ARGOS-SC01_Follow-up

Follow-up of the first in man, prospective, open-label, single arm, multicenter clinical investigation to assess the long-term safety and performance of the ARGOS-SC suprachoroidal pressure sensor system in patients with glaucoma underwent non-penetrating glaucoma surgery (Follow-up Month 12 – Month 36)

Reference Number: ARGOS-SC01_Follow-up

Statistical Analysis Plan (SAP)

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0.1	17.08.2022	First draft version
0.2	26.08.2022	Second draft version after internal review
0.3	01.09.2022	Third draft version review by IOP
1.0	01.09.2022	Final version

Table of Contents

1 Abbreviations

A	
AE	Adverse Event
AS	Anterior Segment
C	
CCT	Central corneal thickness
CIP	Clinical Investigation Plan
CRF	Case report form
CRO	Clinical Research Organisation
D	
DCT	Pascal Dynamic Contour Tonometry
E	
eCRF	Electronic Case Report Form
F	
FAS	Full Analysis Set
G	
GAT	Goldman Applanation Tonometry
I	
ICH (guideline)	International Conference of Harmonization
ICH	Intracranial Hemorrhage
M	
Max	Maximum
Mean	Arithmetic Mean
Min	Minimum
N	
N	Number of Patients (total population)
n	Number of Patients with non-missing Data
O	
OCT	Optical coherence tomography
OPA	Ocular Pulse Amplitude
P	
PS	Posterior Segment
Q	
Q1	Lower Quartile
Q3	Upper Quartile
S	
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis Systems

SD	Standard Deviation
T	
TFLs	Tables, Figures and Listings
V	
V	Visit
VFQ-25	National Eye Institute – Vision related Quality of Life Questionnaire-25

2 Introduction

This Statistical Analysis Plan (SAP) provides a comprehensive and detailed description of the strategy and statistical procedures for analysing the data from study

ARGOS-SC01_Follow-up
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"ARGOS-SC01_Follow-up"

The SAP includes the analysis specification regarding efficacy and safety as well as data conventions and calculation rules for derived data.

The plan is developed according to the International Conference on Harmonization (ICH) guideline E9 "Statistical Principles for Clinical Trials".

The basis of the SAP is the study protocol version Rev.C dated 27.05.2021.

The SAP will be produced by CRO Dr. med. Kottmann GmbH & Co. KG, finalized prior to data base lock, and approved in writing by the sponsor.

The SAP will incorporate all protocol amendments prepared for the study. In case of an amendment to the protocol after the SAP finalization date, an amendment to this SAP may be written.

Any deviations from this SAP will be described and justified in the Clinical Study Report.

All tables, figures, and listings (TFLs), and the statistical analysis will be produced by CRO Dr. med. Kottmann GmbH & Co. KG. A table of contents of the TFLs is given in the appendix.

3 Study Design

3.1 Study design

This study is designed as a prospective, open-label, multicenter, single-arm clinical investigation. Subjects will be followed up at regular intervals for 2 years (Month 12 – Month 36) after the ARGOS-SC implantation to collect safety and performance information

3.2 Study groups

ARGOS-SC System

Since this is a single arm study, there is no comparator in this study.

3.3 Sample size calculation

Given by the exploratory nature of this study, the sample size is not driven by the need for a formal statistical hypothesis test with a certain degree of power. Instead, this study is driven by the desire to obtain a clinically meaningful amount of data to evaluate the long-term safety and performance of the ARGOS-SC system in patients who have been already implanted with the study device. Therefore, the maximum sample size is 24. The minimal sample size for this study is at the Sponsor's direction. This is considered to be appropriate since no experimental treatments are planned and all assessments with exception of IOP measurement using the ARGOS-SC device are established standard methods.

