listings	Safety analysis set
	Figures	Not applicable

Vitals signs will be summarized as follows:

Table 24. Summary of Vital Signs (Safety set) Summary of quantitative vital signs assessments will be presented by treatment group using default summary statistics. At each assessed visit, summary statistics will be presented also for the change from baseline at each post-baseline visit.

In addition to the tables the vital signs will be presented in subject data listings as follows:

Listing 22. Vital Signs in the Multidose Phase Vital signs data will be presented by-subject and within-subject by visit.

Listing 23. Vital Signs in the single dose phase Vital signs data in the single dose phase will be presented by subject.

Graphical representation of the trend over the whole study of each vital sign will be provided by means of line graphs.

5.2.3 Analysis of Other Variables

An analysis of the bioavailability evaluated in the first single dose phase of the study will be performed.

The following pharmacokinetic properties will be evaluated:

- Area under the curve (microg/ml x h) ≥ 5
- C_{\max} (microg/ml x h) $\geq 0,8$
- T_{\max} (hours) ≥ 3
- Elimination half-life ($t_{\frac{1}{2}}$)

The plasma concentration is recorded at Visit 1 at moment 0 (before COQUN intake), hour 1, hour 2, hour 4, hour 8 and hour 12.

Collected Variables

- Plasma concentration of coenzyme Q10 [CRF – Visit 1]


Derived Variables

The parameters AUC_t , AUC_{∞} , C_{\max} , T_{\max} , $t_{\frac{1}{2}}$ and their computation have been described in section 5.2.1 *Primary Efficacy Analysis*. Please refers to the mentioned section for details.

Analysis of Primary Efficacy variable:

Descriptive statistics such as mean \pm standard deviation, median with interquartile range, minimum, maximum and coefficient of variation will be presented for the plasma concentration of coenzyme Q10 at each time point in the entire sample of subjects. 95% confidence interval will be provided as well.

An explorative analysis on gender will be performed showing descriptive statistics for plasma concentration of coenzyme Q10 divided by gender. The effect of gender will be explored by means of a mixed model for repeated measures with covariates *gender*, time and the interaction term *gender*time*.

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Change of plasma concentration versus baseline (i.e. change versus hour 0 values) will be computed for each study visit both for the whole sample and by gender. Change will be computed in the following way:

$$\text{Change (\%)} = \frac{\text{Value at Visit X} - \text{Baseline Value}}{\text{Baseline Value}} \times 100$$

Area under the curve, maximum concentration in the plasma, time of maximum concentration and terminal half-life and half-life will be presented descriptively on the original scale.

95% confidence interval will be provided for the means of the parameters AUC_t , C_{max} and T_{max} and terminal half life in the single dose phase i.e. following a single intake of COQUN oral formulation.

A concentration by time graph will be presented for the single dose phase in order to have a graphical visualization of the pharmacokinetics properties over time.

Line graphs will be provided for the concentration of coenzyme Q10 in the whole sample and by gender.

In performing statistical analysis, it is important to assess the statistical outliers. In fact, inclusion or exclusion of outlying subjects may lead to a different conclusion in assessment of differences in bioavailability between two formulations. It is therefore important to identify these outliers and study their effects.

Analysis will be evaluated on the ITT population and analysis will be replied on the PP population. Results obtained on the PP population will be considered as supportive of those obtained on the ITT set.

Imputations for missing values: No imputation of missing data will be performed

Analysis Sets to be used for:	Tables	ITT and PP analysis set
	Listings	ITT analysis set
	Figures	ITT and PP analysis set

Plasma concentration of coenzyme Q10 in the single dose phase will be summarized as follows:

Table 25. Plasma Concentration of Q10 in the Single Dose Phase (ITT Analysis Set)

Default summary statistics for plasma concentration of Coenzyme Q10 at each time point will be presented for the ITT analysis set. This table will be replied on the PP analysis set.

Table 26. Plasma Concentration of Q10 in the Single Dose Phase by gender (ITT Analysis Set)

Default summary statistics per gender for the Plasma concentration of Coenzyme Q10 at each time point will be presented for the ITT analysis set. This table will be replied on the PP analysis set.

Table 27. Change versus baseline by gender (ITT Analysis Set)

Default summary statistics by gender for the change versus baseline at each time point will be presented for the ITT analysis set. This table will be replied on the PP analysis set.


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Table 28. Pharmacokinetic Parameters in the Single Dose Phase (ITT Analysis Set)

Default summary statistics for each pharmacokinetic parameter will be presented for the ITT analysis set together with confidence intervals at 95% for the means of the pharmacokinetics parameters. This table will be replied on the PP analysis set.

Plasma concentration of Q10 will be presented in subject data listings as follows:

Listing 24. Listing of Plasma Concentration of Q10 in the Single Dose Phase

A listing of the values for plasma concentration of Coenzyme Q10 in the single dose phase, sorted by screening number and within subjects by time point will be presented.

Listing 25. Listing of Pharmacokinetic parameters in the Single Dose Phase

A listing of the values for the pharmacokinetic parameters in the single dose phase, sorted by screening number will be presented.

Plasma concentration of Q10 will be presented in a graph as follows:

Figure 6. Concentration by time plot for the single dose phase (ITT Analysis Set)

A concentration by time graph will be presented for the single dose phase in the ITT analysis set. This plot will be replied in the PP analysis set.

Figure 7. Concentration by time plot by gender for the single dose phase (ITT Analysis Set)

A concentration by time graph will be presented for the single dose phase by gender in the ITT analysis set. This plot will be replied in the PP analysis set.

