Clinical Investigation of the Safety and Effectiveness of FINEVISION HP Trifocal IOL

Protocol Number: PHY1903

Sponsor: Beaver-Visitec International, Inc

Version Number: v.1.7

09 Feb 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 _____

Investigator Address _____

_____

[redacted]

[redacted]

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SSTATEMENT 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.

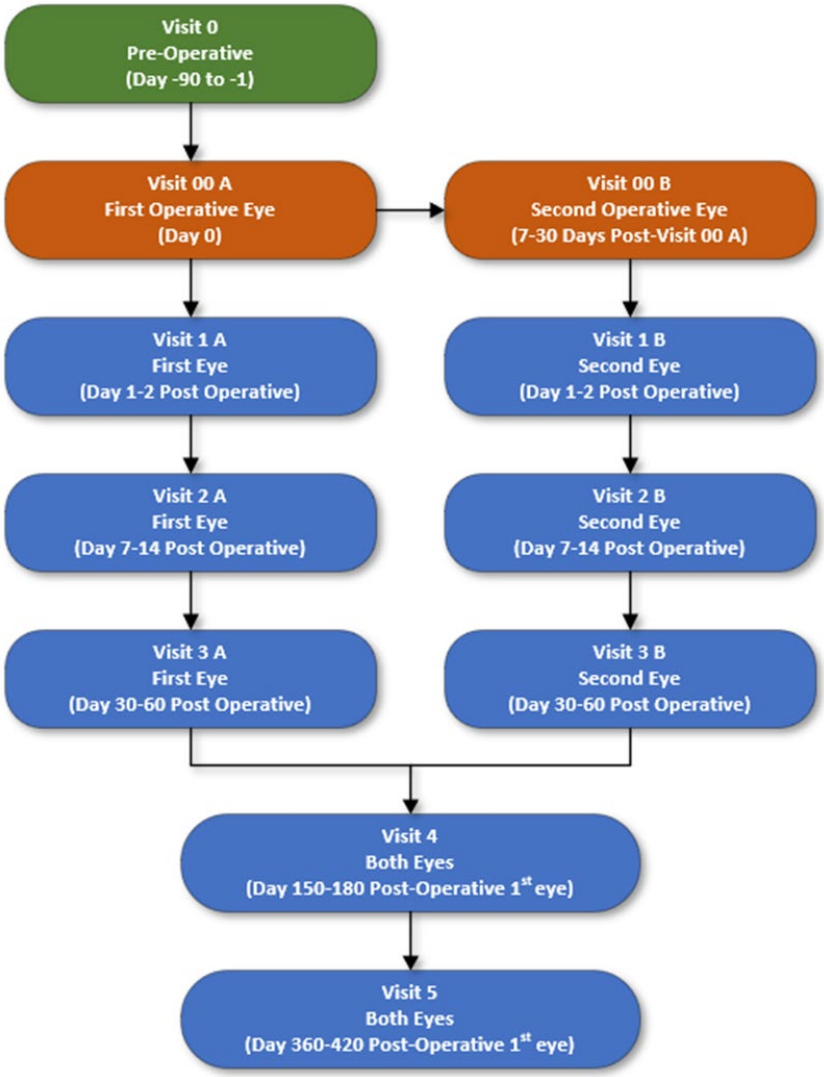
1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	Clinical investigation of the safety and effectiveness of FINEVISION HP Trifocal IOL
Study Description:	This study is a prospective, multicenter, randomized, double masked confirmatory trial comparing an investigational trifocal intraocular lens (IOL) and a commercially available monofocal IOL.
Objectives:	Co-primary effectiveness objectives are to: • Demonstrate non-inferiority of FINEVISION HP trifocal IOL to the control in mean photopic monocular BCDVA (best corrected distance visual acuity) for the first operative eye at Month 6 (Visit 4). • Demonstrate superiority of FINEVISION HP trifocal IOL to the control in mean photopic monocular DCNVA (distance corrected near visual acuity) for the first operative eye at Month 6 (Visit 4) Co-primary safety objectives are to: • Estimate the cumulative rate of SSIs related to the optical properties of the IOL for the first operative eye up to Month 12 (Visit 5) • Evaluate the mean monocular contrast sensitivity for the first operative eye, with and without glare for mesopic conditions and photopic conditions, at Month 12 (Visit 5) The secondary effectiveness objective is to: • Demonstrate superiority of FINEVISION HP trifocal IOL to the control in mean photopic monocular DCVA at intermediate (66 cm) for the first operative eye at Month 6 (Visit 4) The secondary safety objectives are to evaluate: • Rates of cumulative and persistent adverse events in first operative eyes at Month 12 (Visit 5) in comparison to the ISO Safety and Performance Endpoint (SPE) rates as described in ISO 11979-7

	• Visual disturbances using the Quality of Vision (QoV) questionnaire and QoV Supplemental Questions at Month 12 (Visit 5)
Study Population:	The subject population will consist of subjects with operable bilateral cataracts in each eye. Up to 539 subjects are to be enrolled, with 501 subjects planned to undergo phacoemulsification cataract surgery with IOL implantation in both eyes. Prior to cataract surgery in the first operative eye, subjects will be randomly assigned at a 2:1 ratio to receive either the investigational FINEVISION HP or the control IOL, Alcon AcrySof SN60AT[redacted] IOL. The second operative eye will undergo cataract surgery 7 – 30 days afterwards, with the same model IOL implanted.
Phase:	Pivotal
Description of Sites/Facilities Enrolling Participants:	Subjects will be enrolled at up to 24 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.
Description of Study Intervention:	The study intervention is an IOL to be implanted via routine small incision cataract surgery. Subject eyes in the test arm will be implanted with an investigational trifocal IOL, while the eyes in the control arm will be implanted with a commercially available monofocal IOL. IOLs are implantable medical devices intended for long term use over the lifetime of the subject.
Study Duration:	Study duration is estimated to be approximately 24 months based on an estimated enrollment period of 10 months and subject participation period of 14 months (calculated as the difference between the time of the Preoperative Visit to completion of 12-month follow-up on the second operative eye)
Participant Duration:	It is estimated that the duration of each subject's participation in the study will be approximately 14 months (calculated as the difference between the time of the Preoperative Visit to completion of 12-month follow-up on the second operative eye).

1.2 SCHEMA



Note: *For study visits designated A or B, 'A' represents the first eye implanted (Eye A), and 'B' represents the second eye implanted (Eye B). Monocular assessments will be performed at* ***Visits 00 A/B, 1 A/B, 2 A/B****, and* ***3 A/B*** *for only* ***Eye A*** *or only* ***Eye B****, respectively, unless binocular assessments are specified (See Schedule of Activities, Section 1.3). At Visits 4 and 5, monocular assessments and binocular assessments will be completed for both eyes.*

1.3 SCHEDULE OF ACTIVITIES (SOA)

			Visit 0	Visit 00 A	Visit 00 B	Visit 1 A/B	Visit 2 A/B	Visit 3 A/B	Visit 4	Visit 5	USV[2]
Examination	**Light Condition**	**Monocular / Binocular**	**Pre-Op / Screen D -90 to -1**	**Implant A[1] D 0**	**Implant B[1] (D 7 to D 30 after Visit 00 A)**	**Post-Op D 1-2**	**Post-Op D 7-14**	**Post-Op D 30-60**	**Post-Op D 150-180 (from 1st eye)**	**Post-Op D 360-420 (from 1st eye)**	**N/A**
Informed Consent and HIPAA			X								
Demographics			X								
Inclusion & Exclusion Criteria Evaluation			X								
Inclusion & Exclusion Criteria Review				X							
Ocular and non-ocular Medical History			X	X	X	X	X	X	X	X	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	X
Corneal Topography			X								
Manifest Refraction (ETDRS) – 4 meters			X				X	X	X	X	X
Randomization			X								
Operative Procedures				X	X						
Patient Reported Outcome Questionnaires[3]			X						X	X	X
Pupil Size Measurements[4]	Photopic	Monocular	X						X	X	
	Mesopic		X						X	X	
Intraocular Pressure			X			X	X	X	X	X	X
Slit Lamp Examination			X			X	X	X	X	X	X
IOL Tilt and Decentration Grading						X	X	X	X	X	X

