STATISTICAL ANALYSIS PLAN

Protocol Title :	Real-world evidence observational study to evaluate performance and safety of intravesical sodium hyaluronate (Cystistat®) in the treatment of patients with interstitial cystitis (IC)/bladder pain syndrome (BPS)
Protocol No.:	CYST-SLZ-7001
Protocol Date:	06APR2022 (Version 1.0)

Prepared By:
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Approver	**Designation**	**Signature**	**Date**

Sponsor Signature

I hereby declare that I have reviewed the statistical analysis plan and agree to its form and content. In addition, I confirm that the outlined statistical analysis plan contains all relevant information for the data analysis to be performed in the Protocol No. CYST-SLZ-7001 study.

Represented by:

Name	Designation	Signature & Date
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Document Creation History:

Version No. of the SAP	Version Date	Author	Description of Modifications from Previous Version
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Table of contents

List of Abbreviations and Definition of Terms

Abbreviation	Definition
AE	Adverse Event
ANCOVA	Analysis of Covariance
BPS	Bladder Pain Syndrome
BPIC-SS	Bladder Pain/Interstitial Cystitis Symptom Score
CBC	Complete Blood Count
CI	Confidence Interval
CRF	Case Report Form
CRO	Contract Research Organization
CSR	Clinical Study Report
EOS	End Of Study
FAS	Full Analysis Set
GCP	Good Clinical Practice
GAG	Glycosaminoglycan
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IC	Interstitial Cystitis
IP	Investigational Product
MDR	Medical Device Regulation
PGA	Patient Global Assessment
PT	Preferred Term
QoL	Quality of Life
SAE	Serious Adverse Events
SAF	Safety population
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
SOP	Standard Operating Procedures
TEAE	Treatment-emergent Adverse Events
VAS	Visual Analogue Scale
WHODD	World Health Organization Drug Dictionary

1.0 INTRODUCTION

This Statistical Analysis Plan (SAP) provides a comprehensive and detailed description of strategy and statistical technique to be used to realize the analysis of data for Viatris protocol CYST-SLZ-7001, "Real-world evidence observational study to evaluate performance and safety of intravesical sodium hyaluronate (Cystistat®) in the treatment of patients with interstitial cystitis (IC)/bladder pain syndrome (BPS)".

The reader of this SAP is encouraged to also read the Clinical Investigation Plan (Protocol) for details on the conduct of this study and the operational aspects of clinical assessments and timing for completing a patient in this study. The purpose of this SAP is to outline the planned analyses to be completed to support the completion of the Clinical Study Report (CSR) for protocol CYST-SLZ-7001. The planned analyses identified in this SAP will be included in regulatory submissions if applicable and/or future manuscripts. In addition, exploratory analyses not necessarily identified in this SAP may be performed to support the clinical development program. Any post-hoc, or unplanned, analyses which are not identified in this SAP and will be performed, will be clearly identified in the respective CSR.

2.0 DESCRIPTION OF THE PROTOCOL

2.1 Protocol Number

CYST-SLZ-7001

2.2 Protocol Title

Real-world evidence observational study to evaluate performance and safety of intravesical sodium hyaluronate (Cystistat®) in the treatment of patients with interstitial cystitis (IC)/bladder pain syndrome (BPS).

2.3 Date

Version 1.0, 06APR2022

2.4 Amendment

None

3.0 STUDY OBJECTIVES AND ENDPOINTS

The study objectives and corresponding endpoints are given below:

3.1 OBJECTIVES	3.2 ENDPOINTS
3.1.1 Primary objective	**3.2.1 Primary endpoint**
To collect data on the performance of Cystistat on patients' overall IC/BPS	Responder rate to treatment at end of treatment or latest at week 12 as indicated by change on a seven-point Patient Global

