ReUnion TSA Statistical Analysis Plan (SAP)

CLINICAL INVESTIGATION TITLE:	A Post-Market Clinical Evaluation of the ReUnion TSA System
DEVICE NAME:	ReUnion TSA System
STATISTICAL ANALYSIS PLAN (SAP) VERSION:	2
CLINICAL INVESTIGATION PLAN (CIP) VERSION:	1
INDICATIONS:	This study will adhere to the indications and contraindications for the ReUnion TSA System as are detailed in the device's Instructions for Use.
CLINICAL INVESTIGATION DESIGN:	• Post-Market • Multicenter • Prospective • Non-Randomized
CONFIDENTIALITY STATEMENT:	This Statistical Analysis Plan contains confidential information and its' use is limited to investigational staff intending to conduct the clinical investigation, Institutional Review Boards (IRBs)/Ethics Committees (ECs) and any others charged with reviewing the clinical investigation.
DATE:	28 May 2021

Approval Page

APPROVERS			
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1. Administrative Information

1.1. LIST OF ABBREVIATIONS

Acronym	Definition
ADE	Adverse Device Event
AE	Adverse Event
ASES	American Shoulder and Elbow Surgeons
CI	Confidence Interval
CIP	Clinical Investigation Plan
CRF	Case Report Form
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
FR	Final Report
ICF	Informed Consent Form
IFU	Instructions for Use
IR	Interim/Annual Report
IRB	Institutional Review Board
ITT	Intent-to-Treat
LTFU	Lost to Follow-Up
PP	Per Protocol
RSA	Reverse Shoulder Arthroplasty
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
TFL	Tables, Figures, Listings
TSA	Total Shoulder Arthroplasty
UADE	Unanticipated Adverse Device Effect

1.2. STATISTICAL ANALYSIS PLAN REVISION HISTORY

Version	Effective Date	Description	Reason
1	27OCT2020	Initial Version	
2	28MAY2021	Distinction interim/final Analysis Amendment Table Templates section 7	Revision DQI 20-048

1.3. ROLES AND RESPONSIBILITIES

Role	Contributor	Affiliation
Author	Sascha Lorenzen	Stryker
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2. Introduction

2.1. BACKGROUND AND RATIONALE

The ReUnion TSA System is designed as an anatomical total shoulder or hemi-shoulder endoprosthesis to address advanced arthritic disorders affecting the shoulder joint in subjects having intact or repairable rotator cuff function. The ReUnion TSA System consists of a completely modular shoulder platform including a Humeral Stem, Humeral Head and Glenoid. The intended purposes of the ReUnion TSA System are to achieve pain relief, improvement of range of motion and restoration or improvement of the shoulder function while ensuring long-term replacement of the shoulder joint with sufficient stability of all endoprosthesis components.

2.2. CLINICAL INVESTIGATION DESIGN

This investigation is a prospective, multicenter clinical investigation. It is anticipated that a total of one hundred (100) subjects will be enrolled at approximately 4-7 sites. Neither subjects nor investigators are blinded to treatment and the clinical investigation does not include a contemporaneous control. The clinical investigation has been designed to follow the surgeon's standard of care for shoulder arthroplasty subjects, which entails clinical evaluation on a regular ongoing basis, or as needed should the subject become symptomatic in the treated joint. The enrollment period is expected to occur over 14 months.

3. Research Goals

3.1. FRAMEWORK

All quantitative variables, including those based on calculations (secondary elements), will be analyzed with a case summary evaluation before the detailed characteristics and parameters can be evaluated. A case summary contains a listing of the number of valid cases/values, missing cases/values (if any) and total cases/values in the specific analysis. In general, a central position parameter for quantitative variables the mean, median and mode will be analyzed. As variation parameter the standard deviation, 95% confidence interval of the mean, interquartile range and range (based on maximum and minimum) will be calculated. All quantitative variables will be assessed for normality using the Shapiro-Wilk test. For optional visualization of quantitative variables, box-and-whisker plots will be used. Additional analyses like skewness and kurtosis measures or standard errors are optional also.

All qualitative variables, including those based on summaries (secondary elements), will be analyzed listing the proportions, frequencies, column and row totals, and missing proportion (if any).

3.1.1. Primary Analysis / Endpoint

The objective of the clinical investigation is to demonstrate non-inferiority (equal or better) of the ASES Shoulder Score in relationship to the officially cleared indications in comparison to respective clinical outcome data in the scientific literature.

Data collection of ASES Shoulder Score will start pre-operatively and will be collected according to schedule in Table 4.4 This will be repeated annually in all subjects who have the total or partial prosthesis with full or partial implant survival (including all subjects without removal of all endo-prosthesis components).

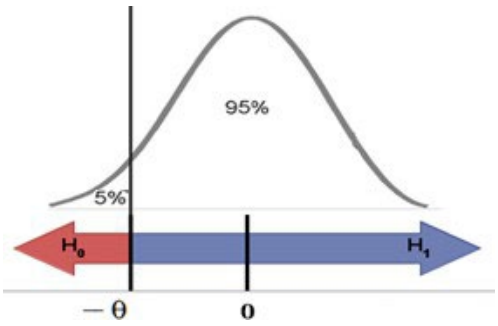
The 24 months postoperative results for subjects implanted with ReUnion TSA System will be compared to a historical group and results reported by respective clinical outcome data in the scientific literature. The benchmark sources and values will serve as the control group for the ReUnion TSA System subjects.

Higher ASES Shoulder Score results are linked to better subject results and vice versa.

The clinical investigation endpoint is non-inferiority to the control, meaning the clinical investigation result should be equal or better than the control. In this clinical investigation, an equal or better ASES Shoulder Score result means equal or more (≥). As only results from samples will be captured, results mostly are estimates of the true population parameter. These estimates vary by a certain area, where it is expected that the true population parameter falls within. Based on this, it is required to specify a lower limit for the acceptable difference or zone of indifference, denoted as -θ.

Hypotheses were developed to allow for a comparison of the 24 months postoperative ASES Shoulder Score effectiveness / performance between the two underlying populations. The 24 months postoperative ASES Shoulder Score is the primary endpoint of this clinical investigation. Hypothesis tests will be one-sided with a significance level α of 5%.

Hypothesis	**Equations**	**Interpretation**
Null (H0)	$A - B < -\theta$ ReUnion TSA System – Control (Benchmark) $< -\theta$	Central tendency of A is inferior to the central tendency of B.
Alternative (H1)	$A - B \geq -\theta$ ReUnion TSA System – Control (Benchmark) $\geq -\theta$	Central tendency of A is non-inferior to the central tendency of B.



Possible Evidence (p)	**Possible Decisions**	**Possible Conclusions – ASES Shoulder Score**

p-value > α (0.05)	Fail to reject null hypothesis (H0)	ReUnion TSA System < Control (Benchmark) Insufficient evidence to reject the null hypothesis (H0: A - B < - θ) at the pre-determined significance level of 5%.
p-value ≤ α (0.05)	Reject null hypothesis (H1)	ReUnion TSA System ≥ Control (Benchmark) Sufficient evidence to reject the null hypothesis (H0: A - B < - θ) at the pre-determined significance level of 5%.

