Alcon

Clinical Trial Protocol

Post-Market Clinical Investigation of the Clareon® IOL

Protocol Number:	ILJ466-P003 / NCT03316885
Sponsor Name & Address:	Alcon Research, Ltd. and its affiliates ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099
Test Article(s) / Product(s):	Clareon® aspheric hydrophobic acrylic monofocal IOL (Model SY60WF)
Investigator Agreement:	I have read the clinical study described herein, recognize its confidentiality, and agree to conduct the described trial in compliance with Good Clinical Practice (GCP), ISO 14155, the ethical principles within the Declaration of Helsinki, this protocol, and all applicable regulatory requirements. Additionally, I will comply with all procedures for data recording and reporting, will permit monitoring, auditing, and inspection of my research center, and will retain all records until notified by the Sponsor.

Principal Investigator: _____

Signature Date

Name and Investigator Number:

Address:

Telephone:

Release Date:

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1 PROTOCOL SYNOPSIS

Financial Disclosure for US FDA Submission Required?	☐ Yes ☒ No
Test Article(s) / Product(s):	Clareon aspheric hydrophobic acrylic monofocal intraocular lens (IOL) Model SY60WF Hereto referred to as Clareon IOL
Objective(s):	**Primary Objective:** To evaluate the long-term (3 years) favorable visual acuity and adverse event outcomes for the Clareon IOL. A comparison to historical safety and performance endpoint (SPE) rates as reported in EN ISO 11979-7:2014 will be conducted for Visual Acuity and Adverse Events at one year. **Secondary Objective:** To evaluate the visual acuity outcomes with the Clareon IOL.
Clinical Trial Design:	A prospective, multicenter, single group safety and performance clinical trial.
No. of Subjects:	a) Required for statistical analysis: 125 subjects (evaluable) completed b) Planned (enrolled): Approximately 200 subjects implanted bilaterally (n = 400 eyes) c) Each site should target approximately 10 subjects.
Region(s):	EU and Australia (approximately 10-20 sites)
Clinical Trial Duration:	a) Total expected duration of the clinical investigation: Approximately 43 months

	b) Expected duration of each subject's participation: Approximately 36 months c) Planned follow-up duration: 36 months post-bilateral implantation d) Estimated time needed to select the number of subjects (ie, enrollment period): Approximately 6 months	
Clinical Trial Population:	Adult subjects, 22 years of age or older, with no ocular pathology (other than cataract) that could confound study outcomes, who require cataract extraction in both eyes will be considered for enrollment in this study. Full details are found in Section 10 SUBJECT POPULATION.	
Treatments:	***Test Article***:	Clareon IOL (Model SY60WF).
	Administration:	Routine small incision cataract surgery with unilateral IOL implantation.
	General Description:	A range of commonly used spherical powers (diopters) will be available, from 15 to 25D in 0.50D steps.
	Duration of Treatment:	Intraocular lenses are implantable medical devices and are intended for long term use over the lifetime of the cataract subject.
	Control Article:	N/A ***Note:*** Historical safety and performance endpoints rates will serve as a comparator (EN ISO 11979-7:2014).
	Administration:	N/A

	General Description:	N/A
	Duration of Treatment:	N/A
Inclusion & Exclusion Criteria:	Details can be found in Section 10: SUBJECT POPULATION	
Performance	• Monocular best corrected distance visual acuity (BCDVA) • Monocular uncorrected distance visual acuity (UCDVA)	
Safety	• Adverse events (AEs), including Secondary Surgical Interventions (SSIs) • Device deficiencies • Surgical problems • Other procedures during surgery • Intraocular pressure (IOP) • Slit-lamp examination • IOL observations • IOL position change • Subjective posterior capsule opacification (PCO) • Posterior capsulotomy • Dilated fundus examination (DFE)	
Other	• Manifest refraction • Keratometry • Axial length (AL) • Anterior chamber depth (ACD)	

	[redacted]

Planned Analyses

The primary analysis set for effectiveness analyses will be the All-Implanted Analysis Set (AAS). AAS includes all eyes with successful test article implantation. [redacted]

The Safety Analysis Set will include all eyes with attempted implantation with the test article (successful or aborted after contact with the eye) and will be used for the safety analyses.

The performance target in support of the primary effectiveness objective is to demonstrate that the one-sided exact 95% upper confidence limit for the percentage of subjects with monocular best corrected distance visual acuity (BCDVA) of 0.3 logMAR or better at 1 year (Visit 5A) is not worse than SPE rate of 92.5% for AAS (as reported in EN ISO 11979-7:2014).

Descriptive statistics (mean, median, standard deviation, number of subjects/eyes, minimum, maximum, and the two-sided 95% confidence interval) will be provided for effectiveness endpoints, separately for first implanted eyes and second implanted eyes.

The primary safety objective is to evaluate the safety of the Clareon IOL for first and second operative eyes separately up to 3 Years (Visit 7A). Adverse Events rates at 1 year (Visit 5A) will be compared to historical safety and performance endpoint (SPE) rates as reported in EN ISO 11979-7:2014.

Descriptive statistics for adverse events (including SSIs) will be presented separately for first and second eyes. The one-sided exact 95% lower confidence limits for incidence rates observed up to one year of study follow-up (ie, after all subjects have completed Visit 5A) will be compared to the cumulative and persistent adverse event SPE rates (as reported in EN ISO 11979-7:2014), separately for first implanted eyes and second implanted eyes.

For the remaining study endpoints, descriptive statistics generated for effectiveness and

safety parameters will be based upon the type of parameter (ie, whether the data were categorical or continuous) being analyzed. For categorical parameters, the statistics used to summarize the data descriptively included sample size, number in the category, and percent in the category. For continuous parameters, sample size, mean, median, standard deviation, minimum, and maximum will be presented.

[redacted]

Sample Size Justifications

If more than 110 of 125 eyes show monocular best corrected distance visual acuity (BCDVA) of 0.3 logMAR or better at 1 year (Visit 5A), the one-sided exact 95% upper confidence limit for the rate is not worse than SPE rate of 92.5%. Assuming that the mean and the standard deviation of monocular BCDVA are 0.0 and 0.18 logMAR respectively, the study has greater than 99% chance to meet this performance target.

For any event where zero incidence is observed in 125 first-operative eyes with Clareon IOL, the one-sided exact 95% upper confidence limit for the adverse event rate is less than 2.4%. Thus, with 95% confidence, the true adverse event rate is less than 2.4%.

Approximately 200 subjects will be bilaterally implanted with the Clareon IOL in order to ensure at least 125 evaluable subjects complete the study.

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3 ABBREVIATIONS

Abbreviation	Definition
AAS	All-Implanted Analysis Set
ACD	Anterior chamber depth
ADE	Adverse device effect
AE	Adverse event
AL	Axial length
ASADE	Anticipated serious adverse device effect
[redacted]	[redacted]
BCDVA	Best corrected distance visual acuity
BSS	Balanced salt solution
CE	*Conformité Européene* or European Conformity
CFR	Code of Federal Regulations
CM	Clinical manager
CRF	Case report form
CSM	Clinical site manager
D	Diopter
DFE	Dilated fundus examination
DFU	Directions for use
DoH	Declaration of Helsinki
eCRF	Electronic case report form
EDC	Electronic data capture
EN	European Standard
EU	European Union
FA	Fluorescein angiography
FDA	Food and Drug Administration
FLACS	Femtosecond laser-assisted cataract surgery
GCP	Good Clinical Practice
HCL	Hydrogen chloride
ICF	Informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Humans Use
IEC	Independent ethics committee
IOL	Intraocular lens
IOP	Intraocular pressure
IRB	Independent review board
IP	Investigational product
ISO	International Organization for Standardization
LASIK	Laser-assisted in-situ keratomileusis
logMAR	Logarithm of minimum angle of resolution
MedDRA®	Medical Dictionary for Regulatory Activities
m	Meter
mm	Millimeter
mmHg	Millimeters of mercury

Abbreviation	Definition
MOP	Manual of procedures
N/A	Not applicable
[redacted]	[redacted]
OCT	Optical coherence tomography
OD	Right eye
OVD	Ophthalmic viscosurgical device
PC	Posterior capsulotomy
PCO	Posterior capsule opacification
RD	Retinal detachment
SADE	Serious adverse device effect
SAE	Serious adverse event
SOP	Standard operating procedure
SPE	Safety and Performance Endpoints
SSI	Secondary surgical intervention
SUN	Standardization of Uveitis Nomenclature
UCDVA	Uncorrected distance visual acuity
USADE	Unanticipated serious adverse device effect
US	United States
USV	Unscheduled visit
UV	Ultraviolet
WHO	World Health Organization
wk	Week

4 GLOSSARY OF TERMS

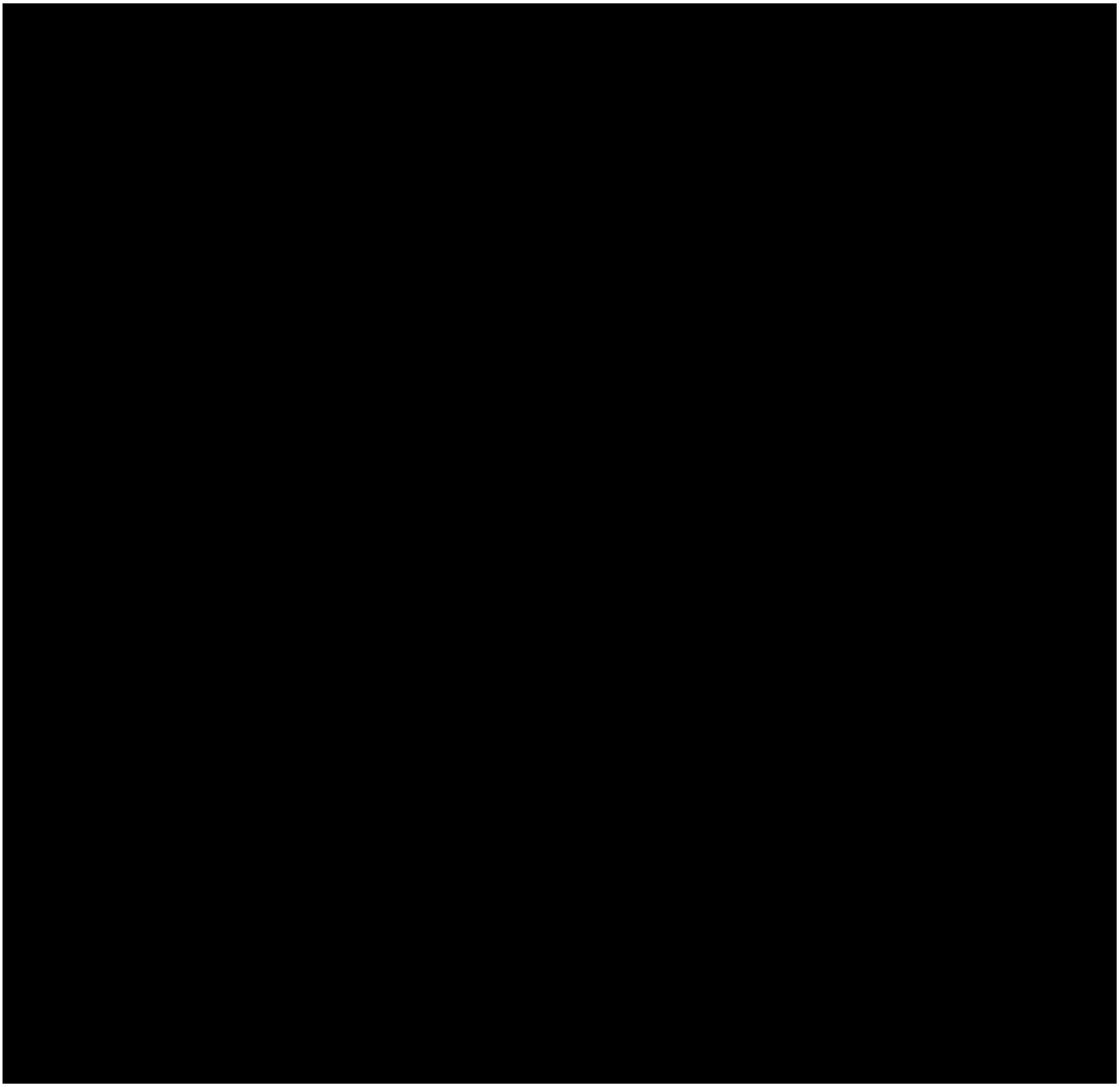
Adverse Device Effect (ADE)	Adverse event related to the use of an investigational medical device or comparator, if applicable. *Note: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation; any malfunction; and use error or intentional misuse of the investigational medical device or comparator, if applicable.*
Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device. *Note: For subjects, this definition includes events related to the investigational medical device, the comparator, or the procedures involved. For users or other persons, this definition is restricted to events related to investigational medical devices.*
Anticipated Serious Adverse Device Effect (ASADE)	Serious adverse device effect which by its nature, incidence, severity, or outcome has been identified in the risk analysis.
Assessment	A procedure used to generate data required by the study.
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. *Note: This definition includes malfunctions, misuse or use errors, and inadequate labeling.*
Performance (Clinical)	Behavior of a medical device or response of the subject to that medical device in relation to its intended use, when correctly applied to appropriate subjects.
Malfunction	Failure of an investigational medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical investigation plan.
Nonserious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.
Period	A minor subdivision of the study timeline; divides phases into smaller functional segments such as screening, baseline, operative, post-implantation, etc.
Randomization Number	A unique identifier assigned to each randomized subject, corresponding to a specific treatment arm assignment.

Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Serious Adverse Event (SAE)	Adverse event that led to any of the following: • Death. • A serious deterioration in health that either resulted in: a) a life-threatening illness or injury. *Note: Life-threatening means that the individual was at immediate risk of death from the event as it occurred, ie, it does not include an event which hypothetically might have caused death had it occurred in a more severe form.* b) any potentially sight-threatening event or permanent impairment to a body structure or a body function. c) in-patient hospitalization or prolonged hospitalization. *Note: Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigation plan, without serious deterioration in health, is not considered a serious adverse event. In general, hospitalization signifies that the individual remained at the hospital or emergency ward for observation and/or treatment (usually involving an overnight stay) that would not have been appropriate in the physician's office or an out-patient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred, the event should be considered serious.* d) a medical or surgical intervention to prevent a) or b), or any ocular secondary surgical intervention excluding posterior capsulotomy. e) any indirect harm as a consequence of incorrect diagnostic test results when used within manufacturer's instructions for use. • Fetal distress, fetal death, or a congenital abnormality or birth defect.
Subject Number	A number assigned to each subject who enrolls in the study. When combined with the site number, a unique identifier is created for each subject in the study.

Unanticipated Serious Adverse Device Effect (USADE)	Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the risk analysis.

5 AMENDMENTS

Modification of the protocol is prohibited without prior written agreement in the form of a protocol amendment. All amendments must be created by the Study Sponsor and must be approved by an Independent Ethics Committee (IEC)/Institutional Review Board (IRB) prior to implementation except when required to mitigate immediate safety risks or when the changes involve only logistical or administrative revisions.



6 SCHEDULE OF VISITS

Activity	Visit 0 Pre-Operative (-60 –Day 0)	Visit 00[d]: First Eye Surgery	Visit 1[d]: Day 1-2[b]	Visit 2[d]: Day 7-14[b]	Visit 00A[d]: Second Eye Surgery, 2-21 Days from V00)	Visit 1A[d]: Day 1-2[c]	Visit 2A[d]: Day 7-14[c]	Visit 3A: Day 30-45[c]	Visit 4A: Day 120-180[c]	Visit 5A: Day 330-420[c]	Visit 6A: Day 630-780[c]	Visit 7A\Early Exit: Day 990-1140[c]	Unscheduled Visit
Informed Consent	X												
Demographics	X												
Medical History	X												
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine Pregnancy Test[a]	X												
Inclusion/Exclusion	X	X			X								
Keratometry	X							X	X	X			
Axial Length (optical biometry)	X							X	X	X			
Anterior Chamber Depth (optical biometry)	X							X	X	X			
Manifest Refraction (4 m)	X			X			X	X	X	X	X	X	X
Monocular BCDVA	X			X			X	X	X	X	X	X	X
Monocular UCDVA	X		X	X		X	X	X	X	X	X	X	X
Slit-Lamp Examination	X		X	X		X	X	X	X	X	X	X	X
Intraocular Pressure	X		X	X		X	X	X	X	X	X	X	X
Dilated Fundus Examination	X								X	X	X	X	X
Operative Eye		X			X								

Activity	Visit 0 Pre-Operative (-60 –Day 0)	Visit 00[d]: First Eye Surgery	Visit 1[d]: Day 1-2[b]	Visit 2[d]: Day 7-14[b]	Visit 00A[d]: Second Eye Surgery, 2-21 Days from V00)	Visit 1A[d]: Day 1-2[c]	Visit 2A[d]: Day 7-14[c]	Visit 3A: Day 30-45[c]	Visit 4A: Day 120-180[c]	Visit 5A: Day 330-420[c]	Visit 6A: Day 630-780[c]	Visit 7A\Early Exit: Day 990-1140[c]	Unscheduled Visit
Surgical Report (including lens power, implant success, target refractive error, and FLACS/no FLACS surgery, IOL calculation formula, capsule polishing, IOL capsule coverage)		X			X								
Surgical Problems		X			X								
Other Procedures at Surgery		X			X								
[redacted]								[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
Subjective posterior capsule opacification (PCO)			X	X		X	X	X	X	X	X	X	X
Posterior Capsulotomy			X	X		X	X	X	X	X	X	X	X
IOL Position Change (tilt and decentration)			X	X		X	X	X	X	X	X	X	X
IOL Observations			X	X		X	X	X	X	X	X	X	X
Adverse Events (including SSIs)	X	X	X	X	X	X	X	X	X	X	X	X	X
Device Deficiencies		X	X	X	X	X	X	X	X	X	X	X	X

[a] In women of child bearing potential only. | [b] Time from first eye surgery. | [c] Time from second eye surgery | [d] Operative eye only

7 INTRODUCTION

7.1 Background

The Clareon IOL (Model SY60WF) is a foldable, monofocal IOL intended as an optical implant for the replacement of the human crystalline lens in the visual correction of aphakia in adult patients following cataract surgery. The lens IOL is intended to be placed in the capsular bag in the posterior chamber of the eye.

The Clareon IOL is a UV-absorbing IOL composed of a high refractive-index foldable acrylic material. Its design is equivalent in dimensions to the globally approved ACRYSOF Natural IQ IOL (Model SN60WF). The Clareon IOL is a monofocal lens of single-piece construction, with a 6.0 mm diameter asymmetric biconvex posterior optic with an aspheric surface incorporated on the anterior side of the optic, and an overall length of 13.0 mm. The haptics are constructed from the same material as the optic with no angulation. The Clareon IOL is qualified for use with existing Alcon Monarch III-D cartridge and delivery systems (see Table 11-2 for more information).

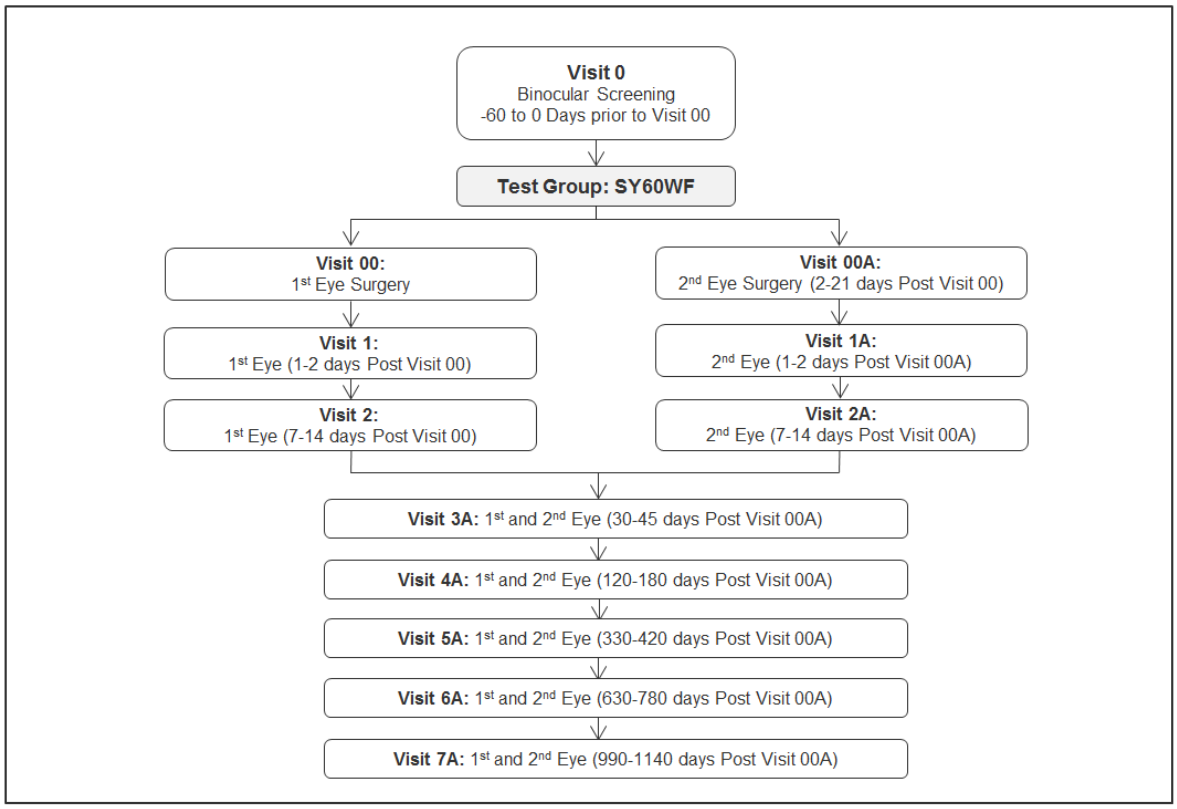
A summary of known and potential risks and benefits to humans of the Clareon IOL, as identified in the literature or through preclinical testing and/or prior clinical evaluations, for the investigational product can be found in the Directions for Use (DFU).

The rationale to conduct this post-market study is to provide long-term (3 years) safety and effectiveness data on the Clareon IOL to support the Market Access requirements including the development of a product value dossier.

7.2 Clinical Trial Design

An overview of the study flow is depicted in Figure 7–1.

Figure 7–1 Study Design



8 CLINICAL TRIAL OBJECTIVES

8.1 Primary Objective

The primary objective of this study is to evaluate the long-term (3 years) favorable visual acuity and adverse event outcomes for the Clareon IOL.

One-year visual acuity and adverse event outcomes will be compared to historical SPE rates as reported in EN ISO 11979-7:2014.

8.2 Secondary Objectives

The secondary objective of this study is to evaluate the visual acuity outcomes obtained with up to 3 years follow-up in eyes implanted with the Clareon IOL.

8.4 Study Endpoints

8.4.1 Primary Effectiveness Endpoint

Percentage of subjects achieving BCDVA of 0.3 logMAR or better at 1 year post-implantation (Visit 5A).

8.4.2 Secondary Effectiveness Endpoints

- Percentage of subjects achieving BCDVA of 0.3 logMAR or better at 2 years post-implantation (Visit 6A)
- Percentage of subjects achieving BCDVA of 0.3 logMAR or better at 3 years post-implantation (Visit 7A)
- UCDVA at 1 year (Visit 5A) post-implantation
- UCDVA at 2 years (Visit 6A) post-implantation

- UCDVA at 3 years (Visit 7A) post-implantation

8.5 Safety Endpoints

The following safety endpoints will be collected:

- AEs (ocular and nonocular, serious and non-serious) including SSIs
- Device deficiencies
- IOL observations
- Surgical problems
- Intraocular pressure
- Posterior capsular opacification
- Posterior capsulotomy
- IOL position change (tilt and decentration)

9 INVESTIGATIONAL PLAN

9.1 Outline of Clinical Trial

The current study is designed as a prospective, multicenter, single-arm trial assessing the long-term (3-year) safety and effectiveness of the Clareon IOL. The study includes adults (≥ 22 years of age) who require bilateral cataract extraction and who meet study entry criteria. Subjects will attend a total of 12 study visits over a period of approximately 36 months. Of these twelve visits, one is a preoperative screening visit (Visit 0) and two are operative visits (Visit 00 and Visit 00A). The remaining nine are post-implantation visits (Visits 1-7A) which will occur at the following intervals: Visit 1 and Visit 1A (Day 1-2 post-implantation, first and second eye), Visit 2 and 2A (Day 7-14 post-implantation, first and second eye), Visit 3A (Day 30-45 post-implantation from 2nd eye surgery), Visit 4A (Day 120-180 post-implantation from 2nd eye surgery), Visit 5A (Day 330-420 post-implantation from 2nd eye surgery), Visit 6A (Day 630-780 post-implantation from 2nd eye surgery), and Visit 7A (Day 990-1140 post-implantation from 2nd eye surgery). Visit day calculations for Visits 1 and 2 are based off of the day of first eye surgery (Visit 00) and calculations for Visits 1A-7A are based off of the day of second eye surgery (Visit 00A). Unscheduled visits may be conducted if needed for medical attention. Refer to Figure 7-1 above for a study outline diagram.

