

**Evaluation of Long-Term Safety and Performance of
AcrySof PanOptix Trifocal and PanOptix
Toric Trifocal IOLs**

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Evaluation of Long-Term Safety and Performance of AcrySof PanOptix Trifocal and PanOptix Toric Trifocal IOLs

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Researchers are conducting this study in compliance with good clinical practice, including archiving of essential documentation.



Statistical Analysis Plan - Approval

Evaluation of Long-Term Safety and Performance of AcrySof PanOptix Trifocal and PanOptix Toric Trifocal IOLs

Protocol:

Number: ILH297-I001

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EXECUTIVE SUMMARY

The purpose of this Post-Market Clinical Follow-up (PMCF) study is to describe the long-term safety and performance of the AcrySof Panoptix and AcrySof Panoptix Toric Intraocular Lens (IOL) models in subjects bilaterally implanted with these IOLs for 3 to 5 years (+/- 90 days). In addition, it will ensure the continued acceptability of the benefit-risk ratio and to identify possible systematic misuse or off-label use of the device.

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Abbreviations

Abbreviation	Definition
ACD	Anterior Chamber Depth
ADE	Adverse Device Effect
AE	Adverse Event
BAS	Best Case Analysis Set
BCDVA	Best Corrected Distance Visual Acuity
CI	Confidence Interval
CME	Cystoid Macular Edema
CRF	Case Report Form
D	Diopter
DCIVA	Distance corrected intermediate visual acuity
DCNVA	Distance corrected near visual acuity
DFE	Dilated Fundus Examination
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ETDRS	Early Treatment Diabetic Retinopathy Study
FAS	Full Analysis Set
HIV	Human Immunodeficiency Virus
ICF	Informed consent form
IEC	Independent Ethics Committee
IOL	Intraocular Lens
IOP	Intraocular Pressure
IRB	Institutional Review Board
ISO	International Organization for Standardization
logMAR	Logarithm of the minimum angle of resolution
m	Meter
Max	Maximum
Min	Minimum
mm	Millimeter
mmHg	Millimeters of Mercury
MedDRA	Medical Dictionary for Regulatory Activities
MRSE	Manifest Refraction Spherical Equivalent
NA	Not Applicable
N	Number
OD	Oculus Dexter (right eye)
OS	Oculus Sinister (left eye)
PCO	Posterior Capsule Opacification
PMCF	Post-Market Clinical Follow-Up
PT	Preferred Term
PRRE	Predicted Residual Refractive Error
Q	Question
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SD	Standard Deviation
SOC	System Organ Class
SOP	Standard Operating Procedures
SSI	Secondary Surgical Intervention
UCDVA	Uncorrected distance visual acuity
UCIVA	Uncorrected intermediate visual acuity
UCNVA	Uncorrected near visual acuity
VA	Visual Acuity
YAG	Yttrium Aluminium Garnet

1 STUDY OBJECTIVES AND DESIGN

The study objectives are as follows.

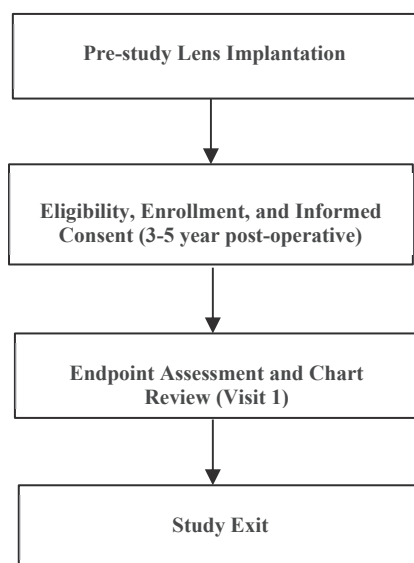
1.1 STUDY OBJECTIVES

The purpose of this Post-Market Clinical Follow-up (PMCF) study is to describe the long-term safety and performance of the AcrySof Panoptix and AcrySof Panoptix Toric IOL models in subjects bilaterally implanted with these IOLs for 3 to 5 years (\pm 90 days). In addition, it will ensure the continued acceptability of the benefit-risk ratio and to identify possible systematic misuse or off-label use of the device.

1.2 STUDY DESCRIPTION

This will be a multicenter, ambispective study with a retrospective chart review for preoperative, operative, and postoperative data, and a prospective visit to collect key long-term safety and performance endpoints in a sample of subjects commercially implanted with the subject devices in the real world. The overall study design is shown in the figure below.

Figure 1. Overall Study Design



The study population consists of adult subjects (18 years or older) who have been bilaterally implanted with the study IOL models (see Section 3) for 3 to 5 years (\pm 90 days). To fulfill the requirements of post-market clinical follow-up, only subjects implanted with the target IOLs will be recruited. Subjects will be recruited from clinical sites in the European Union (English and Spanish speaking countries only). The inclusion and exclusion criteria of this study are less strict to allow the inclusion of a real-world sample per the indication, including patients that have undergone either cataract surgery or refractive lens exchange.

The study will recruit a total of 210 subjects for both AcrySof PanOptix IOL models to obtain 200 evaluable subjects (100 evaluable subjects in each family of implants, described in section 9). Retrospective data will be collected from the preoperative and surgical visits and any safety outcomes reported prior to enrollment. Prospective data will be collected at study enrollment 3 to 5 years (+/- 90 days) after IOL implantation.