Table 3.1.1: Research Goal and Hypothesis (Primary Endpoint)

To test non-inferiority, the 24 months mean ASES Shoulder Score result of the ReUnion TSA System group will be compared to the mean estimate of the control group, 82.16 points.

To be able to identify an acceptable difference or zone of indifference (-θ), the pooled standard deviation of the ASES Shoulder Score result at 24 months postoperative in the control group (Benchmark) was used as lower limit (pooled standard deviation of control is 16.76 points). The lower maximum acceptable difference (-θ) is 65.40 points (mean of control - θ or 82.16 – 16.76 = 65.40 points).

Based on the underlying distribution of the data and the result of the normality assessment, either the parametric one-sample t-test or the non-parametric one-sample sign test will be used to compare the 24 months postoperative ASES Shoulder Score results of the ReUnion TSA System against the value of 65.40 points.

The analysis of the primary endpoint / objective will be conducted when all subjects have completed the 24 months postoperative including the ASES Shoulder Score.

3.1.2. Secondary Analyses

For safety, the incidence of device-related adverse events/incidents will be assessed up to 10 years after the index procedure and monitored through collection and analyses.

Furthermore, time to (earliest) Device-Related Adverse Events will be analyzed as well. For analysis of the time to the (earliest) Device-Related Adverse Events, the Kaplan-Meier method will be used. Considered variables, the level of measurement and the planned analysis steps are listed in detail in the SAP. These analyses will be part of the final report.

3.1.3. Additional Analyses

Additional Analyses are outlined in the subsequent sections. Analysis details (variables, level of measurement, planned steps) are listed in-depth in the SAP.

- **Mortality**
  For analysis of the time to death or mortality, the Kaplan-Meier method will be used. The times between surgery and the last available assessment will be used together with the times between date of surgery and the date of death. This analysis will be part of the final report.

- **ASES Total Score – Within subject changes by visit**
  The within subject score changes of the ASES Total Score from visit to visit will be analyzed to help identify the changes on the subject level. This analysis will be part of the final report.

3.2. SAMPLE SIZE

The determination of sample size is based on benchmark sources and values. To account for an estimated appropriate overall drop-out rate, Stryker intends to enroll the calculated number of subjects, multiplied

by the number of cleared indications to reflect the underlying subject population adequately. For details, please see Table 3.2.

Benchmark and Objectives for Clinical Investigation	
Endpoint	Non-inferiority (equal or better) of the ASES Shoulder Score in relationship to the officially cleared indications in comparison to respective clinical outcome data in the scientific literature.
Estimated drop-out rate	56% (confirmed by Medical Expert, see Cuff et al.) *Cuff et al. Reverse Shoulder Arthroplasty for the Treatment of Rotator Cuff Deficiency: A Concise Follow-up, at a Minimum of 10 Years, of Previous Reports. J Bone Joint Surg Am. 2017 Nov 15;99(22):1895-1899. doi: 10.2106/JBJS.17.00175.*

Benchmark Sources & Values ASES [points]

Source		**n**	**Mean**	**Std. Dev.**	**Comments No.**
No.	**Title**				
1	Irlenbusch et al. [10]	73	77.9	N/A	Conflict related to Follow-Up times in abstract vs method vs result section.
2	Flurin et al. [20]	73	90.3	14.6	Not clear if SD or 95% CI
3	Press et al. [22]	34	82.6	19.4	
4	Hsu et al. [23]	25	94.4	N/A	
5	Kiet et al. [26]	40	80	21	N changed from 45 to 40
6	Steen et al. [29]	96	80.4	22.4	Not clear if SD or 95% CI
7	Gulotta et al. [34]	40	80.1	10.1	
8	Petri et al. [49]	43	83.5	13.1	
9	Schoch et al. [62]	78	88.4	16.7	
10	Alentorn-Geli et al. [70]	38	64	N/A	TSA und HA combined.

Identified Cleared Indications

No.	**Indication**
1	Post-traumatic arthritis
2	Degenerative arthritis
3	Rheumatoid arthritis
4	Revision of previously failed shoulder joint replacement
5	Aseptic necrosis

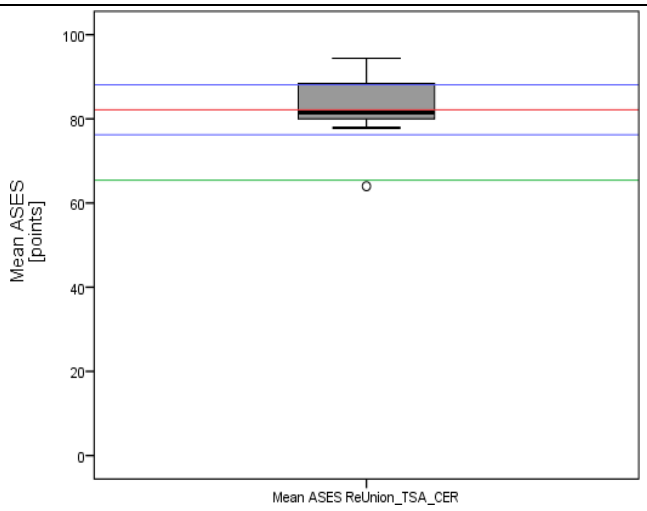
Explorative Meta-Analysis - ASES (single group)	
Acceptance Criteria	
Confidence Interval (CI)	0.95 (95%) two-sided
Software Used	IBM SPSS V20

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Mean ASES ReUnion_TSA_CER	10	100,0%	0	0,0%	10	100,0%
Std.Dev. ASES ReUnion_TSA_CER	7	70,0%	3	30,0%	10	100,0%

Descriptives

			Statistic
Std.Dev. ASES ReUnion_TSA_CER	Mean		16,7571
	95% Confidence Interval for Mean	Lower Bound	12,6353
		Upper Bound	20,8790
	Median		16,7000
	Std. Deviation		4,45678
	Minimum		10,10
	Maximum		22,40
	Interquartile Range		7,90
Mean ASES ReUnion_TSA_CER	Mean		82,1600
	95% Confidence Interval for Mean	Lower Bound	76,2372
		Upper Bound	88,0828
	Median		81,5000
	Std. Deviation		8,27945
	Minimum		64,00
	Maximum		94,40
	Interquartile Range		9,40



Red line: Pooled mean ASES

Blue lines: 95% CI of pooled mean ASES

Black line: Pooled median pooled ASES

Box: Interquartile Range

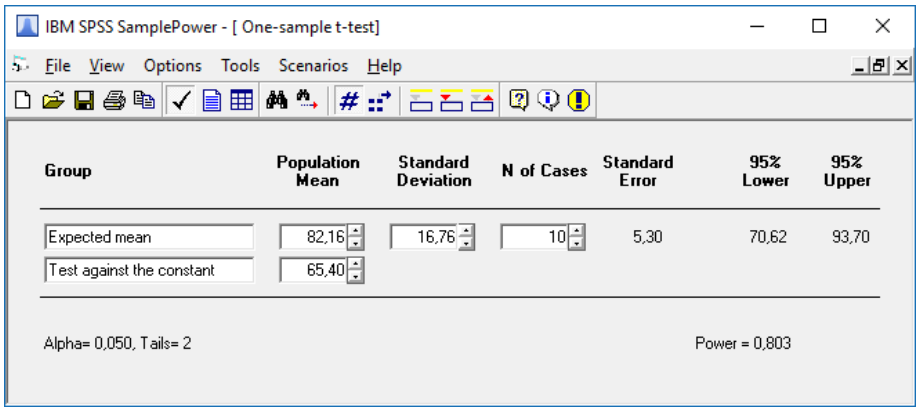
Green Line: Pooled mean ASES minus pooled std. dev. ASES (16.76)