Primary endpoint data will be collected at Visit 5A (330-420 days post-implantation from 2nd eye surgery), and secondary endpoint data will be collected at Visit 5A (330-420 days post-implantation from 2nd eye surgery), Visit 6A (630-780 days post-implantation from 2nd eye surgery) and Visit 7A (990-1140 days post-implantation from 2nd eye surgery). The study will be considered successful if the data at Visit 5A indicate a favorable outcome in relation to the SPE rates as reported in EN ISO 11979-7:2014. Additional details, including a risk-benefit assessment can be found in the sections below.

Section 12 CLINICAL TRIAL PROCEDURES outlines the procedures and assessments to be conducted at each study visit. This information is presented in tabular format in Section 6 SCHEDULE OF VISITS.

9.2 Study Design

This is a prospective, multicenter, single-arm safety and performance clinical study, requiring no masking. The trial will evaluate the safety and performance of the Clareon IOL in approximately 200 bilaterally implanted subjects. To qualify for enrollment into the trial,

adult (≥ 22 years of age) subjects must require routine, bilateral cataract surgery. Potential subjects will be screened for enrollment into the trial in accordance with the entry criteria found in Section 10 SUBJECT POPULATION. Subjects will attend a total of 12 study visits (7 post-implantation) over a period of approximately 3 years.

Primary endpoint data will be collected at Visit 5A (330-420 days post-implantation from 2nd eye surgery).

[redacted] Final data analysis will be conducted at study completion (Visit 7A, 990-1140 days post implantation from the date of 2nd eye surgery.

The study will be considered successful if the data at Visit 5A indicate a favorable outcome in relation to the SPE rates as informed by EN ISO 11979-7:2014. Although study follow-up will continue until Visit 7A is completed for all subjects, the comparison of the vision and adverse events data to the SPE rates will be performed once all subjects have completed Visit 5A. This comparison will only be performed at Visit 5A, as the SPE rates in EN ISO 11979-7:2014 were developed from 1-year post-op clinical investigations (ie, the SPE rates are not appropriate for studies with greater than one year of follow up). Additional details, including a risk-benefit assessment can be found in the sections below.

Section 12 CLINICAL TRIAL PROCEDURES outlines the procedures and assessments to be conducted at each study visit. This information is presented in tabular format in Section 6 SCHEDULE OF VISITS.

9.3 Rational for Study Design

The design of this study will allow for the assessment of long-term (3-year) safety and efficacy of the Clareon monofocal IOL.

9.4 Procedures Per Study Visit

Section 12 CLINICAL TRIAL PROCEDURES contains procedures per study visits.

9.5 Risk Benefit Assessment

For a full and comprehensive risk benefit assessment including a summary of known and potential risks and benefits to humans as identified in the literature, through pre-clinical

testing, or via prior clinical investigations, refer to the DFU. Abbreviated details are provided in Section 9.6 and 9.7 below.

Based on the below outlined risks and benefits, the risk of unanticipated adverse device effects with use of the Clareon IOL is considered to be low and the benefits of receiving the IOL should outweigh the risks for subjects that qualify for implantation in this study.

9.6 Known and Potential Risks

Complications may occur on the surgery day or throughout the postoperative period. Known and potential risks of the Clareon IOL are outlined here.

Surgical Risk

As with any type of intraocular surgery, there is a possibility of complications due to anesthesia, drug reactions, and surgical problems. The surgical procedure can exacerbate a pre-existing ocular condition. Possible problems during surgery include corneal endothelial touch, detached Descemet's membrane, iris damage, iris prolapse, iris trauma, iris incarceration, zonular rupture, vitreous loss, capsulorhexis tear, capsular rupture, uncontrollable intraocular pressure (IOP), hyphema, and retinal damage. An IOP increase may occur from the surgical procedure, residual viscoelastic in the eye, or a steroid response to post-implantation medications.

Post-implantation Risk

Potential post-implantation adverse events include, but are not limited, to corneal stromal edema, cystoid macular edema, endophthalmitis, hypopyon, iritis, lens dislocation, membrane formation on the IOL, pupillary block, retinal detachment, cyclitic membrane, transient or persistent glaucoma, retinal tear, vitritis, iris touch, pupil ovalization, posterior synechiae, ocular inflammation, ocular discomfort or pain, inflammation, decreased vision, decreased contrast sensitivity, decreased color perception, visual disturbances, and corneal endothelial cell loss.

An IOL replacement or explantation may be appropriate in some cases of significant residual refractive error, ocular infection, subject dissatisfaction, or visual disturbances (eg, glare, halos, starbursts, hazy vision, blurred vision, double vision, visual distortions, and color distortions). In most/majority of cases, spectacles or contact lenses may be prescribed to resolve residual refractive error. Other secondary surgical interventions include, but are not limited to: IOL repositioning, refractive laser treatment, paracentesis, vitreous aspirations,

and iridectomy or laser iridotomy for pupillary block, wound leak repair, and retinal detachment repair.

Unknown Risk

There may also be unknown risks with the use of the Clareon IOL. Any foreseen risk to subjects in this clinical study will be minimized by compliance with the eligibility criteria, study procedures, and clinical monitoring.

9.7 Potential Benefits

Known and potential benefits of the Clareon IOL are outlined here.

Cataract surgery with IOL lens implantation benefits patients by restoring sight - the result of replacing the natural cataractous lens with an IOL. IOL implantation may also improve color vision, enhance image sharpness, and decrease nighttime photic phenomena (eg, glare, halo). This enhancement of vision may increase overall lifestyle satisfaction (eg, more independence, participation in social and/or sporting activities). The Clareon IOL is expected to have benefits comparable to other available monofocal IOLs.

This clinical trial may benefit the medical community and future cataract patients via contribution to the available scientific literature and the potential availability of an IOL with a new lens material.

10 SUBJECT POPULATION

The study population includes approximately 200 bilaterally implanted subjects, enrolled at approximately 10-20 investigative sites, over an enrollment period of approximately 6 months. Each Investigator will implant approximately 10 subjects with no Investigator implanting more than 25% of the total study population. Each site will use only one implanting surgeon.

To participate in the clinical trial, subjects must be an adult (age 22 years or older at time of surgery) requiring routine, bilateral cataract surgery. A full list of entry criteria is provided in Sections 10.1 to 10.3 below. The Investigator may also refer to the lens DFU for further guidance, and may exclude potential subjects based upon his/her medical judgement.

Subjects will be implanted bilaterally and both eyes must meet all ocular inclusion/exclusion criteria to qualify for participation in the study. In the event that *either* eye fails to meet entry criteria, the subject *may not* be re-screened at a later date for qualification into the study.

10.1 Inclusion Criteria

Listed below are criteria that must be met for inclusion into the study. Criteria must be met in both eyes unless noted otherwise.

1. Adults, 22 years of age or older at the time of surgery, of either gender or any race, diagnosed with bilateral cataracts
2. Able to comprehend and willing to sign an IRB/IEC approved statement of informed consent and complete all required post-implantation visits
3. Planned small incision cataract removal surgery

[redacted]

[redacted]

10.2 Exclusion Criteria (Prior to Surgery)

Listed below are criteria that exclude entry into the study. Ocular criteria must be met in both eyes.

1. Subjects who may reasonably be expected to require an ocular surgical treatment at any time during the study [redacted]
2. Previous refractive surgery or planned refractive surgery procedures throughout the entire duration of the subjects' participation in the clinical study (including, but not limited to LASIK, astigmatic keratotomy and limbal relaxing incisions)
3. Clinically significant corneal abnormalities including corneal dystrophy (eg, epithelial, stromal, or endothelial dystrophy), inflammation or edema per the Investigator's expert medical opinion
   (Note: Conditions including, but not limited to: keratitis, keratoconjunctivitis, keratouveitis, keratopathy, or keratectasia should be excluded.)

[redacted]

18. Pregnancy or lactation current or planned during the course of the study

10.3 Reasons for Discontinuation During Surgery

Listed below are criteria that, when occurring at the time of first eye surgery, may result in discontinuation from the study. A subject discontinuing at the time of surgery for the first eye will be not be considered a screen failure.

In the event that a criterion listed below occurs for either eye during surgery, do not implant the study lens. Proceed according to the physician's professional medical judgement for what is in the best interest of the subject, including, if warranted, an alternate lens. See protocol Section 12.14 Aborted Implantation and Manual of Procedures (hereto referred to as MOP) Table 5-1 Subject Status After Exclusion During Surgery for additional instructions regarding follow-up.

20. Any other additional procedures during the cataract removal and IOL implant due to intraoperative complications that require further intervention (including but not limited to posterior rupture, with vitreous loss, zonular dehiscence that may make the IOL implant less stable

21. Uncontrolled intraocular pressure

22. Significant anterior chamber bleeding

23. Excessive iris mobility

24. Mechanical or surgical intervention required to manipulate the pupil
    Note: Pupil size must be 4.5mm or larger just prior to implantation

25. Any capsulorhexis other than continuous curvilinear capsulorhexis (eg, no anterior radial inconsistencies in the capsulorhexis such as anterior capsular tears or any areas of "can-opener" capsulotomy)

26. Unrecognized (pre-existing but discovered during surgery) ocular conditions or complications in which the IOL positions could be less stable, including zonular weakness

27. Zonular or capsular rupture

28. Bag-sulcus, sulcus-sulcus, or unknown placement of the IOL haptics
    Note: Intended IOL haptic placement in this study is bag-bag.

11 TREATMENT

Throughout the clinical study, the Investigator is responsible for the accounting of all IP and must ensure that the clinical study product is used in accordance with the manufacturer's DFU.

All consented and qualified subjects will be implanted bilaterally with the test article. No control article is available in this study.

11.1 Investigational Products

Test Article: Refer to Table 11-1 below for test article details.

