NCT04089371

ReUnion RFX Statistical Analysis Plan (SAP)

CLINICAL INVESTIGATION TITLE:	A Post-Market Clinical Evaluation of the ReUnion Reversible Fracture (RFX) System
DEVICE NAME:	ReUnion RFX System
STATISTICAL ANALYSIS PLAN (SAP) VERSION:	2
CLINICAL INVESTIGATION PLAN (CIP) VERSION:	2
INDICATIONS:	This study will adhere to the indications and contraindications for the ReUnion RFX System as are detailed in the device's Instructions for Use.
CLINICAL INVESTIGATION DESIGN:	• Post-Market • Multicenter • Prospective • Two Arms • 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			
Role	**Name**	**Signature**	**Date**
Author	Sascha Lorenzen	*Sascha Lorenzen* *Electronically signed by: Sascha Lorenzen Reason: I am signing as the Author of this document Date: May 28, 2021 13:43 GMT+2*	28-May-2021
Statistician	Claudia Beimel	*Claudia Beimel* *Electronically signed by: Claudia Beimel Reason: I approve this document Date: May 28, 2021 14:27 GMT+2*	28-May-2021
Clinical Research Head (CRH)	Rebecca Gibson	*Rebecca Gibson* *Electronically signed by: Rebecca Gibson Reason: I approve this document Date: May 28, 2021 08:37 EDT*	28-May-2021
Clinical Investigation Manager (CIM)	Susanne Höfer	*Susanne Höfer* *Electronically signed by: Susanne Höfer Reason: I approve this document Date: May 28, 2021 13:44 GMT+2*	28-May-2021

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1. Administrative Information

1.1. LIST OF ABBREVIATIONS

Acronym	Definition
AE	Adverse Event
ASES	American Shoulder and Elbow Surgeons Shoulder Score
CI	Confidence Interval
CIP	Clinical Investigation Plan
CRF	Case Report Form
eCRF	Electronic Case Report Form
EC	Ethics Committee
EDC	Electronic Data Capture
FR	Final Report
HA	Hemi-Shoulder Arthroplasty
ICF	Informed Consent Form
ICH-GCP	International Conference of Harmonisation Good Clinical Practice
IFU	Instructions for Use
IR	Interim/Annual Report
ITT	Intent-to-Treat
Intra-Op	Intra-Operative
IRB	Institutional Review Board
LTFU	Lost to Follow-Up
PP	Per Protocol
Preop	Preoperative
RFX	Reversible Fracture
RSA	Reverse Shoulder Arthroplasty
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
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	08OCT2019	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
(Senior) Statistician	Claudia Beimel	Stryker
Clinical Research Head (CRH)	Rebecca Gibson	Stryker
Clinical Investigation Manager (CIM)	Susanne Höfer	Stryker

2. Introduction

2.1. BACKGROUND AND RATIONALE

The ReUnion RFX System is indicated for use as a hemiarthroplasty (HA), total shoulder arthroplasty (TSA) or reverse shoulder arthroplasty (RSA). It includes a RFX Stem that can utilize either the ReUnion TSA or ReUnion RSA humeral and glenoid components.

2.2. CLINICAL INVESTIGATION DESIGN

This investigation is a prospective, multicenter study. It is anticipated that a total of one hundred (100) subjects will be enrolled at approximately 5-10 sites. Neither subjects nor investigators are blinded to treatment and the study does not include a contemporaneous control. The study has been designed to follow the surgeon's standard of care for joint arthroplasty patients, which entails clinical evaluation on a regular ongoing basis, or as needed should the patient become symptomatic in the treated joint. The enrollment period is expected to occur over 20 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, as 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 also optional.

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 the 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 be collected according to the schedule in Table 1, Schedule of Events. This will be repeated annually in all subjects who have the prosthesis with

full or partial implant survival (including all subjects without removal of all endo-prosthesis components).

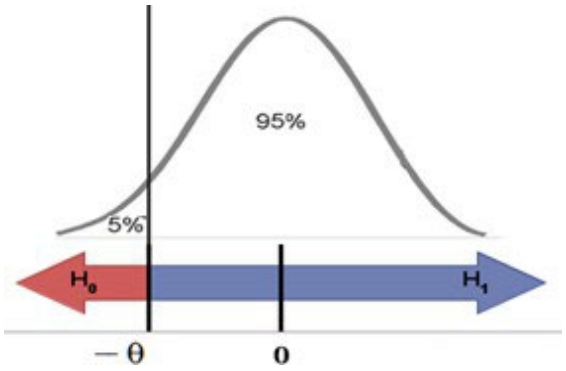
The 24 months postoperative results for subjects implanted with ReUnion RFX System will be compared to a historical group and results reported by respective clinical outcome data in the scientific literature.