Table 1. Study Devices

Model Name	Model Numbers	Indications for Use Statements
AcrySof IQ PanOptix IOL	TFNT00	The AcrySof IQ PanOptix IOL is intended for primary implantation in the capsular bag in the posterior chamber for the visual correction of aphakia secondary to removal of a cataractous lens or clear lens in adult patients with and without presbyopia, who desire near, intermediate and distance vision with increased spectacle independence.
AcrySof IQ PanOptix Toric IOL	TFNT20 TFNT30 TFNT40 TFNT50 TFNT60	The AcrySof IQ PanOptix® Toric Trifocal IOL is intended for primary implantation in the capsular bag in the posterior chamber of the human eye for the visual correction of aphakia and pre-existing corneal astigmatism secondary to removal of a cataractous lens or clear lens in adult patients with and without presbyopia, who desire near, intermediate and distance vision with increased spectacle independence.

1.3 INCLUSION AND EXCLUSION CRITERIA

1.3.1 Inclusion Criteria

Subjects will be eligible to participate in the study if **all** of the following conditions exist:

1. Subjects must be 18 years old or older.
2. Subject or legally authorized representative must be able to understand and sign an IRB/IEC approved informed consent form (ICF).
3. Subject must have had bilateral implantation of AcrySof PanOptix or AcrySof PanOptix Toric models for 3 years to 5 years prior to enrolment, including implantation up to 90 days before the 3-year timepoint and up to 90 days after the 5-year timepoint. A subject may have a Toric lens in one eye and a non-Toric in the fellow eye.
4. Subject must have a documented medical history and required preoperative and operative information available for retrospective data collection.

1.3.2 Exclusion Criteria

Subjects will be excluded from participation in the study if any of the following conditions exist:

1. Subject is currently participating in another investigational drug or device study.
2. Subject has had corneal refractive surgery after of AcrySof PanOptix or AcrySof PanOptix Toric IOL implantation.
3. Subject exposed to a study IOL for a minimum of 3 years (-90 days) prior to Visit 1 that have subsequently undergone an IOL exchange and are no longer implanted with a study IOL at the time of enrollment.
4. Subject is pregnant or nursing at the time of enrollment.
5. Childbirth after IOL implantation.
6. Subject's retrospective data were not properly documented

1.3.3 Exit/Discontinuation Criteria

Subjects will exit the study if **any** of the following conditions exist:

1. Subject voluntarily withdraws from the study.
2. Subject death.
3. Subject completes the protocol.
4. Subject is non-compliant with the protocol
5. Subject's well-being, in the opinion of the Investigator, would be compromised by study continuation.

1.4 RANDOMIZATION

Not applicable.

1.5 MASKING

This is an open-label study.

1.6 INTERIM ANALYSIS

There are no interim analyses planned for this study.

1.7 FINAL ANALYSIS

Database lock will occur no later than 5 weeks following the last subject enrolled (targeting a number of 200 enrolled subjects). A detailed description of the planned final effectiveness and safety analyses are in Section 5 and Section 6, respectively.

2 ANALYSIS SETS

2.1 SUBJECT POPULATION(S) FOR ANALYSIS

Subject populations for analysis include:

The FAS population will be the primary population for all safety analyses and effectiveness analyses include all eyes of enrolled subjects who pass the screening criteria and had non-key ICF PDs noted in the PDCF.

3 ANALYSIS STRATEGY

3.1 STUDY SUMMARIES FOR TABLES AND LISTINGS

All summary statistics will be based on the type of variable. For categorical variables (e.g., sex, race), the number and percentage of eyes within each category of interest will be presented. For continuous variables (e.g., age, VA), number of subjects with non-missing data, mean, median, standard deviation, minimum and maximum, and two-sided 95% confidence interval (CI) for the mean, when applicable, will be reported. Tables will be presented by subjects or eyes as applicable. All data listings will include the following subject characteristics: age and sex. Age, race, ethnicity, and sex are required fields; as such, there should be no missing data for these variables across tables and listings, when presented.

3.2 PRESENTATION OF TABLES AND LISTINGS

In general, tables will be stratified by model (toric and non-toric). Subjects implanted with a toric lens in one eye and a non-toric in the other will be assigned as toric in the subject level tables. Eye-

level tables will be further stratified by first eye and second eye (if applicable), separately, and by all eyes. For subjects bilaterally implanted on the same day, OD is assigned as first eye, and OS is assigned as second eye.

Listings will be organized by lens model and will be sorted by 1/ IOL type (toric/non-toric), 2/ model number, and 3/subject ID. In tables where visit data are presented, only scheduled visits are included.

4 SUBJECT CHARACTERISTICS AND STUDY CONDUCT SAMPLES

Subject characteristics and study conduct summaries include tables and/or listings such as a subject disposition table, demographics, baseline characteristics tables (including age, sex, race, ethnicity, keratometry, biometry), summary of subjects by site, and a listing of screen failures by reason. Retrospectively collected preoperative baseline characteristics will include surgical report data, such as lens power and IOL calculation method, biometry (axial length, Anterior Chamber Depth [ACD], as well as white-to-white and lens thickness if available), keratometry (corneal cylinder [K2(D) – K1(D)]), and preoperative manifest refraction spherical equivalent (MRSE) and preoperative predicted residual refractive error (PRRE) (cylinder and spherical equivalent). Further details are provided in the section below.

Unless otherwise stated, the analysis population for analyses in Section 4 is the FAS, as defined in Section 2.1.

4.1 SUBJECT DISPOSITION

A subject disposition table that displays the number of all enrolled subjects, the number of subjects who completed the study, the number of subjects discontinued, and premature study discontinuation reasons for each subject, including screen failures, who discontinued the study will be presented. Two additional tables will be output – one table that displays the number and percentage of subjects enrolled and their completion status (e.g., completed, discontinued) by site and one table that displays the number and percentage of enrolled eyes for each study device and model number by first eye, second eye (if applicable), and all eyes.