3.4 Study Assessments

The following table shows the schedule of assessments:

Table 1: Assessment Schedule ARGOS-SC01_Follow-up

Visit	**V09**	**V10**	**V11**	**V12**	**V13**
Indicative Days (D) Visit window	**Month 12 Last Visit of ARGOS SC01 (Baseline)**	**Month 18 (Day 540) +/- 3 weeks**	**Month 24 (Day 720) +/- 3 weeks**	**Month 30 (Day 900) +/- 3 weeks**	**Month 36 (Day 1080) +/- 3 weeks**
General					
Informed consent signed	X				
Inclusion & exclusion criteria	X				
Past and current significant medical history	X				
Vision related Quality of Life (VQoL) questionnaire	X		X		X
Visual acuity (ETDRS)[1] (OU)	X	X	X	X	X
Perimetry[2] (OU)	X	X	X	X	X
Heidelberg Engineering ANTERION®	X	X	X	X	X
External eye photography[3]	X	X	X	X	X
User acceptance questionnaire (patient)	X				X
User acceptance questionnaire (investigator)	X				X
Concomitant medication	X	X	X	X	X
AE/ADE/SAE/SADE	X	X	X	X	X
Device malfunction	X	X	X	X	X
Anterior Segment (OU)					
Optical Coherence Tomography[4]	X	X	X	X	X
Slit-lamp biomicroscopy[5]	X	X	X	X	X
Gonioscopy[6]	X	X	X	X	X
Posterior Segment (OU)					
Funduscopy[7]	X	X	X	X	X

Optical coherence tomography (OCT)[8]	X	X	X	X	X
Fundus photography[9]	X		X		X
IOP Measurements					
Goldmann Applanation Tonometry[10] (OU)	X	X	X	X	X
Pascal Dynamic Contour Tonometry[10] (OU)	X	X	X	X	X
ARGOS-SC pressure sensor measurement[10]	X	X	X	X	X
ARGOS-SC pressure sensor self measurement[11]	X	X	X	X	X

1 The best corrected visual acuity will be determined after objective and subjective determination of refraction with the ETDRS chart in accordance with the ETDRS protocol.

2 Perimetry is performed to obtain an accurate examination of the peripheral extent of the visual field. Automated perimeters will be used either with standard glaucoma field, field 30-2 or equivalent.

3 External eye photography is performed through a slit lamp camera or equivalent. The outer eye shall be photographed in order to document potential changes to the iris or pupil structure.

4 Anterior segment OCT is performed to evaluate effects on change in chamber angle after non-penetrating glaucoma surgery and to assess corneal thickness.

5 Slit-lamp biomicroscopy is performed through an undilated pupil to assess the following anatomic parameters of the anterior segment: lids, conjunctiva, cornea, anterior chamber, iris, pupil, lens and anterior vitreous body.

6 Standard gonioscopy is used to confirm glaucoma classification and to evaluate the presence of iris tumors, foreign bodies, anterior synechiae and to predict the anterior chamber angle. The gonioscopic grading system according to Shaffer is used in this clinical investigation.

7 Funduscopy is performed by means of indirect ophthalmoscopy on a slit lamp with the aid of a 90D or "Superfield" or comparable lenses. For this examination the pupil needs to be dilated by the use of mydriatic agents. This method is used to evaluate the following parameters: optic nerve lesions, other posterior pole lesions, vitreous opacities, optic nerve head, fundus lesions, retinal arteries and veins (AV), macular area, fundus periphery, normal and abnormal variations of the fundus.

8 Posterior segment OCT is used to assess macular structures and the peripapillary nerve fiber layer thickness (RNFLT) and if possible Minimum rim width at Bruch membrane opening (BMO-MRW).

9 The fundus should be photographed in order to document potential changes to the optic nerve (cup/disc ratio) and nerve fiber layer (red-free illumination).

10 IOP measurements will be made in series of 2 GAT measurements (in case of a difference of more than 2 mmHg, a third GAT measurement is required) followed by 3 directly consecutive ARGOS-SC system measurements; *if DCT is available:* additionally followed by 2 Pascal DCT measurements (in case of a difference of more than 2 mmHg, a third Pascal DCT measurement is required) and 3 directly consecutive ARGOS-SC system measurements. For the non-study eye, only GAT and DCT measurements will be performed as described above. All measurements should be performed directly one after another.

