Study Protocol

CLINICAL INVESTIGATION OF THE SAFETY AND EFFECTIVENESS OF AN INVESTIGATIONAL MODEL OF THE TECNIS® INTRAOCULAR LENS

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Clinical Investigation of the Safety and Effectiveness of an Investigational Model of the TECNIS® Intraocular Lens

IDE Number: G190057

PROTOCOL NUMBER: SUR-CAT-652-2001

SPONSOR: Johnson & Johnson Surgical Vision, Inc.
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Santa Ana, CA 92705
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Investigator Agreement

As an Investigator, I agree to:

- Implement and conduct this study diligently and in strict compliance with this agreement; the protocol; Good Clinical Practices; 21CFR812, ISO 14155:2011 and all other applicable FDA regulations; conditions of approval imposed by the reviewing Institutional Review Board (IRB), FDA or other regulatory authorities; and all other applicable laws and regulations.
- Supervise all testing of the device where human subjects are involved.
- Ensure that the requirements for obtaining informed consent are met.
- Obtain authorization for use/disclosure of health information (e.g., HIPAA authorization or equivalent).
- Maintain all information supplied by Johnson & Johnson Surgical Vision in confidence and, when this information is submitted to an independent IRB or any other group, it will be submitted with a designation that the material is confidential.

I have read this protocol in its entirety and I agree to all aspects.

Investigator Printed Name	Signature	Date
Sub-Investigator Printed Name	Signature	Date
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1. SYNOPSIS

PROTOCOL: Clinical Investigation of the Safety and Effectiveness of an Investigational Model of the TECNIS® Intraocular Lens

Protocol Number: SUR-CAT-652-2001

STUDY TREATMENTS: Investigational Lens:
TECNIS IOL Model ZFR00V (presbyopia-correcting IOL made with OptiBlue material, which contains a violet-blocking chromophore)

Control Lens:
TECNIS IOL Model ZCB00 (colorless monofocal, Johnson & Johnson Surgical Vision,), commercially available

STUDY OBJECTIVE: The purpose of this clinical trial is to evaluate the safety and effectiveness of the investigational IOL Model ZFR00V in comparison to a monofocal IOL.

CLINICAL HYPOTHESIS: The investigational IOL Model ZFR00V will provide improved distance-corrected near visual acuity, as well as decreased spectacle wear compared to the monofocal control TECNIS 1-piece IOL Model ZCB00. The mean best-corrected distance acuity of the investigational IOL Model ZFR00V will be non-inferior to that of the monofocal control IOL Model ZCB00.

Complication and adverse event rates associated with the investigational IOL Model ZFR00V will be within the rates for posterior chamber IOLs given in ISO 11979-7:2018.

OVERALL STUDY DESIGN:

Structure: Prospective, multicenter, bilateral, three-way masked (sponsor, subject and evaluator), randomized clinical trial

Number of sites: Up to 15 sites in the United States

Duration: 6 months postoperative follow-up

Administration: Surgeons will perform routine, small-incision, cataract surgery and implant the study lenses using a

sponsor-recommended implantation system. Refractive target outcomes will be emmetropia for both eyes.

Visit Schedule: Subjects will be randomized to a treatment group (masked) and bilaterally implanted with the same lens type; the second eye is to be implanted within 1 month of the first eye surgery.

All subjects will undergo 9 scheduled visits: Preoperative for both eyes; Operative, 1-day, and 1-week visits for each eye; and 1-month and 6-month visits for both eyes.

STUDY POPULATION CHARACTERISTICS:

Condition: Bilateral cataracts with otherwise-healthy eyes

Number of Subjects: Up to 300 subjects (150 per lens group) will be enrolled, allowing for 10% screening failures, to achieve approximately 135 bilaterally-implanted subjects in each lens group. Allowing for 10% lost to follow-up, this will achieve approximately 122 evaluable subjects at 6 months postoperative in each lens group in the study.

Each site should enroll approximately 20 subjects, and no site may enroll more than 25% of the enrollment total.

Inclusion Criteria (all criteria apply to each study eye):

- Minimum 22 years of age
- Bilateral cataracts for which posterior chamber IOL implantation has been planned
- Preoperative best-corrected distance visual acuity (BCDVA) of 20/40 Snellen or worse with a glare source or 20/40 Snellen or worse without a glare source
- Potential for postoperative BCDVA of 20/30 Snellen or better
- Corneal astigmatism:
  - Normal corneal topography
  - Predicted postoperative corneal astigmatism of less than 1.00 D in both eyes, including posterior corneal astigmatism (PCA)
- Clear intraocular media other than cataract in each eye
- Availability, willingness and sufficient cognitive awareness to comply with examination procedures and study visits
- Signed informed consent and HIPAA authorization or equivalent documentation necessary to comply with applicable privacy laws pertaining to medical treatment in the governing countries
- Ability to understand and respond to a questionnaire in English.

