Contralateral Study of Clareon PanOptix Pro vs. Clareon PanOptix

STUDY ID

ILQ137-C002 Study A

PROTOCOL v2

18-Mar-2025

NCT06400745

Device Protocol for ILQ137-C002

Title: Contralateral Study of Clareon PanOptix Pro vs. Clareon PanOptix

Protocol Number:	ILQ137-C002
Clinical Investigation Type:	Post Market Interventional / Confirmatory
Test Product:	Clareon™ PanOptix™ Pro Trifocal IOL, Model PXYWT0 Clareon™ PanOptix™ Pro Trifocal IOL, Model PAYWT0
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 trial 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:

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1 GLOSSARY OF TERMS

Names of Test Product(s)	Throughout this document, test product(s) will be referred to as Clareon PanOptix Pro, Model PXYWT0 and Clareon PanOptix Pro, Model PAYWT0 When Clareon PanOptix Pro is used it refers to both models independently: Model PAYWT0 or Model PXYWT0
Name of Comparator Product(s)	Clareon PanOptix, Model CNWTT0
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 Trial	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 trial, 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).
Noninterventional Study	Clinical investigation that draws inferences about the possible effect of an intervention on subjects, but the investigator has not assigned subjects into intervention groups based on a protocol and has not made any attempts to collect data on variables beyond those available throughout the course of normal clinical practice and burden to the subject. NOTE: The term "noninterventional" is synonymous with "observational."
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 labeling 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.
Randomized Subject	Any subject who is assigned a randomized treatment.
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 trial, 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
AAS	All-Implanted Analysis Set
ACD	Anterior chamber depth
ADE	Adverse device effect
AE	Adverse event
[redacted]	[redacted]
ASADE	Anticipated serious adverse device effect
BAS	Best Case Analysis Set
BCDVA	Best corrected distance visual acuity
CFR	Code of Federal Regulations
CIP	Clinical investigation plan
cm	Centimeter
Clareon PanOptix, Model CNWTT0	Clareon PanOptix Trifocal IOL, Model CNWTT0
Clareon PanOptix Pro	Clareon PanOptix Trifocal IOL, Model PAYWT0 and Clareon PanOptix Trifocal IOL, Model PXYWT0
Clareon PanOptix Pro, Model PAYWT0	Clareon PanOptix Pro Trifocal IOL, Model PAYWT0
Clareon PanOptix Pro, Model PXYWT0	Clareon PanOptix Pro Trifocal IOL, Model PXYWT0
CPO	Clareon PanOptix, Model CNWTT0
CPO Pro	Clareon PanOptix Pro Trifocal IOL, Model PAYWT0 or Clareon PanOptix Pro Trifocal IOL, Model PXYWT0
CRF	Case report form
D	Diopter
[redacted]	[redacted]
[redacted]	[redacted]
eCRF	Electronic case report form
EDC	Electronic data capture
EC	Ethic Committee
eIFU	Electronic instructions for use
EN	European standard
ETDRS	Early treatment diabetic retinopathy study
GCP	Good Clinical Practice
IB	Investigator's brochure
ICF	Informed consent form
IFU	Instructions for use
IOL	Intraocular lens

Abbreviation	Definition
IOP	Intraocular pressure
IP	Investigational product
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
[redacted]	[redacted]
MTF	Modulation Transfer Function
n	Number
Nd:YAG	Neodymium-doped yttrium aluminum garnet
NI	Noninferiority
nm	nanometer
N/A	Not applicable
OD	Right eye
OS	Left eye
OUS	Outside of the United States
PCO	Posterior capsular opacification
S	Superior
SADE	Serious adverse device effect
SAE	Serious adverse event
SAS	Safety Analysis Set
Std.	Standard
SSI	Secondary surgical intervention
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
USA	United States of America
USADE	Unanticipated serious adverse device effect
VA	Visual acuity

3 PROTOCOL SUMMARY

Investigational product type	Device
Study type	Interventional
Investigational products	Test Products: Clareon PanOptix Pro Trifocal IOL, Model PXYWT0 and Clareon PanOptix Pro Trifocal IOL, Model PAYWT0 Comparator Product: Clareon PanOptix Trifocal IOL, Model CNWTT0
Purpose and Scientific Rationale for the Study	The studies under this protocol (sub-study A and sub-study B) will establish the safety and effectiveness of two Clareon PanOptix Pro models (Models PXYWT0 and PAYWT0). [redacted]
Brief Summary of the Protocol	The objective of the studies under this protocol is to evaluate the safety and effectiveness of the two Clareon PanOptix Pro models: Model PXYWT0 and Model PAYWT0 compared to Clareon PanOptix. Subjects will be implanted contralaterally with Clareon PanOptix Pro (test) and Clareon PanOptix (comparator). Each of the Clareon PanOptix Pro models represents an incremental change to Clareon PanOptix, as such, the indications for use for each model is the same. Subjects will be randomized to one of two sub-studies. Sub-study A will evaluate Model PXYWT0 and sub-study B will evaluate Model PAYWT0. Subjects randomized to sub-study A will be further randomized to receive Model PXYWT0 or Clareon PanOptix in the first surgical eye, and the second eye will receive the other lens. Similarly, subjects randomized to sub-study B will be further randomized to receive Model PAYWT0 or Clareon PanOptix in the first surgical eye and the second eye will receive the other lens. The 1st surgical eye will be the eye with the worse BCDVA at screening. When the BCDVA is equal between the two eyes, the right eye (OD) will be the 1st surgical eye.

	Subjects in each study will be followed for a total of approximately 6 months postoperatively with key endpoints being assessed at the 2-month postoperative follow-up visit (Visit 3A).
Objective(s)	**Primary Effectiveness Objectives (Sub-Study A and Sub-Study B):** To demonstrate noninferiority of monocular photopic BCDVA of the Clareon PanOptix Pro models compared to Clareon PanOptix at 2 months postoperative (Visit 3A).

Endpoint(s)	**Primary Effectiveness (Sub-Study A and Sub-Study B)**
	• Mean monocular photopic BCDVA (logMAR) at 4 m at 2 months postoperative (Visit 3A).
	Safety (Sub-Study A and Sub-Study B)
	• AEs
	• Device deficiencies
	• IOP
	• Slit lamp examination findings including:
	  • Proportion of eyes with subjective posterior capsular opacification (PCO)
	  • Proportion of eyes with posterior capsulotomy
	  • IOL observations
	• Dilated fundus examination findings, including fundus visualization
	• Intraoperative surgical problems
	• Other procedures at surgery (combined and/or additional)
	• SSIs

Assessment(s)	**Effectiveness** [redacted] • Monocular photopic BCDVA (logMAR) at 4 m **Safety** • Slit lamp examination, including:

	• Posterior capsule opacification evaluation • Posterior capsulotomy evaluation • IOL observations • Intraocular pressure • Dilated fundus examination • Ocular and nonocular AEs • Device deficiencies • SSIs
Study Design	This is a prospective, multicenter, randomized, assessor and subject masked, contralateral, active controlled study. The study protocol contains two sub studies: Sub-study A and Sub-study B • Sub-study A (n = ~66 implanted subjects) – Subjects implanted contralaterally with Clareon PanOptix Pro, Model PXYWT0 in 1 eye and Clareon PanOptix, Model CNWTT0 in the fellow eye • Sub-study B (n = ~66 implanted subjects) – Subjects implanted contralaterally with Clareon PanOptix Pro, Model PAYWT0 in 1 eye and Clareon PanOptix, Model CNWTT0 in the fellow eye Subjects at each site will be randomized to either sub-study A or sub-study B. The protocol will be executed simultaneously and identically for both sub-studies by the sites. Segregation by sub-study A and sub-study B will only be used for analysis and reporting. (See additional information in Appendix B and Appendix C). Enrollment will commence at approximately 10 investigative sites. All of the study sites will be located in one country, the United States. The total duration of a subject's participation in the study is approximately 7 months, attending 9 study visits (which includes the Screening Visit). Subjects will be followed for a total of approximately 6 months postoperatively [redacted]

<table>
<tr><td>Subject population</td><td>Adult subjects with bilateral cataracts and less than 1.00 D of preoperative corneal astigmatism.

Planned number of subjects enrolled/consented: Approximately 158

Planned number of treated/implanted/randomized subjects: Approximately 132

Planned number of completed subjects: Approximately 120</td></tr>
<tr><td>Sites and Locations</td><td>Planned number of clinical sites: Approximately 10 sites

Planned locations (initial list of locations, which may change during start up or conduct according to study needs): United States</td></tr>
<tr><td>Key inclusion criteria
(See Section 8.1 for a complete list of inclusion criteria)</td><td>Adults (22 years or older at the time of participation in the study) with bilateral cataracts.

Preoperative corneal astigmatism less than 1.00 D in each eye.</td></tr>
<tr><td>Key exclusion criteria
(See Section 8.2 for a complete list of exclusion criteria)</td><td>Subjects who desire monovision correction.

Predicted residual astigmatism of > 0.50 D between the two eyes.</td></tr>
<tr><td>Data analysis and sample size justification</td><td>A total of 132 subjects will be randomized (approximately 66 per sub-study). Assuming a drop-out rate of 10%, approximately 60 subjects will be evaluable at the 2-month postoperative period (visit 3A) for each sub-study. The power estimates for each of the powered analyses are presented below:

<table>
<tr><td>Order</td><td>Endpoint</td><td>Comparison</td><td>Expected difference</td><td>Std. Dev^</td><td>Power</td></tr>
<tr><td colspan="6">Sub-study A and Sub-Study B</td></tr>
<tr><td>Primary</td><td>Monocular BCDVA</td><td>NI</td><td>0</td><td>.08</td><td>>99.9%</td></tr>
<tr><td colspan="6">[redacted]A NI margin of 0.1 logMAR is used for the non-inferiority comparisons above.</td></tr>
</table>
</td></tr>
</table>

Associated materials	None

Table 3-1 Schedule of Study Procedures and Assessments

	Visit 0	Visit 00[b]	Visit 1	Visit 2	Visit 00A[c]	Visit 1A	Visit 2A	Visit 3A[d]	Visit 4A	USV[e]
Procedure/Assessment	Screening **Preoperative**	Day 0 **1st Eye Surgery**	Day 1-2 Post Visit 00	Day 7-14 Post Visit 00	Day 0 for **2nd Eye Surgery**	Day 1-2 Post Visit 00A	Day 7–14 Post visit 00A	Day 45-70 (2 Months) Post Visit 00A	Day 180-210 (6 Months) Post Visit 00A	Unscheduled Visit
Informed Consent	X									
Demographics	X									
Medical History	X									
Concomitant Medications	X	X	X	X	X	X	X	X	X	X
Urine Pregnancy Test[a*]	X									
Inclusion/Exclusion criteria	X	X			X					
Slit lamp Exam	X[h]		X	X		X	X	X	X	(X)
Dilated fundus examination	X[h]								X	(X)
Keratometry	X[h]									
Axial length	X[h]									
Anterior Chamber Depth	X[h]									
Target Residual Refractive Error	X[h]									
Predicted Residual Astigmatism	X[h]									
Intraocular pressure	X		X	X		X	X	X	X	(X)