82.16 – 16.76 = **65.40 points**

Acceptance Criteria for Sample Size Calculation		
Significance Level (α)	0.05 (5%)	
Power (1-β)	0.80 (80%)	
Confidence Interval (CI)	0.95 (95%)	
Tails	2	
Path	Non-inferiority – ReUnion TSA (A) ≥ Benchmark (B, explorative meta-analysis in this document)	
Hypotheses Pair	Null (H_0)	A – B < -θ
	Alternative (H_1)	A – B ≥ -θ
Benchmark Timepoint	24 months postoperative	
Benchmark n (sources)	10	
Benchmark Mean	**82.16** (pooled mean ASES [points])	
Benchmark Std. Dev.	**16.76** (pooled std. dev. ASES [points])	
Benchmark Value **Non-Inferiority Margin (-θ)**	Pooled mean ASES minus pooled std. dev. ASES (16.76) 82.16 – 16.76 = **65.40 points**	
Software Used	IBM SPSS Sample Power V3.0	

IBM SPSS Sample Power Output

One goal of the proposed clinical investigation is to test the null hypothesis that the population mean is 82.16 points. The criterion for significance (alpha) has been set at 0.05. The test is 2-tailed, which means that effects in both directions will be interpreted. With the proposed sample size of 10 cases, the clinical investigation will have power of 80.3% to yield a statistically significant result. This computation assumes

<table>
<tr><td colspan="2">that the population from which the sample will be drawn has a mean of 82.16 points with a standard deviation of 16.76 points. The observed value will be tested against a theoretical value (constant, non-inferiority margin) of 65.40 points.</td></tr>
<tr><td colspan="2">IBM SPSS Sample Power Output – Screenshot
 

Estimated overall drop-out rate is 56% which leads to the requirement of enrolling additional 6 subjects into the clinical investigation.</td></tr>
<tr><td>Sample Size</td><td>Number of subjects to be enrolled: 16 subjects (rounded up to 20 subjects)</td></tr>
<tr><td>Overall Sample Size (multiplied by number of indications (=5)</td><td>100 subjects</td></tr>
</table>

Table 3.2: Sample Size Justification

In conclusion, the calculated number of subjects to be enrolled (10), plus the estimated overall drop-out rate of 56%, leads Stryker´s enroll 20 subjects per cleared indication (5) to reflect the underlying subject population adequately. As a result, an enrollment target of 100 subjects in total will be aspired (ideally, but not necessarily, composed with 20 subjects per indication).

4. Methods

4.1. RANDOMIZATION

No specific methods for assigning subjects will be used for this clinical investigation. A consecutive series of subjects at each site meeting all the eligibility criteria will be enrolled in this clinical investigation.

4.2. STATISTICAL INTERIM ANALYSES AND STOPPING GUIDANCE

Interim analyses will be performed on a yearly basis. The progress of the clinical investigation will be reported together with the interim results on the variable level according to the analysis plan.

The analysis of the primary endpoint / objective will be part of the related interim / annual report when all subjects have completed the 24 months postoperative including the ASES Shoulder Score.

There will be no stopping rules specified for this clinical investigation.

4.3. TIMING OF FINAL ANALYSES

The full final report with complete analysis, progress and conduct reporting will be created at the end of this clinical investigation.

4.4. TIMING OF OUTCOME ASSESSMENT

Subjects in this clinical investigation will be evaluated at Pre-Operative, Operative/Discharge, and at 6 Weeks (4 weeks – 8 weeks), 6 Months (24 weeks – 28 weeks), 12 Months (48 weeks- 56 weeks), 24

Months (100 weeks – 108 weeks) and annually after the index procedure. The follow-up evaluations will include assessment of device-related AEs/incidents, radiographs and ASES Shoulder Score.

Assessment	Preoperative	Operative/ Discharge	6 Weeks [a, b] (+/- 2 weeks)	6 Months [a, b] (+/- 3weeks)	12 Months [a, b] (+/- 4 weeks)	24 Months [a, b] (+/- 4 weeks)	Annually [b]
Informed Consent	X						
Demographics & Medical History	X						
Inclusion/Exclusion	X						
Physical Exam	X		X[c]	X[c]	X[c]	X[c]	X[c]
Surgical Procedure		X					
ASES Shoulder Score	X		X[d]	X[d]	X[d]	X[d]	X[d]
Image Evaluation [e, f]	X	X	X	X	X	X	X
Subject Disposition [g]			X	X	X	X	X
	Device-Related AEs/Incidents & Reoperations will be collected throughout the course of the clinical investigation.						
	a. Follow-up visit schedule to reflect Institutions' Standard of Care practices b. If the subject misses a visit and is outside of the visit window, then every effort should be made to collect data instead of noting visit as missed. c. Evaluation may be collected when subject presents in-clinic for study visit. d. Evaluation can be collected via phone. e. Radiograph collection should follow Institution's Standard of Care practices and no additional x-rays should be made for study purposes. f. CT scans may be collected if part of Institution's Standard of Care practices. g. Subject Disposition assessment will occur at any time point for subject withdrawal prior to the completion of the clinical investigation.						

Table 4.4: Schedule of Events

4.5. STATISTICAL SOFTWARE

Statistical Analysis will be performed using IBM SPSS, IBM SPSS Sample Power as well as established standard software packages (e.g. MS Excel).

4.6. MISSING DATA

The intent is to collect as complete a dataset as possible. Nevertheless, in some situations missing data cannot be avoided. The reports and tables therefore will show the number and percentage of missing cases for each analyzed variable in relation to the enrolled cases for each postoperative assessment

Any deviations from Statistical Analysis Plan will be listed in the annual or final reports.

4.7. CONFIDENCE INTERVALS AND P-VALUES

The following acceptance / rejection criteria were used for this clinical investigation:

Parameter	**Acceptance / rejection criteria**
Confidence level (1-α)	0.95 (95%)
Significance level (α)	0.05 (5%)
Power (1-β)	0.80 (80%)
Beta-level (β)	0.20 (20%)
Confidence interval of mean	95%
p-value indicating significance	≤ 0.05

Table 4.7: Acceptance / Rejection Criteria

4.8. UNITS

See analysis chapter for details related to units used for the different variables and calculations.

In case of collection of variables with non-SI units (e.g. pounds instead to kilograms), conversion of such data into SI units (and vice versa) will be ensured and both results will be reported for the full set of available subjects next to each other in the interim/annual and/or final reports.

4.9. CALCULATIONS AND TRANSFORMATIONS

Distances between times and differences between score results will be calculated. For full details of variables used for calculations and the creation of new variables based on these calculations, see analysis chapter.

4.10. ASSUMTIONS

In case of deviation from assumptions (e.g. normality), non-parametric methods will be used for analysis. No transformation of such data will be performed.

