Title

Clinical Investigation of the Visual Outcomes and Safety after Bilateral Implantation of a Trifocal Presbyopia Correcting IOL in A Korean Population

Protocol Number:	ILH297-P004 / NCT03268746
Development Stage of Project:	Product Support
Sponsor Name and Address:	Alcon Research, Ltd. and its affiliates ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099 Alcon Korea Ltd. 6F Glasstower, Teheran-ro 534 Gangnam-gu, Seoul 06181, Korea
Test Product:	The ACRYSOF® IQ PanOptix™ Presbyopia Correcting intraocular lens (IOL), Model TFNT00
Investigator Agreement:	I have read the clinical study described herein, and recognize its confidentiality. I agree to conduct this study in accordance with the ethical principles contained within the Declaration of Helsinki, and the described study in compliance with the protocol, Good Clinical Practice (GCP), ISO 14155, and all applicable regulatory requirements. Additionally, I will comply with all procedures for data recording and reporting, will permit monitoring, auditing, and inspection of my research center, and will retain all records until notified by the Study Sponsor.
Principal Investigator:	

_____

Signature Date

Name and professional position:

Address:

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1 GLOSSARY OF TERMS

Names of test product(s)	Throughout this document, the test product(s) will be referred to as "The ACRYSOF IQ PanOptix Presbyopia Correcting intraocular lens (IOL), Model TFNT00."
Name of Control Product(s)	N/A
Adverse Device Effect	Adverse event related to the use of an investigational medical device (test product) or control product. *Note: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation; any malfunction; and use error or intentional misuse of the test product or control product.*
Adverse Event	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device (test product). *Note: For subjects, this definition includes events related to the test product, the control product, or the procedures involved. For users or other persons, this definition is restricted to events related to the test product.* Requirements for reporting Adverse Events in the study can be found in Section 11.
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. *Note: This definition includes malfunctions, use errors, and inadequate labeling.* Requirements for reporting Device Deficiencies in the study can be found in Section 11.

Enrolled Subject	Any subject who signs an informed consent form for participation in the study.
Interventional Clinical Trial	A research trial that prospectively assigns, whether randomly or not, human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes, and/or a research trial in which diagnostic or monitoring procedures beyond standard of care are conducted and generate outcomes for use in analysis of data.
Investigational Product	Is defined as a preventative (vaccine), a therapeutic (drug or biologic), device, diagnostic, or palliative used as a test or control product in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the authorized form, or when used for an unauthorized indication, or when used to gain further information about the authorized form.
Malfunction	Failure of a medical device to meet its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the labeling of the device. The intended performance of the device refers to the intended use for which the device is labeled or marketed.
Non-serious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.
Postmarketing/Post-authorization study	Any study conducted within the conditions laid down in product labelling and other conditions laid down for the marketing of the product or under normal conditions of use. A postmarketing study falls either within the definitions of an interventional or a non-interventional study and may also fall within the definition of a post-approval study.

Produ ct Complaint s	Any oral, electronic, or written communication that alleges deficiencies related to the identity (labeling), quality, durability, reliability, safety, effectiveness, or perfo1mance of a marketed product, including failure of the product, labeling or packaging to meet specifications, whetheror not the product is related to or caused the alleged deficiency. A complaint may allege that an adverse event or medical device malfunction has occuffed.
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Serious Adverse Event (SAE)	Adverse event that led to any of the following: • Death. • A serious deterioration in the health of the subject that either resulted in: a. A life-threatening illnessor injmy. *Note: Life-threatening means that the individual was at immediate risk of death from the event as it occurred, ie, it does not include an event which hypothetically might have caused death had it occurred in a more severe form.* b. Any potentially sight-threatening event or pe1manent impai1ment to a body strncture or a body function. c. fu -patient hospi ta lizatio n or prolonged hospitalization. *Note: Planned hospitalization for a pre-existing condition, without serious deterioration in health, is not considered a serious adverse event. In general, hospitalization signifies that the individual remained at the hospital or emergency ward*

	for observation and/or treatment (usually involving an overnight stay) that would not have been appropriate in the physician's office or an out-patient setting. Complications that occur during hospitalization are adverse events. If a complication prolongs hospitalization orfulfills any other serious criteria, the event is serious. When in doubt as to whether " hospitalization" occurred, the event should be considered serious. *d.* A medical or surgical intervention to prevent a) or b). Or any ocular secondaly surgical intelvention excluding posterior capsulotomy. *e.* Any indirect harm as a consequence of incon ect diagnostic test results when used within manufacturer's instructions for use. • Fetal distress, fetal death, or a congenital abn01ma1ity or biith defect. *Refer to Section 11 for additional SAEs.*
Use En or	Act or omission of an act that results in a different medical device response than intended by manufacturer or expected by user. *Note: This definition includes slips, lapses, and mistakes. An unexpected physiological response of the subject does not in itself constitute a use error.*

2 LIST OF ACRONYMS AND ABBREVIATIONS

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

Abbreviation	Definition
AAS	All-implanted analysis set
ACD	Anterior chamber depth
ADE	Adverse device effect
AE	Adverse event
AL-8739	N-2-[3-(2-Methylphenylazo)-4-hydroxyphenyl]ethyl metharcylamide
BCVA	Best corrected visual acuity
BCDVA	Best corrected distance visual acuity
BDDA	1,4-Butanediol diacrylate
BSS	Balanced salt solution
°C	Degrees Celsuis
CFR	Code of Federal Regulations
CI	Confidence interval
CRF	Case report form
cm	Centimeter
CM	Clinical manager
D	Diopter
DEP	Deviations and Evaluability Plan
eCRF	Electronic case report form
EDC	Electronic data capture
ETDRS	Early Treatment Diabetic Retinopathy Study
EU	European Union
FAS	Full Analysis Set
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
I/A	Irrigation/aspiration
IEC	Independent ethics committee
ICF	Informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IOL	Intraocular lens
IOP	Intraocular pressure
IP	Investigational product
IRB	Institutional review board
ISO	International Organization for Standardization
LASIK	Laser assisted in situ keratomileusis
LogMAR	Logarithm of the minimum angle of resolution
MedDRA	Medical Dictionary for Regulatory Activities
MFDS	Ministry of Food and Drug Safety
m	Meter
mm	Millimeter

Abbreviation	Definition
mmHg	Millimeters of mercury
MOP	Manual of procedures
N/A	Not applicable
OD	Right eye
oMTP	o-Methallyl Tinuvin P
OVD	Ophthalmic viscosurgical device
PC	Posterior capsulotomy
PCO	Posterior capsular opacification
PEA	2-Phenylethyl acrylate
PEMA	2-Phenylethyl methacrylate
SADE	Serious adverse device effect
SAE	Serious adverse event
SLE	Slit-lamp exam
SOP	Standard operating procedures
SSI	Secondary surgical intervention
UCDVA	Uncorrected distance visual acuity
UCIVA	Uncorrected intermediate visual acuity
UCNVA	Uncorrected near visual acuity
US	United States
VA	Visual acuity
WHO	World Health Organization
YAG	Yttrium aluminium garnet

3 PROTOCOL SUMMARY

Investigational product type	Device
Study type	Interventional
Investigational products	Test Product: The ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 is a single-piece ultraviolet and blue light filtering foldable multifocal IOL. The biconvex optic is 6.0 mm in diameter and the lens has an overall diameter of 13.0 mm. The multifocal optic diffractive structure is in the central 4.5 mm portion of the anterior surface of the optical zone and divides the incoming light to create a +2.17 D intermediate and a +3.25 D near add power (IOL plane). The anterior surface is designed with 0.1 microns of negative spherical aberration to compensate for the positive spherical aberration of the average human cornea. This product is a multifocal IOL that corrects aphakia, a condition that prevents patients from

	seeing things at near and/or at distance, by replacing the cataractous lens after cataract surgery in an adult patient. It is inserted into the capsular bag and has near vision and intermediate add power (3.25 D, 2.17 D).
Purpose and rationale	The ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 has a multifocal design and provides a near focal point at 40 cm and distance vision similar to a traditional multifocal IOL, but with the additional benefit to patients of an intermediate focal point at 60 cm. The present study (ILH297- P004) is intended to confirm the effectiveness of the investigational lens in a Korean population, especially for visual performance, quality of vision, and subject satisfaction with the visual outcome, as well as the safety of the lens.
Objective(s)	Primary effectiveness objectives: Describe binocular defocus curve at 3 months (Visit 4A) post bilateral implantation of the ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 in a Korean population. Secondary effectiveness objectives: 1. Describe binocular defocus curve at 1 month (Visit 3A) post bilateral implantation. 2. Describe binocular BCVA at 4 m at 1 and 3 months (Visit 3A and Visit 4A) post bilateral implantation. 3. Describe both uncorrected binocular and monocular mean VA at 1 and 3 months (Visit 3A and Visit 4A) post bilateral implantation. 4. Describe photopic contrast sensitivity at 3 months (Visit 4A) post bilateral implantation. 5. Describe subjective symptom questions outcome at 3 months (Visit 4A) post bilateral implantation. [redacted]

	[redacted]
	Safety objectives: Assess safety during the study up to 3 months (Visit 4A) post bilateral implantation of the ACRYSOF IQ PanOptix Presbyopia Con ecting IOL, Model TFNTOO in a Ko rean pop ul ation.
Endpoin t(s)	Prima 1y Effectiveness: • Binocular defocus curve at 3 months (Visit 4A) post bilateral implantation Seconda1y Effectiveness: • Binocular defocus curve at 1 month (Visit 3A) post bilateral implantation • Best conected binocular visual acuity at distance (4 m) at 1 and 3 months (Visit 3A and Visit 4A) post bilateral implantation. • Mean visual acuity at 1 and 3 months (Visit 3A and Visit 4A) post bilateral implantation. o Monocular UCDVA (4 m) o Monocular UCIVA (60 cm) o Monocular UCNVA(40 cm) o BinocularUCDVA(4m) o Binocular UCIVA (60 cm) o Binocular UCNVA (40 cm) • Photopic best conected binocular contrast sensitivity with and without glare at 3 months (Visit 4A) post bilateral implantation. • Subjective symptoms questions at preoperatively and 3 months (Visit 4A) post bilateral implantation.
	[redacted]

	Safety: • All adverse events (ocular and nonocular, serious and non-serious) including seconda1y surgical interventions (SSis) related to the optical prope1iies of the IOL for either eye. • Device deficiencies • Posterior capsule opacification • Posterior capsulotomy • IOL position change (tilt and decentration) • Intraocular pressure • Surgical problems
Assessment(s)	Effectiveness: All the effectiveness assessments will be conducted in photopic lighting conditions except the subjective symptoms assessment. • Distance VA(4 m), o Monocular (1st and/or 2nd eye) UCDVA o Binocular UCDVA o Binocular BCDVA • Inte1mediate VA (60 cm) o Monocular (1st and/or 2nd eye) UCIVA o Binocular UCIVA • Near VA (40 cm) o Monocular (1st and/or 2nd eye) UCNVA o Binocular UCNVA • Binoc ular defocus curve • [redacted] • [redacted] • Best conected binocular contrast sensitivity with & without glare • Subjective symptoms

