A Phase 1/2a Pilot Study of Intravesical TSD-001 for Treatment of Low-Grade, Stage Ta, Non-Muscle Invasive Bladder Cancer

Study Number: TD-001

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Approval Page

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ABBREVIATIONS

AE	adverse event
ATC	Anatomical Therapeutic Chemical
BMI	body mass index
BP	blood pressure
BT	body temperature
°C	degrees Celsius
CTCAE	Common Terminology Criteria for Adverse Events
DCL	DCL Pathology (central pathologist)
DLT	dose-limiting toxicity
ECG	electrocardiogram
eCRF	electronic case report form
HR	heart rate
IPSS	International Prostate Symptom Score
Kg	kilogram
Max	maximum
MDD	maximum deliverable dose
MTD	maximum tolerated dose
MedDRA	Medical Dictionary for Regulatory Activities
Min	minimum
MITT	modified intent-to-treat
MLRR	marker lesion response rate
mm Hg	millimeter of mercury
MTD	maximum tolerated dose
N/A	not applicable
NCI	National Cancer Institute
NMIBC	non-muscle invasive bladder cancer
OAB-q	Overactive Bladder Questionnaire
PK	pharmacokinetic
PP	per protocol
PRA	PRA Health Sciences (Bioanalytical Lab)
RR	respiratory rate
SAE	serious adverse event
SD	standard deviation
SEM	standard error of the mean
TCC	transitional cell carcinoma
TURBT	transurethral resection of bladder tumor
WHO DRUG	World Health Organization drug dictionary

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1. STUDY OBJECTIVES

This is a phase 1/2a study to evaluate the safety of TSD-001, the local and systemic paclitaxel pharmacokinetic (PK) concentrations after intravesical exposure to TSD-001, the recurrence-free survival after TURBT and intravesical TSD-001, and the marker lesion response rate after TSD-001 treatment in subjects with low-grade, stage Ta NMIBC.

The primary objective for **part 1** is to establish the maximum tolerated dose (MTD), defined as the dose immediately preceding the dose at which dose-limiting toxicity (DLT) occurs or when a maximum deliverable dose (MDD) is reached. The severity and frequency of adverse events (AEs) will be assessed in the weeks following TSD-001 administration, and defined according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0.

The secondary objectives for **part 1** are to determine the local (bladder urine) and systemic (peripheral blood) paclitaxel PK concentrations before and after intravesical exposure to TSD-001 at all doses. Blood and urine samples will be collected 15 (± 15 minutes) before and 2 hours (± 10 minutes) after each instillation.

Exploratory objectives for **part 1** include evaluation of the change from baseline to last post-dose time point (Week 16) in urinary HRQOL as measured by the International Prostate Symptom Score (IPSS) (men only) and Overactive Bladder Questionnaire (OAB-q) scores.

The primary objective for **part 2** is to assess the marker lesion response rate using the MTD/MDD established in part 1. For subjects in **part 2**, cohort 1, the assessment will occur 12 weeks (± 7 days) after Day 1 at the MTD/MDD. Subjects in **part 2**, cohort 2 will have the marker lesion response rate determined 15 weeks (± 7 days) after Day 1.

Complete marker lesion response requires no evidence of transitional cell carcinoma (TCC) on cystoscope-directed biopsy or cystoscope, if biopsy is not technically possible or safe to perform. Partial response is at least a 30% decrease in marker lesion size (Eisenhauer et al., 2009) as measured by longest diameter.

The secondary objectives of **part 2** are to: 1) determine the systemic (peripheral blood) paclitaxel PK concentrations before and after the third intravesical exposure to TSD-001; and 2) characterize the severity and frequency of AEs following intravesical administration of TSD-001 at the MTD/MDD established in **part 1**, as defined according to CTCAE.

Paclitaxel PK concentration measurements of peripheral blood during **part 2** will be obtained at the following time points: A) 2 hours (± 10 minutes) after the first intravesical instillation, and B) 15 minutes (± 15 minutes) before, and 2 hours (± 10 minutes) after the third intravesical exposure of TSD-001 at the MTD/MDD.

Exploratory endpoints of **part 2** include change from baseline to the end of the treatment in IPSS (men only) and OAB-q scores and paclitaxel levels in voided urine samples at 24, 48, and 72 hours after the third instillation of TSD-001.

Part 1 and **2** safety assessments will be evaluated by analyzing results of AE, laboratory test, vital signs, electrocardiogram (ECG), and physical examination assessments.

The exploratory endpoint of **part 3** (surveillance) will be disease-free survival of subjects exposed to TSD-001 in **part 1 and part 2** who have had a complete response. The endpoint will be a time to event (recurrence) after the last instillation of TSD-001 after TURBT (Day -12 in part 1, Day 1 in part 2), and with recurrence free survival at 12 and 24 months. Cystoscopic surveillance as per standard of care will be performed approximately every 3 months from last endoscopic assessment in **part 1** or **part 2** until 24 months (from initial instillation). Disease-free survival will be defined as no histological tissue diagnosis evidence of recurrence. Histological tissue diagnosis evidence is any diagnosis of urothelial carcinoma (i.e., TCC), including all grades and stages. Due to pandemic circumstances in 2020, and for the safety of study subjects, LIPAC made the decision to suspend the Phase 2a, part 3 registry**.** This decision in May 2020 means p**art 2** subjects will not complete 12- and 24-month assessments. Available data for the available **part 2** subject visits in the long-term surveillance portion (i.e. **part 3)** will be presented within the body of the final CSR.

2. OVERALL STUDY DESIGN

This is a single-arm, phase 1/2a study of intravesical proliposomal formulated paclitaxel (TSD-001) in subjects with low-grade (WHO, 2004), stage Ta, NMIBC. These patients have low to intermediate risk non-muscle invasive bladder cancer (NMIBC). An enrollment of up to 21 subjects (6 in **part 1** and up to 15 in **part 2**) is planned. Any subject that receives at least two treatments in **part** 1 or **part 2** is eligible for surveillance in **part 3**. Subject eligibility will be determined during the screening period based on the subject meeting all of the inclusion and none of the exclusion criteria.

The study comprises a screening period, a six-dose escalation safety and paclitaxel PK concentration assessment (**part 1**), and a stable dosing phase assessing the marker lesion response rate, safety, and (in **part 2**) a paclitaxel PK concentration assessment after the first and third intravesical instillations. Study **part 1** will include a cystoscopy about 13 weeks (± 7 days) after transurethral resection of bladder tumor (TURBT). Study **part 2** cohort 1 will include a cystoscopy and biopsy (or TURBT) under general/regional anesthesia 12 weeks (± 7 days) after Day 1. Study **part 2** cohort 2 will include a cystoscopy and biopsy (or TURBT) under general/regional anesthesia 15 weeks (± 7 days) after Day 1.

The study has a total of 17 planned clinic visits for **part 1** and 14 planned clinic visits for **part 2**, cohort 1 or 16 planned clinic visits for **part 2**, cohort 2, including office visits in each part for study drug administration and additional office visits for safety and paclitaxel concentration assessments. **Part 3** has an additional 7 planned clinic visits.

For the first 3 subjects (cohort 1) in **part 1**, study drug will be administered every 2 weeks at a starting dose of 10 mg TSD-001 and increased according to the schedule (25, 50, 75, 100, 150 mg) every 2 weeks for a total of 6 intravesical treatments. The starting dose for the next three subjects in **part 1** (cohort 2) will be 90 mg, and increased according to the schedule (180, 270, 360, 450, 540 mg). In **part 1**, peripheral blood and urine samples will be collected for paclitaxel concentrations 15 minutes (±15 minutes) before and 2 hours (± 10 minutes) after each instillation. Thirteen weeks (± 7 days) after TURBT, an office cystoscopy will be performed.

During **part 2**, up to 15 additional subjects with low-grade, stage Ta NMIBC will have weekly intravesical instillations of TSD-001 at the highest nontoxic dose (MTD/MDD) established in **part 1**. Paclitaxel PK concentration measurements of peripheral blood during **part 2** will be obtained at the following time points: A) 2 hours (± 10 minutes) after the first intravesical instillation, and B) 15 (± 15 minutes) before, and 2 hours (± 10 minutes) after the third instillation of TSD-001. All subjects in **part 2** will also have additional urine samples collected after their third intravesical instillation. Voided urine paclitaxel levels will be determined for urine samples taken at 24, 48, and 72 hours after instillation of TSD-001 as an exploratory endpoint.

For **part 2** cohort 1, the marker lesion response assessment will be performed at Week 12 (i.e., 7 weeks [± 7 days] after the last TSD-001 intravesical instillation). For **part 2** cohort 2, the marker lesion response assessment will be performed at Week 15 (i.e., 8 weeks (± 7 days) after the last intravesical instillation). Subjects will report to the study site prepared to undergo cystoscopy and bladder biopsy under general anesthesia. Complete marker lesion response requires no evidence of TCC on cystoscope-direct biopsy or cystoscope alone, if biopsy is not technically possible or safe to perform. Partial response is at least a 30% decrease in marker lesion size as measured by longest diameter.

Before each of the planned intravesical treatment visits in **part 2**, the subjects will report to the study site as directed. Intravesical instillation of study drug will be performed with dwell time of up to 2 hours (1 hour or more will be acceptable, depending on subject's tolerability of the procedure). Subjects will be observed within the study site for any AEs during the 2-hour intravesical dwell and for 30 minutes after completing intravesical administration.

Subject questionnaires (IPSS, OAB-q) will be administered at baseline enrollment, day of last treatment, and the end of treatment part on Day 92 (Week 13) for **part 2** cohort 1 or Day 113 (Week 16) for **part 2** cohort 2.

Safety analysis will be performed on data collected through Week 16 of **part 1** and Week 13 of **part 2** cohort 1, and Week 16 of **part 2** cohort 2. In case of withdrawal due to an adverse event, the subject is to be followed until resolution of the AE or for 30 days.

Upon or after completion of **part 1** or **part 2** (treatment part) of the study, the subject may be entered into **part 3** (surveillance). In **part 3**, subjects will be followed for disease-free survival and receive cystoscopic assessments approximately every 3 months as part of standard care following treatment of low-grade NMIBC. Subjects will receive no intravesical administrations of TSD-001 during **part 3,** and subjects will only be followed until recurrence or up to 2 years after first exposure of TSD-001.

If there is evidence of recurrence upon cystoscopic examination in **part 3**, then subjects will have additional standard care. If known, the determination of grade, stage, and results of urine cytology will be recorded in the electronic case report form (eCRF). In addition, any treatments administered as part of standard care for the NMIBC recurrence will be recorded as concomitant medication(s). During **part 3**, AEs continued from **part 1** or **part 2** will be followed until resolution or stabilization, but no new AEs (other than SAEs) will be recorded.

Study assessments will be performed as noted in the schedules of events provided in Appendix 1.

