# Clareon Toric vs Eyhance Toric

STUDY ID:

ILS241-P002

PROTOCOL

Version 4, 29 Jun 2023

ClinicalTrials.gov ID:

NCT05481125

# Device Protocol for ILS241-P002
# Title: Clareon Toric vs Eyhance Toric

| | |
|---|---|
| Protocol Number: | ILS241-P002 |
| Clinical Investigation Type: | Postmarket Interventional / Confirmatory |
| Test Product: | Clareon Aspheric Hydrophobic Acrylic Intraocular Lens (IOL) and Clareon Toric Aspheric Hydrophobic Acrylic IOL (Models SY60WF, CNW0T3, CNW0T4, CNW0T5, CNW0T6) |
| Sponsor Name and Address: | Alcon Research, LLC, and its affiliates (“Alcon”)<br>6201 South Freeway<br>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.

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

Principal investigator:

| | Signature Date |
|---|---|
| Name and professional position: | |
| Address:<br>Phone Number:<br>Off-hours Emergency Phone Number: | |

# Table of Contents

## List of Tables

# List of Figures

# 1 GLOSSARY OF TERMS

| | |
|---|---|
| Names of Test Products | Throughout this document, test products Clareon Aspheric Hydrophobic Acrylic IOL and Clareon Toric Aspheric Hydrophobic Acrylic IOL (Models SY60WF; CNW0T3, CNW0T4, CNW0T5, CNW0T6) will be referred to as Clareon/Clareon Toric IOLs. |
| Name of Comparator Products | Throughout this document, comparator products TECNIS Eyhance/Eyhance Toric II IOL with TECNIS Simplicity Delivery System (Models DIB00; DIU150, DIU225, DIU300, DIU375) will be referred to as Eyhance/Eyhance Toric IOLs. |
| Adverse Device Effect (ADE) | Adverse events related to the use of an investigational medical device (test product) or control product.<br><br>*Note: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation; any malfunction; and use error or intentional misuse of the investigational medical device (test product) or comparator product.* |
| Adverse Event (AE) | Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device (investigational product).<br><br>*Note: For subjects, this definition includes events related to the test product, the control product, or the procedures involved. For users or other persons, this definition is restricted to events related to the test product*<br><br>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. |

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| 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.<br><br>*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, safety, or performance.<br><br>*Note: This definition includes malfunctions, use errors, inadequate labelling.*<br><br>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 |

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| | 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 a medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical investigation plan (CIP). |
| Nonserious Adverse Event | Adverse event that does not meet the criteria for a serious adverse event. |
| Postmarket / Postauthorization study | Any study conducted within the conditions laid down in product labelling and other conditions laid down for the marketing of the product or under normal conditions of use. A postmarket 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:<br>• Death.<br>• A serious deterioration in the health of the subject, that either results in:<br>a) a life-threatening illness or injury<br>*Note: Life-threatening means that the individual was at* |

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| | *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.*<br><br>b) any potentially sight-threatening event or permanent impairment to a body structure or a body function.<br><br>c) inpatient hospitalization or prolonged hospitalization. *Note: Planned hospitalization for a preexisting condition, without serious deterioration in health, is not considered a serious adverse event. In general, hospitalization signifies that the individual remained at the hospital or emergency ward for observation and/or treatment (usually involving an overnight stay) that would not have been appropriate in the physician's office or an outpatient setting. Complications that occur during hospitalization are adverse events. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred, the event should be considered serious.*<br><br>d) a medical or surgical intervention to prevent a) or b). This includes any ocular secondary surgical intervention excluding posterior capsulotomy.<br><br>e) any indirect harm as a consequence of incorrect diagnostic test results when used within manufacturer's instructions for use.<br><br>• Fetal distress, fetal death, a congenital abnormality or birth defect.<br><br>*Refer to Section 11 for additional SAEs.* |
| Serious Health Threat | Any event type which results in imminent risk of death or a serious deterioration in state of health, or serious illness that requires prompt remedial action.<br><br>This would include: Events that are of significant and unexpected nature such that they become alarming as a potential public health |

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| | hazard, e.g., human immunodeficiency virus (HIV) or Creutzfeldt-Jacob Disease (CJD). |
| Study Start | The start of the study is considered to coincide with the enrollment of the first subject. |
| 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 | Act or omission of an act that results in a different medical device response than intended by the manufacturer or expected by the user.<br><br>*Note: This definition includes slips, lapses, and mistakes. An unexpected physiological response of the subject does not in itself constitute 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 |
| AL | Axial length |
| ANSI | American National Standards Institute |
| ASADE | Anticipated serious adverse device effect |
| [redacted] | [redacted] |
| BCDVA | Best corrected distance visual acuity |
| [redacted] | [redacted] |
| CRF | Case report form |
| CIP | Clinical investigation plan |
| CIR | Clinical investigation report |
| CJD | Creutzfeldt-Jacob Disease |
| D | Diopter |
| [redacted] | [redacted] |
| DFU | Directions for use |
| eCRF | Electronic case report form |
| EDC | Electronic data capture |
| [redacted] | [redacted] |
| eIFU | Electronic instructions for use |
| EoS | End of surgery |
| FLACS | Femtosecond laser-assisted cataract surgery |
| GCP | Good Clinical Practice |
| GPCMS | Global Product Complaint Management System |
| HIV | Human immunodeficiency virus |
| ICF | Informed consent form |
| IEC | Independent ethics committee |
| IFU | Instructions for use |
| IOL | Intraocular lens |
| [redacted] | [redacted] |
| IOP | Intraocular pressure |
| IP | Investigational product |
| IRB | Institutional Review Board |
| ISO | International Organization for Standardization |
| [redacted] | [redacted] |
| LASIK | Laser-assisted in situ keratomileusis |
| logMAR | Logarithm of minimum angle of resolution |
| [redacted] | [redacted] |
| LRI | Limbal relaxing incision |

| Abbreviation | Definition |
|---|---|
| m | Meter |
| mm | Millimeter |
| MOP | Manual of procedures |
| MRSE | Manifest refractive spherical equivalent |
| N/A | Not applicable |
| Nd:YAG | Neodymium-doped yttrium aluminum garnet |
| °C | Celsius |
| OD | Oculus dexter |
| OS | Oculus sinister |
| ORA | Optiwave Refractive Analysis |
| OVD | Ophthalmic Viscosurgical Devices |
| [redacted] | [redacted] |
| PCO | Posterior Capsule Opacification |
| SADE | Serious adverse device effect |
| SAE | Serious adverse event |
| SAS | Safety analysis Set |
| SAP | Statistical analysis plan |
| [redacted] | [redacted] |
| SPH | Sphere |
| SSI | Secondary surgical interventions |
| SOC | Standard of care |
| SOP | Standard operating procedure |
| µm | Micrometer |
| [redacted] | [redacted] |
| [redacted] | [redacted] |
| US | United States |
| USADE | Unanticipated serious adverse device effect |
| USV | Unscheduled visit |
| UV | Ultraviolet |
| VA | Visual acuity |

# 3 PROTOCOL SUMMARY

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|---|---|
| **Investigational product type** | Device |
| **Study type** | Interventional |
| **Investigational products** | Test Product: Clareon/Clareon Toric IOLs. Models SY60WF; CNW0T3, CNW0T4, CNW0T5, CNW0T6.<br><br>Comparator Product: Eyhance/Eyhance Toric IOLs. Models DIB00; DIU150, DIU225, DIU300, DIU375. |
| **Purpose and Scientific Rationale for the Study** | To compare visual and subject reported outcomes between Clareon/Clareon Toric and Eyhance/Eyhance Toric IOLs to support scientific messaging. |
| **Objectives** | **<u>Primary Objective:</u>**<br>• To demonstrate noninferiority of the Clareon/Clareon Toric IOLs to the Eyhance/Eyhance Toric IOLs in binocular BCDVA at 3 months postoperative. |

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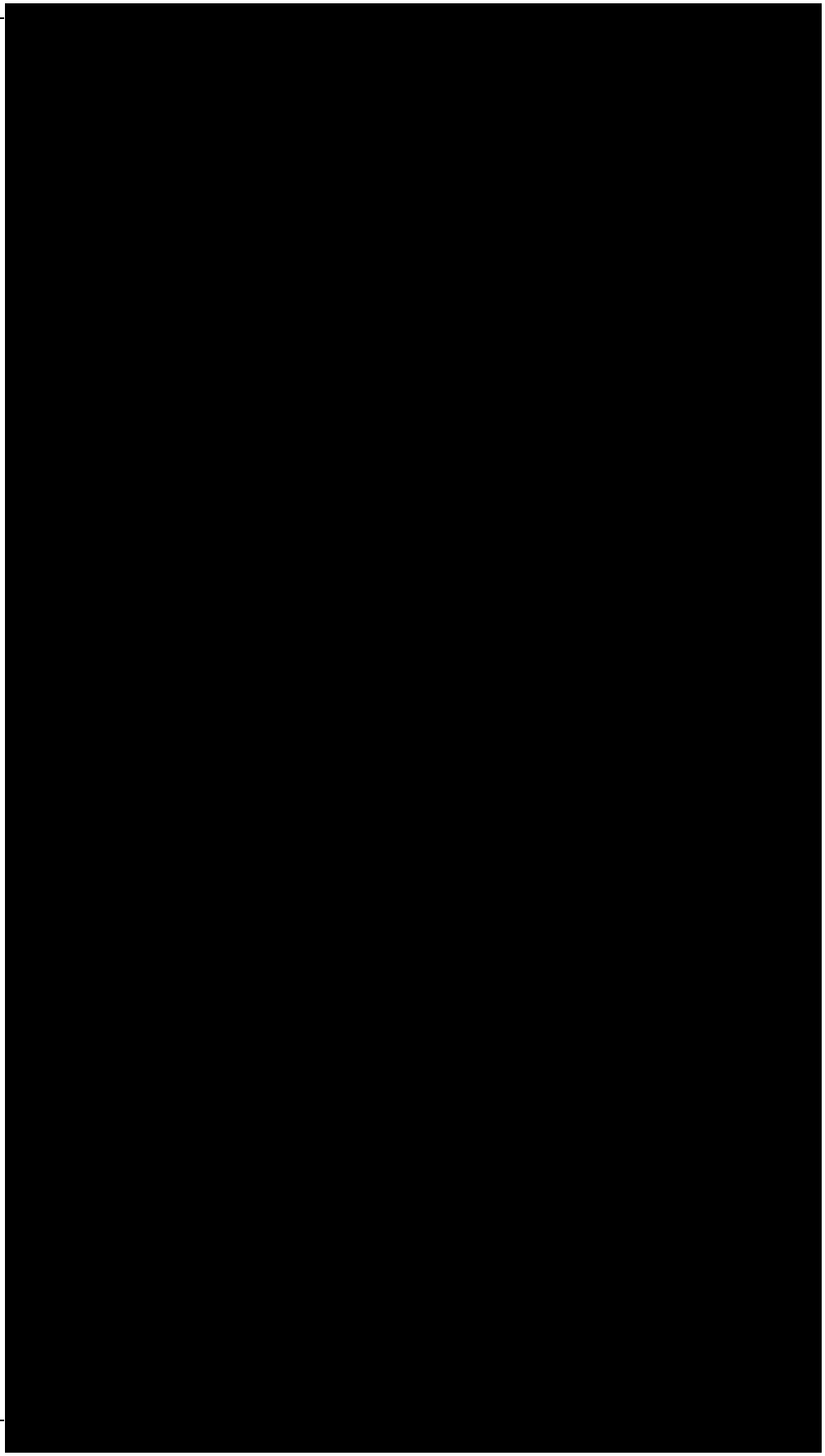
| | [redacted] |
| **Endpoints** | **Primary Effectiveness:**<br>• Mean binocular BCDVA (4 m) (bright lighting conditions) at 3 months postoperative |
| | [redacted] |