11 All patients will receive a MESOGRAPH reading device after implantation in order to measure the IOP daily at home. Measurements will be taken at least 4 times per day (morning, noon, afternoon, evening). The MESOGRAPH reading device will be connected to an external GSM module, which will transfer the measured value directly to a secure database. Investigators can log into the database in order to track the pressure levels of their patients as required.

4 Study Objectives and Endpoints

4.1 Study objectives

The purpose of this study is to evaluate the long-term safety and performance of the ARGOS-SC suprachoroidal pressure sensor in patients with glaucoma who underwent non-penetrating glaucoma surgery.

4.1.1 Primary objectives

Performance:
To evaluate the limits of agreement between measurements with the GAT, DCT and the ARGOS-SC system from month 12 throughout month 36 following implantation.

4.1.2 Secondary objectives

Safety:
To evaluate the safety and tolerability of the ARGOS-SC pressure sensor throughout a follow-up period from V09 (month 12) throughout V13 (month 36).

Performance:
To evaluate the performance of the ARGOS-SC system from V09 (month 12) throughout V13 (month 36).

4.2 Study endpoints

4.2.1 Primary endpoint

Performance:
Level of agreement between measurements made using GAT, Pascal DCT and the ARGOS-SC system from V09 (month 12) throughout V13 (month 36).

4.2.2 Secondary endpoints

Safety:
Number of patients experiencing a device-related SAE (SADE) at any from V09 (month 12) throughout V13 (month 36).

Incidence, nature, severity and seriousness of observed adverse events and adverse device events at any time from V09 (month 12) throughout V13 (month 36).

Performance:
Incidence, nature and seriousness of observed device malfunctions during from V09 (month 12) throughout V13 (month 36).

Repeatability of ARGOS-SC measurement

Utility
User acceptance of the ARGOS-SC system at the investigational site by means of evaluation of physician acceptance questionnaires (by investigators)

User acceptance of the ARGOS-SC system at home by means of evaluation of patient acceptance questionnaires (patients)

5 Sample Size and Power

Given by the exploratory nature of this study, the sample size is not driven by the need for a formal statistical hypothesis test with a certain degree of power. Instead, this study is driven by the desire to obtain a clinically meaningful amount of data to evaluate the long-term safety and performance of the ARGOS-SC system in patients who have been already implanted with the study device. Therefore, the maximum sample size is 24. The minimal sample size for this study is at the Sponsor's direction. This is considered to be appropriate since no experimental treatments are planned and all assessments with exception of IOP measurement using the ARGOS-SC device are established standard methods.

6 Analysis Sets

There will be only one analysis set defined in this study:

- Full Analysis Set (FAS):
  The FAS defined according to the intention-to-treat principle will include all patients of the ARGOS-SC01 clinical investigation with an implanted ARGOS-SC pressure sensor and given their informed consent.

7 Statistical Considerations

7.1 Derived variables

The table below provides the list of derived variables applicable for this study.

Variables	Formula
Demographic and baseline characteristics	
Age [years]	Year of baseline visit – year of birth
Derivation of duration	
Study duration [days]	Date of patient's last visit or date of study discontinuation (whatever the later date is) – date of baseline visit + 1

7.2 Handling of missing data

In general, missing data will not be replaced. In tables of categorical data, missing data will be included as 'Missing' and included in the calculation of percentages.

If not otherwise specified and the calculation of periods requires the full date format dd-mm-yyyy, missing start date entries will be set to the first possible day of the month for a missing day and in case of a missing month, the first possible month of a year will be set. Missing stop date entries will be set to the last possible day of the month for a missing day and in case of a missing month, the last possible month of a year will be set.

7.3 Methods for handling dropouts

All patients will be analysed as far as documented.

7.4 Handling of outliers

Since all primary and secondary outcome measures and most of the other variables are based on categorical variables, there is no need regarding a specific handling of outliers.