3. DETERMINATION OF MTD

Maximum tolerated dose (**part 1**) will be determined by a rule-based method as follows:

- Highest dose at which no DLT (defined as grade 3 or grade 4 toxicity related to study drug), OR prolonged (more than 14 days) Grade 2 toxicity, occurs
  - If no DLT occurs at any dose, the dose just before the dose at which > 33% of the study subjects experience grade 2 toxicity related to study drug.
  - Or if the MDD is reached. The MDD by formulation is set at 540 mg.
  - Or if MDD is reached. The MDD is defined as the highest dose without evidence of precipitation.

4. SIZE OF TRIAL POPULATION

The study is a proof-of-concept study designed to establish the MTD in **part 1**, and to assess preliminary efficacy via a marker lesion method in **part 2**. Local and systemic paclitaxel exposure will be measured in study **part 1** and **part 2**. Given these goals, a sample size of at least 6 subjects for **part 1** and up to 15 for **part 2,** for a total of up to 21, has empirically been planned as sufficient to achieve the study goals.

5. PERSONNEL RESPONSIBLE FOR DATA ANALYSIS

Analyses will be carried out by personnel from LIPAC Oncology LLC or designee.

6. STATISTICAL METHODS

All tests of significance will be assessed at alpha = 0.05, 2-sided. All statistical analyses and data presentations (tables and listings) will be conducted using SAS for Windows (version 9.4, or higher, Cary, NC). All study data, including data not appearing in tables, will be presented in by-subject data listings.

7. ANALYSIS POPULATIONS

Analyses will be based on the safety, modified intent-to-treat (MITT), per protocol (PP), and PK populations.

- **Safety Population**: The safety population will include all enrolled subjects who receive at least one dose of study drug.

- **MITT Population**: The MITT population will include all enrolled subjects who receive at least one dose of study drug and have at least one post-baseline measurement of paclitaxel concentration.
- **PP Population**: The PP population will include subjects in the MITT population who have no major protocol violations. All protocol violations will be defined before hard lock of the database.
- **PK Population:** All subjects who receive study drug and complete paclitaxel PK concentration measurements.

All efficacy analyses will be conducted based on the MITT population as well as the PP population. The PK population will be analyzed for the PK analyses. All safety analyses will be conducted on the safety population. Additional exploratory analyses of the data may be conducted as appropriate.

8. DATA SOURCES

8.1. Missing or Incomplete Data

There will be no imputation of missing data.

8.2. EDC Data

The clinical study database and data entry screens will be developed by the CRO, Linical Accelovance, using Medrio's electronic data capture (EDC) product. Medrio is a clinical trials software provider and will provide software hosting for this study.

Linical will provide LIPAC with interim transfers during the study as requested. The transfers will contain the current study data with coding and will be provided in SAS datasets. All electronic data transfers will occur through Linical's secured website, Egnyte. In the course of development and sometimes due to Protocol Amendments data collection fields in Medrio EDC were superseded. These fields were subsequently made unenterable so that they appeared on the form (as reference) but could not be queried or updated.

These will be left in the SDTM datasets but are not shown in any tables, figures, or listings.

8.3. Central Pathologist Data

DCL Pathology is the central pathologist. Data transfers are formatted and delivered according to a joint Data Transfer Agreement between DCL, LIPAC, and Linical.

8.4. Bioanalytical Laboratory

PRA Health Sciences is the bioanalytical laboratory providing method development, method validation, and delivery of measurements of paclitaxel levels from subject urine and plasma samples. Data transfers from PRA are formatted and delivered according to a joint Data Transfer Agreement between PRA, LIPAC, and Linical.

9. PRESENTATION OF SUBJECT DISPOSITION

Frequency counts and percentages for all subjects who are enrolled, eligible for the safety population, eligible for the MITT population, eligible for the PP population, eligible for the PK population, completed the study, and did not complete the study will be presented for **part 1** cohort 1, **part 1** cohort 2, **part 2** cohort 1, **part 2** cohort 2 and **part 3**. In addition, frequency counts and percentages of subjects' reported reasons for discontinuation will be summarized for each part and cohort.

10. PRESENTATION OF SCREENING VARIABLES

Variables collected at the screening visits will be summarized and presented for **part 1** cohort 1, **part 1** cohort 2, **part 2** cohort 1, **part 2** cohort 2 and **part 3**, separately. Descriptive statistics (number of subjects, mean, standard deviation, standard error of the mean (SEM), median, minimum, and maximum values) will be presented for the continuous variables. Frequency counts and percentages will be presented for the categorical variables for each category. The following variables will be presented:

- ➢ Demographic characteristics
  - Sex (male, female)
  - Age (years)
  - Ethnicity (Non-Hispanic/Latino, Hispanic/Latino)
  - Race (American Indian/Alaskan Native, Asian, Black/African American, Native Hawaiian/Other Pacific Islander, White, or Other)
  - Weight (kg)
  - Height (cm)
  - BMI (kg/m^2)

- ➢ Vital signs measurements (Screening)
  - Systolic blood pressure (mm Hg)
  - Diastolic blood pressure (mm Hg)
  - Heart rate (bpm)
  - Respiratory rate (breaths/minute)
  - Body Temperature (°C)

- ➢ Bladder Characteristics (Screening/Baseline)
  - NMIBC Recurrent (yes, no)
  - Number of Tumor Locations (solitary, multifocal)
  - Previous Intravesical Therapy (yes, no)
  - EAU Risk Stratification (low risk, intermediate risk)

Recurrence will be identified by Medical History documentation of NMIBC and TURBT within 1 year prior to study TURBT. Solitary will be identified as one tumor location identified at the

Day -12 TURBT (Part 1) or the Day 1 TURBT (Part 2). Multifocal will be identified by more than one tumor location at the Day -12 TURBT (Part 1) or the Day 1 TURBT (Part 2).

Table 1: Risk Stratification for TD-001

Low Risk	Intermediate Risk	High Risk
Primary, solitary, Low Grade/G1 <3cm, no CIS	All tumors not defined in the two adjacent categories	*T1 tumor *High Grade/G3 tumor *CIS *Multiple, recurrent, and large (>3cm) Ta G1G2 tumors (all conditions must be present)

11. EXTENT OF EXPOSURE

For each subject, the following will be calculated:

- Duration of exposure (mg*hours)
- Total dose (mg)
- Total hours exposed
- Mean hours exposed per subject per dose.

Duration of exposure will be calculated by multiplying the dose administered by the number of hours from treatment administration start time to treatment administration stop time.

Descriptive statistics (number of subjects, mean, standard deviation, standard error of the mean (SEM), median, minimum and maximum values) will be presented for each exposure parameter for all subjects and **part 1** cohort 1, **part 1** cohort 2, **part 1**, **part 2** cohort 1, **part 2** cohort 2, and **part 2**. The exposure table will also be presented for female subjects and male subjects.

12. EFFICACY PARAMETERS: PART 1

12.1. Primary Endpoint

The primary endpoint of **part 1** is the MTD, defined as the dose immediately preceding the dose at which DLT occurs or when a MDD is reached. The severity and frequency of AEs will be documented following TSD-001 administration, and defined according to NCI CTCAE Version 5.0.

12.2. Secondary and Exploratory Endpoints

The secondary endpoints of **part 1** are to determine paclitaxel PK concentrations in the urine and the peripheral blood before and after intravesical exposure to TSD-001. Paclitaxel concentrations will be limited to pre-instillation (trough) and to post-instillation (peak) concentration measurements of urine and plasma. The goal is to define the local and systemic exposure of the study subjects to paclitaxel .

Exploratory endpoints of **part 1** include the following:

- Change from screening to Week 10 (or last TSD-001 exposure) in IPSS total score (men only)
- Change from screening to Week 16 (or last collection for subject) in IPSS total score (men only)

For the OAB-q, the following domains and total score will be calculated according to the "Scoring Guide for the OAB-q" in Appendix 2:

- Symptom Severity
- HRQL – Coping
- HRQL – Concern
- HRQL – Sleep
- HRQL –Social
- HRQL - Total

For each domain and total score the following endpoints will be calculated:

- Change from screening to Week 10 (or last TSD-001 exposure) in OAB-q
- Change from screening to Week 16 (or last collection for subject) in OAB-q

12.3. Endpoint Analysis

The dose at which DLT occurs or when a MDD is reached will be presented with the MTD.

Descriptive statistics (number of subjects, mean, standard deviation, SEM, median, minimum and maximum) will be presented for urine and plasma concentrations collected at each visit (Day 1, Week 2, Week 4, Week 6, Week 8 and Week 10) and nominal time point (15 minutes pre-instillation and 2 hours post-instillation) for all samples.

After the TD-001 study was begun, the urine paclitaxel concentration method development identified that Tween should be added to the urine collection container to reduce the urine paclitaxel negative bias. Therefore, the urine paclitaxel concentrations will also be presented by Tween category (absent, incomplete, complete).

Comparisons between Tween addition categories may be assessed by an analysis of variance model with urine paclitaxel concentration as the dependent variable and Tween addition as the independent variable.

Additionally, for the 2-hour post-instillation urine concentrations, Pearson correlation coefficients will be generated for the following:

- Number of AEs per subject at each instillation visit
- Change from screening to Week 10 in IPSS total score (men only)
- Change from screening to Week 10 in OAB-q total score

Scatter plots, including the linear regression line and equation, for each comparison will be provided.

Urine precipitation in post-instillation void was collected for **part 2**. For each subject and visit collected, a histogram will be constructed displaying the amount of precipitation (none, observed, high amount).

For IPSS and OAB-q scores, descriptive statistics will be presented for screening, Week 10 (or last TSD-001 exposure), Week 16 (or last collection for subject) and for the changes from screening to Weeks 10 (or last TSD-001 exposure) and 16 (or last collection for subject). The changes from screening will be assessed by the paired t-test or Wilcoxon signed rank test, as appropriate.

13. EFFICACY PARAMETERS: PART 2

13.1. Primary Endpoint

The primary endpoint of **part 2** is to determine the marker lesion response rate (MLRR) using the MTD/MDD established in **part 1** at the final endoscopic assessment after weekly instillations of TSD-001. The final endoscopic assessment will be 12 weeks (± 7 days) after Day 1 (i.e., 7 weeks [± 7 days] after last intravesical TSD-001 instillation) for subjects in **part 2** cohort 1 and 15 weeks (± 7 days) after Day 1 (i.e., 8 weeks [± 7 days] after the last intravesical instillation) for subjects in **part 2** cohort 2.

The MLRR (**part 2**) will be determined by the percentage of subjects at completion cystoscopy and biopsy to have a partial or a complete response (no evidence of TCC on cystoscope-directed biopsy or cystoscope, if biopsy is not technically possible or safe to perform). Partial response will be determined by comparing the pretreatment marker lesion size (i.e. longest dimension of the marker lesion at Day 1 [or Screening if Day 1 TURBT not performed – i.e. solitary lesion]) to the post-treatment size using the greatest (longest) dimensions. Longest dimension is the largest measurable diameter of the lesion. Partial response is defined as at least a 30% decrease in marker lesion size (Eisenhauer et al., 2009) as measured similarly by the longest dimension (in mm).