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| | [redacted]<br>**Safety endpoints**<br>• Adverse events (ocular and non-ocular, serious and non-serious)<br>• Secondary surgical interventions (SSI)<br>• Device deficiencies<br>• IOL observations<br>• IOL position change (tilt and decentration) from slit lamp examination<br>• Posterior Capsule Opacification (PCO)<br>• Posterior capsulotomy<br>• Surgical problems<br>• Other surgical procedures<br>• Slit lamp examination<br>• Dilated fundus examination<br>• IOP |
| **Assessments** | **Effectiveness:**<br>• Distance Visual Acuity at 4 m<br>○ BCDVA (bright lighting conditions, [redacted] |

| | |
|---|---|
| | [redacted] |
| | **Safety:**<br>• Adverse events<br>• SSI<br>• Device deficiencies<br>• IOL observations<br>• IOL position change (tilt and decentration) from slit lamp examination<br>• PCO<br>• Posterior capsulotomy |

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| | • Surgical problems<br>• Slit lamp examination<br>• Dilated fundus examination<br>• Tonometry<br>**Additional**:<br>• Ocular Biometry (Keratometry Axial Length (AL), and Anterior Chamber Depth (ACD) with corneal thickness))<br>• Urine pregnancy<br>• Pupil size<br>*Note: Refer to Schedule of Study Procedures and Assessments (Tables 3-1) for a comprehensive list of study assessments.* |
| **Study Design** | This study is a prospective, multicenter, randomized, double masked, parallel group, postmarket study. |
| **Subject population** | Adults 22 years of age or older, diagnosed with bilateral cataracts, who require bilateral cataract extraction by phacoemulsification<br><br>Planned number of enrolled/consented subjects: Approximately 185 subjects (approximately 93 subjects per group)<br>Planned number of randomized subjects: Approximately 168 subjects (approximately 84 subjects per group)<br>Planned number of completed subjects: Approximately 140 subjects (approximately 70 subjects per group) |
| **Sites and Locations** | Planned number of clinical sites: ~10 sites<br>Planned locations: US |
| **Key inclusion criteria**<br>(See Section 8.1 for a complete list of inclusion criteria) | • Adults (at least 22 years of age or older at the time of screening) diagnosed with cataract in both eyes.<br>• Planned bilateral cataract removal by routine small incision phacoemulsification surgery |

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| | • Planned implantation of either test or comparator IOL (per randomization) from the following model numbers: CNW0T3, CNW0T4, CNW0T5, CNW0T6 or DIU150, DIU225, DIU300, DIU375 in at least one eye with approximately 1.00 – 3.00 D of preoperative corneal astigmatism<br>• Predicted postoperative astigmatism of ≤ 0.5 D in both operative eyes based on a Toric calculator<br>• Pupil restriction with a penlight to ≤ 3.5 mm |
| **Key exclusion criteria**<br>(See Section 8.2 for a complete list of exclusion criteria) | • Any disease or pathology, other than cataract, that (in the investigator's opinion) may reduce the potential BCDVA to a level worse than 0.2 logMAR<br>• Clinically significant (in the investigator's opinion) corneal pathology (epithelial, stromal, endothelial), dry-eye or ocular surface disease that would adversely affect a) the biometry measures and/or toric calculations and b) the visual outcome. This includes, but is not limited, to old significant corneal scars (including Salzman's nodular degeneration), corneal irregularity (including dry eye syndrome), 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.<br>• History of previous intraocular or corneal surgery (including iridotomy and laser-assisted in situ keratomileusis (LASIK)).<br>• Any other planned ocular surgical procedures including but not limited to limbal relaxing incision (LRI), astigmatic keratotomy, LASIK, and retinal laser treatment within the study time frame. |

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| **Data analysis and sample size justification** | **Analysis sets:**<br><br>The all-implanted analysis set (AAS) will include all eyes with successful study IOL implantation and with at least one postoperative visit.<br><br>[redacted]<br><br>All eyes with attempted study IOL implantation (successful or aborted after contact with the eye) will be considered evaluable for the safety analysis set (SAS).<br><br>The primary analysis set for effectiveness will be the AAS.[redacted]<br><br>**Analysis:**<br><br>The null and alternative hypotheses to be evaluated for the primary [redacted] noninferiority objectives are as stated below:<br><br>$$H_0: \mu_{Test} - \mu_{Comparator} \geq \Delta$$<br><br>$$H_1: \mu_{Test} - \mu_{Comparator} < \Delta$$<br><br>where, Δ refers to the noninferiority margin, set at 0.1 logMAR, and $\mu_{Test}$, $\mu_{Control}$ refers to the mean values of binocular BCDVA [redacted] |

[redacted] at 3 months post-implantation.

The primary effectiveness [redacted] will be evaluated with a *t*-test of noninferiority assuming equal variances, unless a Levene's test of equal variances is significant at the 5% level. In that case, the hypothesis test will be conducted with a *t*-test of noninferiority allowing for unequal variances.

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

[redacted]

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| **Associated materials** | Systane preservative free eye drops and surgical disposables used in conjunction with the IP (e.g., OVDs, cartridges) as per the DFU and standard of care. |

**Table 3-1 Schedule of Study Procedures and Assessments**

| | Both Eyes | First Operative Eye[1] | Second Operative Eye[1] | First Operative Eye | Second Operative Eye | Both eyes | | Applicable eye |
|---|---|---|---|---|---|---|---|---|
| | *Pre-op* Visit 0 | Visit 00 | Visit 00A | Visit 1 | Visit 1A | Visit 2A | Visit 3A/Exit Visit | Unscheduled visit |
| | | Day 0 | Day 0A | Day 1-2 | Day 1-2 | Day 30-60 (1month) | Day 90-120 (3months) | N/A |
| Informed consent | X | | | | | | | |
| Demographics | X | | | | | | | |
| Medical history[2] | X | | | | | | | |
| Concomitant medications[2] | X | X | X | X | X | X | X | (√) |
| Urine pregnancy test[3] | X | | | | | | | |
| Inclusion/exclusion criteria | X | | | | | | | |
| Target refractive error (aiming for emmetropia or first minus) | X | | | | | | | |
| Manifest refraction | X | | | | | X | X | (√) |
| Corneal Tomography | X | | | | | X | X | |
| Biometry (Keratometry, AL, and ACD with corneal thickness) | X | | | | | X | X | |
| [redacted] | | | | | | | | |
| Dilated pupil size | X | | | | | | | |
| Toric IOL calculator | X | | | | | | | |
| Lens information | | X | X | | | | | |
| Randomization[5] | X | | | | | | | |
| Cataract surgery | | X | X | | | | | |
| Incision size and location | | X | X | | | | | |
| [redacted] | | | | | | | | |

| | Both Eyes | First Operative Eye[1] | Second Operative Eye[1] | First Operative Eye | Second Operative Eye | Both eyes | | Applicable eye |
|---|---|---|---|---|---|---|---|---|
| | *Pre-op* Visit 0 | Visit 00 | Visit 00A | Visit 1 | Visit 1A | Visit 2A | Visit 3A/Exit Visit | Unscheduled visit |
| | | Day 0 | Day 0A | Day 1-2 | Day 1-2 | Day 30-60 (1month) | Day 90-120 (3months) | N/A |
| [redacted] | | | | | | | | |
| Binocular BCDVA<br>• Bright lighting conditions | | | | | | X | X | |
| [redacted] | | | | | | | | |

| | Both Eyes | First Operative Eye[1] | Second Operative Eye[1] | First Operative Eye | Second Operative Eye | Both eyes | | Applicable eye |
|---|---|---|---|---|---|---|---|---|
| | *Pre-op* Visit 0 | Visit 00 | Visit 00A | Visit 1 | Visit 1A | Visit 2A | Visit 3A/Exit Visit | Unscheduled visit |
| | | Day 0 | Day 0A | Day 1-2 | Day 1-2 | Day 30-60 | Day 90-120 | N/A |
| [redacted] | | | | | | | | |
| **Safety** | | | | | | | | |
| All adverse events including SSI | X | X | X | X | X | X | X | (√) |
| Device deficiencies | | X | X | X | X | X | X | (√) |
| IOL observations | | | | X | X | X | X | (√) |
| PCO assessment | | | | X | X | X | X | (√) |
| Posterior capsulotomy assessment | | | | X | X | X | X | (√) |
| Surgical problems | | X | X | | | | | |
| Other surgical procedures at surgery | | X | X | | | | | |
| Reasons for discontinuation during surgery | | X | X | | | | | |
| Slit lamp examination | X | | | X | X | X | X | (√) |
| Dilated fundus examination | X | | | | | X | X | (√) |
| IOP | X | | | X | X | X | X | (√) |

| | Both Eyes | First Operative Eye[1] | Second Operative Eye[1] | First Operative Eye | Second Operative Eye | Both eyes | | Applicable eye |
|---|---|---|---|---|---|---|---|---|
| | ***Pre-op* Visit 0** | **Visit 00** | **Visit 00A** | **Visit 1** | **Visit 1A** | **Visit 2A** | **Visit 3A/Exit Visit** | **Unscheduled visit** |
| | | **Day 0** | **Day 0A** | **Day 1-2** | **Day 1-2** | **Day 30-60 (1month)** | **Day 90-120 (3months)** | **N/A** |
| IOL position change (tilt and decentration) | | | | X | X | X | X | (√) |

NOTES:

1 It is recommended that Visit 00 (1st eye surgery) occur within 0 to 30 calendar days after the Preoperative Visit (Visit 0). Visit 00A (2nd eye surgery) may have the option to occur same day as Visit 00 (1st eye surgery) and it is recommended that the 2nd eye surgery occur within 14 days after the 1st eye surgery.

