PMCF Evaluation of Clareon Vivity/Vivity Toric

STUDY ID

ILE632-C002

PROTOCOL

Version 1

13-Mar-2023

NCT05852470

Device Protocol for ILE632-C002

Title: PMCF Evaluation of Clareon Vivity/Vivity Toric

Protocol Number:	ILE632-C002
Clinical Investigation Type:	Post market Interventional
Test Product:	Clareon™ Vivity/Vivity Toric Extended Vision IOLs (CNWET0, CNWET3-T6, CCWET0, CCWET3-T6)
Sponsor Name and Address:	Alcon Research, LLC, and its affiliates (“Alcon”) 6201 South Freeway Fort Worth, Texas 76134-2099

Investigator Agreement:

- I have read the clinical study described herein, recognize its confidentiality, and agree to conduct the described study in compliance with Good Clinical Practices; applicable international and national regulations, laws, guidelines, and standards; the conditions of approval imposed by the reviewing IRB or regulatory authority; and in accordance with the ethical medical research principles outlined in the Declaration of Helsinki.
- I will supervise all testing of the device involving human subjects and ensure that the requirements relating to obtaining informed consent and IRB review and approval are met in accordance with applicable local and governmental regulations.
- I have read and understand the appropriate use of the investigational product(s) as described in the protocol, current investigator's brochure, product information, or other sources provided by the sponsor.
- I understand the potential risks and side effects of the investigational product(s).
- I agree to maintain adequate and accurate records in accordance with government regulations and to make those records available for inspection.
- I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements of the sponsor and government agencies.
- I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed of their obligations in meeting the above commitments.

Have you ever been disqualified as an investigator by any Regulatory Authority? ☐ No ☐ Yes
Have you ever been involved in a study or other research that was terminated? ☐ No ☐ Yes If yes, please explain here:

Principal investigator:

Signature Date

Name and professional position:

Address:

Table of Contents

List of Tables

List of Figures

1 GLOSSARY OF TERMS

Names of Test Product(s)	Throughout this document, test product(s) will be referred to as Clareon Vivity/Vivity Toric IOL(s).
Name of Comparator Product(s)	Throughout this document, comparator product(s) will be referred to as Clareon/Clareon Toric Aspheric IOL(s)
Adverse Device Effect (ADE)	Adverse event related to the use of an investigational medical device or comparator. *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.*
Adverse Event (AE)	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 or comparator and whether anticipated or unanticipated. *Note: For subjects, this definition includes events related to the investigational medical device, comparator, or the procedures involved. For users or other persons, this definition is restricted to the use of the investigational medical device or comparator.* Requirements for reporting Adverse Events in the study can be found in Section 11.
Anticipated Serious Adverse Device Effect (ASADE)	An effect which by its nature, incidence, severity, or outcome has been identified in the risk assessment.
Clinical Investigation Plan (CIP)	The document(s) stating the rationale, objectives, design, and prespecified analysis, methodology, organization, monitoring, conduct, and record-keeping of the clinical investigation.

	Note: The protocol and other documents referenced in the protocol (for example, the Statistical Analysis Plan, the Manual of Procedures, the Deviations and Evaluability Plan, and the Protocol Monitoring Plan) comprise the CIP.
Clinical Investigation Report (CIR) / Clinical Study Report	The document describing the design, execution, statistical analysis, and results of a clinical investigation. The Clinical Investigation Report is synonymous with the Clinical Study Report.
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety, or performance. *Note: This definition includes malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling related to the investigational medical device or the comparator.* Requirements for reporting Device Deficiencies in the study can be found in Section 11.
Enrolled Subject	Any subject who signs an informed consent form for participation in the study.
Point of Enrollment	The time at which, following recruitment and before any clinical investigation-related procedures are undertaken, a subject signs and dates the informed consent form.
Interventional Clinical Study	A pre- or postmarket clinical investigation where the assignment of a subject to a particular medical device is decided in advance by a clinical investigation plan, or diagnostic or monitoring procedures requested in the CIP are in addition to those available as normal clinical practice and burden the subject.
Investigational Product	A preventative (vaccine), a therapeutic (drug or biologic), device, diagnostic, or palliative used as a test or comparator product in a clinical study, including a product with a marketing authorization when used or assembled

	(formulated or packaged) in a way different from the authorized form, or when used for an unauthorized indication, or when used to gain further information about the authorized form.
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 (CIP), or investigator's brochure (IB).
Nonserious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.
Postmarketing / Postauthorization study	Any study conducted within the conditions laid down in product labelling and other conditions laid down for the marketing of the product or under normal conditions of use. A postmarketing study falls either within the definitions of an interventional or a noninterventional study and may also fall within the definition of a postapproval study.
Product Complaint	Any oral, electronic, or written communication that alleges deficiencies related to the identity (labeling), quality, durability, reliability, safety, effectiveness, or performance of a marketed product, including failure of the product, labeling, or packaging to meet specifications, whether or not the product is related to or caused the alleged deficiency. A complaint may allege that an adverse event or medical device malfunction has occurred.
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 the health of the subject, users or other persons as defined by one or more of the following:

	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, i.e., 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 including chronic diseases. c) inpatient hospitalization or prolonged hospitalization. d) a medical or surgical intervention to prevent a) or b). This includes 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, congenital abnormality or birth defect including physical or mental impairment. *Note: Planned hospitalization for a preexisting condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.* *Refer to Section 11 for additional SAEs.*
Serious Health Threat	Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users, or other persons, and that requires prompt remedial action for other subjects, users, or other persons. *Note: This would include events that are of significant and unexpected nature such that they become alarming as a*

	potential serious health hazard or possibility of multiple deaths occurring at short intervals.
Study Start	The start of the study is considered to coincide with the enrollment of the first patient.
Study Completion	The completion of the study is considered to coincide with the study-level last subject last visit or the decision to terminate the study, whichever is later.
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 assessment.
Use Error	User action or lack of user action while using the medical device that leads to a different result than that intended by the manufacturer or expected by the user. *Note:* *a) Use error includes the inability of the user to complete a task.* *b) Use errors can result from a mismatch between the characteristics of the user, user interface, task, or use environment.* *c) Users might be aware or unaware that a use error has occurred.* *d) An unexpected physiological response of the patient is not by itself considered a use error.* e) *A malfunction of a medical device that causes an unexpected result is not considered a use error."*
Vulnerable Subject	An individual who is unable to fully understand all aspects of the investigation that are relevant to the decision to participate, or who could be manipulated or unduly influenced as a result of a compromised position, expectation of benefits or fear of retaliatory response.

2 LIST OF ACRONYMS AND ABBREVIATIONS

Table 2–1 List of Acronyms and Abbreviations Used in This Protocol

Abbreviation	Definition
ADE	Adverse device effect
AE	Adverse event
ASADE	Anticipated serious adverse device effect
BCDVA	Best corrected distance visual acuity
cm	Centimeter
CFR	Code of Federal Regulations
CRF	Case report form
D	Diopter
DCIVA	Distance corrected intermediate visual acuity
DCNVA	Distance corrected near visual acuity
DFU	Directions for use
eCRF	Electronic case report form
EDC	Electronic data capture
ETDRS	Early Treatment Diabetic Retinopathy Study
FAS	Full Analysis Set
GCP	Good Clinical Practice
GPCMS	Global Product Complaint System
IB	Investigator's brochure
IEC	Independent ethics committee
ICF	Informed consent form
IOL	Intraocular lens
IOLSAT	Intraocular Lens Satisfaction
IOP	Intraocular pressure
IP	Investigational product
IEC	Independent Ethics Committee
IRB	Institutional review board
ISO	International Organization for Standardization
LogMAR	Logarithm of the minimum angle of resolution
m	Meter
mm	Millimeter
MOP	Manual of procedures
N/A	Not applicable
OD	Right eye
OS	Left eye
PCO	Posterior capsular opacification
[redacted]	[redacted]
Q	Question
QUVID	Questionnaire for Visual Disturbances
SADE	Serious adverse device effect
SAE	Serious adverse event

Abbreviation	Definition
SD	Standard deviation
[redacted]	
US	United States
USADE	Unanticipated serious adverse device effect
VA	Visual acuity

3 PROTOCOL SUMMARY

Investigational product type	Device
Study type	Interventional
Investigational products	Test Product: Clareon Vivity/Vivity Toric Extended Vision IOLs (CNWET0, CNWET3-T6, CCWET0, CCWET3-T6) Comparator Product: Clareon/Clareon Toric Aspheric IOLs (SY60WF, CNW0T3-T6, CC60WF, CCW0T3-T6) and Clareon with AutonoMe (CCA0T0, CNA0T0) ***Note:*** *Subjects enrolled in this study will be 3 to 6 months (90 to 180 days) post implantation (after second eye implant) with the commercially available Test product or Control product at the time of Visit 1.* *No investigational products are being implanted during the study.*
Purpose and Scientific Rationale for the Study	Registration of the Clareon Vivity and Clareon Vivity Toric IOLs has been achieved utilizing clinical safety and performance data from its parent IOL models: AcrySof IQ Vivity, AcrySof IQ Toric, and Clareon monofocal. This study seeks to generate clinical data from previously implanted subjects to augment parent model data and support the clinical benefits statements with model-specific data.