In addition, pathology tissue specimens of the marker lesion have parameters also measured in millimeters (in 3 dimension). Exploratory representation of marker lesion response rate will compare the longest dimension of the marker lesion at Day 1 (or Screening if Day 1 TURBT not performed – i.e. solitary lesion) to the longest dimension of the pathology tissue sample.

As an exploratory analysis, the Pearson correlation coefficient between the longest dimension obtained at Week 12/Week 15 and the longest dimensions reported by DCL Pathology (DCL) will be calculated. Scatter plots for Week 12/Week 15 will be presented. The partial response rate will also be calculated using the DCL measurements. External independent validation of the Week 12/Week 15 marker lesion longest dimension as determined by the investigator (using cystoscopy) and the longest dimension determined by DCL pathologist (using microscopy) will be performed, and analyzed by Pearson correlation coefficient.

13.2. Secondary and Exploratory Endpoints

The secondary endpoints of **part 2** are:

1) to determine paclitaxel concentration parameters in the peripheral blood after instillation of the MTD/MDD of TSD-001, and
2) to characterize the severity and frequency of AEs after the MTD/MDD of TSD-001 is intravesically administered weekly for 6 administrations (cohort 1) or 8 administrations (cohort 2).

Exploratory endpoints of **part 2** include the following:

- Paclitaxel levels in voided urine samples at 24, 48, and 72 hours after the third instillation of TSD-001.

For **part 2** cohort 1:

- Change from screening to Week 5 in IPSS total score (men only)
- Change from screening to Week 13 in IPSS total score (men only)
- Change from screening to Week 5 in OAB-q for each domain and total score
- Change from screening to Week 13 in OAB-q for each domain and total score

For **part 2** cohort 2:

- Change from screening to Week 7 in IPSS total score (men only)
- Change from screening to Week 16 in IPSS total score (men only)
- Change from screening to Week 7 in OAB-q for each domain and total score
- Change from screening to Week 16 in OAB-q for each domain and total score

13.3. Endpoint Analysis

Marker lesion response rate (**part 2**) will be determined by the percentage of subjects at completion TURBT or biopsy to have 1) a reduction of the marker lesion of at least 30% in longest dimension (partial response) and 2) and no biopsy (or cystoscope, if biopsy is not technically possible or safe to perform) evidence of residual disease (complete response).

Additionally, marker lesion response rate in **part 2** will be stratified by EAU risk category at screening (low risk or intermediate risk).

The severity and frequency of AEs will be summarized as described in Section 15.1.

more subjects will be summarized by system organ class and preferred term in descending frequency by preferred term.

Additionally, adverse events will be presented by relationship to study drug, severity, relationship to study drug and severity, adverse events meeting DLT criteria (**part 1** only), serious adverse events and serious treatment-related adverse events. If subject experiences the same adverse event more than once, the most severe or most closely related will be presented. Listings of adverse events meeting DLT criteria and serious adverse events will be provided.

15.2. Vital Signs Measurements

Descriptive statistics will be presented for the vital signs measurements (systolic blood pressure, diastolic blood pressure, pulse rate, respiratory rate, and body temperature) for each visit collected and for the changes from baseline (Day 1) for **part 1** and **part 2**, separately. Note that **part 2** cohort 1 and **part 2** cohort 2 will be combined for all possible study days. The Week 13 visit from cohort 1 and Week 16 visit from cohort 2 will be combined as the End of Study visit.

15.3. Laboratory Measurements

Descriptive statistics will be presented for continuous laboratory parameters for each visit collected and for the changes from screening for **part 1** and **part 2**, separately. Additionally, shift tables will be constructed to display the number and percentage of values normal and abnormal at Screening to normal and abnormal at each subsequent visit will be presented for each parameter.

15.4. 12-Lead ECG

Descriptive statistics will be presented for the ECG parameters (heart rate, PR interval, QRS interval, QT interval, atrial rate and ventricular rate) for screening, study exit and for the changes from screening to study exit for **part 1** and **part 2**, separately. Additionally, for the overall ECG interpretation (normal; abnormal, not clinically significant; abnormal, clinically significant), ST segment (normal, abnormal), T-wave (normal, abnormal), interval (normal, abnormal), rhythm (no sinus rhythm, sinus rhythm), the number and percentage of subjects will be presented as shift tables from screening to study exit for **part 1** and **part 2**, separately.

15.5. Physical Examinations

For each body system, a shift table will be constructed to display the number and percentage of subjects per category (normal; abnormal, not clinically significant; abnormal, clinically significant) at screening to study exit for **part 1** and **part 2**, separately.

15.6. Concomitant Medications

Concomitant medications will be classified by site of action and therapeutic and clinical characteristics using the World Health Organization drug dictionary (WHO DRUG Enhanced

Sep-2017 B2 (Hierarchy and Ingredients)). Concomitant medications will be summarized by WHO Preferred term and Level 4 Anatomical Therapeutic Chemical (ATC) for **part 1** cohort 1, **part 1** cohort 2, **part 1** (cohorts 1 and 2 combined), **part 2** cohort 1, **part 2** cohort 2, and **part 2** (cohorts 1 and 2 combined). For subjects with more than one instance of WHO Preferred term and Level 4 ATC, only the first occurrence will be tabulated.

15.7. Protocol Deviations

Protocol deviations will be summarized by deviation classification and severity for **part 1** cohort 1, **part 1** cohort 2, **part 2** cohort 1, **part 2** cohort 2 and all subjects. The total number of deviations per classification and severity will be presented with the number and percentage of subjects.

16. DEVIATIONS FROM STATISTICAL PLAN AND OTHER ISSUES

During the analysis and reporting process, any deviations from the statistical plan designed for this protocol will be described and justified in the clinical study report.

Table C.2.5	Part 1: Correlation Coefficients for 2-hour Urine Concentrations: Per Protocol Population
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20. PLANNED TABLES

Table A.1.1
Subject Disposition
All Enrolled Subjects

		TSD-001			
Number of Subjects	**All Subjects (N=)**	**Part 1 Cohort 1 (N=)**	**Part 1 Cohort 2 (N=)**	**Part 2 Cohort 1 (N=)**	**Part 2 Cohort 2 (N=)**
Enrolled	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Safety Population	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
MITT Population	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PP Population	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PK Population	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Completed Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Did Not Complete Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Discontinued due to:					
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dose Limiting Toxicity	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ineligible to Continue	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Deterioration of Subject's Clinical Condition	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Significant Protocol Deviation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subject Noncompliance	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Withdrawal of Consent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lack of Efficacy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lost to Follow-Up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Deceased	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[a] Part 3 was only available for enrollment to subjects with a Complete Response.
Part 3 was available to all Part 1 subjects because they had Complete Response after the TURBT procedure.
For Part 2 subjects, Part 3 was not available due to the Complete Response requirement and COVID-19.

Table A.1.2
Demographic Characteristics
Safety Population

		TSD-001				
Characteristic		**All Subjects (N=)**	**Part 1 Cohort 1 (N=)**	**Part 1 Cohort 2 (N=)**	**Part 2 Cohort 1 (N=)**	**Part 2 Cohort 2 (N=)**
Sex	Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Age (years)	n	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Ethnicity	Hispanic Or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Not Hispanic Or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Race	Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Height (cm)	n	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Weight (kg)	n	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
BMI (kg/m)	n	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx

Note: This table will be repeated for the MITT Population, the PP Population and the PK Population

Table A.1.3
Vital Signs Measurements at Screening
Safety Population

		TSD-001				
Parameter		**All Subjects (N=)**	**Part 1 Cohort 1 (N=)**	**Part 1 Cohort 2 (N=)**	**Part 2 Cohort 1 (N=)**	**Part 2 Cohort 2 (N=)**
Systolic Blood Pressure (mm Hg)	n	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Diastolic Blood Pressure (mm Hg)	n	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Pulse Rate (bpm)	n	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Respiratory Rate (breaths/min)	n	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Body Temperature (C)	n	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx

Note: This table will be repeated for the MITT Population, the PP Population and the PK Population

Table A.1.4
Bladder Characteristics at Screening
Safety Population

			TSD-001			
Characteristic		**All Subjects (N=)**	**Part 1 Cohort 1 (N=)**	**Part 1 Cohort 2 (N=)**	**Part 2 Cohort 1 (N=)**	**Part 2 Cohort 2 (N=)**
NMIBC Recurrent	Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of Tumor Locations	Solitary	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Multifocal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Previous Intravesical Therapy	Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
EAU Risk Stratification[a]	Low Risk	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Intermediate Risk	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[a] Low risk defined as: Primary, Solitary, Low Grade/G1 <3cm, no CIS
Intermediate risk defined as: All tumors not defined as Low risk or High risk
High risk defined as: *T1 tumor, *High Grade/G3 tumor, *CIS. *Multiple, recurrent, and large (>3cm) Ta G1G2 tumors (all conditions must be present)

Note: This table will be repeated for the MITT Population, the PP Population and the PK Population

Table A.1.5
Extent of Exposure
Safety Population

		TSD-001						
			Part 1				Part 2	
Parameter		**All Subjects (N =)**	**Part 1 Cohort 1 (N =)**	**Part 1 Cohort 2 (N =)**	**Part 1 (N =)**	**Part 2 (N =)**	**Part 2 Cohort 1 (N =)**	**Part 2 Cohort 2 (N =)**
Duration of Exposure (mg*hours)	n	xx	xx	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Total Dose (mg)	n	xx	xx	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Total Hours Exposed	n	xx	xx	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Mean Hours Exposed per Subject	n	xx	xx	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx

Note: This table will be repeated for the MITT Population, the PP Population and the PK Population

Table A.1.5.1
Extent of Exposure
Safety Population: Female

		TSD-001						
			Part 1			Part 2		
Parameter		**All Subjects (N =)**	**Part 1 Cohort 1 (N =)**	**Part 1 Cohort 2 (N =)**	**Part 1 (N =)**	**Part 2 (N =)**	**Part 2 Cohort 1 (N =)**	**Part 2 Cohort 2 (N =)**
Duration of Exposure (mg*hours)	n	xx	xx	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Total Dose (mg)	n	xx	xx	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Total Hours Exposed	n	xx	xx	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Mean Hours Exposed per Subject	n	xx	xx	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx

Note: This table will be repeated for the MITT Population, the PP Population and the PK Population

Table A.1.5.2
Extent of Exposure
Safety Population: Male

		TSD-001						
		Part 1				Part 2		
Parameter		**All Subjects (N =)**	**Part 1 Cohort 1 (N =)**	**Part 1 Cohort 2 (N =)**	**Part 1 (N =)**	**Part 2 (N =)**	**Part 2 Cohort 1 (N =)**	**Part 2 Cohort 2 (N =)**
Duration of Exposure (mg*hours)	n	xx	xx	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Total Dose (mg)	n	xx	xx	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Total Hours Exposed	n	xx	xx	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx
Mean Hours Exposed per Subject	n	xx	xx	xx	xx	xx	xx	xx
	Mean (SEM)	xx.xx	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)	xx.xx	xx.xx (xx.xx)
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx	xx.xx, xx.xx