Control Article: N/A

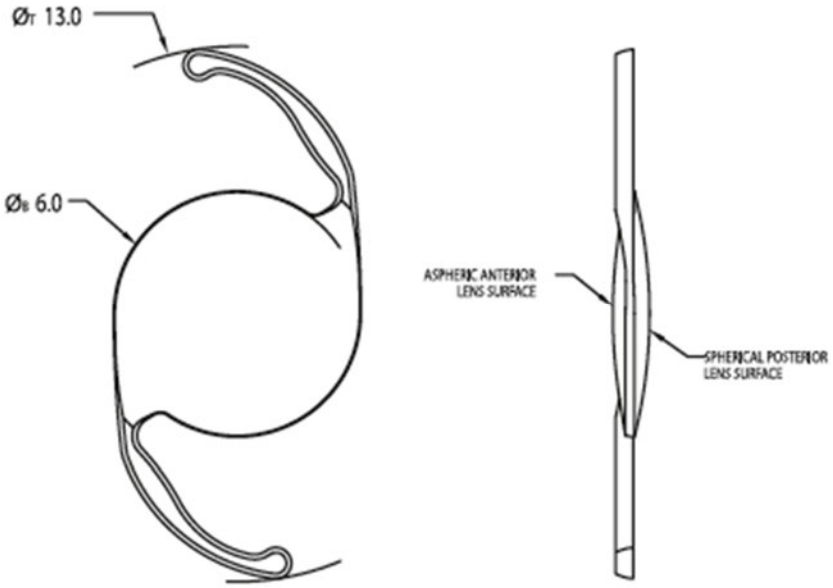
Table 11–1 Test Article

Test Product	Clareon aspheric hydrophobic acrylic intraocular lens (IOL) Model SY60WF
Manufacturer	Alcon
Indication for use	This 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 in adult patients.
Intended Purpose in the current study	The Clareon Aspheric Hydrophobic Acrylic IOL is a foldable single-piece posterior chamber IOL intended as an optical implant for the replacement of the human crystalline lens in the visual correction of aphakia in adult patients following cataract surgery. The lens is intended to be placed in the capsular bag in the posterior chamber of the eye.
Product description and parameters available for this study	Optic Type – Anterior asymmetric biconvex
	Optics Material – Ultraviolet and blue light filtering acrylate/ methacrylate copolymer
	Optic Powers: 15.0 to 25.0 D in 0.5 D steps

	Index of Refraction: 1.55
	Haptic Configuration: STABLEFORCE® Modified-L Haptics
	Haptic Material: Ultraviolet and blue light filtering hydrophobic acrylate/methacrylate copolymer
	Optic Diameter (mm): 6.0
	Overall Length (mm): 13.0
	Haptic Angle: 0°
Formulation	N/A
Usage	IOLs are implantable medical devices and are intended for long-term use over the lifetime of the pseudophakic subject.
Number/Amount of Product to be Provided to the Subject	Each subject is planned to have bilateral IOL implantation.
Packaging description	Each IOL will be individually packaged and will have a unique serial number. The IOL package will contain the following items: • The IOL • A subject registration card (Lens Implant Card) • A subject identification card • Adhesive labels containing the IOL information and unique serial number • A package insert containing directions for use
Labeling description	Packaged in a standard Alcon IOL carton. The carton is labeled with the following information: name of the lens, model number, overall diameter, optic diameter, diopter power, serial number, name of the manufacturer, storage condition, expiration date, sterile, single use, and per any local country requirements, when applicable.

Storage conditions	The IP must be stored in a safe, secure location with limited access separated from general stock. Transportation of product from one address to another must be documented and a Transportation Log (or similar documentation) used for appropriate accountability.
Additional information	In order to implant the test article in a study subject, the surgeon participating in the study must be a licensed ophthalmologist with cataract surgery experience and trained on the protocol. More information on the test article can be found in the product DFU (Clareon Aspheric Hydrophobic Acrylic IOL Model SY60WF).
Supply	Investigators and study sites will obtain IOLs from Alcon through their regular commercial ordering process.

Figure 11–1 Clareon aspheric hydrophobic acrylic intraocular lens (IOL) Model SY60WF



11.2 Usage

The Clareon IOL is a foldable single-piece posterior chamber IOL intended as an optical implant for the replacement of the human crystalline lens in the visual correction of aphakia in adult patients following cataract surgery. The lens is intended to be placed in the capsular bag in the posterior chamber of the eye. Additional information regarding the use of this IOL can be found in the DFU.

Each study surgeon should follow his/her routine cataract procedure for all study surgeries, and according to the site's surgical protocol documented for the study (see Section 14.3, Data Review and Clarifications, for additional details). Femtosecond laser-assisted cataract surgery (FLACS) is permitted for Investigators that currently use this procedure as part of their standard of care for cataract surgery; however, it is **NOT** required. FLACS may **ONLY** be used for the following:

- Primary and sideport incisions
- Capsulorhexis
- Lens fragmentation

The IOL must be delivered via an Alcon qualified delivery system and viscoelastic combination. The qualified combinations are provided below in Table 11-2.

Table 11-2 Qualified Combinations of Compatible Products

Lens Model	Cartridge	Handpiece	Viscoelastic
SY60WF	Monarch® III D Product Reference Number: 8065977763	Monarch III (blue) Product Reference Number: 8065977773	Viscoat® Provisc®

- Surgeons will use his/her clinical judgement when selecting the most suitable IOL power using one of the five available formulae: SRK/T, Holladay I, Hoffer Q, Haigis, or Holladay 2
- A reference provisional lens SRK/T A-constant value of 119.1 for optical biometry equipment is listed on the outer label
- Surgeons should **not** personalize any of the derived provisional A-constants
- Study eyes must be targeted for emmetropia (±0.50 D Spherical Equivalent)
- Use of any intraoperative power assessment is not permitted during surgery

The surgeon must have at least 2 IOLs in the subject's required power available for use during the surgery. One IOL will serve as a reserve lens in the event the first lens cannot be implanted. No more than 2 implantation attempts should be initiated. Refer to Section 10.3 Reasons for Discontinuation During Surgery, Section 12.14 Aborted Implantation, and the MOP Table 5-1 Subject Status after Exclusion During Surgery regarding subject study status and required follow-up. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS and APPENDICES Tables 18-1 and 18-2 for information on device deficiency identification and reporting.

The SY60WF IOL is a CE Marked device approved for use in the countries with participating Investigators as well as other countries across the globe. The Investigator will procure all investigational products used in this trial. Details related to the procurement, labeling, handling, dispensing and final disposition are outlined below. The product must be tracked/accounted for through all steps of the procedure.

11.2.1 Procurement

The Investigator shall locally procure each product (test lens and control lens) through his/her standard Alcon commercial channel.

11.2.2 Labeling

Each IOL will be individually packaged and will have a unique serial number. The IOL package will contain the following items:

- The IOL
- A subject registration card (Lens Implant Card)
- A subject identification card
- Adhesive labels containing the IOL information and unique serial number
- A package insert containing directions for use

Product is locally procured via Alcon commercial channel and will arrive in country compliant commercial packaging with commercial label.

11.2.3 Handling

Once designated for trial use, product will be stored in a safe, secure location with limited access separated from general stock. Transportation of product from one address to another must be documented and a Transportation Log (or similar documentation) used for appropriate accountability.

11.2.4 Dispensing and Accountability Procedures

Upon receipt of IPs, the Investigator or delegate must conduct an inventory of all lenses, by serial number, complete study specific confirmation of receipt procedures as described in the MOP, and retain any required documentation in the Investigator's clinical study records. Throughout the study, the Investigator or delegate must maintain records of IP dispensation for each subject. This record must be made available to the study monitor for the purposes of verifying the disposition of all received IP. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded along with an explanation. All IP obtained by the Investigator must be accounted for by Study Sponsor personnel, and in no case be used in an unauthorized manner.

If possible, return to the Study Sponsor investigational and control products associated with a device deficiency. Refer to Section 12.14 of this protocol and the MOP Section 8 for additional information.

The Investigator is responsible for proper disposition of all unused IP at the conclusion of the study, according to instructions provided by the Sponsor.

12 CLINICAL TRIAL PROCEDURES

12.1 Clinical Trial Assessments

The following section describes in general the assessments to be performed in this clinical trial. Assessments are described in detail in the MOP. Refer to Section 6 SCHEDULE OF VISITS for an overview of assessments by visit.

Refer to Section 10 SUBJECT POPULATION for information on subject selection. AEs are collected and reported for both eyes. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS and APPENDICES Tables 18-1 and 18-2.

12.2 Identification of Potential Subjects

Identify potential subjects most likely to meet the qualifications for participation in the study based on available medical records and exams. Invite those candidates who may qualify for the study to learn more about the trial. For those interested in participation, carry out the informed consent process. Refer to Section 16.2 Informed Consent Procedures.
Note: Subjects must formally consent to the trial prior to any study specific testing.

12.3 Prohibited Procedures

Refractive surgical procedures are prohibited at surgery and throughout the duration of the subject's participation in the clinical study. Prohibited procedures include, but are not limited to, LASIK, astigmatic keratotomy, and limbal relaxing incisions.

12.4 Preoperative Screening Visit (Visit 0)

Subjects will be considered enrolled upon consent. Each subject that signs a consent form must be entered into the EDC system. Upon entry into the system, each subject will be assigned a number. This subject number will be used to identify the subject throughout the study.

Below is a list of study procedures to be undertaken at Visit 0 (-60 to 0 days preoperative). The order of procedures is recommended. All assessments must be documented in source documentation and eCRFs (if applicable).

For Visit 0, data from the Investigator's previous routine clinical evaluation for DFE may be used, if the data 1) meet the requirements of this protocol and MOP, and 2) were collected within 30 days prior to the preoperative screening visit date. All other ocular assessments

must be collected after the subject signs the Informed Consent Form, and should be conducted in the order recommended.

1. Ensure subject has been properly consented for trial participation. Refer to Section 15.2 Informed Consent Procedures.
2. Document demographics, ocular and nonocular medical history, ocular and nonocular concomitant medications and pregnancy status (where applicable).
3. Perform a urine pregnancy test IF the subject is a woman of child-bearing potential.
4. Assess biometry measures including AL, keratometry, and ACD.
   [Both eyes]
5. Perform manifest refraction.
   Note: UCDVA may be performed prior to manifest refraction.
   [Both eyes]
6. Perform monocular UCDVA and BCDVA testing with study specified equipment.
   Note: Lighting conditions must be measured and recorded in source prior to vision testing.
   [Both eyes]
7. Perform an ophthalmic examination including slit-lamp, and DFE (if required, ie historical DFE not available within 30 days prior to screening).
   [Both eyes].
8. Perform tonometry to measure the IOP.
   [Both eyes]
9. Calculate the required lens power for an emmetropic spherical equivalent target (defined as 0.00 ± 0.50 D). See Section 11.2 Usage for available IOL calculation formulae.
   [Both eyes]
10. Record the target refractive error based on IOL power selected.
    [Both eyes]
11. Assess, document and report adverse events. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.
12. Review inclusion/exclusion criteria and subject's willingness to continue participation.
13. Identify the 1st surgical eye. This is defined as the eye with the worse BCDVA. If the BCDVA is the same in both eyes, identify the right eye (OD) as the 1st surgical eye.
14. Document the subject status (eg, continuing, screen failure). If the subject is a screen failure, document the primary reason the subject fails to qualify.
15. Schedule the subject for surgery within 60 days if they qualify.

16. Order lenses for each eye (ensure a back-up lens is available and order if necessary) in the selected IOL power through local commercial channel prior to surgery.

12.5 Operative Visit (Visit 00 and Visit 00A)

Below is a list of study procedures to be undertaken at Visit 00 (Day 0, first eye surgery) and Visit 00A (Day 0, second eye surgery). The order of procedures is recommended. All assessments must be documented in source documentation and eCRFs (if applicable). The Visit 00A window may overlap with other study visit windows (eg, Visit 2). In this case, both visits may be conducted on the same day at the discretion of the Investigator.

1. Prior to treatment, review inclusion/exclusion criteria and ensure the subject has been properly consented for participation in the trial.
2. Document any changes to ocular and nonocular concomitant medications.
3. Record operative eye.
4. Proceed with Investigator's routine cataract procedure while following guidance in Section 11 TREATMENT.
   [Operative Eye Only]
5. Document the Surgical Report outcomes, including use of FLACs, implant success, target refractive error, IOL calculation formula, capsule polishing, and IOL capsule coverage. Refer to MOP for further detail.
   [Operative Eye Only]
6. Document any problems during surgery including intraoperative complications and other procedures at surgery. Other procedures include those performed outside of routine cataract surgery.
   [Operative Eye Only]
7. Record the lens information that is located on the IOL sticker, including lens power. Both successful and aborted (if applicable) investigational product information should be recorded.
   [Operative Eye Only]
8. Record any AEs including SSIs.
   Note: SAEs including SSIs must be entered into Electronic Data Capture (EDC) system within 24 hours of the Investigator or site's knowledge. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.

9. Record any device deficiencies. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.
10. Document the subject status (eg, continuing).

12.6 1-2 Days Post-implantation Visit (Visit 1 and Visit 1A)

Below is a list of study procedures to be undertaken at Visit 1 (1-2 days post-implantation, first eye) and Visit 1A (1-2 days post-implantation, second eye). The order of procedures is recommended. All assessments must be documented in source documentation and eCRFs (if applicable).