5.3 Pharmacokinetic (PK)/ Pharmacodynamic (PD)


Pharmacokinetic properties evaluated for this study are the following:

- Area under the curve (AUC_t)
- Maximum concentration in the plasma (C_{max})
- Time taken to reach the maximum concentration (T_{max})
- Elimination half-life ($t_{\frac{1}{2}}$)

The detailed description of the analysis of pharmacokinetic variables is provided in section 5.2.1 *Primary efficacy analysis*.


5.4 Interim Analysis

Not applicable in this study.

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6. CHANGES TO THE ANALYSIS AS LAID DOWN IN THE PROTOCOL AND AMENDMENTS

No changes to the analysis as laid down in the protocol were made.

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8. APPENDICES

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8.2 Statistical Output Templates

8.2.1 Tables

8.2.1.1 Baseline Characteristics

Table 1. Number of Subjects and Subjects Disposition (Total set)

	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Number of Subjects Screened	n			X
Number of Subjects Randomized	n	X	X	X
Number of Subjects in the safety set	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Number of Subjects in the Intention to treat analysis set (ITT)	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Number of Subjects in the Per Protocol set (PP)	n (%)	X (X.X%)	X (X.X%)	X (X.X%)

N: Number of subjects in specified treatment group

n: Number of subjects with data available

?: Percentage based on N

Notes: a) Percentages are based on the number of all randomized subjects.

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Table 2. Reasons for premature study termination (All Randomized Subjects)

	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Number of Subjects Who Completed the Study	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Number of Subjects Prematurely Terminated the Study	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Primary Reason for Premature Study Termination:				
Screening failures	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Subject retrieved its consent	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Adverse event	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Subject non compliance	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Other reason (1)	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Other reason (2)	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Other reason (3)	n (%)	X (X.X%)	X (X.X%)	X (X.X%)

N: Number of subjects in specified treatment group

n: Number of subjects with data available

?: Percentage based on N

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Table 3. Analysis Sets (All Randomized Subjects)

	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Number of Subjects in the SAFETY Set	n (%)	XX (XXX%)	XX (XXX%)	XX (XXX%)
Number of Subjects excluded from the SAFETY Set	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Reason for exclusion from the SAFETY Analysis Set:				
Reason 1	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Reason 2	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Number of Subjects in the ITT Analysis Set	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Number of Subjects excluded from the ITT Analysis Set	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Reason for exclusion from the ITT Set:				
Reason 1	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Reason 2	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Number of Subjects in the PP Analysis Set	n (%)	X (XX.X%)	X (XX.X%)	XX (XX.X%)
Number of Subjects excluded from the PP Analysis Set	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Reason for exclusion from the PP Set:				
Reason 1	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Reason 2	n (%)	X (X.X%)	X (X.X%)	X (X.X%)

N: Number of subjects in specified treatment group
n: Number of subjects with data available
%: Percentage based on N

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Table 4. Study Status by Visit (All Randomized Subjects)

	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Attended Visit:				
Visit X	n	X	X (X.X%)	X
Visit X	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Visit X	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Visit X	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Visit X	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
Visit X	n (%)	X (X.X%)	X (X.X%)	X (X.X%)

N: Number of subjects in specified treatment group
n: Number of subjects with data available
%: Percentage based on N

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Table 5. Demographics (Safety set)

Characteristic	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Age (years)	n	XX	XX	XX
	Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
	Median	XX.X	XX.X	XX.X
	Min/Max	XX/XX	XX/XX	XX/XX
Height (cm)	n	XX	XX	XX
	Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
	Median	XX.X	XX.X	XX.X
	Min/Max	XX/XX	XX/XX	XX/XX
Weight (kg)	n	XX	XX	XX
	Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
	Median	XX.X	XX.X	XX.X
	Min/Max	XX/XX	XX/XX	XX/XX
Gender				
	Female	n (%)	XX (XX.X%)	XX (XX.X%)
	Male	n (%)	XX (XX.X%)	XX (XX.X%)
Ethnic group				
	Caucasian	n (%)	XX (XXX.X%)	XX (XXX.X%)
	Black	n (%)	XX (XXX.X%)	XX (XXX.X%)
	Asian	n (%)	XX (XXX.X%)	XX (XXX.X%)
	Other (1)	n (%)	XX (XXX.X%)	XX (XXX.X%)
	Other (2)	n (%)	XX (XXX.X%)	XX (XXX.X%)
	Other (3)	n (%)	XX (XXX.X%)	XX (XXX.X%)
BMI (kg/m ²)	n	XX	XX	XX
	Mean (SD)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
	Median	XX.X	XX.X	XX.X
	Min/Max	XX/XX	XX/XX	XX/XX

N: Number of subjects in specified treatment group
n: Number of subjects with data available
%: Percentage based on N
SD = Standard deviation


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Table 6. Compliance to Investigational Product (Safety set)

Characteristic	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Was the investigational device delivered to the subject [Visit 2]?				
Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Was the investigational device taken correctly [Visit 3]?				
Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Was the investigational device taken correctly [Visit 4]?				
Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Was the investigational device taken correctly [Visit 5]?				
Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX

N: Number of subjects in specified treatment group
n: Number of subjects with data available
%: Percentage based on N
SD = Standard deviation



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Table 7. Compliance to The Study Procedures (Safety set)

Characteristic	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Was the subject fasting for at least 10 hours before IP intake [Visit 1]?				
Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Was the investigational device taken by the subject [Visit 1]?				
Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Was the blood sampling taken [Visit 1]?				
Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Was the blood sampling taken [Visit 2]?				
Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Was the blood sampling taken [Visit 3]?				
Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Was the blood sampling taken [Visit 4]?				
Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Was the blood sampling taken [Visit 5]?				
Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX

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Was the V1-V2 diary given to the subject? [Visit 1]?

Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX

Was the V1-V2 diary checked and retrieved from subject [Visit 2]?

Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX

Was the V2-V5 diary given to the subject [Visit 2]?

Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX

Was the V2-V5 diary given back to the subject [Visit 3]?

Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX

Was the V2-V5 diary given back to the subject [Visit 4]?


Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX

Was the V2-V5 diary checked [Visit 3]?

Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX

Was the V2-V5 diary checked [Visit 4]?

Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX

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Was the V2-V5 diary checked [Visit 5]?

Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX

Was the investigational product retrieved from subject [Visit 5]?

Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX

Was the V2-V5 diary retrieved from subjects [Visit 5]?

Yes	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
No	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX
Missing	N	XX	XX	XX
	%	XX.XX	XX.XX	XX.XX

N: Number of subjects in specified treatment group
n: Number of subjects with data available
%: Percentage based on N

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Table 8. Major/Minor Protocol Violations (ITT set)

Violation Category Type of violation	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Total	n (%)	XXX (XXX.X%)	XXX (XXX.X%)	XXX (XXX.X%)
No Major Violation	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At Least One Major Violation	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
MAJOR VIOLATION CATEGORY 1	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
MAJOR VIOLATION CATEGORY 2	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
MAJOR VIOLATION CATEGORY 3	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
MAJOR VIOLATION CATEGORY 4	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
MAJOR VIOLATION CATEGORY 5	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
etc.				
No Minor Violation	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
At Least One Minor Violation	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
MINOR VIOLATION CATEGORY 1	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
MINOR VIOLATION CATEGORY 2	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
MINOR VIOLATION CATEGORY 3	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
MINOR VIOLATION CATEGORY 4	n (%)	X (X.X%)	X (X.X%)	X (X.X%)
etc.				

N: Number of subjects in specified treatment group
n: Number of subjects with data available
%: Percentage based on N

Notes:

- a) Subjects may be counted in more than one major protocol violation category.
- b) Subjects may be counted in more than one minor protocol violation category.

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Table 9. Physical Examination Findings by Body System (Safety set)

Characteristic	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Number of subjects with Abnormal findings at:				
Skin	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Eyes	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Ears-nose-throat	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Breast	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Head&neck	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Lungs	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Heart	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abdomen	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Extremities	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Lymphonodes	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Musculoskeletal	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Peripheral vascular	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Genitourinary	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Other	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

N: Number of subjects in specified treatment group
n: Number of subjects with data available
%: Percentage based on N

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Table 10. Pregnancy test (Safety set)

Characteristic	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Number of subjects with positive pregnancy test	n (%)	XXX(XX.X%)	XXX(XX.X%)	XXX(XX.X%)

N: Number of subjects in specified treatment group
n: Number of subjects with data available
%: Percentage based on N

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Table 11. Medical History (safety set)

	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Number of subjects with any medical history	n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Number of subjects with at least one:				
infections and infestations	n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
neoplasms	n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
blood and lymphatic system	n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
...				
surgical procedures	n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
other	n (%)	XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)

N: Number of subjects in specified treatment group
n: Number of subjects with data available
%: Percentage based on N

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Table 12. Concomitant and Prior Medication (Safety set)

Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Number of subjects with any prior medications	n (%) XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)
Number of subjects with any concomitant medications	n (%) XXX (XX.X%)	XXX (XX.X%)	XXX (XX.X%)

N: Number of subjects in specified treatment group
n: Number of subjects with data available
%: Percentage based on N

Notes:

- a) Prior medications are defined as those starting and ending prior to the first administration of investigational study medication.
- b) Concomitant medications are defined as medications started at or after first administration of investigational study medication and include medications started prior to the first administration of investigational study medication but continued during the study.

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8.2.1.2 Efficacy Analysis

Table 13. Primary Efficacy Variable at Each Study Visit (ITT Analysis Set)

Plasma Concentration of Coenzyme Q10				
Visit	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Visit 2	n	XX	XX	XX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile			
	Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX
Visit 3	n	XX	XX	XXX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile			
	Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX
Visit 4	n	XX	XX	XXX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile			
	Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX
Visit 5	n	XX	XX	XXX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile			
	Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX

N: Number of subjects in specified treatment group

n: Number of subjects with data available

SD = Standard deviation

CV = Coefficient of variation


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Table 14. Plasma concentration of coenzyme Q10 by gender (ITT Analysis Set)

Visit	Statistic	Female (N=XXX)	Male (N=XXX)	Total (N=XXX)
Visit 2	n	XX	XX	XXX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile			
	Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX
Visit 3	n	XX	XX	XXX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile			
	Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX
Visit 4	n	XX	XX	XXX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile			
	Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX
Visit 5	n	XX	XX	XXX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile			
	Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX

N: Number of subjects in specified treatment group
n: Number of subjects with data available
SD = Standard deviation
CV = Coefficient of Variation


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Table 15. Change versus baseline by Treatment (ITT Analysis Set)

Plasma concentration Of Coenzyme Q10	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Change from baseline at Visit 3	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Change from baseline at Visit 4	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Change from baseline at Visit 5	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X

N: Number of subjects in specified treatment group
n: Number of subjects with data available
SD = Standard deviation
Note: a) Baseline is defined as value observed at Visit 2.