Brief Summary of the Protocol	This study seeks to generate clinical data from subjects previously implanted with the Clareon Vivity/Clareon Vivity Toric IOLs or Clareon Monofocal/Clareon Toric IOLs. This study will assess key performance endpoints to support clinical benefits with model-specific data.
Objective(s)	Co-Primary Effectiveness: • To demonstrate that Clareon Vivity/Vivity Toric IOL is non-inferior to Clareon Monofocal/Clareon Toric IOL in mean binocular photopic best corrected distance visual acuity (BCDVA) at 3 to 6 months (90 to 180 days) postoperatively. • To demonstrate that Clareon Vivity/Vivity Toric IOL is superior to Clareon Monofocal/Clareon Toric IOL in mean binocular photopic distance corrected intermediate visual acuity (DCIVA) (66 cm from spectacle plane) at 3 to 6 months (90 to 180 days) postoperatively. Secondary Effectiveness: • To demonstrate that Clareon Vivity/Vivity Toric IOL is superior to Clareon Monofocal/Clareon Toric IOL in mean binocular photopic distance corrected near visual acuity (DCNVA) (40 cm from spectacle plane) at 3 to 6 months (90 to 180 days) postoperatively. • To demonstrate that Clareon Vivity/Vivity Toric IOL is superior to Clareon Monofocal/Clareon Toric IOL with respect to proportion of subjects who respond "Never" to Q1 of the IOLSAT questionnaire (Overall, in the past 7 days, how often did you need to wear eyeglasses to see?) at 3 to 6 months (90 to 180 days) postoperatively. Safety: • To describe the adverse event rates of Clareon Vivity/Vivity Toric IOL and Clareon Monofocal/Clareon Toric IOL collected in this study.

	• To describe monocular (first eye implanted) and binocular mesopic contrast sensitivity test (with and without glare) outcomes at 3 to 6 months (90 to 180 days) postoperatively. • To estimate rates of severe and most bothersome (separately) visual disturbances as reported by subjects using a questionnaire (QUVID) at 3 to 6 months (90 to 180 days) postoperatively.
Endpoint(s)	Primary Effectiveness • Mean Binocular photopic BCDVA (logMAR) at 4 m. • Mean Binocular photopic DCIVA (logMAR) at 66 cm. Secondary Effectiveness • Mean Binocular photopic DCNVA (logMAR) at 40 cm. • Proportion of subjects who respond "Never" to Q1 of the spectacle use questionnaire (IOLSAT) Safety • Adverse events (ocular and non-ocular, serious and non-serious) • Device deficiencies • Proportion of subjects with severe and most bothersome (separately) visual disturbances using the QUVID Questionnaire • Binocular and monocular (first eye implanted) mesopic contrast sensitivity test (with and without glare) • Mean IOP • Slit lamp examination findings including: o IOL observations o Absolute IOL position change (tilt and decentration) o Subjective posterior capsular opacification (PCO) o Presence of posterior capsulotomy • Dilated fundus examination findings
Assessment(s)	Primary and Secondary Effectiveness: • Manifest refraction

	• Binocular photopic BCDVA (logMAR) at 4 m. • Binocular photopic DCIVA (logMAR) at 66 cm. • Binocular photopic DCNVA (logMAR) at 40 cm • IOLSAT questionnaire Safety: • Adverse events (ocular and non-ocular, serious and non-serious) • Device deficiencies • Binocular and monocular (first eye implanted) mesopic contrast sensitivity test (with and without glare) • QUVID Questionnaire (binocular) to assess visual disturbances • Slit Lamp Exam • Dilated Fundus Exam • Tonometry
Study Design	This is a prospective/retrospective, multicenter, nonrandomized, parallel group, controlled, assessor masked interventional study. Both eyes of a subject must qualify for enrollment into this study. To reduce bias, manifest refraction, VA[redacted] and contrast sensitivity assessors will be masked to the IOLs that have been previously implanted in the subject until the end of the study. To minimize bias, Alcon personnel (including biostatistics, masked data manager, and clinical project lead) will also be masked to the IOLs that have been previously implanted in the subject, to the extent possible. A total of 2 scheduled visits are planned and subject participation is expected to last approximately 2 weeks. The visits include a Screening visit (Visit 0) and 1 visit after screening (Visit 1).
Subject population	The study population consists of male and female subjects 18 years of age and older that were previously implanted bilaterally with the Clareon Vivity/Clareon Vivity Toric IOL or Clareon Monofocal/Clareon Toric IOL.

	It is aimed to enroll approximately 210 subjects at up to 12 US investigative sites. Site specific targets will be adjusted based on individual site capabilities. Enrollment projections are as follows: 210 subjects to be enrolled/sign consent (approximately 9.5% screen failure rate is expected) 190 subjects to successfully complete final study visit (Visit 1) 95 subjects in the Clareon Vivity/Clareon Vivity Toric arm 95 subjects in the Clareon Monofocal/Clareon Toric arm
Sites and Locations	Planned number of clinical sites: up to 12 sites Planned locations (initial list of locations, which may change during start up or conduct according to study needs): United States
Key inclusion criteria (See Section 8.1 for a complete list of inclusion criteria)	Adults (18 years or older at the time of participation in the study) with previous bilateral implantation of Clareon Vivity/Clareon Vivity Toric or Clareon Monofocal/Clareon Toric IOLs for at least 3 months and up to 6 months (90 to 180 days) after second eye implant.
Key exclusion criteria (See Section 8.2 for a complete list of exclusion criteria)	History of clinically significant ocular co-morbidities that would affect surgical outcomes based on investigator expert medical opinion. Subjects who were targeted to monovision defined as ≥ 1.50 D of anisometropia. Clinically significant PCO affecting vision.
Data analysis and sample size justification	The Full Analysis Set (FAS) will be the primary analysis set for effectiveness and will be used for all safety analyses. [redacted] The null and alternative hypotheses to be evaluated in support of the primary endpoints are:

	• Clareon Vivity/Vivity Toric IOL is non-inferior compared to Clareon/Clareon Toric IOL with respect to mean binocular best-corrected distance visual acuity at the postoperative visit. The non-inferiority margin will be 0.1 logMAR. • Clareon Vivity/Vivity Toric IOL is superior to Clareon/Clareon Toric IOL with respect to mean binocular distance-corrected intermediate visual acuity (66 cm) at the postoperative visit. Analysis of the first primary endpoint (non-inferiority for binocular BCDVA) will be based on a two-sample t-test assuming equal variances with testing based on a one-sided lower tailed test conducted at the 0.05 significance level. A corresponding two-sided 90% confidence interval for the difference in means (Clareon Vivity/Vivity Toric IOL minus Clareon/Clareon Toric IOL) will be presented. Non-inferiority is demonstrated if the one-sided p-value for the t-test is less than 0.05 or, equivalently, the upper limit of the two-sided 90% confidence interval is less than the non-inferiority margin. A two-sided 95% confidence intervals will also be provided for descriptive purposes. Analysis of the second primary endpoint (superiority test for binocular DCIVA) will be based on a two-sample t-test assuming equal variances with testing based on a one-sided lower tailed test conducted at the 0.05 significance level. A two-sided 95% confidence interval for the difference in means (Clareon Vivity/Vivity Toric IOL minus Clareon/Clareon Toric IOL) will be presented. The null and alternative hypotheses to be evaluated in support of the secondary endpoints are: • Clareon Vivity/Vivity Toric IOL is superior to Clareon/Clareon Toric IOL with respect to mean binocular distance-corrected near visual acuity (40 cm) at the postoperative visit. • Clareon Vivity/Vivity Toric IOL is superior to Clareon/Clareon Toric IOL with respect to the proportion of subjects who respond “Never” to Q1 of the spectacle use questionnaire (IOLSAT) at the postoperative visit. Analysis of the first secondary endpoint (binocular DCNVA) will be based on a two-sample t-test assuming equal variances with testing based on a one-sided lower tailed test conducted at the 0.05 significance level. A two-sided 95% confidence interval for the difference in means

(Clareon Vivity/Vivity Toric IOL minus Clareon/Clareon Toric IOL) will also be presented.

Analysis of the second secondary endpoint (Q1 for IOLSAT) will be based on a Chi-squared test of two proportions with testing based on a one-sided upper tailed test carried out at the 0.05 significant level. The proportion of subjects who respond "Never" to Q1 of the spectacle use questionnaire (IOLSAT) in each group will be presented.

In general, descriptive statistics generated for an endpoint will be based upon the type of parameter (i.e., whether the data is categorical or continuous) being analyzed. 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, sample size, mean, median, standard deviation, minimum, and maximum will be presented. Summaries of logMAR visual acuity may include two-sides 95% confidence intervals for the difference between treatment groups.