	Safety • Adverse DeviceEvents including Seconda1y Surgical Interventions (SSis) related to the optical prope1iies of the IOL • Device deficiencies • Fundus examination and fundus visualization • Intraocular pressure • Slit-lamp examination • IOL observations • Surgical problems • Subjective posterior capsule opacification • Posterior capsulotomy • Lens decentration and tilt
Study Design	This is a prospective, single aim, unmasked, non-randomized, multi-center study. Study subjects will be followed for 90-120 days.
Subject population	The study population consists of adult Korean males and females, at least 20 years of age or older at the time of screening, with no ocular pathology that could confound study outcomes, who require cataract extraction in both eyes and desire an IOL that provides the potential for near, inte1mediate, and distance vision.
Key inclusion criteria (See Section 8.1 for a complete list of inclusion criteria)	• Adults, at least 20 years of age or older at the time of screening, of either gender in Korea, who require cataract extraction in both eyes. • Clear intraocular media other than cataract in both eyes. • Calculated lens power between+16.0 and +24.0 D. • Preoperative OR expected postoperative regular corneal astigmatism of < 1.00 D.
Key exclusion criteria (See Section 8.2 for a complete list	• Pregnancy or lactation • Clinically significant corneal abn01malities including corneal dystrophy (eg, epithelial, stromal or endothelial dystrophy), inflammation or edema per the Investigator's expe1i medical

of exclusion critelia)	op1mon. Note: Conditions including, but not limited to: keratitis, keratoconjunctivititis, keratouveitis, keratopathy, or keratectasia should be excluded. • Previous corneal transplant. • Ocular trauma, previous refractive surgery , or refractive procedures throughout the entire duration of the subjects' participation in the clinical study (including, but not limited to LASIK, astigmatic keratotomy, and limbal relaxing incision). • Hist01y of or conc un ent retinal conditions or predisposition to retinal conditions, previous histo1y of, or a predisposit ion to, retinal detachment or presence of diabetic retinopathy that the Investigator judges could confound outcomes. Note: Including but not limited to background diabetic retinopathy, diabetic macular edema, or proliferative diabetic retinopathy, macular degeneration. • Amblyopia. • Rubella, congenital, traumatic, or complicated cataract. • Extremely shallow anterior chambe r (:S 2.5 mm), not due to swollen cataract. • Any cmTent ante rior or posterior segment inflammation of any etiology, and/or histo1y of any disease producing an intraocular inflammat01y reaction . • Iris neovascularization. • Optic nerve atrophy. • Subjects with diagnosed degenerative eye disorder (eg, macular degeneration or other retinal disorders). • Known color vision deficiencies. • Subjects who may reasonably be expected to require an ocular surgical treatment at any time dming the surge1y (other than YAG capsulotomy).

	• Situations where the need for a large capsulotomy can be anticipated (eg, diabetics, retinal detachment in the fellow eye, peripheral retinal pathology). • Subjects who are expected to require retinal laser treatment. • Any subjects cun ently paiticipating in another investigational mug or device study that may confound the results of this investigation. • Any other conditions that may not be appropriate to this study, as per the Investigator's expert medical opinion. (In the expert opinion of the Investigator, any condition that would be expected to reduce the potential postoperative BCDVA to a level worse than 0.30 logMAR.)
Data analysis and sample size justification	All patients with attempted IOL implantation (successful or aborted after contact with the eye) are considered evaluable for the safety analysis. All patients with successful bilateral IOL implantation and have the bilateral measmements for defocus curve are considered evaluable for Full analysis set with effectiveness analysis. Effectiveness Analysis No formal statistical hypothesis testing is planned for the effectiveness endpoints. The data will be summarizedusing descriptive statistics. All continuous variables will be presented with the following summary statistics: mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized by count and percentage. The con esponding two-sided 90% confidence intervals will be presented for the effectiveness variables if deemed appropriate. Prima1y Effectiveness Binocular defocus will be summarized, and a plot will be generated for the defocus curve with amount of defocus along the x-axis and logMAR visual acuity at each defocus along the y-axis for the Month 3 visit. Seconda1y [redacted] Effectiveness For both seconda1y [redacted] effectiveness variables, the data

	will be summarized descriptively. Binocular defocus curve will be summarized, and a plot will be generated for the defocus curve with amount of defocus along the x-axis and logMAR visual acuity at each defocus along the y-axis for the Month 1 visit. Binocular BCVA at distance, and monocular and binocular UCVA at near, intermediate, and distance will be summarized by visit with descriptive statistics. Binocular contrast sensitivity with/without glare will be summarized descriptively at the Month 3 visit. Subjective symptoms outcome will be summarized per symptom with frequency and percentage presented for each modality of responses. [redacted] <u>Safety</u> Rate of SSIs related to the optical properties of the IOL for either eye during the study will be summarized by eye. All AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) and will be presented by severity (mild, moderate, or severe) and relationship to the test product. Device deficiencies, posterior capsule opacification, posterior capsulotomy, surgical problems, and IOL position change (tilt and decentration) will be summarized descriptively. Intraocular pressure at each visit and change from baseline will be summarized accordingly, Assuming a standard deviation of 0.17 logMAR with defocus visual outcomes, 40 subjects will have more than 99% probability to observe the half width of 90% two-sided confidence interval will be no more than 0.06 logMAR at each defocus. The precision of estimates are within ±3 letters with visual outcomes. Assuming a dropout rate of 10% at Month 3, approximately 44 subjects will be bilaterally implanted to ensure that data for at least 40 subjects is available at Month 3.
Clinical trial duration	a. Total expected duration of the clinical investigation: approximately 12 months b. Expected duration of each subjects' participation : approximately between 3 ~7 months

	c. Planned follow-up duration: about 3 – 4 months post 2nd eye implantation d. Enrollment period : approximately 5 months (The recruit period can be extended if 44 bilaterally implanted subjects cannot achieve 40 evaluable due to unilateral implantation or exclusion after screening visit.).
Key words	Prospective, Single Arm, Unmasked, Non-Randomized, Multi-Center Study, Cataract, Bilateral implantation, The ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00, Trifocal, Korea
Associated materials	Biohazard labeled bag

Table 3-1 Schedule of Study Procedures and Assessments

		1 Operative Eye			2n Operative Eye			Both Eyes		
Visit										
General Assessments and Procedur										
Inf01med Consent	X									
Demo graphics	X									
Medical Hist01y	X									
Concomitant Medications	X	X	X	X	X	X	X	X	X	X
Urine Pre anc Test	X									
Inclusion/Exclusion	X	X			X					
Administer Treatment(s)		X			X					
0 _ hthalmic Assessments										
Distance VA at 4 m										
• Monocular Unconected				X9			xio	X6	X6	
• Bino c u l ar Uncon e cte d								X	X	
• Monocular Best Conected	X									
• Binocular Best Conected	X							X	X	
Intermediate VA at 60 cm										

		1st Operative Eye			2nd Operative Eye			Both Eyes		
Visit										
• Monocular Uncorrected				x9			xlO	x6	x6	
• Binocular Uncorrected								X	X	
Near VA at 40 cm										
• Monocular Uncorrected				x9			XlO	x6	x6	
• Binocular Uncorrected								X	X	
Limiting measurements	X			X			X	X	X	
Photopic Best Corrected Contrast Sensitivity with & without Glare									X	
Subject symptoms	X								X	
Slit-Lamp Examination	X		X	X		X	X	X	X	X'
IOL Observations			X	X		X	X	X	X	X'
Lens decentration and tilt (IOL Position Change)			X	X		X	X	X	X	x1
Subjective PCO			X	X		X	X	X	X	X'
Posterior Capsulotomy			X	X		X	X	X	X	X'
Dilated Fundus Examination	X							X	X	X'

		1st Operative Eye			2nd Operative Eye			Both Eyes		
Visit	**Visit 0** Day -60-0 Preoperative	**Visit 00**[1] Day 0 Operative	**Visit 1** Day 1-2 Post Visit 00	**Visit 2** Day 7-15 Post Visit 00	**Visit 00A**[2] 2-30 Days Post Visit 00	**Visit 1A** Day 1-2 Post Visit 00A	**Visit 2A** 7-15 Days Post Visit 00A	**Visit 3A** 30-60 Days Post Visit 00A	**Visit 4A**[3] 90-120 Days Post Visit 00A	**Unscheduled Visit**
Fundus Visualization								X	X	
Intraocular Pressure	X		X	X		X	X	X	X	X[7]
Surgical Procedure & Assessments										
Surgical report (including implanting surgeon, lens power, implant success, OVD and target refractive error[5])		X			X					
Operative eye		X			X					
Surgical problems		X			X					
Lens Information		X			X					
Final Incision Size		X			X					
IOL damage		X			X					
Other Surgical Procedures		X			X					
Adverse Events & Device Deficiencies										
Adverse Events[8]	X	X	X	X	X	X	X	X	X	X
Secondary Surgical Interventions		X	X	X	X	X	X	X	X	X
Device Deficiencies		X	X	X	X	X	X	X	X	X

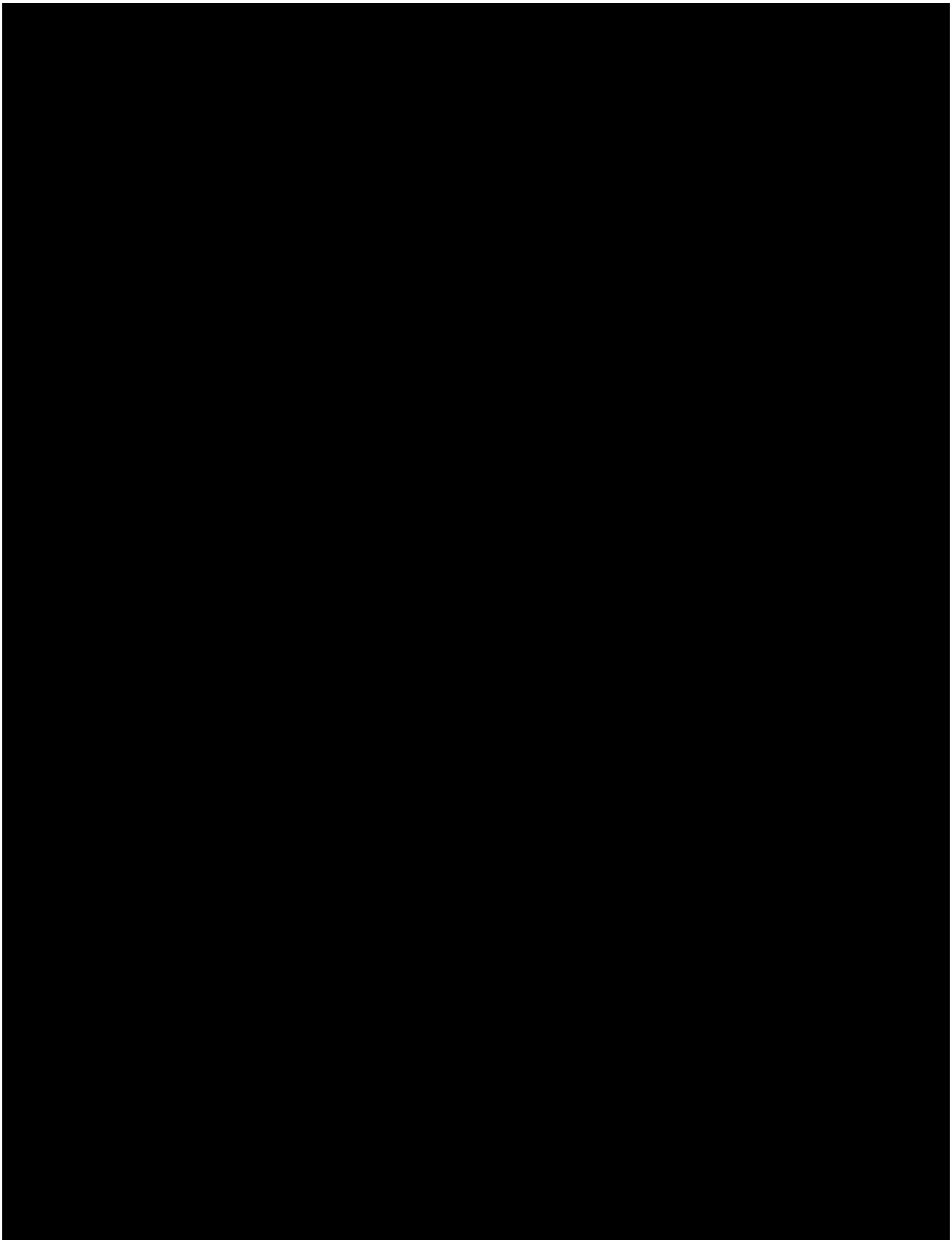
1. Visit 00 (1st eye surgery) must occur within 60 calendar days from Preoperative Visit (Visit 0).
2. Visit 00A (2nd eye surgery) must occur after a minimum of 2 calendar days and a maximum of 30 calendar days after Visit 00.
3. If necessary, Visit 4A may be completed over 2 days within a two-week period. Both days must fall within the specified visit window.