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

Arm A (TSA/HA)		
Hypothesis	**Equations**	**Interpretation**
Null (H_0)	$A - B < -\theta$ ReUnion RFX System (TSA/HA) – Control (Benchmark) < -θ	Central tendency of A is inferior to the central tendency of B.
Alternative (H_1)	$A - B \geq -\theta$ ReUnion RFX System (TSA/HA) – Control (Benchmark) ≥ -θ	Central tendency of A is non-inferior to the central tendency of B.



Possible Evidence (p)	**Possible Decisions**	**Possible Conclusions – ASES score**
p-value > α (0.05)	Fail to reject null hypothesis (H_0)	ReUnion RFX System (TSA/HA) < Control (Benchmark) Insufficient evidence to reject the null hypothesis (H_0: A – B < -θ) at the pre-determined significance level of 5%.
p-value ≤ α (0.05)	Reject null hypothesis (H_1)	ReUnion RFX System (TSA/HA) ≥ Control (Benchmark)

		Sufficient evidence to reject the null hypothesis (H_0: A – B < -θ) at the pre-determined significance level of 5%.

Table 3.1.1.1: Arm A (TSA/HA)

The primary objective of the clinical investigation is to demonstrate non-inferiority of the ASES Shoulder Score at 24 months post-operative compared to the benchmark literature for Arm A. The 24 months mean ASES Shoulder Score result of the RFX System (TSA/HA) will be compared to the pooled postoperative mean estimate of the control group (58.74 points). The pooled standard deviation of the post-operative ASES Shoulder Score result of the benchmark (20.33 points) was used to determine lower limit. The lower maximum acceptable difference (-θ) is 38.41 points (mean of control - θ or 58.74 – 20.33 = 38.41 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 RFX System (TSA/HA) against the value of 38.41 points.

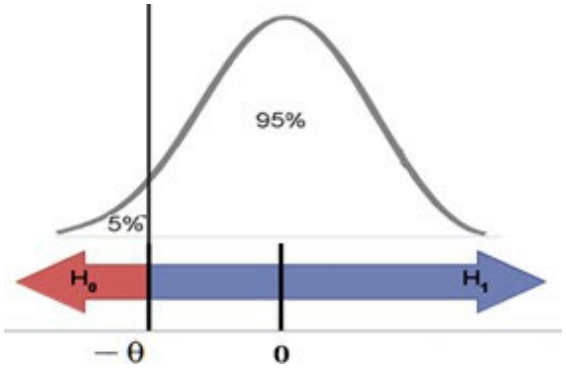
Arm B (RSA)		
Hypothesis	**Equations**	**Interpretation**
Null (H_0)	A – B < -θ ReUnion RFX System (RSA) – Control (Benchmark) < -θ	Central tendency of A is inferior to the central tendency of B.
Alternative (H_1)	A – B ≥ -θ ReUnion RFX System (RSA) – Control (Benchmark) ≥ -θ	Central tendency of A is non-inferior to the central tendency of B.
		
Possible Evidence (p)	**Possible Decisions**	**Possible Conclusions – ASES score**
p-value > α (0.05)	Fail to reject null hypothesis (H_0)	ReUnion RFX System (RSA) < Control (Benchmark) Insufficient evidence to reject the null hypothesis (H_0: A – B < -θ) at the pre-determined significance level of 5%.
p-value ≤ α (0.05)	Reject null hypothesis (H_1)	ReUnion RFX System (RSA) ≥ Control (Benchmark) Sufficient evidence to reject the null hypothesis (H_0: A – B < -θ) at the pre-determined significance level of 5%.

Table 3.1.1.2: Arm B (RSA)

The primary objective of the clinical investigation is to demonstrate non-inferiority of the ASES score at 24 months post-operative compared to the benchmark literature for Arm B. The 24 months mean ASES Shoulder Score result of the RFX System (RSA) will be compared to the pooled postoperative mean estimate of the control group (74.48 points). The pooled standard deviation of the post-operative ASES Shoulder Score result of the benchmark (11.08 points) was used to determine the lower limit. The lower maximum acceptable difference (-θ) is 63.40 points (mean of control - θ or 74.48 – 11.08 = 63.40 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 RFX System (RSA) against the value of 63.40 points.