condition at end of treatment or latest at week 12 in routine clinical practice.	Assessment (PGA) scale where the patient is able to evaluate the overall change in her/his IC/BPS condition as markedly improved, moderately improved, slightly improved, no change, slightly worse, moderately worse or markedly worse. For the primary analysis, a responder is defined as a patient who has experienced an improvement on the PGA scale (i.e., PGA evaluated as markedly improved, moderately improved, or slightly improved. In case of slightly improved, patients will only be considered as responder if the question "Did therapy have a positive effect on your life and would you undergo this treatment again?" is answered with "Yes".).
3.1.2 Secondary objectives	**3.2.2 Secondary endpoints**
• Evaluation of the change of morning voiding volume over time (until month 6)	• Morning voiding volume over time (from patient diaries, until month 6).
• Evaluation of the change of 24-hour urinary frequency and voiding volume (daytime and nighttime) over time (until month 6)	• Total number of voids and total voiding volume (daytime and nighttime) over the last 24 hours (from patient diaries, until month 6)
• Evaluation of change from baseline in Bladder Pain/Interstitial Cystitis Symptom Score (BPIC-SS) (at end of treatment or latest at week 12 and at month 6)	• Change from baseline to end of treatment or latest to week 12 and to month 6 in Bladder Pain/Interstitial Cystitis Symptom Score (BPIC-SS).
• Evaluation of patients' overall IC/BPS condition at month 6 (using the same approach as for the primary objective)	• Percent responders at month 6 as indicated by improvement on the 7-point Patient Global Assessment (PGA) scale using the same responder definition as for the primary endpoint.
• Evaluation of patients' overall IC/BPS condition at end of treatment or latest at week 12 and at month 6 (using the PGA but with an alternative responder definition)	• Percent responders at end of treatment or latest at week 12 and at month 6 as indicated by improvement on the 7-point Patient Global Assessment (PGA) scale using an alternative responder definition (i.e. a responder is defined as a patient who experiences moderate or marked improvement).

• Evaluation of the change from baseline in bladder pain and urinary urgency on Visual Analogue Scale (VAS) (until month 6)	• Change from baseline to end of treatment or latest to week 12 and to month 6 in bladder pain and urinary urgency on Visual Analogue Scale (VAS) scored from 0 to 100.
• Evaluation of the change from baseline in quality of life (QoL) on Visual Analogue Scale (VAS) (until month 6)	• Change from baseline to end of treatment or latest to week 12 and to month 6 in quality of life (QoL) on Visual Analogue Scale (VAS) scored from 0 to 100.
• Evaluation of concomitant IC/BPS and pain medication use (until month 6)	• Use of concomitant IC/BPS and pain medication count (until month 6).
• Evaluation of flares (symptom deterioration) (until month 6)	• Occurrence of flares (documented as adverse events) and additional BPIC-SS (at the time of occurrence) (until month 6).
• Evaluation of premature termination of treatment	• Premature termination of treatment.
• Assessment of tolerability and safety (until month 6)	• Safety assessments: Adverse events and incidents (until month 6).

4.0 STUDY METHODS

4.1 Study Design and Plan

The present study is a prospective, multicenter, non-interventional study to be conducted in several European countries. It is planned to include approximately 15 study sites. The recruitment will be competitive, with a maximum of approximately 15 patients per site.

4.2 Study Initiation and Completion

The study duration for a patient will be approximately 6 months. The observation period for a patient in this study will end approximately 6 months after start of treatment (irrespective of the duration of treatment). If required, treatment will be continued thereafter under regular medical care.

4.3 Selection of Study Population

Approximately 74 female patients with IC/BPS should be included in the study.

4.4 Study Subject Group

There is one group of treatment in the study:

All patients will receive commercially available Cystistat according to the instructions for use.

Cystistat is a clear colourless solution presented in a 50 mL glass vial containing 40 mg sodium hyaluronate. It is manufactured by Mylan [redacted] and distributed by third companies in some countries.

4.5 Study Background

Cystistat is supplied as a 50 mL solution containing 40 mg of sodium hyaluronate. It is indicated for the temporary replacement of the GAG layer in the bladder.

Hyaluronan, the biologic form of hyaluronic acid, is found in numerous tissues in the human body. It is part of interstitial fluids in connective tissues and is also an important contributor to surface barriers. Specifically, the importance of hyaluronan as the predominant substance of the GAG layer that protects the urothelial surface of the urinary bladder has been well investigated and documented.

The benefit of GAG substitution therapy in such cases of GAG layer injury has been well documented in several clinical studies since then. Various investigators have reported clinically significant remission rates for intravesical hyaluronan instillation therapy. Several uncontrolled as well as controlled studies have shown remission rates between 60 and 85%. In addition to its efficacy, Cystistat is known to have a good safety profile with a low level of adverse events.

4.6 Study Rationale

Real world evidence observational studies are considered as an expedient tool to reflect the use of a product under real life conditions. However, due to the known difficulties with the diagnosis of IC/BPS, only clinical sites using state of the art diagnostic measures according to current therapeutic guidelines will be selected for this study.