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Table 16. Pharmacokinetic Parameters by Treatment (ITT Analysis Set)

Parameter	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
AUC _t	n	XX	XX	XXX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX
	C _{max}	n	XX	XX
Mean (SD)		X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
95% CI		XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
CV (%)		XX.XX	XX.XX	XX.XX
Median		X.XXX	X.XXX	X.XXX
Interquartile Range		XX.X	XX.X	XX.X
Min/Max		XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX
T _{max}		n	XX	XX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX
	t _(1/2)	n	XX	XX
Mean (SD)		X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
95% CI		XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
CV (%)		XX.XX	XX.XX	XX.XX
Median		X.XXX	X.XXX	X.XXX
Interquartile Range		XX.X	XX.X	XX.X
Min/Max		XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX

N: Number of subjects in specified treatment group
n: Number of subjects with data available
SD = Standard deviation
CV = Coefficient of Variation

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Table 17. Confidence Interval and Results of T-test for Primary Efficacy Variable (ITT Analysis Set)

Parameter	Mean	95% Confidence Interval		Difference between the means of the two groups	P-value
		Lower Limit	Upper Limit		
AUC _t	X.XX	X.XX	X.XX	X.XX	X.XXXX
C _{max}	X.XX	X.XX	X.XX	X.XX	X.XXXX
T _{max}	X.XX	X.XX	X.XX	X.XX	X.XXXX
t _(1/2)	X.XX	X.XX	X.XX	X.XX	X.XXXX

Notes:

P-values are referred to a Student t-test comparing means of the two groups. A p-value less than 0.05 indicates a statistically significant difference.

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8.2.1.3 Safety Analysis

Table 18. Summary of Adverse Events in the Single Dose Phase (Safety set)

Characteristic	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Number of Subjects With at Least One AE	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of Subjects With at Least One related AE	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of Subjects With at Least One serious AE	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of Subjects With at Least One severe AE	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of Subjects who Prematurely Terminated the Study Due to AE	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of AEs	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of serious AEs	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of related AEs	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of severe AEs	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of deaths	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)

N: Number of subjects in specified treatment group

n: Number of subjects with data available

#: Percentage based on N

Notes: a) serious AE are AE with seriousness recorded as "yes";

b) related AE are AE with relationship with study device recorded as "definitive", "probable", "possible";

c) severe AE are AE with severity recorded as "severe", "life threatening or disabling";

d) Subjects who prematurely terminated the Study Due to AE are defined as those subjects with an adverse event for which the reason for early termination in the CRF end of study has been recorded as "adverse event".


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Table 19. Summary of Adverse Events in the Multidose Phase (Safety set)

Characteristic	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Number of Subjects With at Least One AE	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of Subjects With at Least One related AE	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of Subjects With at Least One serious AE	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of Subjects With at Least One severe AE	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of Subjects who Prematurely Terminated the Study Due to AE	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of AEs	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of serious AEs	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of related AEs	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of severe AEs	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)
Number of deaths	n (%)	XXX (X.X%)	XXX (X.X%)	XXX (X.X%)

N: Number of subjects in specified treatment group

n: Number of subjects with data available

%; Percentage based on N

Notes: a) serious AE are AE with seriousness recorded as "yes";

b) related AE are AE with relationship with study device recorded as "definitive", "probable", "possible";

c) severe AE are AE with severity recorded as "severe", "life threatening or disabling";

d) Subjects who prematurely terminated the Study Due to AE are defined as those subjects with an adverse event for which the reason for early termination in the CRF end of study has been recorded as "adverse event".

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Table 20. AEs of Special Interest in the Single Dose Phase (Safety set)

	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Total	n (%)	XXX (XXX.X%)	XX (XXX.X%)	XXX (XXX.X%)
Insomnia	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Elevated levels of liver enzymes	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Rash	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Nausea	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Upper abdominal pain	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Dizziness	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Sensitivity to light	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Irritability	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Headache	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Heartburn	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Fatigue	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

N: Number of subjects in specified treatment group

n: Number of subjects with data available

%; Percentage based on N

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Table 21. AEs of Special Interest in the Multidose Phase (Safety set)

	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Total	n (%)	XXX (XXX.X%)	XX (XXX.X%)	XXX (XXX.X%)
Insomnia	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Elevated levels of liver enzymes	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Rash	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Nausea	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Upper abdominal pain	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Dizziness	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Sensitivity to light	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Irritability	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Headache	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Heartburn	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Fatigue	n (%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

N: Number of subjects in specified treatment group
n: Number of subjects with data available
%: Percentage based on N

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Table 22. AEs by Relationship (Safety set)

Statistic	Number of Subjects With at Least One AE in the single dose phase	Number of Subjects With at Least One AE in the multidose phase
TREATMENT A (N=XXX)		
Definitive	n (%) XX (XX.X%)	XX (XX.X%)
Probable	n (%) XX (XX.X%)	XX (XX.X%)
Possible	n (%) XX (XX.X%)	XX (XX.X%)
Unlikely	n (%) XX (XX.X%)	XX (XX.X%)
None	n (%) XX (XX.X%)	XX (XX.X%)
TREATMENT B (N=XXX)		
Definitive	n (%) XX (XX.X%)	XX (XX.X%)
Probable	n (%) XX (XX.X%)	XX (XX.X%)
Possible	n (%) XX (XX.X%)	XX (XX.X%)
Unlikely	n (%) XX (XX.X%)	XX (XX.X%)
None	n (%) XX (XX.X%)	XX (XX.X%)
TOTAL (N=XXX)		
Definitive	n (%) XX (XX.X%)	XX (XX.X%)
Probable	n (%) XX (XX.X%)	XX (XX.X%)
Possible	n (%) XX (XX.X%)	XX (XX.X%)
Unlikely	n (%) XX (XX.X%)	XX (XX.X%)
None	n (%) XX (XX.X%)	XX (XX.X%)