Examination		Light Condition	Monocular / Binocular	Visit 0 Pre-Op / Screen D -90 to -1	Visit 00 A Implant A[1] D 0	Visit 00 B Implant B[1] (D 7 to D 30 after Visit 00 A)	Visit 1 A/B Post-Op D 1-2	Visit 2 A/B Post-Op D 7-14	Visit 3 A/B Post-Op D 30-60	Visit 4 Post-Op D 150-180 (from 1st eye)	Visit 5 Post-Op D 360-420 (from 1st eye)	USV[2] N/A
[redacted]					[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Dilated Fundus Examination				X					X	X	X	X
Posterior Capsule Assessment (PCO grade assessment)							X	X	X	X	X	X
IOL Observations							X	X	X	X	X	X
Adverse Events				X	X	X	X	X	X	X	X	X
Device Deficiencies					X	X	X	X	X	X	X	X
Concomitant Medications				X	X	X	X	X	X	X	X	X
Exit from Study											X	
Visual Acuity	UCDVA (4 meters)	Photopic	Monocular	X			X	X	X	X	X	X
			Binocular					X	X	X	X	X
	BCDVA (4 meters)	Photopic	Monocular	X				X	X	X	X	X
			Binocular					X	X	X	X	X
	UCNVA (40 cm)	Photopic	Monocular						X	X	X	
			Binocular						X	X	X	
	BCNVA (40 cm)	Photopic	Monocular						X	X	X	
			Binocular						X	X	X	
	DCNVA (40 cm)	Photopic	Monocular						X	X	X	
			Binocular						X	X	X	
		Mesopic	Monocular						X	X	X	
			Binocular						X	X	X	
	[redacted]	[redacted]	[redacted]						[redacted]	[redacted]	[redacted]	
			[redacted]						[redacted]	[redacted]	[redacted]	
	UCIVA (66 cm)	Photopic	Monocular						X	X	X	
			Binocular							X	X	

Examination		Light Condition	Monocular / Binocular	Visit 0 Pre-Op / Screen D -90 to -1	Visit 00 A Implant A[1] D 0	Visit 00 B Implant B[1] (D 7 to D 30 after Visit 00 A)	Visit 1 A/B Post-Op D 1-2	Visit 2 A/B Post-Op D 7-14	Visit 3 A/B Post-Op D 30-60	Visit 4 Post-Op D 150-180 (from 1st eye)	Visit 5 Post-Op D 360-420 (from 1st eye)	USV[2] N/A
	DCIVA (66 cm)	Photopic	Monocular						X	X	X	
			Binocular							X	X	
		Mesopic	Monocular						X	X	X	
			Binocular							X	X	
	[redacted]	[redacted]	[redacted]						[redacted]	[redacted]	[redacted]	
										[redacted]	[redacted]	
		[redacted]	[redacted]						[redacted]	[redacted]	[redacted]	
										[redacted]	[redacted]	
	[redacted]	[redacted]	[redacted]						[redacted]	[redacted]	[redacted]	
										[redacted]	[redacted]	
Contrast Sensitivity with Glare – 2.5 meters		Photopic	Monocular							X	X	
Contrast Sensitivity without Glare – 2.5 meters										X	X	
Contrast Sensitivity with Glare – 2.5 meters		Mesopic	Monocular							X	X	
Contrast Sensitivity without Glare – 2.5 meters										X	X	
Defocus Curve (Best Distance Corrected) – 4 meters[6]			Monocular							X	X	
			Binocular							X	X	

[1] A – First Operative Eye, B – Second Operative Eye

[2] USV – Unscheduled Visit; for unscheduled visits, mandatory assessments to be completed are defined in the table. Additional assessments may be performed as appropriate, based on the subject's condition.

[3] Patient Reported Outcome Questionnaires include the PRSIQ, QoV and QoV Supplemental Questions

			Visit 0	Visit 00 A	Visit 00 B	Visit 1 A/B	Visit 2 A/B	Visit 3 A/B	Visit 4	Visit 5	USV[2]
Examination	**Light Condition**	**Monocular / Binocular**	**Pre-Op / Screen D -90 to -1**	**Implant A[1] D 0**	**Implant B[1] (D 7 to D 30 after Visit 00 A)**	**Post-Op D 1-2**	**Post-Op D 7-14**	**Post-Op D 30-60**	**Post-Op D 150-180 (from 1st eye)**	**Post-Op D 360-420 (from 1st eye)**	**N/A**

[4] Pupil size measurements in mesopic and photopic lighting conditions must be taken right before contrast sensitivity testing (see instructions for Pupil Size Measurements in Manual of Procedures)

[redacted]

1.4 ABBREVIATIONS

ADE	Adverse device effect
AE	Adverse event
ANSI	American National Standards Institute
BAT	Brightness acuity meter
BCDVA	Best corrected distance visual acuity
BCIVA	Best corrected intermediate visual acuity
BCNVA	Best corrected near visual acuity
CFR	Code of Federal Regulations
CME	Cystoid macular edema
cpd	Cycles per degree
CRF	Case report form
DCIVA	Distance corrected intermediate visual acuity
DCNVA	Distance corrected near visual acuity
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
logMAR	Logarithm of the Minimum Angle of Resolution
MCMC	Markov Chain Monte Carlo
MOP	Manual of procedures
OCT	Optical coherence tomography
PCO	Posterior capsule opacification
PRSIQ	Patient-Reported Spectacle Independence Questionnaire
QoV	Quality of Vision questionnaire
[redacted]	[redacted]
RD	Retinal detachment
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
UCIVA	Uncorrected intermediate visual acuity
UCNVA	Uncorrected near 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 FINEVISION HP Trifocal IOL.

2.2 BACKGROUND

Cataracts are 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. Monofocal IOLs provide adequate distance vision but require spectacle use for activities requiring near or intermediate vision. Multifocal IOLs, including bifocal and trifocal IOLs, have been successfully developed to improve near and intermediate distance vision and increase spectacle independence following cataract surgery. The FINEVISION HP Trifocal IOL is designed to provide distance vision similar to a monofocal IOL, but with improved intermediate and near vision.

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 phimosis
4. Corneal edema
5. Corneal endothelial damage
6. Cystoïd macular edema (CME)
7. Secondary surgical intervention (including, but are 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, multifocal IOLs in particular have been associated with an increased risk of reduced contrast sensitivity and also dysphotopias such as halos and glare, potentially leading to secondary surgical interventions.

2.3.2 POTENTIAL BENEFITS

The possible benefits associated with this study are:

- Improved vision at near, intermediate, and distance
- 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 intermediate and near vision are compared against the risks of reduced contrast sensitivity and visual disturbances, a known risk associated with multifocal IOLs.