3.1.2. Secondary Analyses

The incidence of device-related AEs and implant survivorship will be assessed up to ten years after the index procedure and monitored through collection and analyses.

Furthermore, time to (earliest) device-related AEs will be analyzed as well. For analysis of the time to the (earliest) device-related AEs as well as the time to secondary procedure (revision, removal, reoperation), 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.

- **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.

- **Total 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 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.

3.2.1. Sample Size Justification - Arm A (TSA/HA)

Benchmark and Objectives for Clinical Investigation	
Endpoint	Non-inferiority (equal or better) of the ASES Shoulder Score in relation to the officially cleared indications in comparison to respective clinical outcome data in the scientific literature. Meta-analysis by Shukla et. al., 2016 [1]
Estimated drop-out rate	56% (confirmed by Medical Expert, see Cuff et al. [2]) *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] for Arm A (TSA/HA)
Values from Shukla et. al used that were given for Hemiarthroplasty

Source		Mean	Std. Dev.	Comments
No.	**Title**			
1	Sebastia-Forcada, 2014 [3]	N/A	N/A	No ASES score
2	Baudi, 2014 [4]	51.3	25.4	
3	Chalmers, 2014 [5]	66.0	31.0	
4	Cuff, 2013 [6]	62.0	14.0	
5	Garrigues, 2012 [7]	47.4	12.75	
6	Young, 2010 [8]	67.0	18.5	
7	Gallinet, 2009 [9]	N/A	N/A	No ASES score

Identified Cleared Indications (Arm A & B)

No.	Indication
1	Aseptic necrosis of the humeral head
2	Painful, disabling joint disease of the shoulder resulting from degenerative arthritis, rheumatoid arthritis or post-traumatic arthritis
3	Proximal humeral fractures and/or dislocation
4	Clinical management problems where arthrodesis or alternative reconstructive techniques are less likely to achieve satisfactory results
5	Revision of previous unsuccessful total shoulder replacement, resurfacing or other procedure

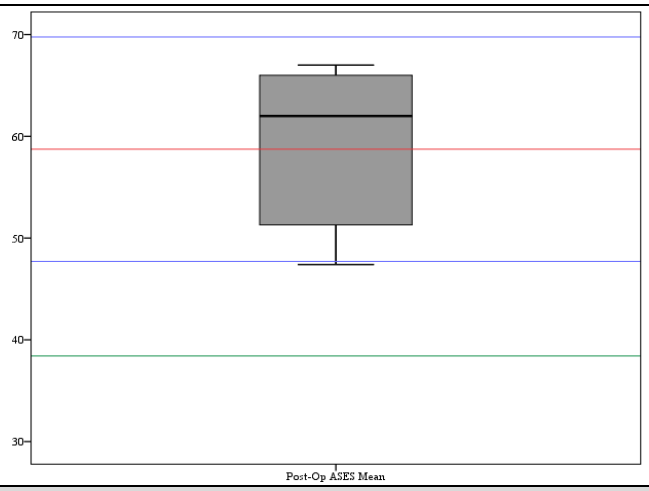
Explorative Analysis - ASES (single group) - for Arm A (TSA/HA)

Acceptance Criteria

Confidence Interval (CI)	0.95 (95%) two-sided
Software Used	IBM SPSS V20

Descriptives

			Statistic	Std. Error
Post-Op ASES Mean	Mean		58,7400	3,97185
	95% Confidence Interval for Mean	Lower Bound	47,7124	
		Upper Bound	69,7676	
	Median		62,0000	
	Std. Deviation		8,88133	
	Minimum		47,40	
	Maximum		67,00	
	Interquartile Range		17,15	
Post-Op ASES Std.Dev.	Mean		20,3300	3,46719



