STATISTICAL ANALYSIS PLAN

EVALUATION OF APPLAUD MEDICAL'S ACOUSTIC ENHANCER WITH LASER LITHOTRIPSY IN THE TREATMENT OF URINARY STONES

CIP-0001

Protocol Revision E (19Jan2022)

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REVISION HISTORY

Table 1 SAP Version History Summary

SAP Version	Approval Date	Change	Rationale
1.0	DDMONYYYY	Not Applicable	Original version

ABBREVIATIONS

ABBREVIATION	DEFINITION OR DESCRIPTION
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
CI	Confidence interval
CRF	Case Report Form
CSR	Clinical Study Report
GMR	Geometric mean ratio
ICH	International Conference on Harmonisation
ITT	Intent-to-treat
MCMC	Markov Chain Monte Carlo
MedDRA	Medical Dictionary for Regulatory Activities
MI	Multiple imputation
PP	Per protocol
PT	Preferred term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOC	System Organ Class
TRE	Total radiant energy
UADE	Unanticipated adverse device effect
WHO	World Health Organization

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1 INTRODUCTION

This statistical analysis plan (SAP) describes the planned analysis and reporting for Applaud Medical's protocol number CIP-0001: Evaluation of Applaud Medical's Acoustic Enhancer with Laser Lithotripsy in the Treatment of Urinary Stones, revision E, dated 19Jan2022. This SAP will be signed off, at a minimum, before the final database lock and contains detailed information to aid in the performance of the statistical analysis and reporting of the study data for use in the final clinical study report (CSR). This SAP is being written with due consideration of the recommendations outlined in the most recent International Conference on Harmonization (ICH) E9 Guideline entitled Guidance for Industry: Statistical Principles for Clinical Trials and the most recent ICH E3 Guideline and the Guidance for Industry: Structure and Content of Clinical Study.

This SAP describes the data that will be analyzed and the subject characteristics, safety, and efficacy assessments that will be evaluated. This SAP provides details of the specific statistical methods that will be used. If additional analyses are performed after database lock and unblinding to supplement the planned analyses described in this SAP, they will be clearly identified as post-hoc in the CSR.

In addition to the study protocol, the case report forms (CRFs) were reviewed in preparation of this SAP.

The reader of this SAP is encouraged to also read the clinical protocol for details on the planned conduct of this study. Operational aspects related to collection and timing of planned clinical assessments are not repeated in this SAP unless relevant to the planned analysis.

1.1 STUDY OBJECTIVES

The purpose of this pivotal study is to evaluate the safety and effectiveness of Applaud Acoustic Enhancer when used in conjunction with conventional ureteroscopic laser systems in the treatment of subjects with urinary stones.

2 STUDY DESIGN AND PROCEDURES

The clinical study is a prospective, multicenter, two-arm, randomized, double blinded study in male or female subjects 18 to 75 years of age with a diagnosis of urinary stone disease. For this study, double blinded means: 1) study subjects will not be informed of their treatment allocation through the index procedure, and 2) in assessing stone fragmentation using a CT image as defined in the primary endpoint, an independent radiologist will conduct the assessment and will be blinded to the treatment allocation of each subject's CT image.

The study visits consist of Screening, Treatment/Procedure [Day 1], Day 14 (+/- 4 days), Day 30 (+14 days), and Day 90 (+/- 21 days). Subjects who have unresolved hydronephrosis at Day 30 need to continue to Day 90. At 90-days post procedure, subjects who have on-going device and/or procedure-related serious adverse events (including device and/or procedure related hydronephrosis) and subjects with pre-existing (prior to treatment) hydronephrosis that have worsened or recurred will continue to be followed until the event has resolved or is deemed stable by the investigator prior to study exit. A total of 196 subjects will be enrolled in this study at up to 27 investigational sites located in the U.S., with each site enrolling no more than 20% of the total.

Following consent and if a subject meets the study's inclusion/exclusion criteria, the subject will be randomly assigned to the investigational arm (Acoustic Enhancer with URS-LL) or

control arm (URS-LL) on the day of the procedure. Random assignment will be conducted using an allocation ratio of 1:1 with one subject randomized to the investigational arm for each subject randomized to the control arm. A minimum of 176 evaluable subjects will be needed for analysis. After randomization and during procedure, eligibility criteria will be verified. If subjects are found to not meet eligibility criteria they will be considered screen failures and will not be considered randomized and treated for analysis purposes.