[redacted]

A total of 210 subjects will be enrolled (approximately 105 per arm). Assuming a screen failure rate of 9.5%, approximately 190 subjects will be evaluable at Visit 1 (95 per arm). The power estimates for the planned analyses are presented below:

Order	Endpoint	Comparison	Noninferiority Margin	Expected difference	SD ^	Power
Co Primary	Binocular BCDVA	Noninferiority	0.10	0.04	0.14	90%
Co Primary	Binocular DCIVA at 66 cm	Superiority	NA	0.085	0.14	> 98%
1st Secondary	Binocular DCNVA at 40 cm	Superiority	NA	0.14	0.14	> 99%
2nd Secondary	Q1 of IOLSAT = NEVER	Superiority	NA	0.14	NA	> 96%

	[redacted] Overall power is estimated based on the assumption that each hypothesis test is independent.
Associated materials	None

Table 3–1 Schedule of Study Procedures and Assessments

	Visit 0 (Screening Visit)	**Visit 1**
	Study Day 0	**Study Day 1 to 14** [e]
Procedure/ Assessment		**3 to 6 months (90-180 days) post 2nd eye implant** [e]
Informed Consent	X	
Demographics	X	
Medical History [c]	X	
Concomitant Medications [c]	X	X
Inclusion/Exclusion	X	
Urine pregnancy test [d]	X	
Photopic Pupil Size	X	
Slit Lamp Examination	X	
Tonometry	X	
Dilated Fundus Examination	X	
Subjective PCO	X	
Presence of Posterior Capsulotomy	X	
IOL Observations	X	
Absolute IOL Position Change (Tilt/Decentration)	X	
Pre-Operative/Operative Information from Chart: • Lens model & power • IOL calculation method • Corneal topography and/or aberrometry (if available) • Biometry & keratometry	X (retrospective)	

	Visit 0 (Screening Visit)	Visit 1
• Predicted residual refractive error • Operating surgeon (first eye) • 1st eye implanted (OD or OS) • Date of Surgery for second eye		
QUVID questionnaire		X
IOLSAT questionnaire		X
Manifest refraction		X
• Binocular BCDVA [redacted]		X [redacted]
• Binocular DCIVA [redacted]		X [redacted]
• Binocular DCNVA [redacted]		X [redacted]
[redacted]		[redacted]
Binocular Mesopic Contrast Sensitivity (with and without glare) Monocular Mesopic Contrast Sensitivity (with and without glare) [b]		X X
Adverse Events	X	X
Device Deficiencies	X	X

[a] First and Second Eye Implanted, [b] First Eye Implanted only, [c] Medical History and Concomitant Meds will be reviewed in source only, [d] in women of childbearing potential only, [e] Visit 1 must occur at least one day after the Screening visit and it is recommended that is occur a max of 14 days after screening. The subject must be 90-180 days post 2nd eye implant at the time of Visit 1.

4 PROTOCOL 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 the IRB/IEC and global and regional health authorities, as applicable, prior to implementation except when required to mitigate immediate safety risks or when the changes involve only logistical or administrative revisions.

Amendments may necessitate that the informed consent and other study-related material be revised. If the consent form is revised, all subjects currently enrolled in the study must sign the approved, revised informed consent (re-consent), as required by the IRB/IEC.

Refer to Appendix A for detailed description of amendments.

5 INTRODUCTION

5.1 Rationale and Background

The Clareon Vivity and Vivity Toric Extended Vision IOLs employ the non-diffractive, wave-front shaping X-WAVE™ technology which, compared to a monofocal IOL, provides an extended range of vision from distance to near while maintaining a low incidence of visual disturbances. The Clareon Vivity Toric Extended Vision IOL models also compensate for corneal astigmatism.

The Clareon Vivity and Vivity Toric Extended Vision IOLs mitigate the effects of presbyopia by providing an extended depth of focus. Compared to an aspheric monofocal IOL, these lenses seek to provide improved intermediate and near visual acuity while maintaining comparable distance visual acuity.

The clinical benefits of the Vivity Extended Vision optical design have been supported by previous studies of the AcrySof IQ Vivity IOLs. This study seeks to generate data to support these benefit statements with model-specific data from Clareon Vivity and Vivity Toric IOLs. The inclusion of Clareon Monofocal as a control (comparator) will allow for comparative analyses to support the benefits of this technology.

5.2 Purpose of the Study

Registration of the Clareon Vivity and Clareon Vivity Toric IOLs has been achieved utilizing clinical safety and performance data from its parent IOL models: AcrySof IQ Vivity, AcrySof IQ Toric, and Clareon monofocal. This study seeks to generate clinical data from previously implanted subjects to augment parent model data and support the clinical benefits statements with model-specific data.

At the end of the study, a clinical study report will be prepared in accordance with applicable regulatory requirements and standards.

There are no immediate plans to submit the results of this study for publication; however, the results may be offered for publication if they are of scientific interest.

5.3 Risks and Benefits

Risk management principles have been applied to both the planning and the intended conduct of the clinical investigation, to ensure the reliability of the clinical data generated and the safety of the subjects. The clinical investigation process risks are managed through appropriate training and monitoring according to the protocol-specific monitoring plan. Investigational device risks, including risks associated with use of device and methods and procedures for application of device, are defined in the investigator's brochure and/or product labeling and are managed through review of safety assessments outlined in this protocol.

This is an interventional study where subjects enrolled into this study will have existing bilateral IOLs implanted with test and control IOL between 3 to 6 months post 2nd eye implant.

Risks of the study are considered to be no greater than a typical eye examination since procedures (e.g., VA testing, IOP, and slit lamp exam) are commonly performed by eye care practitioners. Further, risks are minimized by compliance with the eligibility criteria, study procedures, and clinical monitoring.

Device deficiencies observed during this study for both test and control IOL will be documented and reported as described in Section 11.1.

There is no intended clinical benefit to the subject. This clinical study may benefit the medical community by contributing to the knowledge of IOL development.

Subjects in this study may come away with a sense of wellbeing gained by contributing to the understanding of new or improved IOLs.

Subjects will receive nominal compensation for their time and inconvenience.

6 STUDY OBJECTIVES

6.1 Primary Objective(s)

Table 6–1 Primary Objective(s)

Objective(s)	**Endpoint(s)**
Co-Primary Effectiveness:	
To demonstrate that Clareon Vivity/Vivity Toric IOL is noninferior to Clareon	Mean binocular photopic best corrected distance visual acuity (BCDVA) at 3 to 6

Objective(s)	Endpoint(s)
Monofocal/Clareon Toric IOL in mean binocular photopic best corrected distance visual acuity (BCDVA) at 3 to 6 months (90 to 180 days) postoperatively.	months (90 to 180 days) postoperatively after second eye implant.
To demonstrate that Clareon Vivity/Vivity Toric IOL is superior to Clareon Monofocal/Clareon Toric IOL in mean binocular photopic distance corrected intermediate visual acuity (DCIVA) (66 cm from spectacle plane) at 3 to 6 months (90 to 180 days) postoperatively.	Mean binocular photopic distance corrected intermediate visual acuity (DCIVA) (66 cm from spectacle plane) at 3 to 6 months (90 to 180 days) postoperatively after second eye implant.

6.2 Secondary Objective(s)

Table 6–2 Secondary Objective(s)

Objective(s)	Endpoint(s)
To demonstrate that Clareon Vivity/Vivity Toric IOL is superior to Clareon Monofocal/Clareon Toric IOL in mean binocular photopic distance corrected near visual acuity (DCNVA) (40 cm from spectacle plane) at 3 to 6 months (90 to 180 days) postoperatively.	Mean binocular photopic distance corrected near visual acuity (DCNVA) (40 cm from spectacle plane) at 3 to 6 months (90 to 180 days) postoperatively.
To demonstrate that Clareon Vivity/Vivity Toric IOL is superior to Clareon Monofocal/Clareon Toric IOL with respect to proportion of subjects who respond “Never” to Q1 of the IOLSAT questionnaire (Overall, in the past 7 days, how often did you need to wear eyeglasses to see?) at 3 to 6 months (90 to 180 days) postoperatively.	Proportion of subjects who respond “Never” to Q1 of the IOLSAT questionnaire (Overall, in the past 7 days, how often did you need to wear eyeglasses to see?) at 3 to 6 months (90 to 180 days) postoperatively.