[redacted]

	Visit 0	Visit 00[b]	Visit 1	Visit 2	Visit 00A[c]	Visit 1A	Visit 2A	Visit 3A[d]	Visit 4A	USV[e]
Procedure/Assessment	Screening **Preoperative**	Day 0 **1st Eye Surgery**	Day 1-2 Post Visit 00	Day 7-14 Post Visit 00	Day 0 for **2nd Eye Surgery**	Day 1-2 Post Visit 00A	Day 7–14 Post visit 00A	Day 45-70 (2 Months) Post Visit 00A	Day 180-210 (6 Months) Post Visit 00A	Unscheduled Visit
Monocular Photopic Best Corrected Distance Visual Acuity (4 m)	**X**							**X**	**X**	**(X)[g]**
[redacted]										

	Visit 0	Visit 00[b]	Visit 1	Visit 2	Visit 00A[c]	Visit 1A	Visit 2A	Visit 3A[d]	Visit 4A	USV[e]
Procedure/Assessment	Screening **Preoperative**	Day 0 **1st Eye Surgery**	Day 1-2 Post Visit 00	Day 7-14 Post Visit 00	Day 0 for **2nd Eye Surgery**	Day 1-2 Post Visit 00A	Day 7–14 Post visit 00A	Day 45-70 (2 Months) Post Visit 00A	Day 180-210 (6 Months) Post Visit 00A	Unscheduled Visit
Subjective Posterior Capsule Opacification			**X**	**X**		**X**	**X**	**X**	**X**	**(X)**
Nd:YAG capsulotomy[i]			**(X)**	**(X)**		**(X)**	**(X)**	**(X)**	**(X)**	**(X)**
IOL observations			**X**	**X**		**X**	**X**	**X**	**X**	**(X)**
Secondary Surgical Interventions		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**(X)**
Randomization	X[j]									
Device Deficiencies		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Adverse Events (including SSI), both volunteered and elicited	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**

a. In women of child-bearing potential only
b. It is recommended that Visit 00 (1st eye surgery) occur within 14 days of the Screening Visit (Visit 0).
c. It is recommended that Visit 00A (2nd eye surgery) occur a minimum of 7 days and a maximum of 14 days after Visit 00 (1st eye surgery).
d. If necessary, Visit 3A may be completed over 2 days within a two week period. Visit 3A must be completed within the specified window.
e. Unscheduled Visit: Assessments marked as (X) are optional as per the investigator's discretion.
f. In the surgical eye that is applicable to the visit.
g. Unscheduled Visit: [redacted] monocular photopic BCDVA done using the standard of care method (e.g., Snellen, LogMAR).
h. Historical data collected prior to informed consent and within 60 days of Screening (Visit 0), may be used if collected per study requirements.
i. (X): Procedure performed as necessary.
j. Randomization must occur after confirmation of eligibility and prior to 1st eye surgery.
*Documented in source document only. No entry into database

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.

[redacted].

5 INTRODUCTION

5.1 Rationale and Background

[redacted]

The studies under this protocol seek to understand the safety and effectiveness of the two Clareon PanOptix Pro models (PXYWT0 and PAYWT0). Subjects will be implanted contralaterally with one of the Clareon PanOptix Pro models (test) and Clareon PanOptix (comparator).

5.2 Purpose of the Study

The objective of the studies under this protocol is to:

Evaluate the safety and effectiveness of the two Clareon PanOptix Pro models (Model PXYWT0 and Model PAYWT0) compared to Clareon PanOptix

[redacted]

[redacted]

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 these sub-studies 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, in order 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 product labeling/IFUs and are managed through review of safety assessments outlined in this protocol.

Participation in the clinical study will require the subject to undergo cataract surgery and implantation with one of the Clareon PanOptix Pro models (test) in one eye and Clareon PanOptix (comparator) in the fellow eye. Complications may occur on the surgery day or throughout the postoperative period. 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 preexisting 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, hyphema, and retinal damage. An IOP increase may occur from the surgical procedure, residual viscoelastic in the eye, or a steroid response to postoperative medications. Additionally, potential postoperative AEs 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 residual refractive error, ocular infection, subject dissatisfaction, or visual disturbances (e.g., glare, halos, starbursts, hazy vision, blurred vision, double vision, visual distortions, and color distortions). An SSI (e.g., IOL

repositioning, replacement, or explantation) may be appropriate if the IOL position significantly differs from the intended placement. Alternatively, spectacles or contact lenses may be prescribed to resolve residual refractive error. Other SSIs include, but are not limited to: IOL repositioning, refractive laser treatment, paracentesis, vitreous aspirations, iridectomy or laser iridotomy for pupillary block, wound leak repair, and retinal detachment repair.

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

Refer to the IFUs for additional information.

Clinical evidence from published peer-reviewed clinical literature, clinical experience, and clinical investigations with parent IOLs establishes an acceptable safety and effectiveness profile for the Clareon PanOptix IOL. The Clareon PanOptix IOL is indicated for visual correction of aphakia and treatment of the effects of presbyopia in adult patients. The Clareon PanOptix IOL treats the effects of aphakia and presbyopia by providing near, intermediate, and distance vision following crystalline lens removal and IOL implantation and provides increased spectacle independence. Based on the formal risk assessment, it was concluded that the benefits of increased near and intermediate vision while maintaining good vision at distance significantly outweigh the risks of suboptimal surgical outcomes and increased likelihood of visual disturbances when the Clareon PanOptix IOLs are used in cataract surgery.

The risk/benefit profile for Clareon PanOptix Pro models is expected to be the same as Clareon PanOptix as these newer models represent an incremental change to Clareon PanOptix. Clareon PanOptix Pro has the same indications as Clareon PanOptix and is also indicated for visual correction of aphakia and treatment of the effects of presbyopia in adult patients. This study is designed to assess if the Clareon PanOptix Pro models may provide additional clinical benefits.

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

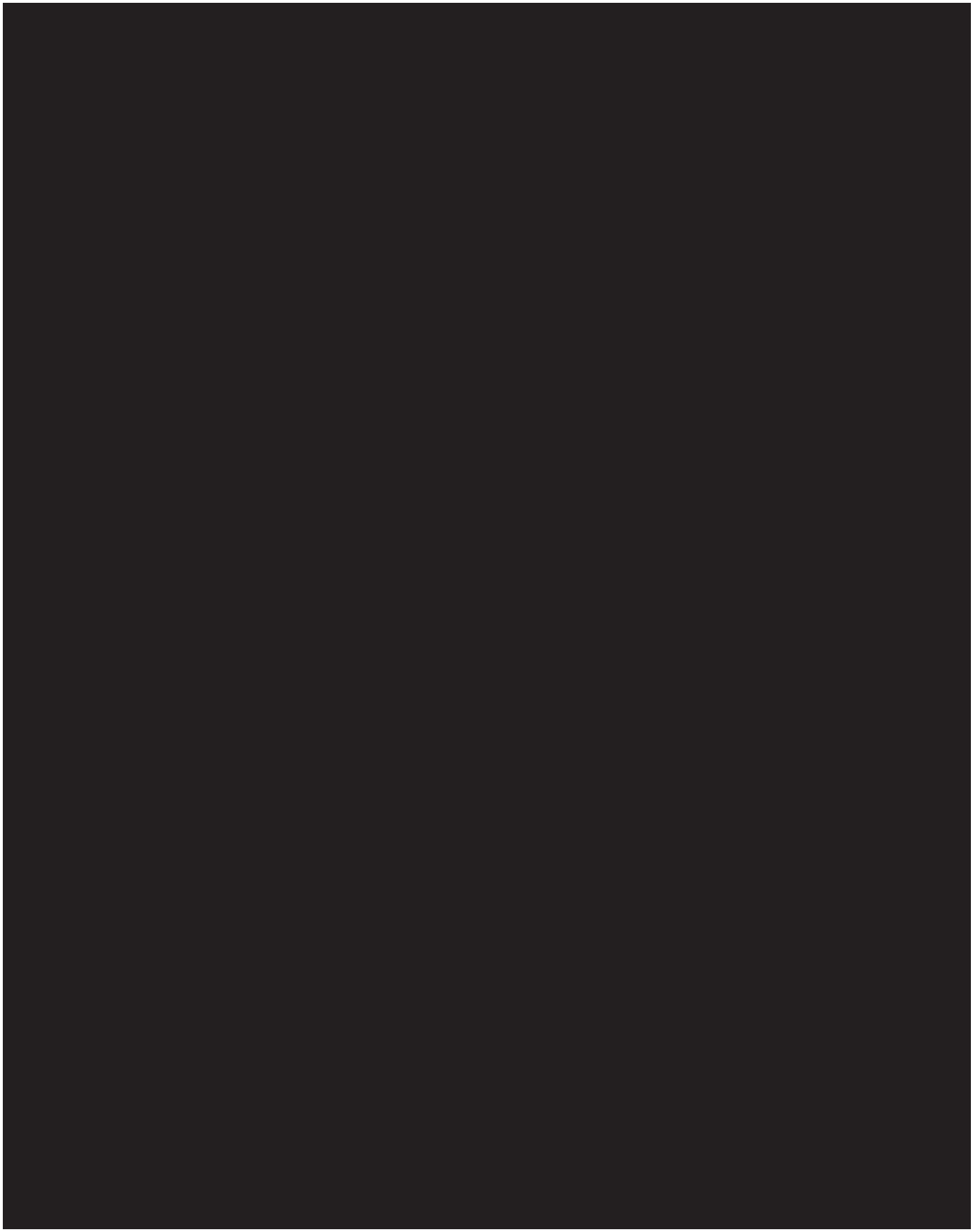
6.1 Primary Objective(s)