5. Population and Progress

5.1. ANALYSIS POPULATION

It is expected that during this clinical investigation only one population for ReUnion TSA System will exist and all subjects will be analyzed "Per Protocol" (PP). However, it cannot be fully avoided that in theory subjects might need to be excluded from the PP population. In this occasion, there will be two groups being fully analyzed to ensure transparency and avoid bias.

The groups are defined as follows:

- **Intent-to Treat Population**

  The Intent-to-Treat (ITT) Population is defined to be all enrolled subjects. An enrolled subject is a subject that has signed informed consent, all screening procedures have been successfully completed, is eligible and can receive treatment. The ITT population will not be analyzed for the annual reports and will only be included in the final report.

- **Per Protocol Population**

  The PP Population is defined to be all subjects in the ITT Population with no major CIP violations. The CIP violations that will exclude a subject are as follows:

  - The subject does not receive the ReUnion TSA System
  - The subject does not meet all eligibility criteria
  - The subject has a clinical investigation plan violation that is considered likely to affect subject outcomes.

  After the clinical investigation has been completed, a review of the data will be conducted to determine which subjects are to be excluded from the PP population.

  The following tables will be created for interim/annual and final reports related to the clinical investigation populations and progress:

Evaluation Variable / Question	Level of Measurement	Analysis Plan
All Forms – Overview & Progress Report		
Counting of available subjects ***Subject Population by Site*** (Variable(s): SITENUM; SUBID)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).
Counting of available subjects ***Subject Population by Visit*** (Variable(s): SITENUM; SUBID; VISITDT)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).
Counting of available subjects ***Subject Population by Visit and by Site*** (Variable(s): SITENUM; SUBID; VISITDT)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).

Table 5.1: Populations and Progress Tables List

5.2. ELIGIBILITY

A subject is defined as eligible if all inclusion and exclusion criteria are fulfilled as it is described in the clinical investigation plan. For details see CIP.

For tables to be created for the interim/annual and final reports, see chapter 6.2 and tables list 6.2.2.

5.3. WITHDRAWAL / FOLLOW-UP

During the clinical investigation if a subject must be withdrawn prematurely from the clinical investigation, then the procedures outlined in the CIP should be followed. These procedures should not interfere with the initiation of any new treatments that are necessary to treat a subject's condition. Information on all withdrawn subjects will be documented.

The following tables will be created for interim/annual and final reports related to the numbers of withdrawn subjects (if any):

Evaluation Variable / Question	Level of Measurement	Analysis Plan
All Forms – Overview & Progress Report		
Counting of withdrawn subjects ***Number of Subjects Withdrawn by Site*** (Variable(s): SITENUM; COMPPROT; PRIMRSN)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).
Counting of withdrawn subjects ***Number of Subjects Withdrawn by Site by Visit*** (Variable(s): SITENUM; COMPPROT; PRIMRSN; VISITDT)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).
Comments related to ***Reasons for Subjects Withdrawn*** (Variable(s): RSNSPF)	Text, String	Listing of reasons for subjects being excluded by subject code/ID

Table 5.3: Withdrawal Tables List

5.4. ADHERENCE AND CIP DEVIATIONS

Any CIP deviations will be listed in the interim/annual and final reports. It is optional to describe this chapter in free text or present it in a tabulated format.

6. Analysis

The following tabulated analysis plan reflects this approach and specifies the variables characteristics (quantitative or qualitative) in detail together with the related analysis strategy. This also includes calculation and summaries based on primary elements and the required analysis.

In addition, it will be defined in the text or directly in the tables below, if the variable must be included in an interim/annual report (IR) and/or in the final report (FR).

6.1. HARMS AND SAFETY

Categorization and definitions of (Serious-, Unanticipated-) Adverse Device Effects, (Serious-) Incidents are given in the CIP.

The following tables will be created for interim/annual and final reports related harms and safety:

Evaluation Variable / Question	Level of Measurement	Analysis Plan	Inclusion		
Adverse Events / Incidents			**IR**	**FR**	**N/A**
Perioperative/Postoperative AE (Variable(s): PERPOST)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).	X	X	
Device-Related Adverse Event / Incident (Variable(s): AEEVENT; AEOTHER)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any). Listing of other Events/Incidents.	X	X	
Describe the AE/Incident (Variable(s): AEDESCRP)	Qualitative, nominal	Listing of other Events/Incidents Description.			X
Unanticipated Adverse Device Event? (Variable(s): AEUADE)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).	X	X	
Severity (Variable(s): AESEVER)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).	X	X	
Action Taken (Variable(s): ACTNONE; ACTMEDS; ACTSURG; ACTSHORT; ACTPROHS; ACTOTHER; ACTOTHSP)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any). Listing of given Other specifications.			X
AE Resolution (Variable(s): AERESOLV)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Outcome (Variable(s): AEONWOTR; AEONWTTR; AEREWOTR; AEREWTTR; AETEDISB; AEPERMD; AESUEXP)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Creation of variable ***Number of Adverse Device Effects by Site*** (Variable(s): AEEVENT; SITENUM)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).	X	X	
Creation of variable ***Number of Adverse Device Effects per Subject and Site*** (Variable(s): AEEVENT; SITENUM; SUBID)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).	X	X	

Table 6.1.1: Adverse Events / Incidents Tables List

Evaluation Variable / Question	Level of Measurement	Analysis Plan	Inclusion		
Reoperation			**IR**	**FR**	**N/A**
Type of Procedure (Variable(s): IRRDEB; SOFTTR; ROTCUFF; OTHSOFT; REVHATSA; REVHATSASP; CONTSAWHS; CONTSAWOHS; CONRSAWHS; CONRSAWOHS; CONHAWHS; CONHAWOHS; CONTRSAWHS; CONTRSAWOHS; REVINFEC; REVINFECSP; RESSALV; ARTHSJ; ORIF; RESOST; PTOTHR; PTOTHSPC)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any). Listings of implant specifications.	X	X	
Reason(s) for Reoperation (Variable(s): WOUNCOM; INFEC; NERPL; DISLOC; OTHSUB; MALIMP; UNDOV; IMPDISL; ROTCUFTR; EROSHA; IMPLOOS; IMPBRKG; WRGLENTSA; PERIFRAC; STIFF; PAIN; HETOSS; RROTH; RROTHSP)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any). Listings of other specifications.	X	X	

Table 6.1.2: Reoperation Tables List

6.2. BASELINE CHARACTERISTICS

Evaluation Variable / Question	Level of Measurement	Analysis Plan	Inclusion		
Preoperative Visit Form – Subject Eligibility – Inclusion & Exclusion Criteria			**IR**	**FR**	**N/A**
Note: Inclusion and exclusion criteria will be checked during monitoring and reported by a statement (e.g. all subjects fulfilled the inclusion criteria).					
Inclusion Criteria Questions (Variable(s): INCLA; INCLB; INCLC; INCLD)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Exclusion Criteria Questions (Variable(s): EXCLA; EXCLB; EXCLC; EXCLD; EXCLE; EXCLF; EXCLG; EXCLH)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
*Creation of variable **No. of Eligible Subjects.** Conclusion of Inclusion and Exclusion Questions.*	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X

Table 6.2.1: Preoperative Visit Form - Subject Eligibility – Inclusion & Exclusion Criteria Tables List