1. Record changes in medical/ocular history and ocular and nonocular concomitant medications.
2. Assess monocular UCDVA. Refer to MOP for further detail.
   [Operative Eye Only]
3. Perform slit-lamp examination of the anterior segment. Include documentation of IOL observations, if applicable.
   [Operative Eye Only]
4. Assess subjective PCO, and record information for any posterior capsulotomy that has occurred since surgery, if applicable.
   [Operative Eye Only]
5. Observe any IOL position changes (ie, tilt and decentration) occurring since the previous visit.
   [Operative Eye Only]
6. Perform tonometry to measure the IOP.
   [Operative Eye Only]
7. Record any AEs including SSIs.
   Note: SAEs including SSIs must be entered into Electronic Data Capture (EDC) system within 24 hours of the Investigator or site's knowledge. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.
8. Record any device deficiencies. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.
9. Document the subject status (eg, continuing).

12.7 1-2 Week Post-implantation Visit (Visit 2 and Visit 2A)

Below is a list of study procedures to be undertaken at Visit 2 (7-14 days post-implantation, first eye surgery) and Visit 2A (7-14 days post-implantation, second eye). The order of procedures is recommended. All assessments must be documented in source documentation and eCRFs (if applicable).

1. Record changes in medical/ocular history and ocular and nonocular concomitant medications.
2. Perform manifest refraction.
   Note: UCDVA may be performed prior to manifest refraction.
   [Operative Eye Only]
3. Assess monocular UCDVA.
   [Operative Eye Only]
4. Assess monocular BCDVA.
   [Operative Eye Only]
5. Perform slit-lamp examination of the anterior segment. Include documentation of IOL observations, if applicable.
   [Operative Eye Only]
6. Assess subjective PCO, and record information for any posterior capsulotomy that has occurred since surgery, if applicable.
   [Operative Eye Only]
7. Observe any IOL position changes (ie, tilt and decentration) occurring since the previous visit. Refer to MOP for further detail.
8. Perform tonometry to measure the IOP. Refer to MOP for further detail.
9. Record any AEs including SSIs.
   Note: SAEs including SSIs must be entered into EDC within 24 hours of the Investigator or site's knowledge. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.
10. Record any device deficiencies. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.
11. Document the subject status (eg, continuing).

12.8 1-Month Post-implantation Visit (Visit 3A)

Below is a list of study procedures to be undertaken at Visit 3A (30-45 days post-implantation from second eye surgery). The order of procedures is recommended. All assessments must be documented in source documentation and eCRFs (if applicable).

1. Record changes in medical/ocular history and ocular and nonocular concomitant medications.
2. Perform manifest refraction.
   Note: UCDVA may be performed prior to manifest refraction.
   [Both eyes]
3. Assess monocular UCDVA.
   [Both eyes]
4. Assess monocular BCDVA.
   [Both eyes]
5. Assess biometry measures including AL, keratometry, and ACD.
   [Both eyes]
6. Perform slit-lamp examination of the anterior segment. Include documentation of IOL observations, if applicable.
   [Both eyes]

[redacted]

8. Assess subjective PCO, and record information for any posterior capsulotomy that has occurred since surgery, if applicable.
   [Both eyes]
9. Observe any IOL position changes (ie, tilt and decentration) occurring since the previous visit.
   [Both eyes]
10. Perform tonometry to measure the IOP.
    [Both eyes]
11. Record any AEs including SSIs.
    Note: SAEs including SSIs must be entered into EDC within 24 hours of the Investigator or site's knowledge. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.
12. Record any device deficiencies. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.
13. Document the subject status (eg, continuing).

12.9 4-6 Month Post-implantation Visit (Visit 4A)

Below is a list of study procedures to be undertaken at Visit 4A (120-180 days post-implantation from 2nd eye surgery). The order of procedures is recommended. All assessments must be documented in source documentation and eCRFs (if applicable).

1. Record changes in medical/ocular history and ocular and nonocular concomitant medications.
2. Perform manifest refraction.
   Note: UCDVA may be performed prior to manifest refraction.
   [Both eyes]
3. Assess monocular UCDVA.
   [Both eyes]
4. Assess monocular BCDVA.
   [Both eyes]
5. Assess biometry measures including AL, keratometry, and ACD.
   [Both eyes]
6. Perform slit-lamp examination of the anterior segment. Include documentation of IOL observations, if applicable.
   [Both eyes]

[redacted]

8. Assess subjective PCO, and record information for any posterior capsulotomy that has occurred since surgery, if applicable.
   [Both eyes]
9. Observe any IOL position changes (ie, tilt and decentration) occurring since the previous visit.
   [Both eyes]
10. Perform tonometry to measure the IOP.
    [Both eyes]
11. Perform fundus exam. Refer to MOP for further detail.
12. Record any AEs including SSIs.
    Note: SAEs including SSIs must be entered into EDC within 24 hours of the Investigator or site's knowledge. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.
13. Record any device deficiencies. Refer to Section 13 DEVICE DEFICIENCIES

AND ADVERSE EVENTS FOR FURTHER DETAIL.

14. Document the subject status (eg, continuing).

12.10 1-Year Post-implantation Visit (Visit 5A)

Below is a list of study procedures to be undertaken at Visit 5A (330-420 days post-implantation). The order of procedures is recommended. All assessments must be documented in source documentation and eCRFs (if applicable).

1. Record changes in medical/ocular history and ocular and nonocular concomitant medications.
2. Perform manifest refraction.
   Note: UCDVA may be performed prior to manifest refraction.
   [Both eyes]
3. Assess monocular UCDVA.
   [Both eyes]
4. Assess monocular BCDVA.
   [Both eyes]
5. Assess biometry measures including AL, keratometry, and ACD.
   [Both eyes]
6. Perform slit-lamp examination of the anterior segment. Include documentation of IOL observations, if applicable.
   [Both eyes]

8. Assess subjective PCO, and record information for any posterior capsulotomy that has occurred since surgery, if applicable.
   [Both eyes]
9. Observe any IOL position changes (ie, tilt and decentration) occurring since the previous visit.
   [Both eyes]
10. Perform tonometry to measure the IOP.
    [Both eyes]
11. Perform fundus exam. Refer to MOP for further detail.
12. Record any AEs including SSIs.
    Note: SAEs including SSIs must be entered into EDC within 24 hours of the Investigator or site's knowledge. Refer to Section 13 DEVICE DEFICIENCIES

AND ADVERSE EVENTS for further detail.

13. Record any device deficiencies. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.
14. Document the subject status (eg, continuing).

12.11 2-Year Post-implantation Visit (Visit 6A)

Below is a list of study procedures to be undertaken at Visit 6A (630-780 days post-implantation). The order of procedures is recommended. All assessments must be documented in source documentation and eCRFs (if applicable).

1. Record changes in medical/ocular history and ocular and nonocular concomitant medications.
2. Perform manifest refraction.
   Note: UCDVA may be performed prior to manifest refraction.
   [Both eyes]
3. Assess monocular UCDVA.
   [Both eyes]
4. Assess monocular BCDVA.
   [Both eyes]
5. Perform slit-lamp examination of the anterior segment. Include documentation of IOL observations, if applicable.
   [Both eyes]

[redacted]

7. Assess subjective PCO, and record information for any posterior capsulotomy that has occurred since surgery, if applicable.
   [Both eyes]
8. Observe any IOL position changes (ie, tilt and decentration) occurring since the previous visit.
   [Both eyes]
9. Perform tonometry to measure the IOP.
   [Both eyes, binocular]
10. Perform fundus exam. Refer to MOP for further detail.
11. Record any AEs including SSIs.
    Note: SAEs including SSIs must be entered into EDC within 24 hours of the

Investigator or site's knowledge. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.

12. Record any device deficiencies. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.
13. Document the subject status (eg, continuing).

12.12 3-Year Post-implantation Visit (Visit 7A/ Early Exit)

Below is a list of study procedures to be undertaken at Visit 7A (990-1140 days post-implantation) or if a subject exits the study early. The order of procedures is recommended. All assessments must be documented in source documentation and eCRFs (if applicable).

1. Record changes in medical/ocular history and ocular and nonocular concomitant medications.
2. Perform manifest refraction.
   Note: UCDVA may be performed prior to manifest refraction.
   [Both eyes]
3. Assess monocular UCDVA.
   [Both eyes]
4. Assess monocular BCDVA.
   [Both eyes]
5. Perform slit-lamp examination of the anterior segment. Include documentation of IOL observations, if applicable.
   [Both eyes]

[redacted]

7. Assess subjective PCO, and record information for any posterior capsulotomy that has occurred since surgery, if applicable.
   [Both eyes]
8. Observe any IOL position changes (ie, tilt and decentration) occurring since the previous visit.
   [Both eyes]
9. Perform tonometry to measure the IOP.
   [Both eyes]

10. Perform fundus exam. Refer to MOP for further detail.
11. Record any AEs including SSIs.
    Note: SAEs including SSIs must be entered into EDC within 24 hours of the Investigator or site's knowledge. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.
12. Record any device deficiencies. Refer to Section 13 DEVICE DEFICIENCIES AND ADVERSE EVENTS for further detail.
13. Complete Disposition status.

12.13 Unscheduled Visits

An unscheduled visit (USV) is defined as follows:

- an ocular examination that is not standard of care and not required by the protocol; and
- an examination conducted by the study staff; and
- a new finding(s), or a change to a previous finding(s) was discovered.

A USV may or may not result in the capture of an AE. Likewise an AE may be captured without the report of a USV (eg, AE identified subsequent to examination by non-study personnel). The assessments captured at the USV are dictated by the Investigator per his/her medical judgment. The following assessments are recommended:

- Concomitant medications
- Monocular UCDVA
- Slit-lamp exam
- IOL position change
- Subjective PCO assessment
- DFE
- IOP
- Adverse events
- Device deficiencies

Note: Assessments are not limited to the above list.

If the subject is discontinued at the USV, perform all Visit 7A/Early Exit procedures. Refer to Section 6 SCHEDULE OF VISITS. For safety purposes, if a USV is required after the final study visit, document the visit. Refer to Section 13.9 Follow-up of Safety Information for further detail.

12.14 Aborted Implantation

If the IOL implantation is attempted and aborted due to a Device Deficiency then a Device Deficiency form must be completed and the IOL must be returned to the Study Sponsor in appropriate safe packaging. Specific guidance with regards to aborted implantation is detailed in the MOP Table 5-1, Subject Status after Exclusion During Surgery.

12.15 Discontinued Subjects

Discontinued subjects withdraw, or are withdrawn from the study after signing consent, and prior to completing all study visits. Subjects signing consent, but withdrawing or withdrawn prior to surgery shall be considered discontinued due to screen failure, and the failed entry criterion documented in source documents and in EDC. Refer to Section 10 SUBJECT POPULATION.

Subjects may discontinue study participation at any time and for any reason. However, it is incumbent upon the Investigator to carefully select subjects who understand the commitment involved in participating in this clinical trial.

Subjects may be discontinued from the study at any time if, in the medical opinion of the Principal Investigator or designated, qualified medical personnel, continued participation poses a health risk to the subject, or other reasonable cause.

Subjects signing consent, but who voluntarily withdraw or are withdrawn by the Investigator prior to the final study visit shall be considered discontinued of study participation. For subjects discontinuing from the study, the Investigator should complete Exit procedures according to Section 12.12 3-Year Post-implantation Visit (Visit 7A/ Early Exit Visit), if the subject is willing and able, and if in the opinion of the Investigator it is safe for the subject to do so. The reason for discontinuation must be documented in source documents and in EDC. To ensure the safety of all subjects who discontinue early, Investigators must assess each subject and, if necessary, advise them of any therapies and/or medical procedures that may be needed to maintain their health.

Subject numbers from discontinued subjects will not be reissued. Discontinued subjects will not be replaced.

12.16 Subject Lost to Follow-up

If a subject is overdue for a visit and all efforts to contact the subject for an examination have failed, this subject is considered lost to follow-up. The Exit Case Report Form should not be completed until after the subject's last visit window closes, in case the subject is able to attend future visits. Any intermediate visits not attended will be considered Missed Visits.

12.17 Clinical Trial Termination

The Sponsor reserves the right to close an investigational site(s) or terminate the study in its entirety at any time, for reasonable cause. The Investigator also may terminate the study at his/her site for reasonable cause. Reasons for the closure of an investigational site or termination of a study may include:

- the Investigator fails to comply with the protocol or Good Clinical Practice (GCP) guidelines;
- inadequate recruitment of subjects by the Investigator; or
- subject safety concerns.