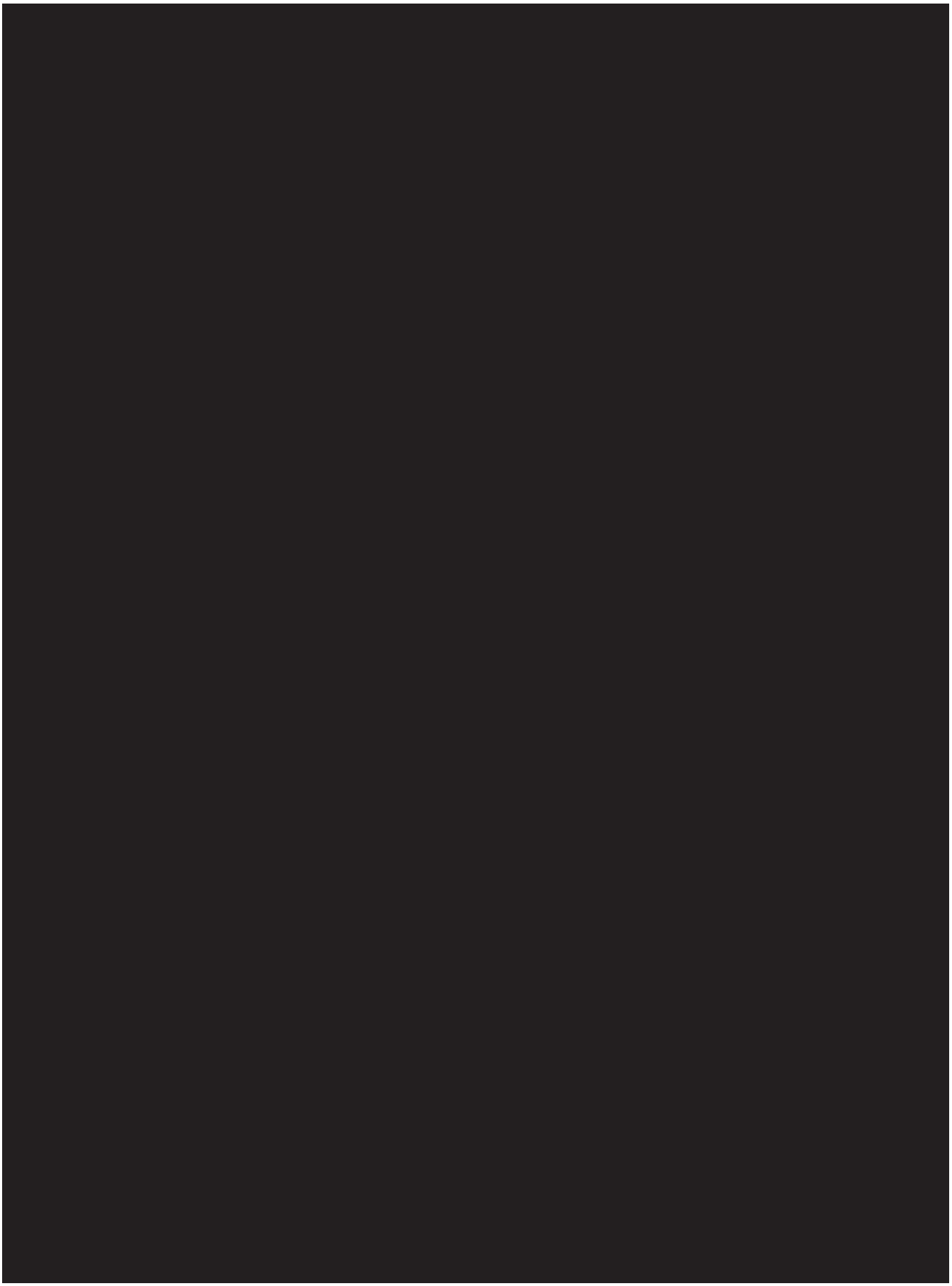
Table 6-1 Primary Objective(s): Sub-Study A and Sub-Study B

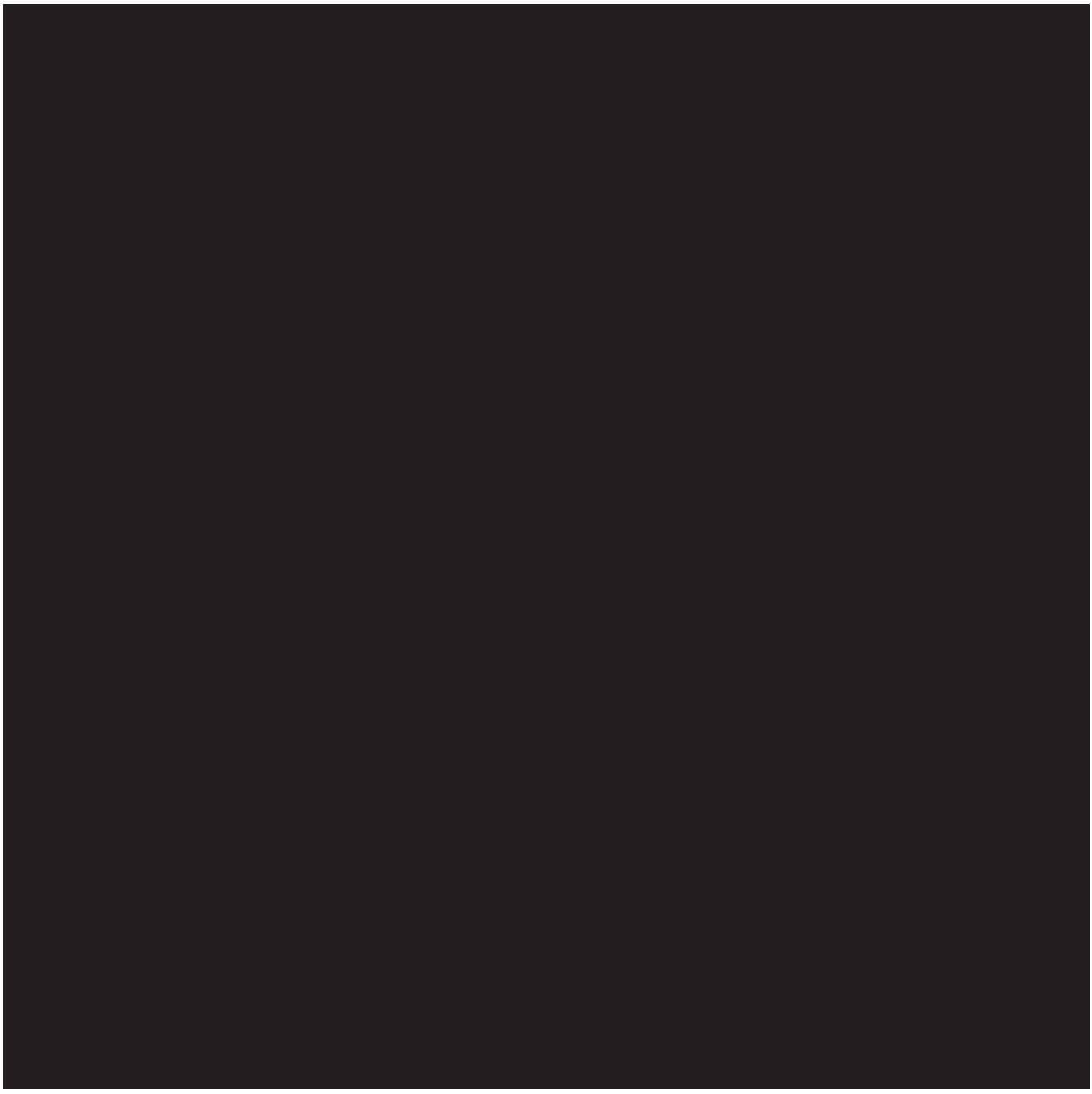
Objective(s)	**Endpoint(s)**
To demonstrate noninferiority of monocular photopic BCDVA of the Clareon PanOptix Pro models compared to Clareon PanOptix at 2 months postoperative (Visit 3A).	Mean monocular photopic BCDVA (logMAR) at 4 m at 2 months postoperative (Visit 3A).

6.2 Secondary Objective(s):

N/A







6.5 Safety Objective(s): Sub-Study A and Sub-Study B

Table 6-5 Safety Objective(s): Sub-Study A and Sub-Study B

Objective(s)	**Endpoint(s)**
To describe the incidence of ocular AEs including SSIs at all visits	• AEs • Device deficiencies • IOP • Slit lamp examination findings including:

Objective(s)	Endpoint(s)
	○ Proportion of eyes with subjective posterior capsular opacification (PCO) ○ Proportion of eyes with posterior capsulotomy ○ IOL observations • Dilated fundus examination findings, including fundus visualization • Intraoperative surgical problems • Other procedures at surgery (combined and/or additional) • SSIs

7 INVESTIGATIONAL PLAN

7.1 Study Design

This is a prospective, multicenter, randomized, assessor and subject masked, contralateral, active controlled study.

The study protocol contains two sub-studies: sub-study A and sub-study B

- Sub-study A (n = ~66 implanted subjects) – Subjects implanted contralaterally with Clareon PanOptix Pro, Model PXYWT0 in one eye and Clareon PanOptix, Model CNWTT0 in the fellow eye
- Sub-study B (n = ~66 implanted subjects) – Subjects implanted contralaterally with Clareon PanOptix Pro, Model PAYWT0 in one eye and Clareon PanOptix, Model CNWTT0 in the fellow eye

After subjects have been screened and met inclusion/exclusion criteria, subjects will be randomized to one of the two sub-studies. Sub-study A will evaluate PXYWT0 and sub-study B will evaluate PAYWT0. Subjects randomized to sub-study A will be further randomized to receive Model PXYWT0 or Clareon PanOptix in the first surgical eye, and the second eye will receive the other lens. Similarly, subjects randomized to sub-study B will be further randomized to receive Model PAYWT0 or Clareon PanOptix in the first surgical eye and the second eye will receive the other lens.

For both groups, the 1st operative eye is defined as the eye with the worse BCDVA at Screening (Visit 0). If the BCDVA is the same in both eyes, the right eye (OD) will be identified as the 1st operative eye.

The protocol will be executed simultaneously and identically for both sub-studies by the sites. (All testing and assessments will be the same for both sub-studies.) Segregation by sub-study A and sub-study B will only be used for analysis and reporting. (See additional information in Appendix B and Appendix C).