A previous randomized, placebo-controlled trial with Cystistat showed limitations of using a placebo group. In this study, the initial response rate in the placebo group was higher than in the Cystistat group, with a turnaround of results at a later timepoint. Several possible explanations for these unexpected findings have been published. As the most likely reason for the placebo efficacy the possible beneficial effect from the alkalizing placebo solution has been assumed.

Based on these considerations and on the known difficulties in recruiting high number of patients in this indication, an observational real world evidence study was chosen as the best feasible way to collect additional data to demonstrate the benefit/risk profile of Cystistat and compliance with the safety and performance requirements of the Medical Device Regulation (MDR).

4.7 Schedule of Study Events

There are below scheduled visits in this study:

Baseline Visit: Baseline, before first treatment

Treatment Visits 1-11: All visits during Treatment, Week 1 to 11

End of Treatment or latest week 12 Visit: Visit with assessment of primary endpoint latest Week 12 (Month 3)

Follow up-Visit: Follow-up, approximately Month 6

4.8 Schedule of Visits and Procedures

	Baseline (1)	During treatment	End of treatment (2)	Follow-up (3)
Study Day	Before first treatment	Week 1-11 (as per standard of care)	Latest week 12 (Month 3)	Approximately Month 6
Written informed consent	X			
Demography and medical history (4)	X			
In-/exclusion criteria	X			
Patient Global Assessment of overall IC/BPS condition improvement (5)			X	X
Assessment of BPIC-SS (6)	X		X	X
Assessment of VAS (7)	X		X	X
Instillation of Cystistat (8)		X	X	(X)
Dispense of diary card (9)	X		X	
Review of diary card		X	X	X
Collection of diary card			X	X
Assessment of concomitant medications (10)		X	X	X
Assessment of adverse events, incidents (11)	X	X	X	X

1 Baseline assessments may be performed on the first treatment visit prior to instillation of Cystistat according to routine clinical practice.

2 This assessment will be performed on the last treatment day or latest at week 12; if required, treatment will be continued after week 12 under regular medical care.

3 Follow-up will be performed as an on-site visit if in accordance with routine clinical practice; if not possible as an on-site visit, the information will be collected remotely (e.g., via phone and postal mail) from the patient.

4 Demography and medical history:

- Patients' demographic and anamnestic background data
- Diagnostic criteria of IC/BPS diagnosis
- Previous and current treatments

5 Patient Global Assessment of overall IC/BPS condition improvement: To be completed at end of treatment or latest at week 12 and at month 6.

6 Bladder Pain/ Interstitial Cystitis Symptom Score (BPIC-SS): To be completed prior to the first treatment, at end of treatment or latest at week 12, and at month 6.

7 Visual Analogue Scale (VAS) for bladder pain, urinary urgency, and quality of life (QoL): To be completed prior to first treatment, at end of treatment or latest at week 12, and at month 6.

8 Instillation of Cystistat: Cystistat will be instilled into the bladder according to the instructions for use; the regimen and duration of treatment will depend on the investigators' discretion; each instillation of Cystistat until month 6 will be recorded in the eCRF; the observation period for this study will end approximately at month 6 (irrespective of the duration of treatment); if required, treatment will be continued after month 6 under regular medical care.

9 Diary card: The following assessments are to be filled out by the patient:
- Morning voiding volume once a week, preferably on the treatment day (until end of treatment or latest week 12) and once at month 6
- Urinary voids and the respective volumes over a period of 24 hours once a week, preferably starting the day before the treatment day (until end of treatment or latest week 12) and once at month 6
- Use of concomitant IC/BPS medication, pain medication, and other relevant concomitant medication (until month 6)
- Adverse events (until month 6)

10 The use of concomitant IC/BPS medication, pain medication, and other relevant concomitant medication will be recorded; it is not required to collect all concomitant medication.

11 Adverse events and incidents will be recorded after the first instillation of Cystistat; prior to first instillation of Cystistat only adverse events will be recorded.

5.0 GENERAL CONSIDERATIONS FOR STATISTICAL ANALYSIS

All analysis will be based on CDISC compliant AdAM data (IG version: 1.1) derived from SDTM datasets (IG version 3.3).

