

# **Clinical Investigation of the Safety and Effectiveness of Monofocal PODEYE TORIC Intraocular Lens (IOL)**

**Protocol Number: PHY2302**

**IDE Sponsor: Beaver-Visitec International, Inc**

**Version Number: v.2.0**

**03 May 2024**

**Investigator Agreement:**

I have read the clinical study described herein, recognize its confidentiality and agree to conduct the described study in compliance with Good Clinical Practices, the ethical principles contained within the Declaration of Helsinki, this protocol and all applicable regulatory requirements.

Investigator

\_\_\_\_\_

Signature

Date

Investigator Name

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Investigator Address

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## Summary of changes

Document	Affected Sections(s)	Summary of Revisions made
[REDACTED]	[REDACTED]	I
[REDACTED]	[REDACTED] [REDACTED]	[REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED]

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## STATEMENT OF COMPLIANCE

This study will be conducted in compliance with the protocol, IRB requirements, FDA Title 21 CFR 812, FDA/ICH GCP, and consistent with the Declaration of Helsinki.

In addition, all applicable local, state, and federal requirements relevant to the use of study devices in the US will be adhered to.

## 1 PROTOCOL SUMMARY

### 1.1 SYNOPSIS

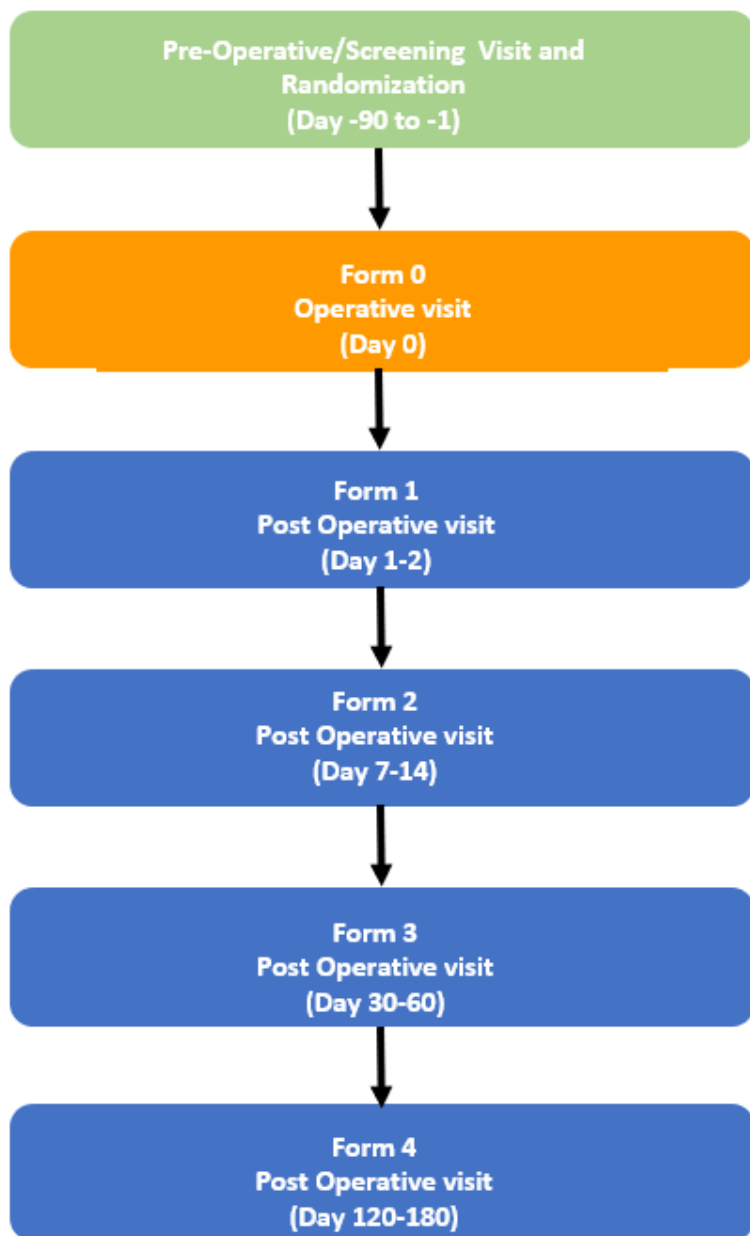
<b>Title</b>	Clinical investigation of the safety and effectiveness of Monofocal PODEYE TORIC Intraocular Lens (IOL)
<b>Study Description</b>	This study is a prospective, multicenter, randomized, double masked trial comparing an investigational Monofocal Toric intraocular lens (IOL) (PODEYE TORIC CYL 1.5 D) and a commercially available non-toric monofocal IOL (Alcon AcrySof SA60AT).
<b>Study Objective</b>	The purpose of this clinical trial is to evaluate the safety and effectiveness of Monofocal PODEYE TORIC Intraocular Lens (IOL)
<b>Endpoints</b>	<p><b>Co-Primary Effectiveness Endpoints</b></p> <p>[REDACTED]</p> <p>4. [REDACTED]</p> <p><b>Co-Primary Effectiveness Endpoint Targets</b></p> <ol style="list-style-type: none"><li>1. Statistically significant smaller residual manifest cylinder in toric arm than in control arm.</li><li>2. 90% of eyes at target.</li><li>3. 95% of eyes at target.</li><li>4. 90% of eyes at target per the ANSI Z80.30 rotation criteria.</li></ol> <p><b>Co-Primary Safety Endpoints</b></p> <ol style="list-style-type: none"><li>1. Cumulative rate of secondary surgical interventions (SSIs) related to the optical properties of the IOL at Form 4, including IOL rotation SSIs for misalignment.</li><li>2. Rates of cumulative and persistent AEs at Form 4 via comparison to the ISO Safety and Performance Endpoint (SPE) rates as described in ISO 11979-7.</li><li>3. BCDVA logMAR of 0.3 or better is not less than ISO 11979-7:2018 tables E.3 and E4 (toric IOL arm only) at Form 4.</li></ol>

<b>Statistical Analysis and Sample Size Calculation</b>	<p>Hypothesis tests for co-primary effectiveness endpoints 1 through 4 must reject their associated null hypotheses in order to claim the effectiveness of the PODEYE TORIC IOL. No multiplicity adjustment of the significance level (i.e., Type I error probability) is performed.</p> <p>[REDACTED]</p> <p>[REDACTED]</p> <p>Based on individual power calculations for each co-primary endpoints 1 through 4, up to 300 eyes enrolled, with 230 eyes randomized to the two IOL groups using a randomization ratio of 1:1 is sufficient for the four hypotheses associated with co-primary endpoints to reject their respective null hypotheses.</p>
<b>Study Population</b>	<p>The subject population will consist of subjects with cataract and pre-existing corneal astigmatism in at least one eye with no other ocular comorbidity and planned for routine cataract surgery.</p>
<b>Phase</b>	<p>Pivotal</p>
<b>Description of Sites/Facilities Enrolling Participants</b>	<p>Subjects will be enrolled at up to approximately 10 study sites and surgeries will be performed in ambulatory surgery centers or hospitals. All study sites and surgery centers will be located in the United States. Each site will be encouraged to randomize a minimum of 20 subjects, and no site will randomize more than 25% of the total number of randomized subjects.</p>
<b>Description of Study Intervention</b>	<p>The study intervention is an IOL to be implanted unilaterally via routine small incision cataract surgery. Subject eyes in the test arm will be implanted with an investigational Toric Monofocal IOL with toricity of 1.5 D (in the IOL plane), while the eyes in the control arm will be implanted with a commercially available monofocal non-toric IOL. IOLs are implantable medical devices intended for long term use over the lifetime of the subject.</p>
<b>Study Duration</b>	<p>Study duration is estimated to be approximately 20 months based on an estimated enrollment period of 8 months, subject participation period of 9 months (calculated as the maximum difference between the time of the Preoperative Visit to completion of Form 4), and 3 months for study close-out, database-lock and Investigative report.</p>

<b>Participant Duration</b>	It is estimated that the duration of each subject's participation in the study will be approximately 9 months (calculated as the difference between the time of the Preoperative Visit to completion of Form 4).
<b>Inclusion Criteria</b>	<ul style="list-style-type: none"> <li>• Male or female adults, age 22 years or older at the Preoperative Visit.</li> <li>• Clinically significant cataract in the study eye eligible for standard phacoemulsification cataract surgery.</li> <li>• Eligible for receipt of an IOL power within the range of the investigational IOL in the study eye. <b>(The Investigational IOL is available in powers from +15 D to +30 D Spherical Equivalent)</b></li> <li>• Pre-operative corneal astigmatism in the range: <math>\geq 0.75</math> D and <math>\leq 1.50</math> D in the study eye</li> </ul> <div style="background-color: black; height: 20px; width: 100%;"></div> <ul style="list-style-type: none"> <li>• Clear intraocular media other than cataract in the study eye.</li> <li>• Best corrected visual acuity equal to or worse than 0.3 logMAR, with or without a glare source in the study eye.</li> <li>• Ability to dilate pupil sufficiently (greater than or equal to 6.0 mm) to allow visualization of Toric IOL axis markings post-implantation in the study eye.</li> <li>• Projected BCDVA of 0.2 logMAR (20/32 Snellen) or better in the study eye after cataract surgery/IOL implantation, as determined by the medical judgment of the Investigator.</li> <li>• Contact lens users must be willing to discontinue wear of their lenses in the study eye in accordance with the following requirements: <ul style="list-style-type: none"> <li>• Rigid gas permeable and toric lenses for <math>\geq 7</math> days prior to the Preoperative Visit</li> <li>• Soft non-toric contact lenses for <math>\geq 3</math> days prior to the Preoperative Visit</li> <li>• All contact lens wearers must demonstrate a stable refraction within <math>\pm 0.50</math> D MRSE and 15 degrees astigmatic axis, on two consecutive examinations at least 1 week apart in an eye to be treated.</li> </ul> </li> <li>• Provide signed written consent prior to participation in any study-related procedures.</li> <li>• Ability, comprehension, and willingness to follow study instructions, and to complete all study visits.</li> <li>• Female subjects must be 1-year postmenopausal, surgically sterilized, or, if of childbearing potential, have a negative urine pregnancy test at the Preoperative Visit. Women of childbearing potential must use an acceptable form of contraception throughout the study. Acceptable methods include at least one of the following: intrauterine (intrauterine device), hormonal (oral, injection, patch, implant, ring), barrier with spermicide (condom, diaphragm), or abstinence.</li> </ul>

