



Statistical Analysis Plan

**Sojournix, Inc.
SJX-653-006**

A Phase 2, Prospective, Randomized, Double-Blind, Placebo-Controlled Clinical Study to Assess the Efficacy, Safety, Tolerability, and Pharmacokinetics of SJX-653 in Postmenopausal Women with Moderate to Severe Vasomotor Symptoms

Protocol Version 2.0 and 2.1: 01 JUL 2020 (Amendment 1.0)

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Approval

Upon review of this document, including the table, listing, and figure shells, the undersigned approves the statistical analysis plan. The analysis methods and data presentation are acceptable.

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LIST OF ABBREVIATIONS

Abbreviation	Full Notations
ADL	activities of daily living
ADME	absorption, distribution, metabolism and excretion
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
AUC	area under the concentration-time curve
AUC(0-24)	area under the concentration-time curve from time 0 to 24 hours
BMI	body mass index
BP	blood pressure
C _{max}	maximum plasma concentration
CSR	Clinical study report
C _{trough}	trough concentration
CYP	cytochrome P450
CYP3A4	cytochrome P450 3A4
DMC	Data Monitoring Committee
ECG	Electrocardiogram
eCRF	electronic case report form
EDC	electronic data capture
eDiary	electronic diary
eGFR	estimated glomerular filtration rate
eITT	exploratory intent-to-treat
EOS	End of Study
EOT	End of Treatment
ePRO	electronic subject reported outcomes
ET	Early Termination
FSH	follicle-stimulating hormone
GCP	Good Clinical Practice
GGT	gamma glutamyl transferase
GnRH	gonadotropin-releasing hormone
HbA1c	glycosylated hemoglobin
HBsAg	hepatitis B surface antigen
HF	hot flash
HFRDIS	Hot Flash Related Daily Interference Scale
HT	hormone therapy
IB	Investigator Brochure
ICF	informed consent form
ICH	International Council for Harmonisation



IEC	Independent Ethics Committee
INR	international normalized ratio
IRB	Institutional Review Board
IRT	Interactive Response Technology
ISI	Insomnia Severity Index
ITT	intent-to-treat
KNDy	kisspeptin, neurokinin B, and dynorphin
LFT	Liver function test
LH	luteinizing hormone
MEDRA	Medical Dictionary for Regulatory Activities
MENQOL	Menopause-Specific Quality of Life
MMRM	Mixed effect Model Repeat Measurement
MS-VMS	moderate to severe vasomotor symptoms
NK3R	neurokinin-3 receptor
NKB	neurokinin B
OOR	out of range
OTC	over the counter
PD	pharmacodynamic(s)
PGI-C	Subject's Global Impression of Change
PK	pharmacokinetic(s)
PMW	postmenopausal women
PSQI	Pittsburgh Sleep Quality Index
QD	once daily
QoL	Quality of Life
QTcF	QT interval corrected by Fridericia formula
RT-PCR	Reverse transcription polymerase chain reaction
SAE	serious adverse event
SAF	safety population
SAP	statistical analysis plan
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SD	standard deviation
SSRI	selective serotonin reuptake inhibitor
SNRI	serotonin and norepinephrine reuptake inhibitor
SUSAR	Suspected Unexpected Serious Adverse Reactions
t _{1/2}	terminal half-life
TEAE	treatment-emergent adverse event
TLF	tables, listings, figures
T _{max}	time to peak plasma concentration
TSH	thyroid-stimulating hormone
ULN	upper limit of normal



VMS vasomotor symptoms



1. INTRODUCTION

This document outlines the statistical methods to be implemented during the analyses of data collected within the scope of Sojournix, Inc. protocol SJX-653-006 [A Phase 2, Prospective, Randomized, Double-Blind, Placebo-Controlled Clinical Study to Assess the Efficacy, Safety, Tolerability, and Pharmacokinetics of SJX-653 in Postmenopausal Women with Moderate to Severe Vasomotor Symptoms]. The purpose of this plan is to provide specific guidelines from which the statistical analyses will proceed. Any deviations from this plan will be documented in the clinical study report (CSR).