N: Number of subjects in specified treatment group
n: Number of subjects with data available
%: Percentage based on N

Notes:

- a) if a subject experienced more than one AE with the same event/diagnosis/sign/symptom, the AE with the strongest relationship will be counted.

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Table 23. AEs by Severity (Safety set)

	Stat- istic	Treatment A (N=XXX)			Treatment B (N=XXX)			Total (N=XXX)		
		Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe
Number of Subjects										
With at Least One AE										
In the single										
dose phase	n (%)	X(X.X%)	X(X.X%)	X(X.X%)	X(X.X%)	X(X.X%)	X(X.X%)	X(X.X%)	X(X.X%)	X(XX.X%) (X.X%)
Number of Subjects										
With at Least One AE										
In the multidose										
phase	n (%)	X(X.X%)	X(X.X%)	X(X.X%)	X(X.X%)	X(X.X%)	X(X.X%)	X(X.X%)	X(XX.X%) (X.X%)	

N: Number of subjects in specified treatment group

n: Number of subjects with data available

#: Percentage based on N

Notes: If a subject experienced more than one AE with the same event/diagnosis/sign/symptom, the AE with the maximum severity will be counted.

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Table 24. Summary of Vital Signs (Safety set)

Characteristic	Statistic	Treatment A (N=XXX)	Treatment B (N=XXX)	Total (N=XXX)
Parameter (unit)				
Visit 1	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Visit 2 (Baseline)	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Visit 3	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Absolute Change from baseline at Visit 3	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Relative Change from baseline at Visit 3	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Visit 4	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Absolute Change from baseline at Visit 4	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Relative Change from baseline at Visit 4	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Visit 5	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Absolute Change from baseline at Visit 5	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Relative Change from baseline at Visit 5	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X

N: Number of subjects in specified treatment group

n: Number of subjects with data available

SD = Standard deviation

Note: a) Baseline is defined as value observed at Visit 2.


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Table 25. Plasma Concentration of Q10 in the Single Dose Phase (ITT Analysis Set)

Plasma Concentration of Coenzyme Q10

Visit 1	Statistic	Total (N=XXX)
Visit 1 - H0	n	XX
	Mean (SD)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X
	CV (%)	XX.XX
	Median	X.XXX
	Interquartile	
	Range	XX.X
	Min/Max	XX.XX/XX.XX
Visit 1 - H1	n	XX
	Mean (SD)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X
	CV (%)	XX.XX
	Median	X.XXX
	Interquartile	
	Range	XX.X
	Min/Max	XX.XX/XX.XX
Visit 1 - H2	n	XX
	Mean (SD)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X
	CV (%)	XX.XX
	Median	X.XXX
	Interquartile	
	Range	XX.X
	Min/Max	XX.XX/XX.XX
Visit 1 - H4	n	XX
	Mean (SD)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X
	CV (%)	XX.XX
	Median	X.XXX
	Interquartile	
	Range	XX.X
	Min/Max	XX.XX/XX.XX
Visit 1 - H8	n	XX
	Mean (SD)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X
	CV (%)	XX.XX
	Median	X.XXX
	Interquartile	
	Range	XX.X
	Min/Max	XX.XX/XX.XX
Visit 1 - H12	n	XX
	Mean (SD)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X
	CV (%)	XX.XX
	Median	X.XXX
	Interquartile	
	Range	XX.X
	Min/Max	XX.XX/XX.XX

n: Number of subjects with data available
SD = Standard deviation
CV = Coefficient of Variation


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Table 26. Plasma Concentration of Q10 in the Single Dose Phase by gender (ITT Analysis Set)

Visit	Statistic	Female (N=XXX)	Male (N=XXX)	Total (N=XXX)
Visit 1 - H0	n	XX	XX	XXX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile			
	Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX
Visit 1 - H1	n	XX	XX	XXX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile			
	Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX
Visit 1 - H2	n	XX	XX	XXX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile			
	Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX
Visit 1 - H4	n	XX	XX	XXX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile			
	Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX
Visit 1 - H8	n	XX	XX	XXX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile			
	Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX
Visit 1 - H12	n	XX	XX	XXX
	Mean (SD)	X.XXX (XX.XX)	X.XXX (XX.XX)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X	XX.X/XX.X	XX.X/XX.X
	CV (%)	XX.XX	XX.XX	XX.XX
	Median	X.XXX	X.XXX	X.XXX
	Interquartile			
	Range	XX.X	XX.X	XX.X
	Min/Max	XX.XX/XX.XX	XX.XX/XX.XX	XX.XX/XX.XX

N: Number of subjects in specified treatment group
n: Number of subjects with data available
SD = Standard deviation
CV = Coefficient of Variation


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Table 27. Change versus baseline by gender (ITT Analysis Set)

Plasma concentration Of Coenzyme Q10	Statistic	Female (N=XXX)	Male (N=XXX)	Total (N=XXX)
Change from baseline at Visit 1 - H1	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Change from baseline at Visit 1 - H2	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Change from baseline at Visit 1 - H4	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Change from baseline at Visit 1 - H8	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X
Change from baseline at Visit 1 - H12	n	XX	XX	XX
	Mean (SD)	X.X (X.XX)	X.X (X.XX)	X.X (X.XX)
	Median	X.X	X.X	X.X
	Min/Max	X.X/X.X	X.X/X.X	X.X/X.X

N: Number of subjects in specified treatment group

n: Number of subjects with data available

SD = Standard deviation

Note: a) Baseline is defined as value observed at Visit 1 - H0.