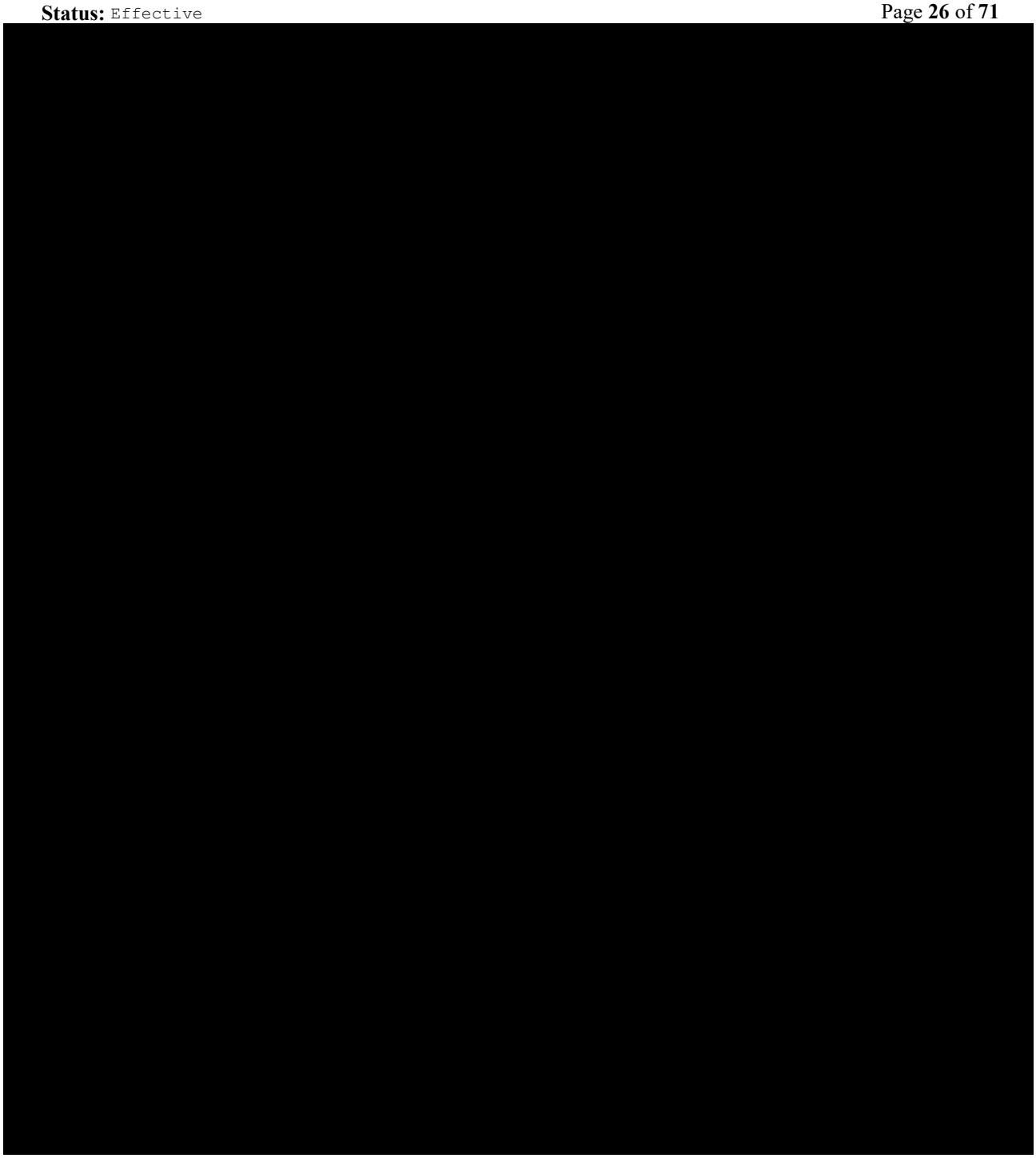
4. In women of child-bearing potential only.
5. Data is reported in EDC at the surgical visit, but may be collected at a previous visit.
6. Testing is conducted monocular bilaterally.
7. Only measure in case considered necessary per the investigator's medical opinion.
8. Collected from time of consent onward.
9. 1st operative eye.
10. 2nd operative eye.

4 PROTOCOL AMENDMENTS

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

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





5 INTRODUCTION

5.1 Rationale and Background

Monofocal IOLs are designed to replace the focusing power of the natural lens (typically after cataract surgery) by providing good visual function through a single, fixed, focal length; thus, generally correcting a subject's distance vision. However, many pseudophakic subjects

implanted with monofocal IOLs ultimately require reading glasses to compensate for the loss of the ability to see clearly at intermediate or near distances. Several IOL designs for compensating the accommodation in pseudophakic subjects exist in modern day clinical practice, including multifocal IOLs. Multifocal IOLs offer subjects an opportunity to overcome the loss of near and intermediate vision by providing multiple focal points. The majority of commercially available multifocal IOLs provide two optical zones for distance and near vision. The ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 uses technology similar to commercially available multifocal IOLs to create an additional focal point for intermediate vision.

The ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 has a multifocal design and provides a near focal point at 40 cm and distance vision similar to a traditional multifocal IOL, but with the additional benefit to patients of an intermediate focal point at 60 cm. The ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 has received CE Marking in European countries and is also approved in many other countries around the world. In Korea, a product import license was granted by the Ministry of Food and Drug Safety on April 12, 2017.

The ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 delivers 3 focal points, including the intermediate range at approximately 60 cm, while competitive trifocal IOLs are at 80 cm. For many patients, critical work is performed at arm's length (60 to 70 cm). The ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 aims to provide greater initial acceptance and patient satisfaction by creating an intermediate focal point at 60 cm as opposed to 80 cm as in competitive trifocal designs. Alcon has received approval to market the ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 with a CE mark in the European Union, and it is currently on the market in the EU and Australia. The interim, 6-month post-implantation results have been presented in ASCRS 2017; the lens demonstrated approximate visual acuity of 20/25 or better from near (40 cm) through intermediate (60 cm) to distance. In Korea, Alcon has also received the approval to market as of April 12, 2017. So far, there were no clinical results in Korean populations for this lens.

Similar to other Asian countries, the prevalence of myopia in South Korea is relevantly high, and many people need to wear glasses from childhood. Relevantly young cataract patients will have a strong desire for an extended range of intermediate vision for daily activities such as computer use, as well as near and distance vision after their cataract surgery; these patients are expected to have a strong desire to be spectacle independent. Additionally, the body height of the Korean population is shorter than the European or Australian population.

According to the Korea National Statistical Office, the average height of a Korean male is 172.2 cm and the average height of a Korean female is 158.6 cm. The average arm length for a Korean male is 58.8 cm and the average arm length for a Korean female is 53.8 cm. Because the ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 is designed to have an intermediate focal point of about 60 cm, it is estimated that Koreans will have greater patient satisfaction with this new trifocal IOL; however, this claim is not currently supported since there are no clinical results in the Korean population.

5.2 Purpose of the Study

The present study (ILH297-P004) is intended to confirm the effectiveness of the investigational lens in a Korean population, especially for visual performance, quality of vision, and subject satisfaction with the visual outcome, as well as the safety of the lens.

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

Results of the study are intended for publication and all data and discoveries arising out of the study, patentable or non-patentable, shall be the sole property of Alcon, Inc. Alcon may use these data now and in the future for presentation or publication at Alcon's discretion or for submission to government regulatory agencies.

5.3 Risks and Benefits

Complications may occur on the surgery day or throughout the postoperative period. As with any type of intraocular surgery, there is a possibility of complications due to anesthesia, drug reactions, and surgical problems. The surgical procedure can exacerbate a pre-existing ocular condition. Possible problems during surgery include corneal endothelial touch, detached Descemet's membrane, iris damage, iris prolapse, iris trauma, iris incarceration, zonular rupture, vitreous loss, capsulorhexis tear, capsular rupture, uncontrollable intraocular pressure, hyphema, and endothelial cell loss. An IOP increase may occur from the surgical procedure, residual viscoelastic in the eye, or a steroid response to postoperative medications.

Additionally, potential postoperative adverse events include corneal stromal edema, cystoid macular edema, endophthalmitis, hypopyon, iritis, lens dislocation, membrane formation on the IOL, pupillary block, retinal detachment, cyclitic membrane, transient or persistent glaucoma, retinal tear, vitritis, irtis touch, pupil ovalization, posterior synechiae, ocular inflammation, and endothelial cell loss.

An IOL replacement or explantation may be appropriate in some cases of residual refractive error, ocular infection, subject dissatisfaction, or visual disturbances (eg, glare, halos, starbusts, hazy vision, blurred vision, double vision, visual distortions, and color distortions).

A secondary surgical intervention (eg, IOL repositioning, replacement, or explantation) may be appropriate if the IOL position significantly differs from the intended placement. Alternatively, spectacles or contact lenses may be prescribed to resolve residual refractive error. Other secondary surgical interventions include, but are not limited to: refractive laser treatment, paracentesis, vitreous aspirations, iridectomy or laser iridotomy for pupillary block, wound leak repair, and retinal detachment repair. Postoperatively, the subject may experience ocular discomfort or pain, inflammation, decreased vision, decreased contrast sensitivity, decreased color perception, and visual disturbances.

The ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 is a multifocal lens intended to provide optical performance and spectacle independence similar to the ACRYSOF IQ RESTOR +3.0 D Multifocal IOL (Model SN6AD1) at near (40 cm) and distance, with the additional benefit of intermediate vision at 60 cm.

After CE mark approval in EU, a postmarket clinical investigation of the ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 was conducted at 14 clinical sites in regions where the ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 is approved for commercial distribution (Australia, Belgium, Chile, France, Germany, Italy, Netherlands, Spain, and the United Kingdom). This study was a prospective, single arm, unmasked, non-randomized, multi-center study. The objective was to describe visual outcomes and confirm long-term safety and performance at 12 months (330-420 days) post bilateral implantation of the ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00. The 6-month interim analysis results showed that the ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00could provide simultaneous visual performance for near, intermediate, and distance with a mean VA of 20/20 for distance and a mean VA of 20/25 for intermediate and near vision. The ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 is safe when implanted according to the approved label.