A listing of screen failures will be provided and will include subject ID, age, sex, lens model, and inclusion/exclusion criteria for subjects that failed. A listing of patients who discontinue or end the study treatment prematurely will also be output and includes subject ID, age, sex, study device, lens model (lens model OD/lens model OS), discontinuation date, discontinuation reason, and if other reason, specify. Lastly, protocol deviations will be presented in a listing and will include subject ID, age, sex, study device, lens model, deviation date, deviation severity (key/non-key), deviation type and sub-type (e.g., procedures and tests, ICF issues, inclusion/exclusion), protocol deviation comment, action taken, and whether the PD resulted in exclusion from the FAS.

4.2 DEMOGRAPHIC AND BACKGROUND CHARACTERISTICS

The demographic and background characteristics listed below will be summarized by the number and percentage of subjects for categorical variables and descriptive statistics for continuous variables (n, mean, standard deviation, median, minimum and maximum). Surgical report data will be presented in a separate table for all eyes by toricity.

Demographics at Visit 1 (subject-level)

Categorical variables

- Age (<65 years, ≥65 years)
- Sex (Female, Male, Unknown, Undifferentiated)
- Race (per CRF, plus “Multiple” if a patient has more than one race identified in the CRF)
- Ethnicity (per CRF)

Continuous variable

- Age (years)

Surgical Report (eye-level)

- Lens power (as a continuous variable, reporting only n, median, min, and max)
- Whether surgical reason was due to refractive lens exchange
- Preoperative IOL calculation method (per CRF)
- Toric IOL calculation method (for toric IOLs only) (per CRF)
- Other surgical procedures during cataract or refractive lens exchange surgery (if applicable)

4.3 MEDICAL HISTORY AND CONCOMITANT MEDICATIONS

A targeted medical history (within 30 days prior to the date of surgery) will be collected for each patient in the study and includes the following: Diabetes, Hypertension, HIV Infection, Multiple Sclerosis, Rheumatoid Arthritis, Sjogren’s Syndrome, Atherosclerosis, Autoimmune disorder, Grave’s disease, Sarcoidosis, Sickle cell disease, and Ocular (specify). The number and percentage of patients with at least one medical condition and within each of the systemic medical histories will be reported in a table by toricity.

Two medical history and concomitant medication listings will be provided for all subjects/eyes. Both listings will include subject, study device, lens model (lens model OD/lens model OS), and the concomitant medication used to treat the medical history condition, when applicable. The systemic medical history listing will also include the targeted systemic medical history term (per the CRF). The ocular medical history listing will also include the ocular medical history term and the affected eye.

4.4 PREGNANCY

Women of childbearing potential are not excluded from participation. Women who gave birth after IOL implantation or who are pregnant or nursing at the time of enrollment are excluded from participation.

4.5 RETROSPECTIVE DATA

If available, retrospective data will be collected regarding the preoperative, operative, and immediate postoperative activities, and will be presented in tables, as described below.

4.5.1 Preoperative Biometry and Keratometry

Preoperative data that includes biometry and keratometry will be extracted from the chart review and presented separately for first implanted eye and second implanted eye (if applicable) and for all eyes by toricity. One table will include both biometry and keratometry data. Biometry data in the table includes axial length, ACD, lens thickness (if available), and white-to-white (if available); keratometry data in the table includes corneal cylinder [K2 (D) – K1 (D)].

Corneal curvatures (K1 and K2) reported in mm should be converted to diopter using the following equation.

Corneal curvature (diopter) = $337.5 \div \text{corneal curvature in (mm)}$

4.5.2 Preoperative Manifest Refraction and PRRE

Preoperative MRSE (defined as the sum of the sphere with half of the cylinder, reported value without taking the absolute value) and PRRE spherical equivalent will be summarized descriptively as a continuous variable (n, mean, median, standard deviation, minimum and maximum, and two-sided 95% CI for the mean) by toricity separately for first implanted eye and second implanted eye (if applicable) and for all eyes. For toric lenses, PRRE cylinder and axis will also be reported. PRRE cylinder should be converted to absolute values to allow for accurate analysis of plus and minus cylinder input from the CRF. Signs should be maintained for MRSE and PRRE.

5 EFFECTIVENESS ANALYSIS STRATEGY

EFFECTIVENESS ENDPOINTS

5.1.1 Primary Effectiveness Endpoint

The primary effectiveness endpoint is measured using the mean Binocular BCDVA (at 4 m) at Visit 1 (3-5 years postoperative, +/- 90 days).

5.2 EFFECTIVENESS HYPOTHESES

No hypothesis testing is planned.

5.3 STATISTICAL METHODS FOR EFFECTIVENESS ANALYSIS

Except otherwise stated, the analysis set for all effectiveness analyses is the FAS as defined in Section 2.1. In the event there is a 10% exclusion in subjects when comparing the FAS and BAS populations, effectiveness analysis tables will be presented for both the FAS and BAS, if requested.

Performance outcome measures will be stratified by the subgroups defined in section 10.4.