Random assignment will be conducted using a stratified permuted block design generated separately for each clinical site.

3 DETERMINATION OF SAMPLE SIZE

A sample size of 196 enrolled and randomized subjects randomized 1:1 to the investigational arm (Acoustic Enhancer with URS-LL) and the control arm (URS-LL) was selected based on consideration of the primary endpoint. Assuming no more than 10% non-evaluable subjects, this provides a randomized sample size 176 subjects (88 per arm).

The primary hypothesis test for the treatment success outcome is as follows:

$$H_0: p_{AE} \leq p_{Control} \text{ vs } H_1: p_{AE} > p_{Control}$$

Where p_{AE} is the acoustic enhanced response rate and $p_{Control}$ is the control response rate (no acoustic enhancement). Using a one-sided 0.025 Farrington-Manning test, a 55% response rate in the control arm, and a 75% response rate in the investigational arm, the sample size provides 80% power for the analysis. The 55% control arm response rate is based on reported results for laser lithotripsy with CT-based follow-up as described in the protocol, while the 75% response rate in the investigational arm is based on exploratory clinical studies.

4 STUDY ASSESSMENTS

All assessments related to primary and secondary endpoints are included in a separate analysis plan.

4.1 LASERING TIME AND INTERVENTIONAL STONE PROCEDURES

While the secondary endpoint, total radiant energy (TRE), is a more rigorous and broadly applicable indicator of improved stone erosion, pitting and fragmentation through the generation of additional stone-fragmenting shockwaves, a demonstration of lower mean lasering time in the Acoustic Enhancer arm compared to the standard laser arm could be clinically important. Total lasering time (seconds) will be summarized as a numeric variable during the Treatment/Procedure [Day 1].

Interventional stone procedure(s) on stone(s) that were treated as part of the AEROLITH study will be identified as basketing for retrieval of stone material and other as collected on the procedure CRF page. This will be summarized categorically.

5 GENERAL ANALYSIS AND REPORTING CONSIDERATIONS

The primary efficacy analysis will be included in a separate analysis plan and is not covered in this SAP.

P-values for the analysis covered by this SAP will be rounded to three decimal places. If a p-value is less than 0.001 it will be reported as “< 0.001.” If a p-value is greater than 0.999 it

will be reported as "> 0.999." Where reported, all confidence intervals will be two-sided 95% confidence intervals (CIs).

Continuous data will be summarized using descriptive statistics: n, mean, standard deviation, median, minimum and maximum, unless otherwise noted.

Categorical variables will be summarized using frequency counts and percentages. When count data are presented, the percentage for zero counts will be suppressed in order to draw attention to the non-zero counts. The denominator for all percentages will be the number of subjects in that treatment group within the population of interest, unless otherwise noted.

The following conventions will be used throughout the study analysis:

- Day 0 is the date of the procedure.
- Baseline value is defined as the last measurement prior to the procedure.
- Change from baseline is defined as post-baseline value minus baseline value.
- Duration of an AE will be computed in days, calculated by using stop date minus the start date if AE occurs on or after the procedure. If reported as ongoing at the time of database lock, the duration will be calculated using the date of the last visit or the last date of any AE for the subject in the database, whichever is later. Missing dates will be imputed as described in Table 2.
- The number of days in the study is computed as: [Date of study completion or withdrawal minus the date of procedure].
- If duplicate values are obtained at a given visit (e.g., repeated vital sign measurements), the last value will be used unless it is noted that the measurement was in error for that value. Values that compromise interpretation will not be used in summaries (e.g., values that were obtained post-procedure will not be summarized as pre-procedure values).

5.1 ADJUSTMENTS FOR COVARIATES

5.2 NO ADJUSTMENTS FOR COVARIATES ARE PLANNED.HANDLING OF MISSING DATA

No imputation or adjustment for missing assessment data will be used.

See the following table for imputation rules for partial to fully missing or medication dates.