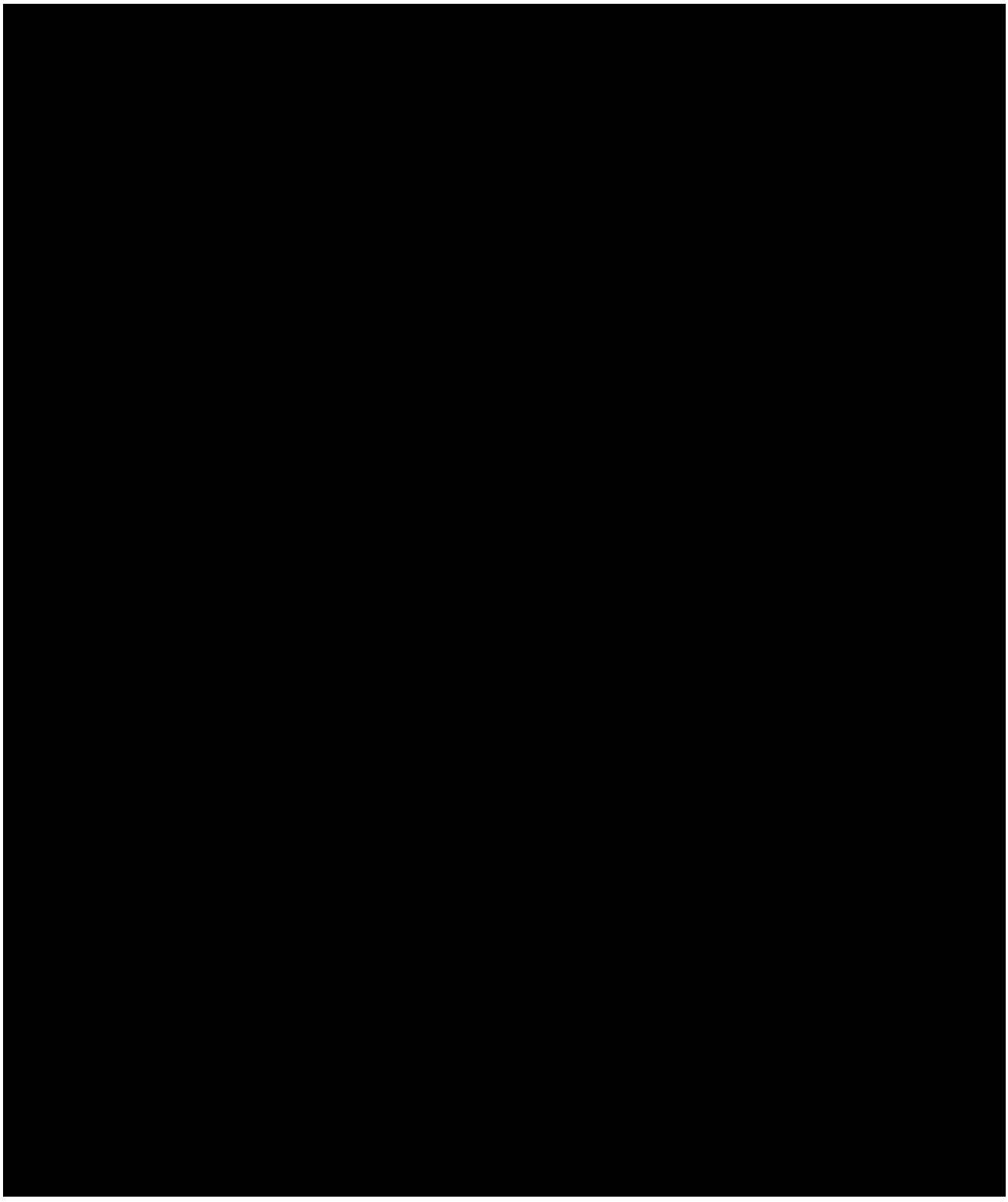


Table 6–4 Safety Objective(s)

Objective(s)	**Endpoint(s)**
To describe the adverse event rates of Clareon Vivity/Vivity Toric IOL and Clareon Monofocal/Clareon Toric IOL collected in this study	Adverse events (ocular and non-ocular, serious and non-serious)
To describe monocular (first eye implanted) and binocular mesopic contrast sensitivity test (with and without glare) outcomes at 3 to 6 months (90 to 180 days) postoperatively.	Binocular and monocular (first eye implanted) mesopic contrast sensitivity test (with and without glare)
To estimate rates of severe and most bothersome (separately) visual disturbances as reported by subjects using a questionnaire (QUVID) at 3 to 6 months (90 to 180 days) postoperatively	Proportion of subjects with severe and most bothersome (separately) visual disturbances using the QUVID Questionnaire

7 INVESTIGATIONAL PLAN

7.1 Study Design

This is a prospective/retrospective, multicenter, nonrandomized, parallel group, controlled, assessor masked interventional study. Both eyes of a subject must qualify for enrollment into this study. To reduce bias, manifest refraction, VA [redacted] and contrast sensitivity assessors will be masked to IOLs that have been previously implanted in the subject until the end of the study. To minimize bias, Alcon personnel (including biostatistics, masked data manager, and clinical project lead) will also be masked to the IOLs that have been previously implanted in the subject, to the extent possible.

A total of 2 scheduled visits are planned and subject participation is expected to last approximately 2 weeks. The visits include a Screening visit (Visit 0) and 1 visit after screening (Visit 1) that should occur 1 to 14 days after Visit 0. The subject must be 90-180 days post 2nd eye implant at the time of Visit 1. Visit 1 must occur at least one day after the Screening visit and it is recommended that is occur a max of 14 days after screening. The study is expected to be completed in approximately 5 months.

The study population consists of male and female subjects 18 years of age and older that were previously implanted bilaterally with the Clareon Vivity/Clareon Vivity Toric IOLs or Clareon Monofocal/Clareon Toric IOLs. Visit 1 must occur at least 3 months and up to 6 months (90 to 180 days) after second eye implant.

The first operative eye is defined as the eye that was implanted first. The second operative eye is defined as the eye that was implanted second. (Note: Eyes that are implanted on the same day are acceptable in this study.)

It is aimed to enroll approximately 210 subjects to complete approximately 190 subjects at the final study visit (approximately 95 in each arm). This assumes approximately a 9.5% screen failure rate. Up to 12 US investigative sites are planned for this study. Site specific targets will be adjusted based on individual site capabilities.

7.2 Rationale for Study Design

Registration of the Clareon Vivity and Clareon Vivity Toric IOLs has been achieved utilizing clinical safety and performance data from its parent IOL models: AcrySof IQ Vivity, AcrySof IQ Toric, and Clareon monofocal. This study seeks to generate clinical data from previously implanted subjects to augment parent model data and support clinical benefit statements with model specific data.

Subjects in this study, in both test and control groups, have prior bilateral IOL implants with no new surgical interventions under the current protocol. The assessments are similar to a typical eye examination since procedures (e.g., VA/performance testing, slit lamp exam) are commonly performed by eye care practitioners. Other assessments such as contrast sensitivity may not be commonly used but are established techniques for ocular assessments that have been well studied in the literature.

To reduce bias, manifest refraction, VA[redacted] and contrast sensitivity assessors will be masked to IOLs that have been previously implanted in the subject until the end of the study and testing methods have predefined procedures.

7.2.1 Purpose and Timing of Interim Analyses and Resulting Design Adaptations

Not applicable

7.3 Rationale for Duration of Treatment/Follow-Up

No treatment will be undertaken during the course of the study as the subject population has been previously implanted. Subjects will attend one visit (Visit 1) after screening to collect assessment data.

7.4 Rationale for Choice of Comparator Product

The test group includes subjects previously implanted bilaterally with Clareon Vivity/Clareon Vivity Toric IOLs. The control (comparator) group includes subjects previously implanted bilaterally with Clareon Monofocal/Clareon Toric IOLs. Both groups were chosen to generate clinical data to augment parent model data and support the clinical benefits with model-specific data. Clareon Monofocal was chosen as the control (comparator) to support clinical benefit statements in which the performance of Clareon Vivity/Vivity Toric is compared to a monofocal IOL.

7.5 Data Monitoring Committee

Not applicable

8 STUDY POPULATION

The study population consists of male and female subjects (18 years or older at the time of participation in the study) with previous bilateral implantation of Clareon Vivity/Clareon Vivity Toric or Clareon Monofocal/Clareon Toric IOLs for at least 3 months and up to 6 months (90 to 180 days) after second eye implant. It is aimed to enroll (consent) approximately 210 subjects at up to 12 sites in the United States, with a target of 190 subjects completing the study. The investigators and sites should also target equal numbers of subject in each group: Clareon Vivity/Clareon Vivity Toric or Clareon Monofocal/Clareon Toric, if possible. This is recommended but not required. Site-specific targets will vary based upon individual site capabilities. Estimated time needed to recruit subjects for the study is approximately 4 months; however, unanticipated circumstances may shorten or lengthen this time and would not require amendment of this protocol. Because a 9.5% screening failure rate is expected, approximately 210 subjects are expected to be enrolled.

This protocol allows enrollment of the following vulnerable population(s), with associated justification for each population:

Elderly – It is appropriate to include the elderly in this clinical study, as IOL implantation is intended to treat age-related cataract formation and is common to this population.

The elderly will be protected through the informed consent process, which will include any risks specific to the elderly subjects, as well as any specific responsibilities associated with their participation. In addition, an IRB/IEC will review and approve the inclusion of elderly subjects in this clinical study prior to enrollment of elderly subjects. Any specific requirements imposed by the IRB/IEC regarding participation of elderly subjects will be

implemented and documented, as appropriate. Upon conclusion of the clinical study, all subjects, including elderly subjects, will return to standard medical care for ongoing conditions.

8.1 Inclusion Criteria

Written informed consent must be obtained before any study specific assessment is performed. Upon signing informed consent, the subject is considered enrolled in the study.

Subjects eligible for inclusion in this study must fulfill **all** of the following criteria:

1. Subject must be able to understand and sign an IRB/IEC approved Informed Consent form.
2. Willing and able to attend all scheduled study visits as required per protocol.
3. Adults (18 years or older at the time of participation in the study) with previous bilateral implantation of Clareon Vivity/Clareon Vivity Toric or Clareon Monofocal/Clareon Toric IOLs for at least 3 months and up to 6 months after second eye implant.

   The IOL spherical power must be within the 10.0 to 30.0 D range in both eyes and for both lens types. If a Toric lens was used, the cylinder power at the IOL plane must be in the range +1.50 to +3.75 Diopters in 0.75 D increments for each eye.

   A subject may have a Toric lens in one eye and a non-Toric in the fellow eye as long as the IOL type is matched (e.g., Clareon Vivity/Vivity Toric or Clareon Monofocal/Monofocal Toric).
4. Documented medical history and required preoperative baseline information available for retrospective data collection.

8.2 Exclusion Criteria

Subjects fulfilling **any** of the following criteria are not eligible for participation in this study.

1. Women of childbearing potential, defined as all women who are physiologically capable of becoming pregnant and who are not postmenopausal for at least 1 year or are less than 6 weeks since sterilization, are excluded from participation if any of the following apply:
   a. they are currently pregnant,

b. have a positive urine pregnancy test result at Screening,

c. intend to become pregnant during the study period,

d. are breastfeeding.