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 std. dev. ASES

58.74 – 20.33 = **38.41 points**

Acceptance Criteria for Sample Size Calculation

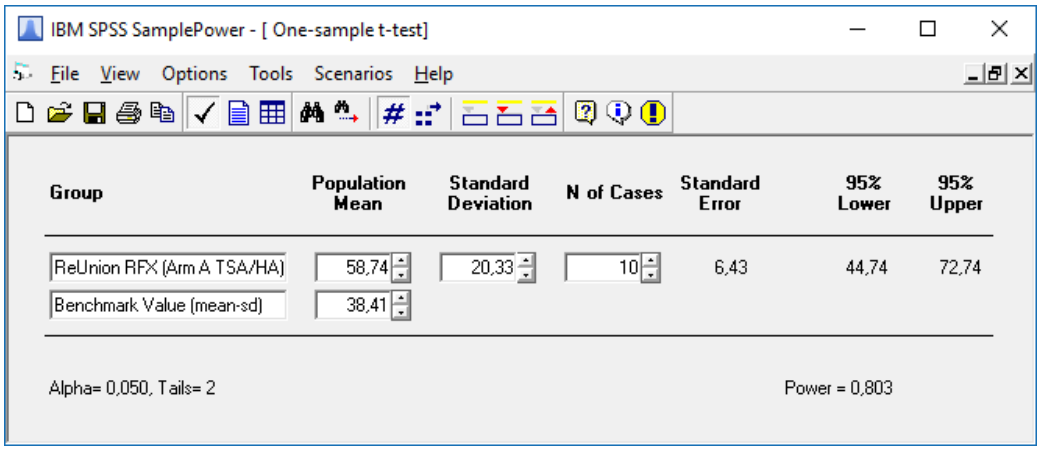
Significance Level (α)	0.05 (5%)
Power (1-β)	0.80 (80%)

Confidence Interval (CI)	0.95 (95%)	
Tails	2	
Path	Non-inferiority – ReUnion RFX Arm A (TSA/HA) (A) ≥ Benchmark (B, explorative analysis in this document)	
Hypotheses Pair	Null (H_0)	$A - B < -\theta$
	Alternative (H_1)	$A - B \geq -\theta$
Benchmark Timepoint	24 months postoperative	
Benchmark no. of sources	5	
Benchmark Mean	**58.74** (pooled mean ASES [points])	
Benchmark Std. Dev.	**20.33** (pooled std. dev. ASES [points])	
Benchmark Value Non-Inferiority Margin (-θ)	Pooled mean ASES minus pooled std. dev. ASES **58.74 – 20.33 = 38.41 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 58.74 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 that the population from which the sample will be drawn has a mean of 58.74 points with a standard deviation of 20.33 points. The observed value will be tested against a theoretical value (constant, non-inferiority margin) of 38.41 points.

IBM SPSS Sample Power Output – Screenshot



Estimated overall drop-out rate is 56% which leads to the requirement of enrolling an additional 6 subjects into the clinical investigation.

Sample Size	**Overall number of subjects to be enrolled: 16 subjects (rounded up to 20 subjects)**
Overall Sample Size (multiplied by number of indications = 5)	**100 subjects**

Table 3.2.1: Sample Size Justification Arm A (TSA/HA)

3.2.2. Sample Size Justification - Arm B (RSA)

Benchmark and Objectives for Clinical Investigation	
Endpoint	Non-inferiority (equal or better) of the ASES Shoulder Score in relation to the officially cleared indications in comparison to respective clinical outcome data in the scientific literature. Meta-analysis by Shukla et al., 2016 [1]
Estimated drop-out rate	56% (confirmed by Medical Expert, see Cuff et al. [2])

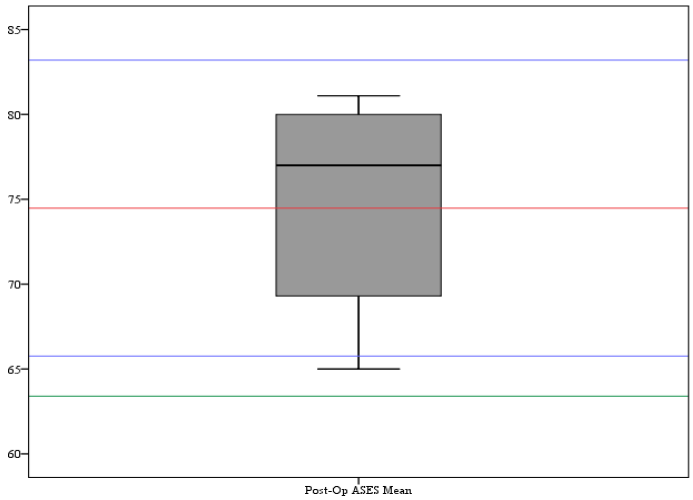
Benchmark Sources & Values ASES [points] for Arm B (RSA)				
Source		Mean	Std. Dev.	Comments
No.	Title			
1	Sebastia-Forcada, 2014 [3]	N/A	N/A	No ASES score
2	Baudi, 2014 [4]	69.3	25.4	
3	Chalmers, 2014 [5]	80.0	11.0	
4	Cuff, 2013 [6]	77.0	3.75	
5	Garrigues, 2012 [7]	81.1	3.25	
6	Young, 2010 [8]	65.0	12.0	
7	Gallinet,2009 [9]	N/A	N/A	No ASES score