Based upon the formal risk assessment, the ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 demonstrates a favorable risk profile that is comparable to previously approved ACRYSOF multifocal IOLs. The ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 is designed to provide the benefit of increased intermediate vision while maintaining visual performance at near and distance. Potential risks following implantation of ACRYSOF IQ PanOptix Presbyopia Correcting IOL include visual

disturbances such as glare and halos, which are known risks for multifocal IOLs. The benefits of improved intermediate vision, when weighed against the risks of visual disturbances, result in a benefit to risk profile that is favorable for the ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00.

There may also be unknown risks with the use of ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00. Any risk to subjects in this clinical study will be minimized by compliance with the eligibility criteria and study procedures, as well as clinical oversight and monitoring. The risk uncertainty is quite low due to the commercialization of PanOptix.

Refer to the product label for additional information.

6 STUDY OBJECTIVES

6.1 Primary Objective(s)

Table 6–1 Primary Objective(s)

Objective(s)	Endpoint(s)
Describe visual outcomes (binocular defocus curve) at 3 months (90-120 days) post bilateral implantation of the ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 in a Korean population.	Binocular defocus curve at 3 months post-implantation (Visit 4A, 90-120 days)

6.2 Secondary Objective(s)

Table 6–2 Secondary Objective(s)

Objective(s)	Endpoint(s)
1. Describe binocular defocus curve at 1 month (30-60 days) post bilateral implantation.	1. Binocular defocus curve at 1 month post-implantation (Visit 3A, 30-60 days)
2. Describe BCDVA 4m at 1 and 3 months (Visit 3A and Visit 4A) post bilateral implantation.	2. Best corrected binocular visual acuity at distance (4 m) at 1 and 3 months post-implantation (Visit 3A and Visit 4A)
3. Describe mean UCVA at 1 and 3 months (Visit 3A and Visit 4A) post	3. Mean visual acuity at 1 & 3 months

bilateral implantation.

4. Describe contrast sensitivity at 3 months (Visit 4A) post bilateral implantation.

5. Describe subjective symptom at 3 months (Visit 4A) post bilateral implantation.

post-implantation (Visit 3A and Visit 4A)

a) Monocular UCDVA (4 m)

b) Monocular UCIVA (60 cm)

c) Monocular UCNVA (40 cm)

d) Binocular UCDVA (4 m)

e) Binocular UCIVA (60 cm)

f) Binocular UCNVA (40 cm)

4. Photopic best corrected binocular contrast sensitivity at 3 months post-implantation (Visit 4A)

5. Subjective symptom questions preoperatively and 3 months post-implantation (Visit 4A)

6.4 Safety Objective(s)

Table 6–4 Safety Objective(s)

Objective(s)	**Endpoint(s)**
Assess safety during the study up to 3 months (90-120 days) post bilateral implantation of the ACRYSOF IQ PanOptix	1. All adverse events (ocular and nonocular, serious and non-serious) including secondary surgical

Presbyopia Correcting IOL, Model TFNT00 in a Korean population.	interventions (SSIs) related to the optical properties of the IOL for either eye. 2. Device deficiencies 3. Posterior capsule opacification 4. Posterior capsulotomy 5. IOL position change (tilt and decentration) 6. Intraocular pressure 7. Surgical problems

7 INVESTIGATIONAL PLAN

7.1 Study Design

This is a prospective, single-arm, unmasked, non-randomized, multi-center study of the ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00.

Both eyes of a subject must require cataract surgery to qualify for enrollment into this study.

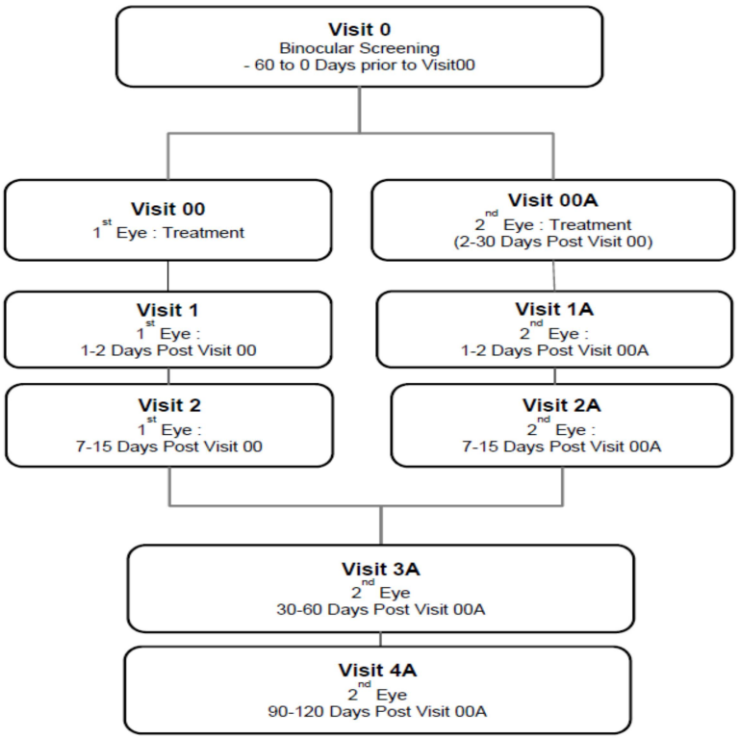
The first operative eye is defined as the eye with the worse BCDVA at screening visit. If BCDVA is the same in both eyes, identify the right eye (OD) as the first operative eye. The second eye implant can occur according to each participating site's standard visit schedule; however, it must occur within 30 days of the first eye implant.

A total of 9 scheduled visits are planned (some scheduled visits may be conducted on the same day due to the visit window) and subject participation is expected to last 3-7 months. The visits include a Screening visit (Visit 0), 2 Operative Visits (Visit 00 and Visit 00A), and 6 postoperative visits at the following intervals: Day 1-2 (Visit 1/1A), Day 7-15 (Visit2/2A), Day 30-60 (Visit 3A), and Day 90-120 (Visit 4A) (See Figure 7-1 Study Design). Primary endpoint data will be collected at the Month 3 visit / Visit 4A (90-120 day post 2nd eye implantation).

Note: Visit 4A may be completed over 2 days within a 2-week period. Both days must fall within the specified visit window.

The schedule of visits is shown below:

Figure 7-1 Study Design



7.2 Rationale for Study Design

The ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 has a multifocal design and provides a near focal point at 40 cm and distance vision similar to a traditional multifocal IOL, but with the additional benefit to patients of an intermediate focal point at 60 cm. Since ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 was approved in EU countries, its safety and effectiveness has been proven through postmarketing clinical use and clinical trials. However, no formal clinical trial has been conducted in Korea to demonstrate the safety and effectiveness in the Korean patient population since its approval.

The purpose of this clinical study is to describe the visual outcomes of this lens at near, intermediate, and distance, and to confirm the expected multifocal vision with this lens by measuring the binocular defocus curve in a Korean population. With well-established safety and effectiveness from EU clinical use data and an acknowledged standard of visual outcomes, a single arm, multi-center study was considered sufficient to describe the visual outcomes and safety of the ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 in a Korean population.

The study is also designed to assess performance and safety parameters of interest in compliance with guidance from ISO 11979-9:2006(E), with minor modifications reflecting the standard visit schedule of modern teaching university hospitals in South Korea.

7.2.1 Purpose and Timing of Interim Analyses and Resulting Design Adaptations

Not applicable.

7.3 Rationale for Duration of Treatment/Follow-Up

The duration of use of the product is in accordance with product labeling. The follow-up visit schedule is in accordance with clinical practice, and the follow-up duration is sufficient based upon the well-established effectiveness and safety profile of the ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 in the EU and Australia.

7.4 Rationale for Choice of Control Product

Not applicable.

7.5 Data Monitoring Committee

Not applicable.

8 STUDY POPULATION

The study population consists of adult Korean males and females, at least 20 years of age or older at the time of screening, with no ocular pathology that could confound study outcomes, who require cataract extraction in both eyes and desire an IOL that provides the potential for near, intermediate, and distance vision. Bilateral cataract extraction is planned in approximately 44 subjects in approximately 4 sites in Korea, with a target of 5 to 15 subjects per site. Site-specific targets may vary based upon individual site capabilities. Estimated time needed to recruit subjects for the study is approximately 5 months. The recruit period can be extended if 44 bilaterally implanted subjects cannot achieve 40 evaluable due to unilateral implantation or exclusion after screening visit. Assuming a 20% screening failure rate, approximately 55 subjects are expected to be enrolled.

8.1 Inclusion Criteria

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

Subjects eligible for inclusion in this study must fulfill **all** of the following criteria (ocular criteria must be met in both eyes):

1.	Subject or legally authorized representative must be able to understand and sign an IRB/IEC approved Informed Consent form.
2.	Willing and able to attend all scheduled study visits as required per protocol.
3.	Adults, at least 20 years of age or older at the time of screening, of either gender in Korean, who require cataract extraction in both eyes.
4.	Clear intraocular media other than cataract in both eyes.
5.	Calculated lens power between +16.0 and +24.0 D.
6.	Preoperative OR expected postoperative regular corneal astigmatism of < 1.00 D.

8.2 Exclusion Criteria

Subjects fulfilling **any** of the following criteria are not eligible for participation in this study. Ocular criteria must not be met in either eye.

1.	Women of childbearing potential, defined as all women who are physiologically capable of becoming pregnant and who are not postmenopausal for at least 1 year or are less than 6 weeks since sterilization, are excluded from participation if any of the following apply: a. they are currently pregnant, b. have a positive urine pregnancy test result at Screening, c. intend to become pregnant during the study period, d. are breast-feeding. Subjects who become pregnant during the study will not be discontinued; however, data will be excluded from the effectiveness analyses because pregnancy can alter refraction and visual acuity results.
2.	Clinically significant corneal abnormalities including corneal dystrophy (eg, epithelial, stromal or endothelial dystrophy), inflammation, or edema per the

	Investigator's expert medical opinion.
3.	Previous corneal transplant.
4.	Ocular trauma, previous refractive surgery, or refractive procedures throughout the entire duration of the subjects' participation in the clinical study (including, but not limited to LASIK, astigmatic keratotomy, and limbal relaxing incision).
5.	History of or concurrent retinal conditions or predisposition to retinal conditions, previous history of, or a predisposition to, retinal detachment or presence of diabetic retinopathy that the Investigator judges could confound outcomes (NOTE: Including but not limited to background diabetic retinopathy, diabetic macular edema or proliferative diabetic retinopathy, macular degeneration).
6.	Amblyopia.
7.	Rubella, congenital, traumatic or complicated cataract.
8.	Extremely shallow anterior chamber (≤ 2.5 mm), not due to swollen cataract.
9.	Any current anterior or posterior segment inflammation of any etiology, and/or history of any disease producing an intraocular inflammatory reaction.
10.	Iris neovascularization.
11.	Optic nerve atrophy.
12.	Subjects with diagnosed degenerative eye disorder.
13.	Known color vision deficiencies.
14.	Subjects who may reasonably be expected to require an ocular surgical treatment at any time during the surgery (other than YAG capsulotomy).
15.	Situations where the need for a large capsulotomy can be anticipated (eg, diabetics, retinal detachment in the fellow eye, peripheral retinal pathology).
16.	Subjects who are expected to require retinal laser treatment.
17.	Any other additional procedures during the phacoemulsification and IOL implant due to intraoperative complications that require further investigation (including but not

	limited to posterior capsule rupture, vitreous loss, zonular dehiscence that may make the IOL implant less stable, etc).
18.	Zonular or capsule rupture.
19.	Excessive iris mobility.
20.	Significant anterior chamber bleeding.
21.	Uncontrolled intraocular pressure.
22.	Unrecognized (pre-existing but discovered during surgery ocular conditions or complications in which the IOL stability could be compromised, including zonular weakness).
23.	Bag-sulcus, sulcus-sulcus, or unknown placement of the haptics.
24.	Capsulorhexis tears or any areas of "can-opener" capsulotomy.
25.	Any subjects currently participating another investigational drug or device study that may confound the results of this investigation.
26.	Any other conditions that may not be appropriate to this study, as per the Investigator's expert medical opinion.