2. STUDY DOCUMENTS

The following study documents are used for the preparation of the SAP:

- Protocol version 2.0 and 2.1, 01JUL2020
- Annotated electronic eSource forms: Capture, 24MAR2021;
- Data management plan version 2.0, 18FEB2021

3. STUDY OBJECTIVES

3.1 Primary Objective

The primary objective of the study is to evaluate the effect of oral 20 mg SJX-653 once daily (QD) for 4 weeks in postmenopausal women (PMW) with moderate to severe vasomotor symptoms (VMS) on VMS frequency after 4 weeks of treatment.

3.2 Secondary Objectives

Secondary objectives include:

- Effect of SJX-653 on measures of VMS severity and frequency by study week
- Safety and tolerability of SJX-653
- Pharmacokinetics (PK) of SJX-653

3.3 Exploratory Objectives

Exploratory objectives include:

- Measures of VMS severity and frequency by study day during the first week
- Daytime and nighttime measures of VMS severity and frequency by study week
- Sleep and Quality of Life (QOL)



4. STUDY DESIGN AND PLAN

This is a multicenter, prospective, randomized, double-blind, placebo-controlled, parallel-group, Phase 2 study of SJX-653 in PMW with moderate to severe VMS. It will be conducted at approximately 20 sites in Europe.

PMW with moderate to severe VMS who sign an informed consent will undergo a Screening process for up to 4 weeks including a 14-day Run-in Period. During the Run-in Period (Day -14 to Day -1), subjects will record the frequency and severity of daytime VMS in the hot flash (HF) eDiary for a period of 14 days. These data will determine each subject's Baseline VMS frequency per the Schedule of Assessments in the protocol. Subjects will be trained in the use of the HF eDiary and will be required to complete the HF eDiary on at least 12 days during the 14-day Run-in Period to be eligible for the study. At the end of the Run-in Period, eligibility will be determined by the investigator.

Eligible subjects will be randomized in a 1:1 ratio to the following treatment groups:

- 20 mg SJX-653 (Treatment Group)
- Matching placebo (Placebo Group)

Subjects will receive their randomized study medication QD for 4 weeks. The Treatment Period will be followed by a 2-week Follow-up Period during which subjects must continue to adhere to all protocol restrictions, including prohibited medications and supplements. Data on efficacy, tolerability, safety, PK, and PD will be collected according to the Schedule of Assessments in the protocol. Monitoring of severe acute respiratory syndrome – coronavirus 2019 (SARS-CoV-2) by a validated reverse transcription-polymerase chain reaction (RT-PCR) method will also be conducted prior to and during the study through EOS visit.

Frequency and severity of daytime VMS will be recorded by subjects in the HF eDiary during the day; VMS occurring during the night can be entered into the HF eDiary either during the night or the following morning.

Subjects will complete QoL assessment Hot Flash Related Daily Interference Scale (HFRDIS) on Baseline, Day 14 and at Day 28/End of Treatment (EOT) and Insomnia Severity Index (ISI) at Baseline and (EOT) visits.

PK sampling will occur prior to dosing on Day 28/EOT, and on Day 7, also prior to dosing if possible.

Safety and tolerability will be assessed by adverse event (AE) collection, physical examination, vital signs, 12-lead ECG, and safety laboratory parameters per the Schedule of Assessments included as Table 1 in the protocol.