2 CRF data will be targeted:

Medical History: All ocular history, targeted systemic history within 30 days prior to screening visit

Concomitant medications: All ocular medications, targeted systemic medications within 30 days prior to screening visit

3 In women of childbearing potential only.

4 Preoperative pupil size is the ability to constrict with a penlight.

5 It is recommended that randomization occur within 14 days prior to 1st eye surgery.

[redacted]

(√) Assessment performed as necessary

# 4 PROTOCOL AMENDMENTS

Modification of the protocol is prohibited without prior written agreement in the form of a protocol amendment. All amendments must be created by the study sponsor and must be approved by the IRB/IEC and global and regional Health Authorities, as applicable, prior to implementation except when required to mitigate immediate safety risks or when the changes involve only logistical or administrative revisions.

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

Refer to Appendix A for detailed description of amendments.

# 5 INTRODUCTION

## 5.1 Rationale and Background

Despite the recent prolific innovation and development of multifocal intraocular lenses (IOLs), monofocal IOLs remain the most common choice for implantation during cataract surgery (Mencucci 2020). They provide the best distance vision with the lowest incidence of photic phenomenon at a relatively low cost (Jeon 2021).

This multi-site, prospective, randomized, double-masked (subject and VA assessor) study will compare visual [redacted] outcomes between two partially corneal asphericity correcting monofocal IOLs, Clareon and Eyhance, [redacted] aiming to simulate real world conditions under a controlled comparison. The study will target toric IOLs to provide the best optical correction.

## 5.2 Purpose of the Study

This postmarket study is designed to compare the visual and patient reported outcomes of Clareon/Clareon Toric IOLs to Eyhance/Eyhance Toric IOLs in binocular BCDVA at 3 months postoperative. The data are intended to support scientific messaging.

Results of the study may be used for publication and presentation at ophthalmology conferences globally. Alcon reserves the right of prior review for any publication or presentation of information related to the study.

## 5.3 Risks and Benefits

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 and are managed through review of safety assessments outlined in this protocol.

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 pre-existing ocular condition. Possible problems during surgery include: corneal endothelial touch, detached Descemet's membrane, iris damage, iris prolapse, iris trauma, iris incarceration, zonular rupture, vitreous loss, capsulorhexis tear, capsular rupture, uncontrollable IOP, 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 adverse events include but are not limited to: corneal stromal edema, cystoid macular edema, endophthalmitis, hypopyon, iritis, lens dislocation, membrane formation on the IOL, pupillary block, retinal detachment, cyclitic membrane, transient or persistent glaucoma, retinal tear, vitritis, iris touch, pupil ovalization, posterior synechiae, ocular inflammation, ocular discomfort or pain, inflammation, decreased vision, decreased contrast sensitivity, decreased color perception, visual disturbances and corneal endothelial cell loss.

An IOL replacement or explantation may be appropriate in some cases of significant residual refractive error, ocular infection, subject dissatisfaction. In most of cases, spectacles or contact lenses may be prescribed to resolve residual refractive error. Other secondary surgical interventions include but are not limited to: IOL repositioning, refractive laser treatment, paracentesis, vitreous aspirations, iridectomy or laser iridotomy for pupillary block, wound leak repair, and retinal detachment repair.

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

# 6 STUDY OBJECTIVES

## 6.1 Primary Objective

The primary objective of this study is to demonstrate noninferiority of the Clareon/Clareon Toric IOLs to the Eyhance/Eyhance Toric IOLs in binocular BCDVA at 3-months postoperative.

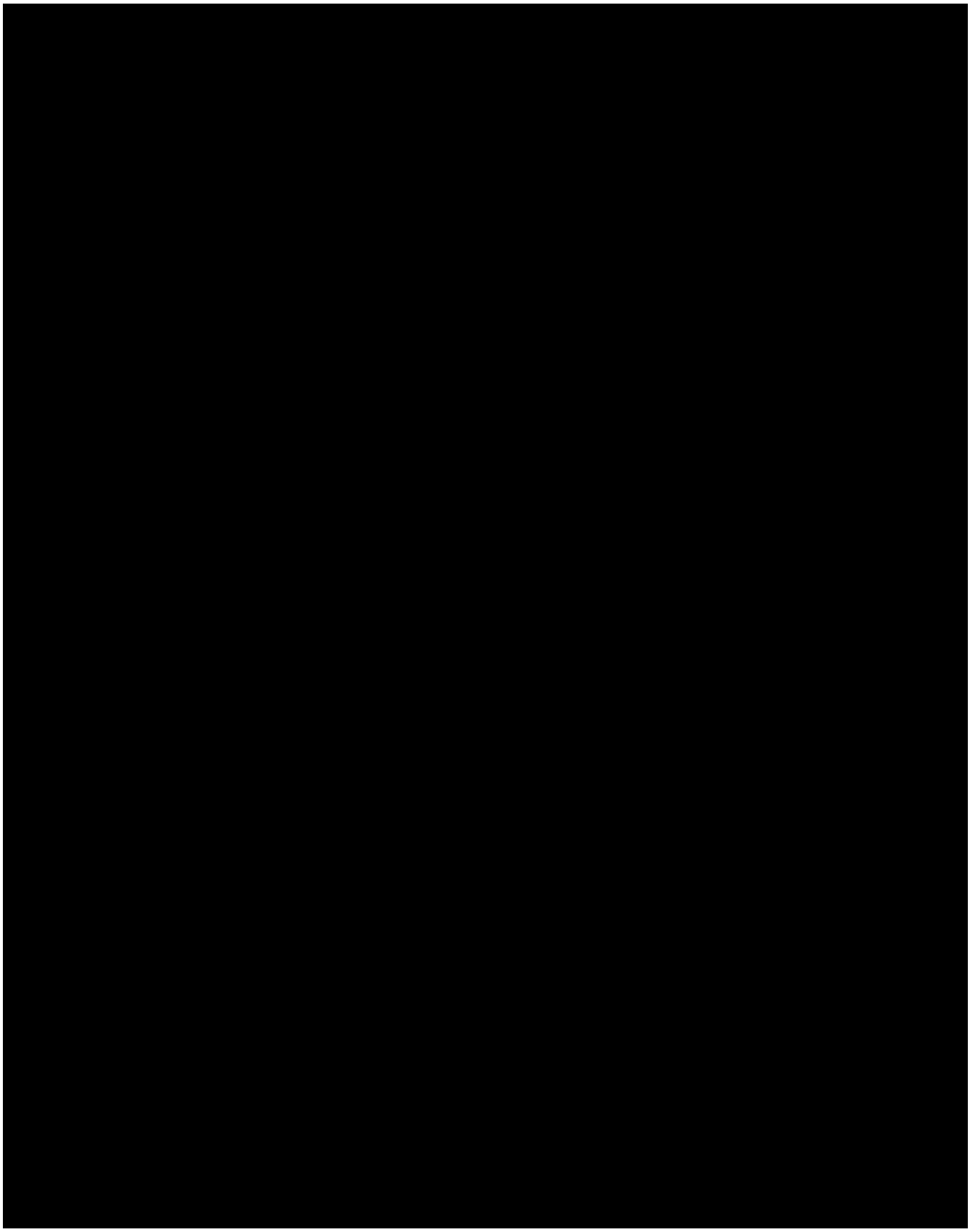
**Table 6-1 Primary Objective**

| **Objective** | **Endpoint** |
|---|---|
| To demonstrate noninferiority of the Clareon/Clareon Toric IOLs to the Eyhance/Eyhance Toric IOLs in binocular BCDVA at 3 months postoperative. | Mean binocular BCDVA under bright lighting conditions at 4 m at 3 months postoperative visit. |

## 6.2 Secondary Objective

Not applicable. There are no secondary objectives in this study.

[redacted]



[redacted]

## 6.5 Safety Objectives

There are no safety objectives. However, safety endpoints will be collected and summarized.

**Table 6-3 Safety Objectives**

| **Objectives** | **Endpoints** |
|---|---|
| None | • All adverse events (ocular and non-ocular, serious and non-serious)<br>• SSI<br>• Device deficiencies<br>• IOL observations<br>• IOL position change (tilt and decentration) from slit lamp examination |

| Objectives | Endpoints |
|---|---|
| | • PCO<br>• Posterior capsulotomy<br>• Surgical problems<br>• Other surgical procedures<br>• Slit lamp examination<br>• Dilated fundus examination<br>• IOP |

# 7 INVESTIGATIONAL PLAN

## 7.1 Study Design

This is a prospective, multi-center, randomized, double masked (subject and VA assessor), parallel group, postmarket study.

The study will enroll approximately 185 subjects who will be randomized to bilateral implantation of either Clareon/Clareon Toric IOLs or Eyhance/Eyhance Toric IOLs. The study will include adults 22 years of age and older, diagnosed with cataracts in both eyes, and planned bilateral cataract removal by routine small incision phacoemulsification surgery.

Eligible subjects should have planned implantation of a toric IOL, either test or comparator IOL per randomization from the following model numbers: CNW0T3, CNW0T4, CNW0T5, CNW0T6 or DIU150, DIU225, DIU300, DIU375 with approximately 1.00 - 3.00 D of preoperative corneal astigmatism in at least one eye at the Preoperative Visit (Visit 0). **It is preferred that both eyes have preoperative astigmatism between 1.00 – 3.00 D.** It is recommended that the eye with the highest astigmatism be implanted first. If the astigmatism is the same in both eyes, it is at the surgeon's discretion to determine which eye is implanted first.