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Table 28. Pharmacokinetic Parameters in the Single Dose Phase (ITT Analysis Set)

Parameter	Statistic	Total (N=XXX)
AUC _t	n	XX
	Mean (SD)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X
	CV (%)	XX.XX
	Median	X.XXX
	Interquartile	
	Range	XX.X
	Min/Max	XX.XX/XX.XX
C _{max}	n	XX
	Mean (SD)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X
	CV (%)	XX.XX
	Median	X.XXX
	Interquartile	
	Range	XX.X
	Min/Max	XX.XX/XX.XX
T _{max}	n	XX
	Mean (SD)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X
	CV (%)	XX.XX
	Median	X.XXX
	Interquartile	
	Range	XX.X
	Min/Max	XX.XX/XX.XX
t _(1/2)	n	XX
	Mean (SD)	X.XXX (XX.XX)
	95% CI	XX.X/XX.X
	CV (%)	XX.XX
	Median	X.XXX
	Interquartile	
	Range	XX.X
	Min/Max	XX.XX/XX.XX

n: Number of subjects with data available
SD = Standard deviation
CV = Coefficient of Variation

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8.2.2 Listings

Listing 1. Subjects Who Prematurely Terminated the Study Prior to Randomization

Total Set (Screening failures only)

Screening number	Date of Study Termination	Primary Reason of Premature Termination	Comment, if applicable
XXXXXXXX 099-9999	DDMMYYYY 22SEP2007	XXXXXXXXXXXXXXXXXXXX Lost to follow-up	XX Subject did not come to Visit 1

etc.

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Listing 2. Randomized Subjects Who Prematurely Terminated the Study


All Randomized Subjects

Screening number	Treatment group	Last visit attended	Study Termination (Last Contact):		Last study Medication administration:		Primary Reason of Premature Termination	Comment, if applicable
			Date	Treatment Day	Date	Treatment Day		
XXXXXXXX 099-9999	XXXXXXXXXXXX Treatment A	XX V2	DDMMYYYY 22SEP2007	XX 20	DDMMYYYY 17SEP2007	XX 15	XXXXXXXXXXXXXXXXXXXX Adverse Event	XXXXXXXXXXXXXXXXXXXXXXXXXXXX

etc.

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Listing 7. Treatment Compliance

Safety analysis set

Screening Number	Treatment Group	Visit	Was the investigational product delivered to the subject?	Was the investigational product taken correctly?
XXXXXXXX	XXXXXXXX	XXX	XXX	XXX
XXXXXXXX	Treatment A	Visit 2	/	YES

etc.

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Listing 8. Compliance to study procedures [1]

Safety analysis Set

Screening Number	Treatment Group	Visit	Was the subject fasting for at least 10h before IP intake	Was the device taken by subject	Was the blood sampling taken	Was the V1-V2 diary given to subject	Was the V1-V2 diary checked and retrieved	Was the V2-V5 diary given to subject
XXXXXXXX	XXXXX	Visit X	XXX	XXX	XXX	XXX	XXX	XXX
XXXXXXXX	Treatment A	Visit X	YES	YES	YES	YES	YES	YES

etc.

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Listing 9. Compliance to study procedures [2]

Safety analysis Set

Screening Number	Treatment Group	Visit	Was the V2-V5 diary given back to subject	Was the V2-V5 diary checked	Was the investigational product retrieved from subject	Was the V2-V5 diary retrieved from subject
XXXXXXXX	XXXXX	Visit X	XXX	XXX	XXX	XXX
XXXXXXXX	Treatment A	Visit X	YES	YES	YES	YES

etc.

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Listing 13. Medical History

Total Set

Screening Number	Treatment Group	Disease category	Details	Start date	Stop date	Ongoing
XXXXXXXX 099-9999 etc.	XXXXXX Treatment A	XXXXXXXXXX hepatobiliary	XXXXXXXXXXXXXXXXXX ILATERAL	DDMMYYYY --JAN2005	DDMMYYYY --FEB2005	No

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Listing 14. Inclusion Criteria


Total Set

Screening Number	Eligibility
XXXXXXXX 099-9999 etc.	XXX Yes

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Listing 15. Exclusion Criteria

Total Set

Screening Number	Eligibility
XXXXXXXX	XXX
099-9999	YES
etc.	


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Listing 16. Listing of Primary Efficacy Variable

ITT Analysis Set

Screening Number	Treatment Group	Visit	Plasma concentration of coenzyme Q10
XXXXXXXXXX	XX	XXXX	XX
099-9999	A	Visit 2	XX
...			

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Listing 17. Listing of Pharmacokinetic parameters

ITT Analysis Set

Screening Number	Treatment Group	AUC_t	C_max	T_max	Clearance	Volume of distribution	T_1/2
XXXXXXXXXX 099-9999	XX A	XXXX XXXX	XXXX XXXX	XXXX XXXX	XXXX XXXX	XXXX XXXX	XXXX XXXX
Etc.							