5.3.1 Primary Effectiveness Analysis

5.3.1.1 *Mean Binocular Best Corrected Distance Visual Acuity (BCDVA)*

Mean binocular BCDVA is performed for distance visual acuity (VA) at the retrospective postoperative visit (1 to 6 months) and at prospective Visit 1 using ETDRS charts validated for testing at 4 m for logarithm of the minimum angle of resolution (LogMAR) chart. The primary effectiveness endpoint, binocular BCDVA, will be summarized descriptively as a continuous variable (n, mean, median, standard deviation, minimum and maximum, and two-sided 95% CI for the mean) prospectively at Visit 1. The number and percentage of subjects in each of the following visual acuity categories will also be presented in the table:

Snellen categories:

- 20/20 or better (≤ 0.04 LogMAR)
- 20/25 or better (≤ 0.14 LogMAR)

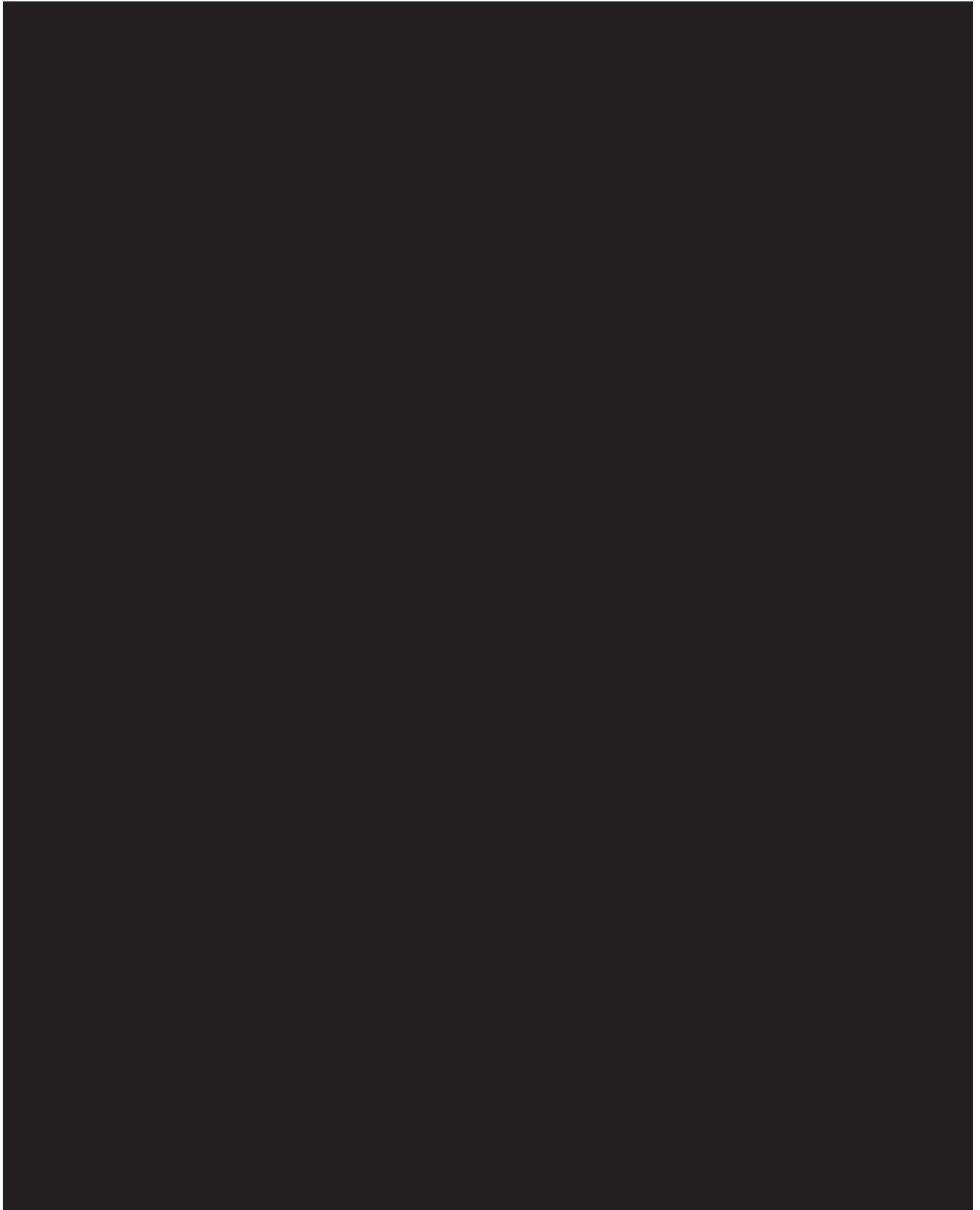
- 20/32 or better (≤ 0.24 LogMAR)
- 20/40 or better (≤ 0.34 LogMAR)
- Worse than 20/40 (> 0.34 LogMAR)