<p><b>Exclusion criteria</b></p>	<ul style="list-style-type: none"> <li>• Subjects with irregular corneal astigmatism in the study eye</li> <li>• Subjects with clinically significant corneal pathology potentially affecting corneal topography in the study eye.</li> <li>• Subjects with a traumatic cataract in the study eye.</li> <li>• Subjects with uncontrolled glaucoma in the study eye.</li> <li>• Subjects with diagnosed degenerative visual disorders (e.g., macular degeneration or other retinal disorders) that are predicted to cause future acuity losses to a level of 0.2 logMAR or worse in the study eye.</li> <li>• Subjects with conditions associated with increased risk of zonular rupture during the cataract extraction procedure which may affect the postoperative centration or tilt of the lens in the study eye.</li> <li>• Significant anterior segment pathology that might increase intraoperative risk or compromise IOL stability (e.g., pseudoexfoliation syndrome) in the study eye.</li> <li>• Reasonably expected to require secondary ocular surgical intervention or laser treatment other than YAG capsulotomy in study eye during the study participation period.</li> <li>• Presence of one or more clinically significant corneal abnormalities in study eye, including corneal dystrophy, irregularity, or edema.</li> <li>• Previous intraocular, corneal, or retinal detachment surgery, including corneal transplant, LASIK, astigmatic keratotomy and limbal relaxing incisions in the study eye.</li> <li>• Clinically significant ocular inflammation or infection present <math>\leq 30</math> days in either eye prior to the Preoperative Visit.</li> <li>• Subjects with potential BCDVA of 20/200 or worse in the fellow eye.</li> <li>• Subjects with a difference of greater than 0.50 D of corneal astigmatism as measured with the IOL master/Lenstar/Argos and the topographer in the study eye using vector analysis.</li> <li>• Presence or history of one or more severe/serious ocular conditions (e.g., glaucoma, uveitis, ocular infection, severe dry eye) in the study eye, or any other unstable medical condition (e.g., uncontrolled diabetes) that in the opinion of the Investigator would put the subject's health at risk, confound the results of the study and/or prevent the subject from completing all study visits.</li> <li>• Use of medications known to interfere with visual performance, pupil dilation, or iris structure <math>\leq 30</math> days prior to the Preoperative Visit.</li> <li>• Participation in any study of an investigational, interventional product within 30 days prior to the Preoperative Visit or at any time during the study period.</li> <li>• Pregnant or nursing females.</li> </ul>
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## 1.2 SCHEMA



### 1.3 SCHEDULE OF ACTIVITIES (SOA)

Examination		Pre-operative/Screening Visit	Form 0	Form 1	Form 2	Form 3	Form 4	USV <sup>1</sup>
Informed Consent and HIPAA		X						
Demographics		X						
Inclusion & Exclusion Criteria Evaluation		X						
Inclusion & Exclusion Criteria Review			X					
Ocular and non-ocular Medical History		X						
Urine Pregnancy Test (if applicable)		X						
Projected Visual Acuity		X						
Target Refraction		X						
IOL power calculation		X						
Axial Length and Anterior Chamber Depth		X						
Keratometry measurement		X				X	X	X
PhysIOL Toric Calculator		X						
Corneal Topography		X						
Manifest Refraction (ETDRS)-4 meters		X			X	X	X	X
Randomization		X						
Operative Procedures			X					
Intraocular Pressure		X		X	X	X	X	X
Slit Lamp Examination		X		X	X	X	X	X
IOL Tilt and Decentration Grading				X	X	X	X	X
IOL Axis Orientation <sup>2</sup>			X	X	X	X	X	X
Dilated pupil size		X						
Dilated Fundus Examination		X				X	X	X
IOL Observations				X	X	X	X	X
Adverse Events		X	X	X	X	X	X	X
Device Deficiencies			X	X	X	X	X	X
Concomitant Medications		X	X	X	X	X	X	X
Exit from Study							X	
Visual Acuity	UCDVA	X		X	X	X	X	X
	BCDVA	X			X	X	X	X

<sup>1</sup>USV- Unscheduled Visit; specific assessments to be completed may be determined by the investigator as appropriate based on the subject's condition. Recommended assessments for Investigator consideration are denoted in the table.

<sup>2</sup>Subjects must be dilated for IOL axis of orientation assessment.

## 1.4 ABBREVIATIONS

ADE	Adverse device effect
AE	Adverse event
ANSI	American National Standards Institute
BCDVA	Best corrected distance visual acuity
CFR	Code of Federal Regulations
CME	Cystoid macular edema
CRF	Case report form
DFU	Directions for Use
eCRF	Electronic case report form
ETDRS	Early Treatment Diabetic Retinopathy Study
FDA	Food and Drug Administration
FLACS	Femto Laser-Assisted Cataract Surgery
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed consent form
ICH	International Conference on Harmonization
IOL	Intraocular lens
IOP	Intraocular pressure
IP	Investigational Product
IRB	Institutional/Independent Review Board
ISO	International Organization for Standardization
ITT	Intent to Treat
logMAR	Logarithm of the Minimum Angle of Resolution
MOP	Manual of procedures
OCT	Optical coherence tomography
PCO	Posterior capsule opacification
PP	Per Protocol
RD	Retinal detachment
SA	Spherical Aberration
SAE	Serious adverse event
SOA	Schedule of activities
SPE	Safety and Performance Endpoints
SSI	Secondary surgical intervention
TASS	Toxic anterior segment syndrome
UADE	Unanticipated Adverse Device Effect
UCDVA	Uncorrected distance visual acuity
USV	Unscheduled visit
VA	Visual Acuity

## 2 INTRODUCTION

### 2.1 STUDY RATIONALE

The purpose of this clinical study is to evaluate the safety and effectiveness of the PODEYE TORIC IOL.

### 2.2 BACKGROUND

Cataract is a common condition in adults over 40 years of age, and surgical replacement of the cataractous lens with an intraocular lens (IOL) remains an effective way to restore vision to cataract patients. Some of the cataract patients may have pre-existing corneal astigmatism which contributes to blurred vision. Monofocal non-toric IOLs provide adequate distance vision but do not address astigmatism which can adversely affect the quality of vision. The PODEYE TORIC IOL is designed to optically correct corneal astigmatism and restore distance vision after cataract surgery.

### 2.3 RISK/BENEFIT ASSESSMENT

#### 2.3.1 KNOWN POTENTIAL RISKS

Potential complications accompanying cataract or IOL implant surgery may include the following:

1. Ocular infection (endophthalmitis, microbial keratitis)
2. Inflammatory reaction [e.g., uveitis, Toxic anterior segment syndrome (TASS), hypopyon]
3. Anterior capsular contraction syndrome (ACCS) (phimosis)
4. Corneal edema
5. Corneal endothelial damage
6. Cystoid macular edema (CME)
7. Secondary surgical intervention (including, but not limited to, lens repositioning, lens replacement, vitreous aspiration, iridectomy for pupillary block, wound leak repair, and retinal detachment repair)
8. IOL dislocation, tilt, decentration, luxation, rotation
9. Elevated intraocular pressure
10. Pupillary block
11. Posterior capsular opacification (PCO)
12. Chromatic aberrations
13. Dysphotopsia
14. Loss of visual acuity
15. Deviation from target refraction
16. Hyphema
17. Retinal detachment
18. Iris or pupil damage
19. Posterior capsular rupture
20. Vitreous loss
21. Wound leak (positive Seidel)

In addition to these risks associated with cataract surgery and IOLs in general, misalignment of the axis of toric IOLs may compromise its astigmatic correction. Such misalignment can result from inaccurate keratometry or marking of the cornea, inaccurate placement of the toric IOL axis during surgery, an unanticipated surgically induced change in the cornea, or physical rotation of the toric IOL after implantation.

### 2.3.2 POTENTIAL BENEFITS

The possible benefits associated with this study are:

- Improvement in visual acuity
- Astigmatism reduction
- Furthering the understanding of vision care

### 2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

Based on a formal risk assessment, the benefit to risk profile is favorable as the benefits of improved vision outweigh the risks of cataract surgery and implantation of a Toric IOL.

## 3 OBJECTIVES AND ENDPOINTS

### 3.1 PRIMARY OBJECTIVES

The objectives are based on ANSI Z80.30 (2018) and ISO 11979-7 (2018).

#### Co-Primary Effectiveness Endpoints

1. [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]

With performance goals of:

1. Statistically significant smaller residual manifest cylinder, of 0.4D or greater, in toric arm than in control arm.
2. 90% of eyes at target
3. 95% of eyes at target
4. 90% of eyes at target

#### Co-primary Safety Endpoints

1. Characterize the cumulative rate of SSIs related to the optical properties of the IOL at Form 4, including IOL rotation SSIs for misalignment.
2. Rates of cumulative and persistent AEs at Form 4 via comparison to the ISO Safety and Performance Endpoint (SPE) rates as described in ISO 11979-7.
3. BCVA logMAR of 0.3 or better at Form 4 for all-implanted and best-case test eyes.

**Additional Safety endpoints**

The incidence of all adverse events other than those listed in ISO 11979-7 (2018) tables E.3 and E.4.

**4 STUDY DESIGN****4.1 OVERALL DESIGN**

This study is a prospective, multicenter, randomized, active controlled, double masked pivotal study to demonstrate the effectiveness and safety of a monofocal toric IOL, PODEYE TORIC. The control IOL will be a commercially available monofocal non-toric IOL, AcrySof SA60AT (Alcon). The study will include adult subjects with operable cataract in at least one eye along with pre-existing corneal astigmatism who are eligible for phacoemulsification cataract surgery followed by IOL implantation. Potential subjects, after signature of the study informed consent document, will be screened for eligibility, except that assessments which are part of the Investigator's routine standard of care for cataract patients may be performed prior to obtaining informed consent. Only one eye per patient will be included in the study. In cases where a subject has significant cataracts and plans to undergo cataract surgery in both eyes, it is recommended that cataract surgery is performed in one eye prior to the subject being enrolled in the study. Once a subject has been enrolled, it is recommended that the fellow eye does not undergo cataract surgery (except for a YAG capsulotomy) throughout the duration of the study. At screening, if both eyes qualify for the study, the eye to undergo cataract surgery and IOL implantation should be the eye with worse pre-operative BCDVA. If pre-operative BCDVA is the same for each eye, the right eye will be the study eye. Subjects who meet all protocol-specified eligibility criteria will be randomized at a 1:1 ratio to receive either the PODEYE TORIC CYL 1.5 D IOL (test) or the AcrySof SA60AT IOL (control) in the study eye. Only unilateral implantation of either Test or Control IOL will be performed. Subjects will attend regular visits where they will undergo ophthalmic examinations over a period of approximately 6 months.