8 Statistical Methods

8.1 General statistical conventions

8.1.1 Statistical analyses in SAS

All analyses will be conducted descriptively. The tables, graphics and statistical analyses will be performed using the statistical software SAS® 9.4 (TS1M6; or later) for Microsoft Windows.

8.1.2 Statistical outputs

8.1.2.1 Tables and graphics

Percentages will be based on the number of subjects in the analysis set.

Categorical variables will be summarized by the number of patients (n) and percentages (%). Percentages will be rounded to one decimal place.

In addition, for the primary endpoints (response rates) the 95% confidence intervals will be calculated.

Continuous variables will be summarized using descriptive statistics, including

- number of patients with non-missing data (n)
- arithmetic mean (Mean)
- 95% confidence interval of mean (if indicated)
- standard deviation (SD)
- median (Median)
- lower (25%, Q1) and upper (75%, Q3) quartile
- minimum (Min) and maximum (Max).

Analyses by visit will be performed irrespective of any time window deviations.

Some mock-up tables are presented in the appendix of this SAP.

8.1.2.2 Patient data listings

Disposition of patient, concomitant medication, adverse events, device deficiencies, abnormal findings of ophthalmic examination will be presented in individual patient data listings. All listings will be sorted by patient ID and visit (if applicable). Unless otherwise stated, data listings will be based on the FAS.

One mock-up listing is presented in the appendix of this SAP.

8.1.3 Level of significance

All analyses will be conducted descriptively, so that no statistical tests will be performed. All confidence intervals which will be calculated will be two-sided 95% confidence intervals.

8.1.4 Subgroup analyses

The performance of subgroup analyses will be decided at a final data review meeting preceding the statistical analysis, based on the actual distribution of subjects.

8.1.5 Interim analyses

Interim analyses are not planned.

8.2 Disposition of patients

The number and percentage of those who complete the follow-up study will be tabulated. The number and percentage of early withdrawals will also be tabulated, along with the reason for the drop-out. Patient disposition will be listed.

8.3 Demographic and other baseline characteristics

Demographic characteristics (age, sex, educational level), lens status, anti-glaucoma medication, and other previous and concurrent treatments will be tabulated.

Specifications of specific medication will be listed only.

8.4 Treatment

Not applicable

8.5 Primary endpoint

8.5.1 Performance

Level of agreement between measurements made using GAT, Pascal DCT and ARGOS-SC system at visit V09 - V13.

The primary outcome measures of the study eye are:

- Average of 2 – 3 measurements using GAT system at visit V09 – V13
- Average of 2 – 3 measurements using ARGOS-SC system at visit V09 – V13 roughly contemporaneous with the GAT measurements

Descriptive statistics for the GAT and ARGOS-SC measures per visit.

Descriptive statistics for the absolute difference between ARGOS-SC and GAT measures per visit.

The absolute difference between the ARGOS-SC and GAT measures will be scaled in ≤ 5mmHg and > 5 mmHg and the frequency distribution will be displayed.

The concordance of the intraindividual measurement values of GAT and ARGOS-SC will be indicated by the concordance correlation coefficient r_{ccc} (→ see section 11.1), separate for each visit.

The Bland-Altman (mean-difference) plot and a X-Y -plot (Scatter-Plot) should illustrate the comparison of the two methods (→ see section 11.2).

The level of agreement between Pascal DCT and ARGOS-SC will be evaluated analogously.

8.6 Secondary outcome measures

The secondary outcome measures are divided in three areas:

- Safety
- Performance
- Utility

8.6.1 Safety

- Number of patients experiencing a device-related SAE (SADE) from V09 (month 12) to V13 (month 36). This parameter will be analysed using a frequency table.
- Incidence, nature, severity and seriousness of observed adverse events and adverse device events at any time from V09 (month 12) throughout V13 (month 36). This parameter will be analysed using a frequency table.

8.6.2 Performance

- Incidence, nature and seriousness of observed device malfunctions from V09 (month 12) throughout V13 (month 36). This parameter will be analysed using a frequency table.
- The variables
  - Standard deviation of 2 – 3 measurements using GAT system
  - Standard deviation of 2 – 3 measurements using ARGOS-SC system

  at visit V09 – V13 will be analysed descriptively per visit and overall.