Note: When criteria 17-24 occur prior to IOL implantation, the study lens should not be implanted. This is true for both eyes.

8.3 Rescreening of Subjects

Rescreening of subjects is not allowed in this study.

9 TREATMENTS ADMINISTERED

9.1 Investigational Product(s)

Test Product(s): The ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00

Control Product(s) (If applicable): Not applicable

Table 9-1 Test Product

Test Product	The ACRYSOF IQ PanOptix Presbyopia Conecting IOL, Model TFNT00
Manufacturer	**License Holder:** Alcon Laboratories, Inc. 6201 South Freeway Fo1tWo1th, Texas 76134-2099 USA **Manufacturer:** Alcon Research Ltd 6065 Kyle Lane Huntington West Virginia, 25702 USA
Indication for use and intended pmpose in the cun ent study	The ACRYSOF IQ PanOptix Presbyopia Conecting IOL, Model TFNT00 is a multifocal IOL that conects aphakia, a condition that prevents patients from seeing things that are at near and/or at distance, by replacing the cataractous lens after cataract surge1y in an adult patient. It is inse1t ed into the capsular bag and has near vision and inte1mediate add power (3.25 D, 2.17 D).
Product description and parameters ava ilable for this study	• Optic Type: Biconvex Aspheric Optic • Optics Material: Ultraviolet and blue light filtering Ac1ylate/ Methac1ylate Copolymer • Optic Powers: 16.0 to 24.0 D in 0.5 D steps • Index of Refraction: 1.55 in air • Haptic Configuration: STABLEFORCE*Modified-L Haptics • Haptic Material: Ultraviolet and blue light filtering Ac1ylate/Methac1ylate Copolymer • Optic Diameter (mm): 6.0 • Overall Length (mm): 13.0 • Haptic Angle: 0°
Formulation	PEA, PEMA, BDDA, oMTP, AL-8739

Usage	IOLs are implantable medical devices and are intended for long-term use over the lifetime of the pseudophakic subject.
Number/Amount of product to be provided to the subject	Each subject will be bilaterally implanted with the test article.
Packaging description	Each IOL will be individually packaged and will have a unique serial number. The IOL package will contain the following items: • The IOL • A subject registration card (Lens Implant Card) • A subject identification card • Adhesive labels containing the IOL information and unique serial number • A package insert containing directions for use
Labeling description	• Primary: polypropylene wagon wheel case • Secondary: Polyester/Tyvek sterilization pouch / Cardboard box with polyprolylene film • Traceability shall be achieved by assignment of lot numbers, batch numbers or serial numbers. • Korean label (not applicable to English label) o Korean only, labeling components should be same as Korea license information approved by MFDS o Font size should be 6 or 7 point o 7 point: name of product & model, year and month of manufacture (use-by date) o 7 point and bold stroke/text box: warning/caution, "Medical Device", "Single use & prohibit re-use", "For clinical investigation. Exclusively for clinical investigation" o 6point: name & address of manufacturer & importer, product license number, packing unit, instmction of use, precautions in use, pmpose of use, storage method, year & month written on the Korean label • Lot number and expiration date: refer to the info1mation on the

	original package.
Storage conditions	< 45°C The IP must be stored in a safe, secure location within limited access separated from general stock. Transportation of product from one address to another must be documented and a Transportation Log (or similar documentation) utilized for appropriate accountability.
Additional information	In order to implant IOLs in study subjects, the surgeons participating in the study must be licensed ophthalmologists with cataract surgery experience and trained on the protocol. Subjects should be targeted for emmetropia postoperative refraction. The surgeon should target lens power that is expected to deliver the best visual outcome based on their medical judgement.
Supply	A designated amount of IOLs will be supplied to the site by the Sponsor.

The ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00 must be maintained within specified environmental conditions, per the labeling.

A temperature log must be maintained documenting appropriate IP storage conditions as described in the MOP, and must be made available for inspection.

More information on the test product can be found in the Package Insert of the ACRYSOF IQ PanOptix Presbyopia Correcting IOL, Model TFNT00.

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

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

9.3 Treatment Assignment / Randomization

Only after signing the ICF, a subject will be assigned a subject number by the electronic data capture system.

9.4 Treatment masking

All members associated with the study (at the site and the Study Sponsor) are unmasked to the assigned treatment.

9.5 Accountability Procedures

Upon receipt ofI Ps, the Investigator or delegate must conduct an invento1y of ACRYSOF IQ PanOptix Presbyopia Con ecting IOL, Model TFNT00 by serial number, complete study-specific confi1mation of receipt procedures as described in the MOP, and retain any required documentation in the Investigator's clinical study records. Throughout the study, the Investigator or delegate must maintain records of IP use and collection for each subject. This record must be made available to the study monitor for the purposes of verifying the accounting of IP supplies. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded along with an explanation.All IPs sent to the Investigator must be accounted for by Study Sponsor personnel, and in no case be used in an unauthorized manner.

- Return to the Study Sponsor investigational and control products associated with a device deficiency. Refer to Section 11 of this protocol for additional information on the reporting of device deficiencies and to the MOP for information on return of study products associated with these events.

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

9.6 Changes to concomitant medications, treatments/ procedures

After the subject is enrolled into the study, the Investigator must instru ct the subject to notify the study site about:

- Any new medications
- Alterations in dose or dose schedules for cunent medications,
- Any medical procedure or hospitalization that occuned or is planned
- Any non-dtug therapies (including physical therapy and blood tr·ansfusions).

The Investigator must document this inf01mation in the subject's case hist01y source document s.

10 STUDY PROCEDURES AND ASSESSMENTS

10.1 Informed Consent and Screening

The Investigator or delegate must explain the purpose and nature of the study, and have the subject or legally authorized representative read, sign, and date the IRB/IEC-approved infmmed consent document. The delegate should be a licensed medical doctor of ophthalmology. The subject must sign the ICF BEFORE any study-specific procedures or assessments can be performed, including study-specific screening procedures. Additionally, have the individual obtaining consent from the subject and a witness, if applicable, sign and date the info1med consent document. The subjects should be provided with enough time for his/her decision on participation on the trial, and shouldhave options to discuss with his/her family members or relatives about the participation to the investigation.

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

10.2 Description of Study Procedures and Assessments

Effectiveness assessments:

Below assessments will be conducted in the photopic lighting condition except subjective symptoms,

- Distance VA (4 m),
    - Monocular (1st and/or 2nd eye) UCDVA
    - Binocular UCDVA
    - Binocular BCDVA
- Inte1mediate VA (60c m)
    - Monocular (1st and/or 2nd eye) UCIVA
    - Binocular UCIVA
- Near VA (40 cm)
    - Mono cular (1st and/or 2nd eye) UCNVA
    - Binocular UCNVA
- Binocular defocus curve

- [redacted]
- [redacted]
- Best corrected binocular contrast sensitivity with & without glare
- Subjective symptoms

Safety assessments:

- Adverse Device Events including Secondary Surgical Interventions (SSIs) related to the optical properties of the IOL
- Device deficiencies
- Fundus examination and fundus visualization
- Intraocular pressure
- Slit-lamp examination
- IOL observations
- Surgical problems
- Subjective posterior capsule opacification
- Posterior capsulotomy
- Lens decentration and tilt

Preoperative assessments:

- Urine Pregnancy Test
- [redacted]

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

10.2.1 Demographics

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

10.2.2 Medical History

Collect medical history information, including information on all medications used within the past 30 days. Include herbal therapies, vitamins, and all over-the-counter medications as well

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

10.2.3 Concomitant Medication

Concomitant medications can be ocular or nonocular. Details are provided in the MOP.

10.2.4 Inclusion/Exclusion Criteria

At the conclusion of Visit 0, verify the subject meets all eligibility criteria as detailed in the protocol, Section 8.1 Inclusion Criteria and Section 8.2 Exclusion Criteria.

10.2.5 Investigational Product compliance

N/A

10.2.6 Urine Pregnancy Test

For women of childbearing potential, request a urine pregnancy test be taken at the Investigator's office.

[redacted]

[redacted]

10.2.9 Visual Acuity: Effectiveness Assessment

ETDRS visual acuity testing for both eyes must be performed prior to any assessment requiring administration of eye drops to dilate the eyes, or any assessment requiring contact

with the eye. When assessing BCDVA, refractive correction is required. All visual acuity tests will be conducted in the photopic lighting conditions. Lighting measurement and manifest refraction details are provided in the MOP.

Visual acuity must be obtained by study personnel who have been successfully trained. For Preoperative Visit (Visit 0), data from the Investigator's previous routine cataract evaluation may be used, if the data 1) meet the requirements of this protocol and MOP, and 2) were collected less than 2 months before the ICF signed for the study.

10.2.10 Binocular Defocus Curve: Effectiveness Assessment

Defocus assessment requires the subject's best distance correction be varied from +2.00 D to -5.00 D in 0.50 D increments. The purpose of the defocus evaluation is to compare binocular clinical performance to the theoretical lens design. Defocus curve is commonly used clinical endpoints to evaluate the effectiveness of presbyopia correcting intraocular lenses, as well as with visual acuity.

10.2.12 Photopic Best Corrected Contrast Sensitivity: Effectiveness Assessment

Photopic best corrected contrast sensitivity with and without glare test will be conducted to assess the effect on visual quality of the trifocal IOL at distance.

10.2.13 Subjective symptoms: Effectiveness Assessment

Provide the subject the patient satisfaction questions prior to seeing a physician or any clinical exam. Assess the subjective visual status/satisfaction on daily activities.

10.2.14 Adverse Events including Secondary Surgical Interventions: Safety Assessment

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

10.2.15 Device Deficiencies: Safety Assessment

Assess and record any device deficiencies that are reported or observed, including those associated with changes in concomitant medication dosing since the previous visit. Requirements for reporting device deficiencies in the study can be found in Section 11.

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

10.2.16 Slit-Lamp Examination: Safety Assessment

SLE of the cornea, iris/anterior chamber, and lens must be performed in both eyes before instillation of any diagnostic eye drops. For Preoperative Visit (Visit 0), data from the Investigator's previous routine cataract evaluation may be used, if the data 1) meet the requirements of this protocol and MOP, and 2) were collected less than 2 months before the ICF signed for the study.

Note: This exam must be completed by a medical doctor, or Ophthalmological technician.

10.2.17 Fundus examination and Fundus Visualization: Safety Assessment

For fundus examination, document the assessment of vitreous, retina, macula, choroid, optic nerve, and cup/disc ratio.

For fundus visualization, document whether the lens causes any difficulty in viewing and/or examining the retina or posterior segment, or affects the surgeon's ability to administer vitreal/retinal treatments, as compared to experience with monofocal IOLs. For Preoperative Visit (Visit 0), data from the Investigator's previous routine cataract evaluation may be used, if the data 1) meet the requirements of this protocol and MOP, and 2) were collected less than 2 months before the ICF signed for the study.