Identified Cleared Indications (Arm A & B)	
No.	Indication
1	Aseptic necrosis of the humeral head
2	Painful, disabling joint disease of the shoulder resulting from: degenerative arthritis, rheumatoid arthritis, or post-traumatic arthritis
3	Proximal humeral fractures and/or dislocation
4	Clinical management problems where arthrodesis or alternative reconstructive techniques are less likely to achieve satisfactory results
5	Revision of previous unsuccessful total shoulder replacement, resurfacing or other procedure

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

Descriptives

			Statistic	Std. Error
Post-Op ASES Mean	Mean		74,4800	3,14124
	95% Confidence Interval for Mean	Lower Bound	65,7585	
		Upper Bound	83,2015	
	Median		77,0000	
	Std. Deviation		7,02403	
	Minimum		65,00	
	Maximum		81,10	
	Interquartile Range		13,40	
Post-Op ASES Std.Dev.	Mean		11,0800	4,00595



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

74.48 – 11.08 = **63.40 points**

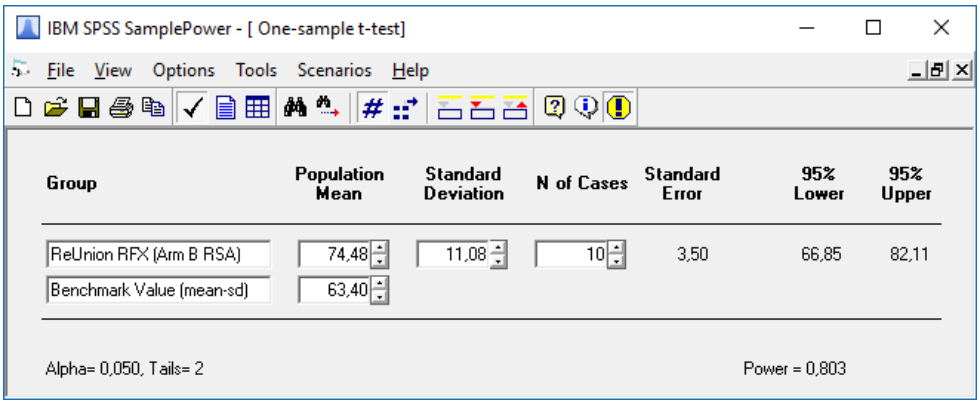
Acceptance Criteria for Sample Size Calculation	
Significance Level (α)	0.05 (5%)
Power (1-β)	0.80 (80%)
Confidence Interval (CI)	0.95 (95%)

Tails	2	
Path	Non-inferiority – ReUnion RFX Arm B (RSA) (A) ≥ Benchmark (B, explorative analysis in this document)	
Hypotheses Pair	Null (H_0)	A – B < -θ
	Alternative (H_1)	A – B ≥ -θ
Benchmark Timepoint	24 months postoperative	
Benchmark no. of sources	5	
Benchmark Mean	**74.48** (pooled mean ASES [points])	
Benchmark Std. Dev.	**11.08** (pooled std. dev. ASES [points])	
Benchmark Value **Non-Inferiority Margin (-θ)**	Pooled mean ASES minus pooled std. dev. ASES **74.48 – 11.08 = 63.40 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 74.48 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 that the population from which the sample will be drawn has a mean of 74.48 points with a standard deviation of 11.08 points. The observed value will be tested against a theoretical value (constant, non-inferiority margin) of 63.40 points.

IBM SPSS Sample Power Output – Screenshot



Estimated overall drop-out rate is 56% which leads to the requirement of enrolling an additional 6 subjects into the clinical investigation.