8.6.3 Utility

- User acceptance of the ARGOS-SC system at the investigational site by means of evaluation of physician acceptance questionnaires by investigators (18 items) at V09 (month 12) and V13 (month 36). All these parameters will be analysed using a frequency table.
- User acceptance of the ARGOS-SC system at home by means of evaluation of patient acceptance questionnaires by patients (16 items) at V09 (month 12) and V13 (month 36). All these parameters will be analysed using a frequency table.

8.7 Further analyses

- Vision related Quality of Life (VQoL) questionnaire at visit V09, V11 and V13.
- Visual acuity (ETDRS) on both eyes at visit V09 – V13
- Perimetry on both eyes at visit V09 – V13
- The ANTERION® from Heidelberg Engineering performed at V09 – V13
- Anterior eye segment measurement on both eyes at visit V09 – V13:
  - Optical coherence tomography (OCT), Central cornea thickness (CCT)
  - Slit-lamp biomicroscopy (Lids, Conjunctiva, Cornea, Anterior chamber, Iris Pupil, Lens, Anterior vitreous body)
  - Gonioscpoy (angle open to (Shaffer), pigmentation of Trabecular meshwork)
- Posterior eye segment measurement:
  - Biomicroscopy (dilated, fundus) on both eyes at visit V09 – V13
  - Optical coherence tomography (OCT) on both eyes at visit V09 – V13

8.8 Further safety analyses

8.8.1 Adverse events

All safety analyses will be conducted on the FAS set.

The AE terms will be coded according MedDRA into System Organ Class (SOC) and Preferred Terms (PT) of *Implandata Ophthalmic Products*.

Number of adverse events as well as the number and relative frequency of patients reporting adverse events will be tabulated by System Organ Class and Preferred terms.

The incidences of AEs will be stratified by:

- Seriounsness
- Severity
- Relationship to medical device
- Expectedness
- Action taken
- Outcome
- Criterion to classify as serious

The incidence of AEs will be summarized to include only one occurrence of an AE class per patient. If a patient has multiple AEs of the same class, then that term will only be counted once. All AEs will be listed.

8.8.2 Device deficiencies

The parameters

- involved components
- safety and well-being of the patient affected
- consequences of the device deficiency

will be analysed using a frequency table.

Other details regarding the device deficiency will be listed only.

8.8.3 Medication

Coding of concomitant medication by ingredients will be conducted of *Implandata Ophthalmic Products*.

Concomitant medication during the Follow-up Phase (V09 until V13) will be shown as follows:

- Concomitant glaucoma medication of the study eye in total (N,%) and stratified by ingredients (N,%)
- Concomitant glaucoma medication other than study eye in total (N,%) and stratified by ingredients (N,%)
- Concomitant medication other indication than glaucoma in total (N,%) and stratified by ingredients (N,%)

The details regarding application forms, dosages, specified medications will be listed only.

9 Changes to Planned Analysis from Study Protocol

ARGOS-SC self-measurements were not recorded

Interim analyses are not performed according Note to File of 29.08.2022

10 References

1. ICH Topic E3: Structure and Content of Clinical Study Reports (CPMP/ICH/137/95 – July 1996).
2. ICH Topic E9: Statistical Principles for Clinical Trials (CPMP/ICH/363/96 – September 1998).
3. ARGOS-SC01_Follow-up (Clinical Investigation Plan), Rev. C, 27.05.2021.
4. Lawrence I-Kuei Lin (March 1989). "A concordance correlation coefficient to evaluate reproducibility". Biometrics. 45 (1): 255–268

11 Appendix

11.1 Concordance correlation coefficient

Concordance correlation coefficient (r_{ccc}) measures the agreement between two variables X and Y. Lawrence Lin has defined the form of the concordance correlation r_{ccc} as[4]

$$r_{ccc} = 2\, r\, s_x\, s_y \,/\, ((s_x^2 + s_y^2) + (m_x - m_y)^2)$$

with

$r = s_{xy}/(s_x\, s_y)$ (Pearson correlation coefficient)
m_x = mean of X
m_y = mean of Y
s_x = standard deviation of X
s_y = standard deviation of Y
s_{xy} = covariance of x and Y