No interim analysis of data is planned.

Up to 300 subjects shall be screened and approximately 230 subjects will be randomized and implanted, allowing [REDACTED]. A drop-out rate of [REDACTED] is expected after the subjects have been implanted with the test/control IOL.

Standard clinical trial methods will be used to minimize bias, including the use of masked vision assessors, masking of subjects, use of standardized test procedures, common investigator training, and common inclusion and exclusion criteria.

## 4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

The purpose of this clinical study is to compare the visual outcomes and safety of the PODEYE TORIC IOL to that of the AcrySof monofocal non-toric IOL Model SA60AT. The study is designed to meet the requirements specified for Toric IOLs in ANSI Z80.30: 2018 standard.

## 4.3 END OF STUDY DEFINITION

The end of the study is defined as completion of the last procedure specified for the last visit as shown in the Schedule of Activities (SOA), Section 1.3, by all subjects who did not terminate study participation early.

Subjects will be considered to have completed the study if they did not terminate study participation prior to completion of visual acuity, IOL rotation, and safety assessments at the 6-month study visit (Form 4).

## 5 STUDY POPULATION

The study population consists of subjects with a diagnosis of cataract with pre-existing corneal astigmatism, eligible for phacoemulsification surgery followed by IOL implantation.

Subjects will be enrolled at up to 10 investigational sites. Investigators will be encouraged to perform cataract surgery/IOL implant for at least 20 subjects per site; no Investigator may implant more than 25% of the total number of subjects planned. Site enrollment will be closely monitored to facilitate achievement of the stated enrollment goals and an even distribution across all sites.

### 5.1 INCLUSION CRITERIA

Eligible subjects must meet all the following inclusion criteria to be eligible for study participation:

1. Male or female adults, age 22 years or older at the Preoperative Visit.
2. Clinically significant cataract in the study eye eligible for standard phacoemulsification cataract surgery.
3. Eligible for receipt of an IOL power within the range of the investigational IOL in the study eye. **(The Investigational IOL is available in powers from +15 D to +30 D Spherical Equivalent)**
4. Pre-operative corneal astigmatism in the range:  $\geq 0.75$  D and  $\leq 1.50$  D in the study eye
6. Clear intraocular media other than cataract in the study eye.
7. Best corrected visual acuity equal to or worse than 0.3 logMAR, with or without a glare source in the study eye.
8. Ability to dilate pupil sufficiently (greater than or equal to 6.0 mm) to allow visualization of Toric IOL axis markings post-implantation in the study eye.
9. Projected BCDVA of 0.2 logMAR (20/32 Snellen) or better in the study eye after cataract surgery/IOL implantation, as determined by the medical judgment of the Investigator.

10. Contact lens users must be willing to discontinue wear of their lenses in the study eye in accordance with the following requirements:
  - i. Rigid gas permeable and toric lenses for  $\geq 7$  days prior to the Preoperative Visit
  - ii. Soft non-toric contact lenses for  $\geq 3$  days prior to the Preoperative Visit
  - iii. All contact lens wearers must demonstrate a stable refraction within  $\pm 0.50$  D MRSE and 15 degrees astigmatic axis on two consecutive examinations at least 1 week apart in an eye to be treated.
11. Provide signed written consent prior to participation in any study-related procedures.
12. Ability, comprehension, and willingness to follow study instructions, and to complete all study visits.
13. Female subjects must be 1-year postmenopausal, surgically sterilized, or, if of childbearing potential, have a negative urine pregnancy test at the Preoperative Visit. Women of childbearing potential must use an acceptable form of contraception throughout the study. Acceptable methods include at least one of the following: intrauterine (intrauterine device), hormonal (oral, injection, patch, implant, ring), barrier with spermicide (condom, diaphragm), or abstinence.

## 5.2 EXCLUSION CRITERIA

Subjects with any of the following diseases, surgeries or conditions are ineligible for study participation.

1. Subjects with irregular corneal astigmatism in the study eye (Note: corneal incisions intended to reduce astigmatism are not permitted)
2. Subjects with clinically significant corneal pathology potentially affecting corneal topography in the study eye.
3. Subjects with a traumatic cataract in the study eye.
4. Subjects with uncontrolled glaucoma in the study eye.
5. Subjects with diagnosed degenerative visual disorders (e.g., macular degeneration or other retinal disorders) that are predicted to cause future acuity losses to a level of 0.2 logMAR or worse in the study eye.
6. Subjects with conditions associated with increased risk of zonular rupture during the cataract extraction procedure which may affect the postoperative centration or tilt of the lens in the study eye.
7. Significant anterior segment pathology that might increase intraoperative risk or compromise IOL stability (e.g., pseudoexfoliation syndrome) in the study eye.
8. Reasonably expected to require secondary ocular surgical intervention or laser treatment other than YAG capsulotomy in study eye during the study participation period.
9. Presence of one or more clinically significant corneal abnormalities in study eye, including corneal dystrophy, irregularity, or edema.
10. Previous intraocular, corneal, or retinal detachment surgery, including corneal transplant, LASIK, astigmatic keratotomy and limbal relaxing incisions in the study eye.
11. Clinically significant ocular inflammation or infection present  $\leq 30$  days in either eye prior to the Preoperative Visit.
12. Subjects with potential BCDVA of 20/200 or worse in the fellow eye.

13. Subjects with a difference of greater than 0.50 D of corneal astigmatism as measured with the IOL master/Lenstar/Argos and the topographer in the study eye using vector analysis.
14. Presence or history of one or more severe/serious ocular conditions (e.g., glaucoma, uveitis, ocular infection, severe dry eye) in the study eye, or any other unstable medical condition (e.g., uncontrolled diabetes) that in the opinion of the Investigator would put the subject's health at risk, confound the results of the study and/or prevent the subject from completing all study visits.
15. Use of medications known to interfere with visual performance, pupil dilation, or iris structure  $\leq$  30 days prior to the Preoperative Visit.
16. Participation in any study of an investigational, interventional product within 30 days prior to the Preoperative Visit or at any time during the study period.
17. Pregnant or nursing females.

### 5.3 REASONS NOT TO IMPLANT A STUDY IOL

At the time of cataract surgery, but prior to IOL implantation there are intraoperative adverse events that may prevent implantation of the designated IOLs for this clinical study. These criteria include, but are not limited to:

- 1) Intraoperative complications during phacoemulsification that require any other additional procedures or further intervention, e.g., vitrectomy.
- 2) Significant detachment of Descemet's membrane
- 3) Significant corneal endothelial damage
- 4) Wound burn
- 5) Capsular tear, iris incarceration or damage, posterior capsular rupture, vitreous loss or prolapse, or zonular weakness, dehiscence or rupture
- 6) Significant anterior chamber bleeding
- 7) Excessive iris mobility or need for iris manipulation
- 8) Mechanical or surgical manipulation required to enlarge the pupil prior to or at IOL implantation
- 9) Other ocular conditions or complications that could compromise IOL stability
- 10) Bag sulcus, sulcus-sulcus or unknown placement of haptics
- 11) Any method of anterior capsulotomy other than circular continuous curvilinear capsulorhexis (e.g., anterior capsular tears or any areas of 'can-opener' capsulotomy or FLACS)
- 12) Capsular fibrosis or other opacity
- 13) Optic and/or haptic damage/amputation
- 14) Inability to fixate IOL in desired position

If an operative adverse event prevents implantation of the investigational IOL and the IOL did not touch the eye, the subject should be implanted with an approved non-study IOL instead and followed until resolution or stability of that adverse event before discontinuation from the study. Later, the subject should be followed under the Investigator's normal standard of care.

If an operative adverse event prevents implantation of the investigational IOL and the IOL touched the eye, the subject should be implanted with an approved non-study IOL (if applicable). The Investigator should follow the subject through resolution of any adverse events (AEs) and then discontinue the

subject, followed under the Investigator's normal standard of care. In this case, the subject will be included in the Safety population.

#### 5.4 SCREEN FAILURES

An enrolled subject who fails to meet eligibility criteria and/or discontinues from the study before the randomization will be considered a screen failure and exited from the study.

A subject who has failed screening will not be allowed to be rescreened.

#### 5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

Study participants will be recruited from the investigator's patient population, referrals, or other outreach methods. Written recruitment materials directed to potential study participants must be approved by the overseeing IRB.

Where possible, candidate participants may be pre-screened via review of their medical charts to evaluate potential eligibility based on study inclusion/exclusion criteria. During the informed consent discussion, the potential participant's willingness and ability to meet the follow-up requirements will be evaluated. Those who elect to sign the study informed consent form (ICF) will be considered enrolled in the study and given a study identification code. At/after the time of enrollment, the subject will be evaluated at the Preoperative Visit for study eligibility based on inclusion/exclusion requirements.

Study site personnel should take the following steps to minimize the likelihood of early termination during the study:

- During the Preoperative Visit, emphasize the importance of returning for all study follow-up visits and thoroughly evaluate the study subject for potential health or motivational issues or other life circumstances that may negatively affect compliance with the study follow-up visit schedule.
- Evaluate research staff flexibility to work around personal difficulties encountered by the subject related to protocol compliance (e.g., appointment times).
- Schedule subject follow-up visits early in the visit window to facilitate rescheduling within the window, if necessary.
- Follow-up on subjects who do not return for scheduled examinations.

### 6 STUDY INTERVENTION

#### 6.1 STUDY DEVICES

##### 6.1.1 INVESTIGATIONAL DEVICE DESCRIPTION

PODEYE TORIC IOL is a posterior chamber intraocular lens intended for primary implantation in the capsular bag of the eye for visual correction of aphakia after removal of a cataractous lens in adult patients with pre-existing corneal astigmatism. The refractive power of the lens has a spherical and a cylindrical component to allow for the compensation of pre-existing corneal astigmatism. The single-piece IOL has a double-C-loop haptic design with ridge technology on the haptics to prevent sticking of the haptics to the optic. A sketch of the IOL is depicted in Figure 1 and the main specifications are summarized in Table 1.