3 OBJECTIVES

3.1 PRIMARY OBJECTIVES

Co-primary effectiveness objectives are to:

- Demonstrate non-inferiority of FINEVISION HP trifocal IOL to the control in mean photopic monocular BCDVA (best corrected distance visual acuity) for the first operative eye at Month 6 (Visit 4)
- Demonstrate superiority of FINEVISION HP trifocal IOL to the control in mean photopic monocular DCNVA (distance corrected near visual acuity) for the first operative eye at Month 6 (Visit 4)

Co-primary safety objectives are to:

- Estimate the cumulative rate of SSIs related to the optical properties of the IOL for the first operative eye up to Month 12 (Visit 5)
- Evaluate the mean monocular contrast sensitivity for the first operative eye, with and without glare for mesopic conditions and photopic conditions, at Month 12 (Visit 5)

Primary Effectiveness Variables

- Photopic monocular logMAR best corrected distance visual acuity (BCDVA) in first operative eyes at Month 6 (Visit 4)

- Photopic monocular logMAR near (40 cm) visual acuity with distance correction (DCNVA) in first operative eyes at Month 6 (Visit 4)

Primary Safety Variables

- Cumulative rate of secondary surgical interventions (SSIs) related to the optical properties of the IOL in first operative eyes through Month 12 (Visit 5)

- Mean monocular distance contrast sensitivity (mesopic with and without glare at 1.5, 3, 6, and 12 cpd measured at 2.5 m, and photopic with and without glare at 3, 6, 12, and 18 cpd, measured at 2.5 m) in first operative eyes at Month 12 (Visit 5)

3.2 SECONDARY OBJECTIVES

The secondary effectiveness objective is to:

- Demonstrate superiority of FINEVISION HP trifocal IOL to the control in mean photopic monocular DCVA at intermediate (66 cm) for the first operative eye at Month 6 (Visit 4)

The secondary safety objectives are to evaluate:

- Rates of cumulative and persistent adverse events in first operative eyes at Month 12 (Visit 5) in comparison to the ISO Safety and Performance Endpoint (SPE) rates as described in ISO 11979-7
- Visual disturbances using the Quality of Vision (QoV) questionnaire and QoV Supplemental Questions at Month 12 (Visit 5)

Secondary Effectiveness Variables

- Photopic monocular logMAR intermediate (66 cm) visual acuity with distance correction (DCIVA) in first operative eyes at Month 6 (Visit 4)

Secondary Safety Variables

- Rates of cumulative and persistent adverse events in first operative eyes through Month 12 (Visit 5), compared to the ISO SPE rates as described in ISO 11979-7
- Visual disturbances using the Quality of Vision (QoV) questionnaire and QoV Supplemental Questions at Month 12 (Visit 5)

3.3 ADDITIONAL OBJECTIVES

[redacted]

- [redacted]

Additional effectiveness objectives are to:

- Characterize all visual acuity measurements at Months 6 and 12 (Visits 4 and 5)
- Characterize monocular and binocular defocus curves at Month 6 (Visit 4)
- Evaluate spectacle independence using the Patient-Reported Spectacle Independence Questionnaire (PRSIQ) at Month 6 (Visit 4)

[redacted]

- [redacted]

Additional Effectiveness Variables

- Photopic monocular logMAR BCDVA, [redacted], DCIVA (66 cm), and DCNVA in first operative eyes at Month 6 (Visit 4) and Month 12 (Visit 5)
- Mesopic monocular logMAR [redacted], DCIVA (66 cm), and DCNVA in first operative eyes at Month 6 (Visit 4) and Month 12 (Visit 5)
- Photopic binocular logMAR BCDVA, [redacted] DCIVA (66 cm), and DCNVA at Month 6 (Visit 4) and Month 12 (Visit 5)
- Mesopic binocular logMAR [redacted], DCIVA (66 cm), and DCNVA at Month 6 (Visit 4) and Month 12 (Visit 5)
- Photopic monocular logMAR UCDVA, [redacted] UCIVA (66 cm), and UCNVA in first operative eyes at Month 6 (Visit 4) and Month 12 (Visit 5)
- Photopic binocular logMAR UCDVA, [redacted], UCIVA (66 cm), and UCNVA at Month 6 (Visit 4) and Month 12 (Visit 5)
- Photopic monocular logMAR [redacted] and BCNVA in first operative eyes at Month 6 (Visit 4) and Month 12 (Visit 5)
- Photopic binocular logMAR [redacted] and BCNVA at Month 6 (Visit 4) and Month 12 (Visit 5)
- Monocular and binocular defocus curves at Month 6 (Visit 4)
- Spectacle Independence using the Patient-Reported Spectacle Independence Questionnaire (PRSIQ) at Month 6 (Visit 4)

4 STUDY DESIGN

4.1 OVERALL DESIGN

This study is a prospective, multicenter, randomized, active controlled, double masked pivotal study. It compares an investigational trifocal IOL, FINEVISION HP Trifocal IOL, and a commercially available monofocal IOL, AcrySof SN60AT[redacted] Monofocal IOL Model SN60AT[redacted] (Alcon). The study will include adult subjects with operable cataracts in both eyes 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. Subjects who meet all protocol-specified eligibility criteria will be randomized at a 2:1 ratio to receive either the FINEVISION HP Trifocal IOL (test) or the AcrySof SN60AT[redacted] Monofocal IOL (control) in both eyes. The first eye undergoing cataract surgery/IOL implantation will be the eye with the worse preoperative BCDVA. If BCDVA of both eyes is the same, the first operative eye will be the right eye. Subjects will undergo cataract surgery/IOL implantation in the second operative eye 7 – 30 days subsequent to primary eye surgery. Subjects will attend regular visits where they will undergo ophthalmic examinations over a period of approximately 12 months.

Standard clinical trial methods will be used to minimize bias, such as the use of a masked vision assessor as well as masking of subjects, standardized test procedures, common investigator training and common inclusion and exclusion criteria. [redacted]

4.2 [redacted]

[redacted]

4.3 SCIENTIFIC RATIONALE FOR STUDY DESIGN

The purpose of this clinical study is to compare the visual outcomes and safety of the FINEVISION HP Trifocal IOL to that of the AcrySof Monofocal IOL Model SN60AT[redacted] Visual outcomes evaluated will include distance, intermediate and near visual acuity. The study is designed to meet the requirements specified for multifocal IOLs in the ISO 11979-7, ISO 11979-9, and ANSI Z80.12 standards.

4.4 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 and safety assessments at the 12-month study visit (Visit 5).

5 STUDY POPULATION

The study population consists of subjects with a diagnosis of bilateral cataracts, eligible for phacoemulsification surgery followed by IOL implantation.

Subjects will be enrolled at up to 24 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 in order to achieve an even distribution across all sites.

5.1 INCLUSION CRITERIA

Eligible subjects must meet all the following inclusion criteria in order to be eligible for study participation. Ocular criteria must be met for both eyes:

1) Male or female adults, age 22 years or older at the Preoperative Visit.
2) Visually significant cataracts in both eyes that are eligible for phacoemulsification cataract surgery.
3) Willing to undergo cataract surgery in the second operative eye within 7 – 30 days after surgery in the first eye.
4) Projected BCDVA of 0.2 logMAR (20/32 Snellen) or better in each eye after cataract surgery/IOL implantation, as determined by the medical judgement of the Investigator
5) Eligible for receipt of an IOL power within the range of the investigational IOL (+10.0 D to +30.0 D, in 0.50 D increments) in each eye
6) Contact lens users must be willing to discontinue wear of their lenses in accordance with the following requirements:
   - Rigid gas permeable lenses for ≥ 7 days prior to the Preoperative Visit
   - Soft contact lenses for ≥ 3 days prior to the Preoperative Visit

   Contact lens wearers must demonstrate a stable refraction (within ±0.50 D for both sphere and cylinder) in each eye, as determined by manifest refraction on two consecutive examination dates at least one week apart after discontinuation of contact lens wear.
7) Provide signed written consent prior to participation in any study-related procedures.