Subjects who become pregnant during the study will not be discontinued;

2. Subjects currently participating in another investigational drug or device study.

3. History of clinically significant ocular co-morbidities that would affect surgical outcomes based on investigator expert medical opinion.

4. History of corneal refractive surgery.

5. Subjects who were targeted to monovision defined as ≥ 1.50 D of anisometropia.

6. Clinically significant PCO affecting vision.

7. History of Amblyopia or Monofixation syndrome with poor stereoscopic vision.

8.3 Rescreening of Subjects

Rescreening of subjects is not allowed in this study.

9 TREATMENTS ADMINISTERED

9.1 Investigational Product(s)

Test Product(s):	Clareon Vivity/Vivity Toric Extended Vision IOLs (CNWET0, CNWET3-T6, CCWET0, CCWET3-T6)
Comparator Product(s) (If applicable):	Clareon/Clareon Toric Aspheric (SY60WF, CNW0T3-T6, CC60WF, CCW0T3-T6) and Clareon with AutonoMe (CCA0T0, CNA0T0)

Table 9–1 Test Product

Test Product	Clareon Vivity/Vivity Toric Extended Vision IOLs (CNWET0, CNWET3-T6, CCWET0, CCWET3-T6)
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
Indication for use and intended purpose in the current study	The Clareon Vivity™ Extended Vision Hydrophobic IOLs are indicated for primary implantation for the visual correction of aphakia in adult patients with < 1.00 D of preoperative corneal astigmatism, in whom a cataractous lens has been removed by extracapsular cataract extraction. The Clareon Vivity™ Toric Extended Vision IOLs are indicated for primary implantation for the visual correction of aphakia and for reduction of residual refractive astigmatism in adult patients with pre-existing corneal astigmatism, in whom a cataractous lens has been removed by extracapsular cataract extraction. Both the Clareon Vivity and Clareon Vivity Toric lenses mitigate the effects of presbyopia by providing an extended depth of focus. Compared to an aspheric monofocal IOL, the lens provides improved intermediate and near visual acuity, while maintaining comparable distance visual acuity and intended for capsular bag placement only.

Product description and parameters available for this study	No investigational products are being implanted during the study. Information on Clareon Vivity/Vivity Toric Extended Vision IOLs may be found in the DFU.
Formulation	N/A
Usage	N/A
Packaging description	N/A
Labeling description	N/A
Training and/or experience requirements for device	No additional training or experience is required to administer the test product as no test product is being implanted.
Storage conditions	N/A
Additional information	N/A
Supply	N/A

Table 9–2 Comparator Product

Comparator Product(s)	Clareon/Clareon Toric Aspheric (SY60WF, CNW0T3-T6, CC60WF, CCW0T3-T6) and Clareon with AutonoMe (CCA0T0, CNA0T0)
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
Indication for Use	The Clareon™ Aspheric Hydrophobic Acrylic IOLs are indicated for primary

	implantation in the capsular bag in the posterior chamber of the eye for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed. The Clareon™ Toric Aspheric Hydrophobic Acrylic IOLs are indicated for primary implantation in the capsular bag in the posterior chamber of the eye for visual correction of aphakia and preexisting corneal astigmatism to reduce residual refractive cylinder and improve uncorrected distance vision in adult patients in whom a cataractous lens has been removed.
Product description and parameters available for this study	No investigational products are being implanted during the study. Information on Clareon Vivity/Vivity Toric Extended Vision IOLs may be found in the DFU.
Formulation	N/A
Usage	N/A
Packaging description	N/A
Labeling description	N/A
Training and/or experience requirements for device	No additional training or experience is required to administer the test product as no test product is being implanted.
Storage conditions	N/A
Additional identifying information	N/A

Supply	N/A

9.2 Other Medical Device or Medication Specified for Use During the Study

No other medical devices or medications are required to be used in conjunction with the treatments during the clinical study.

9.3 Treatment Assignment / Randomization

Only after signing the ICF, a subject will be assigned a subject number by the electronic data capture system. This study is not randomized.

9.4 Treatment masking

This study is ONLY assessor-masked for manifest refraction, VA, [redacted] and contrast sensitivity. To minimize bias, Alcon personnel (including biostatistics, masked data manager, and clinical project lead) will also be masked to the IOLs that have been previously implanted in the subject, to the extent possible. All other members associated with the study (at the site and the study sponsor) are unmasked.

This level of masking will be maintained throughout the conduct of the study. Unmasking will occur only after all planned study data have been validated, and the database locked.

Masked study personnel must avoid seeking information that may compromise masking. Unmasked study personnel must not disseminate information that is potentially unmasking to any masked personnel. The masked and unmasked site personnel must coordinate all study activities as necessary to protect masking and minimize bias during the study. Any unmasking of assessor or subject must be reported to Alcon.

9.5 Accountability Procedures

Not applicable

9.6 Changes to concomitant medications, treatments/ procedures

After the subject is enrolled into the study, the investigator must instruct the subject to notify the study site about:

- Any new medications

- Alterations in dose or dose schedules for current medications
- Any medical procedure or hospitalization that occurred or is planned
- Any nondrug therapies (including physical therapy and blood transfusions).

The investigator must document this information in the subject's case history source documents.

10 STUDY PROCEDURES AND ASSESSMENTS

This section describes the procedures and assessments for this clinical study. There are two study Visits in this study.

Visit 0 is the screening visit. Informed consent procedures as well as eligibility are performed at this visit.

Visit 1 will occur 3 to 6 months (90 to 180 days) after the second eye implant of the subject being enrolled. Visit 1 must occur at least one day after the screening visit and it is recommended that is occur a maximum of 14 days after screening. Endpoint assessments and study exit are performed at this visit.

10.1 Informed Consent and Screening

The investigator or delegate must explain the purpose and nature of the study, and have the subject read, sign, and date the IRB/IEC-approved informed consent document. The subject must sign the ICF BEFORE any study-specific procedures or assessments can be performed, including study-specific screening procedures. Additionally, have the individual obtaining consent from the subject and a witness, if applicable, sign and date the informed consent document.

The investigator or delegate must provide a copy of the signed document to the subject and place the original signed document in the subject's chart, or provide documentation as required by local regulations.

10.2 Description of Study Procedures and Assessments

Study-specific procedures and assessments described here may include standard of care; other standard of care procedures performed in the clinical management of the subject are not excluded.

Detailed descriptions of assessments and procedures are provided in the MOP. The investigator is responsible for ensuring responsibilities for all procedures and assessments are delegated to appropriately qualified site personnel.

10.2.1 Demographics

Obtain demographic information including age, race, ethnicity, and sex.

10.2.2 Medical History and Concomitant Medication

Medical History and Concomitant Medications will be documented in the subject's source but will not be collected in the eCRF for this study.

10.2.3 Urine Pregnancy: Entry Criteria

Perform urine pregnancy test according to the manufacturer's procedure on female subjects of child-bearing potential.

10.2.4 Preoperative/Operative Chart Review Information: Entry Criteria and Effectiveness Assessment

From preoperative/operative chart review, collect and record the lens model implanted, the IOL power, biometry, keratometry, the predicted target residual refractive error for each eye, operating surgeon (first eye), 1st operative eye (OD/OS), date of surgery for second eye. Also collect the IOL calculation method used (e.g., Barrett) in each eye. If a separate Toric calculator was used in addition to the IOL power calculation, document the Toric calculator used in each eye.

Note: To qualify for study participation the subject must have the Clareon Vivity/Vivity Toric bilaterally or Clareon Monofocal/Toric bilaterally and an IOL spherical power must be within the 10.0 to 30.0 D range in both eyes and for both lens types. If a Toric lens was used, the cylinder power at the IOL plane must be in the range +1.50 to +3.75 Diopters in 0.75 D increments for each eye. A subject may have a Toric lens in one eye and a non-Toric in the fellow eye as long as the IOL type is matched (e.g., Clareon Vivity/Vivity Toric or Clareon Monofocal/Monofocal Toric).

Subjects who were targeted to monovision defined as ≥ 1.50 D of anisometropia do not qualify for the study and should be excluded.

Review for exclusion criteria.

If corneal topography and/or aberrometry are/is available in the chart, collect this information for each eye.

Refer to MOP for details.

10.2.5 Photopic Pupil Size: Effectiveness Assessment

During manifest refraction/VA assessment, perform and record photopic pupil size in both eyes at 4 m and record to the nearest 0.5 mm.

10.2.6 Slit Lamp Biomicroscopy: Safety Assessment

Slit lamp examination must be performed in both eyes. Record any slit lamp findings, absolute IOL position change (tilt and decentration), any IOL observations, any subjective PCO and the subject has the presence of a posterior capsulotomy. Refer to MOP for details. This assessment must be performed by medically qualified study staff.

10.2.7 Tonometry: Safety Assessment

Perform tonometry assessment in both eyes according to the to the investigator's standard of care. Record IOP.

10.2.8 Dilated Fundus: Entry Criteria/Safety Assessment

Dilated fundus examination includes ophthalmoscopic assessments of the vitreous, retina, macula, choroid, and optic nerve of both eyes. This assessment must be performed by medically qualified study staff.

10.2.9 IOLSAT Questionnaire: Effectiveness Assessment

Provide the IOLSAT questionnaires to the subject for completion. It is recommended that the questionnaire be completed (after the QUVID questionnaire) by the subject prior to performance of manifest refraction, VA, [redacted] and contrast sensitivity assessments.