If the clinical study is prematurely terminated or suspended, the Sponsor will inform the Investigator and the regulatory authorities of the termination/ suspension and the reason(s) for the termination/suspension. The Investigator should promptly notify the IEC/IRB of the termination or suspension and of the reasons. If the Sponsor terminates the study for safety reasons, it will immediately notify the Investigator(s), and provide written instructions for study termination and applicable subject follow-up.

13 DEVICE DEFICIENCIES AND ADVERSE EVENTS

13.1 General Information

An Adverse Event (AE) is any untoward medical occurrence in a subject who is administered a clinical trial treatment (ie, implant with an investigational device) regardless of whether or not the event has a causal relationship with the treatment. An AE, therefore, can be any unfavorable or unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the clinical trial treatment, whether or not related to the treatment. Below are Figures that categorize AEs and SAEs.

Figure 13-1 Categorization of all Adverse Events

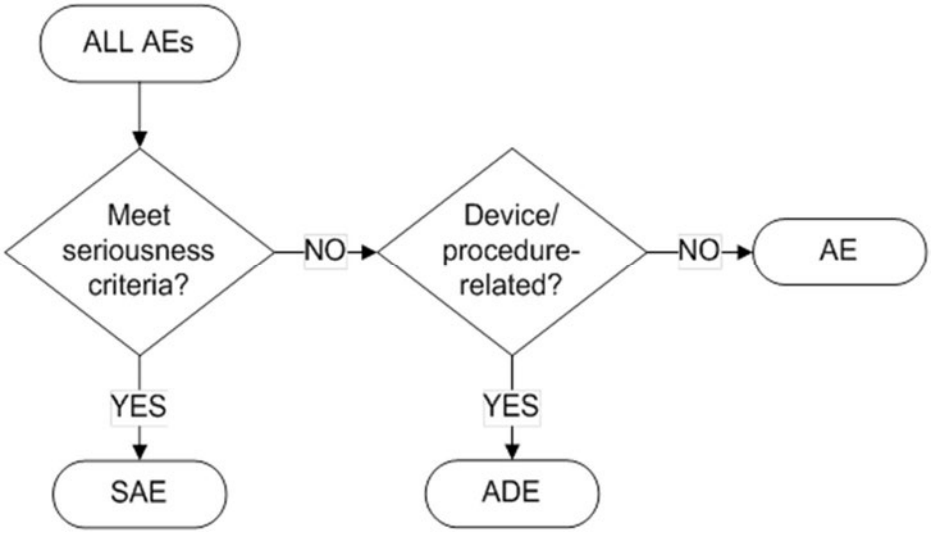
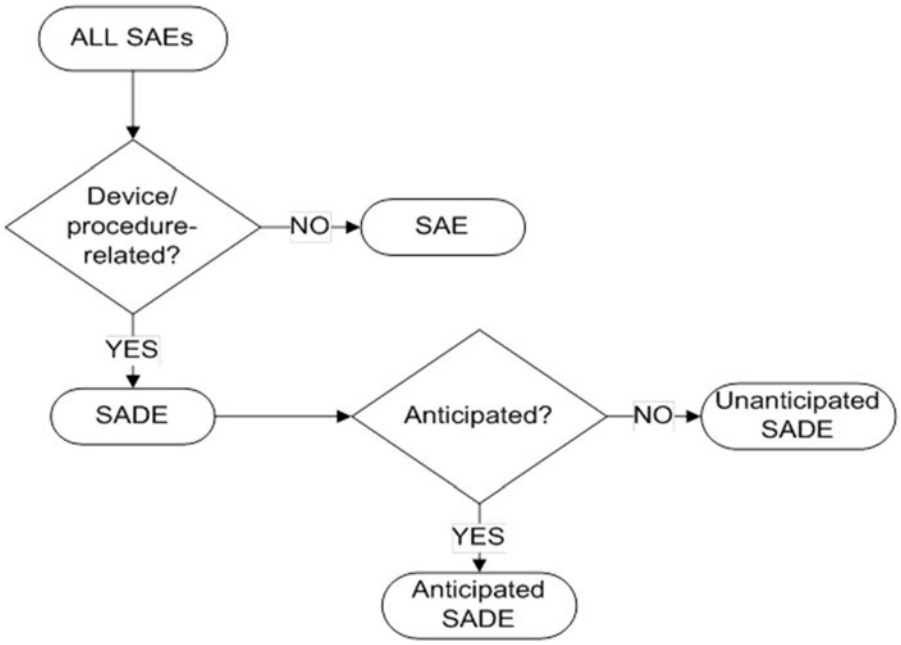


Figure 13–2 Categorization of all Serious Adverse Events



13.2 Serious Adverse Events (SAEs)

A serious adverse event is an AE that led to any of the following:

- Death
- A serious deterioration in the health of the subject that either resulted in:

  a) a life-threatening illness or injury.

  NOTE: *Life-threatening means that the individual was at immediate risk of death from the event as it occurred, ie, it does not include an event which hypothetically might have caused death had it occurred in a more severe form.*

  b) any potentially sight-threatening event or permanent impairment to a body structure or a body function.

  c) in-patient hospitalization or prolonged hospitalization.

  NOTE: *Planned hospitalization for a pre-existing condition, without serious deterioration in health, is not considered a SAE. In general, hospitalization signifies*

that the individual remained at the hospital or emergency ward for observation and/or treatment (usually involving an overnight stay) that would not have been appropriate in the physician's office or an out-patient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred, the event should be considered serious.

d) a medical or surgical intervention to prevent a) or b) or any ocular secondary surgical intervention (excluding PC).

e) any indirect harm as a consequence of incorrect diagnostic test results when used within manufacturer's instructions for use.

- Fetal distress, fetal death, or a congenital abnormality or birth defect.

Potentially sight-threatening events may also be considered serious based on the judgment of the Investigator and should be reported appropriately as delineated in Section 13.7 Procedures for Recording and Reporting.

13.2.1 Cumulative Serious Adverse Events

Total number of Adverse Events that have occurred at any time up to a specified time point postoperatively.

- Cystoid macular edema
- Hypopyon
- Endophthalmitis
- Lens dislocation from posterior chamber
- Pupillary block
- Retinal detachment
- Secondary surgical intervention (excluding PC)

13.2.2 Persistent Serious Adverse Events

- Corneal stromal edema
- Cystoid macular edema

- Iritis
- Raised IOP requiring treatment

This list is consistent with the categories provided in EN ISO 11979-7:2014. A persistent AE is an AE that is present at the conclusion of a clinical investigation per EN ISO 11979-7:2014. Any other potentially sight-threatening event may also be considered serious based on the judgement of the Investigator and must be reported appropriately as delineated in Section 13.2. Serious Adverse Events (SAEs).

13.3 Device Deficiencies

A device deficiency may or may not be associated with subject harm (ie, ADE or SADE); however, not all ADEs or SADEs are due to a device deficiency. The Investigator should determine the applicable category for the identified or suspect device deficiency and report any subject harm separately. Examples of device deficiencies include the following:

- Failure to meet product specifications (eg, incorrect IOL power)
- IOL defect
- Broken IOL optic
- Broken IOL haptic
- Scratched IOL optic
- Unsealed device packaging
- Suspect product contamination
- Lack of effectivity

13.4 Supportive Characterization of Ocular Adverse Events

Additional supportive characterizations of ocular adverse events will be assessed by the Investigator according to the terms and definitions in Section 18, APPENDICES, Table 18-1.

13.5 Secondary Surgical Interventions (SSI)

Secondary surgical interventions reporting will be sub-categorized using the following terminology: exchange, removal, and repositioning. Indications and associated definitions for these outcomes are provided in Section 18, APPENDICES, Table 18-2.

13.6 Monitoring for Adverse Events

At each visit, after the subject has had the opportunity to spontaneously mention any problems, the Investigator should inquire about AEs by asking the standard questions such as:

- "Have you had any health problems since your last study visit?"
- "Have there been any changes in the medicines you take since your last study visit?"

Changes in any protocol-specific ocular or systemic parameter evaluated during the study are to be reviewed by the Investigator. In addition, the subject's responses to any questionnaire utilized during the study are to be reviewed by the Investigator. Any untoward (unfavorable and unintended) change in a protocol-specific parameter or questionnaire response that is clinically relevant, in the opinion of the Investigator, is to be reported as an AE. These clinically relevant changes will be reported regardless of causality.

13.7 Procedures for Recording and Reporting

AEs are collected from the time of informed consent. Any pre-existing medical conditions or signs/symptoms present in a subject prior to the start of the study (ie, before ICF is signed) are not considered AEs in the study and should be recorded in the Medical History section of the eCRF.

In addition, aqueous cells and flare, corneal edema, raised IOP and superficial punctate keratitis are examples of early post-operative findings that are typically observed following ocular surgery. These are not considered AEs if they can be reasonably expected to resolve within a week and not result in any untoward long term visual outcome impact.

For each recorded event, the ADEs and SAEs documentation must include: date of occurrence, severity, treatment (if applicable), outcome, and assessments of the seriousness and causality. In addition, the Investigator must document all device deficiencies reported or observed with test and control articles on the Device Deficiency eCRF. The site must submit all available information on ADEs, SAEs, and device deficiencies to the Study Sponsor immediately as follows:

- **ADEs or SAEs are documented on the Adverse Device Effect and Serious Adverse Event eCRF within 24 hours of the Investigator's or site's awareness.**

- **Device deficiencies are documented on the Device Deficiency eCRF within 24 hours of the Investigator's or site's awareness. Please include a printed copy of the completed Device Deficiency eCRF with product returns.**
- **Additional relevant information after initial reporting is to be entered into the eCRF as soon as the data become available.**
- **Document any changes to concomitant medications on the appropriate eCRFs.**
- **All relevant documentation such as Discharge Summary, Autopsy Report, Certificate of Death, etc, should be faxed to the Study Sponsor at 1-817-302-1927.**
- **USADEs must be reported to the IRB/IEC as soon as possible, but not later than 10 working days after the investigator's or site's awareness.**

NOTE: Should the EDC system become non-operational, the site must complete the appropriate paper Adverse Device Effect and Serious Adverse Event Form or Device Deficiency Form. The completed form is faxed to the Study Sponsor at 1-817-302-1927 or emailed to FTW.medical_safety@alcon.com within 24 hours of the Investigator's or site's awareness; however, the reported information must be entered into the EDC system once it becomes operational.

Any AEs and device deficiencies for non-study marketed devices/products (ie, BSS, OVD, delivery systems) will be considered and processed as spontaneous (following the post-market vigilance procedures) and should be communicated to the device's/product's manufacturer as per local requirements.

Study Sponsor representatives and their contact information are provided in the Manual of Procedures that accompanies this protocol.

Further, depending upon the nature of the AE or device deficiency being reported, the Study Sponsor may request copies of applicable portions of the subject's medical records. The Investigator must also report all AEs and device deficiencies that could have led to a SADE according to the requirements of regulatory authorities or IEC/IRB.

Intensity and Causality Assessments

For every AE and device deficiency, the Investigator must assess the causality as Related or Not Related to the medical device or test procedure in the study. An assessment of causality

will also be performed by a study Sponsor physician utilizing the same definitions, as shown below:

Causality

Related	An AE or device deficiency classified as related may be either definitely related or possibly related where a direct cause and effect relationship with the medical device or test procedure has not been demonstrated, but there is a reasonable possibility that the AE or device deficiency was caused by the medical device or test procedure.
Not Related	An AE or device deficiency classified as not related may either be definitely unrelated or simply unlikely to be related (ie, there are other more likely causes for the AE or device deficiency).

Where appropriate, the Investigator must assess the intensity (severity) of the AE as mild, moderate, or severe, based on medical judgment with consideration of any subjective symptom(s), as defined below:

Intensity (Severity)

Mild	An AE is mild if the subject is aware of but can easily tolerate the sign or symptom.
Moderate	An AE is moderate if the sign or symptom results in discomfort significant enough to cause interference with the subject's usual activities.
Severe	An AE is severe if the sign or symptom is incapacitating and results in the subject's inability to work or engage in their usual activities.

The Investigator must document any action taken (ie, medication, intervention, or treatment plan) and outcome of the AE or device deficiency when applicable.