Table 2: Table of Imputation Rules for Missing Medication Dates

Missing Start Date Portion	*Prior to Treatment*	*Same as Treatment Start Date*	*After Treatment Start Date*
Day	Month and Year < Month and Year of first treatment: Start Day = 1 Stop Day = last day of the month	*Month and Year = Month and Year of first treatment:* Start Day = Day of first treatment Stop Day= last day of the month	*Month and Year > Month and Year of First Treatment:* Start Day = 1 Stop Day= last day of the month
Day and Month Define Day as above, then:	*Year < Year of first treatment:* Start Month = Jan Stop Month = Dec	*Year = Year of first treatment:* Start Month = Month of first treatment Stop Month = Dec	*Year > Year of first treatment:* Month = Jan Stop Month = Dec
Day, Month, and Year	To be conservative, completely missing start dates will be set to the date of first treatment, completely missing end dates will be set to the date of last contact.		

After following these imputation rules, if the start date is imputed as a date after the end date, the start date will be set to the end date to provide a positive duration for the event incidence.

Applaud's medical monitor will assess missing AE study medication relationship or severity which will be used analysis purposes.

No other imputation is planned for safety data.

5.3 **ASSESSMENT TIME WINDOWING**

No visit windows will be utilized in this study and all safety and efficacy assessment summaries will be based on the nominal protocol-specified assessment times. Thus, if the protocol specified Day 30 visit occurs on study Day 31, it will still be summarized as a “D30” assessment.

5.4 **POOLING OF INVESTIGATOR SITES**

No pooling is planned for this study.

5.5 ADJUSTMENTS FOR MULTIPLICITY

The study will include a single primary effectiveness endpoint to be tested at the one-sided 0.025 level. If that hypothesis is met, two other endpoints will be considered sequentially. If the first secondary hypothesis is statistically significant, the second hypothesis will also be assessed. Hence, the overall Type I error for the study is controlled for the specified hypotheses.

5.6 EXAMINATION OF SUBGROUPS

No subgroup analysis is planned.

6 SUBJECT SUMMARIES

6.1 ANALYSIS POPULATIONS

6.1.1 Intent-to-Treat (ITT) Population

The ITT population consists of all randomized subjects who meet the study inclusion/exclusion criteria. Subjects who develop UTI or having their stone move to the middle/distal ureter between the time they were screened and were found to be eligible at the time they were randomized, or who no longer meet any of the other inclusion/exclusion criteria at the time of the procedure, will not be treated under the protocol. These subjects will not be included in the ITT analysis. The ITT population will be used for all effectiveness analyses with groups based on the randomized treatment.

6.1.2 Per-Protocol (PP) Population

The Per-Protocol population will consist of all subjects who complete the primary endpoint information without a major protocol deviation; determination of protocol deviation severity will follow Sponsor procedure, CAP-0017. PP will include subjects who have evaluable CTs both at baseline and at 30-day follow-up. The PP population analyses will be completed based on the randomized treatment arm. The PP population may be used for all effectiveness analyses as sensitivity analyses with groups based on the randomized treatment.

The definition of major protocol deviations is defined in CAP-0017. The list of deviations will be reviewed, and deviations that will exclude subjects from the PP population will be identified and documented in an Excel file that will be approved by the Sponsor. The approved Excel file will be incorporated into analysis programming and used to exclude subjects from the PP population. Subjects who are screened but not randomized will not be included in analysis. Subjects who were randomized but failed screening intraoperatively will not be included in the analysis. Any information on these subjects will be made available in a listing if requested by the IRB or FDA.

6.1.3 Safety Population

The Safety population consists of all subjects who had a procedure performed. The Safety population will be used for the safety summaries (AEs) with groups based on the actual treatment received.

6.2 PATIENT DISPOSITION

The number of subjects included in each analysis population (ITT, Safety, and PP) will be summarized by treatment group and overall for all randomized subjects. The number of subjects screened, enrolled, randomized, randomized and not treated, completed the study, and discontinued the study early (including the reasons for discontinuation such as randomized and not treated due to a screen failure) will be summarized for each treatment group and overall.

Subjects who are excluded from an analysis population will be summarized by the reasons for exclusion by treatment group and overall.

6.3 SUBJECT ACCOUNTABILITY

At each post-treatment visit, the number of subjects who should theoretically be included, the number of deaths, the number of subjects not yet overdue, the expected number of subjects, the number of subjects with actual data, and percent follow-up will be summarized by count only.