Figure 1: PODEYE TORIC IOL

**Table 1: PODEYE TORIC specifications**

Designation	Technical Specifications
Material	Hydrophobic acrylic
Optical diameter	6.00 mm
Total diameter	11.40 mm
Optic	Biconvex aspheric aberration-correcting (-0.11 $\mu$ SA)
Haptic design	Double C-loop
Filtration	UV & Blue light
Refractive index	1.53
Abbe number	42
Angulation	5°
Spherical power	From +15.0 D to +30.0 D in 0.50 D steps
Cylindrical power (IOL plane)	1.5 D
Cylindrical power (Corneal plane)	1.03 D
Recommended corneal astigmatism correction range (based on pre-operative Keratometry values excluding SIA)	0.75-1.50 D

## **Optical Design**

PODEYE TORIC IOL is an aspheric monofocal toric IOL which provides patients with distance vision and corneal astigmatism correction. The front surface is aspherical to yield an optic with a spherical aberration of -0.11 micrometers at 5.0 mm aperture to partially compensate the positive spherical aberration of the cornea and to achieve a high contrast sensitivity of the pseudophakic eye. The cylinder correction is located on the posterior surface. The IOL displays 2 series of three physical indicators (dots, see Figure 1) visible to the surgeon during implantation, which align with the meridian of lowest dioptric power (flattest meridian).

The injector to be used for PODEYE TORIC IOL over the course of the study is [REDACTED]

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### **6.1.2 CONTROL DEVICE DESCRIPTION**

AcrySof SA60AT Monofocal IOL from Alcon (Fort Worth, TX) is a non toric, hydrophobic, ultraviolet filtering, foldable monofocal IOL with biconvex single-piece design comprised of a central optic and 2 open-loop haptics. The optic is 6.0 mm in diameter and the lens has a total diameter of 13.0mm. The lenses will be available in powers +15.0 D to +30.0 D in 0.50 D increments.

## **6.2 DEVICE ACCOUNTABILITY AND STORAGE**

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### **6.2.1 ACQUISITION AND ACCOUNTABILITY**

Throughout the clinical study, the Investigator will be responsible for the accounting of all test and control IOLs and will ensure that the investigational products are used in accordance with the manufacturer's manual of procedures (MOP) and directions for use (DFU).

Upon receipt of the investigational product (IP), PODEYE TORIC IOL, shipment records will be verified by comparing the Shipping Receipt Confirmation to the devices actually received at the site. If a discrepancy is noted, the Sponsor or designee must be notified immediately. Accurate records of receipt and disposition (dispensing log) of the study devices (e.g., dates, subject number) must be maintained by the Investigator or authorized site representative.

Throughout the study, the Investigator must maintain records of IP dispensed and implanted for each subject. All IP sent to the Investigator must be accounted for and in no case be used in an unauthorized manner.

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

The control IOLs (AcrySof SA60AT) shall be procured by the Investigator from the corresponding manufacturer (Alcon).

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### **6.2.2 PACKAGING AND LABELING**

The PODEYE TORIC investigational lenses will be provided sterile in blisters and labeled with the lens ID, lot number, expiry date. Each IOL will bear a sticker with the following statement: 'CAUTION-- Investigational device. Limited by Federal (or United States) law to investigational use.'

The AcrySof SA60AT Monofocal IOL control lenses will be provided sterile in blisters and labeled with the lot number and expiry date along with the standard manufacturer's packaging instructions.

To maintain product sterility and integrity, the study devices will be supplied in their original packaging and used according to the appropriate device instructions.

### 6.2.3 PRODUCT STORAGE AND STABILITY

Study devices should be stored in a secure area according to the package labels.

## 6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND MASKING

Subjects will be randomly assigned to receive either the investigational PODEYE TORIC CYL 1.5D IOL or the AcrySof monofocal non-toric IOL in the study eye according to the randomization schedule (1:1 ratio) provided. The randomization schedule will be computer-generated and programmed by an independent statistician who is not involved in the day-to-day conduct of the study. Randomization is to occur following the completion of informed consent and screening procedures. Randomization will be stratified by site.

To minimize bias, site personnel performing postoperative study assessments of visual performance, including manifest refraction and visual acuity, will be masked to subject treatment assignment until after the final database lock ("masked assessors"). Any unmasking of the masked assessor or any study subjects must be reported to the Sponsor. Every attempt should be made to have the same masked assessor perform the same postoperative measurements for an individual subject throughout the subject's study participation.

Subjects will also be masked to their assigned treatment group (test or control group). Any material that may indicate the subjects' assigned treatment (e.g., packaging, documents) will be removed from areas where subjects and/or masked personnel may see it. Unmasked personnel should further be instructed to avoid conversation and communication with masked personnel, subjects, and persons other than the study investigator regarding subjects' assignments, outcomes, clinical courses and all other information potentially relevant to the study and its conduct.

## 7 PARTICIPANT DISCONTINUATION/ WITHDRAWAL

### 7.1 PARTICIPANT DISCONTINUATION/ WITHDRAWAL FROM THE STUDY

Discontinued subjects are those who withdraw from the study after the study informed consent document is signed and before the final visit is completed. Subjects who sign the study consent document but fail to meet eligibility criteria or withdraw prior to randomization shall be considered discontinued due to screen failure.

A subject may be discontinued prior to the final study visit for any of the following reasons, including but not limited to:

- Screen failure
- Adverse event(s); note that subjects should be followed within the study until adverse event resolution or stability

- Investigator's request (medical decision to ensure patient safety)
- Voluntary withdrawal (subject's request)
- Death
- Study terminated by Sponsor
- Loss to follow-up

Prior to discontinuing a subject, every effort should be made to contact the subject to schedule a final study visit and obtain as much follow-up data as possible. Discontinued subjects should thereafter be followed outside of the study protocol according to the Investigator's normal standard of care.

The reason for participant discontinuation or withdrawal from the study will be recorded on the Exit Case Report Form (CRF).

Randomized subjects who do not receive a study IOL or who receive a study IOL and are discontinued or withdraw from the study afterwards will not be replaced.

## 7.2 LOST TO FOLLOW-UP

The following actions must be taken if a participant fails to return to the clinic for a required study visit:

- The site will attempt to contact the participant by telephone, electronic, or regular mail to reschedule the missed visit. At least 3 documented attempts to contact the subject must be made. If the subject does not respond to these attempts, a certified letter must be sent to the participant's last known mailing address.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

These actions will be recorded in the source documents and a copy of the certified follow-up letter maintained in the source documents. The date of discontinuation for subjects lost to follow-up will be 7 calendar days after the date that the unanswered certified letter was sent.

## 8 STUDY ASSESSMENTS AND PROCEDURES

Study participants will be evaluated at a Preoperative Visit. The subjects who qualify for further study participation will be randomized to receive the assigned study IOL, and the cataract surgery/IOL implantation will be scheduled to occur between 1 and 90 days after the Preoperative visit. The subjects will be scheduled to return for follow-up visits and examinations at the Day 1-2, Week 1-2, Month 1-2, and Month 4-6 time periods, consistent with study visits described in ISO 11979-7 (Form 0 through Form 4). Data collected from each visit, including any abnormal findings, will be documented in the source records and recorded on study eCRFs.

The timing and type of assessments/procedures to be performed at each visit is outlined in the SOA. Methods for study examinations is presented in the Manual of Procedures.

### 8.1 PREOPERATIVE VISIT (DAY -90 TO DAY -1)

The Preoperative Visit must occur no more than 90 days and no less than 1 day prior to the Operative Visit. Informed consent must be obtained prior to performing study-specific procedures not part of the

investigator's routine standard of care. Subjects who sign the ICF will be given a unique 5-digit screening number, where the first two digits correspond to the site number.

At this visit, the following activities will be performed:

1. Biometry<sup>a</sup>
  - Keratometry\*
  - Target refraction\*
  - IOL power calculation\*
  - Axial length\*
  - Anterior chamber depth\*
  - Toric Power calculation
2. Corneal Topography\*
3. Inclusion/Exclusion Criteria Evaluation
4. Demographics
5. Concomitant Medications
6. Ocular and Significant Non-ocular Medical History\*
7. Urine Pregnancy Test (if applicable)
8. Manifest Refraction (ETDRS) – 4 m\*
9. BCDVA - Photopic, Monocular (ETDRS) – 4 m\*
10. UCDVA - Photopic, Monocular (ETDRS) – 4 m\*
11. Projected Visual Acuity\*
12. Slit lamp Examination\*
13. Intraocular Pressure\*
14. Dilated pupil size\*
15. Dilated Fundus Exam\*
16. Randomization
17. Adverse Events

*\* These assessments, if performed during routine standard of care exams up to 90 days before the subject Preoperative Visit, may be used as qualifying preoperative assessments prior to consent. All study specific evaluations not included in a routine cataract evaluation must be performed in the preoperative time period (Day -90 to Day -1).*

*<sup>a</sup> Biometry (if not done during routine standard of care exams), to be done before inclusion/exclusion criteria evaluation.*

Subjects must be targeted as closely as possible to emmetropia. **For PODEYE TORIC IOL, SRK/T formula and A-constant 119.4 should be used to determine IOL power.** Surgeons may use their personalized A-constant for model SA60AT.

The SIA value an investigator will use in this study must be a predetermined single value (each investigator may use their own personal SIA value) that is reported to the sponsor at the beginning of the study and consistently used for all subjects treated by the investigator.

The subjects will be randomized in 1:1 ratio to either Study arm or control arm, as per the randomization schedule.

## 8.2 OPERATIVE VISIT (DAY 0): FORM 0

At the Operative Visit, prior to surgery, subjects will be assessed to reconfirm eligibility and any changes in concomitant medications and medical/ocular conditions will be recorded on the appropriate CRF. If the subject is determined no longer to be eligible, he/she will be discontinued from the study prior to cataract surgery.

All cataract surgical procedures will be performed by a qualified Investigator according to the Investigator's usual standard of care, using a phacoemulsification system adjusted according to the Investigator's customary settings. Surgery may be performed under either local or topical anesthesia, with or without intracameral ophthalmic anesthesia. Subjects must be targeted as closely as possible for emmetropia. Surgeons may use their personalized A-constant for model SA60AT. For PODEYE TORIC, surgeons must use the SRK/T formula and an A-constant of 119.4. The Investigator must also reference the Directions for Use for the PODEYE TORIC IOL and AcrySof SA60AT Monofocal IOL.