Note: This exam must be completed by a medical doctor, or Ophthalmological technician.

10.2.18 Subjective PCO including Posterior Capsulotomy: Safety Assessment

During the slit-lamp examination, assess the presence of PCO. For posterior capsulotomy assessment, indicate whether a posterior capsulotomy was performed since the last visit.

10.2.19 IOL Position Change: Safety Assessment

After surgely, examine the IOL with the slit-lamp. Indicate whether the lens has changed position, tilted, or decentered since the last visit.

10.2.20 Other Surgical Procedures: Safety Assessment

During cataract surgely, document whether any additional procedures (eg, anterior vitrectomy, capsular tension ring) were performed. Evaluate whether the procedure meets the definition of anAE and repo1taccordingly.

10.2.21 Problems during Surgery: Safety Assessment

Document whether any problems arose during surgely. Examples of problems include anterior capsular tear, intraoperative loss of pupil dilation, bag-sulcus haptic placement. Evaluate whether the problem meets the definition of an AE and rep01t accordin gly.

10.2.22 Surgical Report: Safety Assessment

Implant the lens via clear cornea incision using the surgeon's standard operating procedures and in accordance with IOL directions for use. Keep an accurate and complete operative repo1t in the source documentation.

10.2.23 Lens Information: Safety Assessment

Post lens implantation, retain the IOL adhesive label in the subject source.

10.2.24 Intraocular Pressure: Safety Assessment

Intraocular pressure must be measured in both eyes following Investigator's standard of care. Within a single subject utilize the same instmment type to measure IOP during each visit. Record the measurement in mmHg. For Preoperative Visit (Visit 0), data from the Investigator's previous routine cataract evaluation may be used, if the data 1) meet the requirements of this protocol and MOP, and 2) were collected less than 2 months before the ICF signed for the study.

10.3 Unscheduled Visits

If a subject visit occurs between any regularly scheduled visits, this visit must be documented as an Unscheduled Visit. During all unscheduled visits, the Investigator must conduct the following procedures:

- Record changes in medical condition or concomitant medication

- Collect Adverse Event inf01mation
- Re cord seco ndaly sur gical inter ven tion s that have occuned sin ce surge1y, if applicable.
- Evaluate and record any device deficiencies.

The Investigator may perform additional procedures for proper diagnosis and treatment of the subject as below. The Investigator must document this info1mation in the subject's case hist01y source document s.

- Perform manifest refraction
- Perform slit-lamp examination including IOL obse1vations (if any).
- Obse1ve any IOL position changes (ie, tilt and decentration) occuning since the previous visit. [Both Eyes, Bilateral]
- Assess subjective PCO, and record information for any PC that has occmTed since surgery , if applicable. [Both Eyes, Bilateral]
- Perform tonometry to measure IOP.

If during an Unscheduled Visit, the subject is discontinuing the IP or discontinuing from the study, the Investigator must conduct Exit procedures (refer to Visit 4A for the exit procedure) according to Table 3-1 Schedule of Study Procedures and Assessments and Section 10.4.3, as possible.

10.4 Directions Related to Secondary Surgical Intervention

This section is intended to provide guidance on the documentation and procedures related to SSis in this investigation. The investigator must consider subject complains and clinical outcome in his or her consideration of the need for a SSI, determine whether the cause of a needed SSI is due to optical properties of the IOL , and repo1tfindings to the Sponsor with defined timelines in Section in the Section 11.3 Procedure for Recording and Rep01ting.

The main procedural steps in the decision process for SSis and notification to the Sponsor are detailed below:

1. The Investigator must dete1mine whether an SSI is related to the optical properties of the IOL.

2. Any SSI (other than posterior capsulotomy laser treatment) perf01med for any reason should be recorded as a serious adverse event and reported to the Sponsor within 24 hours of its occmTence.

Note: If the SSI is a lens exchange or repositioning, the subsequent study post-operative visits should be based on the date of its surgery. Unscheduled Visit Case Report Forms (CRFs) should be used for other post-operative follow-up visits, where applicable. If the study lens is exchanged and replaced with a non-study lens, the subject will be required to complete all original subsequent study lens visit through Visit 4A (3 months).

Evaluation of Need for a Secondary Surgical Intervention:

The Need for consideration of an SSI includes one or more of the followings:

1. An Investigator assessment of subject's clinical outcome
2. A subject spontaneously complaining about visual symptoms to the investigational site personnel
3. Other reason(s) for an SSI, e.g. retained lens fragments

The Investigator should perform a thorough evaluation including diagnostic testing as needed and a subject interview to understand subject observations in detail to determine if an SSI is the appropriate treatment for the subject's undesired outcome (e.g., blurred vision, visual disturbances/distortions, or other reasons). Case management should be based on the Investigator's clinical assessment with consideration of the subject's postoperative UCDVA, BCDVA, IOL stability after implantation, and any subjective complaints. Careful consideration of the potential risks and benefits associated with the SSI for the subject is required, and these should be discussed with the subject prior to reposition or explant the IOL or otherwise surgically intervene.

10.5 Discontinued Subjects

10.5.1 Screen Failures

Screen failures are subjects who were excluded from the study after signing the informed consent and prior to administering treatment.

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

Subject numbers must not be re-used.

10.5.2 Discontinuations

Discontinued subjects are individuals who voluntarily withdraw or are withdrawn from the study by the Investigator after informed consent is signed and before the last visit is completed.

Subject numbers of discontinued subjects must not be re-used.

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

If a subject discontinues from study treatment, every effort must be made to keep the subject in the study and to continue with the study assessments as specified in the schedule of study procedures and assessments until the final visit.

For subjects discontinuing from the study, the Investigator must complete all Exit procedures according to Table 3-1 Schedule of Study Procedures and Assessments and Section 10.4.3, if the subject is willing and able, and if in the opinion of the Investigator it is safe for the subject to do so.

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

To ensure the safety of all subjects who discontinueearly, Investigatorsmust assess each subject and, if necessary, advise them of any therapies and/or medical procedures that may be needed to maintain their health.

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

In the case of subjects who discontinue IP but do not discontinue from the study, subjects must be assessed with below tests till the end of study, if applicable.

Effectiveness assessment (photopic light conditions)	Safety assessment
Distance VA (4 m), • Monocular (1st and/or 2nd eye) UCDVA • Binocular UCDVA	Adverse Device Events including Secondary Surgical Interventions (SSIs) related to the optical properties of the IOL

• Binocular BCDVA	
lnte1mediate VA (60 cm) • Monocular (1st and/or 2nd eye) UCIVA • Binocular UCIVA	Device Deficienc ies
Near VA (40 cm) • Monocular (1st and/or 2nd eye) UCNVA • Binocular UCNVA	Fundus Visualization Fundus Examination
Photopic binocular defocus cmve	Intraocular Pressure
[redacted]	[redacted]
[redacted]	[redacted]
Photopic best conected binocular contrast sensitivity with & withoutglare	Surgical problems
Subjective symptoms	Subjective Posterior Capsule Opacification
	Posterior Capsulotomy
	Lens decentration and tilt

Depending on the circumstance, the subject may continue in the study or may be discontinued as outlined asbelow.

Eye	Conditions	Status/Follow-up
1st Operative Eye	• Exclusion during surge1y • Lens does not touch eye	Subject discontinued
	• Exclusion during surge1y • Lens touches eye • Lens is not implanted	• Subject continued • 1st eye: 0 *No* effectiveness assessments conducted 0 *Monocular* safety

		assessments conducted at postoperative visits • 2nd eye: Not implanted
	• Exclusion during surgely • Lens implanted	• Subject continued • **1st** eye: 0 *Monocular* **and** *binocula r* effectiveness assessments conducted at postoperati ve visits 0 Safe ty ass ess ment s cond ucted at pos toperati ve visits • 2nd eye: Proceed to implant study lens as scheduled
2nd Ope rative Eye	• Exclusion during surgely • Lens does not touch eye	• Subject continued • 1st eye: 0 *Monocular* effectiveness assessments perf01med at postoperative visits 0 Safety assessments perf01med at postopera tive visits • **2nd eye:** 0 No effectiveness assessments conducted • Rep01t AEs and Device Deficiencies, if any
Eye	**Conditions**	**Status**
2 nd0 per·atlve Eye	• Exclu sion during surgely	• Subject continued • 1st eye:

	• Lens touches eye • Lens not implanted	○ *Monocular* effectiveness assessments performed at postoperative visits ○ *Monocular* safety assessments performed at postoperative visits • 2nd eye: ○ No effectiveness assessments conducted ○ *Monocular* safety assessments performed at postoperative visits
	• Exclusion during surgely • Lens implanted	• Subject continued • **1st** eye: ○ *Monocular* **and** *binocular* effectiveness assessments conducted at postoperative visits ○ Safety assessments conducted at postoperative visits • **2nd eye:** ○ *Monocular* and *binocular* effectiveness assessments conducted at postoperative visits ○ Safety assessments conducted at postoperative visits

10.6 Clinical Study Termination

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

If the clinical study is prematurely terminated or suspended by the Study Sponsor:

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

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

10.6.1 Follow-up of subjects after study participation has ended

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

11 ADVERSE EVENTS AND DEVICE DEFICIENCIES

11.1 General Information

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

Figure 11-1 Categorization of All Adverse Events

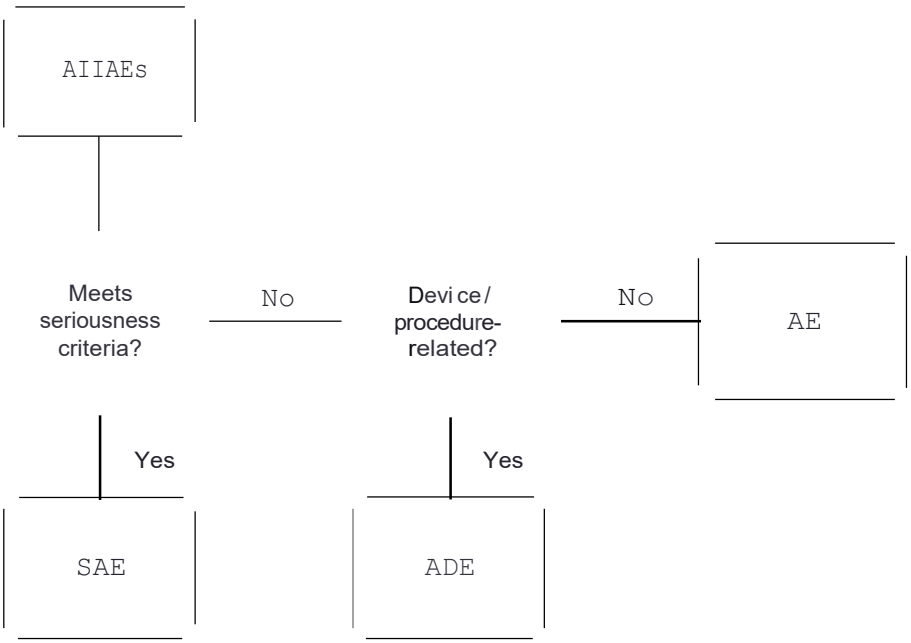
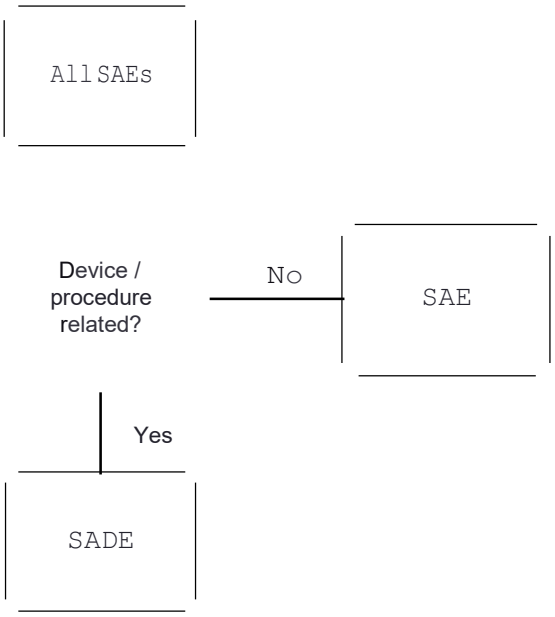


Figure 11-2 Categorization of All Serious Adverse Events



In addition to rep01ting all AEs (serious and non-serious) meeting the definitions, the Investigator must repo1t any occunence of the following as an SAE:

Cumulative Serious Adverse Events

- Cystoid macular edema

- Hypopyon
- Endophthalmitis
- Lens dislocation
- Pupillary block
- Retinal detachment
- Secondary surgical intervention (excluding posterior capsulotomy)

Persistent Serious Adverse Events

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

This list is consistent with the categories provided in EN ISO 11979-7:2014. A persistent AE is an AE that is present at the conclusion of a clinical investigation per EN ISO 11979-1:2012. Any other potentially sight-threatening event may also be considered serious based upon the judgment of the Investigator and should be reported appropriately as delineated in Section 11.3.