8) Ability, comprehension, and willingness to follow study instructions, and likely to complete all study visits.
9) 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. Subjects may not participate if either eye meets any of the ocular exclusion criteria:

1) History or presence of, or predisposition to, degenerative visual disorders (e.g., macular degeneration, retinal detachment, proliferative diabetic retinopathy, or other retinal disorders) predicted to result in BCDVA worse than 0.2 LogMAR (20/32 Snellen) in either eye during the study participation period.
2) Significant anterior segment pathology in either eye that might increase intraoperative risk or compromise IOL stability (e.g., pseudoexfoliation syndrome)
3) Reasonably expected to require secondary ocular surgical intervention or laser treatment other than YAG capsulotomy in either eye during the study participation period.
4) Presence of one or more clinically significant corneal abnormalities in either eye, including corneal dystrophy, irregularity, or edema per the Investigator's medical opinion.
5) Previous intraocular, corneal, or retinal detachment surgery, including corneal transplant, LASIK, astigmatic keratotomy and limbal relaxing incisions in either eye
6) Rubella, congenital, traumatic or complicated cataract in either eye
7) Preoperative keratometric astigmatism > 1.0 D or irregular corneal astigmatism in either eye (Note: corneal incisions intended to reduce astigmatism are not permitted)
8) Clinically significant ocular inflammation or infection present ≤ 30 days in either eye prior to the Preoperative Visit.
9) Presence or history of one or more severe/serious ocular conditions (e.g., glaucoma, uveitis, ocular infection, severe dry eye) in either 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.
10) Use of medications known to interfere with visual performance, pupil dilation, or iris structure ≤ 30 days prior to the Preoperative Visit.
11) 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.
12) 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 operative adverse events that may prevent implantation of the designated IOLs for this clinical study. There criteria include, but are not limited to:

1) Intraoperative complications during the phacoemulsification and IOL implant that require any other additional procedures or further intervention
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 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 in the first eye and the IOL did not touch the eye, the subject should be implanted with a non-study IOL instead and discontinued from the study, followed under the Investigator's normal standard of care.

If an operative adverse event prevents implantation of the investigational IOL in the first eye and the IOL touched the eye, the Investigator should follow the subject through resolution of any adverse events (AEs) and then discontinue the subject. If an operative AE prevents implantation of the investigational IOL in the second operative eye, the Investigator should follow the subject through resolution of any AEs for the second operative eye and the subject should remain in the study and attend all study visits for the first operative eye.

5.4 SCREEN FAILURES

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

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).
- Attempt to schedule subject follow-up visits early in the visit window to facilitate rescheduling within the window, if necessary.
- Attempt to follow-up on subjects who do not return for scheduled examinations.

6 STUDY INTERVENTION

6.1 STUDY DEVICES

6.1.1 INVESTIGATIONAL DEVICE DESCRIPTION

The FINEVISION HP Trifocal IOL, shown in Figure 1, is a diffractive IOL designed to provide recipients with intermediate, near and distance vision. These lenses provide three focal points by combining two superimposed diffractive profiles, one with a +1.75 D addition at the IOL plane for intermediate vision, and the other with a +3.50 D addition for near vision. The light-energy distribution sends the greatest amount of light to distance, then near, and the least to intermediate.

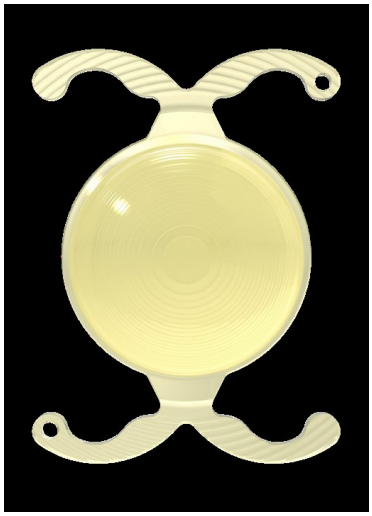


Figure 1: FINEVISION HP Trifocal IOL

The FINEVISION HP Trifocal IOL is available in powers from +10.0 D to +30.0 D in 0.50 D steps. The single-piece IOL has a double-C-loop haptic design and 5° vault. The 4 haptics are of 0.34 mm thickness. The optic portion diameter is 6.0 mm and the IOL total diameter is 11.4 mm. The device has a square edge of 360° aiming at optimal lens-tissue contact. The IOL has a biconvex aspheric optic (-0.11 microns of spherical aberration at 5 mm pupil) to adjust for the positive spherical aberration of the cornea. [redacted]

The IOL is made with the proprietary medical quality hydrophobic acrylic (GFY) (meth) acrylic material. The material includes an UV blocker and a blue light filtering chromophore.

[redacted]

6.1.2 CONTROL DEVICE DESCRIPTION

AcrySof SN60AT[redacted] Monofocal IOL Model SN60AT[redacted] from Alcon (Fort Worth, TX) is a 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 +10.0 D to +30.0 D in 0.50 D increments. [redacted] T[redacted]

6.2 DEVICE ACCOUNTABILITY AND STORAGE

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), 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, etc.) 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.

6.2.2 PACKAGING AND LABELING

The FINEVISION HP 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 SN60AT[redacted] Monofocal IOL Model SN60AT[redacted] 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 FINEVISION HP IOL or the AcrySof monofocal IOL in both eyes according to the randomization schedule (2:1 ratio) provided. Randomization will be stratified by site. The randomization schedule will be created using computer-generated randomization methodology 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.

In order to minimize bias, site personnel performing postoperative study assessments of visual performance, including manifest refraction, visual acuity, defocus curve testing and contrast sensitivity 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, etc., should 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 study IOL implantation in the first eye 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 (e.g. medical decision)
- 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 may be replaced. Randomized subjects 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. For subjects who qualify for further study participation, the primary eye will be determined, the subject will be randomized to receive the assigned study IOL, and surgery will be scheduled to occur between 1 and 90 days after the Preoperative visit. Cataract surgery/IOL implantation will be performed for the primary eye and the subject will be scheduled to return for follow-up visits and examinations at the Day 1, Week 1, Month 1, Month 6, and Month 12 time periods, consistent with study visits described in ISO 11979-7 (Form 0 through Form 5). Cataract surgery/IOL implantation in the second operative eye will be scheduled 7 – 30 days after primary eye surgery in a manner such that follow-up examinations for the second operative eye may be performed when the subject returns for scheduled primary eye visits. Data collected from each visit, including any abnormal findings, will be documented in the source records and recorded on study eCRFs.

The timing and frequency of assessments/procedures to be performed at each visit is outlined in the SoA.

Methodology for study examinations is presented in the Manual of Procedures.

8.1 PREOPERATIVE VISIT (DAY -90 TO DAY -1): VISIT 0

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 4-digit screening number, where the first two digits corresponds to the site number.

At this visit, the following activities will be performed:

- Ocular and significant non-ocular medical history*
- Projected Visual Acuity*
- UCDVA*
- BCDVA*
- Target Refraction/IOL power calculation/Axial Length/Anterior Chamber Depth (biometry)*
- Keratometry*
- Corneal Topography*
- Manifest Refraction (ETDRS)*
- Photopic/mesopic pupil size*
- Intraocular Pressure*
- Slit Lamp Exam*
- Dilated Fundus Exam*

** 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).*

For those determined to be eligible for cataract surgery/IOL implantation, the eye with the worse BCDVA will be scheduled for surgery first. If BCDVA is the same for both eyes, the right eye will be implanted first. The randomization assignment will be determined indicating which IOL will be used, and the subject's surgery will be scheduled.