[REDACTED] must be used to implant the PODEYE TORIC in accordance with [REDACTED]. A qualified delivery system should be used for the AcrySof SA60AT IOL, in accordance with the Alcon Directions for Use.

[REDACTED]

[REDACTED]

No additional refractive procedures are to be performed during the operative procedure or throughout the postoperative study period. Femtosecond laser-assisted cataract surgery (FLACS) must not be performed to create corneal incisions, to adjust astigmatism during the study period, or for any other reason. (Note: Corneal incisions intended to reduce corneal astigmatism (e.g., Limbal relaxing incisions and astigmatic keratotomy are not permitted)

If operative complications prevent implantation of the investigational Study IOL (PODEYE TORIC or Control IOL) (see Section 5.3 – Reasons Not to Implant a Study IOL), a non-study IOL may be implanted instead. Subjects who were not exposed to the study IOL will be exited from the study and followed per the investigator's standard of care.

The Investigator should refer to the Manual of Procedures for more detailed guidance on PODEYE TORIC and AcrySof SA60AT implantation.

After the operative procedure but at the same visit, IOL axis orientation retro-illuminated slit lamp images must be taken for the subjects implanted with PODEYE TORIC IOL. Refer to the Manual of Procedures for more guidance.

## 8.3 POSTOPERATIVE VISITS: FORM 1 THROUGH FORM 4

Postoperative visits should be scheduled according to the following visit window schedule:

- Form 1: 1-2 days after surgery on the study eye
- Form 2: 7-14 days after surgery on the study eye
- Form 3: 30-60 days after surgery on the study eye
- Form 4: 120-180 days after surgery on the study eye

Refer to the Schedule of Activities in Section 1.3 and the MOP for detailed procedures to be performed at these scheduled postoperative visits.

#### 8.4 UNSCHEDULED VISITS

Unscheduled visits are those which are not required by the study protocol, but which occur due to an ocular intervention or a subject complaint.

If a subject visit occurs between any regularly scheduled visits, this visit is to be documented as an Unscheduled Visit. During all unscheduled visits, the Investigator should conduct assessments as appropriate given the subject's condition. Recommended assessments include:

- Concomitant medication
- Manifest refraction
- BCDVA at 4 m- Photopic, Monocular (ETDRS) for study eye
- UCDVA at 4 m- Photopic, Monocular (ETDRS) for study eye
- Keratometry
- Slit lamp exam
- IOL observations
- IOL tilt and decentration grading
- Intraocular pressure (IOP)
- IOL Axis Orientation (retro-illuminated slit lamp photo in a **dilated** eye, only for subjects implanted with PODEYE TORIC IOL)
- Dilated Fundus Exam
- Adverse events
- Device deficiencies

The Investigator may perform additional procedures for proper diagnosis and treatment of the subject according to SOA in Section 1.3. The Investigator must document this information in the subject's source documents and record it on the USV eCRF.

If, during an Unscheduled Visit, the subject is discontinuing from the study, the Investigator must complete the Exit CRF.

Visits intended to fulfill scheduled visit requirements that fall outside the designated scheduled visit window are not Unscheduled Visits. In these cases, the visit data will be collected and transcribed to the appropriate scheduled visit CRF, and a protocol deviation should be reported, if applicable.

## 8.5 CONCOMITANT MEDICATION

Documentation of all medications used by the subject within 30 days of the Preoperative Visit and during the study will be entered in the Concomitant Medication CRF. Pre-, intra-, and postoperative medications may be administered per the Investigator's standard of care and documented in source documents only (not to be entered in CRFs). A complete list of the Investigator's standard regimen of these medications will be provided to the Sponsor or its designee and approved by the Medical Monitor prior to initiation of the study. Medications known to interfere with visual performance, pupil dilation, or iris structure are prohibited for the duration of the study. For more details on these medications, refer to the MOP.

## 8.6 SECONDARY SURGICAL INTERVENTION (SSI)

The study Investigator must assess the subject to determine if a secondary surgical intervention (SSI) is needed. This assessment should be based on the Investigator's assessment of the subject's clinical outcome, subject's feedback related to visual symptoms, and any other applicable reasons. The Investigator's assessment of the need for SSI should be based on a thorough examination including diagnostic testing as appropriate. Consideration of BCDVA, IOL stability and subjective complaints such as blurred vision or visual disturbances should be considered, with an assessment of the potential risks and benefits associated with the SSI.

The Investigator must assess if an SSI is related to the optical properties of the IOL, i.e., rotation of a toric IOL. Situations requiring SSIs that are not considered related to the optical properties of the IOL include:

- Posterior capsular opacification (PCO; note that YAG for PCO is not considered an SSI but an analysis of rates will be performed)
- Macular edema confirmed by optical coherence tomography and/or fluorescein angiography
- Corneal disorders (e.g., dry eye syndrome, edema, and corneal irregularities)
- Pre-existing or newly developed ocular pathologies
- Surgical complications noted at the operative visit that may reasonably be expected to affect postoperative outcomes

Subjects that have a secondary surgery that is targeted to correct for postoperative toric IOL rotation shall have their clinical results prior to that surgical intervention carried forward as the final results for that subject. In cases where axis misalignment measured at follow up visits after a secondary surgical intervention (SSI) is greater than the axis misalignment prior to SSI, the greater misalignment error shall be considered final.

Secondary IOL interventions should be categorized as IOL exchange (the investigational device is replaced with the same lens model), IOL removal (the investigational device is removed and replaced with a non-investigational lens or no lens is implanted), IOL repositioning (the existing IOL is surgically moved to another location or rotated), or other. Indications for device exchange, removal, or repositioning will be recorded in the CRF.

The investigator should consult with the Medical Monitor to determine if an SSI is warranted. If there is any uncertainty as to whether the SSI is related to the optical properties of the IOL or to some other

unrelated factor, the Investigator should consult with the Medical Monitor. The Investigator should determine the most suitable SSI procedure for each case. Note that limbal relaxing incisions during cataract surgery and refractive procedures to address residual refractive error are disallowed by the protocol.

An SSI must be reported to the sponsor or designee within 7 days of the date of SSI.

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#### 8.6.1 IOL EXCHANGE

An IOL exchange, where the IOL is replaced with the same lens model, is only allowed at the Operative visit (Form 0). If the IOL needs to be replaced sometime later after the operative visit, the replacement IOL cannot be the investigational IOL model.

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#### 8.6.2 IOL REPOSITIONING

If IOL repositioning is required, it should be done in the early postoperative period, preferably within the first 30 days following surgery. Repositioning should only be considered in cases where IOL rotation, tilt, or decentration is such that repositioning is necessary to improve the visual outcomes of the subject or prevent damage to the eye.

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#### 8.6.3 IOL EXPLANTATION AND REPLACEMENT

If IOL explantation and replacement is required, it should be done in the early postoperative period. In the case of an incorrect IOL power or residual refractive error, if IOL replacement is expected to improve the subject's visual outcomes, the IOL should be replaced with a new lens; however, the replacement IOL cannot be the investigational IOL model.

The Investigator should consult with the Medical Monitor and carefully consider the potential risks and benefits of the SSI.

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### 8.7 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, UNANTICIPATED ADVERSE DEVICE EFFECTS AND DEVICE DEFICIENCIES

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#### 8.7.1 DEFINITION OF ADVERSE EVENTS

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical sign (including an abnormal laboratory finding) or symptom in subjects whether or not related to an investigational device.

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#### 8.7.2 DEFINITION OF SERIOUS ADVERSE EVENTS

A serious adverse event (SAE) is defined as any untoward medical occurrence that meets any of the following:

- Requires inpatient hospitalization or prolongation of existing hospitalization;
- Requires medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure;
- Is life threatening (places the subject at immediate risk of death from the event as it occurred) or sight threatening;

- Results in permanent impairment of a body function or permanent damage to a body structure;
- Results in death
- May jeopardize the subject and require medical or surgical intervention to prevent one of the other outcomes.

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#### 8.7.2.1 CUMULATIVE ADVERSE EVENTS

In addition, the total number of the following adverse events that have occurred at any time will be reported as cumulative AEs, consistent with categories provided in ISO 11979-7:

- Cystoid macular edema
- Hypopyon
- Endophthalmitis - defined as intraocular inflammation leading to diagnostic vitreous tap and treated with intraocular antibiotics
- Lens dislocation from posterior chamber
- Pupillary block - shallowing of anterior chamber due to obstruction of aqueous humor flow from the posterior to anterior chamber through the pupil
- Retinal detachment
- Secondary surgical intervention (excluding posterior capsulotomies)

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#### 8.7.2.2 PERSISTENT ADVERSE EVENTS

The total number of the following adverse events that are present at the conclusion of the clinical investigation will be reported as persistent AEs, consistent with categories provided in ISO 11979-7:

- Corneal stromal edema
- Cystoid macular edema
- Iritis
- Raised intraocular pressure (IOP) requiring treatment.

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#### 8.7.3 DEFINITION OF ADVERSE DEVICE EFFECTS AND UNANTICIPATED ADVERSE DEVICE EFFECTS

An Adverse Device Effect (ADE) is any adverse event related to the use of a study device. This definition includes any events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation or operation, or any malfunction of the device. This definition also includes any event resulting from use error or from intentional misuse of a study device.

An Unanticipated Adverse Device Effect (UADE) is any serious adverse effect on subject health or safety, or any life-threatening problem or death caused by or associated with the investigational device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the study protocol.

## 8.7.4 CLASSIFICATION OF AN ADVERSE EVENT

### 8.7.4.1 SEVERITY OF EVENT

The investigator must determine the intensity of the event.

<i>Mild</i>	Awareness of sign or symptom, but easily tolerated
<i>Moderate</i>	Discomfort enough to cause interference with normal daily activities
<i>Severe</i>	Inability to perform normal daily activities

### 8.7.4.2 RELATIONSHIP TO STUDY INTERVENTION

All adverse events (AEs) must have their relationship to study intervention assessed by the Investigator based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

#### **Relationship of the AE to Study Device or Surgical Procedure:**

<i>Definite</i>	A clear-cut causal relationship and no other possible cause
<i>Probable</i>	A causal relationship is likely although alternate etiologies are also possible
<i>Possible</i>	A causal relationship is not definite, alternate etiologies are also possible
<i>Not Related</i>	The AE has no causal relationship and/or there is evidence of alternative etiology such as concurrent medication or illness.