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Listing 18. Listing of AEs: General

Safety Analysis Set

Screening Number	Treatment Group	Gender/ Age/Ethnicity	Event	Outcome	Severity	Treatment	Relationship with study device	Action Taken	Pattern	Serious	Start date	End date
XXXXXXXXXX 099-9999	XX A	XX/XX/XXX F/52/ASIAN	XXXXXXXXX FIBROMYOMA	XXX UNKNOWN	XXXX MODERATE	XXXX NONE	XXXX NONE	XXXX NONE	XXXX OTHER	XX NO	DDMMYYYY 23FEB2006	DDMMYYYY 25FEB2006
...												

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Listing 19. Listing of Deaths

Safety analysis Set


Screening Number	Treatment Group	Gender/Age/ Ethnicity	Event	Date Started /Date Stopped /Treatment Days	Severity /Serious	Drug Event Relation-ship	Action Taken With Study Medication/ Concomitant Therapy Introduced	Outcome /Led to Study Termina-tion
XXXXXXXXXX	XXXXXXXXXXXXXXXXXX	X/XX/XXXXX/ XXXXXXXXXX	XXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXX	DDMMYYYY/ DDMMYYYY/ XX/XX	XXXX/XX	XXXXXXXXXX	XXXXXXXXXX/ XXXXXXXXXX	XXXXXXXX/ XX
099-9999	Treatment A	F/54/ HISPANIC	FIBROMYOMA RIGHT SIDE	23FEB2006/ ONGOING/ 25	MODERATE /YES	UNRELATED	NA/NO	UNKNOWN/ YES

Notes: a) Death is defined as a fatal outcome of an (S)AE.

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Listing 20. Listing of SAEs

Safety Analysis Set

Screening Number	Treatment Group	Gender/ Age/Ethnicity	Event	Outcome	Severity	Treatment	Relationship with study device	Action Taken	Pattern	Start date	End date
XXXXXXXXXX	XX	XX/XX/XXX	XXXXXXXX	XXX	XXXX	XXXX	XXXX	XXXX	XXXX	DDMMYYYY	DDMMYYYY
099-9999	A	F/52/ASIAN	FIBROMYOMA	UNKNOWN	MODERATE	NONE	NONE	NONE	OTHER	23FEB2006	25FEB2006
...											


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Listing 21. Listing of AEs Leading to Study Termination

Safety Analysis Set

Screening Number	Treatment Group	Gender/ Age/Ethnicity	Event	Outcome	Severity	Treatment	Relationship with study device	Action Taken	Pattern	Serious	Start date	End date
XXXXXXXXXX	XX	XX/XX/XXX	XXXXXXXX	XXX	XXXX	XXXX	XXXX	XXXX	XXXX	XX	DDMMYYYY	DDMMYYYY
099-9999	A	F/52/ASIAN	FIBROMYOMA	UNKNOWN	MODERATE	NONE	NONE	NONE	OTHER	NO	23FEB2006	25FEB2006
...												

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Listing 22. Vital Signs in the Multidose Phase

Safety analysis Set

Screening Number	Treatment Group	Assessment Date	Visit	Sitting SBP (mmHg)	Sitting DBP (mmHg)	Heart Rate (beats/min)	Respiratory Rate (acts/min)	Temperature (kg)
XXXXXXXXXX	Treatment A	DDMMYYYY	Visit X	XXX	XXX	XXX	XXX	XXX
		DDMMYYYY	Visit X	XXX	XXX	XXX	XXX	XXX
		DDMMYYYY	Visit X	XXX	XXX	XXX	XXX	XXX
		DDMMYYYY	Visit X	XXX	XXX	XXX	XXX	XXX
		DDMMYYYY	Visit X	XXX	XXX	XXX	XXX	XXX
		DDMMYYYY	Visit X	XXX	XXX	XXX	XXX	XXX

Etc.

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Listing 23. Vital Signs in the single dose phase

Safety analysis Set

Screening Number	Assessment Date	Visit	Sitting SBP (mmHg)	Sitting DBP (mmHg)	Heart Rate (beats/min)	Respiratory Rate (acts/min)	Temperature (kg)
XXXXXXXXXX	DDMMYYYY	Visit 1	XXX	XXX	XXX	XXX	XXX
XXXXXXXXXX	DDMMYYYY	Visit 1	XXX	XXX	XXX	XXX	XXX

Etc.

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Listing 24. Listing of Plasma Concentration of Q10 in the Single Dose Phase

ITT Analysis Set

Screening Number	Time Point	Plasma concentration of coenzyme Q10
XXXXXXXXXX	XXXX	XX
099-9999	Visit 1 - H1	XX
...		

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Listing 25. Listing of Pharmacokinetic parameters in the Single Dose Phase

ITT Analysis Set

Screening Number	AUC_t	C_max	T_max	Clearance	Volume of distribution	t_1/2
XXXXXXXXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX
099-9999	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX
Etc.						