Sample Size	**Overall number of subjects to be enrolled: 16 subjects (rounded up to 20 subjects)**
Overall Sample Size (multiplied by number of indications = 5)	**100 subjects**

Table 3.2.2: Sample Size Justification Arm B (RSA)

In conclusion, the calculated number of subjects to be enrolled (10) plus the estimated overall drop-out rate of 56% predicts enrollment of 16 subjects (rounded up to 20) per indication. Since the five cleared indications and the proposed sample sizes are identical for the two clinical investigation arms, the sample size of one indication (n=20) will be multiplied by five 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 post-operative including the ASES score.

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

4.3. TIMING OF FINAL ANALYSES

The full final report with complete analyses, 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 (up to ten years) after the index procedure. The follow up evaluations will include assessment of complications and adverse events and ASES Shoulder Score.

Assessment	Pre-Operative	Operative/ Discharge	6 Weeks [a, b] (+/- 2 weeks)	6 Months [a, b] (+/- 3 weeks)	12 Months [a, b] (+/- 4 weeks)	24 Months [a, b] (+/- 4 weeks)	Annually [b] (+/- 4 weeks)
Informed Consent	X						
Demographics & Medical History	X						
Inclusion/Exclusion	X						
Primary Diagnosis	X						
Surgical Procedure		X					
ASES Shoulder Score	X		X	X	X [c]	X [c]	X [c]
Subject Disposition [d]			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 missed a visit and outside of visit window, every effort should be made to collect data instead of noting visit as missed. Visit windows are calculated from index event, and not from previous visit. c. Evaluation can be collected via phone. d. Subject Disposition assessment would 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 post-operative 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 RFX 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 Per Protocol (PP) Population is defined to be all subjects in the ITT Population with no major clinical investigation plan / protocol violations. The clinical investigation plan / protocol violations that will exclude a subject are as follows:

  - The subject does not receive the ReUnion RFX System
  - The subject does not meet all eligibility criteria
  - The subject has a clinical investigation plan / protocol 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 protocol. 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

If, during the clinical investigation, a subject must be prematurely withdrawn from clinical investigation, procedures are outlined in the CIP. 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) divided into both groups (Arm A; Arm B):

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.

All analyses described in this section, will be split in the two groups (Arm A; Arm B).

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.

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;	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X

ACTPROHS; ACTOTHER; ACTOTHSP)		Listing of given Other specifications.			
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; SOFTTRL; ROTCFRP; OTHTISRP; RVHARSA; RVHARSASP; REVRSA; REVRSASP; CHATSAWHS; CHATSAWOHS; CHARSAWHS; CHARSAWOHS; CTSAHAWHS; CTSAHAWOHS; CTSARSAWHS; CTSARSAWOHS; CRSAHAWHS; CRSAHAWOHS; REVFINF; REVFINFSP; RESARTH; ARTHOD; ORIF; RESOSSIF; TYPEOTH; TYPEOTHSP)	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; NERPAL; DISLC; OTSUBLUX; MALPOS; UNDROVR; IMPDISL; ROTCFTR; ERGLEN; IMPLOOS; IMPBRKG; WRGLEN; PERFRAC; STIFF; PAIN; HETOSSIF; RESOTH; RESOTHSPC)	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)	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). Listing of given specifications.	X	X	
Height [captured in inches] 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] 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).	X	X	

		Listing of given specifications.			

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). Listing of given specifications.		X	
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?	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X

(Variable(s): PNKLR)					
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	X	X	

		cases/values (if any) and total cases/values. Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.			
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 Score (post fracture, prior to surgery) Tables List

6.3. INTRA-OPERATIVE 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	
Which humeral and glenoidal components were used? (Variable(s): COMPUSED)	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): HSREFRSA)	Qualitative, nominal	None, used to populate diameter, length, press-fit textured or smooth uncoated stem details Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Humeral Cup Lot/Serial # (Variable(s): HCREFRSA)	Qualitative, nominal	None, used to populate diameter and thickness details Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Humeral Insert Lot/Serial # (Variable(s): HIREFRSA)	Qualitative, nominal	None, used to populate diameter, thickness, standard or constrained insertion details Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Glenosphere Lot/Serial # (Variable(s): GLREFRSA)	Qualitative, nominal	None, used to populate diameter, offset, concentric or eccentric glenosphere details Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Central Screw Lot/Serial # (Variable(s): CSREFRSA)	Qualitative, nominal	None, used to populate length details Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Peripheral Screw #1 Lot/Serial # (Variable(s): PSREF1RSA)	Qualitative, nominal	None, used to populate length details Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Peripheral Screw #2 Lot/Serial # (Variable(s): PSREF2RSA)	Qualitative, nominal	None, used to populate length details Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Third peripheral screw used (Variable(s): PS3USED)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Peripheral Screw #3 Lot/Serial # (Variable(s): PS3REFRSA)	Qualitative, nominal	None, used to populate length details		X	