Device Deficiencies

A device deficiency may or may not be associated with subject harm (ie, ADE or SADE); however, not all ADEs or SADEs are due to a device deficiency. The Investigator should determine the applicable category for the identified or suspect device deficiency and report any subject harm separately.

- Failure to meet product specifications (eg, incorrect IOL power)
- IOL defect
- Broken IOL optic
- Broken IOL haptic
- Scratched IOL optic
- Unsealed device packaging
- Suspect product contamination (IOL)

11.2 Monitoring for Adverse Events

At each visit, after the subject has had the oppo1tunity to spontaneously mention any problems, the Investigator should inquire about AEs by asking the standard questions:

- "Have you had any health problems since yom last study visit?"
- "Have there been any changes in the medicines you take since your last study visit?"

Changes in any protocol-specific parameters and/or questionnaires evaluated during the study are to be reviewed by the Investigator.Any untoward (unfavorable and unintended) change in a protocol-specific parameter or questionnaire response that is clinically relevant, in the opinion of the Investigator, is to be rep01ied as an AE. These clinically relevant changes will be repo1ied regardless of causality.

11.3 Procedures for Recording and Reporting

AEs are collected from the time of inf01med consent. Any pre-existing medic al conditi ons or sign s/symptoms present in a subject prior to the stali of the study (ie, before info1med consent is signed) are not considered AEs in the study and should be recorded in the Medical Hist01y sect ion of the eCRF.

In addition, aqueous cells and flare, corneal edema, raised IOP, and superficial punctate keratitis are examples of early postoperative findings that are typically observed following ocular surgery. The se are not considered AEs if they can be reasonably expected to resolve within a week and not result in any untoward long te1m visual outcome impact.

For each recorded event, the ADEs and SAEs documentation must include: date of occmTence, seve rity, treatment (if applicable), outcome, and assessments of the seriousness and causality. In addition, the Investigator must document all device deficiencies reported or observed with test a li cles on the Device Deficiency eCRF. The site must submit all available information on ADEs, SAEs, and device deficiencies to the Study Sponsor immediately as follows:

- All SAEs must be repo1ied immedia tely (within 24 homs) of the Investigator's or site's awareness.
- ADEs that do not meet seriousness criteria and device deficiencies must be reporied within 10 calendar days of the Investigator's or site's awareness.
- A printed copy of the completed Serious Adverse Event and Adverse Device Effect and/or Device Deficiency eCRF must be included with product retmns.

- Additional relevant information after initial reporting must be entered into the eCRF as soon as the data become available.
- Document any changes to concomitant medications on the appropriate eCRF.
- Document all relevant information from Discharge Summary, Autopsy Report, Certificate of Death etc, if applicable, in narrative section of the Adverse Device Effect (for related AEs) and Serious Adverse Event eCRF.

Note: Should the EDC system become non-operational, the site must complete the appropriate paper Serious Adverse Event and Adverse Device Effect and/or Device Deficiency Form. The completed form is faxed or emailed to the Study Sponsor (Korean Novartis Patient Safety Desk) at or is faxed at or [redacted]) according to the timelines outlined above; however, the reported information must be entered into the EDC system once it becomes operational.

Any AEs and device deficiencies for non-study marketed devices/products (ie, but not limited to BSS, OVD, Delivery systems, Phacoemulsification systems, VA handpieces) will be considered and processed as spontaneous (following the postmarket vigilance procedures) and should be communicated to the device's/product's manufacturer as per local requirements.

Study Sponsor representatives may be contacted for any protocol related question and their contact information is provided in the Manual of Procedures (MOP) that accompanies this protocol.

Further, depending upon the nature of the AE or device deficiency being reported, the Study Sponsor may request copies of applicable portions of the subject's medical records. The Investigator must also report all AEs and device deficiencies that could have led to a SADE according to the requirements of regulatory authorities or IRB/IEC.

Intensity and Causality Assessments

Where appropriate, the Investigator must assess the intensity (severity) of the AE based upon medical judgment with consideration of any subjective symptom(s), as defined below:

Intensity (Severity)

Mild: An AE is mild if the subject is aware of but can easily tolerate the sign or symptom.

Moderate: An AE is moderate if the sign or symptom results in discomfort significant enough to cause interference with the subject's usual activities.

Severe: An AE is severe if the sign or symptom is incapacitating and results in the subject's inability to work or engage in their usual activities.

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

Causality

1. Definitely related

   Event which has definitive time relationship to the use of the device of interest, cannot be explained by other reasons but the device of interest, has symptom disappearance to discontinuation of the device of interest and reappears when the device of interest is rechallenged (only when rechallenge is possible to do so).

   Also event is consistent to already known information of the device of interest or other devices of the same class.

2. Probably related

   Event where there is evidence that the device of interest was used, has reasonable time relationship to the use of device of interest, can be explained mainly by the device of interest rather than other reasons, and has symptom disappearance to discontinuation of the device of interest.

3. Possibly related

   Event where there is evidence that the device of interest was used has plausible time relationship to the use of device of interest, device of interest and other reasons have similar chances of resulting to an event, has symptom disappearance to discontinuation of the device of interest.

4. Possibly not related

   Event where there is evidence that the device of interest was used, can be reasonably explained by other reasons, has symptom disappearance or there is uncertainty of the symptom when device of interest is discontinued has no symptom reappearance or there is uncertainty of the symptom when device of interest is rechallenged (only when rechallenge is possible to do so).

5. Definitely not related

   Event where device of interest was not used has no reasonable time relationship to the use of device of interest, can be explained by other reasons.

6. Unknown

   Cannot be judged because information is insufficient or contradictory and cannot be supplemented or confirmed.

※Assessment criteria used in reporting to Novartis Patient Safety based upon the 6 classifications

Safety Reporting Form	MFDS Guideline
Suspected	Definitely related, Probably related, Possibly related, Unknown
Not suspected	Possibly not related, Definitely not related

The Study Sponsor will assess the AEs and may upgrade the Investigator's assessment of seriousness and/or causality. The Study Sponsor will notify the Investigator of any AEs that are upgraded from non-serious to serious or from unrelated to related.

11.4 Return product analysis

Study Sponsor representatives and their contact information are provided in the Manual of Procedures (MOP) that accompanies this protocol.

Alcon products associated with device deficiencies and/or product related AEs should be returned and must include the Complaint # which will be provided by Study Sponsor after the case is entered in the iTrack (Sponsor's Medical Safety Database).

11.5 Unmasking of the Study Treatment

Not applicable; this study is open-label, unmasked study.

11.6 Follow-Up of Subjects with Adverse Events

The Investigator is responsible for adequate and safe medical care of subjects during the study and for ensuring that appropriate medical care and relevant follow-up procedures are maintained after the study.

The Investigator should provide the Study Sponsor with any new safety information (which includes new AEs and changes to previously reported AEs) that may affect the safety evaluation of the device. For AEs that are unresolved/ ongoing at time of subject exit from

study, any additional information received at follow-up should be documented in the eCRF up to study completion (ie, database lock).

All complaints received after this time period will be considered and processed as spontaneous (following the postmarket vigilance procedures) and should be communicated to the medical device's manufacturer as per local requirements.

The Investigator should also report complaints on non-Alcon products directly to the manufacturer as per the manufacturer's instructions or local regulatory requirements.

11.7 Pregnancy in the Clinical Study

Pregnancy is not reportable as an AE; however, complications may be reportable and will be decided on a case–by-case basis. An Alcon form will be utilized to capture all pregnancy-related information until birth of the child.

12 ANALYSIS PLAN

12.1 Subject Evaluability

The final subject evaluability will be determined using the Deviations and Evaluability Plan (DEP) prior to locking the database.

12.2 Analysis Sets

All effectiveness analyses will be based on the full analysis set (FAS). All-implanted analyses set (AAS) will be used only for effectiveness analyses of monocular assessments.

All subjects with successful bilateral IOL implantation and have the bilateral measurements for defocus curve will be evaluable for the FAS.

All-implanted analysis set (AAS) is defined as all subjects with successful implantation of the test product in at least one eye.

The safety analysis set will include all patients with attempted IOL implantation (successful or aborted after contact with the eye).

12.3 Demographic and Baseline Characteristics

Demographics and baseline characteristics will be summarized for FAS, AAS and safety analysis set. Demographics include age, sex, ethnicity, height, [redacted] and race. [redacted]

[redacted]

Summaries of continuous variables will include the number of observations, mean, standard deviation, median, minimum, and maximum.Summaries of categorical variables will include count and percentage.

12.4 Effectiveness Analyses

This is a single aim descriptive study. No formal statistical hypothesis testing is planned for any endpoint. Rather the data will be summarized using descriptive statistics.

12.4.1 Analysis of Primary Effectiveness Endpoint

The primary effectiveness endpoint is:

- Binocular defocus cmve at 3 months (Visit 4A) post bilateral implantation

12.4.1.1 Statistical Hypotheses

No hypothesis testing of the primary effectiveness endpoint is planned.

12.4.1.2 Analysis Methods

The visual acuity data in logMAR for binocular defocus cmve at Month 3 will be summarized with the number of observations, mean, standard deviation, median, minimum, and maximum, two-sided 90% CI of the mean. A plot will be generated for the defocus curve with amount of defocus along the x-axis and logMAR visual acuity at each defocus along the y-axis.

12.4.2 Analysis of Secondary Effectiveness Endpoints

The seconda1yeffectiveness endpoints are:

- Binocular defocus cmve at 1 month post-implantation (Visit 3A)
- Best conected binocula·i visual acuity at distance (4 m) (Visits 3A, 4A)
- Unconected monocular & binocular visual acuity at 1 & 3 months post-implantation (Visits 3A, 4A) at 40 cm, 60 cm and 4 m
- Photopic best con ected binoculai· contrast sensitivity with & without glare at 3 months post-implantation (Visit 4A)

- Subjective symptom questions at preoperatively and postoperatively: 3 months post-implantation (Visit 4A)

12.4.2.1 Statistical Hypotheses

No hypothesis testing of the seconda1y effectiveness endpoints is planned.