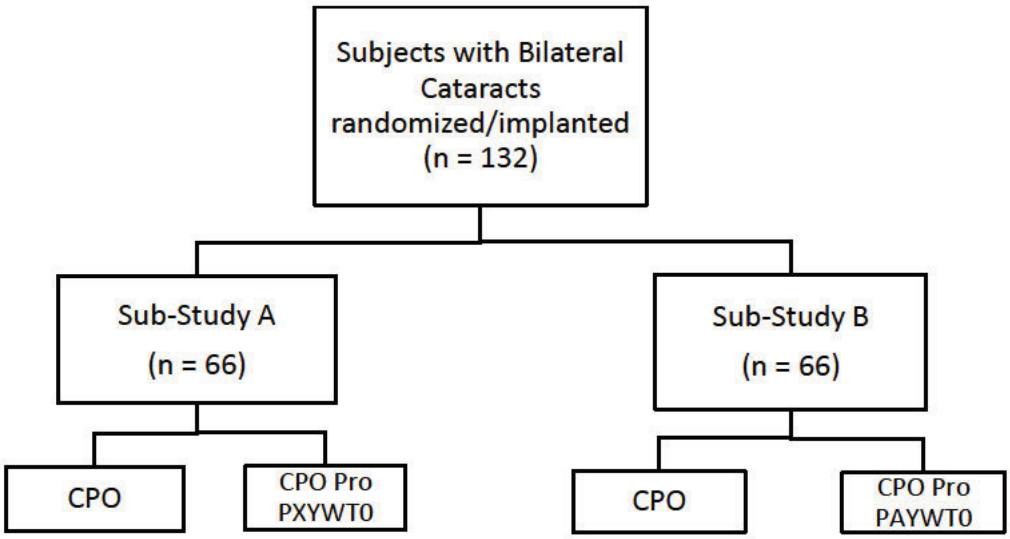
Enrollment will commence at approximately 10 investigative sites. All of the study sites will be located in one country, the United States.

The total duration of a subject's participation in the study is approximately 7 months, attending 9 study visits (which includes the Screening Visit). Subjects will be followed for a total of approximately 6 months postoperatively [redacted]

The duration of the entire study is approximately one year.

Exposure to IP is designed to remain in the eye for a lifetime of the subject.

Figure 7-1 Study Design Flowchart



7.2 Rationale for Study Design

This study design is justified based upon an evaluation of the results of relevant preclinical and clinical testing, as described within the IFUs. This will be a prospective, randomized, controlled contralateral implant study to investigate key safety and effectiveness endpoints.

- The two sub-studies under this protocol will establish the safety and effectiveness of two Clareon PanOptix Pro models (PXYWT0 and PAYWT0). A sub-study design was selected, as opposed to two separate protocols, for efficiency of execution since the

protocol will be executed simultaneously and identically for both sub-studies by the sites.

- Subjects will be implanted contralaterally with Clareon PanOptix Pro (test) and Clareon PanOptix (comparator). The contralateral study design allows for assessment of subject response and will confirm noninferiority of the Clareon PanOptix Pro [redacted]

- To reduce bias, testing methods have predefined procedures. Also, this study is assessor and subject-masked. [redacted] Masked assessors will be masked to IOLs implanted in the subject until the time of the final database lock. Subjects will be masked to the IOLs implanted until the end of their study exit visit.

7.2.1 Purpose and Timing of Interim Analyses and Resulting Design Adaptations

Two interim analyses are planned for this study. The first interim analysis will occur when approximately 40 subjects (20 subjects in each sub-study; minimum of 30 subjects total) have completed the 2-month visit (Visit 3A). This analysis is designed to review preliminary safety and effectiveness results for strategic business decisions.

The second interim analysis will be conducted after all treated subjects have completed the 2-month visit (Visit 3A) and all inferential analysis will be conducted.

No changes will be made to the design or conduct of the ongoing study as a result of the interim analyses.

7.3 Rationale for Duration of Treatment/Follow-Up

All subjects will be followed for approximately 6 months postoperatively. This period will allow sufficient subject recovery from surgery and stability of visual outcomes. Additionally, this postoperative period will ensure adequate evaluation of the primary [redacted] endpoints being assessed at the 2-month (Visit 3A) postoperative visit, and to adequately assess device safety.

7.4 Rationale for Choice of Comparator Product

The comparator used in this study, Clareon PanOptix IOL, Model CNWTT0 is a well-established trifocal IOL with proven benefits and safety profile. It was chosen to allow confirmation of noninferiority of the Clareon PanOptix Pro models [redacted]

7.5 Data Monitoring Committee

Not applicable

8 STUDY POPULATION

The study population consists of male and female subjects (age 22 or older at the time of participation in the study) with a diagnosis of bilateral cataracts. It is aimed to enroll (consent) approximately 158 in approximately 10 sites in the United States, with a target of 132 contralaterally implanted subjects, with approximately 13 to 22 subjects per site. Site-specific targets may vary based upon individual site capabilities. Estimated time needed to recruit subjects for the study is approximately 6 months; however, unanticipated circumstances may shorten or lengthen this time and would not require amendment of this protocol.

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

Elderly – It is appropriate to include elderly subjects in this clinical trial, as cataract formation is a known age-related occurrence and is common to this population. The investigational IOL under study is intended for implantation upon the removal of a cataractous crystalline lens to alleviate this age-related condition common to the elderly population. It is necessary to include elderly subjects in this clinical trial to gain data regarding the safety and effectiveness of the investigational IOL in this population.

The elderly population 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 trial 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 trial, 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.

Both eyes of a subject must qualify for enrollment into this 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 (22 years or older at the time of participation in the study) with bilateral cataracts
4.	Planned bilateral cataract extraction by routine phacoemulsification
5.	Calculated IOL power between +15 D and +25 D in each eye when targeting emmetropia, defined as IOL power with amount of targeted postoperative refractive error closest to 0 D based on power calculation
6.	Preoperative corneal astigmatism less than 1.00 D in each eye
7.	Potential postoperative BCDVA of 0.2 logMAR or better in each eye in the expert medical opinion of the investigator

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; however, data will be excluded from selected analyses (described in Section 12.2) because pregnancy can alter refraction and VA results
2.	History of anterior segment (corneal, anterior chamber, sulcus) or posterior segment (uveal, vitreoretinal) pathologic change including retinal vascular occlusive disease, retinal detachment or peripheral retinal laser photocoagulation, ARMD, glaucoma, diabetic retinopathy, retinitis pigmentosa, and any pathologic changes associated with the optic nerve
3.	History of recurrent anterior segment/posterior segment inflammation
4.	Clinically significant corneal diseases (epithelium, stromal, and/or endothelium) that may, according to the investigator's medical opinion, adversely affect visual outcomes. These ocular pathologies include but are not limited to old significant corneal scars (including Salzman's nodular degeneration), active or inactive keratitis with compromise of the refractive capability of the cornea, keratoconjunctivitis sicca with compromise of visual function, active keratouveitis, endothelial dystrophy (Fuch's and non-guttate), keratoconus, etc. *Note: Patients with any pathological manifestations that may potentially affect postoperative VA should not be included in this study*
5.	Clinically significant/severe dry eye that would affect study measurements based on the investigator's expert medical opinion
6.	History of previous intraocular or corneal (refraction or trauma related) surgery
7.	Current or past history of amblyopia or monofixation syndrome with poor stereoscopic vision
8.	Subjects currently participating in another investigational drug or device study that may confound the results of this investigation
9.	Any other ocular or systemic comorbidity that, in the investigator's medical opinion, may confound the results of this study or prohibit the completion of the study assessments or increase the risk for the subject
10.	Subjects with conditions that increase the risk of zonular rupture during cataract extraction procedure that may affect the postoperative centration or tilt of the IOL (e.g., patients of exfoliation syndrome, Marfan syndrome)
11.	Subjects who desire monovision correction
12.	Predicted residual astigmatism of > 0.50 D between the two eyes

	Note: A toric calculator should be used to verify predicted residual astigmatism in each eye. Incisions to reduce astigmatism during surgery are allowed in this study and must be taken into account when calculating predicted residual astigmatism.
Intraoperative Exclusion Criteria	
13.	Surgical complications including, but not limited to: Loss of zonular integrity/zonular weakness, zonular rupture, anterior or posterior capsule rupture interfering with the stability of the IOL, any evidence of fluid misdirection during the cataract procedure with progressive shallowing of the anterior chamber, and/or uncontrollable IOP **during surgery**
14.	Mechanical or surgical manipulation of the pupil **during surgery**
15.	Excessive iris mobility **during surgery**
16.	Inability to place the IOL in the capsular bag due to surgical complications **during surgery**

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 PanOptix Pro Trifocal IOL, **Model PXYWT0**
Clareon PanOptix Pro Trifocal IOL, **Model PAYWT0**

Comparator Product: Clareon PanOptix Trifocal IOL, **Model CNWTT0**

Table 9-1 Test Products

Test Product	Clareon PanOptix Pro Trifocal IOL, Model PXYWT0
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
Indication for use and intended	Indication: The Clareon PanOptix Pro Trifocal IOL is indicated for primary implantation in the capsular bag in the posterior chamber of the eye for the visual correction of aphakia in adult patients, with

purpose in the current study	less than 1 D of preexisting corneal astigmatism, in whom a cataractous lens has been removed. The lens mitigates the effects of presbyopia by providing improved intermediate and near VA, while maintaining comparable distance VA with a reduced need for eyeglasses, compared to a monofocal IOL. Intended purpose: The Clareon PanOptix Pro IOL is intended for use by a trained ophthalmic surgeon. The IOL is intended to be placed in the capsular bag in the posterior chamber of the eye, replacing the natural crystalline lens. This position allows the IOL to function as a refractive medium in the correction of aphakia. This IOL has a biconvex optic containing an aspheric design and a diffractive structure on the anterior surface. The diffractive structure divides incoming light to provide a range of vision from distance to intermediate to near. This IOL provides an option for clinicians to provide patients an intermediate add power of +2.17 D and a near add power of +3.25 D at the IOL plane (representing +1.65 D and +2.35 D at the corneal plane after implantation, respectively, for an average human eye). The aspheric biconvex optic compensates for the positive spherical aberration of the cornea as compared to a standard spherical optic.
Product description and parameters available for this study	Compared to Clareon PanOptix IOL Model CNWTT0, this Clareon PanOptix Pro IOL improves the fidelity of the diffractive structure to enhance the overall light utilization and image quality between the distance and intermediate peaks. • Optic type: Single-piece IOL with diffractive aspheric biconvex optic • Optics material: Blue light filtering acrylate/methacrylate copolymer • Optic powers (spherical equivalent diopters): +15.0 through +25.0 D in 0.5 D increments • Index of refraction: 1.55 • Haptic configuration: STABLEFORCE™ Modified-L Haptics • Haptic material: Blue light filtering 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.
Packaging description	Alcon standard package contains below items: • The IOL • A subject registration card in case it is needed for the Alcon market (lens implant reply card) • A subject identification card, for the patient (implant card) • Adhesive labels containing the IOL information and unique serial number • eIFU reference card
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 manufacture, storage condition, expiration date, sterile, and single use.
Training and/or experience requirements for device	In order to implant IOLs in study subjects, the surgeons participating in the study must be licensed ophthalmologists with cataract surgery experience and trained on the protocol.
Storage conditions	N/A
Additional information	More information on the test article can be found in the test article IFU
Supply	Alcon will supply a consignment of this test article in the diopter range +15.0 D and +25.0 D