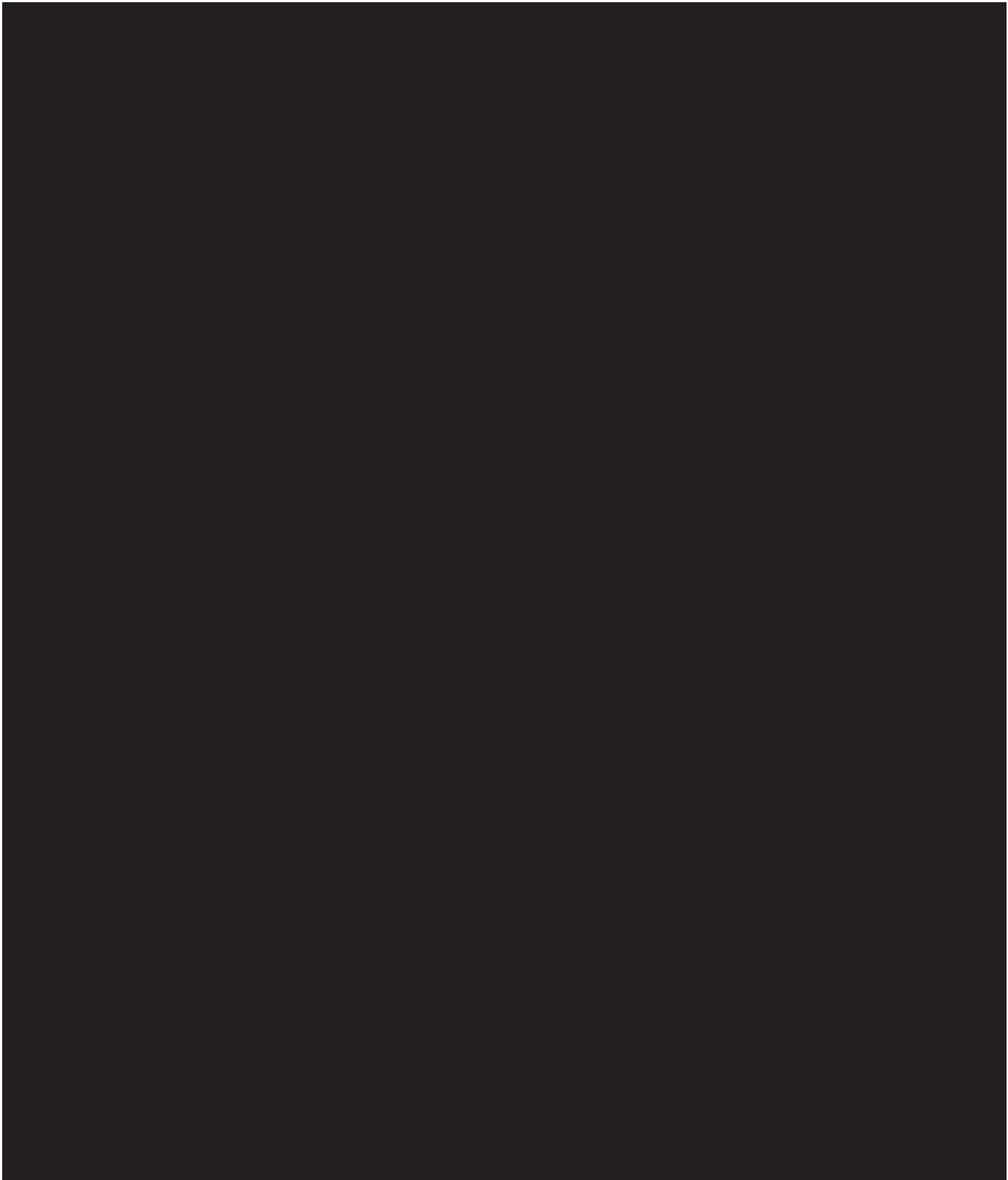
The table will also be output for the retrospective postoperative visit (1 to 6 months post-op).

A listing for binocular BCDVA for patients with a 0.20 LogMAR or higher/worse will be output and includes the following variables: subject, age, sex, study device, lens model (OD/OS), visit, days from surgery, whether surgery was done due to refractive lens exchange (OD and OS, separately), BCDVA (converted to LogMAR), and Snellen Category. All visits for patients meeting the criteria will be included in listing to provide a comprehensive picture of the subject's visual acuity over the duration of the study. Snellen categories for the listing will be as follows:

- ≤ -0.14 LogMAR = "Better than 20/16"
- < -0.14 to -0.04 LogMAR = "~20/16"
- < -0.04 to 0.04 LogMAR = "~20/20"
- < 0.04 to 0.14 LogMAR = "~20/25"
- < 0.14 to 0.24 LogMAR = "~20/32"
- < 0.24 to 0.34 LogMAR = "~20/40"
- < 0.34 to 0.44 LogMAR = "~20/50"
- < 0.44 to 0.51 LogMAR = "~20/60"
- < 0.51 to 0.57 LogMAR = "~20/70"
- < 0.57 to 0.65 LogMAR = "~20/80"
- < 0.65 to 0.74 LogMAR = "~20/100"
- < 0.74 to 0.80 LogMAR = "~20/120"
- < 0.80 to 0.85 LogMAR = "~20/130"
- < 0.85 to 0.90 LogMAR = "~20/150"
- < 0.90 to 0.96 LogMAR = "~20/170"
- < 0.96 to 1.05 LogMAR = "~20/200"
- < 1.05 to 1.14 LogMAR = "~20/250"
- < 1.14 to 1.24 LogMAR = "~20/300"
- < 1.24 to 1.35 LogMAR = "~20/400"
- < 1.35 to 1.46 LogMAR = "~20/500"
- < 1.46 to 1.56 LogMAR = "~20/650"
- < 1.56 to 1.65 LogMAR = "~20/800"
- < 1.65 to 1.75 LogMAR = "~20/1000"
- < 1.75 to 1.85 LogMAR = "~20/1250"
- < 1.85 to 1.95 LogMAR = "~20/1600"
- < 1.95 to 2.05 LogMAR = "~20/2000"
- > 2.05 LogMAR = "Worse than 20/2000"









6.2 SAFETY HYPOTHESES

There are no formal safety hypotheses in this study.

6.3 STATISTICAL METHODS FOR SAFETY ANALYSIS

The focus of the safety analysis will be to conduct a comprehensive descriptive assessment of AEs and other listed parameters in the safety analysis set and provide listings if necessary. Except otherwise stated, the analysis set for all safety analyses is the FAS as defined in Section 2.1. For this study, AEs from time of exposure to the study model IOL to the prospective study visit are considered.

All safety outcome measures will be stratified by the subgroups defined in section 10.4.

While imputation is not defined for this study, adverse events with partial AE dates will be considered for analysis if the AE occurs within the same month of implantation or if the AE can be determined as occurring after implantation using the partial date.