The descriptive statistics for continuous variables will be presented with number (n) of non-missing observations, number of missing observations (nmiss), mean, standard deviation (SD), minimum, 5% percentile (P5), lower quartile (Q1), median, upper quartile (Q3), 95% percentile (P95) and maximum (range). For categorical data, number (n) and percentage of observations in the various categories of the endpoint will be presented, where percentage will be based on the total number of patients in the respective population or analysed subgroup if not stated otherwise. Individual patient data listings will also be provided. Depending on the study population, data compiled up to the point of discontinuation will be used for analysis. Subjects who are withdrawn prematurely from the study treatment will be included in all analyses (up to the date of withdrawal), regardless of the duration of treatment.

5.1 Sample Size Determination

Approximately 74 patients (including approximately 10% dropouts before end of treatment or latest week 12), are planned to be included in this study. [redacted]

[redacted]

[redacted]

Accounting for approximately 10% dropouts before end of treatment or latest week 12, further 7 patients and a total of 74 patients will be included in this study.

5.2 Analysis Population

5.2.1 Enrolled population

The enrolled population includes all patients that have signed the ICF for this study.

5.2.2 Safety (SAF) population

All enrolled patients confirmed by the investigator and who received at least one instillation of Cystistat.

5.2.3 Full analysis set (FAS) population

All patients of the SAF who have at least one post baseline assessment of primary or secondary efficacy endpoint.

5.3 Method of Treatment Assignment, Randomization and Blinding

Randomization and blinding are not applicable due to only one treatment group.

5.4 Baseline

Baseline value will be defined as the non-missing value before first treatment.

5.5 Change from Baseline

Value of change from baseline at any post baseline visit will be defined as the difference of the non-missing baseline value to the non-missing post baseline value i.e.

Change from baseline (Δ) = post-baseline value at visit X - baseline value, where both values are non-missing.

Percent change from baseline will be calculated as:

(Assessment value at post-baseline visit X – baseline value) / baseline value * 100.

5.6 End of treatment

This assessment will be performed at end of treatment or latest at week 12.

In this study Follow-up will be performed as an on-site visit if in accordance with routine clinical practice at Month 6.

The end of study is defined as the date of the last visit (or remote contact) of the last patient included in the study.

5.7 Treatment Start Day

Date of first Cystistat instillation date will be used for treatment start day i.e., Visit 2 (Week 1) in this study.

5.8 Treatment End Day

Date of last Cystistat instillation date will be used for treatment end day (i.e., Latest Week 12 (Month 3) or Additional Treatment Visit (After week 12 to Month 6) in this study). If the patient has not completed the study, then the last available non-missing date of Cystistat instillation will be used for treatment end day.

5.9 Duration of treatment exposure

Duration of treatment exposure is defined as the time the subjects will be on treatment during the study.

Duration of treatment exposure: number of days between the last instillation date and the first instillation date + 1 i.e., date of last instillation -date of first instillation +1.

5.10 Multiple Comparisons and Multiplicity

As this study is exploratory in character, no multiplicity adjustment will be performed for different endpoints.

5.11 Methods for Withdrawals, Missing Data

Subjects who are withdrawn prematurely from the study treatment will be included in all analyses (up to the date of withdrawal), regardless of the duration of treatment. The analysis will be done on observed data only, no imputation will be done for missing values.

5.12 Unscheduled visits and Early termination Visit.

As this is a real-life study, no fix visit schedule is foreseen. Therefore, also unscheduled visits are not applicable.

If the patient terminates early, withdraws or is withdrawn, the reason for early termination/withdrawal will be recorded.

5.13 Analysis Software

All analysis will be performed using SAS® Software version 9.4 or later.

6.0 DEMOGRAPHICS AND OTHER BASELINE CHARACTERISTICS

6.1 Demographics

Demographic variables and subject characteristics will be summarized descriptively. Demographic variables will include age, gender, and ethnicity.

6.2 Prior and Concomitant Medications

All prior and concomitant medications will be coded using World Health Organization Drug Dictionary (WHODD), 1st March 2023 or later. The frequency and percent of prior and concomitant IC/BPS and pain medications will be tabulated by using Therapeutic class and Generic name for overall.

IC/BPS Medications: Medications entered with indication 'Study indication (IC/BPS)'.

Pain Medications: Medications classified as "Drugs used in pain therapies" based on WHODrug Standardised Drug Groupings (WHODrug SDGs), version 1st September 2023 or later.

Prior Medications: Medications started and stopped prior to enrolment into the study (i.e. start date and stop date at least one day before baseline visit).