Changes in lens selection (diopter power and/or toricity) are permitted intraoperatively if recommended by the Optiwave Refractive Analysis (ORA) or similar equipment. However, the lens selected intraoperatively must meet the same preoperative requirements of:

1) target emmetropia or first minus for the predicted residual refraction*,

2) have a predicted residual cylinder of ≤ 0.50 D, and

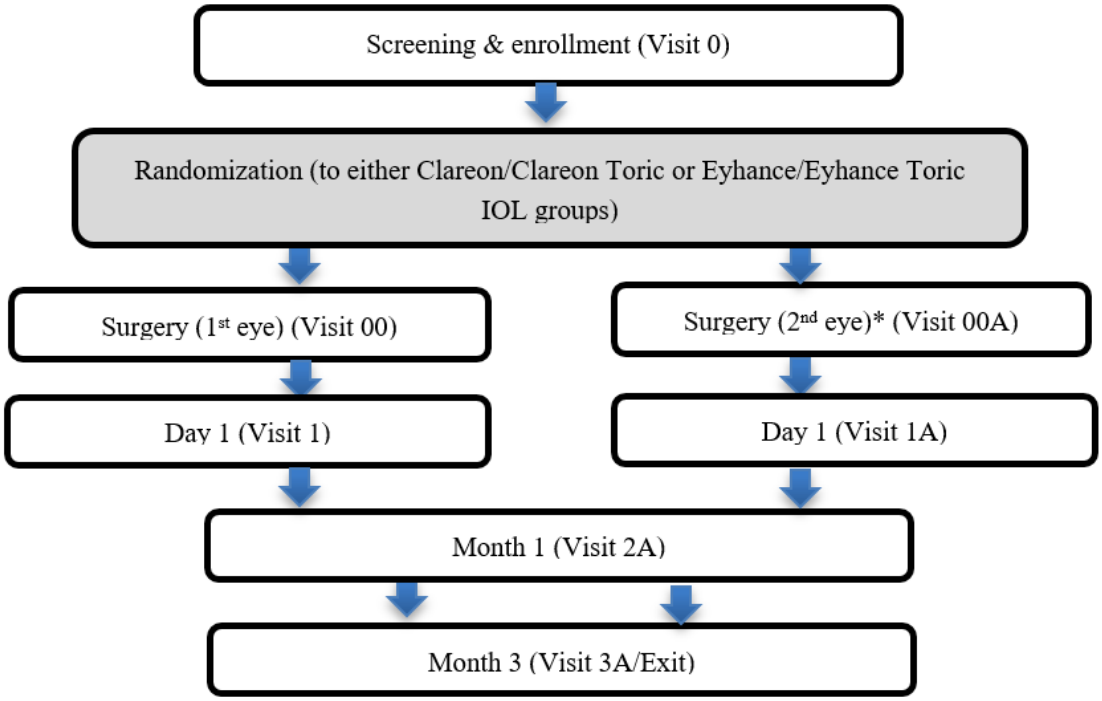
3) be within the diopter range (10.0 – 25.0 D) and toric model up to a maximum of CNW0T6 or DIU375 depending on the randomization group.

*Surgeons may change the planned IOL power and resulting predicted residual refraction for the 2nd eye based on the first eye outcomes so long as the predicted residual refraction within +/- 0.50 D. This should only be used to adjust in the case of a refractive surprise and should NOT be used to implant patients with mini-monovision. If ORA (or similar equipment) recommends that the patient subject receive a non-toric IOL (Clareon SY60WF or Eyhance DIB00), then the subject may receive this non-toric IOL implantation and continue in the study.

It is recommended that Visit 00 (1st eye surgery) occur within 0 to 30 calendar days after the Preoperative Visit (Visit 0). It is allowable for the 2nd eye to be operated on the same day as the 1st eye per the investigator's medical judgement. It is recommended that the 2nd eye surgery occur no longer than 14 days after the 1st eye surgery. **Note**: If a subject must re-schedule 1st eye surgery (Visit 00) and the date exceeds 60 days from Visit 0, the subject may continue study participation if Visit 0 biometry, tonometry, slit lamp examination, and dilated fundus exam assessments are repeated and occur within 60 days of the rescheduled surgery, and the subject is confirmed to continue to meet all entry criteria.

A total of up to 7 scheduled visits are planned: the Screening/Visit 0 and two Operative Visits (Visit 00 and Visit 00A), Visit 1, Visit 1A, Visit 2A and Visit 3A. Postoperative visits must occur at the following intervals: Visit 1/1A (Days 1-2) after 1st and 2nd eye surgery respectively, Visit 2A (Days 30-60) after the 2nd eye surgery, and Visit 3A (Days 90-120) after the 2nd eye surgery.

**Figure 7-1 Study Diagram**




* Option for the 2nd eye to be operated on the same day as the 1st eye. It is recommended that Visit 00 (1st eye surgery) occur within 0 to 30 calendar days after the Preoperative Visit (Visit 0). If not occurring on the same day, the 2nd eye IOL implantation should be conducted within 14 days after 1st eye implantation.

## 7.2 Rationale for Study Design

This prospective, multi-center, randomized, double masked (subject and VA assessor), parallel group, postmarket study aims to compare two partial-corneal correcting aspheric monofocal IOLs with different aspheric profiles. The head-to head design, randomization and double masking provide the most robust method of comparison between the IOLs while reducing potential bias. The IOLs were identified for their potential similarity using pre-clinical testing and clinical literature reviews which have led to the noninferiority statistical plan. Both IOLs will be applied on label and as described within the package insert.

[redacted]

## 7.4 Rationale for Duration of Treatment/Follow-Up

The duration of subject follow-up for this study will allow for the short-term assessment (3 month) of the IOLs included in this study.

Both the Clareon/Clareon Toric IOLs and the Eyhance/Eyhance Toric IOLs are currently marketed products.

## 7.5 Rationale for Choice of Comparator Product

The study lenses are both partial-corneal correcting aspheric monofocal IOLs with different aspheric profiles. The Clareon/Toric IOL has a uniform aspheric surface, and Eyhance/Eyhance Toric IOLs has a graduated aspheric surface. [redacted]. The IOLs were identified for their similarity using pre-clinical testing and clinical literature reviews.

## 7.6 Data Monitoring Committee

Not applicable

# 8 STUDY POPULATION

The study population consists of adults 22 years of age or older, diagnosed with binocular cataract who require bilateral cataract extraction by phacoemulsification.

We aim to enroll (consent) approximately 185 subjects in approximately 10 sites in the US with a target of approximately 23-31 subjects per site. Each site should contribute no more than 25% of the total enrolled study sample size. Site-specific targets may vary based upon individual site capabilities. The estimated time needed to recruit subjects for the study is approximately 5 months, however, unanticipated circumstances may shorten or lengthen this time and would not require amendment of this protocol.

Assuming a 10% screening failure rate and 16% dropout rate, data from approximately 140 subjects (70 subjects per group) will be available for statistical analysis at 3 months. Enrollment projections are as follows:

- Approximately 185 subjects to be enrolled (sign consent) (a 10% screen failure rate is estimated)
- Approximately 168 subjects randomized (approximately 84 per group) to be bilaterally implanted (a 16% dropout rate is estimated)

- Minimum 140 subjects (approximately 70 subjects per group) to successfully complete the final study visit (Visit 3A)

Check all entry criteria at Screening/Visit 0 and at both surgical visits (Visit 00, Visit 00A). If a subject is excluded following enrollment and prior to 1st eye surgery (IOL does not come in contact with the eye), the subject should be discontinued from participation in the study.

Refer to Section 8.4 Reasons for Discontinuation (During Surgery) for further details.

## 8.1 Inclusion Criteria

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

| | |
|---|---|
| 1. | Adults 22 years of age and older (at the time of screening) diagnosed with cataracts in both eyes. |
| 2. | Able to comprehend and willing to sign an IRB/IEC approved informed consent. |
| 3. | Planned bilateral cataract removal by routine small incision phacoemulsification surgery. |
| 4. | Planned implantation of either test or comparator IOL (per randomization) from the following model numbers: CNW0T3, CNW0T4, CNW0T5, CNW0T6 or DIU150, DIU225, DIU300, DIU375 **in at least one eye** with approximately 1.00 – 3.00 D of preoperative corneal astigmatism. |
| 5. | Predicted postoperative astigmatism of ≤ 0.5D in both operative eyes based on a Toric calculator. |
| 6. | Calculated IOL power between 10.0 D and 25.0 D when targeted for emmetropia or first minus residual refraction. |
| 7. | Potential postoperative best corrected distance visual acuity of 0.2 logMAR or better in both eyes based on the Investigator's expert medical opinion (**Note**: Subjects with any pathology that could reduce visual potential should not be enrolled in this study). |
| 8. | Pupil constriction with a penlight to ≤ 3.5 mm. |
| 9. | Pupil able to dilate to > 6.0 mm. |

| | |
|---|---|
| 10. | Clear intraocular media other than cataract. |
| 11. | Willing and able to complete all required postoperative visits. |

## 8.2 Exclusion Criteria

| | |
|---|---|
| 1. | Any disease or pathology, other than cataract, that (in the Investigator's opinion) may reduce the potential BCDVA to a level worse than 0.2 logMAR (including, but not limited to the following: clinically severe corneal dystrophy (e.g., epithelial, stromal, or endothelial dystrophy), diabetic retinopathy, extremely shallow anterior chamber, not due to swollen cataract, microphthalmos, previous retinal detachment, previous corneal transplant, recurrent severe anterior or posterior segment inflammation of unknown etiology, iris neovascularization, glaucoma, aniridia, or optic nerve atrophy, epiretinal membrane, or diagnosis of pseudoexfoliation). |
| 2. | History of or concurrent macular degeneration. |
| 3. | Clinically significant (in the Investigator's opinion) corneal pathology (epithelial, stromal, endothelial), dry-eye or ocular surface disease that would adversely affect a) the biometry measures and/or toric calculations and b) the visual outcome. This includes, but is not limited to old significant corneal scars (including Salzman's nodular degeneration), corneal irregularity (including dry eye syndrome), 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. |
| 4. | Clinically significant ocular trauma or ocular surface disease that would affect study measurements based on the Investigator's expert medical opinion. |
| 5. | History of previous intraocular or corneal surgery (including iridotomy and laser-assisted in situ keratomileusis (LASIK). |
| 6. | 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:<br>a. They are currently pregnant<br>b. Have a positive urine pregnancy test result at Screening<br>c. Intend to become pregnant during the study period<br>d. Are breast-feeding<br>Subjects who become pregnant and/or lactating after a study lens has been implanted in (or contacted) their eye will not be discontinued; however, data will be excluded from the effectiveness analyses because pregnancy and/or lactating can alter refraction and visual acuity results. |
| 7. | History of amblyopia or monofixation syndrome with poor stereoscopic vision. |
| 8. | Any use (current or historical) of an alpha-1-selective adrenoceptor blocking agent or an antagonist of alpha1A adrenoceptor (e.g., Flomax (tamsulosin HCL), Hytrin (terazosin), Cardura (doxazosin), or Uroxatral (alfuzosin)). |
| 9. | Any subject currently participating in another investigational drug or device study that may confound the results of this investigation. |
| 10. | Any other ocular or systemic co-morbidity that, in the Investigator's opinion, may confound the results of this study or prohibit the completion of the study assessments or increase the risk for the subject. |
| 11. | Subjects with conditions that, in the Investigator's opinion, increase the risk of zonular rupture during cataract extraction procedure (e.g., Marfan syndrome) that may affect the postoperative centration or tilt of the lens. |
| 12. | Any other planned ocular surgical procedures including but not limited to limbal relaxing incision (LRI), astigmatic keratotomy, LASIK, and retinal laser treatment within the study time frame. |
| 13. | Patients who desire monovision/mini-monovision. |

| | |
|---|---|
| 14. | Presumed or actual ocular infection (bacterial, viral, fungal) or history of ocular herpes (simplex or zoster) in either eye as determined by subject history and/or examination at Visit 0 per the investigator's expert medical opinion. |

## 8.3 Rescreening of Subjects

Rescreening of subjects is not allowed in this study.