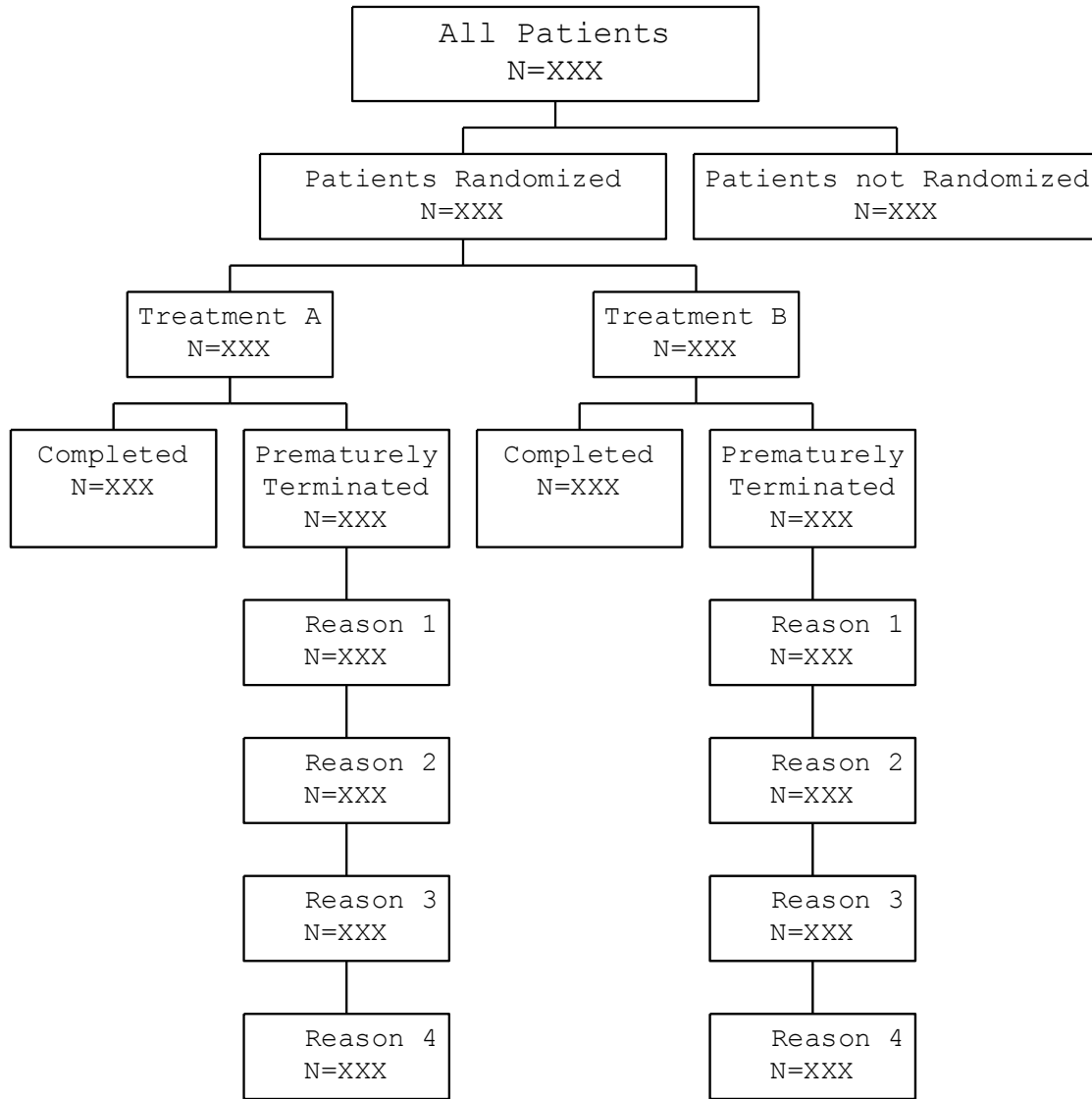
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8.2.3 Figures

Figure 1. Flow Chart of Subjects Disposition




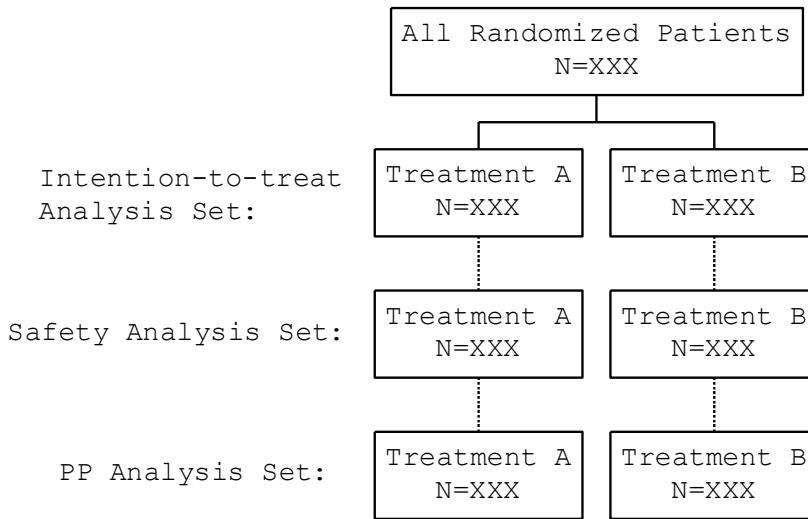
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Figure 2. Flow Chart of Analysis Sets



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Figure 3. Concentration by time plot (ITT Analysis Set)

Figure 4. Concentration by time plot by treatment group (ITT Analysis Set)

Figure 5. Concentration by time plot by gender (ITT Analysis Set)

Figure 6. Concentration by time plot for the single dose phase (ITT Analysis Set)

Figure 7. Concentration by time plot by gender for the single dose phase (ITT Analysis Set)