Concomitant Medications: Medications started after enrolment into the study (i.e. start date on or after the day of baseline visit and stop date on or after day of baseline visit or ongoing).

Prior and Concomitant Medications: Medications started prior to enrolment into the study and continued during the study (i.e. start date at least one day before baseline visit and stop date on or after day of baseline visit or ongoing).

6.3 Baseline and Screening Conditions

6.3.1 Baseline Medical/Surgical History

Medical history will be coded using MedDRA dictionary version 26.0 or higher version. The frequency count (n) and percentage (%) of subjects will be summarized according to the coded terms of system organ class (SOC) and preferred term (PT) for Safety Population (SAF).

6.3.2 Baseline Physical Exam, vital sign and Laboratory assessment

Not Applicable

6.3.3 Measurement of Treatment Compliance

As measurement for compliance the total number of instillations (until end of treatment visit or latest week 12 and until Month 6) done as per instruction will be analysed by counts and percentages.

7.0 EFFICACY ANALYSES

The efficacy analyses will be performed on all the subjects in Full Analysis Set (FAS) if not stated otherwise.

7.1 Primary Efficacy Variable Analysis

The primary efficacy endpoint is the responder rate at the end of treatment or latest at week 12 as indicated by change on a seven-point Patient Global Assessment (PGA) scale where the patient is able to evaluate the overall change in her/his IC/BPS condition as markedly improved, moderately improved, slightly improved, no change, slightly worse, moderately worse or markedly worse. For the primary analysis, a responder is defined as a patient who had an improvement on the PGA scale (i.e. PGA evaluated as markedly improved, moderately

improved, or slightly improved. In case of slightly improved, patients will only be considered as responder if the question "Did therapy have a positive effect on your life and would you undergo this treatment again?" is answered with "Yes".).
PGA categories will be tabulated and responder rate will be calculated using total number of responders and dividing by total number of patients in FAS. The 90% confidence interval of rate will be estimated [redacted]

[redacted]

Additional Analysis of Primary Endpoint:

[redacted]

Additional sensitivity analyses may be performed to address for example the impact of missing data due to dropouts.

7.2 Secondary Efficacy Variable Analysis

Secondary endpoints will be analyzed and reported as described below. Endpoint assessments will be tabulated by timepoint and in case of more than 2 timepoints additionally be displayed graphically as time course.

All changes from baseline will be analyzed by descriptive statistics for actual and change to end of treatment or latest week 12 and month 6 and reported using standard summary statistics. P-value will be calculated by using paired t-test for change form baseline. This is applicable for the following secondary endpoints:

- Morning voiding volume over time (from patient diaries, until month 6).

- Total number of voids and total voiding volume (daytime and nighttime) over the last 24 hours (from patient diaries, until month 6).

All changes from baseline will be analyzed by descriptive statistics for actual and change to end of treatment or latest week 12 and month 6 and reported using standard summary statistics. An ANCOVA model, as described below, will be used for baseline comparisons. This is applicable for the following secondary endpoints:

- Change from baseline to end of treatment or latest to week 12 and to month 6 in Bladder Pain/Interstitial Cystitis Symptom Score (BPIC-SS)
- Change from baseline to end of treatment or latest to week 12 and to month 6 in bladder pain and urinary urgency on Visual Analogue Scale (VAS) scored from 0 to 100.
- Change from baseline to end of treatment or latest to week 12 and to month 6 in quality of life (QoL) on Visual Analogue Scale (VAS) scored from 0 to 100.

The changes from baseline to end of treatment or latest week 12 and month 6 in above listed endpoints will be analyzed by Analysis of Covariance (ANCOVA). For the ANCOVA model, change from baseline will be the dependent variable and baseline will be the covariate. The analysis will be performed by using Proc Mixed. The covariance matrix will be left unstructured and the satterswhaite approximation will be used for degrees of freedom.

Adjusted least square mean and the standard error values along with the p-value and the 95% confidence will be presented. Single effect for Week 12 and Month 6 will be derived as contrast from the overall model.

The Proc mixed procedure of SAS will be used to compare the change from baseline for Bladder Pain/Interstitial Cystitis Symptom Score (BPIC-SS) by adjustement of continuous baseline values.

[redacted]

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The following secondary endpoints will be analyzed and reported like the analysis method and reporting of the primary endpoint as described above:

- Percent responders at month 6 as indicated by change on the 7-point Patient Global Assessment (PGA) scale using the same responder definition as for the primary endpoint.