Exclusion Criteria (all criteria apply to each study eye):

- Requiring an intraocular lens power outside the available range of +14.0 D to +26.0 D
- Any clinically-significant pupil abnormalities (non-reactive, fixed pupils, or abnormally-shaped pupils)
- Inability to focus or fixate for prolonged periods of time (e.g., due to strabismus, nystagmus, etc.)
- Prior corneal refractive (LASIK, LASEK, RK, PRK, etc.) or intraocular surgery, including prophylactic peripheral iridotomies and peripheral laser retinal repairs
- Corneal abnormalities such as stromal, epithelial or endothelial dystrophies (e.g., any observed guttata) that are predicted to cause visual acuity losses to a level worse than 20/30 Snellen during the study
- Irregular corneal astigmatism
- Inability to achieve keratometric stability for contact lens wearers (as defined in Section 10.3 Preoperative Procedures)
- Recent ocular trauma or ocular surgery that is not resolved/stable or may affect visual outcomes or increase risk to the subject
- Subjects with diagnosed degenerative visual disorders (e.g., macular degeneration or other retinal disorders) that are predicted to cause visual acuity losses to a level worse than 20/30 Snellen during the study
- Subjects with conditions associated with increased risk of zonular rupture, including capsular or zonular abnormalities that may lead to IOL decentration or tilt, such as pseudoexfoliation, trauma, or posterior capsule defects
- Use of systemic or ocular medications that may affect vision
- Prior, current, or anticipated use during the course of the 6-month study of tamsulosin or silodosin (e.g., Flomax, Flomaxtra, Rapaflo) that may, in the opinion of the investigator, confound the outcome or increase the risk to the subject (e.g., poor dilation or a lack of adequate iris structure to perform standard cataract surgery)
- Poorly-controlled diabetes
- Acute, chronic, or uncontrolled systemic or ocular disease or illness that, in the opinion of the investigator, would increase the operative risk or confound the outcome of the study (e.g., immunocompromised, connective tissue disease, suspected glaucoma, glaucomatous changes in the fundus or visual field, ocular inflammation, etc.). Note: controlled ocular hypertension without glaucomatous changes (optic nerve cupping and visual field loss) is acceptable.
- Known ocular disease or pathology that, in the opinion of the investigator,
  - may affect visual acuity
  - may require surgical intervention during the course of the study (macular degeneration, cystoid macular edema, diabetic retinopathy, uncontrolled glaucoma, etc.)
  - may be expected to require retinal laser treatment or other surgical intervention during the course of the study (macular degeneration, cystoid macular edema, diabetic retinopathy, etc.)
- Pregnancy, planned pregnancy, presently lactating, or another condition associated with hormonal fluctuation that could lead to refractive changes
- Concurrent participation or participation within 60 days prior to preoperative visit in any other clinical trial

- Desire for monovision correction.

EVALUATION CRITERIA:

The purpose of this clinical study is to evaluate the safety and effectiveness of the investigational IOL Model ZFR00V. Clinical endpoints and success criteria for this evaluation are defined below.

EFFECTIVENESS

The primary effectiveness endpoint for the study is the mean monocular distance-corrected near visual acuity (40 cm) under photopic conditions.

The secondary effectiveness endpoints for the study are:

1. Monocular DCIVA (66 cm) under photopic conditions

2. Monocular DCNVA (33 cm) under photopic conditions

3. Monocular BCDVA under photopic conditions

4. Monocular distance-corrected defocus curve

5. Spectacle wear

SAFETY

Primary Safety:

1. The rate of secondary surgical interventions (SSIs) related to optical properties of the lens in first eyes of subjects in the test group

2. All SPE types of adverse events, including total SSIs, reported among first eyes of subjects in the test group will be compared to ISO SPE rates.

3. All other types of adverse events (non-SPE) will be analyzed

Co-Primary Safety:

1. The proportion of first eyes in the test group that achieves monocular BCDVA percent of 20/40 or better will be compared to the ISO SPE rate.