Test Product	Clareon PanOptix Pro Trifocal IOL, Model PAYWT0
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway

	Fort Worth, Texas 76134-2099 USA
Indication for use and intended purpose in the current study	Indication: The Clareon PanOptix Pro Trifocal IOL is indicated for primary implantation in the capsular bag in the posterior chamber of the eye for the visual correction of aphakia in adult patients, with less than 1 D of preexisting corneal astigmatism, in whom a cataractous lens has been removed. The lens mitigates the effects of presbyopia by providing improved intermediate and near VA, while maintaining comparable distance VA with a reduced need for eyeglasses, compared to a monofocal IOL. Intended purpose: The Clareon PanOptix Pro IOL is intended for use by a trained ophthalmic surgeon. The IOL is intended to be placed in the capsular bag in the posterior chamber of the eye, replacing the natural crystalline lens. This position allows the IOL to function as a refractive medium in the correction of aphakia. This IOL has a biconvex optic containing an aspheric chromatic aberration correcting design and a diffractive structure on the anterior surface. The diffractive structure divides incoming light to provide a range of vision from distance to intermediate to near. This IOL provides an option for clinicians to provide patients an intermediate add power of +2.17 D and a near add power of +3.25 D at the IOL plane (representing +1.65 D and +2.35 D at the corneal plane after implantation, respectively, for an average human eye). The aspheric biconvex optic compensates for the positive spherical aberration of the cornea as compared to a standard spherical optic.
Product description and parameters available for this study	[redacted]

	
Formulation	N/A
Usage	IOLs are implantable medical devices and are intended for long term use over the lifetime of the pseudophakic subject.
Packaging description	Alcon standard package contains below items: • The IOL • A subject registration card in case it is needed for the Alcon market (lens implant reply card) • A subject identification card, for the patient (implant card) • Adhesive labels containing the IOL information and unique serial number • eIFU reference card
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 manufacture, storage condition, expiration date, sterile, and single use.
Training and/or experience requirements for device	In order to implant IOLs in study subjects, the surgeons participating in the study must be licensed ophthalmologists with cataract surgery experience and trained on the protocol.
Storage conditions	N/A
Additional information	More information on the test article can be found in the test article IFU

Supply	Alcon will supply a consignment of this test article in the diopter range +15.0 D and +25.0 D

Table 9-2 Comparator Product

Comparator Product	Clareon PanOptix Trifocal IOL, Model CNWTT0
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
Indication for use and intended purpose in the current study	Indication: The Clareon PanOptix Pro Trifocal IOL is indicated for primary implantation in the capsular bag in the posterior chamber of the eye for the visual correction of aphakia in adult patients, with less than 1 D of preexisting corneal astigmatism, in whom a cataractous lens has been removed. The lens mitigates the effects of presbyopia by providing improved intermediate and near VA, while maintaining comparable distance VA with a reduced need for eyeglasses, compared to a monofocal IOL. Intended purpose: The Clareon PanOptix Pro IOL is intended for use by a trained ophthalmic surgeon. The IOL is intended to be placed in the capsular bag in the posterior chamber of the eye, replacing the natural crystalline lens. This position allows the IOL to function as a refractive medium in the correction of aphakia. The optic portion is biconvex and includes an aspheric surface. The optic diffractive structure is in the central 4.5 mm portion of the optic and divides the incoming light to create a +2.17 D intermediate and a +3.25 D near add power at the IOL plane (representing +1.65 D and +2.35 D at the corneal plane after implantation, respectively, for an average human eye). The anterior aspheric surface of the Clareon PanOptix IOL is designed with negative spherical aberration to compensate for the positive spherical aberration of an average cornea.
Product description and parameters	• Optic type: Single-piece IOL with diffractive aspheric biconvex optic

available for this study	• Optics material: Blue light filtering acrylate/methacrylate copolymer • Optic powers (spherical equivalent diopters): +15.0 through +25.0 D in 0.5 D increments • Index of refraction: 1.55 • Haptic configuration: STABLEFORCE™ Modified-L Haptics • Haptic material: Blue light filtering 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.
Packaging description	Alcon standard package contains below items: • The IOL • A subject registration card in case it is needed for the Alcon market (lens implant reply card) • A subject identification card, for the patient (implant card) • Adhesive labels containing the IOL information and unique serial number • eIFU reference card
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 manufacture, storage condition, expiration date, sterile, and single use.
Training and/or experience requirements for device	In order to implant IOLs in study subjects, the surgeons participating in the study must be licensed ophthalmologists with cataract surgery experience and trained on the protocol.
Storage conditions	N/A

Additional information	More information on the test article can be found in the test article IFU
Supply	Alcon will supply a consignment of this test article in the diopter range +15.0 D and +25.0 D

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. Treatment will be assigned by randomization via the EDC system on the day of or after the Screening visit, if the subject meets all entry criteria.

Subjects will be randomized to one of two sub-studies and to contralateral treatment in a 1:1 ratio. Subjects will be block randomized by investigational site. Subjects at each site will be randomized to one of two sub-studies in a 1:1 ratio. Sub-study A will evaluate Model PXYWT0 and sub-study B will evaluate Model PAYWT0. Subjects randomized to sub-study A will be further randomized to receive Model PXYWT0 or Model CNWTT0 in the first surgical eye, and the second eye will receive the other lens. Similarly, subjects randomized to sub-study B will be further randomized to receive Model PAYWT0 or Model CNWTT0 in the first surgical eye and the second eye will receive the other lens. The 1st surgical eye will be the eye with the worse BCDVA at screening. When the BCDVA is equal between the two eyes, the right eye (OD) will be the 1st surgical eye.

Reminder: The subjects and the study staff members responsible for performing masked assessments must NOT be told of the treatment assignment.

9.4 Lens Power

Lens dioptric power will be determined by each surgeon's standard of care. The subject must be targeted with the IOL power with the amount of targeted postoperative refractive error closest to 0 D based on power calculation.

Note: Preoperative corneal astigmatism must be less than 1.00 D in each eye and the predicated residual astigmatism must NOT be > 0.50 D between the two eyes.

9.5 Treatment Masking

This study is assessor-masked and subject-masked.

[redacted] Alcon personnel (including biostatistics, masked data manager, and clinical project lead) will also be masked. All other members associated with the study (at the site and the study sponsor) are unmasked.

Alcon personnel will be masked to IOLs implanted in the eye until the 2nd interim study database lock. At the 1st interim analysis, unmasking of Alcon personnel will be limited to the subset of subjects included in the 1st interim lock as needed. Masked assessors will be masked to the IOLs implanted until the final database lock.

Subjects will be provided with implant cards by unmasked personnel upon exiting the study and will become unmasked at that time.

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.

9.5 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 use for each subject. This record must be made available to the study monitor for the purposes of verifying the accounting of IP supplies. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded along with an explanation. All IPs sent to the investigator must be accounted for by study sponsor personnel, and in no case be used in an unauthorized manner.

Refer to Section 11 of this protocol for additional information on the reporting of device deficiencies and to the MOP for information on return of investigational products associated with these events.

The investigator is responsible for proper disposition of all unused IPs at the conclusion of the study, according to the instructions provided in the MOP.

9.6 Changes to Concomitant Medications, Treatments/Procedures

9.6.1 Changes to Concomitant Medications

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.

9.6.2 Changes to Treatments/Procedures

In the event an intraoperative exclusion criterion is met during cataract surgery, take appropriate action as described in Table 9-3. The table includes, but is not limited to, the most common or likely complications.

Table 9-3 Procedural Complications

Treatment/Procedure Complication	Precaution(s) and Action(s) to be taken	Subject Status
One or more intraoperative exclusion criteria met during 1st eye surgery; IP **did not touch** the eye.	Do not implant the study IOL. Implant another suitable nonstudy lens per standard of care.	Discontinue subject per Section 10.4.2.
One or more intraoperative exclusion criteria met during 1st eye surgery; IP **touched** the eye.	Do not implant the study IOL. Implant another suitable nonstudy lens per standard of care.	Encourage the subject to remain in the study so as to continue to perform safety assessments only in the 1st eye, per Section 10.4.3.

Treatment/Procedure Complication	Precaution(s) and Action(s) to be taken	Subject Status
		Do not implant the study IOL in the 2nd eye.
One or more intraoperative exclusion criteria met during 2nd eye surgery; IP **did not touch** the eye.	Do not implant the study IOL. Implant another suitable nonstudy lens per standard of care.	Continue to follow the subject for all safety assessments in the 1st eye implanted with the study IOL. Do not perform any assessments on the 2nd eye.
One or more intraoperative exclusion criteria met during 2nd eye surgery; IP **touched** the eye.	Do not implant the study IOL. Implant another suitable nonstudy lens per standard of care.	Continue to follow the subject for all safety assessments in the 1st eye, implanted with the study IOL. Continue to perform safety assessments only on the 2nd eye, per Section 10.4.3.

NOTE: A nonstudy lens is defined as a lens that the clinic has procured on its own (all lenses provided by Alcon for this study (for both the test group and comparator group) are considered in the category of 'study lens').

10 STUDY PROCEDURES AND ASSESSMENTS

This section describes the procedures and assessments for this clinical study.

Prescreening is highly suggested for this study. A prescreening log may be provided to the sites, as needed.

There are 9 study Visits (including the screening visit) in this study.

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

- Visit 00 is the first eye operative visit,
- Visit 00A is the second eye operative visit,

- Visit 1 (1 Day) is Day 1 to Day 2 post 1st eye surgery,
- Visit 1A (1 Day) is Day 1 to Day 2 post 2nd eye surgery,
- Visit 2 (1 Week) is Day 7 to Day 14 post 1st eye surgery,
- Visit 2A (1 Week) is Day 7 to Day 14 post 2nd eye surgery,
- Visit 3A (2 month) is Day 45 to Day 70 post 2nd eye surgery,
- Visit 4A (6 month) is Day 180 to Day 210 post 2nd eye surgery.

If necessary, Visit 3A (2 months) may be completed over 2 days within a two week period, and must be completed within the specified window.

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.

NOTE: Historical data collected prior to informed consent and within 60 days of Screening, may be used if collected per study requirements.