## 8.4 Reasons for Discontinuation (During Surgery)

Below are listed reasons to not implant the study lens.

| | |
|---|---|
| 1. | 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, uncontrollable IOP. |
| 2. | Mechanical or surgical manipulation of the pupil. |
| 3. | Excessive iris mobility. |
| 4. | Inability to place the IOL in the capsular bag due to surgical complications. |

Subjects may be excluded from trial participation during surgery. For specific criteria, refer to protocol Section 8.4 Reasons for Discontinuation During Surgery. Depending on the circumstance, the subject may continue in the study or may be discontinued as outlined in Table 8-1 below. In addition, the subject may be excluded from trial participation if lens implantation was unsuccessfully attempted more than twice. Table 8-1 below applies in these circumstances as well. A subject discontinuing at the time of surgery will not be considered as a screen failure.

**Table 8-1 Subject Status after Exclusion During Surgery**

| Conditions | Status/Follow-up |
|---|---|
| • Exclusion during surgery occurs<br>• IOL **did not** touch eye | • Subject discontinued |

| Conditions | Status/Follow-up |
|---|---|
| • Exclusion during surgery occurs<br>• IOL **did** touch eye<br>• Lens is **not** implanted | • Subject continued<br>• *No* effectiveness assessments conducted at postoperative visits<br>• Safety assessments conducted at postoperative visits |
| • Exclusion during surgery occurs<br>• Lens implanted | • Subject continued<br>• Effectiveness assessments conducted at postoperative visits<br>• Safety assessments conducted at postoperative visits |

**Note**: Unilateral IOL implantation is NOT allowed in this study; thus, if the subject's 1st eye is not implanted with study IOL, the subject should be discontinued from the study.

In the event the 2nd eye is not implanted with study IOL (following a successful implant with a study IOL in the 1st eye), the subject will remain in the study and complete all required testing except for binocular VA assessments and subject questionnaires. Surgeon questionnaires should still be completed for the study eye.

# 9 TREATMENTS ADMINISTERED

## 9.1 Investigational Products

| | |
|---|---|
| *Test Products:* | Clareon/Clareon Toric IOLs. Models SY60WF; CNW0T3, CNW0T4, CNW0T5, CNW0T6. |
| *Comparator Products:* | Eyhance/Eyhance Toric IOLs. Models DIB00; DIU150, DIU225, DIU300, DIU375. |

**Table 9-1 Test Product**

| | |
|---|---|
| Test Products | Clareon/Clareon Toric IOLs. Models SY60WF; CNW0T3, CNW0T4, CNW0T5, CNW0T6 as available. |

| | |
|---|---|
| Manufacturer | Alcon Laboratories, Inc.<br>6201 South Freeway<br>Fort Worth, Texas 76134-2099<br>USA |
| Indication for use and intended purpose in the current study | The Clareon Aspheric Hydrophobic Acrylic Intraocular Len (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 in whom a cataractous lens has been removed.<br><br>The Clareon Toric 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 and pre-existing corneal astigmatism. |
| Product description and parameters available for this study | Clareon IOL (Model SY60WF):<br>• Optic Type: Anterior Asymmetric Biconvex<br>• Optics Material: Ultraviolet and Blue Light Filtering Hydrophobic Acrylate / Methacrylate Copolymer<br>• Optic Powers:<br>  ○ +10.0 to +25.0 diopters (in 0.5 diopter increments) optic powers as available<br>• Index of Refraction: 1.55 at 35°C<br>• Haptic Configuration: STABLEFORCE™ Modified-L Haptics<br>• Haptic Material: Ultraviolet and Blue Light Filtering Hydrophobic Acrylate / Methacrylate Copolymer<br>• Optic Diameter (mm): 6.0<br>• Overall Length (mm): 13.0<br>• Haptic Angle: 0°<br>Clareon Toric IOLs. Models CNW0T3, CNW0T4, CNW0T5, CNW0T6 as available: |

| | |
|---|---|
| | • Optic Type: Biconvex Toric Aspheric Optic<br>• Optics Material: Ultraviolet and Blue Light Filtering Hydrophobic Acrylate / Methacrylate Copolymer<br>• Optic Powers:<br>o +10.0 to +25.0 diopters (in 0.5 diopter increments) optic powers as available<br>• IOL Cylinder Powers (D): 1.00, 1.50, 2.25, 3.00, 3.75, 4.50, 5.25, 6.00 as available<br>• Index of Refraction: 1.55 at 35°C<br>• Haptic Configuration: STABLEFORCE™ Modified-L Haptics<br>• Haptic Material: Ultraviolet and Blue Light Filtering Hydrophobic Acrylate / Methacrylate Copolymer<br>• Optic Diameter (mm): 6.0<br>• Overall Length (mm): 13.0<br>• Haptic Angle: 0° |
| Formulation | N/A |
| Usage | IOLs are implantable medical devices and are intended for long-term use over the lifetime of the pseudophakic subject. |
| Number/Amount of product to be provided to the subject | Each subject will be bilaterally implanted with the test product or comparator. |
| Packaging description | Alcon standard commercial package contains below items:<br>• The IOL<br>• A subject registration card in case it is needed for the Alcon market (Lens Implant Reply Card)<br>• A subject identification card, for the patient (Implant Card)<br>• Adhesive labels containing the IOL information and unique serial number |

| | |
|---|---|
| | • eIFU Reference Card, providing information to access the IFU at ifu.alcon.com |
| 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 | The Clareon Aspheric Hydrophobic Acrylic IOL is intended for use by a trained ophthalmic surgeon. |
| Storage conditions | N/A |
| Additional information | 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.<br><br>More information on the test article can be found in the Package Insert/DFU |
| Supply | The Investigator shall locally procure the test product through his/her standard commercial channel. |

**Table 9-2 Comparator Product**

| | |
|---|---|
| Comparator Products | Eyhance/Eyhance Toric IOLs. Models DIB00; DIU150, DIU225, DIU300, DIU375 as available. |
| Manufacturer | Johnson & Johnson Surgical Vision, Inc<br>1700 E Saint Andrew Pl<br>Santa Ana, CA 92705 |
| Indication for Use | The Eyhance IOL for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed by |

| | |
|---|---|
| | extracapsular cataract extraction. The lens is intended to be placed in the capsular bag.<br><br>The Eyhance Toric IOLs for the visual correction of aphakia and pre-existing corneal astigmatism of one diopter or greater in adult patients with or without presbyopia in whom a cataractous lens has been removed by phacoemulsification and who desire reduction in residual refractive cylinder. The lens is intended to be placed in the capsular bag. |
| Product description and parameters available for this study | Eyhance IOL. Model DIB00<br>• Optics Material: Optically clear, soft foldable hydrophobic acrylic with a covalently bound UV absorber. Full transmission of blue wavelength light for optimal scotopic sensitivity.<br>• Optic Powers:<br>o +10.0 to +25.0 diopters (in 0.5 diopter increments) optic powers as available<br>• Index of Refraction: 1.47 at 35°C<br>• Haptic Configuration: TRI-FIX design Modified C, integral with optic<br>• Haptic Material: Soft foldable hydrophobic acrylic with a covalently bound UV absorber.<br>• Optic Thickness (mm): 0.46<br>Eyhance Toric IOLs. Models DIU150, DIU225, DIU300, DIU375 as available.<br>• Optics Material: Optically clear, soft foldable hydrophobic acrylic with a covalently bound UV absorber. Full transmission of blue wavelength light for optimal scotopic sensitivity.<br>• Optic Powers:<br>o +10.0 to +25.0 diopters (in 0.5 diopter increments) optic powers as available<br>• Index of Refraction: 1.47 at 35°C |

| | |
|---|---|
| | • Haptic Configuration: TRI-FIX design Modified C, integral with optic<br>• Haptic Material: Soft foldable hydrophobic acrylic with a covalently bound UV absorber.<br>Optic Thickness (mm): 0.46 |
| Formulation | N/A |
| Usage | IOLs are implantable medical devices and are intended for long-term use over the lifetime of the pseudophakic subject. |
| Number/Amount of Product to be Provided to the subject | Each subject should be bilaterally implanted with the test product or comparator. |
| Packaging description | Each IOL will be individually packaged and will have a unique serial number. The IOL<br>package will contain the following items:<br>• The IOL<br>• A subject registration card (Lens Implant Card)<br>• A subject identification card<br>• Adhesive labels containing the IOL information and unique serial number<br>• A package insert containing directions for use.<br>More information on the test article can be found in the Package Insert/DFU. |
| Labeling description | Packaged in a Johnson & Johnson Surgical Vision carton. |
| Training and/or experience requirements for device | The Eyhance/Eyhance Toric IOLs are intended for use by a trained ophthalmic surgeon. |
| Storage conditions | N/A |

| | |
|---|---|
| Additional identifying information | 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.<br><br>More information on the test article can be found in the Package Insert/DFU. |
| Supply | The Investigator shall locally procure the test product through his/her standard commercial channel. |

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

Systane preservative free drops are required to be used bilaterally prior to both corneal tomography and biometry measures.

The Clareon/Clareon Toric IOLs must be delivered by the Clareon Monarch IV Delivery System.

Each study surgeon should follow his/her routine cataract procedure for all study surgeries.

Femtosecond laser-assisted cataract surgery (FLACS) is permitted for Investigators that currently use this procedure as part of their standard of care for cataract surgery, however, it is **NOT** permitted on primary incisions.

FLACS may **ONLY** be used for the following:

- Capsulorhexis
- Lens fragmentation

## 9.3 Treatment Assignment / Randomization

Ensure potential subjects are properly consented (i.e., subject has undergone informed consent process and the Informed Consent Form (ICF) is fully signed by all required parties) prior to any study-specific test. Consider subjects enrolled after the ICF signing. Enter the subjects into the electronic data capture (EDC) system for the provision of a subject number.

Subjects will be randomized in a 1:1 manner to receive treatment with either Clareon/Clareon Toric IOLs or Eyhance/Eyhance Toric IOLs, respectively.

It is recommended that randomization occur within 14 days prior to 1st eye surgery. A randomization list will be generated using a validated system that automates the random assignment of treatment arms to randomization numbers in the specified ratio. Subjects will be assigned treatment according to the randomization list uploaded in the EDC system. The randomization list will be generated and maintained by the study sponsor.

## 9.4 Treatment Masking

This study is VA assessor-masked and subject-masked to the IOL group assignment.