10.2.10 QUVID Questionnaire: Safety Assessment

Provide the QUVID questionnaire to the subject for completion. It is recommended that the QUVID be completed before IOLSAT questionnaire. The questionnaire should be completed by the subject prior to administration of manifest refraction VA, [redacted] and contrast sensitivity assessments.

10.2.11 Manifest Refraction: Effectiveness Assessment

Perform and record manifest refraction using technique detailed in the MOP at 4 m. This assessment must be performed by delegated trained masked assessor only.

[redacted]

10.2.13 Best Corrected Distance Visual Acuity: Effectiveness Assessment

Measure and record binocular [redacted] ETDRS BCDVA at 4 m. This assessment must be performed by delegated trained masked assessor only.

[redacted]

10.2.15 Distance Corrected Intermediate Visual Acuity: Effectiveness Assessment

Measure and record binocular [redacted] ETDRS DCIVA at 66 cm. This assessment must be performed by delegated trained masked assessor only.

[redacted]

10.2.17 Distance Corrected Near Visual Acuity: Effectiveness Assessment

Measure and record binocular [redacted] ETDRS DCNVA at 40 cm. This assessment must be performed by delegated trained masked assessor only.

[redacted]

10.2.19 Contrast Sensitivity: Safety Assessment

Measure and record both binocular and first eye monocular contrast sensitivity under mesopic lighting conditions with and without glare. This assessment must be performed by delegated trained masked assessor only. Refer to MOP for details.

10.2.20 Adverse Event Collection: Safety Assessment

Assess and record any adverse events that are observed or reported since the time of consent.

AEs must be recorded for all enrolled subjects from the time of signature of informed consent, regardless of subject enrollment status (screen failure).

10.2.21 Device Deficiencies: Safety Assessment

Assess and record any device deficiencies that are reported or observed since the time of consent. Requirements for reporting device deficiencies in the study can be found in Section 11.

Device deficiencies must be recorded for all enrolled subjects from the time of signature of informed consent, regardless of subject enrollment status (screen failure).

10.3 Unscheduled Visits

If a subject visit occurs between any regularly scheduled visit and the visit is conducted by study personnel, this visit must be documented as an Unscheduled Visit. If the subject seeks medical attention outside the clinic (for example, at an emergency room) or at the clinic but is seen by non-study personnel, the investigator is to capture adverse event-related information on the adverse event form upon becoming aware.

During all unscheduled visits, the investigator must conduct the following procedures:

- Collect adverse event information
- Record changes in medical condition or concomitant medication

The investigator may perform additional procedures for proper diagnosis and treatment of the subject (e.g., subjective VA, slit lamp exam, tonometry, and dilated fundus exam). The investigator must document this information in the subject’s case history source documents.

10.4 Discontinued Subjects

10.4.1 Screen Failures

Subjects who were excluded from the study after signing the informed consent, excluded based on inclusion/exclusion criteria at the Screening Visit, and prior to Visit 1 testing.

The investigator must document the reason for screen failure in the subject's case history source documents.

Subject numbers must not be reused.

10.4.2 Discontinuations

Discontinued subjects are individuals who voluntarily withdraw or are withdrawn from the study by the investigator after inclusion/exclusion criteria has been met at Screening Visit.

Subject numbers of discontinued subjects must not be reused (i.e., subject replacement is not allowed).

Subjects may discontinue from study or study treatment at any time for any reason. Subjects may also be discontinued from study treatment at any time if, in the opinion of the investigator, continued treatment poses a risk to their health.

The investigator must document the reason for study or treatment discontinuation in the subject's case history source documents.

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.

10.4.3 Schedule of Procedures and Assessments for Subjects Discontinued from Investigational Product

Not applicable

10.5 Clinical Study Termination

The study sponsor reserves the right to suspend or close the investigational site or suspend or terminate the study in its entirety at any time.

If the clinical study is prematurely terminated or suspended by the study sponsor:

- The study sponsor must:
    - Immediately notify the investigator(s) and subsequently provide instructions for study termination.
    - Inform the investigator and the regulatory authorities of the termination/suspension and the reason(s) for the termination/suspension.
- The investigator must:
    - Promptly notify the IRB/IEC of the termination or suspension and of the reasons.
    - Provide subjects with recommendations for poststudy treatment options as needed.

The investigator may terminate the site's participation in the study for reasonable cause.

10.5.1 Follow-up of subjects after study participation has ended

Following this study, the subject will return to their eye care professional for their routine eye care.

11 ADVERSE EVENTS AND DEVICE DEFICIENCIES

11.1 General Information

An AE is 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. Refer to the Glossary of Terms and figures below for categories of AEs and SAEs.

Figure 11-1 Categorization of All Adverse Events

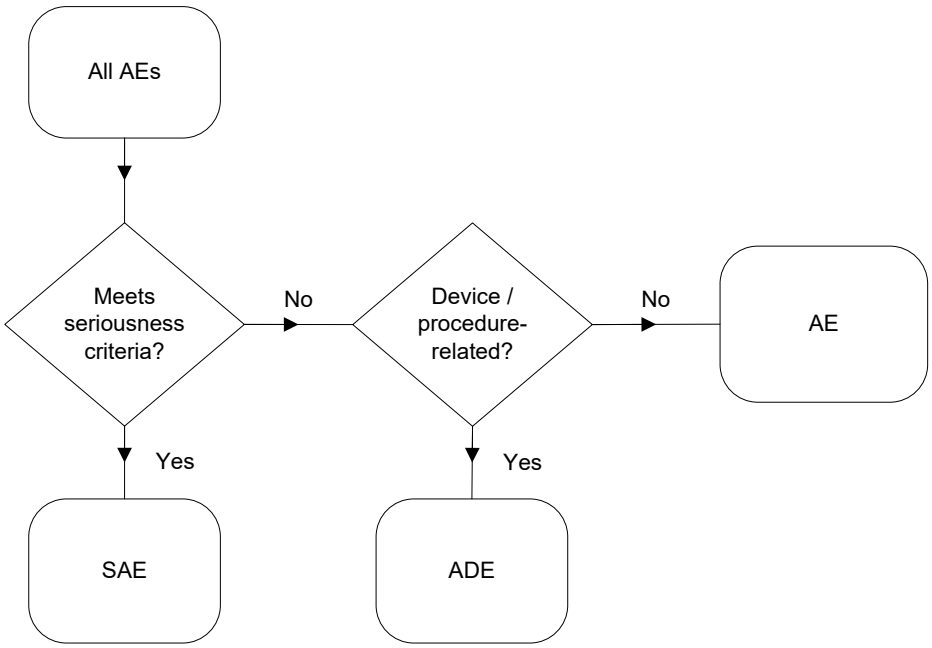
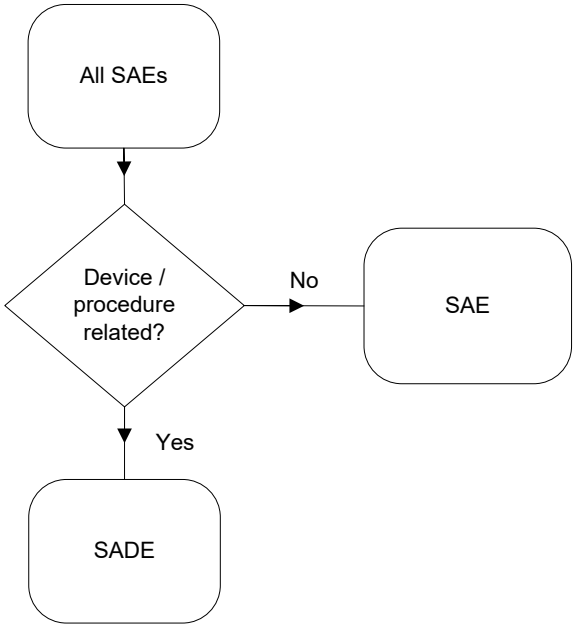


Figure 11-2 Categorization of All Serious Adverse Events



Specific Events Relevant to this Protocol

In addition to reporting all AEs (serious and nonserious) meeting the definitions, the investigator must report any occurrence of the following as an SAE:

- Cystoid macular edema
- Hypopyon
- Endophthalmitis
- Lens dislocation from posterior chamber
- Pupillary block
- Retinal detachment

Any other potentially sight-threatening event may also be considered serious based on the judgment of the investigator and should be reported appropriately as delineated in Section 11.3 (Procedures for Recording and Reporting).

Device Deficiencies

A device deficiency may or may not be associated with subject harm (i.e., 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 (e.g., incorrect IOL power)
- IOL defect
- Scratched IOL
- Lack of performance

11.2 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 shown below and report as applicable:

- “Have you had any health problems since your last study visit?”

- "Have there been any changes in the medications you take because of a new health issue or worsening of an existing health issue since your last study visit?"

In addition, changes in any protocol-specific parameters and/or questionnaires evaluated 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.

11.3 Procedures for Recording and Reporting

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

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 comparator products on the Device Deficiency eCRF. The site must submit all available information on ADEs, SAEs, and device deficiencies to the study sponsor as follows:

- All SAEs must be reported immediately (within 24 hours) of the investigator's or site's awareness.
- ADEs that do not meet seriousness criteria and device deficiencies must be reported within 10 calendar days of the investigator's or site's awareness.
- A printed copy of the completed ***Serious Adverse Event and Adverse Device Effect*** and/or ***Device Deficiency*** eCRF must be included with product returns.
- Additional relevant information after initial reporting must be entered into the eCRF as soon as the data become available.
- Document any changes to concomitant medications on the appropriate eCRFs.
- Document all relevant information from Discharge Summary, Autopsy Report, Certificate of Death etc., if applicable, in narrative section of the *Serious Adverse Event and Adverse Device Effect* eCRF.