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. [redacted]

[redacted].

10.2.1 Demographics: Entry Criteria

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

10.2.2 Medical History and Concomitant Medications: Entry Criteria

Medical history and concomitant medications will be collected in the eCRF as outlined in the MOP.

10.2.3 Urine Pregnancy: Entry Criteria

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

10.2.4 Inclusion/Exclusion Criteria: Entry Criteria

Determine if subject meets entry criteria as outlined in Section 8. Subjects not meeting entry criteria are screen failures and should not continue in the study.

NOTE: Determinations related to entry criteria must be made by medically qualified study staff.

For subjects meeting entry criteria, refer to Section 9.3 for details on treatment assignment.

10.2.5 Keratometry, Axial Length, and Anterior Chamber Depth: Entry Criteria/[redacted]

Measure keratometry, ACD, and AL according to the investigator’s standard of care for each eye.

10.2.6 Target Residual Refractive Error: Entry Criteria/[redacted]

Record target residual refractive error for each eye.

The targeted postoperative residual refractive error for lens selection must be closest to 0 D based on power calculation.

10.2.7 Predicted Residual Astigmatism: Entry Criteria

Record predicted residual astigmatism for each eye. The use of a IOL Toric calculator is required.

Incisions to reduce astigmatism during surgery are allowed in this study and must also be taken into account when calculating predicted residual astigmatism.

A subject with predicted residual astigmatism of > 0.50 D between the two eyes should not be enrolled in the study.

10.2.8 Slit Lamp Biomicroscopy: Safety Assessment

Slit lamp examination must be performed in both eyes. Record any slit lamp findings, any **IOL observations, any subjective PCO.** This assessment must be performed by medically qualified study staff.

10.2.9 Intraocular Pressure: Safety Assessment

Perform tonometry assessment in each eye according to the to the investigator's standard of care. Record IOP results.

10.2.10 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.

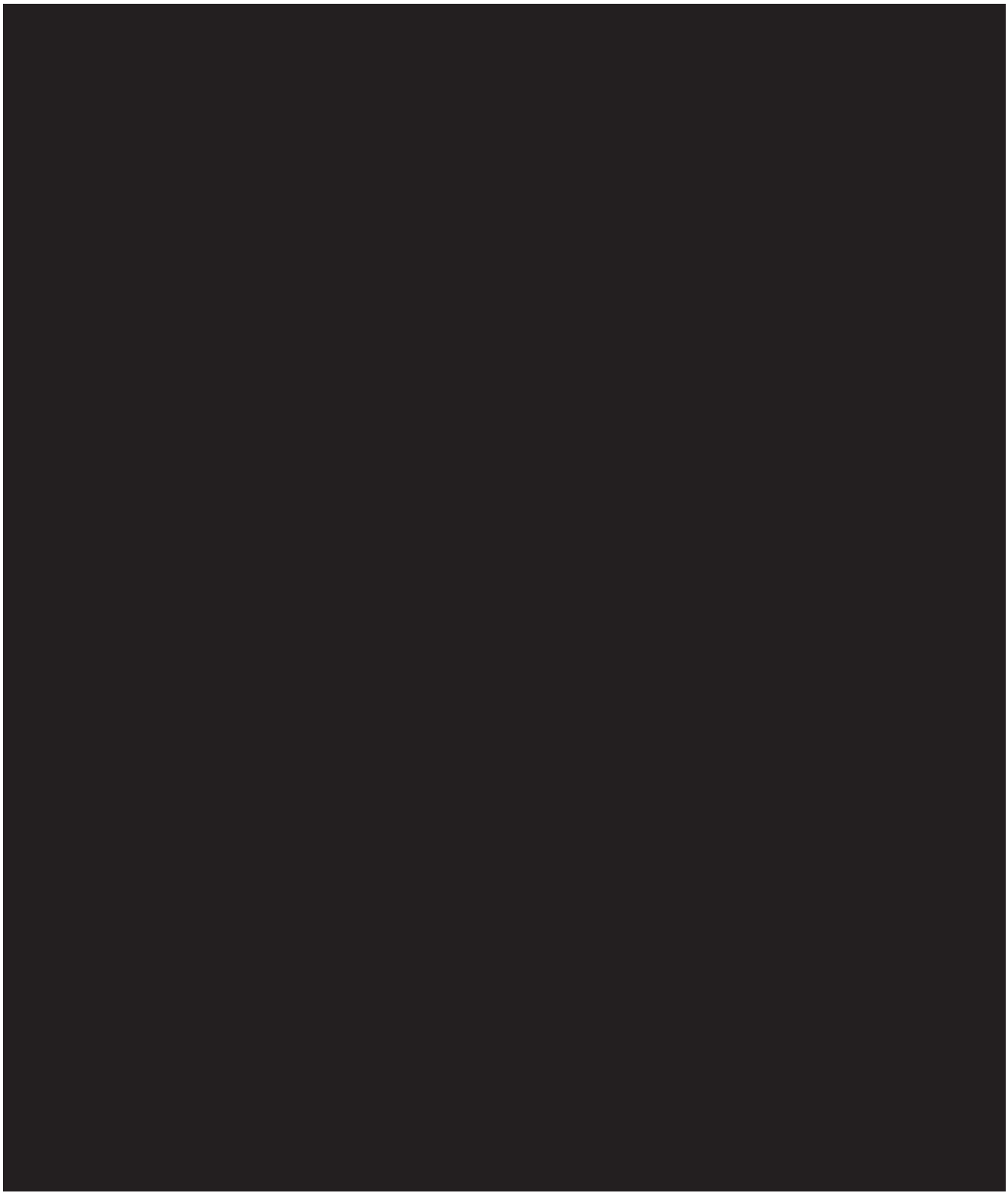
10.2.11 Administration of Treatment (Cataract Surgery): Safety Assessment

Perform cataract surgery in alignment with each subject's assigned treatment from randomization. In both sub-studies, the 1st operative eye is defined as the eye with the worse BCDVA at Screening (Visit 0). If the BCDVA is the same in both eyes, the right eye (OD) will be identified as the 1st operative eye.

[redacted]

10.2.15 Monocular Photopic Best Corrected Distance Visual Acuity: Effectiveness Assessment at 4 m: Effectiveness Assessment

Measure monocular photopic ETDRS BCDVA at 4 m in each eye. This assessment must be performed by delegated trained masked assessor only.



10.2.30 Adverse Event Collection: Safety Assessment

Assess and record any AEs that are observed or reported since the previous visit, including those associated with changes in concomitant medication dosing.

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

10.2.31 Device Deficiencies: Safety Assessment

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

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

10.2.32 IOL Observations: Safety Assessment

Document any observations related to the IOL (e.g., haze, discoloration).

10.2.33 Subjective PCO: Safety Assessment

Assess and document presence of posterior capsule opacification (PCO).

10.2.34 Nd:YAG Capsulotomy: Safety Assessment

If a posterior capsulotomy (i.e., YAG laser treatment) has been performed since last visit, document the treatment including treatment date, eye, and size of the capsulotomy.

10.2.35 SSI: Safety Assessment

Document and report any SSIs (e.g., IOL repositioning) as an SAE.

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 nonstudy personnel, the investigator is to capture AE-related information on the AE form upon becoming aware.

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

- Collect AE information
- Record changes in medical condition or concomitant medication

The investigator may perform optional study assessment as outlined in Table 3-1, if clinically indicated.

The investigator may perform additional non-study procedures for proper diagnosis and treatment of the subject. 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 form and prior to randomization are considered screen failures. Subjects who are deemed no longer eligible to be implanted with a study lens after randomization (due to intraoperative exclusions or other noted issues) will be withdrawn from the study.

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

Subject numbers must not be re-used.

10.4.2 Discontinuations

Discontinued subjects are individuals who voluntarily withdraw or are withdrawn from the study by the investigator after exposure to investigational product.

NOTE: Subjects not implanted at the time of surgery (1st operative eye) and the study IOL **did not** touch the eye must be captured as withdrawn.

Subject numbers of discontinued subjects must not be re-used for another subject (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 Subjects with Aborted Implantation and Explanted IOL(s)

Implantation may be attempted twice. After two aborted attempts to implant, meaning the investigational product touched the eye, the eye must be implanted with a nonstudy provided IOL. Refer to Section 9.6.2 for additional information.

If the IOL implantation is attempted and aborted due to device deficiency, then a device deficiency form must be completed and the IOL must be returned to the study sponsor in appropriate safe packaging.

In case an explant is performed: the explanted eye will be followed for safety as routine standard of care for explants of approved IOLs.

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.

Breaking of the masked treatment codes will be done after locking the database.

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 sign (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device (test product). Refer to the Glossary of Terms for categories of AEs and SAEs.

Figure 11-1 Categorization of All Adverse Events

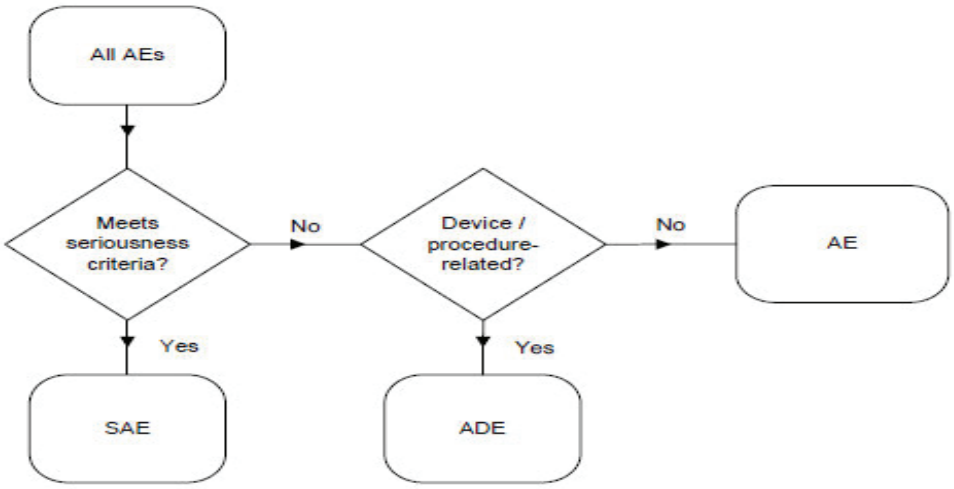
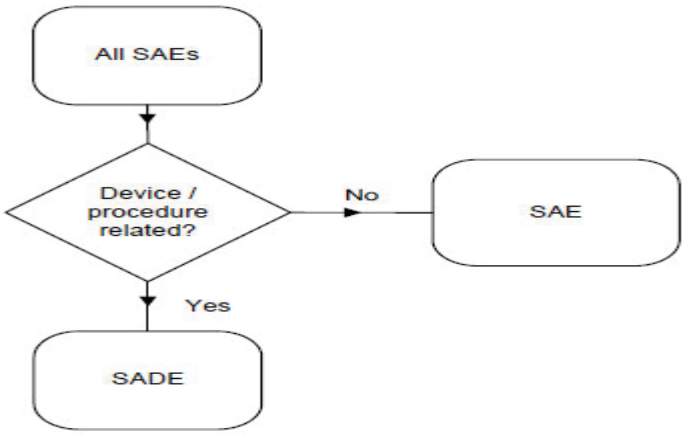


Figure 11-2 Categorization of All Serious Adverse Events



Specific Events Relevant to this Protocol

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

Cumulative (at any visit during the study) Serious Adverse Events:

- Cystoid macular edema
- Hypopyon
- Endophthalmitis
- Lens dislocation
- Pupillary block
- Retinal detachment
- SSI (excluding posterior capsulotomy)

Persistent (still present at conclusion of study) Serious Adverse Events:

- Corneal stromal edema
- Cystoid macular edema
- Iritis
- Elevated IOP requiring treatment

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 11.4.