Evaluation Variable / Question	Level of Measurement	Analysis Plan	Inclusion		
Preoperative Visit Form - Subject Demographics			**IR**	**FR**	**N/A**
*Creation of variable **Age [years]** Difference between **Date of Surgery [dd.mmm.yyyy]** and **Date of Birth/DOB [dd.mmm.yyyy]** in [⎪years⎪]* (Variable(s): BIRTHDT; VISITDT; VISNAME)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.	X	X	
Gender (Variable(s): GENDER)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).	X	X	
Race (Variable(s): AMERIND; ASIAN; BLKAFR; NATHAW; CAUS; RACEOTH; RACEOTHR)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).	X	X	

		Listing of given specifications.			
Height [captured in inches or cm] In the analysis, all values will be reported in inches and cm next to each other. (Variable(s): HGHTM)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.			X
Weight [captured in lbs or kg] In the analysis, all values will be reported in lbs and kg next to each other. (Variable(s): WEIGHTKG)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.			X
Body Mass Index [kg/m^2] (Variable(s): BMI)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.	X	X	

Table 6.2.2: Preoperative Visit Form - Subject Demographics Tables List

Evaluation Variable / Question	**Level of Measurement**	**Analysis Plan**	**Inclusion**		
Preoperative Visit Form – Current Relevant Medical Conditions			**IR**	**FR**	**N/A**
Current Relevant Medical Conditions (Variable(s): CURCOND; CONDSPC)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any). Listing of given specifications.	X	X	

Table 6.2.3: Preoperative Visit Form - Current Relevant Medical Conditions

Evaluation Variable / Question	**Level of Measurement**	**Analysis Plan**	**Inclusion**		
Preoperative Visit Form – Subject Evaluation			**IR**	**FR**	**N/A**
Tobacco Use: (Variable(s): TOBCCO)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).	X	X	
Corticosteroids Taking: (Variable(s): CORTICO)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).	X	X	
Affected (Study) Shoulder (Variable(s): AFFCSHL)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).	X	X	
Primary Shoulder Diagnosis: (Variable(s): PRIMDIAG)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).	X	X	
Shoulder Arthroplasty Procedure: (Variable(s): SHLARPROC)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any). Listing of given specifications.	X	X	
Previous History of Surgery to the Affected Shoulder (Variable(s): PREVHIST)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	

		Listing of given specifications.			
Procedure 1 (Variable(s): PROCNM1)	Text, String	Listing of comments and dates together identified by subject code/ID			X
Procedure Date 1 (Variable(s): PROCDT1)	Quantitative, ratio Date/Time				X
Procedure 2 (Variable(s): PROCNM2)	Text, String	Listing of comments and dates together identified by subject code/ID			X
Procedure Date 2 (Variable(s): PROCDT2)	Quantitative, ratio Date/Time				X
Procedure 3 (Variable(s): PROCNM3)	Text, String	Listing of comments and dates together identified by subject code/ID			X
Procedure Date 3 (Variable(s): PROCDT3)	Quantitative, ratio Date/Time				X
Procedure 4 (Variable(s): PROCNM4)	Text, String	Listing of comments and dates together identified by subject code/ID			X
Procedure Date 4 (Variable(s): PROCDT4)	Quantitative, ratio Date/Time				X

Table 6.2.4: Preoperative Visit Form – Medical History Tables List

Evaluation Variable / Question	**Level of Measurement**	**Analysis Plan**	**Inclusion**		
Preoperative Visit Form – ASES Shoulder Score (prior to surgery)			**IR**	**FR**	**N/A**
Q1 - Usual Work (Variable(s): USWORK)	Text, String	Listing of comments identified by subject code/ID			X
Q2 - Usual Sport/Leisure activity? (Variable(s): USSPRT)	Text, String	Listing of comments identified by subject code/ID			X
Q3 - Do you have shoulder pain at night? (Variable(s): PNNIGHT)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q4 - Do you take pain killers such as paracetamol (acetaminophen), diclofenac, or ibuprofen? (Variable(s): PNKLR)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q5 - Do you take strong pain killers such as codeine, tramadol, or morphine? (Variable(s): CODTRMD)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q6 - How many pills do you take on an average day? (Variable(s): PILLNUM)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.			X
Q7 - Intensity of pain? (Variable(s): PAINC)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.			X
Q8 - Is it difficult for you to put on a coat? (Variable(s): PUTCOAT)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X

Q9 - Is it difficult for you to sleep on the affected side? (Variable(s): DIFSLP)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q10 - Is it difficult for you to wash your back/do up bra? (Variable(s): WASHBCK)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q11 - Is it difficult for you manage toileting? (Variable(s): MNGTOIL)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q12 - Is it difficult for you to comb your hair? (Variable(s): COMBHR)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q13 - Is it difficult for you to reach a high shelf? (Variable(s): HIGHSHL)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q14 - Is it difficult for you to lift 10lbs. (4.5kg) above your shoulder? (Variable(s): LIFT10)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q15 - Is it difficult for you to throw a ball overhand? (Variable(s): BALLOV)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q16 - Is it difficult for you to do your usual work? (Variable(s): DFWORK)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q17 - Is it difficult for you to do your usual sport/leisure activity? (Variable(s): SPRACT)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
ASES Pain Score [points] (Variable(s): PAINSC)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.	X	X	
ASES Functioning Score [points] (Variable(s): FUNSCORE)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.	X	X	
Total ASES Shoulder Score [points] (Variable(s): FINSCORE)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.	X	X	

Table 6.2.5: Preoperative Visit Form – ASES Shoulder Score (post fracture, prior to surgery) Tables List

6.3. INTRAOPERATIVE CHARACTERISTICS

Evaluation Variable / Question	Level of Measurement	Analysis Plan	Inclusion		
Operative Visit – Operative Procedure			**IR**	**FR**	**N/A**
Date of Surgery *[dd.mmm.yyyy]*: (Variable(s): VISITDT; VISNAME)	Date/Time	Listing the first and last surgery in the report text to describe from which date to which date subjects were operated.		X	
Date of Admission *[dd.mmm.yyyy]*: (Variable(s): ADMINDT)	Date/Time	None			X
Date of Discharge *[dd.mmm.yyyy]*: (Variable(s): DISCHRDT)	Date/Time	None			X
Creation of variable ***Difference between Date of Surgery [dd.mmm.yyyy] and Date of Discharge [dd.mmm.yyyy] in [| days |]*** (Variable(s): VISITDT; DISCHRDT; VISNAME)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.		X	
Surgery Start Time (24-hour clock): (Variable(s): SURGSTTM)	Date/Time	None			X
Surgery Stop Time (24-hour clock): (Variable(s): SURGSPTM)	Date/Time	None			X
Difference between Surgery Start Time and Surgery Stop Time in [| hh:mm |] (Variable(s): SURGSTTM; SURGSPTM)	Quantitative, ratio Date/Time	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.		X	
Amount of Blood Infused (Variable(s): BLOODINF)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.		X	
Type of Anesthesia: (Variable(s): TYPANEST)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Were there any technical difficulties during surgery? (Variable(s): SURGDIFF; SURGDESC)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any). Listing of given description.	X	X	
Were any concomitant procedures done during surgery? (Variable(s): CONPROC; CONPROCD)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any). Listing of given description.	X	X	