8.2 OPERATIVE VISIT (DAY 0): VISIT 00 A/B

The Operative Visit for the first operative eye must occur on Day 0. The Operative Visit for the second operative eye must be scheduled between Days 7 – 30, inclusive.

At the Operative Visit, prior to surgery, subjects will be assessed to reconfirm eligibility and any changes in concomitant medications or 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 and considered a screen failure.

If operative complications prevent implantation of the investigational 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.

No additional refractive procedures are to be performed during the operative procedure or throughout the postoperative study period.

The Investigator should refer to the Manual of Procedures for more detailed guidance on FINEVISION HP implantation and AcrySof SN60AT[redacted] implantation. Subjects must be targeted as closely as possible for emmetropia. Surgeons may use their personalized A-constant for model SN60AT[redacted].

For study visits designated A or B, 'A' represents the first eye implanted (Eye A), and 'B' represents the second eye implanted (Eye B). Monocular assessments will be performed at **Visits 00 A/B, 1 A/B, 2 A/B**, and **3 A/B** for only **Eye A** or only **Eye B**, respectively, unless binocular assessments are specified (See Schedule of Activities, Section 1.3). At Visits 4 and 5, monocular assessments and binocular assessments will be completed for both eyes.

8.3 POSTOPERATIVE VISITS: VISIT 1 THRU VISIT 5

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

- Visit 1 A: 1-2 days after surgery on the first eye
- Visit 1 B: 1-2 days after surgery on the second eye

- Visit 2 A: 7-14 days after surgery on the first eye
- Visit 2 B: 7-14 days after surgery on the second eye

- Visit 3 A: 30-60 days after surgery on the first eye
- Visit 3 B: 30-60 days after surgery on the second eye

- Visit 4: 150-180 days after surgery on the first eye
- Visit 5: 360-420 days after surgery on the first eye

IOL implantation in the second operative eye is to be scheduled between 7 to 30 days after IOL implantation in the first operative eye. Subsequent Post-Op visits for the first and second eye are to be conducted as separate visits for Visits 1-3. Visits 4 and 5 must be conducted for both eyes at the same time based on timing from when the first eye was implanted.

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 regarding their eye.

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. Mandatory assessments include:

- Patient Reported Outcomes Questionnaires
- Concomitant medication
- Ocular and non-ocular medical history
- Manifest refraction
- BCDVA at 4 m (photopic) monocularly, binocularly for each implanted eye
- UCDVA at 4 m (photopic) monocularly, binocularly for each implanted eye
- Keratometry
- Slit lamp exam
- Posterior capsule assessment
- IOL observations
- IOL tilt and decentration grading
- Intraocular pressure
- IOL Axis Orientation (retroilluminated slit lamp photo) – selected sites only
- Fundus exam with dilated pupil
- 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.

8.6 SECONDARY SURGICAL INTERVENTION (SSI)

The study Investigator must make an assessment of 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, subjects feedback related to visual symptoms, and other reasons, such as observed retained lens fragments. 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. An SSI is considered related to the optical properties of the IOL if the SSI is due to subject intolerance of visual symptoms not adequately improved by spectacle correction.

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, including those related to decentration, tilt or rotation of the IOL requiring reoperation
- Surgical complications noted at the operative visit that may reasonably be expected to affect postoperative outcomes

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.

8.6.1 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 when tilt or decentration is such that repositioning is necessary to improve the visual outcomes of the subject or prevent damage to the eye.

8.6.2 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.

In the case where the subject reports visual disturbances in the early postoperative period, the surgeon should remind the subject that these symptoms generally improve over time due to neural adaptation. Therefore, adequate time should be allowed for this neural adaptation to occur. The Investigator should consult with the Medical Monitor and carefully consider the potential risks and benefits of the SSI. These should be discussed with the subject; if the subject is intolerant of persistent visual disturbances and the Investigator identifies the IOL properties as being the primary cause then lens replacement should be considered.

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

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.

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:

- Is associated with a loss of 2 or more lines of BCDVA [loss of 10 or more Early Treatment Diabetic Retinopathy Study (ETDRS) letters] at Visit 4 or later from any prior postoperative visit
- 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.

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 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 by the crystalline lens, vitreous face, or implanted device
- Retinal detachment
- Secondary surgical intervention (excluding posterior capsulotomies)

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

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.

Mild	Awareness of sign or symptom, but easily tolerated
Moderate	Discomfort enough to cause interference with normal daily activities
Severe	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:

Definite	A clear-cut causal relationship and no other possible cause
Probable	A causal relationship is likely although alternate etiologies are also possible
Possible	A causal relationship is not definite, alternate etiologies are also possible
Not Related	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.

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.

8.7.7 ANTICIPATED ADVERSE EVENTS

Anticipated AEs associated with cataract surgery and/or premium 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 obscuring the surgeon's view
- Vitreous prolapse
- Wound leak (positive Seidel)
- Posterior capsular rupture
- Choroidal detachment/hemorrhage
- Zonular dialysis
- Thermal injury (phaco burn)

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 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.]
- Corneal edema [corneal swelling (stromal or epithelial) resulting in BCDVA of 0.3 logMAR or worse at Visit 3 or later]
- Cystoid macular edema (CME) diagnosed by clinical exam and adjunct testing (eg. OCT or other method), resulting in BCDVA of ≤ 0.3 logMAR at Visit 3 or later
- Difficulty with tasks in dim light resulting in secondary surgical intervention
- 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
- Hypopyon
- Incorrect IOL power resulting in secondary surgical intervention
- Increased glare or halos
- Increased IOP (elevation of IOP ≥ 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 malposition resulting in secondary surgical intervention
- Iris or pupil damage
    - Best-corrected distance visual acuity loss of 2 lines (10 letters) or more on the ETDRS chart measured at or after postoperative Visit 4 compared to any prior postoperative 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)
- Multiple (or “ghost”) images
    - Chronic pain in the study eye, per subjective patient reporting, graded as ≥ 4 on the standardized pain rating scale (from 0 to 10), present greater than 3 months postoperative
- Reduced contrast sensitivity
- Retained lens material

- Rhegomatogenous retinal detachment (RD) (partial or complete RD associated with retinal tear)
- Secondary IOL intervention (reposition, exchange or removal)
- Synechiae formation
- Toxic anterior segment syndrome (TASS) (An acute, noninfectious inflammation of the anterior segment of the eye that develops within 24 to 48 hours after surgery, usually resulting in hypopyon and commonly presenting with corneal edema, and that improves with steroid treatment)
- Undesirable severe optical phenomena resulting in secondary surgical intervention

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 and 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 regiment (If it persists to 1 week or more it should be reported as an adverse event);
- Increased IOP that is <10mm Hg above baseline or is < 25mmHg and requires no change in standard postoperative medications regiment 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.

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 STATISTICAL HYPOTHESES

Primary Effectiveness Hypotheses

The null and alternative hypotheses for the first co-primary effectiveness analysis are:

H_{01e}: $\mu_{t1e} - \mu_{c1e} \geq 0.10$

H_{11e}: $\mu_{t1e} - \mu_{c1e} < 0.10$

Where μ_{t1e} and μ_{c1e} denote the population mean photopic monocular BCDVA (logMAR) at 4m in the first operative eyes at Month 6 (Visit 4) for the test and control IOLs, respectively.

The null and alternative hypotheses for the second co-primary effectiveness analysis are:

H_{02e}: $\mu_{t2e} - \mu_{c2e} \geq 0$

H_{12e}: $\mu_{t2e} - \mu_{c2e} < 0$

Where μ_{t2e} and μ_{c2e} denote the population mean photopic monocular DCNVA (logMAR) at 40 cm in the first operative eyes at Month 6 (Visit 4) for the test and control IOLs, respectively.