11.2 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 and delivery system defect
- Broken IOL optic
- Broken IOL haptic

- Scratched IOL optic
- Unsealed device packaging
- Suspect product contamination (IOL)

11.3 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 medicines you take since your last study visit?"

In addition, changes in any protocol-specific parameters [redacted] evaluated during the study are to be reviewed by the investigator. Any untoward (unfavorable and unintended) change in a protocol-specific parameter or questions 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.

11.4 Procedures for Recording and Reporting

AEs are collected from the time of signing 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.

In addition, aqueous cells and flare, corneal edema, raised IOP, and superficial punctate keratitis are examples of early postoperative findings that are typically observed following ocular surgery. These are not considered AEs if they can be reasonably expected to resolve within 2 weeks 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 study 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 immediately 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 Adverse Device Effect (for related AEs) and Serious Adverse Event eCRF.

Note: Should the EDC system become non-operational, the site must complete the appropriate paper SAE and ADE 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.

Any AEs and device deficiencies for any non-study marketed devices/products 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. Any AEs and device deficiencies with the test or comparator IP should still be reported in EDC and can enter in the comment the other manufactures product if applicable.

Study sponsor representatives may be contacted for any protocol related questions and their contact information is provided in the MOP 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 study IP device deficiencies that could have led to a SADE according to the requirements of regulatory authorities or IRB/IEC.

11.5 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 non-serious to serious or from unrelated to related.

11.6 Return Product Analysis

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

Alcon study products associated with device deficiencies and/or product related AEs should be returned under conditions described in the MOP.

11.7 Unmasking of the Study Treatment

Masked information on the identity of the assigned medical device should not be disclosed to the masked assessor or to the subject during the study. Refer to Section 9.5 of the protocol. If the treatment code needs to be broken in the interest of subject safety, the investigator is encouraged to contact an appropriate study sponsor representative prior to unmasking the

information if there is sufficient time. Dependent upon the individual circumstances (i.e., medical emergency), the code may be broken prior to contact with the study sponsor. The study sponsor must be informed of all cases in which the code was broken and of the circumstances involved. Additionally, the study sponsor may be required to unmask the information in order to fulfill expedited regulatory reporting requirements.

11.8 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). Any additional data received up to 6 months after subject has completed the study should 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 post-market 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.

11.9 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

All study conduct, effectiveness, and safety data will be reported for each sub-study (A and B) separately.

The primary time point of interest is 2 Months (Visit 3A) postoperative. After all subjects complete the 2-Month Visit (Visit 3A), the study database will be locked to conduct final inferential analyses. The study will be continued until all subjects complete the 6-Month Visit (Visit 4A), at which time the study database will be considered final and locked to report longer term effectiveness and safety results.

12.1 Subject Evaluability

Subject evaluability must be determined prior to breaking the code for masked treatment assignment and locking the database, based upon the deviations and evaluability plan. Subjects will be randomized to sub-study (A or B) and contralateral treatment in a 1:1 ratio to receive the investigational products.

12.2 Analysis Sets

There will be three analysis datasets for each sub-study: the all-implanted analysis set, the best-case analysis set, and the safety analysis set.

The all-implanted analysis set (AAS) will include all subjects with successful test and comparator article contralateral implantation, with at least one postoperative visit.

The best-case analysis set (BAS) will include all subjects with successful contralateral implantation with the test and comparator article that had:

- At least one postoperative visit,
- No preoperative ocular pathology or macular degeneration at any time in either eye and
- No major protocol deviations

Subjects who become pregnant at any time during the study will also be excluded from the BAS.

All eyes with attempted test or comparator article implantation (successful or aborted after contact with the eye) will be considered evaluable for the Safety Set (SAS).

The primary analysis set for effectiveness analyses will be the AAS, [redacted]

All effectiveness analyses will be conducted on an as-treated basis. Eyes will be categorized under the actual study IOL implanted.

12.3 Demographic and Baseline Characteristics

Demographic and baseline characteristics will be summarized for each sub-study on the subject and eye level (by treatment) as applicable. Counts and percentages will be presented for categorical variables such as sex, age group, race, and ethnicity. N, mean, standard deviation, median, minimum, and maximum will be presented for continuous variables that are collected at baseline such as age, eye biometry, monocular VA, and refractive errors.

12.4 Effectiveness Analyses

In general, descriptive statistics will be generated using mean, standard deviation, median, minimum, and maximum, for continuous variables. The number in each category and percentage will be reported for categorical variables. Summaries of logMAR VA may include two-sided 95% confidence intervals for the mean difference between treatment groups.

For statistical inference testing, the overall Type I error will be maintained, within each sub-study, at the alpha 0.05 level (one-sided) using a sequential testing approach that will be detailed in the statistical analysis plan.

See Appendix B for specific effectiveness analyses related to sub-study A and see Appendix C for specific effectiveness analyses related to sub-study B.

12.5 Handling of Missing Data

There will be no imputation of missing data.

12.6 Safety Analyses

The safety objective for this study is to describe the incidence of ocular AEs including SSIs.

The safety endpoints are as follows for sub-study A and B:

- AEs
- Device deficiencies
- IOP
- Slit lamp examination findings including:
    - Proportion of eyes with subjective posterior capsular opacification (PCO)
    - Proportion of eyes with posterior capsulotomy
    - IOL observations

- Dilated fundus examination findings, including fundus visualization
- Intraoperative surgical problems
- Other procedures at surgery (combined and/or additional)
- SSIs

There are no safety hypotheses for either sub-study. The focus of the safety analysis will be a comprehensive descriptive assessment, of occurrence of ocular AEs and SSIs, as well as the other listed parameters. For all safety measures, descriptive statistics generated will be based upon the type of variable. For categorical variables summary statistics will include sample size, number in each category, and percentage in each category. For continuous variables, number of subjects/eyes, mean, median, standard deviation, minimum, and maximum will be reported. Safety measures may be presented in listings as appropriate.

All AEs occurring from the time a subject signs the informed consent form to study exit will be accounted for in the reporting. Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis. Descriptive summaries (counts and percentages) and listings will be presented. Individual subject listings will be provided for AEs that occur after signing the informed consent form but prior to exposure to IP.

12.7 Interim Analyses and Reporting

The first interim analysis will be conducted when approximately 40 subjects (approximately 20 in each sub-study, minimum 30 subjects total) complete the 2-Month postoperative visit. This interim analysis is designed to review preliminary safety and effectiveness results for strategic business decision making purposes. There is no intention of stopping the study early. A second interim analysis will be conducted when all subjects complete the 2-Month postoperative visit, at this point treatment arms will be unmasked and all inferential analysis will be conducted. To control the overall type I error rate (at alpha = 0.05) the Lan-DeMets method with an O'Brien-Fleming alpha spending function will be utilized to distribute the type I error rate between the first and second interim analyses. The first interim analysis will be conducted when approximately 1/3 of the information fraction (in this case 1/3 of the target sample size) is available, therefore the alpha spend will be approximately 0.001 at the first interim analysis and accordingly the significance level at the second interim analysis (which is the primary inferential analysis point) will be 0.049 for all effectiveness endpoints. The power estimates provided below are based on a 0.049 significance level.

12.8 Sample Size Justification

A total of 132 subjects will be randomized (approximately 66 per sub-study). Assuming a drop-out rate of 10%, approximately 60 subjects will be evaluable at 2 months postoperative period (visit 3A) for each sub-study. The power estimates for each of the planned analyses are presented below:

Order	Endpoint	Comparison	Expected difference	Std. Dev^	Power
Sub-study A					
Primary	Monocular BCDVA	NI	0	.08	>99.9%
[redacted]					
Sub-study B					
Primary	Monocular BCDVA	NI	0	.08	>99.9%
[redacted]					

^Estimate of std. dev is based on two recent Alcon studies (ILH297-C001 and ILI875-C002). * Estimated based of simulated results from VirtIOL. **Difference would indicate clinically meaningful effect. A NI margin of 0.1 logMAR is used for all non-inferiority comparisons above.

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 trial 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
- IP accountability records
- 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 trial. For this study, the principal investigator and implanting sub-investigators must be healthcare professionals appropriately trained/licensed/certified to perform surgery/treat subjects with the condition under study.

The study sponsor is financially funding this clinical trial and will compensate the investigator and/or the institution(s) at which the study is conducted in accordance with a signed clinical trial 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 GCP; 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 wellbeing of human subjects under emergency

circumstances. Emergency deviations may proceed without prior approval of the sponsor and the IRB/EC, but shall be documented and reported to the sponsor and the IRB/EC 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 a copy of the IFUs, 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 subject. 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 investigator should document subject withdrawal of consent. The investigator is the designated contact point for any such withdrawals.

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

15.1 Regulations and Standards

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

- EN ISO 11979-7 Ophthalmic implants – Intraocular lenses – Part 7: Clinical Investigations of Intraocular Lenses for the Correction of Aphakia
- EN ISO 14155 - 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 812 - Investigational Device Exemptions
- 21 CFR Part 54 - Financial Disclosure by Clinical Investigators
- The California Bill of Rights, if applicable

15.2 Scientific and Other References

Not applicable. There are no references.

17 APPENDIX B – Sub-Study A

17.1 Analysis of Primary Effectiveness Endpoint(s)

The primary objective of this study is to demonstrate noninferiority of monocular photopic BCDVA of the Clareon PanOptix Pro PXYWT0 model compared to Clareon PanOptix at 2 months postoperative (Visit 3A). The primary endpoint is mean monocular photopic BCDVA (logMAR) at 4 m at 2 months postoperative (Visit 3A).