Sponsor individuals associated with the study who are masked or unmasked, other than the sponsor monitor listed below are detailed in the Statistical Analysis Plan (SAP).

The VA assessor associated with vision testing will be masked in this study. This includes manifest refraction [redacted] **Note**: Any unmasking of the masked assessor or subject must be reported to Alcon.

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 subject will remain masked for the duration of his/her trial participation and will be provided with his/her permanent implant card upon study exit.

[redacted]

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

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

The Investigator will procure both investigational products (test and comparator lenses). Details related to the procurement, labeling, handling, dispensing, and final disposition are outlined below. The implanted lenses must be tracked for the study.

### 9.5.1 Procurement

The Investigator shall locally procure both products (Clareon/Clareon Toric IOLs and Eyhance/Eyhance Toric IOLs) through his/her standard commercial channels.

### 9.5.2 Labeling

Products are locally procured via commercial channel and will arrive in country compliant commercial packaging with commercial label.

### 9.5.3 Handling

IP will be handled according to site practices, SOPs, and product direction of use (DFU). It is the responsibility of the investigator to ensure that the planned IOLs are available for surgery dates.

### 9.5.4 Dispensing

The Investigator is to keep a current record of the dispensing of all test products. This record will be made available to the Sponsor's monitor to account for all test articles. Any discrepancy and/or deficiency must be recorded, with an explanation.

### 9.5.5 Final Disposition

At the conclusion of the trial, remaining product may be returned to the Investigator's general stock.

**Note**: Return deficient product to the manufacturer following each manufacturer's respective complaint process. Refer to Section 11 for further details on the return process for Alcon product. Additionally, the investigator must follow any recalls from the distributor/manufacturer.

## 9.6 Changes to Concomitant Medications, Treatments/Procedures

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

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

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

# 10 STUDY PROCEDURES AND ASSESSMENTS

This section describes the procedures and assessments for this clinical study. The timing of visits is specified as below.

Visit 0 is the screening visit; informed consent procedures as well as eligibility and endpoint assessments are performed at this visit. Visits 00/00A are the operative visits. Visit 1 is Day 1 to Day 2 post 1st eye surgery and Visit 1A is Day 1 to Day 2 post 2nd eye surgery. Endpoint assessments are performed at this visit. Visit 2A is Day 30 to Day 60 post 2nd eye surgery (both eyes). Endpoint assessments are performed at this visit. Visit 3A is Day 90 to Day 120 post 2nd eye surgery (both eyes). Endpoint assessments and study exit are performed at this visit.

## 10.1 Informed Consent and Screening

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

The subject should be provided with enough time for his/her decision on participation in the study and should have options to discuss with his/her family members or relatives about the participation in the investigation as well as have ability to ask questions to the investigator.

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. Note that the applicable privacy regulation requirements must be met.

## 10.2 Description of Study Procedures and Assessments

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

Detailed descriptions of assessments and procedures are provided in the Manual of Procedures (MOP). The Investigator is responsible for ensuring responsibilities for all procedures and assessments are delegated to appropriately qualified study staff.

### 10.2.1 Demographics

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

### 10.2.2 Medical History and Concomitant Medication

Collect Concomitant Medications, including all ocular and systemic medications, within 30 days prior to screening visit, in source documents. Limited concomitant medications will be captured in EDC.

Collect medical history information, including all ocular and nonocular systemic history within 30 days prior to screening visit in source document. Collect all ocular surgery information regardless of date. Limited medical and ocular history will be captured in EDC via prepopulated dropdown field with items of interest listed in EDC.

Throughout the subject's participation, obtain information on any changes in medical health and/or the use of concomitant medications.

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 child-bearing potential.

### 10.2.4 Biometry: Effectiveness Assessment

Add a Systane preservative free drop to both eyes prior to Biometry.

Measure optical biometry according to the Investigator's standard of care noting all available measurements including keratometry, ACD with corneal thickness and AL for both eyes. The targeted residual refractive error for lens selection must be either emmetropia or the first minus. See details in the MOP for detail on targeted residual refractive error and use of a recent generation IOL Toric Calculator.

### 10.2.5 Pupil Size: Entry Criteria

Screening visit (Visit 0):

[redacted]

- Dilated pupil size: Perform and record pupil size in both eyes at 4 m to the nearest 0.1 mm with ruler under standard of care lighting conditions.

[redacted]

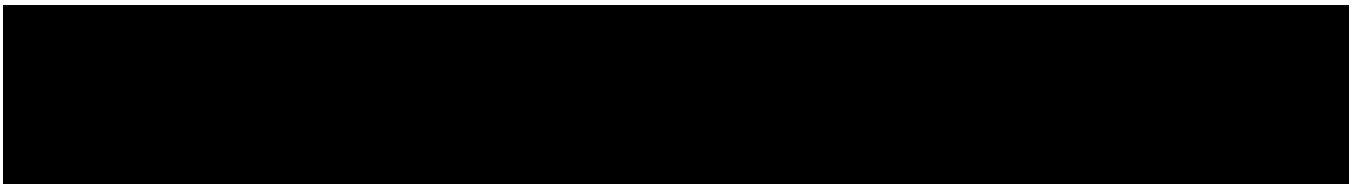
### 10.2.7 Visual Acuity: Effectiveness Assessment

Perform visual acuity as below:

[redacted]

- Measure binocular BCDVA at 4 m (OU) in bright lighting conditions.

[redacted]



These assessments must be performed by delegated trained masked VA assessor only.

### 10.2.10 Slit lamp Examination: Safety Assessment

Slit lamp examination must be performed in both eyes. This assessment must be performed by a delegated investigator. Record any slit lamp findings, IOL Position Change (Tilt and Decentration), any IOL Observations, and any Subjective PCO including Posterior Capsulotomy. Refer to MOP for details.

*For toric IOLs only*: Record the actual axis of IOL orientation at implantation, and at subsequent visits. This assessment must be performed by a delegated investigator.

### 10.2.12 Dilated Fundus Examination: Safety Assessment

Dilated fundus examination must be performed in both eyes. This assessment must be performed by a delegated investigator.

### 10.2.13 Adverse Event: Safety Assessment

Assess and record any AEs that are observed or reported. Causality must be determined by a delegated investigator. Requirements for reporting Adverse Event in the study can be found in Section 11.

### 10.2.14 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.

### 10.2.15 Intraocular Pressure: Safety Assessment

Perform IOP according to the to the Investigator's standard of care.

### 10.2.16 Surgical Procedures and Assessments: Safety Assessment

Perform cataract surgery. Record operative eye, initial and final incision size, incision location, lens information, and any surgical problems that arise during surgery. Refer to the MOP for additional details. During cataract surgery, document whether any additional procedures (e.g., anterior vitrectomy, capsular tension ring) were performed. If subject is discontinued during surgery, record the reason for discontinuation.

**Note**: Nd:YAG capsulotomy should not be performed as a preventive surgery for PCO reoccurrence.

## 10.3 Unscheduled Visits

An unscheduled visit (USV) is defined as follows:

- Ocular examination that is not standard of care and not required by the protocol
- Examination conducted by the study staff
- New findings, or a change to a previous finding was discovered

- Not site standard of care (SOC)/routine

An USV may or may not result in the capture of an adverse event. Likewise, an adverse event may be captured without the report of an USV (e.g., AE identified subsequent to study eye examination by non-study personnel).

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 USV. If the subject seeks medical attention outside the clinic (for example, at an Emergency Room) or at the clinic but is seen by non-study personnel, the investigator is to capture adverse event-related information on the Adverse Event form upon becoming aware.

The assessments captured at the USV are dictated by the Investigator per his/her medical judgement, however, the following assessments are recommended

- Collect Adverse Event information.
- Record changes in medical condition or concomitant medication

[redacted]

- Measure monocular BCDVA at 4 m [redacted].
- Perform tonometry.

[redacted]

- Perform a slit-lamp examination.

[redacted]

- Record IOL observations, if any, for the operative eye(s).

[redacted]

- Perform a dilated fundus examination.
- Record any subjective posterior capsule opacification if present and information for any posterior capsulotomy that has occurred since surgery, if applicable for operative eye(s).
- Record secondary surgical interventions for the operative eye(s) that have occurred since surgery, if applicable.

- Record any adverse events (both volunteered and elicited).
- Record any device deficiencies, if applicable.

*Note: Assessments that may be completed during an unscheduled visit are not limited to the above list. In cases where the Investigator's routine clinic visits are more frequent than study specific visits the additional routine visits would not be considered as unscheduled visits.*

*However, adverse events collected from these routine visits must be reported with the study data. Refer to Section 11 for further details on the AE reporting.*

## 10.4 Discontinued Subjects

Subjects may be discontinued from study participation at any time after informed consent via screen failure or early discontinuation

### 10.4.1 Screen Failures

Subjects who were excluded from the study after signing the informed consent and prior to randomization are considered screen failures. The Investigator must document the reason for screen failure 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 informed consent is signed, are randomized to treatment and before the last study visit is completed.

Subject numbers of discontinued subjects must not be re-used (i.e., subject replacement is not allowed). Subjects may discontinue from the study or study treatment at any time for any reason. Subjects may also be discontinued from study treatment at any time if, in the opinion of the Investigator, continued treatment poses a risk to their health.

The Investigator must document the reason for study or treatment discontinuation in the subject's case history source documents. To ensure the safety of all subjects who discontinue early, Investigators must assess each subject and, if necessary, advise them of any therapies and/or medical procedures that may be needed to maintain their health.

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

Subjects who discontinue the IP (i.e., have study lens explanted) will continue in the study through Visit 3A and be followed for safety. At minimum, safety examinations must include the assessments associated with appropriate medical care. Standard post-surgical assessments are bulleted below:

- UCDVA and/or BCDVA
- Slit-lamp Examination
- Dilated Fundus Examination

### 10.4.4 Subject Lost to Follow Up

If a subject unavoidably misses a scheduled exam, he/she should be rescheduled within the same exam period. The investigational site should show diligence in trying to schedule the subject for all exams. The site must document all attempts to contact the subject in the subject's chart, including dates, times, method of contact, etc. If a subject is unable to return for the Final Study Visit, the Exit Case Report Form should be completed with the appropriate reason for discontinuation indicated. If attempts to contact the subject are unsuccessful, then the Exit Case Report Form for that subject is completed as Lost to Follow-up. The date at which the subject was considered lost to follow-up should also be recorded.

### 10.4.5 Subject Pregnant or Lactating

Subjects who become pregnant after having a study IOL implanted (or the study IOL touches the eye) or are lactating during the study will not be discontinued; [redacted]. Pregnancy, or women who are lactating, should be noted within the source documentation for each visit, and at which time the subject is pregnant or lactating.