Secondary Safety:

The binocular and monocular (first eyes) best-corrected distance contrast sensitivity for the test group will be compared to that of the control (mesopic with and without glare at 1.5, 3, 6, and 12 cpd, photopic with glare at 3, 6, 12, and 18 cpd).

For primary and co-primary safety endpoints, additional secondary analyses consisting of second eyes and all eyes (pooling first and second eyes) will also be included.

OTHER ENDPOINTS

Other endpoints in the study include:

- Binocular distance-corrected defocus
- Monocular (first eye) and binocular mesopic DCNVA at 40 cm
- Monocular (first eye) UCDVA
- Binocular UCDVA, UCIVA, and UCNVA
- Binocular BCDVA and DCNVA at 40 cm
- Medical findings/complications
- Lens findings/complications
- Residual refractive error
- Visual symptoms reported via PRO instrument (Patient Reported Visual Symptoms Questionnaire [PRVSQ]
- Ocular/visual symptoms (non-directed responses to the open-ended question “Are you having any difficulties with your eyes or vision?”)

- Satisfaction and other questionnaire responses

DATA ANALYSIS:

The investigational IOL Model ZFR00V will be compared to the control IOL Model ZCB00. The 6-month postoperative visit is the key analysis time point for all endpoints, although data will be reviewed at other time points as well.

For the primary effectiveness endpoint (DCNVA at 40 cm) and monocular secondary effectiveness endpoints (DCIVA, DCNVA at 33 cm, and BCDVA), the primary analysis population will be a modified Intent-to-Treat (mITT) analysis for all first eyes randomized and implanted with either a test or control lens.

For the spectacle wear secondary endpoints based on binocular measurements, the primary analysis population will be a modified Intent-to-Treat (mITT) analysis that only includes subjects randomized and binocularly implanted with the same lens model (either investigational or control lenses in both eyes). Any missing values at the 6-month postoperative visit will be imputed in ITT and mITT analyses.

Since there are no inferential statistics for the monocular defocus curve secondary endpoint, a safety population (SP), with available data (i.e., no data imputation) and with subjects randomized and implanted with either an investigational or control lens will be the primary analysis population. The SP will also be used for safety endpoints and other endpoints. With the exception of spectacle wear data, binocular, second-eye and pooled eye data will be considered supplementary and will be used for secondary analyses. Per-protocol analysis will be performed for primary and secondary endpoints. Sensitivity analysis will also be performed for primary DCNVA (40 cm) endpoint and secondary DCIVA, DCNVA (33 cm), BCDVA, and spectacle wear endpoints. Please see detailed descriptions of the analysis populations in Section 20.1.

All data will be reported by IOL group.

STUDY VISITS AND PROCEDURES:

Inclusion and exclusion qualifications will be assessed at the preoperative visit according to the inclusion/exclusion criteria. The Informed Consent Form and Authorization for Use/Disclosure of Health Information form (HIPAA authorization) must be signed by any patients who agree to participate in the study prior to undergoing any study-specific procedures. Those subjects who meet the inclusion/exclusion criteria and agree to participate will be randomized to a treatment group in a masked fashion and implanted in both eyes: either the test Model ZFR00V IOL or control Model ZCB00 IOL. The eye implanted first will be considered the primary study eye. All subjects are intended to have bilateral cataract surgery with the second-eye surgery occurring after the 1-week exam for the first eye but no more than 30 days after the first eye surgery. Study subjects as well as personnel performing the postoperative vision testing and refractions

will be masked for the duration of the study. In addition, key Sponsor personnel will be masked during the study, as necessary.

Key preoperative data include ocular health and history, visual acuities, manifest refraction, keratometry, biomicroscopic slit-lamp findings, ocular symptoms, and biometry. The operative visit will include standard procedures for cataract surgery and IOL implantation. Key postoperative data include monocular and binocular uncorrected and distance-corrected visual acuities under photopic and mesopic lighting conditions, contrast sensitivity, defocus curve, slit-lamp findings, non-directed visual symptoms, questionnaires, and adverse events.

2. BACKGROUND/INTRODUCTION

Presbyopia, defined as the age-related loss of accommodative amplitude[1], affects essentially all human beings beyond the age of 45 and impacts the ability of the eye to focus at near distances[2]. Current intraocular lens options for cataract patients who desire improved vision across a range of distances include a choice of monovision or multifocality. Patients implanted with standard monofocal lenses often need spectacles for reading or performing other near tasks, even if a monovision option is selected. Patients implanted with multifocal lenses, while being able to read and perform other near tasks without spectacles, may have limited intermediate ability (e.g., may need spectacles to work on a computer), and may sometimes experience dysphotopsias (e.g., halos), particularly at night. Some accommodating lenses are also available on the market, although their effect depends upon fit within the capsular bag or capsular bag elasticity. The extended range of vision IOL, TECNIS Symfony Model ZXR00, uses diffractive technology to elongate the depth of focus and improve vision range compared to standard monofocal IOLs.