Note: This table will be repeated for the MITT Population, the PP Population and the PK Population

Table A.1.6
Protocol Deviations
Safety Population

		TSD-001									
		All Subjects (N=)		Part 1 Cohort 1 (N=)		Part 1 Cohort 2 (N=)		Part 2 Cohort 1 (N=)		Part 2 Cohort 2 (N=)	
Classification	**Severity**	**Number**	**n (%) of Subjects**	**Number**	**n (%) of Subjects**	**Number**	**n (%) of Subjects**	**Number**	**n (%) of Subjects**	**Number**	**n (%) of Subjects**
Classification #1	Minor	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
	Major	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Classification #2	Minor	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
	Major	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
etc.	etc.	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)

Table B.2.1
Part 1: Maximum Tolerated Dose
MITT Population

	Dose (mg)
Maximum Tolerated Dose	N/A
Dose Limiting Toxicity Occurred at Dose	N/A
Maximum Deliverable Dose Reached	540 mg
Maximum Deliverable Dose Reached due to Precipitation [a]	360 mg

[a] Observed post void precipitation in patients with pH below 6.0

Note: This table will be repeated for the PP Population

Table B.2.2
Part 1: Cohort 1: Paclitaxel Concentration in Urine by Dose Administered and Tween Addition
Descriptive Statistics
MITT Population

Visit	Time Point	Tween Addition	n	Mean	SEM	SD	Min	Median	Max
Day 1: 10 mg	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	Incomplete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	Complete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	All Samples	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Incomplete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Complete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	All Samples	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 2: 25 mg	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	etc.	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 4: 50 mg	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	etc.	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 6: 75 mg	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	etc.	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 8: 100 mg	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	etc.	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 10: 150 mg	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	etc.	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Note: This table will be repeated for the PP Population and the PK Population

Table B.2.3
Part 1: Cohort 2: Paclitaxel Concentration in Urine by Dose Administered and Tween Addition
Descriptive Statistics
MITT Population

Visit	Time Point	Tween Addition	n	Mean	SEM	SD	Min	Median	Max
Day 1: 90 mg	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	Incomplete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	Complete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	All Samples	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Incomplete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Complete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	All Samples	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 2: 180 mg	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	etc.	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 4: 270 mg	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	etc.	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 6: 360 mg	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	etc.	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 8: 450 mg	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	etc.	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 10: 540 mg	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	etc.	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Note: This table will be repeated for the PP Population and the PK Population

Table B.2.4
Part 1: Cohort 1: Paclitaxel Concentration in Plasma by Dose Administered
Descriptive Statistics
MITT Population

Visit	Time Point	n	Mean	SD	SEM	Minimum	Median	Maximum
Day 1	15 minutes pre-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
10 mg	2 hours post-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 2	15 minutes pre-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
25 mg	2 hours post-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 4	15 minutes pre-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
50 mg	2 hours post-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 6	15 minutes pre-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
75 mg	2 hours post-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 8	15 minutes pre-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
100 mg	2 hours post-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 10	15 minutes pre-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
150 mg	2 hours post-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Note: This table will be repeated for the PP Population and the PK Population

Table B.2.4
Part 1: Cohort 2: Paclitaxel Concentration in Plasma by Dose Administered
Descriptive Statistics
MITT Population

Visit	Time Point	n	Mean	SD	SEM	Minimum	Median	Maximum
Day 1	15 minutes pre-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
10 mg	2 hours post-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 2	15 minutes pre-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
25 mg	2 hours post-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 4	15 minutes pre-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
50 mg	2 hours post-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 6	15 minutes pre-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
75 mg	2 hours post-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 8	15 minutes pre-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
100 mg	2 hours post-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 10	15 minutes pre-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
150 mg	2 hours post-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Note: This table will be repeated for the PP Population and the PK Population

Table B.2.5
Part 1: Correlation Coefficients for 2-hour Urine Concentrations
MITT Population

	Number of AEs			IPSS Total Score: Change from Screening to Week 10		OAB-q Total Score: Change from Screening to Week 10	
Visit	**Total # of AEs**	**Pearson Correlation Coefficient**	**p-value**	**Pearson Correlation Coefficient**	**p-value**	**Pearson Correlation Coefficient**	**p-value**
Week 2	xx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
Week 4	xx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
Week 6	xx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
Week 8	xx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
Week 10	xx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx

Note: This table will be repeated for the PP Population

Table B.2.6
Part 1: IPSS Total Score
Descriptive Statistics
MITT Population: Men Only

Visit		n	Mean	SD	SEM	Minimum	Median	Maximum	p-value*
Screening	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
Week 10 (or last TSD-001 exposure)	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx
Week 16 (or last collection for subject)	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx

* P-values generated by the Paired t-test or the Wilcoxon Signed Rank test. (r) indicates Wilcoxon
Note: This table will be repeated for the PP Population

Table B.2.7
Part 1: OAB-q Domains and Total Score
Descriptive Statistics
MITT Population

Symptom Severity									
Visit		**n**	**Mean**	**SD**	**SEM**	**Minimum**	**Median**	**Maximum**	**p-value***
Screening	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
Week 10 (or last TSD-001 exposure)	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx
Week 16 (or last collection for subject)	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx

* P-values generated by the Paired t-test or the Wilcoxon Signed Rank test. (r) indicates Wilcoxon
Note: This table will be repeated for the domains of Coping, Concern, Sleep, Social and Total Score
Note: This table will be repeated for the PP Population

Table B.3.1
Part 2: Marker Lesion Response Rate
MITT Population

	TSD-001		
Response Rate	**Part 2 Cohort 1 (N=)**	**Part 2 Cohort 2 (N=)**	**Part 2 (N=)**
Complete Response Rate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Partial Response Rate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Marker Lesion Response Rate[a]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[a] Marker Lesion Response Rate=Sum of Complete plus Partial Response Rates

Note: This table will be repeated for the PP Population

Table B.3.2
Part 2: Marker Lesion Response Rate as Stratified by EAU Risk Category
MITT Population

		TSD-001		
EAU Risk Category[a]	**Response Rate**	**Part 2 Cohort 1 (N=)**	**Part 2 Cohort 2 (N=)**	**Part 2 (N=)**
LOW RISK	Complete Response Rate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Partial Response Rate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Marker Lesion Response Rate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
INTERMEDIATE RISK	Complete Response Rate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Partial Response Rate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Marker Lesion Response Rate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[a] Low risk defined as: Primary, Solitary, LG/G1 <3cm, no CIS
Intermediate risk defined as: All tumors not defined in the two adjacent categories
Note: Marker Lesion Response Rate=Sum of Complete plus Partial Response Rates

Note: This table will be repeated for the PP Population

Table B.3.3
Part 2: Cohort 1: Paclitaxel Concentration (ug/L) in Urine by 360 mg TSD-001 Dose Administered and Tween Addition
Descriptive Statistics
MITT Population

Visit	Time Point	Tween Addition	n	Mean	SEM	SD	Min	Median	Max
Week 2	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	Incomplete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	Complete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	All Samples	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Incomplete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Complete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	All Samples	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Day 16	24 hrs post	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	24 hrs post	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Day 17	48 hrs post	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	48 hrs post	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Day 18	72 hrs post	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	72 hrs post	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Note: This table will be repeated for the PP Population and the PK Population

Table B.3.4
Part 2: Cohort 2: Paclitaxel Concentration in Urine by 360 mg TSD-001 Dose Administered and Tween Addition
Descriptive Statistics
MITT Population

Visit	Time Point	Tween Addition	n	Mean	SEM	SD	Min	Median	Max
Week 2	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	Incomplete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	Complete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	All Samples	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Incomplete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Complete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	All Samples	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Day 16	24 hrs post	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	24 hrs post	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Day 17	48 hrs post	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	48 hrs post	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Day 18	72 hrs post	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	72 hrs post	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Note: This table will be repeated for the PP Population and the PK Population

Table B.3.5
Part 2: Cohort 1 and Cohort 2: Paclitaxel Concentration in Urine by 360 mg TSD-001 Dose Administered and Tween Addition
Descriptive Statistics
MITT Population

Visit	Time Point	Tween Addition	n	Mean	SEM	SD	Min	Median	Max
Week 2	15 mins pre	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	Incomplete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	Complete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	15 mins pre	All Samples	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Incomplete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	Complete	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hrs post	All Samples	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Day 16	24 hrs post	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	24 hrs post	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Day 17	48 hrs post	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	48 hrs post	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Day 18	72 hrs post	Absent	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	72 hrs post	etc.	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Note: This table will be repeated for the PP Population and the PK Population

Table B.3.6
Part 2: Cohort 1 and 2: Paclitaxel Concentration in Plasma by 360 mg TSD-001 Dose Administered
Descriptive Statistics
MITT Population

Visit	Time Point	n	Mean	SD	SEM	Minimum	Median	Maximum
Day 1	15 minutes pre-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hours post-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 2	15 minutes pre-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	2 hours post-instillation	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Note: This table will be repeated for the PP Population and the PK Population

Table B.3.7
Part 2: Correlation Coefficients for 2-hour Urine Concentrations at Week 2
MITT Population

Total Number of AEs		**Complete Response**		**Partial Response**		**Total Response**	
Pearson Correlation Coefficient	**p-value**	**Spearman Correlation Coefficient**	**p-value**	**Spearman Correlation Coefficient**	**p-value**	**Spearman Correlation Coefficient**	**p-value**
x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx

IPSS Total Score: Change from Screening to Week 5/7		**OAB-q Total Score: Change from Screening to Week 5/7**	
Pearson Correlation Coefficient	**p-value**	**Pearson Correlation Coefficient**	**p-value**
x.xxx	x.xxx	x.xxx	x.xxx
x.xxx	x.xxx	x.xxx	x.xxx
x.xxx	x.xxx	x.xxx	x.xxx
x.xxx	x.xxx	x.xxx	x.xxx
x.xxx	x.xxx	x.xxx	x.xxx

Note: This table will be repeated for the Tween Addition categories of Complete, Incomplete and Absent
Note: This table will be repeated for the PP Population

Table B.3.8
Part 2: IPSS Total Score
Descriptive Statistics
MITT Population

Cohort 1

Visit		n	Mean	SD	SEM	Minimum	Median	Maximum	p-value*
Screening	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
Week 5	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx
Week 13	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx

Cohort 2

Visit		n	Mean	SD	SEM	Minimum	Median	Maximum	p-value*
Screening	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
Week 7	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx
Week 16	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx

Part 2 (Cohort 1 & 2)

Visit		n	Mean	SD	SEM	Minimum	Median	Maximum	p-value*
Screening	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
Interim Visit	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx
Final Study Visit (or last collection for subject)	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx

* P-values generated by the Paired t-test or the Wilcoxon Signed Rank test. (r) indicates Wilcoxon
Note: This table will be repeated for the PP Population

Table B.3.9
Part 2: OAB-q Domains and Total Score
Descriptive Statistics
MITT Population