		Proportions, frequencies, column and row totals, missing proportion (if any).			
Fourth peripheral screw used (Variable(s): PS4USED)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Peripheral Screw #4 Lot/Serial # (Variable(s): PS4REFRSA)	Qualitative, nominal	None, used to populate length details Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Humeral Stem Lot/Serial# (Variable(s):HSREFTSA)	Qualitative, nominal	None, used to populate diameter, length, press-fit textured or smooth uncoated stem details Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Humeral Head Lot/Serial # (Variable(s):HHREFTSA)	Qualitative, nominal	None, used to populate diameter, length, press-fit textured or smooth uncoated stem details Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Glenoid Lot/Serial # (Variable(s): GLENREFTSA)	Qualitative, nominal	None, used to populate diameter, length, press-fit textured or smooth uncoated stem 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): TSA_QA)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Correct sizing of the humeral stem and head (Variable(s): TSA_QB)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Correct positioning of the glenoid component (Variable(s): TSA_QC)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Correct initial positioning of the humeral stem and the humeral cup (Variable(s): TSA_QD)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Correct initial positioning of the baseplate (Variable(s): TSA_QE)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Correct initial positioning of the glenosphere (Variable(s): TSA_QF)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Correct positioning of central and peripheral screws in the glenoid (Variable(s): TSA_QG)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Correct sizing of humeral stem, humeral cup, and glenosphere (Variable(s): TSA_QH)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of intraoperative fracture of the humerus (Variable(s): QI)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	

Radiologic signs of intraoperative fracture of the glenoid (Variable(s): QJ)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Correct cementation of the humeral component (Variable(s): QK)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Correct cementation of the glenoid component (Variable(s): QL)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of humeral cement leakage (Variable(s): QM)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of glenoidal cement leakage (Variable(s): QN)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Others (Variable(s): QO)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).			X
Please describe the findings in detail (Variable(s): QP)	Qualitative, nominal	Listing of comments identified by subject code/ID			X

Table 6.3.3: Operative Visit Form – Radiographic Evaluation Tables List

6.4. EARLY POST-OPERATIVE CHARACTERISTICS

N/A

6.5. POST-OPERATIVE 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.	X	X	

		Mean, median, interquartile range, maximum, minimum, standard deviation, 95% confidence interval for mean, Shapiro-Wilk Test.			
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 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 component dissociation (humeral head from humeral stem (Variable(s): TSAQA)	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): TSAQB)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of breakage of the glenoid component (Variable(s): TSAQC)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of wear of the glenoid component (Variable(s): TSAQD)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of rotator cuff tear (superior/cranial migration) (Variable(s): QE)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiolucency of the glenoid (Variable(s): TSAQF)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Gross loosening of the glenoid component (Variable(s): TSAQG)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Glenoid (select glenoid used) (Variable(s): TSAQH)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	

If pegged glenoid component: (Variable(s): TSAQI)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
If keeled glenoid component (Variable(s): TSAQJ)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Implant component dissociation (humeral cup from humeral stem) (Variable(s): RSAQK)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Implant component dissociation (humeral insert from humeral cup) (Variable(s): RSAQL)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Implant component dissociation (glenosphere from baseplate) (Variable(s): RSAQM)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of breakage of the humeral insert (Variable(s): RSAQN)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of wear of the humeral insert (Variable(s): RSAQO)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Breakage of the humeral cup (Variable(s): RSAQP)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Breakage of the glenosphere (Variable(s): RSAQQ)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Breakage of the baseplate (Variable(s): RSAQR)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Bending or breakage of the central screw (Variable(s): RSAQS)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Bending or breakage of one or more peripheral screw(s) (Variable(s): RSA QT)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of gross loosening of the baseplate and the screws (Variable(s): RSAQU)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Scapular notching (Variable(s): RSAQV)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Stress fracture of the acromion or the scapular neck (Variable(s): RSAQW)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Stress fracture of the coracoid (Variable(s): RSAQX)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Stress fracture of the clavicle (Variable(s): RSAQY; RSAQZ)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any). Listing of given explanation.		X	
Implant dislocation (complete dislocation) (Variable(s): Q2)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Periprosthetic fracture of the humerus (Variable(s): Q3)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Periprosthetic fracture of the glenoid (Variable(s): Q4)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Breakage of the humeral stem (Variable(s): Q5)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Heterotopic ossification (Variable(s): Q6)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	