- Percent responders at the end of treatment or latest at week 12 and at month 6 as indicated by change on the 7-point Patient Global Assessment (PGA) scale using an alternative responder definition (i.e. a responder is defined as a patient who experiences moderate or marked improvement).

The following secondary endpoints will be presented by summary statistics:

- Counts and percentages will be presented for occurrence of flares (documented as adverse events) and descriptive statistics will be presented for additional BPIC-SS (at the time of occurrence) (until month 6) by summary statistics.
- Number and percentage of premature termination of treatment will be presented by using frequency tables.
- Use of concomitant IC/BPS and pain medication count (until month 6) will be presented by using frequency tables.

7.3 Subgroup Analysis

A subgroup of patients who have at least 4 treatments in first 25 days of treatment will be analyzed separately to reflect treatment recommendation, if relevantly different from the Full Analysis Set (FAS) (less than 80% of Full Analysis Set (FAS)). Descriptive statistics will be done for all primary and secondary efficacy analyses by using subgroup analysis population.

If there is a substantial rate of patients with early termination before end of treatment or latest week 12 (n>10), a separate subgroup for patients with available data for end of treatment visit or latest week 12 analyses will be performed.

Additional subgroups regarding concomitant IC/BPS, pain medication, specific treatments schedule or deviation of in-/exclusion criteria might be meaningful and will be analysed exploratively.

8.0 SAFETY AND TOLERABILITY ANALYSES

The safety analysis will be performed on all the subjects in Safety population (SAF).. The descriptive statistics for continuous variables will be presented using standard summary statistics. For categorical data, frequencies and percentages will be presented, where percentage will be based on the total number of subjects in Safety population (SAF)...

This is applicable for Adverse Events and Incidents, including non-related Serious Adverse Events (SAEs) and Serious Incidents.

8.1 Adverse Events and Incidents

All AEs and incidents will be tabulated by number and percentage of subjects and number of events.

The Adverse events and incidents will be coded by System Organ Class (SOC) and Preferred Term (PT) using version 26.0 or higher of Medical Dictionary for Drug Regulatory Affairs (MedDRA) body system. In addition, all incidents will be coded according to IMDRF Problem code A.

All AEs and incidents will be collected, evaluated, and tabulated separately by SOC, PT, related to Cystistat, special interest, seriousness (AE and Incidents), severity, action taken, and outcome, and date of resolution.

All non-related Serious adverse events (SAEs) and Serious Incidents will be listed and summarized.

9.0 INTERIM ANALYSIS

[redacted]

10.0 REPORTING CONVENTIONS

10.1 Reporting of Numeric Values

All raw data will be presented to the original number of decimal places. The mean, median and quartiles will be presented with 1 decimal place more than raw data. The standard deviation (SD), Standard Error of Mean and Confidence Interval (CI) of mean will be presented with 1 decimal place more than mean. The range (minimum and maximum) will be presented as per the raw data Percentages will be presented in xx.x% format. All categories of variables will be presented even if there is no data. Blank cells will be filled by "-"in reporting of results.

Precision of p-values will be 4 decimal places. p-values less than 0.0001 will be presented as <0.0001 and if equal to 1 then ≥ 0.9999.

10.2 Output (Tables, Listings and Graphs) Considerations

The Tables, Listings and Graphs (TLG) layout will be as follows:

Orientation	All pages should preferably be landscape.
Paper Size	Legal size
Margins	Top: 0.75 inch Bottom: 0.75 inch Left: 0.75 inch Right: 0.75 inch
Font	Times New Roman (font size: min. 9 point, max. 12 point)

Headers	**Titles of Table/Listing will be center** **Left** Sponsor: MEDA Pharma GmbH & Co. KG (A Viatris Company) Product: Cystistat Protocol No: CYST-SLZ-7001
Footers	**Left** Analyst Initials: Program Name: Program Run date: time: **Right** Datasets Used: Page XXX of YYY

The bottom and right margin may be reduced to 0.38 inch as necessary to allow additional rows to be presented, but not at the expense of clarity. The date format for all presentations will be 'DDMMMYYYY'.

11.0 REFERENCES

1. Protocol: CYST-SLZ-7001 V1.0_ 06_APR_2022
2. Case Report Form (CRF): CYSTISTAT STUDY eCRF Designing V 0.4 (21-JUN-22)