Symptom Severity

Cohort 1

Visit		n	Mean	SD	SEM	Minimum	Median	Maximum	p-value*
Screening	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
Week 5	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx
Week 13	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx

Cohort 2

Visit		n	Mean	SD	SEM	Minimum	Median	Maximum	p-value*
Screening	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
Week 7	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx
Week 16	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx

Part 2 (Cohort 1 &2)

Visit		n	Mean	SD	SEM	Minimum	Median	Maximum	p-value*
Screening	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
Interim Visit	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx
Final Study Visit (or last collection for subject)	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	x.xxx

* P-values generated by the Paired t-test or the Wilcoxon Signed Rank test. (r) indicates Wilcoxon

Note: This table will be repeated for the domains of Coping, Concern, Sleep, Social and Total Score
Note: This table will be repeated for the PP Population

Table B.3.10
Part 2: Post-Treatment Marker Lesion Sites
Correlation of Maximum Diameter Values of DCL to TURBT/Biopsy Measurements at Day 85/106
MITT Population

				Pearson Correlation	
Specimen Type	**Measurement**	**N**	**Mean (SD)**	**Coefficient**	**p-value**
Single Specimen	CYSTOSCOPY	xx	xx.xx	x.xxx	x.xxx
	DCL	xx	xx.xx	x.xxx	x.xxx
Multiple Specimens	CYSTOSCOPY	xx	xx.xx	x.xxx	x.xxx
	DCL	xx	xx.xx	x.xxx	x.xxx
All Specimens	CYSTOSCOPY	xx	xx.xx	x.xxx	x.xxx
	DCL	xx	xx.xx	x.xxx	x.xxx

Note: This table will be repeated for the PP Population

Table E.1.1
Part 1: Overall Adverse Event Information
Safety Population

	TSD-001		
Number of Subjects:	**Part 1: Cohort 1 (N =)**	**Part 1: Cohort 2 (N =)**	**Part 1 (N =)**
At Least One TEAE	n (%)	n (%)	n (%)
At Least One Treatment-Related TEAE	n (%)	n (%)	n (%)
At Least One TEAE meeting DLT criteria	n (%)	n (%)	n (%)
At Least One Treatment-Related TEAE meeting DLT criteria	n (%)	n (%)	n (%)
At Least One Serious TEAE	n (%)	n (%)	n (%)
At Least One Serious Treatment-Related TEAE	n (%)	n (%)	n (%)
At Least One TEAE Leading to Treatment Discontinuation	n (%)	n (%)	n (%)

TEAE=treatment-emergent adverse event

Table E.1.2
Part 1: Number (%) of Subjects with Treatment-emergent Adverse Events* by System Organ Class and Preferred Term
Safety Population

		TSD-001		
System Organ Class	**Preferred Term**	**Part 1: Cohort 1 (N =)**	**Part 1: Cohort 2 (N =)**	**Part 1 (N =)**
Gastrointestinal Disorders	Diarrhea	n (%)	n (%)	n (%)
	Dyspepsia	n (%)	n (%)	n (%)
	Nausea	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)
Nervous System Disorders	Dizziness	n (%)	n (%)	n (%)
	Headache	n (%)	n (%)	n (%)
	Somnolence	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)
etc.	etc.	n (%)	n (%)	n (%)

*If a subject experiences the same event more than once the first occurrence is tabulated.

Table E.1.3
Part 1: Number (%) of Subjects with Treatment-emergent Adverse Events* by System Organ Class and Preferred Term by Nearest Relationship to Study Drug
Safety Population

			TSD-001		
System Organ Class	**Preferred Term**	**Relationship**	**Part 1: Cohort 1 (N =)**	**Part 1: Cohort 2 (N =)**	**Part 1 (N =)**
Gastrointestinal Disorders	Diarrhea	Not Related	n (%)	n (%)	n (%)
		Unlikely	n (%)	n (%)	n (%)
		Possibly	n (%)	n (%)	n (%)
		Probably	n (%)	n (%)	n (%)
		Definitely	n (%)	n (%)	n (%)
	Dyspepsia	Not Related	n (%)	n (%)	n (%)
		Unlikely	n (%)	n (%)	n (%)
		Possibly	n (%)	n (%)	n (%)
		Probably	n (%)	n (%)	n (%)
		Definitely	n (%)	n (%)	n (%)
	etc.	Not Related	n (%)	n (%)	n (%)
		Unlikely	n (%)	n (%)	n (%)
		Possibly	n (%)	n (%)	n (%)
		Probably	n (%)	n (%)	n (%)
		Definitely	n (%)	n (%)	n (%)
Nervous System Disorders	Dizziness	Not Related	n (%)	n (%)	n (%)
		Unlikely	n (%)	n (%)	n (%)
		Possibly	n (%)	n (%)	n (%)
		Probably	n (%)	n (%)	n (%)
		Definitely	n (%)	n (%)	n (%)
	Headache	Not Related	n (%)	n (%)	n (%)
		Unlikely	n (%)	n (%)	n (%)
		Possibly	n (%)	n (%)	n (%)
		Probably	n (%)	n (%)	n (%)
		Definitely	n (%)	n (%)	n (%)
	etc.	Not Related	n (%)	n (%)	n (%)
		Unlikely	n (%)	n (%)	n (%)
		Possibly	n (%)	n (%)	n (%)
		Probably	n (%)	n (%)	n (%)
		Definitely	n (%)	n (%)	n (%)

*If a subject experiences the same event more than once the most closely related to study drug is tabulated.

Table E.1.4
Part 1: Number (%) of Subjects with Treatment-emergent Adverse Events* by System Organ Class and Preferred Term by Maximum Severity
Safety Population

			TSD-001		
System Organ Class	**Preferred Term**	**CCTAE Grade: Severity**	**Part 1: Cohort 1 (N =)**	**Part 1: Cohort 2 (N =)**	**Part 1 (N =)**
Gastrointestinal Disorders	Diarrhea	Grade 1: Mild	n (%)	n (%)	n (%)
		Grade 2: Moderate	n (%)	n (%)	n (%)
		Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
	Dyspepsia	Grade 1: Mild	n (%)	n (%)	n (%)
		Grade 2: Moderate	n (%)	n (%)	n (%)
		Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
	etc.	Grade 1: Mild	n (%)	n (%)	n (%)
		Grade 2: Moderate	n (%)	n (%)	n (%)
		Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
Nervous System Disorders	Dizziness	Grade 1: Mild	n (%)	n (%)	n (%)
		Grade 2: Moderate	n (%)	n (%)	n (%)
		Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
	Headache	Grade 1: Mild	n (%)	n (%)	n (%)
		Grade 2: Moderate	n (%)	n (%)	n (%)
		Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
	etc.	Grade 1: Mild	n (%)	n (%)	n (%)
		Grade 2: Moderate	n (%)	n (%)	n (%)
		Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)

*If a subject experiences the same event more than once the most severe is tabulated.

Table E.1.5
Part 1: Number (%) of Subjects with Treatment-emergent Adverse Events* by System Organ Class and Preferred Term by Nearest Relationship to Study Drug and Maximum Severity
Safety Population

System Organ Class	Preferred Term	Relationship	CTCAE Grade: Severity	TSD-001 Part 1: Cohort 1 (N =)	TSD-001 Part 1: Cohort 2 (N =)	TSD-001 Part 1 (N =)
Gastrointestinal Disorders	Diarrhea	Not Related	Grade 1: Mild	n (%)	n (%)	n (%)
		Not Related	Grade 2: Moderate	n (%)	n (%)	n (%)
		Not Related	Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Not Related	Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Not Related	Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
		Unlikely	Grade 1: Mild	n (%)	n (%)	n (%)
		Unlikely	Grade 2: Moderate	n (%)	n (%)	n (%)
		Unlikely	Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Unlikely	Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Unlikely	Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
		Possibly	Grade 1: Mild	n (%)	n (%)	n (%)
		Possibly	Grade 2: Moderate	n (%)	n (%)	n (%)
		Possibly	Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Possibly	Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Possible	Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
		Probably	Grade 1: Mild	n (%)	n (%)	n (%)
		Probably	Grade 2: Moderate	n (%)	n (%)	n (%)
		Probably	Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Probably	Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Probably	Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
		Definitely	Grade 1: Mild	n (%)	n (%)	n (%)
		Definitely	Grade 2: Moderate	n (%)	n (%)	n (%)
		Definitely	Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Definitely	Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Definitely	Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)

*If a subject experiences the same event more than once the most closely related to study drug and most severe is tabulated.

Table E.1.6
Part 1: Number (%) of Subjects with Treatment-emergent Adverse Events* Meeting DLT Criteria by System Organ Class and Preferred Term
Safety Population

		TSD-001		
System Organ Class	**Preferred Term**	**Part 1: Cohort 1 (N =)**	**Part 1: Cohort 2 (N =)**	**Part 1 (N =)**
Gastrointestinal Disorders	Diarrhea	n (%)	n (%)	n (%)
	Dyspepsia	n (%)	n (%)	n (%)
	Nausea	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)
Nervous System Disorders	Dizziness	n (%)	n (%)	n (%)
	Headache	n (%)	n (%)	n (%)
	Somnolence	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)

*If a subject experiences the same event more than once the first occurrence is tabulated.

Table E.1.7
Part 1: Number (%) of Subjects with Serious Treatment-emergent Adverse Events* by System Organ Class and Preferred Term
Safety Population

		TSD-001		
System Organ Class	**Preferred Term**	**Part 1: Cohort 1 (N =)**	**Part 1: Cohort 2 (N =)**	**Part 1 (N =)**
Gastrointestinal Disorders	Diarrhea	n (%)	n (%)	n (%)
	Dyspepsia	n (%)	n (%)	n (%)
	Nausea	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)
Nervous System Disorders	Dizziness	n (%)	n (%)	n (%)
	Headache	n (%)	n (%)	n (%)
	Somnolence	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)

*If a subject experiences the same event more than once the first occurrence is tabulated.

Table E.1.8
Part 1: Number (%) of Subjects with Serious Treatment-related, Treatment-emergent Adverse Events* by System Organ Class and Preferred Term
Safety Population

		TSD-001		
System Organ Class	**Preferred Term**	**Part 1: Cohort 1 (N =)**	**Part 1: Cohort 2 (N =)**	**Part 1 (N =)**
Gastrointestinal Disorders	Diarrhea	n (%)	n (%)	n (%)
	Dyspepsia	n (%)	n (%)	n (%)
	Nausea	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)
Nervous System Disorders	Dizziness	n (%)	n (%)	n (%)
	Headache	n (%)	n (%)	n (%)
	Somnolence	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)

*If a subject experiences the same event more than once the first occurrence is tabulated.