12.4.2.2 Analysis Methods

The visual acuity data in logMAR for binocular defocus curve data at Month I will be summarized with the number of observations, mean, standard deviation, median, minimum, and maximum, and two-sided 90% CI of the mean. A plot will be generated for the defocus curve with amount of defocus along the x-axis and logMAR visual acuity at each defocus along the y-axis.

Best con ected binocular visual acuity at distance (Visits 3A, 4A), uncoffected binocular visual acuity at 40 cm, 60 cm and 4 m in logMAR (Visits 3A, 4A) will be summarized by visit with the number of observations, mean, median, standard deviation, minimum, maximum, and two-sided 90% CI of the mean. Additionally, these visual acuity endpoints will also be summarizedin Snellen VA as categorical variables, by visit, with number of non-missing observations, cumulative frequency, and percentage in the following categories:

- 20/20 or better
- 20/25 or better
- 20/32 or better
- 20/40 or better

Unc01Tected mono cular visual acuity will be summarized in the same way as the uncon ected binocular visual acuity. The uncon ected monocular visual at 40 cm, 60 cm and 4 m will be summarized by the first and second operative eye for the following visits: Weeki , Month I and Month 3 for the full analysis set. Besides the FAS analysis, similarly, the uncon ected monocular visual acuity will be summarizedfor AAS as well.

Logarithmic contras t sensitivity for various spatial frequencies at Month 3 with and without glare will be summarized with the number of observations, mean, median, and standard deviation, minimum, maximum, and two-sided 90% CI of the mean. Plots will be generated separately for glare and without glare conditions with spatial frequency along the x-axis and mean logarithmic contrast sensitivity along the y-axis. Numberand percentage of subjects who do not have a record for a spatial frequency will be presented. Descriptive tables and

plots will be generated based on the scoring instructions of Vector Vision, and based on the observed data.

Subjective symptom questions will be summarized by visit (Preoperative, Month 3) per question with total number of non-missing observations, count in the category, and percent in the category.

[redacted]

12.5 Handling of Missing Data

No missing data will be imputed.

12.6 Safety Analyses

The safety endpoints are:

- Adverse events including secondaiy surgical interventions(SSis) related to the optical properties of the IOL.
- Device deficiencies
- Posterior capsule opacification
- Posterior capsulotomy
- IOL position change
- Intraocular pressure
- Surgical problems

Safety analyses will be made based upon the safety analysis set.

Rate of SSis related to the optical prope1iies of the IOL for either eye will be summai·ized by operative eye. All AEs will be coded using the Medical Dictiona1y for Regulato1y Activities (MedDRA) and will be presented by severity (mild, moderate, or severe) and relationship to the study product. Ocular AEs will be summarized byoperative eye. Descriptive tables (count and percentage) and listing will be generated for AEs based upon the categories of ocular and nonocular AEs, serious and non-serious AEs, as appropriate.

Device deficiencies will be listed. The count and percent of device deficiencies will be presented.

Results of posterior capsule opacification will be summarized with count and percentage in each categ01y by operative eye. A list of eyes with posterior capsule opacification will be presented.

Number and percentage of eyes with posterior capsulotomy will be presented by operative eye. A list of eyes with posterior capsulotomy will be presented.

Number and percentage of eyes with an IOL position change (tilted, decentered) will be presented by operative eye. A listing will be presented for eyes with IOL position changes.

Intraocular pressure and its change from baseline will be summarized descriptively with number of observations, mean, median, standard deviation, minimum, and maximum by operative eye. Baseline is defined as the last measurement taken prior to the IOL implantation. Individual listing of intraocular pressure and its change from baseline will be presented.

Count and percentage of eyes with surgical problems will be presented. Individual listings of surgical problems will be presented.

Results of slit-lamp exams, fundus exams, and other procedures at surgery, final incision size, lens information, IOL damage and IOL observations will be listed. If applicable, some of the items will not be listed as safety endpoints, e.g., final incision size without complications.

12.7 Interim Analyses and Reporting

Not Applicable. No interim analysis is planned for this study.

12.8 Sample Size Justification

Assuming a standard deviation of 0.17 logMAR for defocus visual outcomes, a sample size of 40 subjects will ensure more than 99% probability to observe the half width of 90% two-sided confidence interval to be not larger than 0.06 logMAR at a defocus point. The precision of estimates are within ±3 letters with visual outcomes.

Assume a dropout rate of 10% at Month 3, an approximate total of 44 subjects with intended bilateral IOL implantation are planned to be enrolled in the study to achieve 40 subjects with complete data at Month 3.

13 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

13.1 Subject Confidentiality

The Investigator must ensure that the subject's anonymity is maintained throughout the course of the study. In particular, the Investigator must keep an enrollment log with confidential identifying information that corresponds to the subject numbers and initials of each study participant. At the end of the clinical study, the Study Sponsor will collect a copy of the enrollment log ***without any identifying subject information***. All documents submitted to the Study Sponsor will identify the subjects exclusively by number and demographic information. No other personally identifying information will be transmitted to the Study Sponsor.

The Study Sponsor may release anonymized study data to external researchers for purposes of future research directly related to the study objectives, or future research that is beyond the scope of the current study objectives. The Informed Consent Form explains this to study subjects. Anonymization means that all identifiable information will be removed from the dataset and all links to the subjects in the study will be removed. Anonymization of the data will maintain confidentiality of the subjects who participate in the study so that they cannot

be identified by external researchers. The anonymized data set will contain records from all of the subjects in the current study, but the anonymization process might change the data set in some ways, so external researchers will be informed that they might not be able to duplicate some of the results from this study.

13.2 Completion of Source Documents and Case Report Forms

The nature and location of all source documents will be identified to ensure that original data required to complete the CRFs exist and are accessible for verification by the site monitor, and all discrepancies shall be appropriately documented via the query resolution process. Site monitors are appointed by the Study Sponsor and are independent of study site staff.

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

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

- Subject identification (name, sex, race/ethnicity)
- Documentation of subject eligibility
- Date of informed consent
- Dates of visits
- Documentation that protocol specific procedures were performed
- Results of study parameters, as required by the protocol
- IP accountability records
- Documentation of AEs and other safety parameters (if applicable)
- Records regarding medical histories and the use of concomitant therapies prior to and during the study
- Date of study completion and reason for early discontinuation, if applicable

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

Only designated individuals at the site will complete the CRFs. The CRFs must be completed at regular intervals following the clinical study visit schedule. It is expected that all data reported have corresponding entries in the source documents. The Principal Investigator is

responsible for reviewing and certifying that the CRFs are accurate and complete. The only subject identifiers recorded on the CRFs will be subject number, and subject demographic information.

13.3 Data Review and Clarifications

A review of CRF data to the subject's source data will be completed by the site monitor to ensure completeness and accuracy. After the CRFs have been completed, additional data clarifications and/or additions may be needed as a result of the data cleaning process. Data clarifications are documented and are part of each subject's CRF.

Deviations from this protocol and GCP must be recorded. A plan for data validation will be completed, and agreed upon by the study clinical manager (CM) and other team members.

Concomitant medications entered into the database will be coded using the WHO Drug Reference List. Medical history and adverse events will be coded using the medical dictionary for regulatory activities (MedDRA) terminology.

Upon completion of the study and once the database is declared completed and accurate, the database will be locked and data will be available for data analysis.

13.4 Sponsor and Monitoring Responsibilities

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

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

A Coordinating Investigator may be identified by the Study Sponsor to review and endorse the final study report. In cases where a Coordinating Investigator is engaged, the Study

Sponsor will select the Coordinating Investigator based upon their experience, qualifications, active study participation , and their willingness and availability to take on this role.

13.5 Regulatory Documentation and Records Retention

The Investigator is required to maintain up-to-date, complete regulat01y documentation as indicated by the Study Sponsor and the Investigator's files will be reviewed as part of the ongoing study monitoring. Financial information is to be kept separately.

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

13.6 Quality Assurance and Quality Control

The Study Sponsor will secure agreement from all involved parties to ensure direct access to all study related sites, source data and documents, and rep01t s for the purpose of monitoring and auditing by the Study Sponsor, and inspection by domestic and foreign regulatory authorities . Quality control will be applied to each stage of data handling to ensure that all data are reliable and have been processed conectly. Agreements made by the Study Sponsor with the Investigator/Institution and any other parties involved in the clinical study will be provided in writing as pa1t of the protocol or as a separate agreement.

14 ETHICS

This clinical study must be conducted in accordance with the ethical principles contained within:

- The Declaration of Helsinki, and in compliance with the ICH E6 GCP Consolidated Guideline, ISO 14155:2011, and the applicable US FDA 21 CFR Regulations.
- SOPs of the Study Sponsor and contract research organizations participating in the conduct of the clinical study and all other applicable regulations.
- Notifications and timelines for reporting protocol deviations should be based upon applicable Ethics Committee requirements

The Investigatormust ensure that all personnel involved in the conduct of the study are qualified to perform their assigned responsibilities through relevant education, training, and

experience. The Investigator and all clinical study staff must conduct the clinical study in compliance with the protocol. Deviations from this protocol, regulatory requirements and/or GCP must be recorded and reported to the Sponsor prior to database lock. If needed, corrective and preventive action should be identified, implemented, and documented within the study records. Use of waivers to deviate from the clinical protocol is prohibited.

Before clinical study initiation, this protocol, the informed consent form, any other written information given to subjects, and any advertisements planned for subject recruitment must be approved by an IRB/IEC. The Investigator must provide documentation of the IRB/IEC approval to the Study Sponsor. The approval must be dated and must identify the applicable protocol, amendments (if any), informed consent form, assent form (if any), all applicable recruiting materials, written information for subject, and subject compensation programs. The IRB/IEC must be provided with a copy of the Package Insert, any periodic safety updates, and all other information as required by local regulation and/or the IRB/IEC. At the end of the study, the Investigator must notify the IRB/IEC about the study's completion. The IRB/IEC also must be notified if the study is terminated prematurely. Finally, the Investigator must report to the IRB/IEC on the progress of the study at intervals stipulated by the IRB/IEC.

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

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

15 REFERENCES

15.1 References applicable for all clinical studies

- ASCRS 2017 American Society of Cataract and Refractive Surgery 2017
- Korea National Statistical Office
- ISO 11979-9:2006(E)Ophthalmic implants - Intraocular lenses - Part 9: Multifocal intraocular lenses
- EN ISO 11979-7:2014 Ophthalmic implants - Intraocular lenses - Part 7: Clinical Investigations
- ISO 14155:2011 Clinical investigation of medical devices for human subjects - Good clinical practice
- EN ISO 11979-1:2012 Ophthalmic implants - Intraocular lenses - Part 1: Vocabulary

15.1.1 US references applicable for clinical studies

- 21 CFR Part 11 - Electronic Records; Electronic Signatures
- 21 CFR Part 50 - Protection of Human Subjects
- 21 CFR Part 56 - Institutional Review Boards
- 21 CFR Part 812 - Investigational Device Exemptions
- 21 CFR Part 54 - Financial Disclosure by Clinical Investigators

15.2 References for this clinical study

Not applicable.

Date/Time (mm/dd/yyyy GMT):	Signed by:	Justification:
12/07/2017 14:11:31	[redacted]	[redacted]
12/07/2017 14:48:02	[redacted]	[redacted]
12/07/2017 15:40:02	[redacted]	[redacted]
12/08/2017 02:11:59	[redacted]	[redacted]