13.8 Unmasking of the Study Information

Not applicable.

13.9 Follow-up of Safety Information

The Investigator is responsible for adequate and safe medical care of subjects during the study and for ensuring that appropriate medical care and relevant follow-up procedures are maintained after the study.

The Investigator must provide the Study Sponsor with any new safety information (which includes new AEs and changes to previously reported AEs) that may affect the safety evaluation of the device. For AEs that are unresolved/ ongoing at time of subject exit from study, any additional information received at follow-up should be documented in the eCRFs up to study completion (ie, database lock).

Any additional data from these follow-up procedures performed up to 6 months after subject discontinuation or exit must be documented and available upon the Study Sponsor's request. All complaints received after this time period will be considered and processed as spontaneous (following the postmarket vigilance procedures) and should be communicated to the medical device's manufacturer as per local requirements.

The Investigator should also report complaints on non-Alcon products directly to the manufacturer as per the manufacturer's instructions or local regulatory requirements.

14 DATA REVIEW AND HANDLING

14.1 Subject Confidentiality

The Investigator must ensure that the subject's anonymity is maintained throughout the course of the study. In particular, the Investigator must keep an enrollment log with confidential identifying information that corresponds to the subject numbers and initials of each study participant. At the end of the clinical study, the Study Sponsor will collect a copy of the enrollment log **without any identifying subject information**. All documents submitted to the Study Sponsor will identify the subjects exclusively by number and demographic information. No other personally identifying information will be transmitted to the Study Sponsor.

The Study Sponsor may release anonymized study data to external researchers for purposes of future research directly related to the study objectives, or future research that is beyond the scope of the current study objectives. The ICF explains this to study subjects. Anonymization means that all identifiable information will be removed from the dataset and all links to the subjects in the study will be removed. Anonymization of the data will maintain

confidentiality of the subjects who participate in the study so that they cannot be identified by external researchers. The anonymized data set will contain records from all of the subjects in the current study, but the anonymization process might change the data set in some ways, so external researchers will be informed that they might not be able to duplicate some of the results from this study.

External researchers who request permission to use anonymized data from studies for a new medicine or new indication of a medicine (studies for approved medicinal products, small molecule generics, and devices are excluded) must be approved by a central independent review panel that will adjudicate the scientific request and the competency of the external researcher(s), as well as determine the applicability to current standard operating procedures (SOPs). If approved, a data sharing agreement will be executed between the Study Sponsor and the external researcher(s), committing to a specified analysis and publication timeline. Anonymized data will be released to external researchers only after European Union (EU) and/or United States (US) submission of the investigational drug/biologic for the study indication. The Study Sponsor will not be able to influence the analyses that are performed by external researchers using the data from this study once the anonymized data are released.

14.2 Completion of Source Documents and Case Report Forms

The nature and location of all source documents will be identified to ensure that original data required to complete the electronic case report forms (eCRFs) exists and are accessible for verification by the Clinical Site Manager (CSM). It is required that the author of each entry in the source documents be identifiable (eg, initials or signature and date). At a minimum, source documents should include the following information for each subject:

- Subject identification (name, date of birth or age, sex)
- Documentation of subject eligibility
- Date of informed consent
- Dates of visits
- Documentation that protocol-specific procedures were performed
- Results of study testing, as required by the protocol
- Test article accountability records
- Documentation of SAEs and other safety parameters (as applicable)

- Records regarding medical histories and the use of concomitant therapies prior to and during the study
- Date of study completion and reason for early discontinuation, if applicable

Note: If electronic source records are maintained, the method of verification must be determined in advance of starting the study.

It is required that the author of an entry in the source documentation be identifiable. Direct access to source documentation (medical records) must be allowed for the purpose of verifying that the data recorded on the eCRF are consistent with the original source data. Data reported on the eCRFs shall be derived from source documents and be consistent with these source documents, and any discrepancies shall be explained in writing. Any change or correction to data reported on a source document shall be dated, initialed, and explained if necessary, and shall not obscure the original entry (ie, an audit trail shall be maintained); this applies to both written and electronic changes and corrections. eCRFs shall be signed and dated by the Principal Investigator or his/her authorized designee(s).

14.3 Data Review and Clarifications

Upon completion of the eCRFs, targeted data will be reviewed by the assigned Sponsor global CSM team for accuracy and completeness. The planned source document verification and overall monitoring activities for this study are outlined in a separate document, the Protocol Monitoring Plan. Corrections and/or any necessary additions to the data will be applied and if required, queries will be generated. Designated investigative staff are expected to respond to data queries in a timely manner and ensure that the corrections and changes made to the data are reflected in the subjects' source documentation.

Deviations from this protocol, regulatory requirements and GCP must be recorded. An explanation of the deviation should be included, as applicable. In addition, corrective and preventive action should be identified, implemented and documented within the study records. Prior to study start, a plan for data validation will be completed by Alcon clinical data management, and agreed upon by the study clinical manager (CM) and other team members.

Concomitant medications entered into the database will be coded using the WHO Drug Reference List. Medical history and adverse events will be coded using the medical dictionary for regulatory activities (MedDRA) terminology. Upon completion of the study and once the database is declared completed and accurate, the database will be locked and

data will be available for data analysis. Any changes to the database after lock will be implemented upon agreement between the Sponsor's clinical trial management, medical safety clinical data management and biostatistics departments, and will be completed following the Sponsor's procedures for changes to a database after database lock.

14.4 Quality Assurance and Quality Control

The Study Sponsor will secure agreement from all involved parties to ensure direct access to all study related sites, source data and documents, and reports for the purpose of monitoring and auditing by the Study Sponsor, and inspection by domestic and foreign regulatory authorities. Quality control will be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly. Agreements made by the Study Sponsor with the Investigator/Institution and any other parties involved in the clinical study will be provided in writing as part of the protocol or as a separate agreement.

15 ANALYSIS PLAN

15.1 Subject Evaluability

The final subject evaluability will be determined prior locking the database.

15.2 Analysis Data Sets

The primary analysis set for effectiveness analyses will be the All-Implanted Analysis Set (AAS). AAS includes all eyes with successful test article implantation. [redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]

The Safety Analysis Set will include all eyes with attempted implantation with the test article (successful or aborted after contact with the eye) and will be used for the safety analyses.

15.3 Demographics and Baseline Characteristics

Summary statistics will be provided for demographic and baseline characteristics. Number and percentage will be presented for categorical variables and descriptive statistics including mean, standard deviation, minimum, and maximum will be presented for continuous variables.

15.4 Performance Analyses

15.4.1 Primary Performance

The number and percentage of subjects with BCDVA of 0.3 logMAR or better at 1 year postoperative (Visit 5A) will be summarized along with the corresponding one-sided exact 95% upper confidence limit.

The performance target in support of the primary effectiveness objective is to show that the one-sided exact 95% upper confidence limit for the percentage of subjects with monocular BCDVA of 0.3 logMAR or better at 1 year postoperative (Visit 5A) is not worse than the SPE rate of 92.5% for AAS (as reported in EN ISO 11979-7:2014).

15.4.1.1 Statistical Hypotheses

Not applicable.

15.4.1.2 Analysis Methods

Categorical statistics (sample size, number in the category, percent in the category, and the corresponding one-sided exact 95% upper confidence limit) will be provided for the primary endpoint. In addition, descriptive statistics (sample size, mean, median, standard deviation, number of subjects/eyes, minimum, maximum, and the two-sided 95% confidence interval) will be provided for BCDVA.

15.4.2 Secondary Performance

The secondary effectiveness endpoints are:

- Percentage of subjects achieving BCDVA of 0.3 LogMAR or better at 2 years post-implantation (Visit 6A)
- Percentage of subjects achieving BCDVA of 0.3 LogMAR or better at 3 years post-implantation (Visit 7A)

- UCDVA at 1 year (Visit 5A) post-implantation
- UCDVA at 2 years (Visit 6A) post-implantation
- UCDVA at 3 years (Visit 7A) post-implantation

15.4.2.1 Statistical Hypotheses

Not applicable. Only descriptive statistics will be presented.

15.4.2.2 Analysis Methods

For categorical parameters, the statistics used to summarize the data descriptively include sample size, number in the category, and percent in the category. For continuous parameters, the statistics used to summarize the data descriptively include sample size, mean, median, standard deviation, number of subjects/eyes minimum, and maximum.

15.4.3.2 Analysis Methods

For categorical parameters, the statistics used to summarize the data descriptively include sample size, number in the category, and percent in the category. For continuous parameters, the statistics used to summarize the data descriptively include sample size, mean, median, standard deviation, number of subjects/eyes minimum, and maximum.

15.5 Handling of Missing Data

The AAS [redacted] do not include any imputed values. Although missing data will occur, the influence of the missing data is expected to be minimal.

[redacted]

15.7 Safety Analysis

The primary safety objective is to evaluate the safety of the Clareon IOL for first and second operative eyes separately up to 3 years (Visit 7A).

Adverse Events

Descriptive statistics for adverse events will be presented separately for first and second eyes. The one-sided exact 95% lower confidence limits for incidence rates observed up to one year of follow-up (ie, after all implanted subjects have completed Visit 5A) will be compared to the cumulative and persistent adverse event SPE rates in EN ISO 11979-7:2014. An eye with multiple ocular adverse events of the same preferred term is only counted once toward the total of this preferred term. All information obtained on adverse events will be displayed by subject.

Other Safety Assessments

All other safety assessments (such as device deficiencies, surgical problems, other procedures during surgery, IOP, slit-lamp examination, IOL observations, IOL position change, subjective PCO, posterior capsulotomy, and DFE) will be summarized with descriptive statistics. For categorical parameters, the statistics used to summarize the data descriptively include sample size, number in the category, and percent in the category. For continuous parameters, the statistics used to summarize the data descriptively include sample size, mean, median, standard deviation, minimum, and maximum.

[redacted]

15.9 Sample Size Justification

If more than 110 of 125 eyes show monocular BCDVA of 0.3 logMAR or better at 1 year (Visit 5A), the one-sided exact 95% upper confidence limit for the rate is not worse than SPE rate of 92.5%. Assuming that the mean and the standard deviation of monocular BCDVA are 0.0 and 0.18 logMAR respectively, the study has greater than 99% chance to meet this performance target.

For any event where zero incidence is observed in 125 first-operative eyes with Clareon IOL, the one-sided exact 95% upper confidence limit for the adverse event rate is less than 2.4%. Thus, with 95% confidence, the true adverse event rate is less than 2.4%.

Approximately 200 subjects will be bilaterally implanted with the Clareon IOL in order to ensure at least 125 evaluable subjects complete the study.

16 ADMINISTRATIVE PROCEDURES

16.1 Regulatory and Ethical Compliance

This clinical trial will be conducted in accordance with the ethical principles contained within the following:

- the Declaration of Helsinki (DoH), and in compliance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) E6 GCP Consolidated Guideline
- ISO 14155:2011 Clinical investigation of medical devices for human subjects, Good Clinical Practice
- Code of Federal Regulations (CFR), and all other applicable regulations
- Standard Operating Procedures of Alcon

The Investigator and all clinical trial staff will conduct the clinical trial in compliance with this protocol. The Investigator will ensure that all personnel involved in the conduct of the clinical trial are qualified to perform their assigned duties through relevant education, training, and experience.

16.2 Informed Consent Procedures

Voluntary informed consent will be obtained from every subject prior to the initiation of any screening or other clinical trial-related procedures. The Investigator must have a defined process for obtaining consent. Specifically, the Investigator, or designee, will explain the clinical trial to each potential subject and the subject must indicate voluntary consent by signing and dating the approved informed consent form. The subject must be provided an opportunity to ask questions of the Investigator, and if required by local regulation, other qualified personnel. The Investigator must provide the subject with a copy of the consent form written in a language the subject understands. The consent document must meet all applicable local laws and will provide subjects with information regarding the purpose, procedures, requirements, and restrictions of the clinical trial, along with any known risks and potential benefits associated with the investigational product, the available compensation, and the established provisions for maintaining confidentiality of personal, protected health information. Subjects will be told about the voluntary nature of participation in the clinical trial and will be provided with contact information for the appropriate individuals should questions or concerns arise during the clinical trial. The subject also will be told that their

records may be accessed by appropriate authorities and Sponsor-designated personnel. The Investigator must keep the original, signed copy of the consent and must provide a duplicate copy to each subject.