A subject will be considered theoretically included at a given visit if they satisfy the following:

data extraction date – index procedure date > visit date

Where,
data extraction date = date of the data extract used for generation of tables, listings, and figures (TLFs)

index procedure date = date of procedure

visit date = date of visit for which the relevant study day is needed

The number of deaths at each visit is given where the date of death is on or before the upper protocol-specified window limit for a given visit. The number of deaths is cumulative.

A subject will be considered not yet overdue if they have not been evaluated at a given visit, has not experienced death, and the number of days between the data extraction date and the index procedure falls within the upper half of the time window period.

The expected number of subjects is given by subtracting the number of deaths and not yet overdue from the number of subjects that should be theoretically included at a given visit.

A subject will be counted as actual if they have any data available at the given visit.

Percent follow-up is calculated as (Actual/Expected)*100.

6.4 DEMOGRAPHIC AND BASELINE CHARACTERISTICS

6.4.1 Demographic and Baseline Characteristics

Demographic variables will include age, sex, race, and ethnicity. Baseline characteristics include height (cm), weight (kg), and body mass index (BMI; kg/m^2). Demographics and baseline characteristics will be presented in a by-subject listing and summarized overall and by treatment group using the ITT, PP and Safety populations.

6.4.2 Baseline Disease Status/Disease History

Disease history information will be collected on the Urinary Stone History form, which include:

- History of treatment procedures in study/treatment side (Yes/No)
- Existence of stent in place and whether the stent appears calcified or encrusted is in place
- ~~Existence of radiolucent stones on KUB or Scout CT Imaging and the imaging modality used to access radiolucent stones if radiolucent stones are present~~

Disease status information will be collected on the Vital Signs/Physical Exam form and the Stone Location and Measurement form, which includes:

- Conduct of focused urogenital calculus physical exam and abnormality if conducted (Abnormal findings/No abnormal findings)
- Location of each stone (investigator reported)
- Largest diameter (mm) of each stone (investigator reported)
- Cumulative diameter (mm) of all stones (investigator reported)

Urinary stone history and stone location and measurement will be presented in separate by-subject listings and summarized together overall and by treatment group using the ITT, PP and Safety populations.

6.4.3 Medical and Procedural History

Medical and procedural history will be collected at screening for each body system. All medical history will be presented in a by-subject listing.

6.4.4 Prior and Concomitant Medications

Prior medications are those that stop prior to the start of URS-LL with Acoustic Enhancer URS-LL control procedure. Any medication that stops at or after this time or with missing stop dates is considered concomitant medication.

Prior and concomitant medications are collected throughout the study. Prior and concomitant medications will be coded using World Health Organization Drug Dictionary Anatomical Therapeutic Chemical (WHO/ATC) classification index version Global B3, ATC Level 2. The number and percentage of subjects who take prior and concomitant medications will be summarized separately by drug class and preferred term, overall and by treatment group, for the safety population. A separate summary will be summarized for pain medications for kidney stones. Medications will be summarized by timing (prior to treatment, post-treatment, at Day 14, at Day 30), drug class and preferred term, overall and by treatment group, for the safety population.

A separate summary will also be provided for medications of interest. These will include, but are not limited to, prescription medications associated with kidney stones, post operative

pain medications and medications for AEs. ARA will provide a medication list to Applaud and Applaud will identify these medications.

All medications captured in CRFs will appear in by-subject data listings.

6.5 PROTOCOL DEVIATIONS

Protocol deviations will be captured on CRFs and additional tracked by the operational study team members. They will be categorized as Informed Consent, Inclusion/Exclusion, Study Visit, Clinical Exam/Assessment, or Other. Major protocol deviations are defined in Sponsor's CAP-0017 and will be determined by Sponsor's study team prior to final analysis and unblinding. Subjects experiencing a major protocol deviation will be excluded from the PP population during analysis.

Protocol deviations will be summarized as the number of subjects with any protocol deviation, protocol deviations by category and major/minor status within category, overall and by treatment group for the ITT population.