The investigational IOL in this protocol, Model ZFR00V, is a next-generation TECNIS lens that is designed to provide an increased range of vision for intermediate and near tasks as compared to the control IOL Model ZCB00.

3. CLINICAL HYPOTHESIS

The investigational IOL Model ZFR00V will provide improved distance-corrected near visual acuity, as well as decreased spectacle wear compared to the monofocal control, TECNIS 1-piece IOL Model ZCB00. The mean best-corrected distance acuity of the

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[1] Koretz J.F., Kaufman P.L, Neider M.W. Goeckner P.A. Accommodation and Presbyopia in the Human Eye – Aging of the Anterior Segment. Vision Res. 1989;29: 1685-1692.

[2] Benjamin, William, J., Borish, Irvin M. Borish's Clinical Refraction, Philadelphia: 1998, W.B. Saunders, pg 109.

investigational IOL Model ZFR00V will be non-inferior to that of the monofocal control IOL Model ZCB00.

Complication and adverse event rates associated with the investigational IOL Model ZFR00V will be within the rates for posterior chamber IOLs given in ISO 11979-7:2018.

4. STUDY DESIGN

This study is a 6-month, prospective, multicenter, three-way masked (Sponsor, subject and evaluator), bilateral randomized clinical investigation of the TECNIS IOL Model ZFR00V versus the TECNIS Model ZCB00 IOL.

The study will be conducted at up to 15 sites in the U.S.A. and will enroll up to 300 subjects to achieve approximately 270 bilaterally-implanted subjects, resulting in approximately 122 evaluable subjects in each lens group at 6 months. Subjects will be randomized to a treatment group in a masked fashion and be implanted with either the investigational IOL Model ZFR00V or the control IOL Model ZCB00 in both eyes. The eye implanted first will be considered the primary (monocular) study eye.

5. ACRONYMS

The following acronyms are used throughout this document:

- UCDVA: uncorrected distance visual acuity
- BCDVA: best-corrected distance visual acuity
- UCIVA: uncorrected intermediate visual acuity
- DCIVA: distance-corrected intermediate visual acuity
- UCNVA: uncorrected near visual acuity (40 cm)
- DCNVA: distance-corrected near visual acuity (40 cm unless otherwise stated)
- D: diopters

6. STUDY OBJECTIVES AND ENDPOINTS

The purpose of this study is to evaluate the safety and effectiveness of the investigational IOL Model ZFR00V in comparison to a monofocal control IOL. The 6-month postoperative visit is the key analysis time point for all endpoints, although data will be reviewed at other time points as well. Data for other visits will be included in the final analysis.

6.1 PRIMARY EFFECTIVENESS ENDPOINT

MONOCULAR PHOTOPIC DCNVA AT 40 CM

Success criteria: Statistically significant improvement in mean monocular photopic distance-corrected near visual acuity for first eyes in the test group vs.

first eyes in the control group. In addition, clinical significance will be determined if the mean DCNVA for the test group is at least 0.2 LogMAR.

6.2 SECONDARY EFFECTIVENESS ENDPOINTS

1. MONOCULAR PHOTOPIC DCIVA AT 66 CM

Success criteria: Statistically significant improvement in mean LogMAR distance-corrected intermediate visual acuity for first eyes in the test group vs. first eyes in the control group. In addition, clinical significance will be determined if the mean DCIVA at 66 cm for the test group is at least 0.2 LogMAR.

2. MONOCULAR PHOTOPIC DCNVA AT 33 CM

Success Criteria: Statistically significant improvement in mean LogMAR distance-corrected near visual acuity at 33 cm for the test group compared to the control group. In addition, clinical significance will be determined if the mean DCNVA at 33 cm for the test group is at least 0.2 LogMAR.

3. MONOCULAR PHOTOPIC BCDVA

Success criteria: Statistically non-inferior (within 0.1 LogMAR) in mean LogMAR best-corrected distance visual acuity for eyes in the test group vs. eyes in the control group.