## 8.7.5 ADVERSE EVENT REPORTING

All AEs that occur during or after the Preoperative Visit through completion of study participation must be documented. Adverse events are collected from time of informed consent, and may be determined by evaluating the following in relation to the study subject:

- Observed or volunteered problems
- Complaints
- Physical signs and symptoms
- The occurrence of a medical condition during the study, which was absent at baseline
- The worsening of a baseline medical condition during the study

Each subject eye must be examined for the presence/absence of adverse events at all visits, whether scheduled or not. If an AE occurs, the first concern will be the safety and welfare of the subject; treatment should be provided as appropriate for the event.

AEs, regardless of causal relationship, must be assessed by the Investigator and recorded in the subject's CRF. AEs should be recorded in the form of a diagnosis, rather than signs and symptoms. Each AE must be described as ocular or non-ocular along with the following information: date of onset, date of resolution, severity, nature of the event (intermittent, continuous), action taken (none, medical and/or surgical), relationship to study device and surgical procedure, seriousness criteria and expectedness. Any medication or other intervention necessary for the treatment of an AE must be recorded on the appropriate eCRF. If the same type of AE occurs multiple times, each event should be recorded separately.

AEs will be documented beginning at the time of onset, and documentation must continue until recovery is noted. Events that are ongoing at the time of study exit should be followed until resolution or stabilization.

Ocular conditions or diseases noted during the Preoperative Visit that are chronic but stable and meet the inclusion/exclusions criteria should be recorded as Ocular History in the subject's case report form. The worsening of a preoperative condition or disease will be considered an AE. As applicable, signs and symptoms indicating a common underlying pathology should be noted as one comprehensive event.

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#### 8.7.6 EXPEDITED ADVERSE EVENT REPORTING

Any ocular SAE or UADE, whether the event is expected or unexpected, ***must be reported to the Sponsor, or the Sponsor's designee, within 24 hours*** of the Investigator becoming aware of the event. Non-ocular SAEs must be reported within 7 days.

SAEs and UADEs must be recorded in the subject's eCRF. Information provided on the eCRF should be supplemented with hospitalization records, death certificate, clinic notes from specialists evaluating the subject's condition, etc., as applicable for the event. The urgency for reporting SAEs/UADEs is 3-fold:

- To facilitate discussion [and implementation, if necessary] by the Sponsor and the Investigator of appropriate follow-up measures.
- To facilitate Investigator reporting of unanticipated problems involving risk to human subjects to the IRB, and
- To enable the Sponsor to fulfill the reporting requirements to the appropriate regulatory authority.

It is the responsibility of the Investigator to promptly notify the IRB of SAEs per the IRBs reporting requirements. Investigators must report the occurrence of a UADE to their reviewing IRB as soon as possible, but no later than 10 working days after first learning of the event. The Sponsor must report the results of an evaluation of an UADE to FDA and all reviewing IRBs and participating investigators within 10 working days after the Sponsor first receives notice of the effect.

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#### 8.7.7 ANTICIPATED ADVERSE EVENTS

As per ISO 11979-7 (2018) and *The American Academy of Ophthalmology Task Force Consensus Statement on Adverse Events with Intraocular Lenses*<sup>3</sup>, the anticipated AEs associated with cataract

surgery and/or Toric IOL implantation that might reasonably be expected to occur in this study are listed below and include, but are not limited to, the following:

#### Intraoperative Adverse Events

- Anterior capsule tear
- Hyphema
- Vitreous prolapse
- Wound leak (positive Seidel)
- Posterior capsular rupture
- Choroidal detachment/hemorrhage
- Zonular dialysis
- Thermal injury (phaco burn)
- Iris or pupil damage

#### Postoperative Adverse Events

- Anterior uveitis (including iritis and iridocyclitis)
- Capsular block syndrome
- Choroidal detachment/hemorrhage
- Chronic anterior uveitis [anterior segment inflammation characterized by grade 1+ cell or greater (using the Standardization of Uveitis Nomenclature [SUN] criteria) that is persistent for greater than 3 months after surgery, or relapses in less than 3 months after discontinuation of therapy, or the subject is maintained on therapy for more than 3 months to control inflammation.] Note that any iritis present at the final visit is considered significant and should be counted as a 'persistent ISO SPE event'.
- Visually significant corneal edema [corneal swelling (stromal or epithelial) resulting in BCDVA of 0.3 logMAR or worse at Form 3 or later]. Note that any corneal stromal edema present at the final visit is considered significant and should be counted as a 'persistent ISO SPE event'.
- Clinically significant cystoid macular edema (CME) diagnosed by clinical exam and adjunct testing (e.g., OCT or other method), resulting in BCDVA of  $\leq 0.3$  logMAR at Form 3 or later
- Endophthalmitis (intraocular inflammation leading to diagnostic vitreous tap and use of intraocular antibiotics)
- Flat anterior chamber with lens/cornea touch or a shallow chamber with iridocorneal apposition without lens/cornea touch
- Anterior Capsular Contraction Syndrome (ACCS, Phimosis)
- Hypopyon
- Corneal endothelial damage
- Incorrect IOL power resulting in secondary surgical intervention
- Increased IOP (elevation of IOP  $\geq 10$  mmHg above the IOP measured at the Preoperative Visit to a minimum of 25 mmHg)
- Infectious keratitis
- IOL damage resulting in secondary surgical intervention

- IOL dislocation, tilt, decentration, luxation, rotation resulting in secondary surgical intervention
- Best-corrected distance visual acuity loss of 2 lines (10 letters) or more on the ETDRS chart measured at or after postoperative Form 4 compared to any prior postoperative visit
- Best-corrected distance visual acuity loss of 2 lines (10 letters) or more since the prior visit
- Mechanical pupillary block (A shallowing of the anterior chamber due to obstruction of aqueous humor flow from the posterior to anterior chamber through the pupil by the crystalline lens, vitreous face, or implanted device)
- Chronic pain in the study eye, per subjective patient reporting, graded as  $\geq 4$  on the standardized pain rating scale (from 0 to 10), present greater than 3 months postoperative
- Retained lens material
- Rhegmatogenous retinal detachment (RD) (partial or complete RD associated with retinal tear)
- Secondary IOL intervention (Exchange, Removal, or Reposition)
- Secondary surgical intervention (include, but are not limited to lens repositioning, lens replacement, vitreous aspiration, iridectomy for pupillary block, wound leak repair, and retinal detachment repair). It excludes posterior capsulotomies
- Synechiae formation
- Toxic anterior segment syndrome (TASS) (An acute, noninfectious inflammation of the anterior segment of the eye that starts within 24 to 48 hours after surgery, usually resulting in hypopyon and commonly presenting with corneal edema, and that improves with steroid treatment)

Investigators should accurately record the resolution status of all AEs, including all sequelae which could be on ocular structure or ocular (or visual) function.

Early, low grade anterior chamber cell/flare, corneal edema, and increase in IOP can often be considered normal or expected after IOL surgery. They do not need to be reported as adverse events if they occur prior to 1 week postoperatively if they meet the following criteria:

- Anterior chamber cells or flare of grade 2 or less that requires no change in standard postoperative medication regimen (if it persists to 1 week or more it should be reported as an adverse event);
- Corneal edema of grade 2 or less that does not reduce acuity to 0.3 logMAR (20/40) or worse and does not require any change in standard postoperative medication regimen (if it persists to 1 week or more it should be reported as an adverse event);
- Increased IOP that is  $<10$ mm Hg above baseline or is  $<25$ mmHg and requires no change in standard postoperative medications regimen or any other special treatment.

However, note that all secondary surgical interventions (and events that cause these interventions) and all events that have sequelae should be reported as adverse events, regardless of when they occur.

Note: Posterior capsular opacification (PCO) is NOT to be reported as an AE, per ISO 11979-7. YAG capsulotomies should be reported in the subject's case report form.

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#### 8.7.8 DEVICE DEFICIENCIES

Device deficiencies related to the identity (e.g., labeling), quality, durability, reliability, safety, effectiveness, or performance of the study device must be reported to the Sponsor, or Sponsor's designee, within 7 days of the Investigator becoming aware of the deficiency. Device deficiencies must be recorded in the subject's case report form.

Device deficiencies will be categories as one of the following:

- **Device failure:** A device has failed if it is used according to the labeling, including without limitation, instructions for use, and applicable standards of medical practice but does not perform according to the labeling and negatively impacts the treatment.
- **Device malfunction:** A device malfunction is a change in the function of the device that is not described in the labeling and that may or may not affect device performance.
- **Device misuse:** A misused device, i.e., one that is not used by the Investigator (in the study) in compliance with applicable standards of medical practice, including without limitation, those described in the instructions for use and labeling, will not be considered a malfunction.
- **Other:** must be described by the Investigator

## 9 STATISTICAL CONSIDERATIONS

### 9.1 GENERAL

All data analysis will be performed after the study is completed and the database has been locked. Statistical programming and analyses will be performed using SAS Version 9.4 or higher and R Software, Version 4.3.0 or higher. Figures will be produced using R Software, version 4.3.0 or higher. All study data will be listed by subject, and visit, as applicable, in support of summary tables.

For continuous or ordinal measures, descriptive summary statistics will include the number of observations, mean, standard deviation, median, minimum, maximum, as well as the number with results not reported. Minima and maxima will be reported with the same precision as the raw values; means and medians will be presented to 1 additional decimal place than reported in the raw values. Standard deviations will be presented to 2 additional decimal places than reported in the raw values. For categorical measures, the percentage and number of cases for each condition (e.g., subject sex, age grouping), along with a 95% Clopper-Pearson confidence interval, will be reported. The number of subjects without results will be omitted from the numerator and denominator of such calculations. All percentages will be rounded to 1 decimal place (i.e., XX.X%).

### 9.2 ANALYSIS POPULATIONS

The All-enrolled population includes all subjects who sign an informed consent form. This population will be used for disposition summaries.

The Safety population will include all subjects where the test or control IOL touched the eye.

The intent to treat (ITT) population includes all randomized subjects. Missing data will be imputed. Subjects will be analyzed as randomized. The ITT population is the primary analysis population for assessing effectiveness.

The All-implanted population includes all ITT subjects who were successfully implanted with one of the two study IOLs and who attended at least one postoperative visit. Missing data will be imputed. Subjects will be analyzed as randomized. The All-implanted population is supportive of the ITT population for assessing effectiveness.

The Per-Protocol (PP) population includes all subjects in the All-implanted population who have no major protocol deviations that could affect the interpretation of effectiveness. Exclusions from PP will be determined prior to study unmasking. Missing data will not be imputed. Subjects will be analyzed as treated. Analyses based on PP will be supportive of those based on ITT.