Table E.2.1
Part 1: Vital Signs Measurements
Descriptive Statistics
Safety Population

Systolic Blood Pressure (mm Hg)

Visit		n	Mean	SD	SEM	Minimum	Median	Maximum
Day 1	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 1	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 2	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 3	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 4	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 5	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 6	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 7	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 8	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 9	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 10	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 11	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 14	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 15	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 16	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Change = Visit Value minus Day 1

Note: This table will be repeated for diastolic blood pressure, pulse rate, respiratory rate and body temperature

Table E.2.2
Part 1: Laboratory Measurements
Descriptive Statistics
Safety Population

Hemoglobin (%)

Visit		n	Mean	SD	SEM	Minimum	Median	Maximum
Screening	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Day 1	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 1	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 2	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 3	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 4	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 5	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 6	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 7	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 8	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 9	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 10	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 11	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 16	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Change = Visit Value minus Screening

Note: This table will be repeated for all continuous lab parameters

Table E.2.3
Part 1: Laboratory Measurements
Shift from Screening: Number (%) of Subjects
Safety Population

		Normal at Screening to:		**Abnormal at Screening to:**	
Parameter	**Visit**	**Normal**	**Abnormal**	**Normal**	**Abnormal**
Albumin (g/dL)	Week 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Albumin/Globulin (RATIO)	Week 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Alkaline Phosphatase (U/L)	Week 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
etc.	Week 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: This table will be repeated for all lab parameters

Table E.2.4
Part 1: ECG Measurements
Descriptive Statistics
Safety Population

Heart Rate (bpm)

Visit		n	Mean	SD	SEM	Minimum	Median	Maximum
Screening	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 16	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Change = Visit Value minus Screening

Note: This table will be repeated for all continuous ECG parameters

Table E.2.5
Part 1: ECG: ST-segment and Interval Measurements
Shift from Screening: Number (%) of Subjects
Safety Population

		Normal at Screening to:		**Abnormal, NCS at Screening to:**	
Parameter	**Visit**	**Normal**	**Abnormal, NCS**	**Normal**	**Abnormal, NCS**
PR Interval, Aggregate (msec)	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
QRS Duration, Aggregate (msec)	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
QT Interval, Aggregate (msec)	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table E.2.6
Part 1: ECG: Sinus Rhythm
Shift from Screening: Number (%) of Subjects
Safety Population

		Not Sinus Rhythm at Screening to:		**Sinus Rhythm at Screening to:**	
Parameter	**Visit**	**Not Sinus Rhythm**	**Sinus Rhythm**	**Not Sinus Rhythm**	**Sinus Rhythm**
Sinus Node Rhythms	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table E.2.7
Part 1: ECG: Overall Interpretation
Shift from Screening: Number (%) of Subjects
Safety Population

		Normal at Screening to:		Abnormal, NCS at Screening to:	
Parameter	**Visit**	**Normal**	**Abnormal, NCS**	**Normal**	**Abnormal, NCS**
Interpretation	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table E.2.8
Part 1: ECG: T-wave Interpretation
Shift from Screening: Number (%) of Subjects
Safety Population

		Normal at Screening to:		Abnormal at Screening to:	
Parameter	**Visit**	**Normal**	**Abnormal**	**Normal**	**Abnormal**
T Wave	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table E.2.9
Part 1: Physical Examination
Shift from Screening: Number (%) of Subjects
Safety Population

		Normal at Screening to:			Abnormal, NCS at Screening to:		
Parameter	**Visit**	**Normal**	**Abnormal, NCS**	**Abnormal, CS**	**Normal**	**Abnormal, NCS**	**Abnormal, CS**
Allergies	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
Cardiovascular	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
Dermatological	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
Endocrine/Metabolic	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
Extremities	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
Gastrointestinal	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
General Appear/Constitutional Symptoms	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
Genitourinary/Reproductive	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
HEENT	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
Hematologic	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
Hepatic	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
Lymphatic	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
Musculoskeletal	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
Neurological Function	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
Psychiatric	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)
Respiratory	Week 16	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)	xx (x.xx%)

Table E.2.10
Part 1: Concomitant Medications by WHO Preferred Term and Level 4 ATC: Number (%) of Subjects
Safety Population

WHO Preferred Term	**Level 4 ATC**	**TSD-001** Part 1 (N =)	**TSD-001** Part 1 (N =)	**TSD-001** Part 1 (N =)
Preferred Term #1	ATC Term #1	n (%)	n (%)	n (%)
	ATC Term #2	n (%)	n (%)	n (%)
	ATC Term #3	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)
Preferred Term #2	ATC Term #1	n (%)	n (%)	n (%)
	ATC Term #2	n (%)	n (%)	n (%)
	ATC Term #3	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)

*If a subject receives the same medication more than once the first occurrence is tabulated.

Table E.3.1
Part 2: Overall Adverse Event Information
Safety Population

	TSD-001		
Number of Subjects:	**Cohort 1 (N =)**	**Cohort 2 (N =)**	**Part 2 (N =)**
At Least One TEAE	n (%)	n (%)	n (%)
At Least One Treatment-Related TEAE	n (%)	n (%)	n (%)
At Least One TEAE meeting DLT criteria	n (%)	n (%)	n (%)
At Least One Treatment-Related TEAE meeting DLT criteria	n (%)	n (%)	n (%)
At Least One Serious TEAE	n (%)	n (%)	n (%)
At Least One Serious Treatment-Related TEAE	n (%)	n (%)	n (%)
At Least One TEAE Leading to Treatment Discontinuation	n (%)	n (%)	n (%)

TEAE=treatment-emergent adverse event

Table E.3.2
Part 2: Number (%) of Subjects with Treatment-emergent Adverse Events* by System Organ Class and Preferred Term
Safety Population

		TSD-001		
System Organ Class	**Preferred Term**	**Cohort 1 (N =)**	**Cohort 2 (N =)**	**Part 2 (N =)**
Gastrointestinal Disorders	Diarrhea	n (%)	n (%)	n (%)
	Dyspepsia	n (%)	n (%)	n (%)
	Nausea	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)
Nervous System Disorders	Dizziness	n (%)	n (%)	n (%)
	Headache	n (%)	n (%)	n (%)
	Somnolence	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)
etc.	etc.	n (%)	n (%)	n (%)

*If a subject experiences the same event more than once the first occurrence is tabulated.

Table E.3.3
Part 2: Number (%) of Subjects with Treatment-emergent Adverse Events* by System Organ Class and Preferred Term by Nearest Relationship to Study Drug
Safety Population

				TSD-001	
System Organ Class	**Preferred Term**	**Relationship**	**Cohort 1 (N =)**	**Cohort 2 (N =)**	**Part 2 (N =)**
Gastrointestinal Disorders	Diarrhea	Not Related	n (%)	n (%)	n (%)
		Unlikely	n (%)	n (%)	n (%)
		Possibly	n (%)	n (%)	n (%)
		Probably	n (%)	n (%)	n (%)
		Definitely	n (%)	n (%)	n (%)
	Dyspepsia	Not Related	n (%)	n (%)	n (%)
		Unlikely	n (%)	n (%)	n (%)
		Possibly	n (%)	n (%)	n (%)
		Probably	n (%)	n (%)	n (%)
		Definitely	n (%)	n (%)	n (%)
	etc.	Not Related	n (%)	n (%)	n (%)
		Unlikely	n (%)	n (%)	n (%)
		Possibly	n (%)	n (%)	n (%)
		Probably	n (%)	n (%)	n (%)
		Definitely	n (%)	n (%)	n (%)
Nervous System Disorders	Dizziness	Not Related	n (%)	n (%)	n (%)
		Unlikely	n (%)	n (%)	n (%)
		Possibly	n (%)	n (%)	n (%)
		Probably	n (%)	n (%)	n (%)
		Definitely	n (%)	n (%)	n (%)
	Headache	Not Related	n (%)	n (%)	n (%)
		Unlikely	n (%)	n (%)	n (%)
		Possibly	n (%)	n (%)	n (%)
		Probably	n (%)	n (%)	n (%)
		Definitely	n (%)	n (%)	n (%)
	etc.	Not Related	n (%)	n (%)	n (%)
		Unlikely	n (%)	n (%)	n (%)
		Possibly	n (%)	n (%)	n (%)
		Probably	n (%)	n (%)	n (%)
		Definitely	n (%)	n (%)	n (%)

*If a subject experiences the same event more than once the most closely related to study drug is tabulated.

Table E.3.4
Part 2: Number (%) of Subjects with Treatment-emergent Adverse Events* by System Organ Class and Preferred Term by Maximum Severity
Safety Population

			TSD-001		
System Organ Class	**Preferred Term**	**CCTAE Grade: Severity**	**Cohort 1 (N =)**	**Cohort 2 (N =)**	**Part 2 (N =)**
Gastrointestinal Disorders	Diarrhea	Grade 1: Mild	n (%)	n (%)	n (%)
		Grade 2: Moderate	n (%)	n (%)	n (%)
		Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
	Dyspepsia	Grade 1: Mild	n (%)	n (%)	n (%)
		Grade 2: Moderate	n (%)	n (%)	n (%)
		Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
	etc.	Grade 1: Mild	n (%)	n (%)	n (%)
		Grade 2: Moderate	n (%)	n (%)	n (%)
		Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
Nervous System Disorders	Dizziness	Grade 1: Mild	n (%)	n (%)	n (%)
		Grade 2: Moderate	n (%)	n (%)	n (%)
		Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
	Headache	Grade 1: Mild	n (%)	n (%)	n (%)
		Grade 2: Moderate	n (%)	n (%)	n (%)
		Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
	etc.	Grade 1: Mild	n (%)	n (%)	n (%)
		Grade 2: Moderate	n (%)	n (%)	n (%)
		Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)

*If a subject experiences the same event more than once the most severe is tabulated.

Table E.3.5
Part 2: Number (%) of Subjects with Treatment-emergent Adverse Events* by System Organ Class and Preferred Term
by Nearest Relationship to Study Drug and Maximum Severity
Safety Population

					TSD-001	
System Organ Class	**Preferred Term**	**Relationship**	**CTCAE Grade: Severity**	**Cohort 1 (N =)**	**Cohort 2 (N =)**	**Part 2 (N =)**
Gastrointestinal Disorders	Diarrhea	Not Related	Grade 1: Mild	n (%)	n (%)	n (%)
		Not Related	Grade 2: Moderate	n (%)	n (%)	n (%)
		Not Related	Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Not Related	Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Not Related	Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
		Unlikely	Grade 1: Mild	n (%)	n (%)	n (%)
		Unlikely	Grade 2: Moderate	n (%)	n (%)	n (%)
		Unlikely	Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Unlikely	Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Unlikely	Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
		Possibly	Grade 1: Mild	n (%)	n (%)	n (%)
		Possibly	Grade 2: Moderate	n (%)	n (%)	n (%)
		Possibly	Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Possibly	Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Possible	Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
		Probably	Grade 1: Mild	n (%)	n (%)	n (%)
		Probably	Grade 2: Moderate	n (%)	n (%)	n (%)
		Probably	Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Probably	Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Probably	Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)
		Definitely	Grade 1: Mild	n (%)	n (%)	n (%)
		Definitely	Grade 2: Moderate	n (%)	n (%)	n (%)
		Definitely	Grade 3: Severe: Medically Significant	n (%)	n (%)	n (%)
		Definitely	Grade 4: Severe: Life-threatening	n (%)	n (%)	n (%)
		Definitely	Grade 5: Severe: Death related to AE	n (%)	n (%)	n (%)

*If a subject experiences the same event more than once the most closely related to study drug and most severe is tabulated.