7 STUDY PROCEDURE MEASUREMENTS

The following Investigational Device/Unblinded Procedure Details will be summarized overall and by treatment group for the ITT population:

- Treatment Side
- Anesthesia Used
- Were the Laser Pulse Energy settings used throughout the procedure within 0.2 and 1.5 J
- Were the Laser Pulse Repetition Rates used throughout the procedure within 5 Hz to 60 Hz?,
- Did the time-averaged power (defined as the product of the Laser Pulse Energy and the Laser Pulse Repetition Rate) exceed 25 W during any portion of the procedure?,
- Were continuous suction devices (e.g., ClearPetra, LithAssist) Used?,
- Post-Procedure Ureteral Stent
- Was the URS-LL procedure able to be performed
- Did the subject remain blinded to the treatment assignment through procedure?,
- Overnight hospital stay required (>24 hours)?
- Duration of fibre placement (min)
- Total Lasering Time (min)

All procedure details will be provided in three by-subject listings to account for all data collected. Pregnancy tests will also be provided in a by-subject listing.

8 EFFICACY EVALUATION

8.1 EFFICACY ENDPOINT(S)

8.1.1 Primary Efficacy Endpoint

The primary efficacy analysis will be included in a separate analysis plan and is not covered in this SAP.

8.1.2 Secondary Efficacy Endpoint(s)

The secondary efficacy analysis will be included in a separate analysis plan and is not covered in this SAP

8.1.3 Exploratory Efficacy Endpoint(s)

- Mean total lasering time (sec). Lasering time is captured in minutes and seconds but will be converted entirely to seconds for analysis.
- Difference in means of total lasering time between groups
- Number of subjects receiving subsequent additional interventional stone procedures (URS-LL, SWL)) for stone(s) that were treated in the AEROLITH study
- Number and percentage of subjects receiving subsequent additional interventional stone procedures for stone(s)
- Number of secondary stone treatments
- Number of subjects taking prescription pain medication for managing stone-associated pain prior to treatment, post treatment, at Day 14 and at Day 30(defined as a medication categorized as a Pain Medication and answered “Yes” to “Medication taken for Kidney Stones?”)

8.2 EFFICACY ANALYSIS

8.2.1 Primary Efficacy Analysis

The primary efficacy analysis will be included in a separate analysis plan and is not covered in this SAP.

8.2.2 Supportive and Sensitivity Analyses of the Primary Endpoint

The primary efficacy analysis will be included in a separate analysis plan and is not covered in this SAP.

8.2.3 Secondary Efficacy Analyses

The secondary efficacy analysis will be included in a separate analysis plan and is not covered in this SAP.

8.2.4 Exploratory Efficacy Analyses

Mean Total Lasering Time

Mean total lasering time (sec) will be summarized descriptively overall and by treatment group and analyzed as a numeric endpoint using the ITT population. A two-sided t-test with equal variances assumed will be used to evaluate the null hypothesis that mean time is similar in both groups. A 95% two-sided CI for the mean difference will be provided.

An ANOVA will be used to evaluate mean total laser time as a function of location, treatment, and location-treatment interaction. Least square means for the treatment effects and difference of least square means will be provided with the associated p-values.

Pseudo SAS Code:

```
ods output diff=diff;
ods output LSMeanDiffCL=pdiff;
ods output LSMeans=lsm;
```

```
proc glm data = <DATA> plots=none;
  class <TREATMENT> <LOC>;
  model <TIME> = <TREATMENT> <LOC> <TREATMENT>*<LOC>;
  lsmeans <TREATMENT>/alpha=0.05 cl pdiff;
run;
```

Additional Interventional Stone Procedures for Treated Stone(s)

The number and percentage of subjects receiving subsequent additional interventional stone procedures for stone(s) that were treated in this study will be summarized overall and by treatment group using the ITT population. A Likelihood-Ratio chi-square test will be used to evaluate the null hypothesis that the proportion of subjects with at least one secondary stone treatment is equal in both groups. The two-sided 0.05 p-value will be reported.

Pseudo SAS Code:

```
ods output ChiSq=chisq;
proc freq data = <DATA>;
  tables <TREATMENT>*<STREAT>/chisq;
run;
```

Where,
<DATA> is the dataset containing at the minimum, treatment and a binary variable for whether a subject has received additional interventional treatment for stone(s)
<TREATMENT> is the randomized treatment
STREAT> is the binary variable for whether a subject has received additional interventional treatment for stone(s)

Prescription Pain Medication for Kidney Stone-Associated Pain

The number and percentage of subjects who take prescription pain medication for managing stone-associated pain will be summarized by timing (prior to treatment or post-treatment), drug class, and preferred term, overall and by treatment group for the ITT and PP populations.