The Best-Case Set will include subjects in PP with all of the following characteristics:

- No major protocol deviations potentially affecting any of the primary effectiveness endpoints (BCDVA, DCNVA). Major protocol deviations that may potentially affect the primary effectiveness endpoints include, but are not limited to:
  - Inclusion of ineligible subjects
  - Implantation of incorrect IOL
  - Missed assessments for effectiveness endpoints at Form 4
  - Receipt of medication likely to interfere with visual performance at Form 4
- At least one eye implanted with a study lens
- No clinically significant preoperative ocular pathology in the first operative eye, including any of the following present prior to the operative visit
  - Pseudoexfoliation
  - Glaucoma
  - Uveitis
  - Retinal detachment
  - Diabetic retinopathy
  - Macular degeneration
  - Amblyopia
  - Other preoperative pathologies that are likely to affect central acuity
- No macular degeneration detected at any time in the first operative eye
- No previous surgery for the correction of refractive errors in the first operative eye

### 9.3 ANALYSIS SUBSETS

A best-case analysis population is defined for the testing of co-primary endpoint of BCVA logMAR of 0.3 or better at Form 4.

### 9.4 HYPOTHESES

Formal statements for the four effectiveness hypotheses are as follows.

[REDACTED]

[REDACTED]

[REDACTED]

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## 9.5 POWER AND SAMPLE SIZE

A sample size of up to 300 eyes is planned to be enrolled, where a screen failure of up to 70 eyes (23%) is anticipated. Approximately 230 eyes will be randomized and implanted with toric or control IOL.

For co-primary endpoint 3, IOL axis misalignment  $< 20^\circ$  from intended IOL axis of orientation at Form 4, we assume a success rate of 99.0% in toric lenses. Given a target of 95%, and using the testing method employed with SPE endpoints, we have 99% power to show that the upper 95% boundary of a Clopper-Pearson confidence interval of the achieved success rate includes the threshold rate of 95%.

For co-primary endpoint 4, Stability of the toric IOL axis orientation (toric IOL arm only) from Form 3 to Form 4 of  $\leq 5^\circ$  change in orientation, we assume a success rate of 91.46% in toric lenses. Given a target of 90%, and using the testing method employed with SPE endpoints, we have 99% power to show that the upper 95% boundary of a Clopper-Pearson confidence interval of the achieved success rate includes the threshold rate of 90%.

Given that all four co-primary endpoints must be met for study success, the worst-case study power, assuming independence among all tests, is  $0.94 \times 0.99 \times 0.99 \times 0.99 = 91\%$ . However, given any positive correlation among the endpoints, power will exceed 91%.

## 9.6 MULTIPLICITY

All co-primary endpoints must be met for the study to be declared a success. Consequently, no adjustment in alpha is necessary.

## 9.7 MISSING DATA AND IMPUTATION

Missing Form 4 effectiveness endpoint data will be imputed for All-implanted and ITT analyses.

For ITT, All-implanted, and PP analyses, per ANSI Z80.30-2018, eyes that have a secondary surgery that is targeted to correct for postoperative toric IOL rotation shall have their clinical results prior to that surgical intervention carried forward as the final results for analysis. Further, in cases where axis misalignment measured at follow up visits after an SSI is greater than the axis misalignment prior to SSI,

the greater misalignment error shall be considered as the final result for analysis. Repositioning of toric IOLs will result in imputation of worst observed value or assignment failure for the co-primary endpoints at Form 4 analysis, as appropriate. Imputation methods described below will retain these worst-value or failure assignments and will not overwrite them with imputed values.

The primary imputation method for all co-primary endpoints will be by multiple imputation where details of initial seed, predictors and methods will be fully described in the Statistical Analysis Plan. Co-primary endpoint 1, will use 50 imputed datasets for analysis; all other endpoints, being binary and tested by exact methods, are not amenable to combining multiple imputations, so only the first imputed dataset will be used.

In addition, for co-primary endpoint 1, where two arms are involved, a tipping point sensitivity analysis will involve initially setting all control-lens eyes with missing data to the best observed outcome (presumably, 0.0 residual cylinder) and setting all toric-lens eyes with missing data to the worst observed outcome. The best and worst values will be incremented/decremented by 0.125 D until control eyes have the worst and toric have the best value imputed. The point at which, if any, where the results of the hypothesis test changes its results regarding rejection of the null hypothesis will be reported.

For all other co-primary endpoints, the tipping-point sensitivity analysis will be performed in which missing data are initially assumed to be failures. Then, one of the imputed failures will be imputed as a success. Then, a second failure will be assigned to a success. This process will be repeated until all missing data are imputed as successes. The point at which, if any, where the results of the hypothesis test changes its results regarding rejection of the null hypothesis will be reported.

Missing data will not be imputed for PP analyses.

## 9.8 STATISTICAL TESTING OF EFFECTIVENESS ENDPOINTS

For co-primary endpoint 1, the test of superiority of the toric lens over the control lens to result in less residual cylinder, a Wilcoxon rank-sum test will be performed, given that the distribution of residual cylinder will be discrete and likely skewed, the t-test is used only as a preliminary estimate of the needed sample size. Given the loss of power due to the use of a non-parametric test, an assumed loss of power of 5% has been made to accommodate lower power of the Wilcoxon test. The point estimate of the difference and a 95% confidence interval of the treatment effect will be provided based on the mean difference and its standard error.

For co-primary endpoints, where axis stability is examined, the upper 95% boundary of a Clopper-Pearson confidence interval will be used to test if the null hypothesis can be rejected. Number and percentage of eyes achieving various levels of stability will be summarized.

## 9.9 STATISTICAL TESTING OF SAFETY ENDPOINTS

Cumulative and persistent adverse events from ISO 11979-7 (2018) Table E.2 will be summarized using descriptive statistics by AE type and treatment and will be compared to the maximum number of cases allowed before the ISO SPE rate is exceeded. Summaries will be provided for both spherical and toric lenses.

The other safety outcomes, listed in Section 3.1, will be summarized by count and percentage for each IOL type. Adverse events will be tabulated by type (e.g., all, serious, anticipated, unanticipated) and classification by IOL.

[REDACTED]

#### 9.10 POOLABILITY

Poolability of results will be assessed by site. The binary co-primary effectiveness endpoints addressing performance of the toric IOL will be tabulated by site to determine if success rates indicate a difference in effectiveness. Similarly, the degree of superiority of the toric arm in reducing residual cylinder, compared with the control arm, will be tested. Cross-tabulations of site by binary endpoints will be analyzed with a Fisher's exact test and the comparison of residual cylinder between treatment arms will be analyzed with an analysis of variance model with an interaction term for site by treatment. In both cases, a p-value of 0.15 will indicate that potential site differences exist and will require investigation as to the possible causes.

#### 9.11 ADDITIONAL ENDPOINTS AND ASSOCIATED ANALYSES

The following are not subject to hypothesis testing.

- 1) Achievement of  $\leq 0.50$  D reduction in cylindrical power of the eye as a binary endpoint. Analysis will summarize the overall percentage of eyes meeting endpoint 1 as well as by each 0.25 D step of preoperative keratometric cylinder. Tabulation will be by both arms at Form 4.
- 2) Reduction in cylindrical power of the eye at Form 4. Analysis will include summary statistics of reduction in cylinder power of the eye overall and by each 0.25 D step of preoperative keratometric cylinder. Summary statistics will be provided for both treatment arms, with the addition of a 95% confidence interval of the mean for each arm. Number and percentage with an absolute reduction of  $\leq 0.5$  D will be provided for each arm.
- 3) Relationship between reduction in cylindrical power of the eye at the corneal plane and preoperative keratometric cylinder at Form 4. The association will be shown using a scatterplot with a linear regression line for each treatment arm. Intercept and slope, with associated p-values, will be provided. If the scatter of the data do not appear to be linear, a LOESS curve will be added for each arm.
- 4) The surgically induced change in corneal cylinder is calculated by analysis of the preoperative and postoperative keratometric readings (power and axis of meridians of highest and lowest power), converted to components in dioptric space. Change is defined as postoperative component values minus preoperative component values. Change and percentage change from baseline at Form 4 will be summarized with descriptive statistics for each treatment arm, overall, and by preoperative keratometric cylinder categories. Analyses will include:
  - a) Analysis of the error in the predicted magnitude of postoperative astigmatism, including the bias, standard deviation, and mean absolute error, and a similar analysis of error in the predicted axis;

- b) Bar plot of the absolute error in predicted keratometric axis as a function of preoperative corneal astigmatism, and tabulation of the proportion of eyes with absolute error in axis by 5° wide bins (e.g., 0° to 5°, >5° to 10°).
- 5) Achievement of UCDVA of 0.0 logMAR or better, 0.2 logMAR or better, and of 0.3 logMAR or better at Form 4. Results will be tabulated for each treatment arm by N and percentage.
- 6) UCDVA at Form 4. UCDVA will be summarized with summary statistics, overall and by each 0.25 D step of preoperative keratometric cylinder categories. Both treatment arms will be summarized.
- 7) Manifest cylinder at Form 4. Analysis will include summary statistics of manifest cylinder. Summary statistics will be provided for both treatment arms. Results will be summarized overall as well as stratified by each 0.25 D of preoperative keratometric cylinder.
- 8) Achieving accuracy of cylinder to target at Form 4 within 0.25 D, 0.50 D, and 0.75 D. Results will be tabulated for each treatment arm by N and percentage.
- 9) Achieving accuracy of MRSE to target at Form 4 within 0.25 D, 0.50 D, and 0.75 D. Results will be tabulated for each treatment arm by N and percentage.
- 10) Axis misalignment compared to target within specified accuracy at Form 4. Results will be tabulated for the toric lens only, reporting the number and percentage with axis deviation greater than 30° of target.
- 11) Axis misalignment at Form 4. Results for absolute and signed values will be summarized for the toric lens only, with summary statistics of deviation from target. A two-sided tolerance interval around the mean of the signed value, which contains at least 90% of the population (with 95% probability), will be provided.

## 10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

### 10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

#### 10.1.1 INFORMED CONSENT PROCESS

##### 10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

The study ICF has been developed in compliance with 21 CFR Part 50.25. Study ICFs and any other subject-facing materials (e.g., recruitment materials, subject instruction sheets) must be submitted to and approved by the IRB prior to implementation. Any IRB-requested modifications to the consent form must remain in compliance with 21 CFR Part 50.25. Each participant must be provided with a copy of the IRB-approved ICF for their review, and the participants' written approval must be provided prior to initiation of study procedures.