The concordance correlation r_{ccc} has an range of -1 to 1. Values near +1 indicate strong concordance between *x* and y, values near -1 indicate strong discordance and values near zero indicate no concordance. There is no clear-cut agreement as to how to interpret the values, although one approach is to interpret Lin's r_{ccc} as for Pearson's correlation coefficient (e.g. values less than .20 are poor, while values greater than .80 are excellent).

11.2 Bland-Altman Plot

Bland and Altman introduced the Bland-Altman plot to describe agreement between two quantitative measurements by constructing limits of agreement. These statistical limits are calculated by using the mean and the standard deviation (s) of the differences between two measurements. To check the assumptions of normality of differences and other characteristics, they used a graphical approach.

The resulting graph is a scatter plot XY, in which the Y axis shows the difference between the two paired measurements (x-y) and the X axis represents the average of these measures ((x+y)/2). In other words, the difference of the two paired measurements is plotted against the mean of the two measurements. Bland-Altman recommended that 95% of the data points should lie within ± 2s of the mean difference. This is the most common way to plot the Bland-Altman method.

The bias is computed as the value determined by one method minus the value determined by the other method. If one method is sometimes higher, and sometimes the other method is higher, the average of the differences will be close to zero. If it is not close to zero, this indicates that the two assay methods are systematically producing different results.

11.3 Statistical Analysis Package – Table of Contents

11.3.1 Tables

11.3.2 Figures

11.3.3 Listings

11.4 Statistical Analysis Package – Mock-up outputs (examples)

11.4.1 Tables

Table 1.2: Baseline characteristics

Table 1.2: Baseline characteristics		
Age [years]	N	n
	Minimum	xx.x
	Q1	xx.x
	Median	xx.x
	Q3	xx.x
	Maximum	xx.x
	Mean	xx.x
	Standard dev.	xx.x
	Mean [95% CI]	xx.x | x.xx
Gender	N	n
	male	xx (xx.x%)
	female	xx (xx.x%)
Race	N	n
	Asian	xx (xx.x%)
	African	xx (xx.x%)
	Hispanic	xx (xx.x%)
	Caucasian	xx (xx.x%)
Please record the highest educational level the patient has completed	N	n
	Primary	xx (xx.x%)
	Intermediate	xx (xx.x%)
	A level	xx (xx.x%)
	University	xx (xx.x%)
	Vocational	xx (xx.x%)
	Other	xx (xx.x%)

Table 1.2: Baseline characteristics		
Duration of glaucoma [years]	N	n
	Minimum	xx.x
	Q1	xx.x
	Median	xx.x
	Q3	xx.x
	Maximum	xx.x
	Mean	xx.x
	Standard dev.	xx.x
	Mean [95% CI]	xx.x | x.xx
Type of glaucoma	N	n
	POAG	xx (xx.x%)
	NTG	xx (xx.x%)
	OHT/Glaucoma suspect	xx (xx.x%)
	PEX	xx (xx.x%)
	Other	xx (xx.x%)
Study eye	N	n
	left	xx (xx.x%)
	right	xx (xx.x%)