5. DETERMINATION OF SAMPLE SIZE

Sample size requirements were calculated under the following assumptions for the primary efficacy endpoint:

- One-sided $\alpha=0.025$
- Two sided $\alpha=0.05$
- Target power=80%.
- Unpaired t-test with two treatment arms (placebo and 20 mg SJX-653).
- Pooled standard deviation = 4.0 based on the change from Baseline to Week 4/ET for placebo and 20 mg SJX-653
- Drop-out rate of 12%.
- Mean improvement in placebo group from an average daily frequency of 10 moderate to severe VMS/day to 6.0 moderate to severe VMS/day at Week 4.
- Mean improvement in 20 mg SJX-653 group from an average daily frequency of 10 moderate to severe VMS/day to 3.0 moderate to severe VMS/day at Week 4

Under these assumptions, approximately 29 subjects per group need to complete the study to detect a mean 3.0 moderate to severe VMS /day improvement for 20 mg SJX-653 over placebo in the ITT Population. Approximately 66 (33+33) eligible subjects will initially be randomized 1:1 (20 mg SJX-653: placebo) to achieve 58 (29+29) subjects reaching Week 4.

6. GENERAL ANALYSIS CONSIDERATIONS

The statistical analyses will be reported using summary tables, listings, and figures (TLFs). The International Council for Harmonisation (ICH) numbering convention will be used for all TLFs.

Continuous variables will be summarized with means, standard deviations, medians, minimums, and maximums. Other summaries (e.g., 95% confidence intervals) may be used as appropriate and will be mentioned in the respective sections.

Categorical variables will be summarized by counts and by percentage of subjects in corresponding categories. Percentages for missing values are omitted and do not account for the percent calculation of other categories. Percentages are routinely based on the total category count excluding the missing category if not otherwise mentioned. Percentages showing a rate relative to the total number of subjects in this group are given in special tables (e.g., adverse event [AE] tables). Footnotes will specify the percent basis in those cases.

All summary tables will be presented by treatment group and will also include a total column.



Individual subject data obtained from the eSource forms and external vendors (e.g., central clinical laboratory) will be presented in data listings as identified in Sections 9 and 13.

The analyses described in this plan are considered a priori, in that they have been defined prior to breaking the blind.

Any analyses performed subsequent to breaking the blind will be considered post hoc and exploratory. Post hoc analyses will be labeled as such on the output and identified in the CSR.

All analyses and tabulations will be performed using SAS® software Version 9.4 or higher unless otherwise noted. Tables and listings will be presented in RTF format. Upon completion, all SAS® programs will be validated by an independent programmer. In addition, all program output will undergo a senior level statistical review. The validation process will be used to confirm that statistically valid methods have been implemented and that all data manipulations and calculations are accurate. Checks will be made to ensure accuracy, consistency with this plan, consistency within tables, and consistency between tables and corresponding data listings. Upon completion of validation and quality review procedures, all documentation will be collected and filed by the project statistician or designee.

7. NOTATION OF TREATMENT GROUPS AND VISITS

Notation of treatment groups

The following notation of **treatment groups** will be used throughout the report:

<i>Full notation (as used in the study protocol)</i>	<i>Notation as used throughout all tables, listings and figures</i>
20 mg SJX-653 Placebo	20 mg SJX-653 Placebo



Visit terminology

<i>Week</i>	<i>Day</i>	<i>Visit</i>	<i>Notation as used throughout all tables, listings and figures</i>
Week -4 through -1	Day -30 to -1	V1 (Screening)	Screening/Run-In
Week 1	Day 1	V2 (Baseline)	Baseline
Week 1	Day 2 to 7	V3	Day 7
Week 2	Day 8 to 14	V4	Day 14
Week 4	Day 15 to 28	V5	Day 28 / EOT
Week 6	Day 29 to 42	V6	Day 42 / EOS

Days are measured from date of randomization. Study days corresponding to measurements are calculated as:

- Assessment date – date of randomization + 1, if assessment date is on or after the date of randomization.
- Assessment date – date of randomization, if measurement date is before the date of randomization.

8. ANALYSIS SETS

The study was terminated early (see Section 14), and therefore only a safety population is defined. The following population will be used for safety summaries:

- Safety population will include all subjects who receive at least one dose of study drug (Investigational drug or placebo). Treatment assignment will be based on treatment randomization.