The Investigator must notify the sponsor within 24 hours of learning that a subject is pregnant; reporting procedures are noted in Section 11.

### 10.4.6 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.

### 10.4.7 Follow-up of subjects after study participation has ended

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

# 11 ADVERSE EVENTS AND DEVICE DEFICIENCIES

## 11.1 General Information

An AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device (test product). Refer to the Glossary of Terms for categories of AEs and SAEs.

**Figure 11-1 Categorization of All Adverse Events**

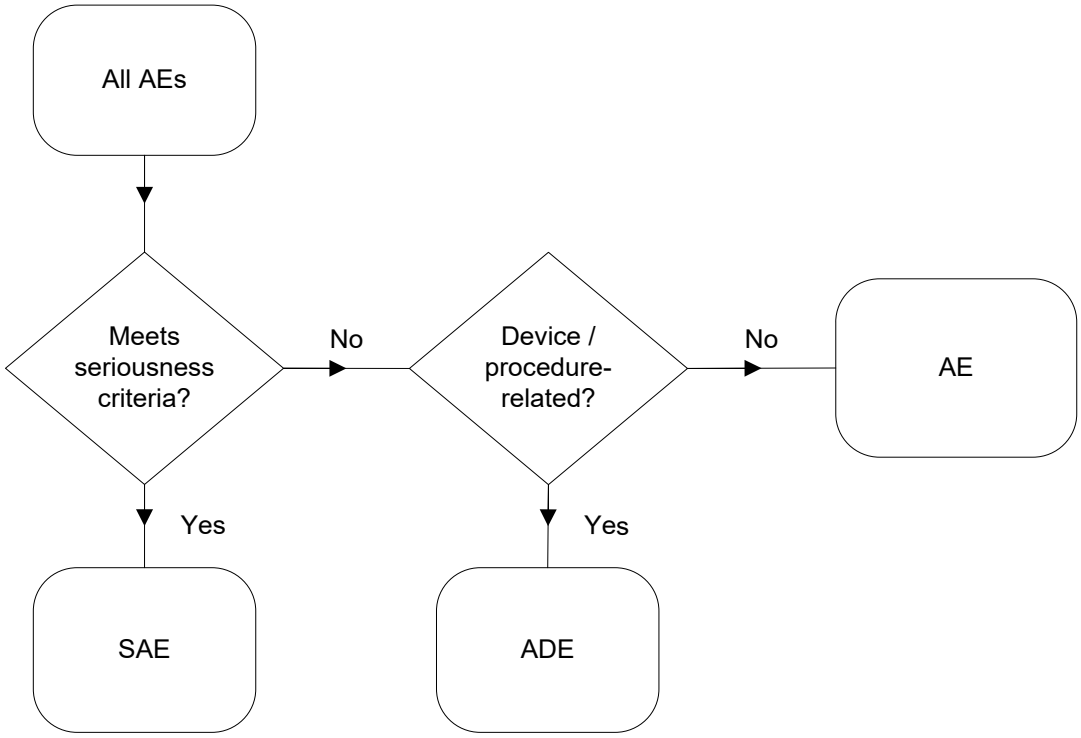
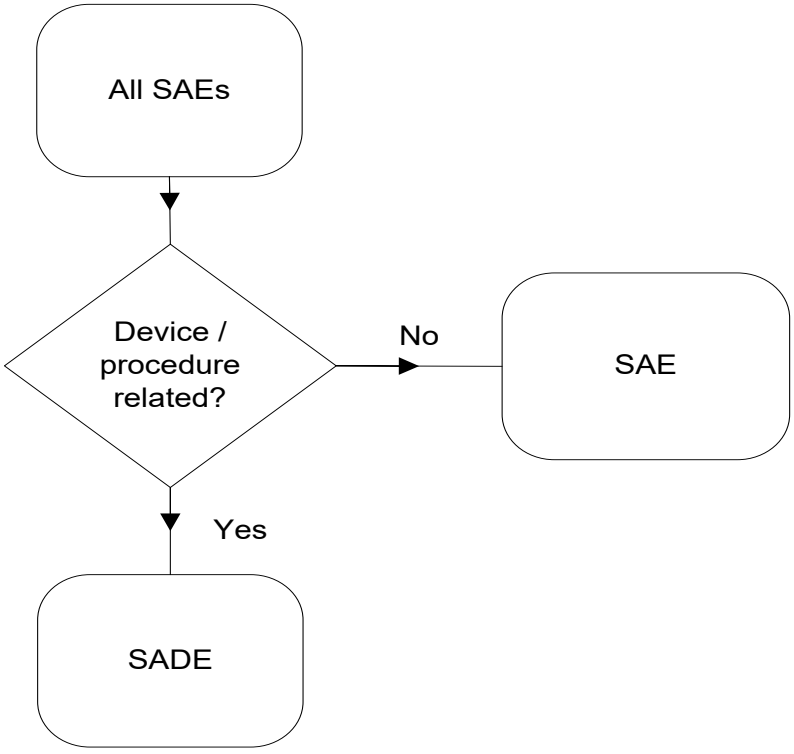



**Figure 11-2 Categorization of All Serious Adverse Events**



**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
- Secondary surgical intervention (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 11.3.

## 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, delivery system)
- Lack of effectiveness
- Injector issue
- Cartridge damage
- Delivery system issue

## 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 and/or questionnaires evaluated during the study are to be reviewed by the Investigator. Any untoward (unfavorable and unintended) change in a protocol-specific parameter or questionnaire response that is clinically relevant, in the opinion of the Investigator, is to be reported as an AE. These clinically relevant changes will be reported regardless of causality.

## 11.4 Procedures for Recording and Reporting

AEs are collected from the time of informed consent. Any pre-existing medical conditions or signs/symptoms present in a subject prior to the start of the study (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 post-operative findings that are typically observed following ocular surgery. These are not considered AEs if they can be reasonably expected to resolve within a week and not result in any untoward long term visual outcome impact.

For each recorded event, the ADEs and SAEs documentation must include: date of occurrence, severity, treatment (if applicable), outcome, and assessments of the seriousness and causality. In addition, the Investigator must document all device deficiencies reported or observed with study test (Clareon / Clareon Toric) and control (Eyhance / Eyhance Toric) 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 Serious Adverse Event and Adverse Device Effect and/or Device Deficiency Form. The completed form is emailed to the Study Sponsor at MSUS.safety@alcon.com according to the timelines outlined above; however, the reported information must be entered into the EDC system once it becomes operational.

Any AEs and device deficiencies for the control IOLs and any non-study marketed devices/products (i.e., Eyhance/Eyhance Toric IOLs and OVDs) 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 control 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 question 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 and must include the Complaint # which will be provided by Study Sponsor after the case is entered in the Study Sponsor's Global Product Complaint Management System (GPCMS).

## 11.7 Unmasking of the Study Treatment

Masked information on the identity of the assigned medical device should not be disclosed during the study. Refer to Section 9.4 "Treatment Masking" 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).

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. An eCRF will be utilized to capture all pregnancy-related and lactating information.

# 12 ANALYSIS PLAN

## 12.1 Subject Evaluability

Final 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 for bilateral treatment in a 1:1 ratio to receive the investigational product.

## 12.2 Analysis Sets

The primary analysis set for effectiveness will be the All-Implanted Analysis Set (AAS). The AAS will include all eyes with successful study IOL implantation and with at least one postoperative visit.

[redacted]

All eyes with attempted study IOL implantation (successful or aborted after contact with the eye) will be considered evaluable for the safety analysis set (SAS).

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

## 12.3 Demographic and Baseline Characteristics

Demographic and baseline characteristics will be summarized by treatment group and overall. Counts and percentages will be presented for categorical variables such as sex, age group (< 65 years and ≥ 65 years), 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, [redacted] binocular VA, refractive errors, and IOP.

## 12.4 Effectiveness Analyses

### 12.4.1 Analysis of Primary Effectiveness Endpoint

The primary objective of this study is to demonstrate noninferiority of the Clareon/Clareon Toric IOLs to the Eyhance/Eyhance Toric IOLs in binocular BCDVA at 3 months postoperative. The primary effectiveness endpoint is, mean binocular BCDVA under bright lightning conditions at 4 m at 3 months postoperative.

### 12.4.2 Statistical Hypotheses

The null ($H_0$) and alternative ($H_1$) hypotheses to be evaluated in support of the primary noninferiority objective are:

$$H_0: \mu_{Test} - \mu_{Comparator} \geq \Delta$$
$$H_1: \mu_{Test} - \mu_{Comparator} < \Delta$$

Where, $\Delta$ refers to the noninferiority margin, set at 0.1 logMAR, and $\mu_{Test}$, $\mu_{Comparator}$ refers to the mean values of binocular BCDVA for the test (Clareon/ Clareon Toric) and comparator (Eyhance/Eyhance Toric) IOLs respectively at 3 months post implantation.

### 12.4.3 Analysis Methods

The noninferiority objective as well as the corresponding hypothesis will be evaluated using a t-test of noninferiority assuming equal variances, if the equality of variance is not rejected, or assuming unequal variance when the equality of variance is rejected based on Levene's test. The null hypothesis is rejected, that is the noninferiority is claimed, if the upper bound of the one-sided 95% confidence interval does not exceeds the noninferiority margin of 0.1 logMAR. Primary analysis will be based on AAS. [redacted]