17.1.1 Statistical Hypotheses

The null and alternative hypotheses to be evaluated in support of the primary non-inferiority objective are as stated below:

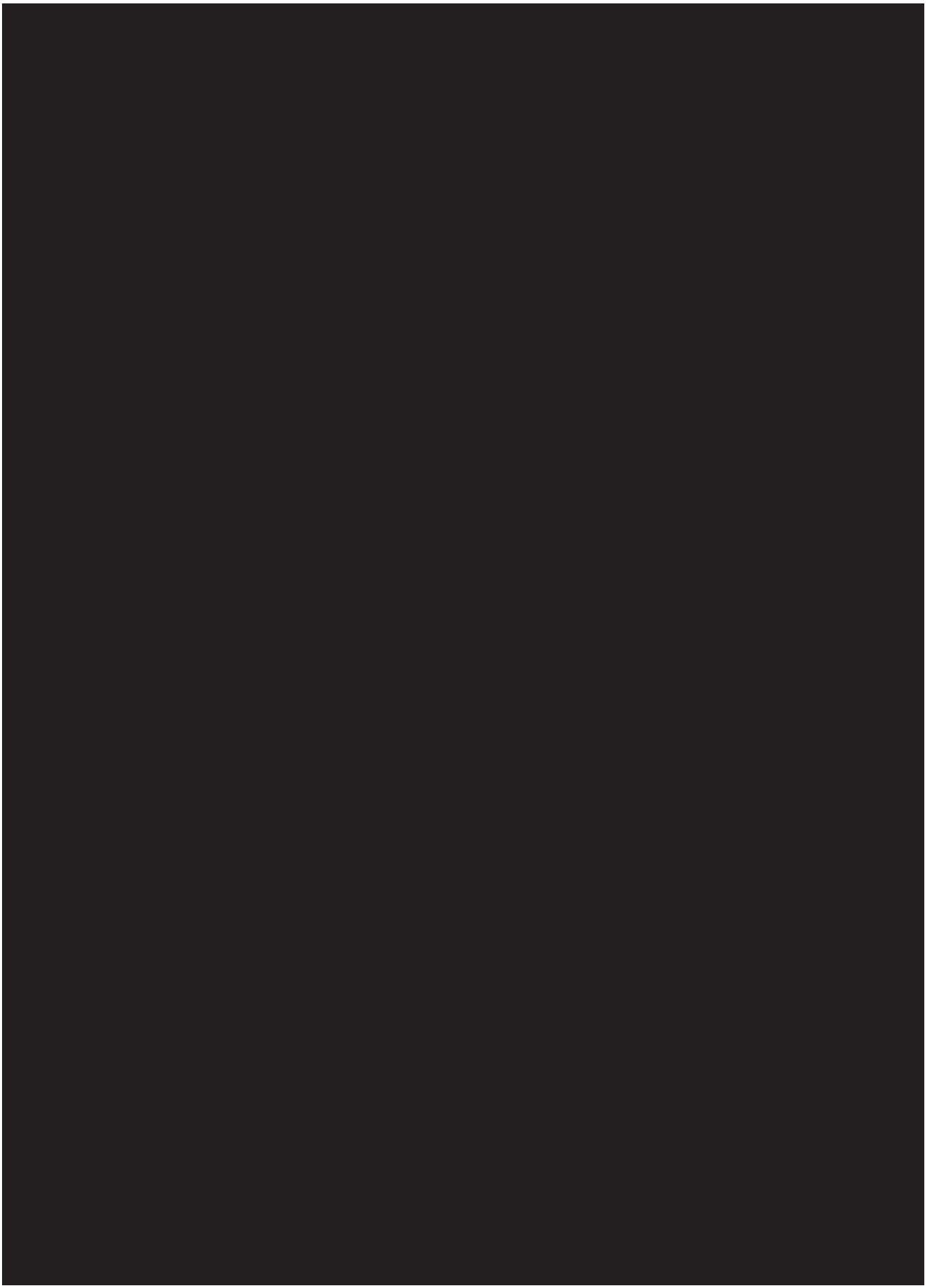
$$H_0: \mu_D \geq \Delta$$

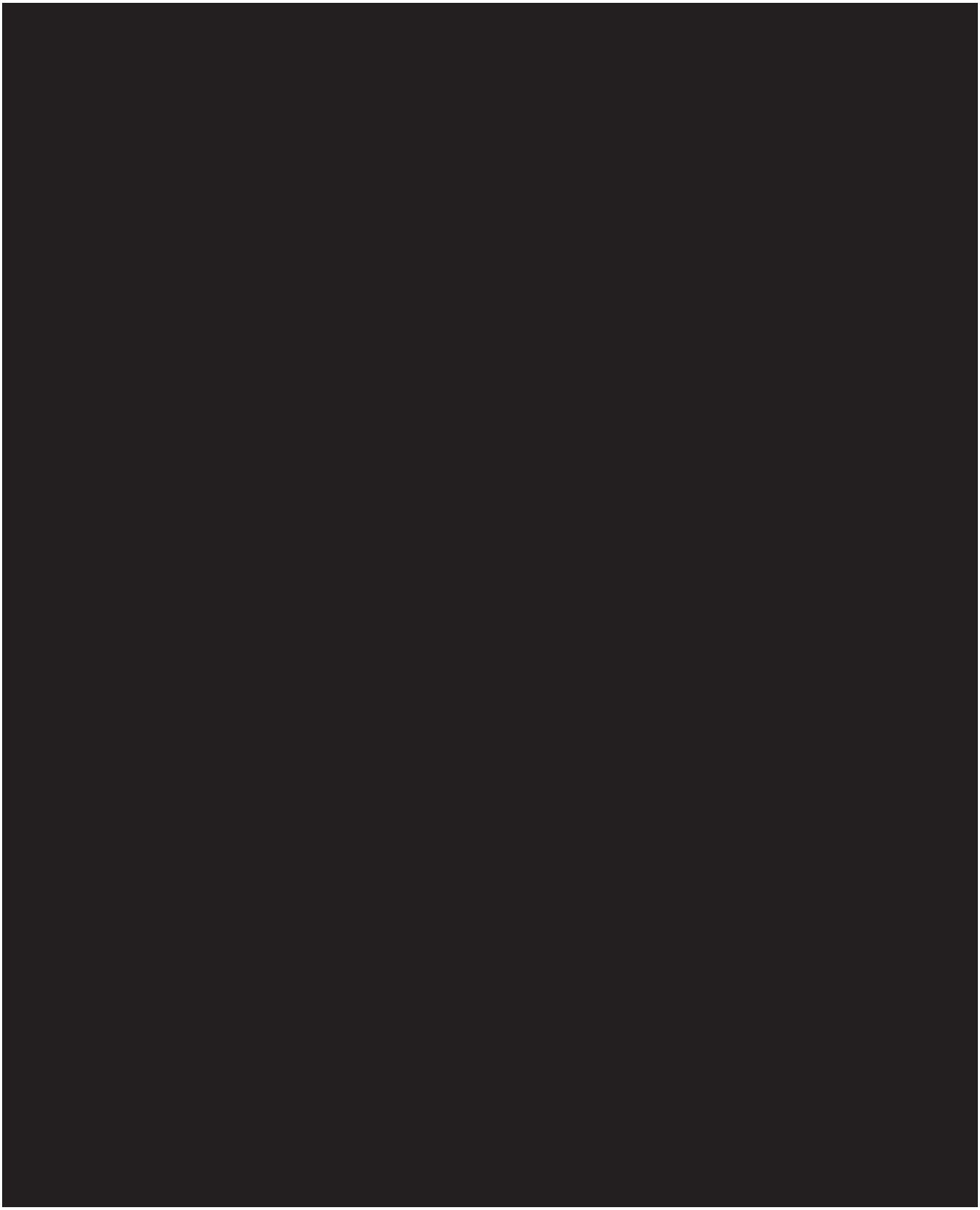
$$H_a: \mu_D < \Delta$$

where, Δ refers to the non-inferiority margin, set at 0.1 logMAR, and μ_D refers to the mean of the difference between paired observations of each subject's eyes (test minus comparator) for monocular photopic BCDVA at 2 months post implantation.

17.1.2 Analysis Methods

The primary effectiveness endpoint, associated with the above hypotheses, will be tested by generating a one-sided 95.1% upper confidence limit based on the mean paired difference (Clareon PanOptix Pro - Clareon PanOptix) using a one-sample t-test. The upper bound of the one-sided 95.1% confidence limit will be compared to the margin, 0.10 logMAR. If the upper bound is less than the margin, the null hypothesis will be rejected and it will be concluded that Clareon PanOptix Pro is noninferior to Clareon PanOptix for monocular photopic BCVDA at 4 m. The difference in means (Clareon PanOptix Pro minus Clareon PanOptix) and the associated one-sided upper confidence limit will be presented.





18 APPENDIX C– Sub-Study B

18.1 Analysis of Primary Effectiveness Endpoint(s)

The primary objective of this study is to demonstrate noninferiority of monocular photopic BCDVA of the Clareon PanOptix Pro PAYWT0 model compared to Clareon PanOptix at 2 months postoperative (Visit 3A). The primary endpoint is mean monocular photopic BCDVA (logMAR) at 4 m at 2 months postoperative (Visit 3A).

18.1.1 Statistical Hypotheses

The null and alternative hypotheses to be evaluated in support of the primary noninferiority objective are as stated below:

$$H_0: \mu_D \geq \Delta$$

$$H_a: \mu_D < \Delta$$

where, Δ refers to the noninferiority margin, set at 0.1 logMAR, and μ_D refers to the mean of the difference between paired observations of each subject's eyes (test minus comparator) for monocular photopic BCDVA at 2 months post implantation.

18.1.2 Analysis Methods

The primary effectiveness endpoint, associated with the above hypotheses, will be tested by generating a one-sided 95.1% upper confidence limit based on the mean paired difference (Clareon PanOptix Pro - Clareon PanOptix) using a one-sample t-test. The upper bound of the one-sided 95.1% confidence limit will be compared to the margin, 0.10 logMAR. If the upper bound is less than the margin, the null hypothesis will be rejected and it will be concluded that Clareon PanOptix Pro is noninferior to Clareon PanOptix for monocular photopic BCVDA at 4 m. The difference in means (Clareon PanOptix Pro - Clareon PanOptix) and the associated one-sided upper confidence limit will be presented.