Secondary Effectiveness Hypothesis

The null and alternative hypotheses for the secondary effective analysis are:

H_{03e}: $\mu_{t3e} - \mu_{c3e} \geq 0$

H_{13e}: $\mu_{t3e} - \mu_{c3e} < 0$

Where μ_{t3e} and μ_{c3e} denote the population mean photopic monocular DCIVA (logMAR) at 66 cm in the first operative eyes at Month 6 (Visit 4) for the test and control IOLs, respectively.

Primary Safety Hypotheses

The null and alternative hypotheses for the first co-primary safety analysis are:

H_{01s}: $p_{t1s} - p_{c1s} \geq 0.014$

H_{11s}: $p_{t1s} - p_{c1s} < 0.014$

Where p_{t1s} and p_{c1s} denote the population proportion of first operative eyes at Month 12 (Visit 5) requiring secondary surgical intervention related to the optical properties of the IOL for the test and control IOLs, respectively.

9.2 SAMPLE SIZE DETERMINATION

As specified in ANSI Z80.12:2007 (R2017) *–C.4*, a minimum of 300 subjects implanted with the investigational IOL and 150 subjects implanted with the comparator IOL must be available for analysis at Visit 5 (postoperative days 330-420). To consider the potential loss of subjects between the time of enrollment and study completion, a total of approximately 501 subjects will be randomized and undergo surgery in this study. It is assumed that of approximately 501 subjects who undergo surgery, 51 subjects (10%) will be discontinued prematurely or lost to follow-up. Subjects will be randomized to receive either the investigational or comparator IOL in a 2:1 ratio. Of 501 subjects who undergo surgery, approximately 334 subjects will receive the investigational IOL and 167 subjects will receive the comparator IOL. Expecting a screen failure rate of 7%, up to 539 subjects will be enrolled in the study to have 501 subjects randomized and scheduled for surgery.

For effectiveness, 300 subjects (first operative eyes) randomized to FINEVISION HP IOL and 150 subjects (first operative eyes) randomized to AcrySof SN60AT [redacted] IOL completing through Month 6 (Visit 4) yields >99% power to reject H_{01e} in favor of H_{11e} and conclude the FINEVISION HP IOL is non-inferior to the AcrySof SN60AT [redacted] IOL in BCDVA (logMAR) at Month 6 (Visit 4), using a one-sided test with an alpha level of 0.05 and assuming no difference in mean BCDVA between test and control IOLs, a common standard deviation of 0.10 logMAR, and a non-inferiority margin of 0.10 logMAR.

Similarly with the sample size required for safety, 300 subjects (first operative eyes) randomized to FINEVISION HP IOL and 150 subjects (first operative eyes) randomized to AcrySof SN60AT [redacted] IOL completing through Month 6 (Visit 4) will have >99% power to demonstrate superiority of FINEVISION HP IOL to AcrySof SN60AT [redacted] IOL in DCIVA (reject H_{03e} in favor of H_{13e}) and DCNVA (reject H_{02e} in favor of H_{12e}) using a two-sided test with an alpha level of 0.05 and assuming a true difference in means of -0.10 logMAR (FINEVISION HP minus AcrySof SN60AT [redacted] with a common standard deviation of 0.14 logMAR.

For safety (based on ANSI Z80.12) 300 first operative eyes with FINEVISION HP IOL and 150 first operative eyes with AcrySof SN60AT [redacted] IOL completing through Month 12 (Visit 5) yields approximately 80% power to reject H_{01s} in favor of H_{11s} and conclude the FINEVISION HP IOL is non-inferior to the AcrySof SN60AT [redacted] IOL in secondary surgical interventions related to the optical properties of the IOL, using a one-sided Farrington-Manning score test with an alpha level of 0.05 and assuming the true proportion of secondary surgical interventions related to the optical properties of the FINEVISION HP IOL and of the AcrySof SN60AT [redacted] IOL is 0.001, and a non-inferiority margin of 0.014 (1.4%). Similarly, ISO 11979-7 specifies that a minimum of 300 subjects should complete a clinical evaluation of an IOL to obtain appropriate specificity around adverse event and visual acuity rates.

9.3 POPULATIONS FOR ANALYSES

Intent-to-Treat Set

The Intent-to-Treat (ITT) Set will include all randomized subjects (eyes).

All-Implanted Analysis Set

The All-Implanted Analysis Set will include all eyes with successful IOL implantation with a least 1 postoperative visit and will be the primary analysis for all effectiveness analysis.

Safety Set

The Safety Set will include all subjects with at least one eye implanted with a study lens.

Best Case Set

The Best Case Set will include subjects 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 Month 6 (Visit 4)
    - Receipt of medication likely to interfere with visual performance at Month 6 (Visit 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

[redacted]

[redacted].

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

Summaries for continuous variables will include the sample size, mean, standard deviation, median, minimum, and maximum. Summaries for discrete (categorical) variables will include the tabulation of frequencies and percentages.

The unit of analysis in this study will be the first operative eye for all primary effectiveness and safety summaries and will be the second operative eye and all eyes for supportive safety summaries; [redacted] Both eyes of each subject will be treated during the study. For those subjects whose eyes are both determined to be eligible for cataract surgery/IOL implantations at Preoperative Visit 0, the eye with the worse best-corrected distance visual acuity (BCDVA) will be scheduled for surgery first. If BCDVA is the same for both eyes, the right eye will be implanted first. Additionally, non-ocular AEs and medical history will be presented at the subject level.

9.4.2 HANDLING OF MISSING DATA

Missing data for primary and secondary efficacy analyses will be imputed under the following strategies.

Nonmonotone missing data will be multiply-imputed using treatment-based Markov Chain Monte Carlo (MCMC) methods; monotone missing data will be multiply imputed using regression methods assuming data as either missing at random or missing not at random as described below.

Primary Strategy

1. Withdrawal due to investigator's request: missing data assumed to be missing not at random. Control-based multiple imputations will be completed for superiority hypotheses and treatment-based multiple imputations will be completed for non-inferiority hypotheses. [hypothetical strategy]
2. Missing data without withdrawal or withdrawal due to reasons other than due to investigator's request: missing data assumed to be missing at random. Treatment-based multiple imputations will be completed. [hypothetical strategy]

Secondary Strategy

1. Withdrawal due to investigator's request: missing data assumed to be missing not at random. Control-based multiple imputations will be completed for superiority hypotheses and treatment-based multiple imputations, *using the worst half of the subjects who have data within the same treatment group*, will be completed for non-inferiority hypotheses. [hypothetical strategy]

2. Missing data without withdrawal or withdrawal due to reasons other than due to investigator's request: missing data assumed to be missing at random. Treatment-based multiple imputations will be completed. [hypothetical strategy]

9.4.3 ANALYSIS OF PRIMARY EFFECTIVENESS ENDPOINTS

The statistical analyses described in ISO 11979-7, ISO 11979-9, and ANSI Z80.12 will be performed unless otherwise specified in the statistical analysis plan.

The co-primary effectiveness endpoints are:

- Photopic monocular logMAR best corrected distance visual acuity (BCDVA) in first operative eyes at Month 6 (Visit 4)
- Photopic monocular logMAR distance corrected near visual acuity (DCNVA) in first operative eyes at Month 6 (Visit 4)

Primary effectiveness endpoint analyses will be based on the All-implanted Analysis Set. Imputation of missing data will be performed utilizing multiple imputation techniques under assumptions of missing at random and missing not at random following the primary strategy presented in Section 9.4.2. As sensitivity analyses, the primary effectiveness analyses will be repeated using the secondary multiple imputation strategies presented in Section 9.4.2, as well as on the ITT and Best Case Sets using the primary multiple imputation strategy only. If the results of the ITT or Best Case Set robustness analyses materially differ from the primary analyses on the All-implanted Analysis Set then the results of investigations into the cause of such differences will be presented.