Table 6.3.1: Operative Visit – Surgical Procedure Tables List

Evaluation Variable / Question	Level of Measurement	Analysis Plan	Inclusion		
Operative Visit – Implant Specification			**IR**	**FR**	**N/A**
Humeral Stem Lot/Serial # (Variable(s): HSREF)	Qualitative, nominal	None, used to populate diameter, length, press-fit		X	

		textured or smooth uncoated stem details Proportions, frequencies, column and row totals, missing proportion (if any).			
Humeral Head Lot/Serial # (Variable(s): HHREF)	Qualitative, nominal	None, used to populate diameter, thickness and standard(eccentric humeral head details Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Glenoid Lot/Serial # (Variable(s): GLENREF)	Qualitative, nominal	None, used to populate size and pegged/keeled glenoid details Proportions, frequencies, column and row totals, missing proportion (if any).		X	

Table 6.3.2: Operative Visit – Implant Specification Tables List

Evaluation Variable / Question	**Level of Measurement**	**Analysis Plan**	**Inclusion**		
Operative Visit – Radiographic Evaluation			**IR**	**FR**	**N/A**
Correct initial positioning of the humeral stem and head (Variable(s): QA)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Correct sizing of the humeral stem and head (Variable(s): QB)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Correct positioning of the glenoid component (Variable(s): QC)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of intraoperative fracture of the humerus (Variable(s): QD)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of intraoperative fracture of the glenoid (Variable(s): QE)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Correct cementation of the humeral component (Variable(s): QF)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Correct cementation of the glenoid component (Variable(s): QG)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of humeral cement leakage (Variable(s): QH)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of glenoidal cement leakage (Variable(s): QI)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Other (Variable(s): QJ)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Please describe the findings in detail (Variable(s): QDTL)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X

Table 6.3.3: Operative Visit Form – Radiographic Evaluation Tables List

6.4. EARLY POSTOPERATIVE CHARACTERISTICS

N/A

6.5. POSTOPERATIVE CHARACTERISTICS

The analysis of the Postoperative data must be performed separately for each follow-up visit listed in table 4.4 in accordance to the following tables in this chapter. New Variables must be created individually for each follow-up visit.

Evaluation Variable / Question	Level of Measurement	Analysis Plan	Inclusion		
Postoperative Visit Form – Date of Visit			**IR**	**FR**	**N/A**
Date of Visit *[dd.mmm.yyyy]*:	Date/Time	None			X
Creation of variable ***Difference between Date of Surgery [dd.mmm.yyyy] and Date of "FU Visit" [dd.mmm.yyyy] In [| days |]*** (Variable(s): VISITID; VISNAME)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.		X	

Table 6.5.1: Postoperative Visit Form – Date of Visit

Evaluation Variable / Question	Level of Measurement	Analysis Plan	Inclusion		
Postoperative Visit Form – ASES Shoulder Score			**IR**	**FR**	**N/A**
Q1 - Usual Work (Variable(s): USWORK)	Text, String	Listing of comments identified by subject code/ID			X
Q2 - Usual Sport/Leisure activity? (Variable(s): USSPRT)	Text, String	Listing of comments identified by subject code/ID			X
Q3 - Do you have shoulder pain at night? (Variable(s): PNNIGHT)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q4 - Do you take pain killers such as paracetamol (acetaminophen), diclofenac, or ibuprofen? (Variable(s): PNKLR)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q5 - Do you take strong pain killers such as codeine, tramadol, or morphine? (Variable(s): CODTRMD)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q6 - How many pills do you take on an average day? (Variable(s): PILLNUM)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.			X
Q7 - Intensity of pain? (Variable(s): PAINC)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.			X
Q8 - Is it difficult for you to put on a coat? (Variable(s): PUTCOAT)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X

Q9 - Is it difficult for you to sleep on the affected side? (Variable(s): DIFSLP)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q10 - Is it difficult for you to wash your back/do up bra? (Variable(s): WASHBCK)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q11 - Is it difficult for you manage toileting? (Variable(s): MNGTOIL)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q12 - Is it difficult for you to comb your hair? (Variable(s): COMBHR)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q13 - Is it difficult for you to reach a high shelf? (Variable(s): HIGHSHL)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q14 - Is it difficult for you to lift 10lbs. (4.5kg) above your shoulder? (Variable(s): LIFT10)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q15 - Is it difficult for you to throw a ball overhand? (Variable(s): BALLOV)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q16 - Is it difficult for you to do your usual work? (Variable(s): DFWORK)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Q17 - Is it difficult for you to do your usual sport/leisure activity? (Variable(s): SPRACT)	Qualitative, Ordinal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
ASES Pain Score [points] (Variable(s): PAINSC)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.	X	X	
ASES Functioning Score [points] (Variable(s): FUNSCORE)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.	X	X	
Total ASES Shoulder Score [points] (Variable(s): FINSCORE)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.	X	X	

Table 6.5.2: Postoperative Visit Form – ASES Shoulder Score Tables List

Evaluation Variable / Question	**Level of Measurement**	**Analysis Plan**	**Inclusion**		
Postoperative Visit Form – Range of Motion			**IR**	**FR**	**N/A**
Flexion (Variable(s): FLEX)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Abduction (Variable(s): ABDC)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	

Extension (Variable(s): EXTN)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
External Rotation (Variable(s): EXROT)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Internal Rotation (Variable(s): INTOR)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	

Table 6.5.3: Postoperative Visit Form – ROM Tables List

Evaluation Variable / Question	**Level of Measurement**	**Analysis Plan**	**Inclusion**		
Postoperative Visit Form – Radiographic Evaluation			**IR**	**FR**	**N/A**
Implant dislocation (complete dislocation) (Variable(s): QA)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Periprosthetic fracture of the humerus (Variable(s): QB)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Periprosthetic fracture of the glenoid (Variable(s): QC)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Implant component dissociation (humeral head from humeral stem) (Variable(s): QD)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of erosion of the glenoid (in hemiarthroplasty only) (Variable(s): QE)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Breakage of the humeral stem (Variable(s): QF)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of breakage of the glenoid component (Variable(s): QG)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of wear of the glenoid component (Variable(s): QH)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of rotator cuff tear (superior/cranial migration) (Variable(s): QI)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Heterotopic ossification (Variable(s): QJ)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiolucency of the humerus (Variable(s): QK)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of gross loosening of the humeral stem (Variable(s): QL)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiolucency of the glenoid (Variable(s): QM)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Gross loosening of the glenoid component (Variable(s): QN)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Non-union of lesser tuberosity osteotomy (Variable(s): QO)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Malunion of lesser tuberosity osteotomy (Variable(s): QP)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Other (Variable(s): QQ)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any). Listing of given description.		X	

Other description (Variable(s): DESC)	Qualitative, Nominal	Listing of given description.			X
Heterotopic ossification (modified BROOKER grading) (Variable(s): QS; QTG0; QTG1; GR1ZN; QTG2, GR2ZN; QTG3, GR3ZN; QTG4; GR4ZN; QTG5)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiolucent lines 2 mm or greater in ≥ 3 zones (Variable(s): QU)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Tilting (> 5°) or subsidence (> 5 mm) of the stem (Variable(s): QV)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Thinning ("scalloping") of the humeral cortex (Variable(s): QW; QX)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any). Listing of given description.		X	
Description of Radiolucency (Variable(s): QY)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
If pegged glenoid component (Variable(s): QZ)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
If keeled glenoid component (Variable(s): QAA)	Qualitative, Nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	

Table 6.5.4: Postoperative Visit Form – Radiographic Evaluation Tables List

6.6. ANALYSIS OF CI ENDPOINTS

Evaluation Variable / Question	**Level of Measurement**	**Analysis Plan**
Endpoints – Primary Endpoint		
Use variable ***Total ASES Shoulder Score 24 Months [points]:*** Based on the underlying distribution of the data and the result of the normality assessment, either the parametric one-sample t-test or the non-parametric one-sample sign test will be used to compare the 24 months postoperative ASES Shoulder Score results of the ReUnion TSA group against the lower maximum acceptable difference (-θ) of 65.40 points. The analysis of the primary endpoint will be part of the final report.		