Note: Should the EDC system become nonoperational, the site must complete the appropriate paper *Serious Adverse Event and Adverse Device Effect* and/or *Device Deficiency* Form. The

completed form is emailed to the study sponsor at msus.safety@alcon.com according to the timelines outlined above; however, the reported information must be entered into the EDC system once it becomes operational.

In addition to recording all AEs into the EDC system, any AEs and device deficiencies for non-study marketed devices/products will be considered and processed as spontaneous following the postmarket vigilance procedures and should be communicated to the device's/product's manufacturer as per local requirements.

Study sponsor representatives may be contacted for any protocol related question and their contact information is 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 IRB/IEC.

Intensity and Causality Assessments

Where appropriate, the investigator must assess the intensity (severity) of the AE 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.

For every AE in the study, the investigator must assess the causality (Related or Not Related to the medical device or study procedure). An assessment of causality will also be performed by study sponsor utilizing the same definitions, as shown below:

Causality

Related An AE classified as related may be either definitely related or possibly related where a direct cause and effect relationship with the medical device or study procedure has not been demonstrated, but there is a reasonable possibility that the AE was caused by the medical device or study procedure.

Not Related An AE classified as not related may either be definitely unrelated or simply unlikely to be related (i.e., there are other more likely causes for the AE).

The study sponsor will assess the AEs and may upgrade the investigator's assessment of seriousness and/or causality. The study sponsor will notify the investigator of any AEs that is upgraded from nonserious to serious or from unrelated to related.

11.4 Return product analysis

Study sponsor representatives and their contact information are provided in the MOP that accompanies this protocol.

Should a product need to be returned, include the Complaint # which will be provided by study sponsor after the case is entered in the study sponsor's Global Product Complaint Management System (GPCMS).

Return any recoverable Alcon Product associated with a product related AE (ADE, SADE) or device deficiency to the sponsor. Procedures vary by country, so investigators must contact their assigned monitor for detailed guidance. Follow biohazard regulations if the product has touched the eye (i.e., place the product in a biohazard labeled bag). Include the SAE/ADE or device deficiency electronic case report form (eCRF) in the return package. Maintain a copy of shipment tracking information and all documents submitted with the product.

11.5 Unmasking of the Study Treatment

This study is assessor-masked for manifest refraction, VA, [redacted] and contrast sensitivity. To minimize bias, Alcon personnel (including biostatistics, masked data manager, and clinical project lead) will also be masked to the IOLs that have been previously implanted in the subject, to the extent possible. All other members associated with the study (at the site and the study sponsor) are unmasked.

This level of masking will be maintained throughout the conduct of the study. Unmasking will occur only after all planned study data have been validated, and the database locked.

11.6 Follow-Up of Subjects with Adverse Events

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 should 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 (i.e., database lock).

All complaints received after study completion 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.

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

12 ANALYSIS PLAN

In general, descriptive statistics generated for an endpoint will be based upon the type of parameter (i.e., whether the data is categorical or continuous) being analyzed. 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, sample size, mean, median, standard deviation, minimum, and maximum will be presented.

Analysis assumptions will be periodically reviewed during study conduct for deviations from analysis assumptions or the presence of outliers. The statistical methods should only be modified if there is a significant risk that the validity of the results can be substantively impacted. Because the study is open label, any discussion of analysis assumptions should not be based on review of any results by treatment group.

12.1 Subject Evaluability

Final subject evaluability must be determined prior to locking the database, based upon the Deviations and Evaluability Plan.

12.2 Analysis Sets

The Full Analysis Set (FAS) will include all eyes for enrolled subjects who are bilaterally implanted with the test or comparator IOL. The FAS will be the primary analysis set for effectiveness and will be used for all safety analyses.

12.3 Demographic and Baseline Characteristics

Demographic and baseline characteristics will be summarized by treatment group and overall. Counts and percentages will be presented for categorical variables such as sex, categorized age group (< 65 years; ≥ 65 years), race, and ethnicity. The number of values, mean, standard deviation, median, and minimum, and maximum values will be presented for continuous baseline variables.

12.4 Effectiveness Analyses

12.4.1 Analysis of Primary Effectiveness Endpoints

The co-primary effectiveness objectives are:

1. To demonstrate that Clareon Vivity/Vivity Toric IOL is non-inferior to Clareon Monofocal/Clareon Toric IOL in mean binocular photopic best corrected distance visual acuity (BCDVA) at 3 to 6 months (90 to 180 days) postoperatively.
2. To demonstrate that Clareon Vivity/Vivity Toric IOL is superior to Clareon Monofocal/Clareon Toric IOL in mean binocular photopic distance corrected intermediate visual acuity (DCIVA) (66 cm from spectacle plane) at 3 to 6 months (90 to 180 days) postoperatively.

The corresponding primary effectiveness endpoints are

- Binocular photopic BCDVA (logMAR) at 4 m.
- Binocular photopic DCIVA (logMAR) at 66 cm.

12.4.1.1 Statistical Hypotheses

The null and alternative hypotheses for the first primary effectiveness endpoint are:

$$H_0: \mu_{Test} - \mu_{Comparator} \geq \Delta$$

$$H_1: \mu_{Test} - \mu_{Comparator} < \Delta$$

where μ_{Test} and $\mu_{Comparator}$ are the means for binocular BCDVA for test (Clareon Vivity/Vivity Toric IOL) and comparator (Clareon Monofocal/Clareon Toric IOL), respectively, at 3 to 6 months (90 to 180 days) postoperatively, and Δ is the noninferiority margin set at 0.1 logMAR.

The null and alternative hypotheses for the second primary effectiveness endpoint are:

$$H_0: \mu_{Test} \geq \mu_{Comparator}$$

$$H_1: \mu_{Test} < \mu_{Comparator}$$

where μ_{Test} and $\mu_{Comparator}$ are the means for binocular DCIVA for test (Clareon Vivity/Vivity Toric IOL) and comparator (Clareon Monofocal/Clareon Toric IOL), respectively, at 3 to 6 months (90 to 180 days) postoperatively.

[redacted]

12.4.1.2 Analysis Methods

The FAS will be used for the primary statistical analyses for both endpoints. [redacted]

Analysis of the first primary endpoint (noninferiority for binocular BCDVA) will be based on a two-sample t-test assuming equal variances with testing based on a one-sided lower tailed test conducted at the 0.05 significance level. A corresponding two-sided 90% confidence interval for the difference in means (Clareon Vivity/Vivity Toric IOL minus Clareon/Clareon Toric IOL) will be presented. Noninferiority is demonstrated if the one-sided p-value for the t-test is less than 0.05 or, equivalently, the upper limit of the two-sided 90% confidence interval is less than the noninferiority margin. A two-sided 95% confidence intervals will also be provided for descriptive purposes.

Analysis of the second primary endpoint (superiority test for binocular DCIVA) will be based on a two-sample t-test assuming equal variances with testing based on a one-sided lower tailed test conducted at the 0.05 significance level. A two-sided 95% confidence interval for

the difference in means (Clareon Vivity/Vivity Toric IOL minus Clareon/Clareon Toric IOL) will be presented.

12.4.2 Analysis of Secondary Effectiveness Endpoints

The secondary effectiveness objectives are:

1. To demonstrate that Clareon Vivity/Vivity Toric IOL is superior to Clareon Monofocal/Clareon Toric IOL in mean binocular photopic distance corrected near visual acuity (DCNVA) (40 cm from spectacle plane) at 3 to 6 months (90 to 180 days) postoperatively.
2. To demonstrate that Clareon Vivity/Vivity Toric IOL is superior to Clareon Monofocal/Clareon Toric IOL with respect to proportion of subjects who respond "Never" to Q1 of the IOLSAT questionnaire (Overall, in the past 7 days, how often did you need to wear eyeglasses to see?) at 3 to 6 months (90 to 180 days) postoperatively.

The corresponding secondary effectiveness endpoints are:

- Mean binocular photopic DCNVA (logMAR) at 40 cm.
- Proportion of subjects who respond "Never" to Q1 of the spectacle use questionnaire (IOLSAT)

12.4.2.1 Statistical Hypotheses

The null and alternative hypotheses for the first secondary endpoint are:

$$H_0: \mu_{Test} \geq \mu_{Comparator}$$

$$H_1: \mu_{Test} < \mu_{Comparator}$$

where μ_{Test} and $\mu_{Comparator}$ are the means for binocular DCNVA for test (Clareon Vivity/Vivity Toric IOL) and comparator (Clareon Monofocal/Clareon Toric IOL), respectively, at 3 to 6 months (90 to 180 days) postoperatively.

The null and alternative hypotheses for the second secondary endpoint are:

$$H_0: p_{Test} \leq p_{Comparator}$$

$$H_1: p_{Test} > p_{Comparator}$$

where p_{Test} and $p_{Comparator}$ are the proportion of subjects who respond "Never" to Q1 of the IOLSAT, for test (Clareon Vivity/Vivity Toric IOL) and comparator (Clareon Monofocal/Clareon Toric IOL), respectively, at 3 to 6 months (90 to 180 days) postoperatively.