Photopic monocular BCDVA in first operative eyes at Postoperative Month 6 (Visit 4) will be primarily summarized using continuous summary statistics by treatment group. The treatment effect [mean Test group IOL visual acuity (VA) minus mean Control group IOL VA] in logMAR units will be presented in addition to a two-sided 90% t-distribution confidence interval around the difference. If the upper confidence limit is less than 0.1, then H_{01e} will be rejected in favor of H_{11e} and the FINEVISION HP IOL will be considered to be statistically non-inferior to the AcrySof SN60AT[redacted] IOL in BCDVA.

Photopic monocular DCNVA in first operative eyes at Postoperative Month 6 (Visit 4) will be summarized using continuous summary statistics in logMAR units by treatment group. The FINEVISION HP IOL will be compared to the AcrySof SN60AT[redacted] IOL using a two-sample t-test with a two-sided alpha of 0.05. If the two-sided p-value < 0.05 in favor of FINEVISION HP IOL for DCNVA, then the FINEVISION HP IOL will be considered to be statistically superior to the AcrySof SN60AT[redacted] IOL in DCNVA.

The study will be considered a success only if both primary effectiveness endpoints are met.

9.4.4 ANALYSIS OF SECONDARY EFFECTIVENESS ENDPOINTS

The secondary effectiveness endpoint is:

- Photopic monocular logMAR DCIVA at 66 cm in first operative eyes at Month 6 (Visit 4)

The secondary effectiveness endpoint will be based on the All-implanted Analysis Set. Imputation of missing data and sensitivity analyses for the secondary effectiveness endpoint will be performed similarly as for the primary effectiveness endpoints.

Photopic DCIVA (66 cm) in first operative eyes at Postoperative Month 6 (Visit 4) will be summarized using continuous summary statistics in logMAR units by treatment group. The FINEVISION HP IOL will be compared to the AcrySof SN60AT[redacted] IOL using a two-sample t-test with a two-sided alpha of 0.05. If the two-sided p-value < 0.05 in favor of FINEVISION HP IOL for DCIVA, then the FINEVISION HP IOL will be considered to be statistically superior to the AcrySof SN60AT[redacted] IOL in DCIVA.

Inference will be conducted for the secondary effectiveness analysis only if all primary effectiveness endpoints are met.

9.4.5 MULTIPLICITY CONSIDERATIONS

The Type I error rate for the primary effectiveness hypothesis tests will be controlled by requiring all primary effectiveness hypothesis test results to be statistically significant to declare success for the study. The overall Type I error rate including the primary and secondary effectiveness hypothesis tests will be controlled by a hierarchical testing strategy in which statistical inference for the secondary effectiveness endpoint will only be performed if the primary effectiveness analyses are successful.

9.4.6 SAFETY ANALYSES

All safety analyses will be based on the Safety Set, unless otherwise specified.

Co-primary Safety Analyses

The co-primary safety endpoints are:

- Cumulative rate of SSIs related to the optical properties of the IOL in first operative eyes through Month 12 (Visit 5)
- Mean monocular distance contrast sensitivity (mesopic with and without glare at 1.5, 3, 6, and 12 cpd measured at 2.5m, and photopic with and without glare at 3, 6, 12, and 18 cpd, measured at 2.5m) in first operative eyes at Month 12 (Visit 5)

Descriptive statistics and analyses of co-primary safety variables will be based on first operative eyes and repeated as supportive analyses using second operative eyes as well as all operative eyes.

Secondary surgical interventions related to the optical properties of the IOL will be summarized by descriptive statistics for each IOL group. Noninferiority of FINEVISION HP IOL compared to AcrySof SN60AT[redacted] IOL in the proportions of first operative eyes with secondary surgical interventions related to the optical properties of the IOL will be evaluated using two-sided 90% Farrington method confidence intervals around the difference in proportions between the FINEVISION HP IOL and AcrySof SN60AT[redacted] IOL. If the upper limit of the confidence interval is less than 0.014, then H_{01s} will be rejected in favor of H_{11s} and the FINEVISION HP IOL will be considered statistically non-inferior to the

AcrySof SN60AT [redacted] IOL in rate of secondary surgical interventions related to optical properties of the IOL.

Monocular best-corrected distance contrast sensitivity (mesopic with and without glare at 1.5, 3, 6, and 12 cpd measured at 2.5m, and photopic with and without glare at 3, 6, 12, and 18 cpd, measured at 2.5m) in first operative eyes based on the Best Case Set will be summarized by descriptive statistics for each IOL group. The treatment group difference (mean Test group contrast sensitivity minus mean Control group contrast sensitivity) in log units will be presented by testing condition and frequency. Additionally, for each testing condition and frequency, the 5th percentile for the control group log contrast sensitivity will be determined and the percentage of subjects in the investigational arm who have achieved a log contrast sensitivity lower than this value will be reported.

Secondary Safety Analyses

The secondary safety endpoints are:

- Rates of cumulative and persistent adverse events in first operative eyes through Month 12 (Visit 5), compared to the ISO SPE rates as described in ISO 11979-7
- Visual disturbances using the QoV questionnaire and QoV Supplemental Questions at Month 12 (Visit 5)

Descriptive statistics and analyses of secondary safety variables will be based on first operative eyes and repeated as supportive analyses using second operative eyes as well as all operative eyes.

Cumulative and persistent adverse events from ISO 11979-7 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.

Visual disturbances will be assessed by the QoV questionnaire with supplemental questions at Month 12 (Visit 5). Total QoV subscale scores (frequency, severity, bothersomeness) will be summarized using continuous summary statistics by treatment group. The frequencies and proportions of subjects for each response category for each question from the QoV Supplemental Questions will be presented by treatment group.

As additional categorical analyses of the QoV questionnaire, the frequencies and proportions of subjects for each response category of frequency, severity, or bothersomeness (separately) at Month 12 (Visit 5) will be presented for each item by treatment group. Subjects' satisfaction with the IOL at Month 12 (Visit 5) will also be summarized by treatment group.

Adverse Events

Analyses of adverse events will be performed separately for first operative eyes, second operative eyes, and all operative eyes.

The incidence of operative eyes with at least one serious adverse event will be summarized using categorical summary statistics by treatment received.

Cumulative and persistent adverse events from ISO 11979-7 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. Additionally, cumulative and persistent adverse events will be summarized separately by age group (< 65 years vs. ≥ 65 years) and by investigator.

The incidence of adverse events based on consensus definitions as set forth by the American Academy of Ophthalmology's Task Force (Masket et al. Ophthalmology 2017) will be summarized by treatment group.

All types of adverse events will be reported and compared between arms using descriptive statistics. Separate analyses will be done for device-related events and events that are of moderate to severe severity. All adverse events reported will be summarized and listed by subject.

Adverse events will also be summarized for all ocular AEs and for all SAEs. All ocular AEs will also be summarized by maximal severity, for AEs related to the study lens, and by study day of onset.

In addition, the following summaries will be provided:

- Ocular AEs by relationship to study device/procedure as well as unrelated Ocular and Non-ocular AEs
- Ocular Serious AEs by relationship to study device/procedure as well as unrelated Ocular and Non-ocular Serious AEs
- Ocular AEs by maximal severity
- Ocular AEs by age group (< 65 years vs. ≥ 65 years)
- Ocular AEs by investigator

Other Safety Endpoints

YAG capsulotomy procedures (number and rate) will be summarized by descriptive statistics for each IOL group.