Table 6.6.1: Endpoints – Primary Endpoint Tables List

Evaluation Variable / Question	**Level of Measurement**	**Recode and Analysis Plan**	**Inclusion**		
Adverse Events – Time to (earliest) Device-Related Adverse Event / *Incident*			**IR**	**FR**	**N/A**
Creation of variable ***Difference between Date of Surgery [dd.mm.yyyy] and Date of First Device Related Adverse Event [dd.mm.yyyy] in [| days |]*** (Variable(s): VISITDT; AEONSTDT)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.		X	
Creation of variable ***Difference between Date of Surgery [dd.mm.yyyy] and Date of "most recent" Visit [dd.mm.yyyy] in [| days |]*** (Variable(s): VISITDT)	Quantitative, ratio	N/A (Analyzed above), used for survivorship		X	

Create new variable ***"Grouping variable – First Device Related Adverse Event"*** (Variable(s): AEONSTDT)	Qualitative, nominal	- censored = survivors - events = first (earliest) Device Related Adverse Event		X	
Create new variable ***"Combined Time – First Device Related Adverse Event"*** (Variable(s): AEONSTDT)	Quantitative, ratio	- Use time between surgery and "most recent" visit for surviving subjects - Use time between surgery and first device related adverse event for subjects with device related adverse event		X	
Use variables ***"Combined Time – First Device Related Adverse Event"*** *and* ***"Grouping variable – First Device Related Adverse Event"***	Qualitative, nominal Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Kaplan-Meier survival analysis: subject ID, time, status, cumulative proportion, Kaplan-Meier estimate, standard error of KM estimate, number of cumulative events, number of remaining cases, mean for survival time with 95% confidence interval, survival graph, hazard graph.		X	

Table 6.6.2: Endpoints – Secondary Endpoint Time to (earliest) Device Related Adverse Event / Incident Tables List

6.7. ADDITIONAL ANALYSIS

6.7.1. ASES Comparison

The comparison of the ASES Shoulder Score must compare all Total ASES Shoulder Scores of all follow-up visits against each other (m x n) in accordance to table 6.7.1.1 and the analysis tables listed in this chapter. This analysis is part of the final report only.

ASES Shoulder Score – Follow-up Visits to be compared													
Comparison		Follow-up Visits (n)											
		Preop	6 Weeks	6 Months	12 Months	24 Months	36 Months	48 Months	60 Months	72 Months	84 Months	96 Months	108 Months	120 Months
Follow-up Visits B (m)	Preop													
	6 Weeks	x												
	6 Months	x	x											
	12 Months	x	x	x										
	24 Months	x	x	x	x									
	36 Months	x	x	x	x	X								
	48 Months	x	x	x	x	X	x							
	60 Months	x	x	x	x	X	x	x						
	72 Months	x	x	x	x	X	x	x	x					
	84 Months	x	x	x	x	X	x	x	x	x				
	96 Months	x	x	x	x	X	x	x	x	x	x			
	108 Months	x	x	x	x	X	x	x	x	x	x	x		
	120 Months	x	x	x	x	X	x	x	x	x	x	x	x	
*All combinations marked with an "x" must be performed														

Table 6.7.1.1: All Assessments – ASES Shoulder Score – Follow-up Visits to be compared

Evaluation Variable / Question	Level of Measurement	Analysis Plan
All Assessments – ASES Shoulder Score Comparison		
*Use **"ASES Total Score m [points]"** and **"ASES Total Score n [points]"***: Based on the underlying distribution of the data in both groups and the result of the normality assessment, either the parametric paired samples t-test or the non-parametric Wilcoxon test will be used to compare ***"ASES Total Score m [points]"*** *and* ***"ASES Total Score n [points]"*** to evaluate the ASES Shoulder Score change by subject (improvement or decrease). The complete available SPSS tables content related to either the paired samples t-test or the Wilcoxon test will be included in the final report. (Variable(s): FINSCORE)		

Table 6.7.1.2: All Assessments – ASES Shoulder Score Comparison Tables List

6.7.2. Mortality

For analysis of the time to death or mortality, the Kaplan-Meier method will be used. The times between surgery and the most recent or last available assessment per subject will be used together with the times between surgery and the date of death. This analysis is part of the final report.

Evaluation Variable / Question	Level of Measurement	Recode and Analysis Plan
All Assessments – Mortality		
Creation of variable ***Difference between Date of Surgery [dd.mm.yyyy] and Date of Death [dd.mm.yyyy] in [| days |]*** (Variable(s): VISITDT; DOSEDD)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.

Creation of variable ***Difference between Date of Surgery [dd.mm.yyyy] and Date of "most recent" Visit [dd.mm.yyyy] in [| days |]*** (Variable(s): VISITDT)	Quantitative, ratio	N/A (Analyzed above), used for survivorship
Create new variable ***"Grouping variable - Mortality"*** (Variable(s): PRIMRSN)	Qualitative, nominal	- censored = survivors - events = death
Create new variable ***"Combined Time - Mortality"*** (Variable(s): VISITDT; DOSEDD)	Quantitative, ratio	- Use time between surgery and most recent visit for surviving subjects - Use time between surgery and death for deceased subject
Use variables ***"Combined Time - Mortality"*** *and* ***"Grouping variable - Mortality"***	Qualitative, nominal Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Kaplan-Meier survival analysis: subject ID, time, status, cumulative proportion, Kaplan-Meier estimate, standard error of KM estimate, number of cumulative events, number of remaining cases, mean for survival time with 95% confidence interval, survival graph, hazard graph.

Table 6.7.2.1: All Assessments – Mortality Tables List

6.7.3. Reoperation Surgery

For analysis of the time to the reoperation surgery, the Kaplan-Meier method will be used. The times between surgery and the most recent or last available assessment per subject will be used together with the times between surgery and the date of reoperation (earliest reoperation in case that one subject experienced more than one reoperation). This analysis is part of the final report.