Table E.3.6
Part 2: Number (%) of Subjects with Serious Treatment-emergent Adverse Events* by System Organ Class and Preferred Term
Safety Population

		TSD-001		
System Organ Class	**Preferred Term**	**Cohort 1 (N =)**	**Cohort 2 (N =)**	**Part 2 (N =)**
Gastrointestinal Disorders	Diarrhea	n (%)	n (%)	n (%)
	Dyspepsia	n (%)	n (%)	n (%)
	Nausea	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)
Nervous System Disorders	Dizziness	n (%)	n (%)	n (%)
	Headache	n (%)	n (%)	n (%)
	Somnolence	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)

*If a subject experiences the same event more than once the first occurrence is tabulated.

Table E.3.7
Part 2: Number (%) of Subjects with Serious Treatment-related, Treatment-emergent Adverse Events* by System Organ Class and Preferred Term
Safety Population

		TSD-001		
System Organ Class	**Preferred Term**	**Cohort 1 (N =)**	**Cohort 2 (N =)**	**Part 2 (N =)**
Gastrointestinal Disorders	Diarrhea	n (%)	n (%)	n (%)
	Dyspepsia	n (%)	n (%)	n (%)
	Nausea	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)
Nervous System Disorders	Dizziness	n (%)	n (%)	n (%)
	Headache	n (%)	n (%)	n (%)
	Somnolence	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)

*If a subject experiences the same event more than once the first occurrence is tabulated.

Table E.4.1
Part 2: Vital Signs Measurements
Descriptive Statistics
Safety Population

Systolic Blood Pressure (mm Hg)

Visit		n	Mean	SD	SEM	Minimum	Median	Maximum
Day 1	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 1	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 2: Day 15	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 2: Day 16	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 2: Day 17	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 2: Day 18	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 3	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 4	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 5	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 6	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 7	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 9	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 12	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 15	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
End of Study	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Change = Visit Value minus Day 1

Note: This table will be repeated for diastolic blood pressure, pulse rate, respiratory rate and body temperature

Table E.4.2
Part 2: Laboratory Measurements
Descriptive Statistics
Safety Population

Hemoglobin (%)

Visit		n	Mean	SD	SEM	Minimum	Median	Maximum
Screening	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Day 1	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 1	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 2	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 3	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 4	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 5	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 6	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 7	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Week 9	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
End of Study	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Change = Visit Value minus Screening

Note: This table will be repeated for all continuous lab parameters

Table E.4.3
Part 2: Laboratory Measurements
Shift from Screening: Number (%) of Subjects
Safety Population

		Normal at Screening to:		**Abnormal at Screening to:**	
Parameter	**Visit**	**Normal**	**Abnormal**	**Normal**	**Abnormal**
Albumin (g/dL)	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Albumin/Globulin (RATIO)	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Alkaline Phosphatase (U/L)	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
etc.	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: This table will be repeated for all lab parameters

Table E.4.4
Part 2: ECG Measurements
Descriptive Statistics
Safety Population

Heart Rate (bpm)

Visit		n	Mean	SD	SEM	Minimum	Median	Maximum
Screening	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
End of Study	Value	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Change	xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

Change = Visit Value minus Screening

Note: This table will be repeated for all continuous ECG parameters

Table E.4.5
Part 2: ECG: ST-segment and Interval Measurements
Shift from Screening: Number (%) of Subjects
Safety Population

		Normal at Screening to:		**Abnormal, NCS at Screening to:**	
Parameter	**Visit**	**Normal**	**Abnormal, NCS**	**Normal**	**Abnormal, NCS**
PR Interval, Aggregate (msec)	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
QRS Duration, Aggregate (msec)	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
QT Interval, Aggregate (msec)	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table E.4.6
Part 2: ECG: Sinus Rhythm
Shift from Screening: Number (%) of Subjects
Safety Population

		Not Sinus Rhythm at Screening to:		**Sinus Rhythm at Screening to:**	
Parameter	**Visit**	**Not Sinus Rhythm**	**Sinus Rhythm**	**Not Sinus Rhythm**	**Sinus Rhythm**
Sinus Node Rhythms	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table E.4.7
Part 2: ECG: Overall Interpretation
Shift from Screening: Number (%) of Subjects
Safety Population

		Normal at Screening to:		Abnormal at Screening to:	
Parameter	**Visit**	**Normal**	**Abnormal**	**Normal**	**Abnormal**
Interpretation	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table E.4.8
Part 2: ECG: T-wave Interpretation
Shift from Screening: Number (%) of Subjects
Safety Population

		Normal at Screening to:		**Abnormal at Screening to:**	
Parameter	**Visit**	**Normal**	**Abnormal**	**Normal**	**Abnormal**
T Wave	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table E.4.9
Part 2: Physical Examination
Shift from Screening: Number (%) of Subjects
Safety Population

		Normal at Screening to:		**Abnormal, NCS at Screening to:**		
Parameter	**Visit**	**Normal**	**Abnormal, NCS**	**Normal**	**Abnormal, NCS**	**Abnormal, CS**
Allergies	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Cardiovascular	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dermatological	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Endocrine/Metabolic	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Extremities	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Gastrointestinal	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
General Appear/Constitutional Symptoms	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Genitourinary/Reproductive	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
HEENT	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hematologic	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hepatic	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lymphatic	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Musculoskeletal	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Neurological Function	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Psychiatric	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Respiratory	Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Week 16	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table E.4.10
Part 2: Concomitant Medications by WHO Preferred Term and Level 4 ATC: Number (%) of Subjects
Safety Population

			TSD-001	
WHO Preferred Term	**Level 4 ATC**	**Cohort 1 (N =)**	**Cohort 2 (N =)**	**Part 2 (N =)**
Preferred Term #1	ATC Term #1	n (%)	n (%)	n (%)
	ATC Term #2	n (%)	n (%)	n (%)
	ATC Term #3	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)
Preferred Term #2	ATC Term #1	n (%)	n (%)	n (%)
	ATC Term #2	n (%)	n (%)	n (%)
	ATC Term #3	n (%)	n (%)	n (%)
	etc.	n (%)	n (%)	n (%)

*If a subject receives the same medication more than once the first occurrence is tabulated.

Table F.1.1
Part 3 (n=6): One Year Recurrence/Disease-Free Survival in Part 1 Subjects
MITT Population

	EAU Risk Category[a]		**TSD-001 (N=)**
One Year Recurrence/Disease-Free Survival	Low Risk	n (%)	n (%)
	Intermediate Risk	n (%)	n (%)
	All Subjects (Part 1)	n (%)	n (%)

[a] Low risk defined as: Primary, Solitary, LG/G1 <3cm, no CIS
Intermediate risk defined as: All tumors not defined as Low risk or High risk
High risk defined as: *T1 tumor, *HG/G3 tumor, *CIS. *Multiple, recurrent, and large (>3cm) Ta G1G2 tumors (all conditions must be present)

Note: This table will be repeated for the PP population

Table F.1.2
Part 3 (n=6): Two Year Recurrence/Disease-Free Survival in Part 1 Subjects
MITT Population

	EAU Risk Category[a]		**TSD-001 (N=)**
Two Year Recurrence/Disease-Free Survival	Low Risk	N	x
		25th Percentile	xx.x
		Median (50th percentile)	xx.x
		75th Percentile	xx.x
	Intermediate Risk	N	x
		25th Percentile	xx.x
		Median (50th percentile)	xx.x
		75th Percentile	xx.x
	All Subjects (Part 1)	N	x
		25th Percentile	xx.x
		Median (50th percentile)	xx.x
		75th Percentile	xx.x

Kaplan-Meier method was used to calculate the 25th, 50th and 75th percentiles.

[a] Low risk defined as: Primary, Solitary, LG/G1 <3cm, no CIS
Intermediate risk defined as: All tumors not defined as Low risk or High risk
High risk defined as: *T1 tumor, *HG/G3 tumor, *CIS. *Multiple, recurrent, and large (>3cm) Ta G1G2 tumors (all conditions must be present)

Note: This table will be repeated for the PP population

21. APPENDIX 1

Table 2: Part 1 Schedule of Assessments

Visit	Screening	Day -12	Day 1	Day 8 Week 1	Day 15 Week 2	Day 22 Week 3	Day 29 Week 4	Day 36 Week 5	Day 43 Week 6	Day 50 Week 7	Day 57 Week 8	Day 64 Week 9	Day 71 Week 10	Day 78 Week 11	Day 99 Week 14	Day 106 Week 15	Day 113 Week 16
Visit Window	**≤ 28 days before Day 1**	**±2 days**	**N/A**	**±1 day**	**±1 day**	**±1 day**	**±2 days**	**±2 days**	**±2 days**	**±2 days**	**±2 days**	**±2 days**	**±2 days**	**±2 days**	**±7 days**	**±7 days**	**±7 days**
Informed consent	X																
Subject demographics	X																
Eligibility criteria	X	X	X														
Medical/surgical history	X																
Hemoglobin A1c	X																
Weight and height	X																X
Drug screen	X																X
Urinalysis with pH[1]	X		X		X		X		X		X		X				X
Pregnancy test (urine)[2]	X		X														X
12-lead ECG[1]	X																X
Vital signs (BP, HR, RR, BT)[1]	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical examination[1]	X																X
Chemistry panel (fasted ≥ 2 hours)[1]	X						X										X
Hematology panel[1]	X		X	X	X	X	X	X	X	X	X	X	X	X			X
Prior/concurrent medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Endoscopic assessment[3]	X[7]	X[8]												X[9]			
Enrollment			X														
Administer study drug[4]			X		X		X		X		X		X				
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Paclitaxel level plasma[5]			X		X		X		X		X		X				
Paclitaxel level urine[6]			X		X		X		X		X		X				
IPSS, OAB-q	X												X				X

Treatment exit[10]																	X

BP = blood pressure; BT = body temperature; ECG = electrocardiogram; HR = heart rate; IPSS = International Prostate Symptom Score (men only); N/A = not applicable; OAB-q = Overactive Bladder Questionnaire; RR = respiratory rate; TURBT = transurethral resection of bladder tumor

1. May also be performed at principal investigator's discretion at any visit (including unscheduled visits).
2. For women of childbearing potential.
3. Endoscopic assessment includes TURBT (Day -12), voided cytology (screening/Day 78), and/or cystoscopy (screening/Day 78).
4. Study drug is administered intravesically using sterile urethral catheter. Intravesical dwell time = 2 hours (1 hour or more will be acceptable, depending on subject's tolerability of the procedure). For study dose escalation, study drug reconstitution, and administration instructions, see Section 7 and Section 8.
5. Peripheral venous blood will be obtained 15 ± 15 minutes before, and 2 hours ± 10 minutes after, intravesical instillation of TSD-001.
6. Urine (duplicate aliquots via catheterized or voided) will be obtained 15 ± 15 minutes before, and 2 hours ± 10 minutes after, intravesical instillation of TSD-001. Urine pH will be measured by urine pH test strips at each timepoint. Select sites will make observations on urine appearance (turbidity and precipitation).
7. Voided cytology and cystoscopy will be performed at screening visit. Positive cytology finding will result in screen failure.
8. TURBT to be performed on Day -12.
9. Voided cytology and cystoscopy performed in office as bladder tumor standard-of-care at screening and Day 78 ± 2 days. A cystoscope and voided urine cytology should be performed at any early treatment part withdrawal visit prior to Day 78.
10. End treatment part, begin surveillance portion of study (**part 3**).