6.3.1 Primary Safety Endpoints

6.3.1.1 *Adverse Events Including Secondary Surgical Interventions*

Adverse Events

The following summary tables and listings will be provided:

1. All Adverse Events (for summary tables and tables by PT (ocular) or SOC/PT (non-ocular))
 - a. Ocular by Toricity (eye-level)
 - b. Non-ocular by Toricity (subject-level)
2. All Adverse Device Effects (tables by PT (ocular) or SOC/PT (non-ocular))
 - a. Ocular by Toricity (eye-level)
 - b. Non-ocular by Toricity (subject-level)
3. All Serious Adverse Events (including Serious Adverse Device Effects (SADEs)) (tables by PT (ocular) or SOC/PT (non-ocular))
 - a. Ocular by Toricity (eye-level)
 - b. Non-ocular by Toricity (subject-level)

4. Listing of all Adverse Events (listings by PT (ocular) or SOC/PT (non-ocular))
 - a. Non-serious Ocular (eye-level)
 - b. Non-serious Non-Ocular (subject-level)
 - c. Serious Ocular (eye-level)
 - d. Serious Non-ocular (subject-level)

Summary tables, by eye and event for ocular AEs and by subject for non-ocular AEs, will be output. For ocular AEs, the table will report the number of eyes experiencing an AE and the number of adverse events for all eyes by toricity and for non-ocular AEs, the table will include the number and percentage of subjects experiencing at least one AE by toricity. Both tables will include the number and percent of AEs related to study devices and/or procedures, and the seriousness criteria for serious AEs (per the CRF). For ocular AE summary tables, the AE event outcome and action taken due to the adverse event will also be reported.

In addition, the number and percentage of all AEs will be tabulated by Preferred Term (PT) for ocular AEs and by System Organ Class (SOC) and Preferred Term (PT) for non-ocular AEs using the Medical Dictionary for Regulatory Activities (MedDRA) dictionary (Version 26.1) for all subjects. If a subject has multiple AEs with the same PT, the PT will only be counted once per subject; similarly for subjects with multiple AEs per SOC, the SOC will only be counted once per subject. AEs will be sorted alphabetically by SOC and then by decreasing total frequency by PT.

Listings of AEs will include subject, age, sex, study device, lens model, implanted eye (first eye, second eye), eye (OD/OS), days from surgery, the MedDRA SOC and PT (for non-ocular listings) or PT (for ocular listings) for the AE, AE description, action taken, severity, causality, duration, and outcome, when available. Surgery eye will only be provided in listings of ocular AE. AEs related to the IOL are referred to as adverse device effects (ADE).

Pregnancy is not reportable as an AE; however, complications may be reportable and will be decided on a case-by-case basis.


Secondary Surgical Interventions (SSIs)

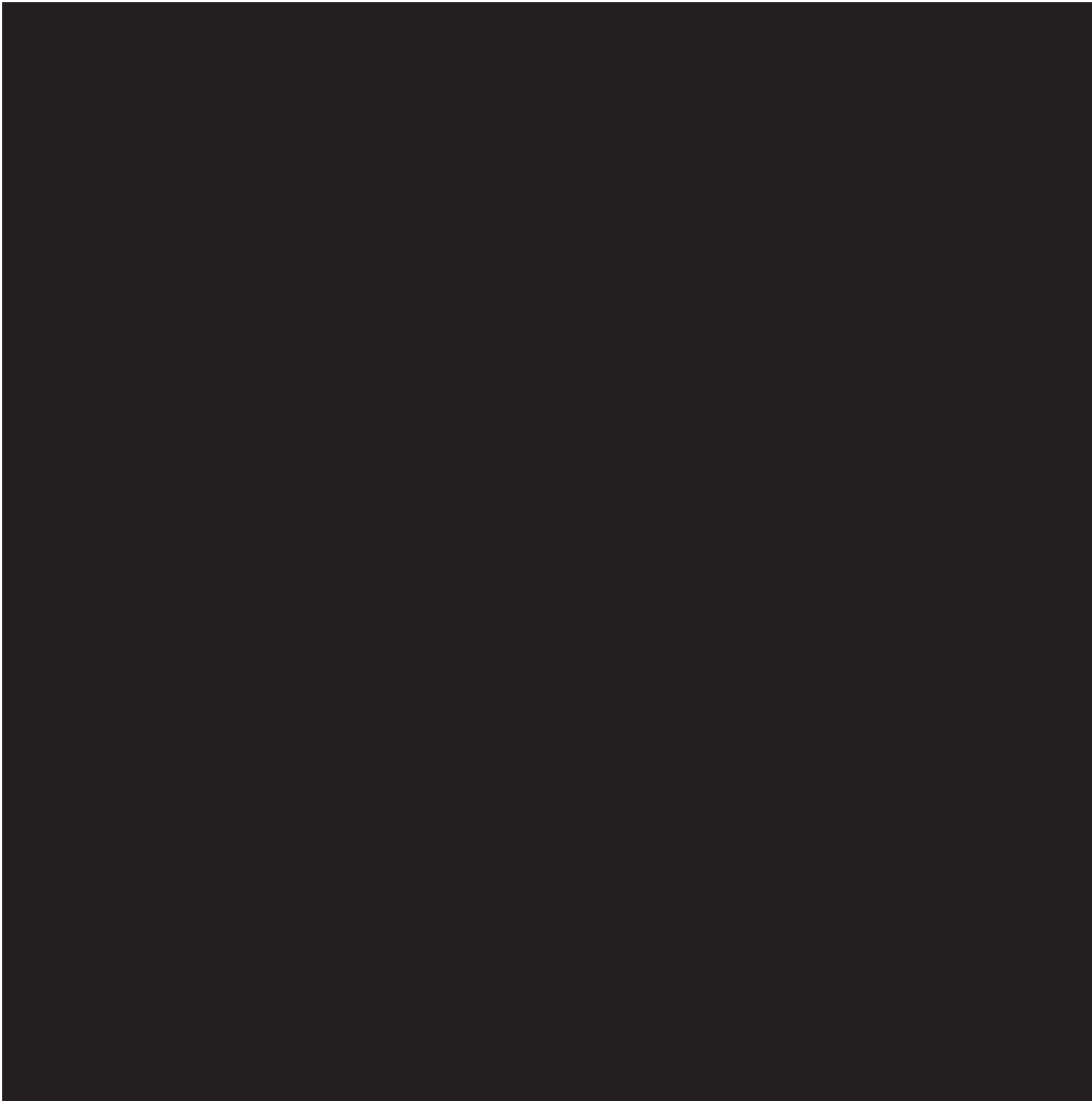
The number and percentage of eyes with secondary surgical interventions (SSIs), secondary surgical intervention type (exchange, removal, reposition), and secondary surgical intervention relationship (related to IOL, unrelated to IOL) will be presented separately for first implanted eye and second implanted eye (if applicable) and for all eyes by toricity.