Other safety endpoints will be summarized descriptively by visit, including but not limited to IOP, slit lamp examination results, dilated fundus exam results, and PCO results. Changes or shifts from baseline will also be summarized where appropriate. In addition, the proportion of eyes with any worsening in BCDVA during the study of 10 letters or more (from a postoperative visit to any later postoperative visit) will be summarized. Reasons for VA worsening by 10 letters or more will be summarized. For assessments performed by eye, first operative eye and second operative eye will be summarized separately.

9.4.7 POOLABILITY ANALYSIS

Consistency of treatment effectiveness for primary and alpha adjusted secondary endpoints across sites will be evaluated through summaries by site and treatment. Additionally, a linear model will be fit with explanatory variables: site, treatment, and the site by treatment interaction, including sites with 6 or more subjects. Sites with fewer than 6 subjects will not be arbitrarily pooled into a single larger site to

be included in this model. If the site by treatment interaction is significant at a 2-sided alpha = 0.15, the cause of the significant interaction will be evaluated and presented.

Consistency of treatment safety across sites will be evaluated through summaries by site and treatment of frequency and proportion of subjects with SSI's related to the optical properties of the IOL and the cumulative and persistent adverse events in first operative eyes through Month 12 (Visit 5) as described in ISO 11979-7, ratings for each response category for each item from the QoV Supplemental Questions at Month 12 (Visit 5), as well as continuous descriptive statistics summarizing distance contrast sensitivity for each test condition at Month 12 (Visit 5) and total QoV subscale scores at Month 12 (Visit 5) by site and treatment.

9.4.8 BASELINE DESCRIPTIVE STATISTICS

Demographic variables collected in this study, including age, sex, race, and ethnicity, and baseline characteristics, including mesopic and photopic pupil size, target refraction, and keratometric cylinder for first operative eyes, will be summarized using descriptive statistics for the All-implanted Analysis Set by treatment group.

9.4.9 [redacted]

[redacted]

[redacted]

9.4.10 SUB-GROUP ANALYSES

Summary statistics for primary and secondary effectiveness endpoints, as well as primary safety endpoints, will be presented by postoperative photopic pupil size (≤ 4mm; > 4mm).

9.4.11 ADDITIONAL EFFECTIVENESS ANALYSES

All additional effectiveness analyses will be based on the All-implanted Analysis Set population unless otherwise stated.

The visual acuity exploratory endpoints are as follows:

- Photopic monocular logMAR BCDVA, [redacted], DCIVA (66 cm), and DCNVA in first operative eyes at Month 6 (Visit 4) and Month 12 (Visit 5)
- Mesopic monocular logMAR [redacted], DCIVA (66 cm), and DCNVA in first operative eyes at Month 6 (Visit 4) and Month 12 (Visit 5)
- Photopic binocular logMAR BCDVA, [redacted], DCIVA (66 cm), and DCNVA at Month 6 (Visit 4) and Month 12 (Visit 5)
- Mesopic binocular logMAR [redacted], DCIVA (66 cm), and DCNVA at Month 6 (Visit 4) and Month 12 (Visit 5)
- Photopic monocular logMAR UCDVA, [redacted], UCIVA (66 cm), and UCNVA in first operative eyes at Month 6 (Visit 4) and Month 12 (Visit 5)
- Photopic binocular logMAR UCDVA, [redacted], UCIVA (66 cm), and UCNVA at Month 6 (Visit 4) and Month 12 (Visit 5)
- Photopic monocular logMAR [redacted] and BCNVA in first operative eyes at Month 6 (Visit 4) and Month 12 (Visit 5)
- Photopic binocular logMAR [redacted] and BCNVA at Month 6 (Visit 4) and Month 12 (Visit 5)

A visual acuity variable will be summarized categorically by logMAR level by presenting the sample size, frequency, and percentage of subjects with logMAR visual acuity within the following visual acuity ranges:

- 0.00 logMAR or better
- 0.10 logMAR or better
- 0.20 logMAR or better
- 0.30 logMAR or better
- Worse than 0.30 logMAR

A visual acuity variable will be summarized categorically by Snellen level by presenting the sample size, frequency, and percentage of subjects with Snellen visual acuity within the following visual acuity ranges:

- 20/20^{-2} or better: ≤ 0.04 logMAR
- 20/25^{-2} or better: ≤ 0.14 logMAR
- 20/32^{-2} or better: ≤ 0.24 logMAR
- 20/40^{-2} or better: ≤ 0.34 logMAR
- Worse than 20/40^{-2}: > 0.34 logMAR

The visual acuity exploratory endpoints will be summarized categorically by logMAR level and Snellen level by treatment group and will also be summarized by treatment group using continuous descriptive statistics.

Additionally, photopic monocular logMAR BCDVA, DCIVA (66 cm), and DCNVA in first operative eyes at Month 12 (Visit 5) will be analyzed by repeating the primary and secondary effectiveness analyses at Month 12 (Visit 5).

The sample size, frequency, and percentage of subjects achieving logMAR visual acuity thresholds at all distances for photopic binocular logMAR UCDVA, UCIVA (66 cm), and UCNVA at Month 6 (Visit 4) and Month 12 (Visit 5) will be presented by treatment group. Similar analyses will also be performed using Snellen visual acuity thresholds.

[redacted] Monocular and binocular defocus curves from Month 6 (Visit 4) based on the Best Case Set will be summarized utilizing continuous descriptive statistics by treatment group. Defocus curve summaries by treatment group will also be presented for each of the following postoperative photopic pupil size groups:

- Small (≤ 2.5mm)
- Medium (> 2.5mm and < 4mm)
- Large (≥ 4mm)

The defocus curve means will be plotted for each treatment group and pupil size group, when applicable, with error bars representing one standard deviation. The defocus curve analyses above will be repeated at Month 12 (Visit 5) as additional analyses.

Spectacle independence as measured by the Patient-Reported Spectacle Independence Questionnaire (PRSIQ) at Month 6 (Visit 4) will be summarized using frequencies and percentages for each response category for each item and viewing distance by treatment group.

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, etc.) 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.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

The Sponsor reserves the right 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 and 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.

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 FDA and other governing regulatory authorities, as well as reviewing IRBs; however, to the extent possible, the subject's identity will not be disclosed.

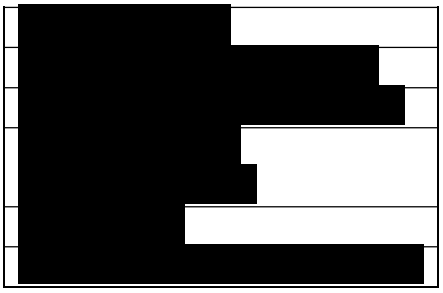
10.1.4 DOCUMENT RETENTION

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.

10.1.5 MEDICAL MONITOR



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.

10.1.7 CLINICAL MONITORING

During the study, the Sponsor or designee will perform periodic monitoring visits to study sites. 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.

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.

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).

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 Harmonisation 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 persons 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 of 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 [redacted]

[redacted]

11 REFERENCES

ANSI Z80.12: 2007 (R2017) *American National Standard for Ophthalmics - Multifocal Intraocular Lenses*

[redacted]

ISO 11979-7: 2014 *Ophthalmic implants – intraocular lenses – part 7: clinical investigations*

ISO 11979-9: 2014 *Ophthalmic implants – intraocular lenses – part 9: multifocal intraocular lenses*

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12 APPENDIX A: [redacted]

Protocol Title: Clinical Investigation of the Safety and Effectiveness of FINEVISION HP Trifocal IOL

Study number: PHY1903

Protocol Date: [redacted]

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.

[redacted]