Evaluation Variable / Question	**Level of Measurement**	**Recode and Analysis Plan**
Adverse Events / Reoperation Surgery		
Creation of variable ***Difference between Date of Surgery [dd.mm.yyyy] and Date of First Reoperation [dd.mm.yyyy] in [| days |]*** (Variable(s): VISITDT)	Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.
Creation of variable ***Difference between Date of Surgery [dd.mm.yyyy] and Date of "most recent" Visit [dd.mm.yyyy] in [| days |]*** (Variable(s): VISITDT)	Quantitative, ratio	N/A (Analyzed above), used for survivorship
Create new variable ***"Grouping variable – First Reoperation"*** (Variable(s): VISITDT)	Qualitative, nominal	- censored = survivors - events = first (earliest) Reoperation
Create new variable ***"Combined Time – First Reoperation"*** (Variable(s): VISITDT)	Quantitative, ratio	- Use time between surgery and most recent visit for surviving subjects - Use time between surgery and first reoperation for subjects with reoperation(s)
Use variables ***"Combined Time – First Reoperation"*** *and* ***"Grouping variable – First Reoperation"***	Qualitative, nominal Quantitative, ratio	Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Kaplan-Meier survival analysis: subject ID, time, status, cumulative proportion, Kaplan-Meier estimate, standard error of KM estimate, number of cumulative events, number of remaining cases, mean for survival time with 95% confidence interval, survival graph, hazard graph.

Table 6.7.3.1: All Assessments – Reoperation Surgery Tables List

6.7.4. ASES Shoulder Score – Within subject changes by visit

The within subject score changes of the ASES Shoulder Score from visit to visit will be analyzed to help identifying the changes on the subject level. This analysis is part of the final report.

The within subject changes by visit of the ASES Shoulder Score must compare all follow-up visits against each other (m x n) in accordance to table 6.7.4.1 and the analysis tables in this chapter.

ASES Shoulder Score – Follow-up Visits to be compared														
Comparison		Follow-up Visits (n)												
		Preop	6 Weeks	6 Months	12 Months	24 Months	36 Months	48 Months	60 Months	72 Months	84 Months	96 Months	108 Months	120 Months
Follow-up Visits B (m)	Preop													
	6 Weeks	x												
	6 Months	x	x											
	12 Months	x	x	x										
	24 Months	x	x	x	x									
	36 Months	x	x	x	x	X								
	48 Months	x	x	x	x	X	x							
	60 Months	x	x	x	x	X	x	x						
	72 Months	x	x	x	x	X	x	x	x					
	84 Months	x	x	x	x	X	x	x	x	x				
	96 Months	x	x	x	x	X	x	x	x	x	x			
	108 Months	x	x	x	x	X	x	x	x	x	x	x		
	120 Months	x	x	x	x	X	x	x	x	x	x	x	x	
*All combinations marked with an "x" must be performed														

Table 6.7.4.1: All Assessments – ASES Shoulder Score – Follow-up Visits to be compared

Evaluation Variable / Question	**Level of Measurement**	**Coding and Analysis Plan**
All Assessments - ASES Shoulder Score Within Subject Changes		
Creation of variable ***"ASES Total Score change between m and n [points]"*** *Difference between* ***"ASES Total Score m [points]"*** *with* ***"ASES Total Score n [points]"*** (Variable(s): FINSCORE)	Quantitative, interval	Calculate difference (could be negative or positive). Case summary with number and percentage of valid cases/values, missing cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.

Table 6.7.4.2: All Assessments – ASES Shoulder Score Within Subject Changes

7. Table Templates (Tables, Figures, Listings - TFL)

Tables must consist of at least a headline, the variable/analysis-object label and column headers. Furthermore, the table headline must contain the "Analysis Section"(e.g. Demographics, Operative) the variable label (e.g. Gender, Age) as well as the table type (Frequencies, Listing). If the table is referring to a subgroup, a notification must be entered in the headline as well. Figures (if any) must be clearly labeled and numbered by a figure number and title in addition to the axis and category labeling created by software packages (e.g. IBM SPSS).

7.1. FREQUENCIES

All answered response options must be listed with the appropriate label, other response options do not have to be displayed necessarily. In the event of missing answers, the frequencies must be included in an extra row as well ("*Missing*"). All given answers must be added up in an extra row ("*Total*"). In addition to the number of frequencies, percentages must be displayed in a separate column.

"Analysis Section" – "Variable Label" – Frequencies

Characteristic		**n**	**%**
"Variable Label"	"Response A"	*"xxx"*	*"xxx"*
	"Response B"	*"xxx"*	*"xxx"*
	Missing	*"xxx"*	*"xxx"*
	Total	*"xxx"*	*"xxx"*

Table 7.1.1: Frequencies Table Template

If multiple subgroups/clusters (e.g. Sites, Visits) should be displayed in one table, an extra column ("*Group X*") and/or extra rows ("*Group Y*") must be added. Same applies to (sub-) questions, which can be merged in one table. It is recommended to add an extra "Total" column and row, for adding up the subgroups, if possible, from a statistical point of view. In addition, subgroups must be named in the headline as well ("*by Group X and by Group Y*").

"Analysis Section" – "Variable Label" – Frequencies – by "Group X" and "Group Y"

Characteristic		***"Group X1"***		***"Group X2"***		**Total**	
		n	**%**	**n**	**%**	**n**	**%**
"Group Y1"	*"Response A"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*
	"Response B"	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*
	Missing	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*
	Total	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*
"Group Y2	*"Response A"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*
	"Response B"	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*
	Missing	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*
	Total	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*
Total	*"Total Response A"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*
	"Total Response B"	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*
	Missing	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*
	Total	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*

Table 7.1.2: Grouped Frequencies Table Template

7.2. DESCRIPTIVE STATISTICS

Descriptive Statistic tables must contain the items listed in Table 7.2.1. Furthermore, the associated unit must be displayed. If the values are referring to a subgroup (n) and not to the overall population (N), a notification must be entered in the headline("*n = xxx*").

"Analysis Section" – "Variable Label" – Descriptive Statistics (n = "xxx")

Characteristic		**["*unit*"]**
"Variable Label"	Mean	*"xxx"*
	Median	*"xxx"*
	SD	*"xxx"*
	IQR	*"xxx"*
	Range	*"xxx"*
	Max	*"xxx"*
	Min	*"xxx"*

Table 7.2.1: Descriptive Statistics Table Template

7.3. LISTINGS

Listing tables must contain one unique identifier (e.g. Subject ID). Furthermore, an additional column must be added, if the specification/description is not referring to one single variable or response option("*Response Option*"), which is already named in the headline. If multiple specifications/descriptions exist for one variable/response (e.g. Drug1, Drug2, Drug3…), further columns must be added ("*Specification/Description A*", "*Specification/Description B*"). Subgroups can be implemented as described in chapter 7.1.

"Analysis Section" – "Variable Label" – Listing

"Unique Identifier"	**Description**	
	"Response Option"	***"Specification/Description A"***
"xxx"	*"xxx"*	*"xxx"*
"xxx"	*"xxx"*	*"xxx"*
"xxx"	*"xxx"*	*"xxx"*

Table 7.3.1: Listing Table Template

8. References

a. ISO 14155 - Clinical Investigation of Medical Devices for Human Subjects

b. ICH-E6 - Harmonized Tripartite Guidelines for Good Clinical Practice

c. ICH-E9 - Statistical Principles for Clinical Trials

d. Declaration of Helsinki

e. Gamble C et. al. Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. AMA. 2017;318(23):2337-2343. doi:10.1001/jama.2017.18556

f. DQP 20-001 Clinical Investigation

g. DQI 20-001 Clinical Investigation - Clinical Investigation Plan

h. DQI 20-004 Clinical Investigation - Master CRF, eCRF and Database Development

i. DQI 20-009 Clinical Investigation - Reports

20210528_ReUnion TSA_SAP

Final Audit Report 2021-05-28

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