9. STUDY POPULATION

9.1 Subject Disposition

Subject disposition information will be summarized for all subjects by treatment group. Summaries will include: the number of subjects screened under protocol Version 2.0 and 2.1, the number of enrolled (randomized) subjects, the number of subjects in the safety population, the number of subjects discontinuing the study, and the primary reason for discontinuation.



9.2 Protocol Deviations

Protocol deviations will be evaluated as per the clinical database and additionally as tracked by operational study team members.

Protocol deviations due to COVID-19 will be summarized by treatment group. Missed assessments due to COVID-19 will be reported in a data listing.

9.3 Demographic and Baseline Characteristics

Demographic and baseline characteristics will be summarized descriptively for the safety population. Demographic characteristics will include age, ethnicity, and race. Age will be calculated in years relative to the informed consent date. Baseline characteristics will include height, weight, and body mass index (BMI).

9.4 Prior and Concomitant Medications

Prior and concomitant medication verbatim terms in the eSource forms will be mapped to Anatomical/Therapeutic/Chemical (ATC) class and preferred names using the WHODrug global dictionary (Version Sep, 2020).

Prior medications are those medications that started before the initial dose of study drug. Concomitant medications are those medications that started after the initial dose of study drug or medications that started before the initial dose of study drug and continued during the treatment period. If no classification to prior and/ or concomitant can be done, the medication will be considered as both prior and concomitant. Concomitant medications will be listed.

SARS-CoV2 test results and antibodies will be listed.

10. EFFICACY ANALYSES

Not applicable. See Section 14.

10.1 Handling of Dropouts or Missing Data

10.1.1 Missing Safety Data

When tabulating AE data, partial dates will be imputed as follows.

- If the day of the month is missing, the onset day will be set to the first day of the month unless it is the same month and year as study treatment. In this case, to conservatively report the event as treatment-emergent, the onset date will be assumed to be the first date of treatment.



- If the onset day and month are both missing, the day and month will be assumed to be January 1, unless the event occurred in the same year as the study treatment. In this case, the event onset will be coded to the first date of treatment in order to conservatively report the event as treatment-emergent. A missing onset date will be coded as the first day of treatment.
- Listings will present all data as reported (i.e., without imputations).

10.2 Interim Analysis and Data Monitoring

An independent Data Monitoring Committee (DMC) will be established for this study. Members of the DMC will be independent of the study Investigators and the sponsor. The DMC will comprise of relevant medical experts in the following disciplines: women's health specialist with experience in management of and clinical research in vasomotor symptoms, clinical drug development in women's health, hepatology. The DMC will also include an independent statistician who will have access to the clinical database and the randomization code. The DMC will review safety data at regular intervals according to the DMC Charter. The DMC Charter will establish meeting frequency, scope and method of data review, maintenance of blind, and the decision-making process, prior to the start of the study. In the event that potential safety issues are identified, the DMC may recommend modification of the study design or study termination, which will be communicated to the Investigators, Institutional Review Boards/Independent Ethics Committees (IRBs/IECs), and regulatory agencies by the Sponsor, in accordance with legal and regulatory requirements. The DMC Charter is finalized in synSOJd_DMC Charter_V2_16JUL2020_Final.doc.pdf.

There are no planned interim efficacy analyses for this study.

10.3 Multicenter Studies

This is multicenter study, with approximately 20 centers participating in the study. Approximately 66 subjects will be randomized, leading to approximately 3 subjects per center.

This expected low number of subjects at some centers does not allow center to be included as a covariate in the statistical model.

11. METHODS OF EFFICACY ANALYSIS

Not applicable. See Section 14.

12. PHARMACOKINETIC ANALYSES

PK sampling will occur prior to dosing on Day 28 (EOT), and on Day 7, also prior to dosing if possible. Trough plasma concentrations of SJX-653 and its 2 metabolites M2 and M3 in steady state will be reported by the PK laboratory. PK data will not be summarized or tabulated.