Table 2.1.1: IOP measures: GAT and ARGOS-SC

Table 2.1.1: IOP measures: GAT and ARGOS-SC						
		Visit V09	**Visit V10**	**Visit V11**	**Visit V12**	**Visit V13**
GAT [mmHg]	N	n	n	n	n	n
	Mean	x.xx	x.xx	x.xx	x.xx	x.xx
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Q1	x.xx	x.xx	x.xx	x.xx	x.xx
	Median	x.xx	x.xx	x.xx	x.xx	x.xx
	Q3	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	x.xx	x.xx	x.xx	x.xx	x.xx
	Maximum	x.xx	x.xx	x.xx	x.xx	x.xx
	95%-CI LL	x.xx	x.xx	x.xx	x.xx	x.xx
	95%-CI UL	x.xx	x.xx	x.xx	x.xx	x.xx
ARGOS-SC [mmHg]	N	n	n	n	n	n
	Mean	x.xx	x.xx	x.xx	x.xx	x.xx
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Q1	x.xx	x.xx	x.xx	x.xx	x.xx
	Median	x.xx	x.xx	x.xx	x.xx	x.xx
	Q3	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	x.xx	x.xx	x.xx	x.xx	x.xx
	Maximum	x.xx	x.xx	x.xx	x.xx	x.xx
	95%-CI LL	x.xx	x.xx	x.xx	x.xx	x.xx
	95%-CI UL	x.xx	x.xx	x.xx	x.xx	x.xx

Table 2.1.1: IOP measures: GAT and ARGOS-SC						
		Visit V09	**Visit V10**	**Visit V11**	**Visit V12**	**Visit V13**
Difference ARGOS-SC - GAT [mmHg]	N	n	n	n	n	n
	Mean	x.xx	x.xx	x.xx	x.xx	x.xx
	SD	x.xx	x.xx	x.xx	x.xx	x.xx
	Q1	x.xx	x.xx	x.xx	x.xx	x.xx
	Median	x.xx	x.xx	x.xx	x.xx	x.xx
	Q3	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	x.xx	x.xx	x.xx	x.xx	x.xx
	Maximum	x.xx	x.xx	x.xx	x.xx	x.xx
	95%-CI LL	x.xx	x.xx	x.xx	x.xx	x.xx
	95%-CI UL	x.xx	x.xx	x.xx	x.xx	x.xx
Difference	N	n	n	n	n	n
	≤ 5 mmHg	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	> 5 mmHg	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pearson Correlation		x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
r_{ccc}		x.xxx	x.xxx	x.xxx	x.xxx	x.xxx

Table 3.1.1: Adverse Events

Table 3.1.1: Adverse events				
SOC	**PT**	**No. of AEs**	**No. of patients**	**%**
Gastrointestinal disorders	Nausea	xx	xx	xx.x
	Diarrhoe	xx	xx	xx.x
	Total (SOC)	xx	xx	xx.x
Nervous system disorders		xx	xx	xx.x
		xx	xx	xx.x
	Total (SOC)	xx	xx	xx.x
	Total	xx	xx	xx.x

Table 3.2.1: Characteristics of Adverse Events

Table 3.2.1: Characteristics of Adverse Events																													
									Relationship with …																				
		Expected-ness		SAE		Severity			Medical Device				Medical Procedure				Other				Action taken			Outcome				
SOC / PT	N	No	Yes	No	Yes	1	2	3	0	2	3	4	0	2	3	4	0	2	3	4	1	2	3	1	2	3	4	5
Gastrointestinal disorders	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
- Nausea	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
- Diarrhoe	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Nervous system disorders	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
-	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
-	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Total	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx

Severity: 1=mild, 2=moderate, 3=severe

Relationship: 0=none, 2=possible, 3=probable, 4=causal relationship

Action taken: 1=ARGOS-SC Sensor removed, 2=subject withdrawn from study, 3=other

Outcome: 1=recovered, 2=recovered with sequeleae, 3=recovering, 4=not recovered, 5=death

11.4.2 Listing

Listing 6: Adverse Events

Listing 6: Adverse Events										
Pat-ID	**AE no**	**AE Description**	**Preferred Term**	**Study eye affected**	**Onset date**	**End date**	**SAE**	**Expected event**	**Severity**	**Outcome**
DE-SC01-1-01	1	R/L Keratokonjunktivitis		X	29/11/2018	21/12/2018	no	no	mild	recovered
	2	Chemosis		X	27/11/2018	21/12/2018	no	yes	mild	recovered
DE-SC01-1-02	1	Pain in study eye after surgery		X	16/01/2019	16/01/2019	no	yes	mild	recovered
	2	Tooth removal			13/08/2019	13/08/2019	no	yes	mild	recovered