6.3.1.2 Device Deficiencies

The number and percentage of eyes with a device deficiency, each device deficiency description category (per CRF), and whether the device deficiency could have led to a serious adverse event will be reported separately for first implanted eye and second implanted eye (if applicable) and for all eyes by toricity. A device deficiencies listing will also be provided and includes the variables subject, age, sex, implanted eye (first eye, second eye), eye (OD/OS), study device, lens model,

days from surgery, the description of the deficiency, the circumstances that led to the device deficiency, whether the deficiency could have led to a SADE, and the medical term for the SADE.





7 INTERIM ANALYSIS STRATEGY

There are no interim analyses planned for this study.

8 FINAL ANALYSIS STRATEGY

The endpoint of interest is 3 to 5 years (+/- 90 days) post implantation. After all subjects complete their follow-up visit, the study database will be locked to conduct final analyses. A full set of output will be generated for review.

9 SAMPLE SIZE AND POWER CALCULATIONS

The study will recruit a total of 210 subjects for both AcrySof PanOptix IOL models to obtain 200 evaluable subjects (n=100 non-toric and n=100 toric). A minimum of 100 subjects bilaterally implanted with AcrySof PanOptix non-Toric should be evaluable. In addition, a minimum of 100 subjects with at least one eye implanted with AcrySof PanOptix Toric should be evaluable. Alcon will attempt to enroll all variants in the AcrySof PanOptix Toric family. ISO 22979 and ISO 11979-7 recommend a sample size of n=100 for IOLs where safety and performance risks can be adequately addressed with the sample size required of a Level B clinical investigation. Therefore, a target enrollment of up to 105 (enrolled) to achieve a goal of 100 evaluable subjects for both AcrySof PanOptix toric and non-toric models is justified by ISO standards for IOLs. Based on a pooled standard deviation of 0.07 logMAR and a t-distributed error, a sample size of 100 subjects gives an expected half width of a 95% confidence interval of 0.014 logMAR. Thus, it can be expected with 95% confidence that the estimated mean binocular BCDVA will be within 0.014 logMAR (< 1 letter on a logMAR visual acuity chart) of the true mean with a sample size of at least 100 subjects and a standard deviation of 0.07 logMAR. Descriptive results from this long-term RWE study are sufficient to provide a comparison to shorter term follow-up data of these models, and SotA safety and performance thresholds. Performance and safety outcome measures will be stratified by models (toric and non-toric).

Table 2. Subject Sample Distributions

AcrySof PanOptix Family Implants	
Toric	100
Non-Toric	100

10 STATISTICAL METHODS

10.1 STATISTICAL RULES

Appropriate descriptive statistics will be computed and presented for all categorical and continuous endpoints. For categorical variables, the number and percentage of subjects/eyes within each category of interest will be presented. The percentages will be calculated based on the respective analysis set or the number of non-missing observations (i.e., the number of patients/eyes assessed) in the respective analysis set where applicable. For categorical variables with at least one missing observation, a category of 'missing' will be added to document the number of missing

observations. If there is no missing observation, a category of ‘missing’ may not be added. Percentages will be rounded to one decimal place.

For continuous variables, the number of subjects/eyes with non-missing data, mean, standard deviation, median, minimum and maximum, and 95% CI of the mean, when applicable, will be calculated. There will be no imputation for missing data. Means and medians will be rounded to one decimal more than that with which the original data are recorded. The standard deviation will be rounded to two decimals more than the original data. Minimum and maximum values will be reported with the same number of decimals with which the original data are recorded.

Theoretical lower limits will be set for 95% CIs of the mean as follows:

- VA – -0.30
- IOP – 0.00
- Absolute Residual Cylinder – 0.00
- Misalignment – 0.0
- IOL Axis – 0.0

10.1.1 Visual Acuity

Visual acuity is measured at the immediate post-op visit (1-6 months post-op) and Visit 1 (3-5 years post-op, +/- 90 days), and other standard of care visits, when applicable [REDACTED]. Distance VA is measured per the site’s standard of care practice using charts validated for the specific testing distance. All distance VA will be converted to LogMAR scale prior to analysis.

For VA not reported in LogMAR, refer to Table 3 to convert the corresponding LogMAR VA. For example, if the distance VA is 20/25 Snellen, then the corresponding LogMAR VA is $-\log_{10}(20/25) = 0.10$.