13. SAFETY ANALYSES

All safety analyses will be based on the safety population defined as all randomized subjects who took at least one dose of study drug, will be descriptive only, and will be presented by treatment group. No inferential testing will be performed. Missing safety data will not be imputed.

13.1 Extent of Exposure

Study drug exposure based on expected exposure will be summarized by treatment group. Expected exposure will be derived as follows:

- Subjects who complete the Day 28/EOT visit: $(64 \text{ tablets dispensed} - \text{number tablets returned} - \text{number tablets lost}) / (2 \times 28)$
- Subjects who prematurely discontinue prior to Day 28/EOT: $(64 \text{ tablets dispensed} - \text{number tablets returned} - \text{number tablets lost}) / 2 \times (12\text{FEB}2021 - \text{date of first dose} + 1)$

Note: 12FEB2021 is the date of sponsor notification of sites of study termination for safety reasons.

13.2 Adverse Events

All AE summaries will be restricted to treatment-emergent AEs (TEAEs), which are defined as those AEs that occurred after dosing and those existing AEs that worsened after start of dosing. If it cannot be determined whether the AE is treatment-emergent due to a partial onset date, then it will be counted as such. Verbatim terms in the eSource forms will be mapped to preferred terms and system organ classes using the Medical Dictionary for Regulatory Activities (MedDRA) (version 23.0).

Each AE summary will be displayed by treatment group. Summaries that are displayed by system organ class and preferred terms will be ordered by descending subject count in the total column by system organ class and preferred term. Summaries of the following types will be presented:

- Overall summary of TEAEs.
- Subject incidence of TEAEs and total number of unique TEAEs by MedDRA system organ class and preferred term.
- Subject incidence of TEAEs of special interest and total number of unique TEAEs by MedDRA system organ class and preferred term.
- Subject incidence of treatment-related TEAEs and total number of unique TEAEs by MedDRA system organ class and preferred term.
- Subject incidence of serious TEAEs and total number of unique serious TEAEs by MedDRA system organ class and preferred term.



- Subject incidence of TEAEs leading to study discontinuation and total number of unique TEAEs leading to study discontinuation by MedDRA system organ class and preferred term.

13.3 Clinical Laboratory Evaluation

Laboratory samples will be analyzed by a central laboratory. The central laboratory will provide normal reference ranges for the laboratory results and a flag for all abnormal values.

Laboratory safety parameters for hematology, serum chemistry, and urinalysis will be summarized descriptively at baseline and at each post-baseline time point (Day 14, 28/EOT, and Day 42/EOS) and will include change from baseline. Baseline is defined as the last non-missing value prior to first dose of study drug.

Laboratory safety parameters for liver function tests (LFTs) will be summarized descriptively at baseline and at each post-baseline time point (Day 7, Day 14, 28/EOT, and Day 42/EOS) and will include frequency count and percent for each test category. Potential Hy's Law cases will be identified using the common criteria of 2x upper limit normal (ULN) total bilirubin concurrent with 3x ULN aspartate aminotransferase (AST) or alanine aminotransferase (ALT) (whichever is higher) when aspartate aminotransferase (ALP) is < 2x ULN.

Categorical parameters for urinalysis laboratory results will not be summarized but will be presented in a data listing.

13.4 Electrocardiogram

Descriptive statistics at baseline and end of treatment (Day 28) as well as changes from baseline will be summarized for each electrocardiogram (ECG) parameter. Baseline is defined as the last non-missing value prior to first dose of study drug.

13.5 Vital Signs

Vital signs will be summarized using descriptive statistics at baseline and at each post-baseline time point (Day 7, 14, 28/EOT, 42/EOS) and will include change from baseline. Baseline is defined as the last non-missing value prior to first dose of study drug.

13.6 Physical Examination

Physical examination results will be listed.