9 SAFETY EVALUATIONS

9.1 OVERVIEW OF SAFETY ANALYSIS METHODS

9.2 ADVERSE EVENTS AND UNANTICIPATED ADVERSE DEVICE EFFECTS

An AE is any undesired clinical response or complication experienced by a subject.

An unanticipated adverse device effect (UADE) is any serious adverse effect on health or safety, any life-threatening problem or death caused by, or associated with a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the clinical investigational plan or risk analysis; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

AEs and UADEs are classified into categories based on Common Terminology Criteria for Adverse Events (CTCAE) and collected as such on the CRFs. All recorded AEs will be listed and summarized.

For evaluation of causal relatedness to device or procedure, the categories are unrelated, possibly related, probably related, or definitely related.

For evaluation of event severity terms, the criteria are

- Grade 1: Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated;
- Grade 2: Moderate; minimal, local or non-invasive intervention indicated; limiting age appropriate instrumental Activities of Daily Living;
- Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care Activities of Daily Living;
- Grade 4: Life-threatening consequences; urgent intervention indicated,
- Grade 5: Death related to AE

An overall summary will be prepared giving for frequency and percentages by treatment group and overall, for the number of subjects with at least one TEAE, TEAE related to study device, TEAE related to study procedure, serious adverse event (SAE), UADE, SAE related to study device, SAE related to study procedure, and TEAEs resulting in death.

The frequency and percentages of subjects with AEs will be summarized overall and for CTCAE. These summaries will be given overall and by treatment in separate tables for each of the following AE event sets:

All events

- Serious events
- UADEs
- Events by maximum severity
- Events by maximum relationship to study device
- Events by maximum relationship to study procedure
- Serious events by maximum severity
- Serious events by maximum relationship to study device
- Serious events by maximum relationship to study procedure

If a given subject experiences an AE with the same CTCAE more than once, the subject will be counted only once for the CTCAE at the greatest severity (i.e., mild, moderate, severe, life threatening, or death) and causality (i.e., attribution to study material).

For the tables classified by severity grade and relationship, if a patient has multiple occurrences of a AE with the same CTCAE, the event with the highest severity or closest relationship will be counted.

No imputation is planned for missing safety data.

In addition to a listing of all AE, a listing will be provided for AE narrativesI. Clinical Laboratory Evaluations

Clinical laboratory evaluations include urinalysis for pH and infection result and serum creatinine (mg/dL). All clinical laboratory evaluations will be presented in a by-subject listing.

9.3 VITAL SIGNS

Vital signs results including blood pressure (systolic and diastolic; mmHg), pulse rate (beats per minute), and body temperature (C) will be listed for individual subjects.

Baseline for vital signs measurements will be defined as the last evaluation before dosing with study medication. Summary statistics, including change from baseline, will be determined for each measure and will be summarized overall by treatment and time point using the Safety population.

9.4 FOCUSED UROGENITAL CALCULUS PHYSICAL EXAMINATION

Focused urogenital calculus physical examinations will be performed at Screening, Day 30, and Day 90 will be performed for assessment of abnormal results. All examination data will be provided in a by-subject listing.

9.5 IMAGING

Imaging includes CT imaging and ultrasound. While collected, reports are not planned for imaging data.

9.6 PREGNANCY TEST

Pregnancy (for female subjects of childbearing potential) will be assessed with a urine pregnancy test on the day of treatment prior to randomization. Results of the pregnancy test will be provided in a by-subject listing.

10 PK/PD ANALYSIS

There are no pharmacokinetic or pharmacodynamic analyses planned.

11 INTERIM ANALYSIS

There is no interim analysis planned.

12 DATA SAFETY AND MONITORING BOARD

There is no Data Safety and Monitoring Board activity planned.

13 CHANGES TO THE ANALYSES PLANNED IN THE PROTOCOL

In the protocol it is stated that the total number of secondary stone treatments will be summarized and a Cochran-Armitage trend test will be used to evaluate the null hypothesis that there is no trend in the number of stones between the groups. This was removed from the SAP. Because subjects exit the study 30 days after receiving treatment, this data is unlikely to be available.

No further changes exist between the protocol-defined statistical analyses and those presented in this statistical plan.

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No figures are planned for reporting.

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16.2.8.3	Safety	Vital Signs
16.2.8.4	Safety	Focused Urogenital Calculus Physical Exam

15 REFERENCES