Radiolucency of the humerus (Variable(s): Q7)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiologic signs of gross loosening of the humeral stem (Variable(s): Q8)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Non-union of lesser tuberosity osteotomy (Variable(s): Q9)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any). Listing of given explanation.		X	
Malunion of lesser tuberosity osteotomy (Variable(s): Q10)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Others (Variable(s): Q11)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any). Listing of given explanation.		X	
Others description (Variable(s): Q12)	Qualitative, nominal	Listing of given explanation.			X
Heterotopic ossification (modified BROOKER grading (Variable(s): Q13)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Description of radiolucency in humeral stems (Variable(s): Q14G0; Q14G1; Q14G1Z; Q14G2; Q14G2Z; Q14G3; Q14G3Z; Q14G4; Q14G4Z; Q14G5)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Radiolucent lines 2 mm or greater in ≥ 3 zones (Variable(s): Q28)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Tilting (> 5°) orsubsidence (> 5 mm) of thestem (Variable(s): Q29)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any).		X	
Thinning ("scalloping")of the humeral cortex (Variable(s): Q30; Q31)	Qualitative, nominal	Proportions, frequencies, column and row totals, missing proportion (if any). Listing of given explanation.		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**	**Inclusion**		
Endpoints – Primary Endpoint Arm A (TSA/HA)			**IR**	**FR**	**N/A**
Use variable ***Total ASES 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 RFX System (TSA/HA) against the value of 38.41 points. The analysis of the primary endpoint will be part of the final report				X	
Endpoints – Primary Endpoint Arm B (RSA)			**IR**	**FR**	**N/A**
Use variable ***Total ASES 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 RFX System (RSA) against the value of 63.40 points. The analysis of the primary endpoint will be part of the final report.				X	

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 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]***	Quantitative, ratio	N/A (Analyzed above), used for survivorship

and Date of "most recent" Visit [dd.mm.yyyy] in [| days |] (Variable(s): VISITDT)		
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.: All Assessments – Mortality Tables List

6.7.3. Reoperation Surgery

For analysis of the time to the reoperation, 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: All Assessments – Revision Surgery Tables List

6.7.4. ASES Total Score – Within subject changes by visit

The within subject score changes of the total 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**	**Recode and Analysis Plan**
All Assessments - ASES Shoulder Score Within Subject Changes		
Creation of variable ***"ASES Total Score change between m visit and n [points]"****Difference between* ***"ASES Total Score m [points]"*** *with* ***"ASES Total Score n [points]"*** (Variable(s): FINSCORE)	Quantitative, ratio	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 Total 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. Each analysis arm must be displayed separately, as well as a overall result of both arms has to be created. The two arms and the overall results can be combined in one table or in three separate tables.

"Analysis Section" – "Variable Label" – Frequencies

Characteristic		**ARM A**		**ARM B**		**Total**	
		n	**%**	**n**	**%**	**n**	**%**
"Variable Label"	"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"*

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

	"Total Response B"	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*
	Missing	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*
	Total	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"xxx"*	*"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		**Arm A**	**Arm B**	**Total**
		["*unit*"]	**["*unit*"]**	**["*unit*"]**
"Variable Label"	Mean	*"xxx"*	*"xxx"*	*"xxx"*
	Median	*"xxx"*	*"xxx"*	*"xxx"*
	SD	*"xxx"*	*"xxx"*	*"xxx"*
	IQR	*"xxx"*	*"xxx"*	*"xxx"*
	Range	*"xxx"*	*"xxx"*	*"xxx"*
	Max	*"xxx"*	*"xxx"*	*"xxx"*
	Min	*"xxx"*	*"xxx"*	*"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

Description		
"Unique Identifier"	***Arm A***	
	"Response Option"	***"Specification/Description A"***
"xxx"	*"xxx"*	*"xxx"*
"xxx"	*"xxx"*	*"xxx"*
"xxx"	*"xxx"*	*"xxx"*
"Unique Identifier"	***Arm B***	
	"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 RFX_SAP

Final Audit Report 2021-05-28

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