14. CHANGES TO PROTOCOL-SPECIFIED ANALYSES

Based on the DMC meeting on Thursday Feb 11th and a subsequent internal company meeting, Sojournix terminated the SJX-653-006 study early. At the time of termination, sites were



informed to stop screening and withdraw all subjects from the study. Subjects on treatment were notified to stop dosing immediately.

Due to limited number of randomized subjects, select safety data will be summarized as outlined in Section 13. Efficacy data will not be summarized or tabulated.

15. REFERENCES

None.



16. APPENDICES

APPENDIX A: PRESENTATION OF DATA AND PROGRAMMING SPECIFICATIONS

General

- Specialized text styles, such as bold, italics, borders, shading, superscripted and subscripted text will not be used in tables, figures, and data listings unless they add significant value to the table, figure, or data listing.
- Only standard keyboard characters are to be used in tables and data listings.
- Special characters, such as non-printable control characters, printer-specific, or font-specific characters, will not be used on a table, figure, or data listing.
- Hexadecimal character representations are allowed (e.g., μ , α , β).
- All footnotes will be left justified and at the bottom of a page. Footnotes should be used sparingly and must add value to the table, figure, or data listing.

Tables

- Means and medians will be presented to one more decimal place than the raw data. Standard deviations will be presented to two more decimal places than the raw data. Minimums and maximums will be reported with the same number of decimal places as the raw data.
- Percentages will be presented with two decimal places.
- For frequency counts of categorical variables, categories whose counts are zero will be displayed for the sake of completeness. For example, if none of the subjects discontinued due to "lost to follow-up," this reason will be included in the table with a count of 0. Categories with zero counts will not have zero percentages displayed.
- Percentiles (e.g., 25%, 75%) should be presented to one decimal place more than the raw/derived data.
- The first footnote will be "Source: xxx", where xxx indicates the source listing number(s) and/or source dataset(s) (e.g., ADaM).

Listings

- If not otherwise specified, all data listings will be sorted by treatment, center, subject number, visit, and date/time as appropriate.
- All date values will be presented in a SAS date (e.g., 29AUG2001) format.
- All observed time values will be presented using a 24-hour clock HH:MM:SS format (e.g., 01:35:45 or 11:26). Seconds will only be reported if they were measured as part of the study.



Standard Calculations

Variables requiring calculation will be derived using the following formulas:

- **Days** – A duration expressed in days between one date (*date1*) and another later date (*date2*) is calculated using the formulas noted below:
$$\text{duration in days} = \text{date2} - \text{date1} + 1$$
- **Months** – A duration expressed in months is calculated using the INTCK function of SAS as follows:
$$\text{duration in months} = \text{intck}(\text{'month'}, \text{'date1'd}, \text{'date2'd}, \text{'continuous'});$$
- **Years** – A duration expressed in years between one date (*date1*) and another later date (*date2*) is calculated as follows:
$$\text{duration in years} = \text{intck}(\text{'year'}, \text{'date1'd}, \text{'date2'd}, \text{'continuous'});$$
- **Change from baseline** – Change from baseline will be calculated as:
$$\text{Change} = \text{post baseline value} - \text{baseline value}$$
- **Percent change from baseline** – Change from baseline will be calculated as:
$$\text{Percent change from baseline} = (\text{post baseline value} - \text{baseline value}) / \text{baseline value} \times 100$$



APPENDIX B: SAS PROGRAMMING QC REQUIREMENTS

Programmer / Validator Review

1. Program Review

- 1.1. **Program name** follows standard naming conventions and is consistent with other study program names.
- 1.2. **Program header** uses standard template with all relevant information completed.
- 1.3. **Program flow** is logical (i.e., header → initialization code → macro variable definitions → format definitions → main body).
- 1.4. **Programmer comments** are included throughout program to describe purpose of individual sections or macros and provide understanding of specific code, if necessary. All comments are clear and up-to-date.
- 1.5. **Hard coding**, if any, is implemented correctly and documented in program header with: date, reason, and reference to sponsor approval. A comment is also inserted at the location of the hard coding.
- 1.6. **SAP Derivation** rules, if any, are followed. Significant deviations from mock table or SAP text are documented in the SAS Program Header.
- 1.7. **Permanent intermediate datasets** utilized as source data have either been fully validated elsewhere or are fully validated within the scope of this QC.
- 1.8. **Program runs** properly and output dataset is generated as intended.