[redacted]

12.4.2.2 Analysis Methods

The FAS will be used for the primary statistical analyses for both endpoints. [redacted]

Analysis of the first secondary endpoint (binocular DCNVA) will be based on a two sample t-test assuming equal variances with testing based on a one-sided lower tailed test conducted at the 0.05 significance level. A two sided 95% confidence interval for the difference in means (Clareon Vivity/Vivity Toric IOL minus Clareon/Clareon Toric IOL) will also be presented.

Analysis of the second secondary endpoint (Q1 for IOLSAT) will be based on a Chi-squared test of two proportions with testing based on a one-sided upper tailed test carried out at the 0.05 significant level. The proportion of subjects who respond "Never" to Q1 of the spectacle use questionnaire (IOLSAT) in each group will be presented.

[redacted]

[redacted]

12.5 Handling of Missing Data

Missing data will not be imputed. Subjects will be included in each respective analysis if there is an observed result for that subject at the specified time point.

12.6 Safety Analyses

12.6.1 Analysis of Safety Endpoints

The safety endpoints are:

- Adverse events
- Device deficiencies
- QUVID subject survey
- Binocular and monocular (first eye implanted) mesopic contrast sensitivity test (with and without glare)
- IOP
- Slit lamp examination findings including:
    - IOL observations
    - Absolute IOL position change (tilt and decentration)
    - Subjective posterior capsular opacification (PCO)
    - Posterior capsulotomy rates
- Dilated fundus examination, including fundus visualization

12.6.1.1 Statistical Hypotheses

No hypothesis testing of the safety endpoints are planned.

12.6.1.2 Analysis Methods

The focus of the safety analysis will be a comprehensive descriptive assessment of occurrence of adverse events and other safety parameters. Descriptive summaries (counts and percentages) and listings will be presented. Individual subject listings will be provided for AEs that occur after signing informed consent.

12.7 Interim Analyses and Reporting

No interim analyses are planned.

12.8 Sample Size Justification

A total of 210 subjects will be enrolled (approximately 105 per arm). Assuming a screen failure rate of 9.5%, approximately 190 subjects will be evaluable at Visit 1 (95 per arm). The power estimates for the planned analyses are presented below:

Order	Endpoint	Comparison	Noninferiority Margin	Expected difference	SD^	Power
Co Primary	Binocular BCDVA	Noninferiority	0.10	0.04	0.14	90%
Co Primary	Binocular DCIVA at 66 cm	Superiority	NA	0.085	0.14	> 98%
1st Secondary	Binocular DCNVA at 40 cm	Superiority	NA	0.14	0.14	> 99%
2nd Secondary	Q1 of IOLSAT = NEVER	Superiority	NA	0.14	NA	> 96%
[redacted]						

Overall power is estimated based on the assumption that each hypothesis test is independent.

13 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

13.1 Subject Confidentiality

The investigator must ensure that the subject's identity is kept confidential 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. The study sponsor may collect a copy of the enrollment log ***without any directly identifying subject information***.

The study sponsor may share patient-level data collected in this study with qualified researchers to help facilitate product development or enhancements in research that is not directly related to the study objectives. The informed consent explains this to the study subject.

13.2 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 CRFs exist and are accessible for verification by the site monitor, and all discrepancies shall be appropriately documented via the query resolution process. Site monitors are appointed by the study sponsor and are independent of study site staff.

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

At a minimum, source documents include the following information for each subject:

- Subject identification (name, sex, race/ethnicity)
- Documentation of subject eligibility
- Date of informed consent
- Dates of visits
- Documentation that protocol specific procedures were performed
- Results of study parameters, as required by the protocol
- Documentation of AEs and other safety parameters (if 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

It is required that the author of an entry in the source documents be identifiable. Direct access to source documentation (medical records) must be allowed for the purpose of verifying that the data recorded on the CRF are consistent with the original source data.

Only designated individuals at the site will complete the CRFs. The CRFs must be completed at regular intervals following the clinical study visit schedule. It is expected that all data reported have corresponding entries in the source documents. The principal investigator is responsible for reviewing and certifying that the CRFs are accurate and complete. The only subject identifiers recorded on the CRFs will be subject number, and subject demographic information.

13.3 Data Review and Clarifications

A review of CRF data to the subject's source data will be completed by the site monitor to ensure completeness and accuracy. After the CRFs have been completed, additional data

clarifications and/or additions may be needed as a result of the data cleaning process. Data clarifications are documented and are part of each subject's CRF.

13.4 Sponsor and Monitoring Responsibilities

The study sponsor will select principal investigators that are qualified by education, training, and experience to assume responsibility for the proper conduct of this clinical study.

The study sponsor is financially funding this clinical study and will compensate the investigator and/or the institution(s) at which the study is conducted in accordance with a signed clinical study agreement.

The study sponsor will designate a monitor to conduct the appropriate site visits at the appropriate intervals according to the study monitoring plan. The clinical investigation will be monitored to ensure that the rights and wellbeing of the subjects are protected, the reported data are accurate, complete, and verifiable from the source documents, and the study is conducted in compliance with the current approved protocol (and amendments[s], if applicable), with current GCP, and with applicable regulatory requirements.

The site may not screen subjects or perform the informed consent process on any subject until it receives a notification from an appropriate study sponsor representative that the site may commence conducting study activities. Monitoring will be conducted periodically while the clinical study is ongoing. Monitoring methods may include site visits, telephone, written and fax correspondence. Close-out visits will take place after the last visit of the last subject at the site.

A coordinating investigator may be identified by the study sponsor to review and endorse the final study report. In cases where a coordinating investigator is engaged, the study sponsor will select the coordinating investigator based upon their experience, qualifications, active study participation, and their willingness and availability to take on this role.

13.5 Regulatory Documentation and Records Retention

The investigator is required to maintain up-to-date, complete regulatory documentation as indicated by the study sponsor and the investigator's files will be reviewed as part of the ongoing study monitoring. Financial information is to be kept separately.

Additionally, the investigator must keep study records and source documents consistent with the terms of the clinical study agreement with the study sponsor. If the investigator retires, relocates, or for any other reason withdraws from responsibility of keeping the study records,

then the study sponsor must be notified, and suitable arrangements made for retention of study records and source documents needed to comply with national and international regulations.

13.6 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.

14 ETHICS

Investigations are conducted in compliance with Good Clinical Practices; international and national regulations, laws and guidelines; ISO 14155; the conditions of approval imposed by reviewing IRBs/IECs or regulatory authorities; and in accordance with the ethical medical research principles outlined in the Declaration of Helsinki

- The SOPs of the study sponsor and contract research organizations participating in the conduct of the clinical study and all other applicable regulations shall apply.
- Notifications and timelines for reporting protocol deviations should be based upon applicable Ethics Committee requirements.

The investigator must ensure that all personnel involved in the conduct of the study are qualified to perform their assigned responsibilities through relevant education, training, and experience. The investigator and all clinical study staff must conduct the clinical study in compliance with the protocol. The investigator is not allowed to deviate from the protocol except to protect the rights, safety, and well-being of human subjects under emergency circumstances. Emergency deviations may proceed without prior approval of the sponsor and the IRB/IEC, but shall be documented and reported to the sponsor and the IRB/IEC as soon as possible. Deviations from this protocol, regulatory requirements, and/or GCP must be recorded and reported to the Sponsor prior to database lock. If needed, corrective and preventive action should be identified, implemented, and documented within the study records. Failure to implement identified corrective and preventative actions may result in site closure by the sponsor. Use of waivers to deviate from the clinical protocol is prohibited.

Before clinical study initiation, this protocol, the informed consent form, any other written information given to subjects, and any advertisements planned for subject recruitment must be approved by an IRB/IEC. The investigator must provide documentation of the IRB/IEC approval to the study sponsor. 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 subject, and subject compensation programs. The IRB/IEC must be provided with any periodic safety updates, and all other information as required by local regulation and/or the IRB/IEC. Any additional requirements imposed by the EC or regulatory authority shall be followed. At the end of the study, the investigator must notify the IRB/IEC about the study's completion. The IRB/IEC also must be notified if the study is terminated prematurely. Finally, the investigator must report to the IRB/IEC on the progress of the study at intervals stipulated by the IRB/IEC.

Voluntary informed consent must be obtained in writing from every. The obtaining of consent shall be documented before any procedure specific to the clinical investigation is applied to the subject.

The investigator must have a defined process for obtaining the required consent. Specifically, the investigator, or their delegate, must explain the clinical study 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 provide subjects with information regarding the purpose, procedures, requirements, and restrictions of the study, along with any known risks and potential benefits associated with the IP and the study, 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 study and must be provided with contact information for the appropriate individuals should questions or concerns arise during the study. The subject also must 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 (file in subject's medical records) and must provide a duplicate copy to each subject according to local regulations.

The study sponsor assures that the key designs of this protocol will be registered on public databases where required by current regulations, and, as applicable, results will be posted.

15 REFERENCES

Not applicable

15.1 Regulations and Standards

The following references may be applicable in whole or in part for this clinical study.

- ISO 14155:2020 - Clinical Investigation of Medical Devices for Human Subjects - Good Clinical Practice
- 21 CFR Part 11 - Electronic Records; Electronic Signatures
- 21 CFR Part 50 - Protection of Human Subjects
- 21 CFR Part 56 - Institutional Review Boards
- 21 CFR Part 54 - Financial Disclosure by Clinical Investigators

15.2 Scientific and Other References

Not applicable

16 APPENDIX A – Protocol Amendments

There are no amendments. This is the first version of the protocol.