Table 3. Distance Visual Acuity Conversion Formula Chart

Visual Acuity	LogMAR
Snellen Feet 20	$LogMAR = -\log_{10}\left(\frac{20}{\text{Snellen Visual Acuity Denominator}}\right)$

10.2 CONVENTIONS

Change in value from 1st visit to follow-up visit

For a given parameter, the change from baseline for postoperative visit, Visit X, will be calculated as:

Change: Follow-up Visit X - Baseline

Percent Change: $[(\text{Follow-up Visit X} - \text{Baseline}) / \text{Baseline}] * 100$

Days from Surgery

Days from surgery will be calculated as: (Date of the event – Date of surgery)

AE duration

End date of AE – Start date of AE + 1

10.3 MISSING DATA

No missing data imputation is planned for this study.

10.4 STRATIFICATION

Performance and safety outcome measures will be stratified by the following subgroups of interest:

- PanOptix toric vs. PanOptix non-toric, where for subject-level data, subjects with at least one eye implanted with a toric IOL are considered to be in the toric group. For eye-level data, toricity is reported by each implanted eye's model. For subjects bilaterally implanted on the same day, OD is assigned as first eye, and OS is assigned as second eye

10.5 ANALYSIS TIME POINTS

Analysis timepoints/windows will not be considered for analysis purposes. All scheduled visit data will be presented based on the visit reported in the CRF. For example, all scheduled Visit 1 data will be reported and analysed as Visit 1, regardless of the number of days the visit occurred from IOL implantation. Any visits occurring outside of a visit window should be logged as protocol deviations (PD) and reported in the PD listing.

10.6 STATISTICAL SOFTWARE

Unless otherwise specified, analyses, summary outputs, listings, and figures will be generated [REDACTED].

10.7 STATISTICAL OUTPUT

Analysis datasets will be created from the raw EDC datasets to facilitate programming of Tables, Figures, and Listings (TFL). Proposed shells for TFL will be provided as listed in the planned output (See Section 14.2). Tables and Figures will be provided in word format. Listings may be prepared in word or excel format.

11 QUALITY CONTROL AND VERSION CONTROL

The Statistical Analyst will direct the project team to apply quality control and data validation programming to ensure consistency and accuracy of the statistical analysis datasets, statistical analyses, and associated output, according to ICON standard operating procedures [REDACTED]

[REDACTED] The review involves, but is not limited to the following: generation of QC statistics, checking calculations of

derived variables, confirmation of analytic cohort, examination of the SAS® LOG or equivalent, confirmation of statistical validity, and consistency of output across tables, listings, and figures.

ICON plc will designate the initial version of the SAP approved by the Sponsor and ICON plc as Version 1.0. ICON plc will document any changes made to the SAP in a new version and the version number updated. ICON plc may complete revisions to SAP attachments without requiring additional revisions and approval to the SAP.

12 REFERENCES

12.1 REFERENCES APPLICABLE TO ALL CLINICAL STUDIES

- ISO 11979-7:2018 Ophthalmic Implants - Intraocular lenses - Part 7: Clinical Investigations
- ISO 22979:2017 Ophthalmic implants — Intraocular lenses — Guidance on assessment of the need for clinical investigation of intraocular lens design modifications
- ISO 14155:2020 Clinical Investigation of Medical Devices for Human Subjects - Good Clinical Practice

13 REVISION HISTORY

Version	Date	Change from Previous Version
V1.0	18Apr2025	Final SAP v1.0

14 APPENDIX

14.1 SCHEDULE OF EVENTS

Event	Retrospective		Prospective	
	Preoperative and Operative Visit	Postoperative Standard of Care & Unplanned Visits	Visit 1 (3-5 Years +/- 90 Days Postoperative)	Unscheduled Visit ^a
Informed Consent			✓	
Eligibility Determination			✓	
Demographics			✓	
Medical History	✓ ^b			
Concomitant Medications	✓***	✓	✓	✓**
Biometry & Keratometry	✓ ^c			
Preoperative Manifest Refraction	✓ ^c			
Predicted Residual Refractive Error	✓*			
Lens Model & Power	✓			
IOL Calculation Method	✓*			
Other Surgical Procedures During Cataract or Refractive Lens Exchange Surgery	✓*			

Manifest Refraction	✓*	✓*	✓	
Binocular UCDVA		✓ [†]	✓	
Monocular BCDVA		✓ [†]	✓	✓**
Binocular BCDVA		✓ [†]	✓	
Binocular UCIVA at 66 cm		✓ [†]	✓	
Binocular DCIVA at 66 cm		✓ [†]	✓	
Binocular UCNVA at 40 cm		✓ [†]	✓	
Binocular DCNVA at 40 cm		✓ [†]	✓	
Slit Lamp Examination (Biomicroscopy)	✓	✓	✓	✓**
Posterior Capsule Opacification (PCO)			✓	✓**
Capsulotomy Assessment			✓	
Tonometry			✓	✓**
Dilated Fundus Examination			✓	✓**
Actual Axis of IOL Orientation	✓*	✓ ^{††}	✓	
Assessment of Adverse Events	✓	✓	✓ ^d	✓**
Assessment of Device Deficiencies	✓*	✓*	✓	✓**
Study Exit			✓	✓**

^a Prospective visit after Visit 1 to monitor subjects with ongoing AEs

^b Medical history includes all relevant systemic and all ocular conditions that began prior to surgery and implantation of study IOL(s).

^c Preoperative keratometry, biometry, and manifest refraction assessments for each eye should have occurred within 90 days of IOL implantation of the respective eye.

^d AEs should be assessed at all postoperative visits through Visit 1 and recorded in EDC.

* If available

** As needed

*** Do not enter medications used for cataract surgery in EDC

[†] Immediate postoperative visual acuity (1-6 months postoperative), if available

^{††} From 1 day postoperative visit, if available