16.3 Responsibilities of the Investigator and IRB/IEC

Before clinical trial initiation, this protocol, the informed consent form, any other written information provided to subject, and any advertisements planned for subject recruitment must be approved by an Institutional Review Board / Independent Ethics Committee (IRB/IEC). Documentation of IRB/IEC approval must be provided to the Sponsor by the Investigator or IRB/IEC. The approval must be dated and must identify the applicable protocol, amendments (if any), informed consent form, assent form (if any), all applicable recruiting materials, written information for subjects, and subject compensation programs (if any). The IRB/IEC must be provided with a copy of the DFU, any periodic safety updates, and all other information as required by local regulation and/or the IRB/IEC. At the end of the clinical trial or in the case of early termination, the Investigator or Sponsor will notify the IRB/IEC of the clinical trial's final status. Finally, the Investigator or Sponsor will report to the IRB/IEC on the progress of the clinical trial at intervals stipulated by the IRB/IEC.

16.4 Sponsor and Monitoring Responsibilities

The Sponsor will designate a monitor to conduct the appropriate site visits at the appropriate intervals. The clinical investigation will be monitored, following the Protocol Monitoring Plan, to ensure that: the rights and well-being of the subjects are protected; the reported data are accurate, complete, and verifiable from the source documents; the equipment used to assess variables in the clinical investigation is maintained and calibrated per manufacturer instructions and Sponsor requirements; the study is conducted in compliance with the current approved protocol (and amendment[s], if applicable), with current GCP, and with applicable regulatory requirements.

All investigative sites must have a site initiation. Prior to screening subjects or performing the informed consent process on any subject, the site must receive a Site Activation Notification from an appropriate study Sponsor representative. Monitoring will be conducted periodically while the clinical study is ongoing. Monitoring methods may include site visits, telephone and written correspondence. Closeout visits will take place after the last visit of the last subject or after the database lock.

16.5 Regulatory Documentation and Records Retention

Essential documents must be retained by the Investigator in compliance with the medical device directive and its local transposition as well as other applicable national and international regulations. The Investigator(s)/institution(s) must comply with record retention stipulations outlined in the Clinical Study Agreement. Additionally the Investigator will be supplied with further instruction at study completion.

16.6 Clinical Trial Results

The Investigator or the Sponsor will notify the IRB/IEC of the end of the study. The end of the study is defined as database lock. In case the study is ended prematurely, the Investigator or the Sponsor will notify the IRB/IEC, including the reasons for the premature termination. Within one year after the end of the study, the Investigator or the sponsor will submit a final study report with the results of the study, including any publications/abstracts of the study, to the IRB/IEC as required.

The Study Sponsor assures that the key design elements of this protocol will be registered in www.clinicaltrials.gov as required by current regulations and, if applicable, other public databases as required by local country regulations. In addition, results of this study will be made publicly available in www.clinicaltrials.gov regardless of outcome as required by current regulations and, if applicable, in other public databases as required by local country regulations.

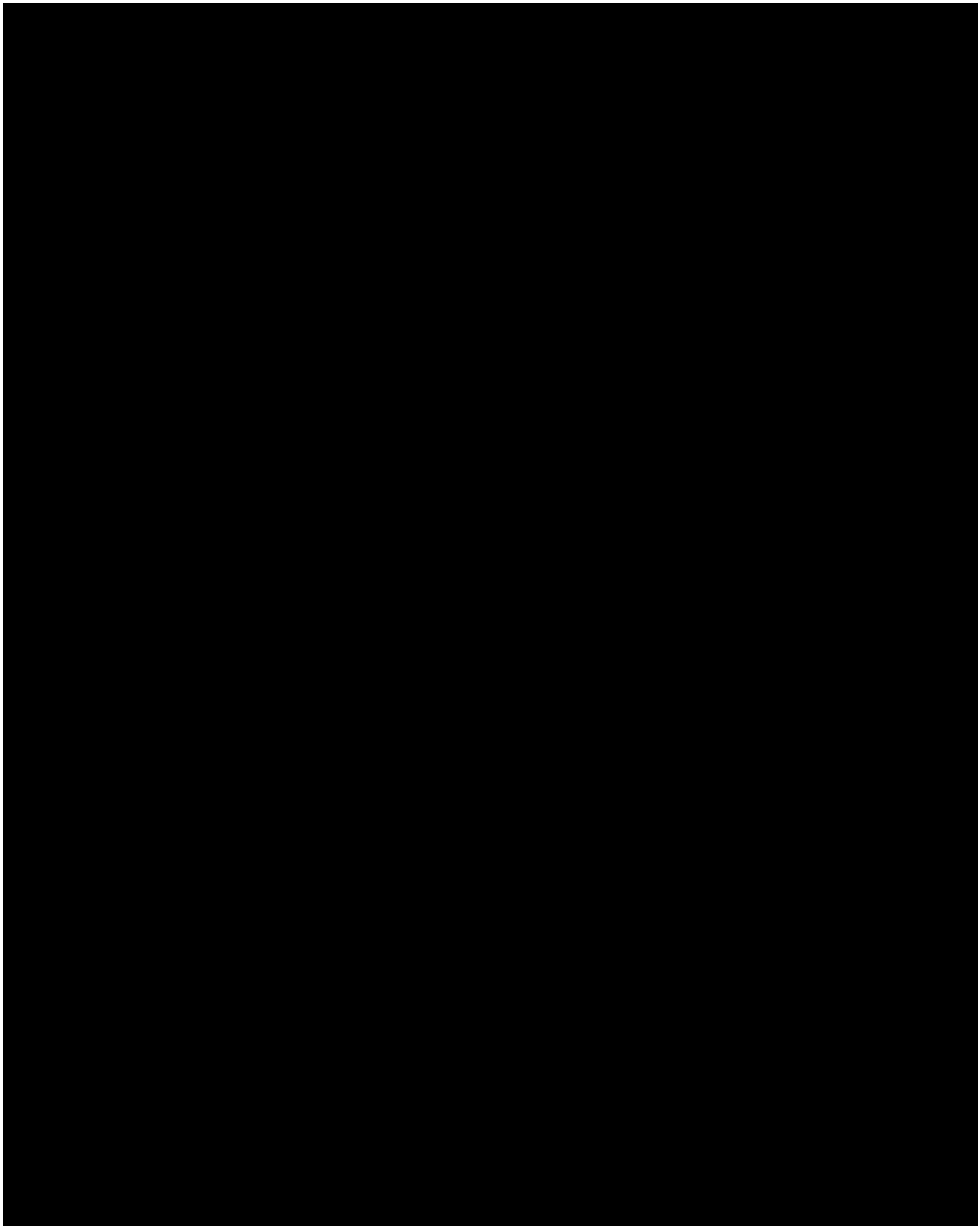
17 REFERENCES

EN ISO 11979-7:2014 Ophthalmic implants – Intraocular lenses – Part 7: Clinical Investigations

Isotani H, Fukumoto Y, Kitaoka H, Furukawa K, Ohsawa N, Utsumi T. Oval pupil in patients with diabetes mellitus: examination by measurement of the dark-adapted pupillary area and pupillary light reflex. Diabetes Res Clin Pract. 1995;29:43-8.

Masket S, Rorer E, Stark W, Holladay J, MacRae S, Tarver ME, et al. Special report: the Academy of Ophthalmology Task Force consensus statement on adverse events with intraocular lenses. Ophthalmology. 2017;124(1):142-4.

[redacted]



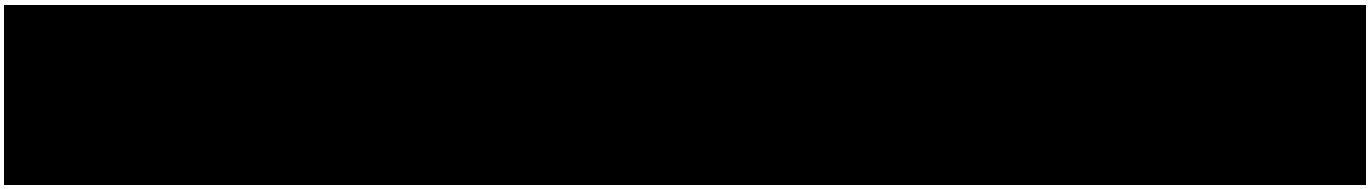


Table 18–1 Postoperative Adverse Event Definitions for Intraocular Events (Masket 2017)

Adverse Event	Definition
Chronic anterior uveitis	Persistent anterior segment inflammation characterized by grade 1+ cell or greater using SUN criteria[3], that is persistent for greater than 3 months after surgery, or relapses in less than 3 months after discontinuation of therapy, or the subject is maintained on therapy for more than 3 months to control inflammation.
Clinically significant cystoid macular edema	Macular edema diagnosed by clinical examination and adjunct testing (eg, OCT, FA) resulting in BCDVA of ≤ 20/40 at ≥ 1 month
Corneal edema	Corneal swelling (stromal or epithelial) resulting in BCDVA of ≤ 20/40 at ≥ 1 month
Endophthalmitis	Intraocular inflammation requiring diagnostic vitreous tap and intraocular antibiotics
Mechanical pupillary block	Shallowing of anterior chamber due to obstruction of aqueous humor flow from the posterior to anterior chamber through the pupil by the crystalline lens, vitreous face, or implanted device
Increased IOP	Elevation of IOP by ≥10 mmHg above baseline to a minimum of 25 mmHg
Rhegmatogenous RD	Partial or complete RD associated with retinal tear
Toxic anterior segment syndrome	Acute, noninfectious inflammation of the anterior segment that starts within 24 hours after surgery, usually resulting in hypopyon and commonly presenting with corneal edema, that improves with steroid treatment
Secondary IOL intervention	
Exchange	The investigational device is replaced with the same lens model.
Removal	The investigational device is removed and replaced with a non-investigational lens or no lens is implanted
Reposition	The existing IOL is surgically moved to another location or rotated

Table 18-2 Definitions of Indications for Device Exchange, Removal, or Reposition (Masket 2017)

Indication	Definition
Capsular block syndrome	Hyper-distention of the lens capsular bag due to the IOL optic blocking egress of fluid through the anterior capsulotomy typically inducing a myopic refractive error
Cataract	Any opacification of the crystalline lens with or without reduced visual acuity
Chronic anterior uveitis	Persistent anterior segment inflammation characterized by grade ≥ 1+ cell using SUN criteria (Isotani 1995)
Endothelial cell loss	Chronic endothelial cell loss at a rate greater than that due to normal aging
Incorrect IOL power	Postoperative refractive error different from predicted and not due to a calculation or other user error
Iris pigment epithelium loss*	New or worsening iris transillumination defects or increase in pigmented cells in the anterior chamber noted after the 1-wk visit when assessed before instillation of any dilating drops
Lens optic abnormality	Unanticipated visual outcome (eg, acuity, contrast sensitivity, symptoms) associated with opacification, vacuoles, microvacuoles, or subsurface nanoglistenings and not due to other causes
Malpositioned IOL Early Late	Decentration, tilt, or rotation of IOL requiring reoperation. [redacted] If noted before 120 days postoperatively If noted at ≥ 120 days postoperatively
Damaged IOL	Crack of lens optic, breakage, or deformity of haptic, or other damage to the IOL; [redacted]
Pupil ovalization	Progressive deformation of the pupil with elongation of the pupil in the meridian of the long axis of the IOL Documentation to be made under photopic conditions Appendix 1 (Masket 2017)
Pain	Graded as ≥ 4 on the standardized pain numeric rating scale of current pain intensity from 0 (no pain) to 10 (worst possible pain)
Peripheral anterior synechiae	Progressive closure of the anterior chamber angle due to propagation of anterior synechiae in the absence of obvious anterior uveitis
Patient-reported undesirable optical phenomena	Dysphotopsia (positive or negative or both), monocular diplopia, intolerable glare, halos, or other visual symptoms, not due to 1 of the indications listed

*If there is a transillumination defect preoperatively, then a photograph should be taken, and then at each subsequent visit, a photograph should be taken and compared with the preoperative photograph via a standardized photographic method.

[redacted]