Table 3: Part 2 Cohort 1 Schedule of Assessments

Visit	Screening	Day 1	Day 8 Week 1	Day 15 Week 2	Days 16,17,18	Day 22 Week 3	Day 29 Week 4	Day 36 Week 5	Day 43 Week 6	Day 64 Week 9	Day 85 Week 12	Day 92 Week 13
Visit Window	**≤ 28 days before Day 1**	**N/A**	**±1 day**	**±2 days**		**±2 days**	**±2 days**	**±2 days**	**±2 days**	**±7 days**	**±7 days**	**±7 days**
Obtain informed consent	X											
Subject demographics	X											
Eligibility criteria	X	X										
Medical/surgical history	X											
Hemoglobin A1c	X											
Weight and height	X											X
Drug screen	X											X
Urinalysis with pH[1]	X	X	X	X		X	X	X				X
Pregnancy test (urine)[2]	X	X										X
12-lead ECG[1]	X											X
Vital signs (BP, HR, RR, BT)[1]	X	X	X	X	X	X	X	X	X	X	X	X
Physical examination[1]	X											X
Chemistry panel (fasted ≥ 2 hours)[1]	X											X
Hematology panel[1]	X	X	X	X		X	X	X	X			X
Prior/concurrent medications	X	X	X	X	X	X	X	X	X	X	X	X
Endoscopic assessment[3]	X[7]	X[8]									X[9,10]	
Enrollment		X										
Administer study drug[4]		X	X	X		X	X	X				
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X
Paclitaxel level plasma[5]		X		X								
Paclitaxel level urine[6]				X	X							
IPSS, OAB-q	X							X				X
Treatment exit[11]												X

BP = blood pressure; BT = body temperature; ECG = electrocardiogram; HR = heart rate; IPSS = International Prostate Symptom Score (men only); N/A = not applicable; OAB-q = Overactive Bladder questionnaire; RR = respiratory rate; TURBT = transurethral resection of bladder tumor

1. May also be performed at principal investigator's discretion at any visit (including unscheduled visit).
2. For women of childbearing potential.

3. Endoscopic assessment includes TURBT (Day 1 for multiple tumor subjects), voided cytology (screening/Day 85), cystoscopy (screening/Day 85), and/or biopsy or TURBT (Day 85).
4. Study drug is administered intravesically using sterile urethral catheter. Intravesical dwell time = 2 hours (1 hour or more will be acceptable, depending on subject's tolerability of the procedure). For study dose escalation, study drug reconstitution and administration instructions see Protocol Section 7.
5. Peripheral venous blood samples will be obtained 2 hours ± 10 minutes after the first intravesical instillation of TSD-001. Peripheral venous blood will also be obtained 15 ± 15 minutes before, and 2 hours ± 10 minutes after the third intravesical instillation of TSD-001.
6. Urine (duplicate aliquots via catheterized or voided) will be obtained 15 ± 15 minutes before, and 2 hours ± 10 minutes after, the third intravesical instillation of TSD-001 only. Urine pH will be measured by urine pH test strips at each timepoint. Select sites will make observations on urine appearance (turbidity and precipitation). Additional urine samples should be obtained on days 16, 17, and 18 (24, 48, and 72 hours, respectively, following the third dose of TSD-001).
7. Voided cytology and cystoscopy will be performed at screening visit. Positive cytology finding will result in screen failure.
8. TURBT to be performed on Day 1 for subjects not meeting solitary tumor eligibility; all tumors except the marker lesion tumor will be removed on Day 1.
9. TURBT performed if evidence of lesion is present.
10. On Day 85, if there is no cystoscopic evidence of bladder tumor, biopsy marker lesion site and obtain urine cytology. Performed at Day 85 or any early treatment part withdrawal before week 12.
11. End treatment part, begin surveillance portion of study (**part 3**).

Table 4: Part 2 Cohort 2 Schedule of Assessments

Visit	Screening	Day 1	Day 8 Week 1	Day 15 Week 2	Days 16, 17, 18	Day 22 Week 3	Day 29 Week 4	Day 36 Week 5	Day 43 Week 6	Day 50 Week 7	Day 64 Week 9	Day 85 Week 12	Day 106 Week 15	Day 113 Week 16
Visit Window	**≤ 28 days before Day 1**	**N/A**	**±1 day**	**±2 days**		**±2 days**	**±2 days**	**±2 days**	**±2 days**	**±2 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**
Obtain informed consent	X													
Subject demographics	X													
Eligibility criteria	X	X												
Medical/surgical history	X													
Hemoglobin A1c	X													
Weight and height	X													X
Drug screen	X													X
Urinalysis with pH[1]	X	X	X	X		X	X	X	X	X				X
Pregnancy test (urine)[2]	X	X												X
12-lead ECG[1]	X													X
Vital signs (BP, HR, RR, BT)[1]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical examination[1]	X													X
Chemistry panel (fasted ≥ 2 hours)[1]	X													X
Hematology panel[1]	X	X	X	X		X	X	X	X	X	X			X
Prior/concurrent medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Endoscopic assessment[3]	X[7]	X[8]											X[9,10]	
Enrollment		X												
Administer study drug[4]		X	X	X		X	X	X	X	X				
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Paclitaxel level plasma[5]		X		X										
Paclitaxel level urine[6]				X	X									
IPSS, OAB-q	X									X				X
Treatment exit[11]														X

BP = blood pressure; BT = body temperature; ECG = electrocardiogram; HR = heart rate; IPSS = International Prostate Symptom Score (men only); N/A = not applicable; OAB-q = Overactive Bladder questionnaire; RR = respiratory rate; TURBT = transurethral resection of bladder tumor

1. May also be performed at principal investigator's discretion at any visit (including unscheduled visit).

2. For women of childbearing potential.
3. Endoscopic assessment includes TURBT (Day 1 for multiple tumor subjects), voided cytology (screening/Day 106), cystoscopy (screening/Day 106), and/or biopsy or TURBT (Day 106).
4. Study drug is administered intravesically using sterile urethral catheter. Intravesical dwell time = 2 hours (1 hour or more will be acceptable, depending on subject's tolerability of the procedure). For study dose escalation, study drug reconstitution and administration instructions see Protocol Section 7.
5. Peripheral venous blood samples will be obtained 2 hours ± 10 minutes after the first intravesical instillation of TSD-001. Peripheral venous blood will also be obtained 15 ± 15 minutes before, and 2 hours ± 10 minutes after the third intravesical instillation of TSD-001.
6. Urine (duplicate aliquots via catheterized or voided) will be obtained 15 ± 15 minutes before, and 2 hours ± 10 minutes after, the third intravesical instillation of TSD-001 only. Urine pH will be measured by urine pH test strips at each timepoint. Select sites will make observations on urine appearance (turbidity and precipitation). Additional urine samples should be obtained on days 16, 17, and 18 (24, 48, and 72 hours, respectively, following the third dose of TSD-001).
7. Voided cytology and cystoscopy will be performed at screening visit. Positive cytology at screening will result in screen failure.
8. TURBT to be performed on Day 1 for subjects not meeting solitary tumor eligibility; all tumors except the marker lesion tumor will be removed on Day 1.
9. TURBT performed if evidence of lesion is present.
10. On Day 106, if there is no cystoscopic evidence of bladder tumor, biopsy marker lesion site and obtain urine cytology. Performed at Day 106 or any early treatment part withdrawal before Week 15.
11. End treatment part 2, begin surveillance portion of study (**part 3**).

Table 5: Surveillance Schedule of Assessments (Part 3)

Visit[1]	Treatment part exit	Month 6 (Day 181)	Month 9 (Day 271)	Month 12 (Day 366)	Month 15 (Day 456)	Month 18 (Day 546	Month 21 (Day 636)	Exit Month 24 (Day 731)
Visit Window		±7 days	±7 days	±7 days	±7 days	±7 days	±7 days	±7 days
Obtain informed consent[2]	X							
Cystoscopy		X	X	X	X	X	X	X
Prior/concurrent medications[3]	X	X	X	X	X	X	X	X
Adverse events[4]/Serious adverse events	X	X	X	X	X	X	X	X
Study surveillance exit								X

AE = adverse event; eCRF = electronic case report form

1. Visit timing is from initial instillation in previous (treatment) part (e.g. Month 6 is approximately 6 months from Day 1 of previous part).
2. If not previously obtained in **part 1** or **part 2**, obtain informed consent for **part 3** at treatment exit visit or first available visit in **part 3**.
3. Only recorded in eCRF if they relate to an AE continuing from **part 1** or **part 2** or a treatment for a recurrence.
4. AEs continued from **part 1** or **part 2**, but no new AEs will be recorded.

22. APPENDIX 2

Scoring Manual for the OAB-q

To calculate a symptom severity score, create a summed score from the listed items and use the formula below the table to transform the value. This will provide symptom scores where higher score values are indicative of greater symptom severity or bother and lower scores indicate minimal symptom severity.

Scale	Sum Item Values	Lowest and Highest Possible Raw Scores	Possible Raw Score Range
Symptom Severity	1 - 8	8,48	40

Transformation for Symptom Severity raw scores ONLY:

$$\text{Transformed Score} = \frac{(\underline{\textit{Actual} \text{ raw score} - \textit{lowest} \text{ possible raw score}})}{\text{Possible raw score range}} \quad \text{X } 100$$

For the HRQL subscales (coping, concern, sleep, and social), create summed scores of the listed items for each individual subscale. To calculate the HRQL total score, sum the value of each individual subscale (do not sum all the individual items). Use the formula below the table to transform all values. Higher scores will be indicative of better HRQL.

Scale	Sum Item Values	Lowest and Highest Possible Raw Scores	Possible Raw Score Range

Coping	9+11+16+21+22+26+32+33	8,48	40
Concern	12+13+14+19+23+25+29	7,42	35
Sleep	10+15+17+24+30	5,30	25
Social	18+20+27+28+31	5,30	25
HRQL Total	Sum of HRQL subscales (not individual items)	25, 150	125

Formula for transformation of HRQL raw scores:

$$\text{Transformed Score} = \frac{(\textit{Highest}\ \text{possible score} - \textit{Actual raw}\ \text{score})}{\text{Possible raw score range}} \times 100$$

Missing Items

For the subscale analyses, if < 50% of the scale items are missing, the scale should be retained with the mean scale score of the items present used to impute a score for the missing items. If ≥ 50% of the items are missing, no scale score should be calculated, the subscale score should be considered missing. If a subscale score is missing, the HRQL Total score cannot be calculated.