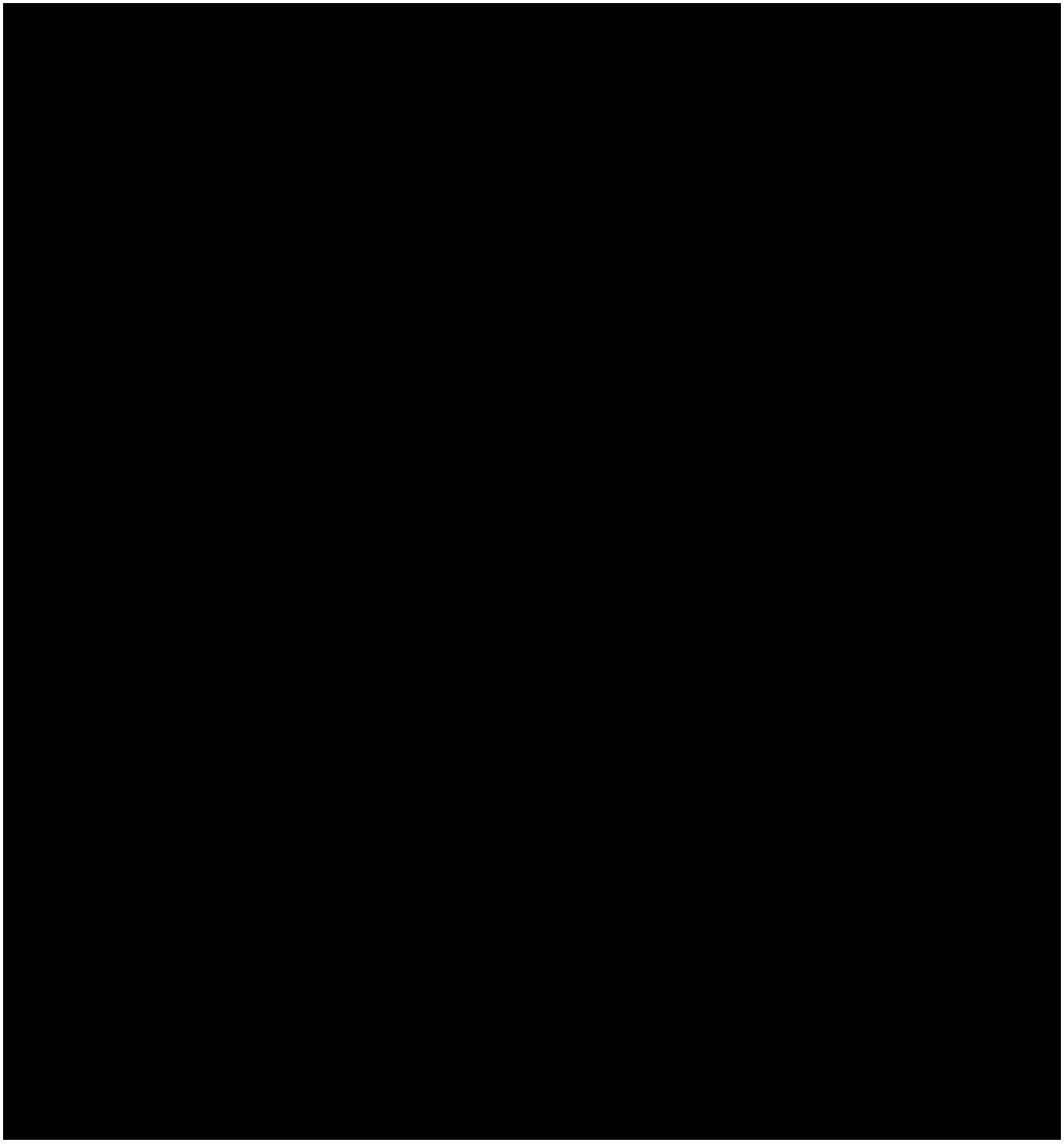
Standard descriptive statistics will be presented for the primary endpoint where the number of subjects/eyes, mean, median, standard deviation, minimum, maximum, and 95% confidence intervals will be reported based on AAS [redacted] at 3 months visit.

### 12.4.4 Analysis of Secondary Effectiveness Endpoints

There are no secondary effectiveness endpoints in this study.

### 12.4.5 Statistical Hypotheses

No hypothesis testing of the secondary effectiveness endpoint(s) is planned.



## 12.5 Handling of Missing Data

There will be no imputation for missing data.

## 12.6 Safety Analyses

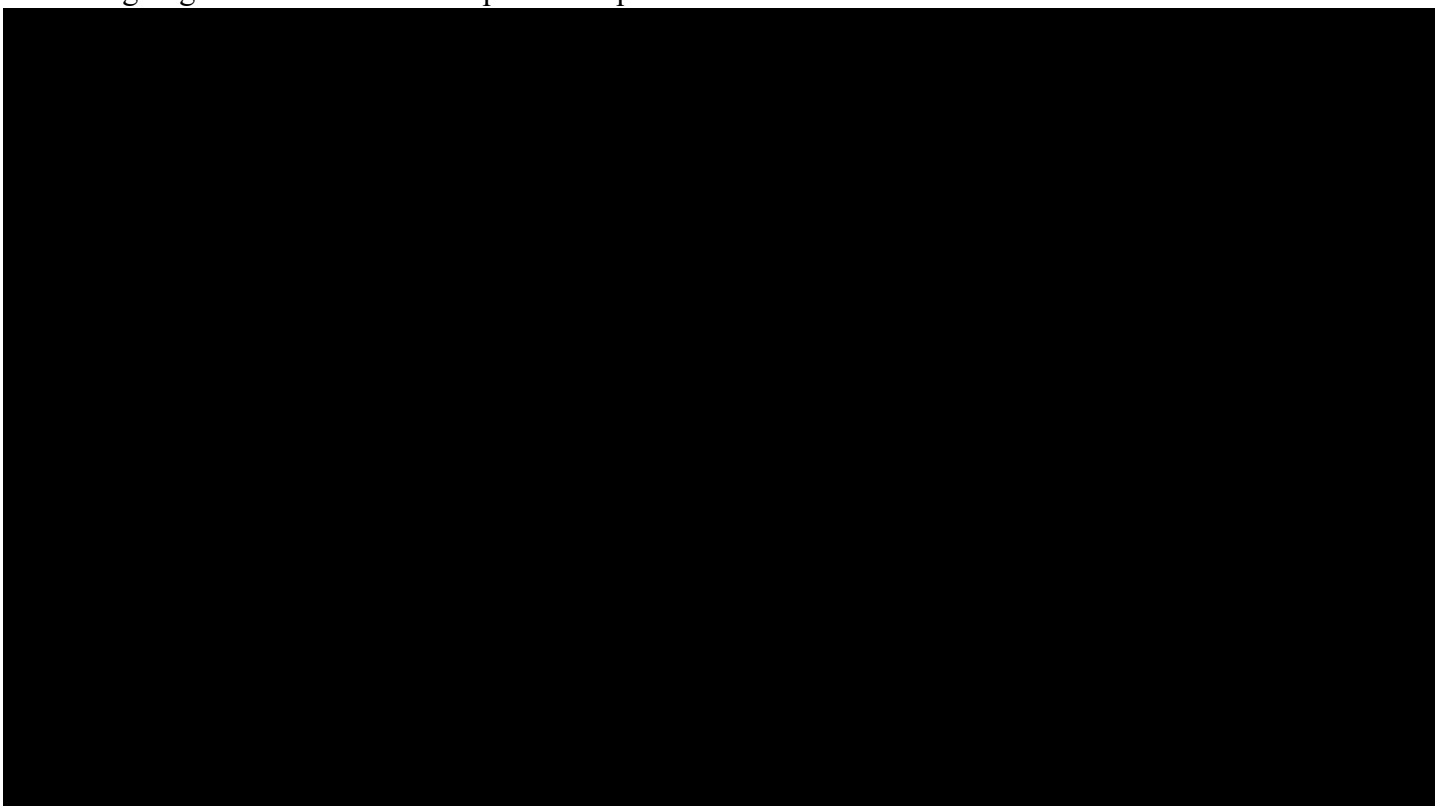
The safety endpoints are:

- All adverse events (ocular and non-ocular, serious and non-serious)
- SSI
- Device Deficiencies
- IOL observations
- IOL position change (tilt and decentration)

- PCO
- Posterior capsulotomy
- Surgical problems
- Other surgical procedures
- Slit lamp examination
- Dilated fundus examination
- IOP

There are no safety hypotheses for this study. 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 category, and % in each category. For continuous variables, number of subjects/eyes, mean, median, standard deviation, minimum, and maximum will be reported.

All adverse events occurring from the time a subject sign informed consent 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 informed consent but prior to exposure to IP.



[redacted]

# 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 dispensing 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 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 well-being 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 email correspondence. Close-out visits will take place after the last visit of the last subject at the site.

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

## 13.5 Regulatory Documentation and Records Retention

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

Additionally, the investigator must keep study records and source documents consistent with the terms of the clinical study agreement with the study sponsor. If the investigator retires, relocates, or for any other reason withdraws from responsibility of keeping the study records, then the study sponsor must be notified, and suitable arrangements made for retention of study records and source documents needed to comply with national and international regulations.

## 13.6 Quality Assurance and Quality Control

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

# 14 ETHICS

Investigations are conducted in compliance with Good Clinical Practices; international and national regulations, laws and guidelines; the conditions of approval imposed by reviewing

IRBs/IECs or regulatory authorities; and in accordance with the ethical medical research principles outlined in the Declaration of Helsinki.

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

The investigator must ensure that all personnel involved in the conduct of the study are qualified to perform their assigned responsibilities through relevant education, training, and experience. The investigator and all clinical study staff must conduct the clinical study in compliance with the protocol. The investigator is not allowed to deviate from the protocol except to protect the rights, safety, and well-being of human subjects under emergency circumstances. Emergency deviations may proceed without prior approval of the sponsor and the IRB/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 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, if appropriate. 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 and/or legal representative, as applicable. The obtaining of consent shall be documented before any procedure specific to the clinical investigation is applied to the subject.

The investigator must have a defined process for obtaining the required consent. Specifically, the investigator, or their delegate, must explain the clinical study to each potential subject and the subject must indicate voluntary consent by signing and dating the approved informed consent form. The subject must be provided an opportunity to ask questions of the investigator, and if required by local regulation, other qualified personnel. The investigator must provide the subject with a copy of the consent form written in a language the subject understands. The consent document must meet all applicable local laws and provide subjects with information regarding the purpose, procedures, requirements, and restrictions of the study, along with any known risks and potential benefits associated with the IP and the study, the available compensation, and the established provisions for maintaining confidentiality of personal, protected health information. Subjects will be told about the voluntary nature of participation in the study and must be provided with contact information for the appropriate individuals should questions or concerns arise during the study. The subject also must be told that their records may be accessed by appropriate authorities and sponsor-designated personnel. The investigator must keep the original, signed copy of the consent (file in subject's medical records) and must provide a duplicate copy to each subject according to local regulations.

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

# 15 REFERENCES

1. AcrySof IQ Vivity IOL DFU
2. Clareon Toric DFU
3. P190018 Physician Labelling (fda.gov)
   https://www.accessdata.fda.gov/cdrh_docs/pdf19/P190018C.pdf
4. Tecnis Eyhance Toric II DFU:
   https://www.jnjvisionpro.com/sites/us/files/public/surgical/IOLs/tecnis_eyhance_toric_ii_iol_dfu_final.pdf
5. Tecnis Eyhance with Simplicity DFU:
   https://www.jnjvisionpro.com/sites/us/files/public/surgical/IOLs/z311524e_a_tecnis_eyhance_iol_with_tecnis_simplicity_delivery_system_us_dfu.pdf

## 15.1 Regulations and Standards

- ISO 14155:2011 Clinical investigation of medical devices for human subjects - Good clinical practice
- ANSI Z80.30-2018 American National Standard for Ophthalmics - Toric Intraocular Lenses

## 15.2 Scientific and Other References

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