##### 10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

The investigator or designee will explain the study purpose, procedures and responsibilities to the potential participant and provide sufficient opportunity to ask questions, while allowing adequate time for

consideration of the information provided. Documentation of written consent for study participation must be present prior to initiation of any study-specific procedure, and subjects will be considered enrolled in the study upon their signature on the ICF.

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#### 10.1.2 STUDY DISCONTINUATION AND CLOSURE

The Sponsor reserves the right to terminate the study at any time. If the clinical study is prematurely terminated or suspended, the Sponsor will inform the Investigators and the regulatory authorities of the reason for the termination/suspension. The Investigator should promptly notify the IRB of the termination or suspension and of the reasons. If the Sponsor terminates the study for safety reasons, it will promptly notify the Investigators and provide written instruction for study termination and applicable subject follow-up.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of insufficient effectiveness that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination of futility

If the study is suspended, it may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the Sponsor, IRB and/or Food and Drug Administration (FDA).

If, in the opinion of the investigator, the clinical observations in the study suggest that it may be unwise to continue, the investigator may terminate the study at his or her site after consultation with the Sponsor. A written statement fully documenting the reasons for such a termination will be provided to the Sponsor.

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#### 10.1.3 CONFIDENTIALITY AND PRIVACY

The investigator will maintain the confidentiality of the identity of subjects enrolled in the study and the information contained in the study records. The records will be made available as required for review by the FDA and other governing regulatory authorities, as well as reviewing IRBs; however, to the extent possible, the subject's identity will not be disclosed.

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#### 10.1.4 DOCUMENT RETENTION

Source documents may include a subject's medical records, hospital charts, clinic charts, the investigator's study subject files, as well as the results of diagnostic tests such as X-rays, laboratory tests, and electrocardiograms. The investigator's copy of the Case Report Forms serves as the investigator's record of a subject's study-related data.

All study related correspondence, patient records, consent forms, record of the use of the study device and copies of case report forms will be maintained on file for at least two years after the last approval of a marketing application and until there are no pending or contemplated marketing applications; or until at least two years have elapsed since the formal discontinuation of clinical development of the investigational device. These documents will be retained for a longer period if required by the applicable

regulatory requirements or by an agreement with the Sponsor. It is the responsibility of the Sponsor to inform the investigator/institution as to when these documents no longer need to be retained or should be forwarded to the Sponsor.

If the responsible investigator retires, relocates, or for other reasons withdraws from the responsibility of keeping study records, custody must be transferred to a person who will accept the responsibility. The Sponsor must be notified in writing of the name and address of the new custodian.

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#### 10.1.5 MEDICAL MONITOR


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#### 10.1.6 INSTITUTIONAL REVIEW BOARD APPROVAL

Before enrollment of study subjects, this protocol must be reviewed and approved by an IRB operating in accordance with 21 CFR Part 50 and all applicable local regulations. Any changes to the study protocol or consent forms must be approved by the IRB prior to implementation. Materials for study patient recruitment and study-specific written materials provided to the subject must also be approved by the IRB prior to use.

Ongoing study progress reports will be submitted to the IRB at least annually, and more frequently if specified by the IRB. Reports of safety events and any protocol deviations that affect the safety and welfare of a study subject will be submitted to the IRB in accordance with United States Food and Drug Administration (FDA) and IRB requirements.

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#### 10.1.7 CLINICAL MONITORING

During the study, the Sponsor or the designee will perform periodic monitoring visits to study sites as per the Clinical Monitoring Plan. During these visits, information recorded on the study eCRFs will be verified against source documents to confirm data capture completeness, accuracy and logical consistency. Study documents will be reviewed to confirm protocol compliance and adherence to IRB and Sponsor-specified reporting requirements, and product accountability will be checked.

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#### 10.1.8 COMPLIANCE WITH PROTOCOL

The Investigator is responsible for complying with the requirements of the study protocol and any amendment or clarification as published by the Sponsor, or Sponsor designee. Subject evaluations will be performed as described in the study protocol. All information generated by the subject evaluation will be recorded using eCRFs with access provided by the Sponsor or Sponsor designee. If applicable, original laboratory reports will be retained by the Investigator, but as the results become available, they will be entered on appropriate eCRFs.

Investigator(s) will not deviate from the study protocol without prior approval of the Sponsor, or Sponsor designee, unless the protection of health, safety or welfare of study subjects requires prompt action.

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#### 10.1.9 DATA HANDLING AND RECORD KEEPING

Procedures for the handling and analysis of data will be conducted using good computing practices meeting International Conference on Harmonization (ICH) and FDA guidelines and all applicable local regulations for the handling and analysis of data for clinical trials.

##### **Data Quality Control and Reporting**

After data have been entered into the study database, a system of computerized data validation checks will be applied and queries pertaining to data omissions and discrepancies will be directed to study sites for resolution within the study database. Study staff will update the database as appropriate to resolve queries generated. All changes to the study database will be documented.

##### **Data Archiving**

Archived versions of the database will be saved by the Sponsor or designee consistent with ICH GCP Guidelines, complying with whichever of the requirements is longer. The Sponsor will notify the investigator when documents should be returned.

##### **Records Retention**

The Investigator's site will retain all records related to the study in compliance with ICH GCP Guidelines.

##### **Protocol Amendments**

Modifications to the approved protocol are only possible using approved protocol amendments and with the agreement of all responsible persons. The procedure for approval of a protocol amendment is identical to that for approval of the protocol. The IRB must review and approve any protocol amendments prior to their implementation at each study site.

The Investigator may not implement any deviation from or change to the protocol, without discussion with, and agreement by the Sponsor and prior review and documented approval/favorable opinion of the amendment from the relevant IRB, except where it is necessary to eliminate an immediate hazard to study subjects, or where the change(s) involves only logistical or administrative aspects of the study (e.g., change in monitor(s), change of telephone number(s)).

Protocol amendments will be submitted to the appropriate authority(ies) as required by the applicable regulatory requirement(s).

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#### 10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site Investigator. The Investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data.

Data recorded in the electronic case report form (eCRF) should be consistent with the data recorded on the source documents.

Clinical data (including the measures as presented in Section 1.3 Schedule of Activities) will be entered into a 21 CFR Part 11-compliant data capture system that includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

#### 10.1.10 PROTOCOL DEVIATIONS

A protocol deviation is any noncompliance with the clinical trial protocol requirements or International Conference on Harmonization Good Clinical Practice (ICH GCP).

Per ICH E3, Structure and Content of Clinical Study Reports and ICH E3, Questions and Answers (R1), major protocol deviations are those that might significantly affect the completeness, accuracy, and/or reliability of study data or that might significantly affect a subject's rights, safety or well-being. For example, major protocol deviations might include enrolling subjects in violation of key eligibility criteria designed to ensure a specific subject population, or failing to collect data necessary to interpret primary endpoints that may compromise the scientific value of the trial.

The site investigator is responsible for knowing and adhering to the reviewing IRB requirements regarding reporting of protocol deviations. Further details about the handling of protocol deviations will be included in the Statistical Analysis Plan.

#### 10.1.11 PUBLICATION AND DATA SHARING POLICY

Any information other than that disclosed upon registration should not be discussed with people outside the study. The protocol, study data, and information related to the study or to BVI's products or research programs that is provided by BVI (Confidential Information) is to be kept confidential, and not disclosed directly or indirectly to any third party other than those involved in the study with a need to know.

All data and discoveries arising out of the study, patentable or non-patentable, shall be the sole property of BVI. BVI reserves the right to prior review of any publication or presentation of information related to the study. BVI may use these data now and in the future for presentation or publication at BVI's discretion or for submission to government regulatory agencies.

### 10.2 PROTOCOL AMENDMENT HISTORY

Version	Section	Description of Change	Brief Rationale


## 11 REFERENCES

<sup>1</sup> ANSI Z80.30: 2018; *American National Standard for Ophthalmics - Toric Intraocular Lenses*

<sup>2</sup> ISO 11979-7: 2018 *Ophthalmic implants – intraocular lenses – part 7: clinical investigations of intraocular lenses for the correction of aphakia*

<sup>3</sup> Masket S, Rorer E, Stark W, Holladay J, MacRae S, Tarver M, Glasser A, Calogero D, Hilmantel G, Nguyen T, Eydelman M. Special Report: The American Academy of Ophthalmology Task Force Consensus Statement on Adverse Events with Intraocular Lenses. *Ophthalmology*, Vol 124, No 1, 2017; 124 (1): 42-144.

<sup>4</sup> Chassain C, Hallak MK, Lesaffre M. Rotational stability and clinical outcomes after implantation of a new monofocal toric intraocular lens with double C-loop design. *J Fr Ophtalmol*. 2023 Jun;46(6):571-580. doi: 10.1016/j.jfo.2022.07.005. Epub 2023 May 11. PMID: 37179129.

<sup>5</sup> ACRYSOF® Single-Piece Posterior Chamber Intraocular Lenses with Toric Optic- Summary of Safety and Effectiveness Data- Premarket Approval Application (PMA) Number: P930014/S15

## 12 APPENDIX A: Sponsor And TrueNorth Approvals

**Protocol Title:** Clinical Investigation of the Safety and Effectiveness of PODEYE TORIC Monofocal IOL

**Study number:** PHY2302

**Protocol Date:** 26 Oct 2023

This clinical study protocol was subject to critical review and has been approved by the Sponsor. The following personnel contributed to writing and/or approving this protocol.

<p>Mattia Ronchetti</p> <p>Senior Director Global Clinical &amp; Regulatory Affairs BVI Medical</p>	<p>.....</p>
<p>Rebecca McQuaid PhD</p> <p>Associate Director Global Clinical Operations BVI Medical</p>	<p>.....</p>
<p>Sonal Shekhawat MD</p> <p>U.S. Clinical Operations Lead BVI Medical</p>	<p>.....</p>
<p>Lavanya Gunasekaran</p> <p>Regulatory Development Manager BVI Medical</p>	<p>.....</p>
<p>[REDACTED]</p> <p>[REDACTED]</p> <p>[REDACTED]</p>	<p>.....</p>
<p>[REDACTED]</p> <p>[REDACTED]</p>	<p>.....</p>