2. SAS Log Review

- 2.1. **Scan of entire log** confirming that each data step and procedure completed properly.
- 2.2. **Critical messages** such as: errors, warnings, merge notes, or uninitialized variables are not found in log. Unavoidable critical messages are verified to not adversely affect the output and the reasons why they are unavoidable are documented.
- 2.3. **Other messages** such as “PUT” or “INFO” messages (e.g., overwritten variables following merge) are handled appropriately, if they are found in log.

3. Output Review

- 3.1. **Output file name** follows standard naming conventions and is consistent with other study output file names.
- 3.2. **Titles and footnotes** are verified against mock table (if available). Discrepancies, including footnotes added for clarification, are noted and verified.
- 3.3. **Column/row header text** is verified against mock table and/or CRF.
- 3.4. **Format and sorting order** are correct relative to mock table and/or CRF.
- 3.5. **Pages breaks** are as intended throughout the document.
- 3.6. **Significant digits** are appropriate for summary results (e.g., mean is one more digit than collected on the CRF, etc.).



- 3.7. **Analysis population totals** are verified as correct based on SAP definitions and are consistent with other tables using the same population(s).
- 3.8. **Inappropriate data:** checked for outliers, invalid numbers, missing results, etc.



1. Verification of Data

1.1. Analysis datasets (ADaM or ADaM-Like)

1.1.1. Programmer

- Each Analysis dataset is opened and data are reviewed for consistency with the protocol, SAP, and/or CRF (no additional QC programming is necessary).

1.1.2. Validator

- Validation is performed against the protocol, SAP, and/or eSource. A spot-check of source data against the output dataset is performed on at least 2 subjects. Each eSource section/form should be populated at least once for the spot-check. If a section/ form is repeated (e.g., at several visits) one repeat per subject has to be spot-checked.

1.2. Tables

1.2.1. Program Review

- Verify that the appropriate datasets, variables, analysis populations, parameters/tests, and visits/timepoints are used.
- Verify that all keyword and positional parameters of the standardized macro call are accurate and are implemented as intended.

1.2.2. Output Review

- All expected data (parameters/tests, visits/timepoints, treatments, totals, etc.) are included on the output.
- Units and the range of values are confirmed to be consistent.
- Percentages are based on the correct denominator and confirmed to not exceed 100%.
- Counts within subgroups or subsets of data are checked for internal consistency (e.g., subset counts do not exceed overall counts).

1.3. Listings

- Listing content is as expected (e.g., listing includes all enrolled subjects, all expected visits, etc.)
- Variables directly from source dataset are spot-checked for accuracy and completeness.
- Derived or calculated variables are compared to corresponding source data and manual calculation for at least 2 subjects are done.



2. Documentation

- 2.1. The Programmer and Validator must document completion of QC (e.g., date of QC and method used) in **TMP-SOP-0205-002 Program Status Document**.
- 2.2. Validator findings and/or comments may be tracked in the Program Status Document along with a description of how the finding was resolved and resolution date.
- 2.3. The following must be retained electronically within the study folder by the Validator as supporting documentation:
 - If a spot-check of subject data is performed, output that clearly identifies the subjects and CRF forms/sections that are checked



APPENDIX C: LIST OF TABLES, LISTINGS, AND FIGURES

The following proposal for section 14 and 16.2 is completed according to ICH E3 guidelines. The ICH heading numbers and description are in **bold**. Minor changes from this planned index do not need to be amended in the SAP.

TABLES, FIGURES AND LISTINGS

Index of Section 14

Table Number	Table Title	Analysis Set
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