4. MONOCULAR DISTANCE-CORRECTED DEFOCUS CURVE

Success Criteria: The mean distance-corrected visual acuity for the investigational lens group is maintained at 0.2 LogMAR or better from 0.0 D to -2.5 D of defocus.

5. SPECTACLE WEAR

Success criteria: Statistically significantly greater proportion of subjects who do not wear spectacles (defined as subjects who wear glasses or contacts “none of the time”) for distance, intermediate, near and overall vision in subjects in the test group vs. control group, as determined from a PRO instrument assessing spectacle wear (PRSIQ). In addition, clinical significance will be determined by 1) at least 50% of subjects in the test group will report wearing glasses “None of the time” for all four conditions (distance, intermediate, near and overall vision) and 2) the proportion of test subjects who report wearing glasses or contacts “None of the time” for all four conditions will be at least 25 percentage points higher than that for the control group.

6.3 SAFETY ENDPOINTS

Primary Safety:

1. The rate of SSIs related to optical properties of the lens in first eyes of subjects in the test group will be analyzed using descriptive statistics and compared to that of the control group.
2. All SPE adverse events, including total SSI, reported among first eyes of subjects in the test group will be compared to ISO SPE rates.
3. All other non-SPE AEs will be analyzed using descriptive statistics comparing the two lens groups.

Co-Primary Safety:

1. The rate of monocular BCDVA 20/40 or better among first eyes of subjects in the test group will be compared to ISO SPE rates.

Additionally, secondary analyses consisting of second eyes and all investigational eyes (pooling first and second eyes together) will also be included for the above primary and co-primary safety endpoints.

Secondary Safety:

As a secondary safety endpoint, the binocular and monocular (first eyes) best-corrected distance contrast sensitivity for the test group will be compared to control (mesopic with and without glare at 1.5, 3, 6, and 12 cpd, photopic with glare at 3, 6, 12, and 18 cpd).

6.4 OTHER ENDPOINTS

Other endpoints in the study include:

- Binocular distance-corrected defocus
- Monocular (first eye) and binocular mesopic DCNVA at 40 cm
- Monocular (first eye) UCDVA
- Binocular UCDVA, UCIVA, and UCNVA
- Binocular BCDVA and DCNVA at 40 cm
- Medical findings/complications
- Lens findings/complications
- Residual refractive error
- Visual symptoms reported via PRO instrument (Patient Reported Visual Symptoms Questionnaire [PRVSQ])
- Ocular/visual symptoms (non-directed responses to the open-ended question “Are you having any difficulties with your eyes or vision?”)
- Satisfaction and other questionnaire responses

7. STUDY PRODUCTS

7.1 INTRAOCULAR LENSES

The two intraocular lens models that will be evaluated in this study are the investigational IOL Model ZFR00V and the control IOL Model ZCB00.

Investigational IOL Model ZFR00V

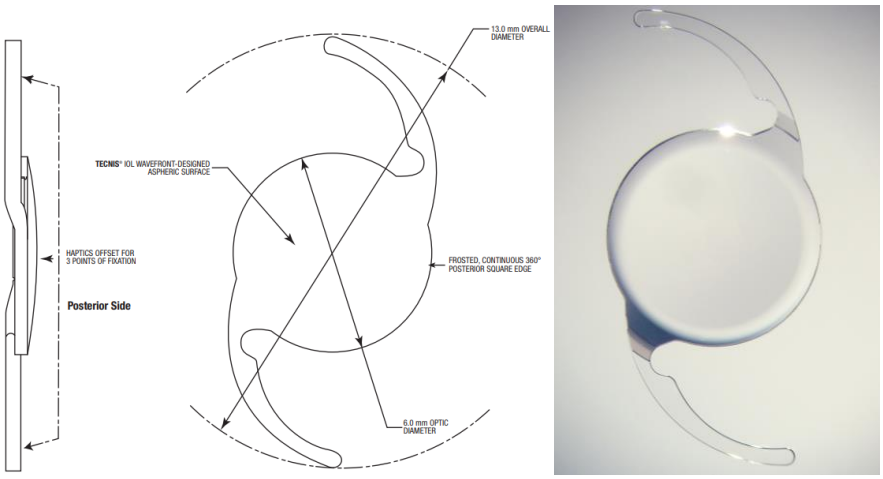
The investigational IOL Model ZFR00V is a posterior chamber, 1-piece, aspheric, diffractive, acrylic, foldable IOL designed for placement in the capsular bag (**Figure 1**). The lens is made of OptiBlue hydrophobic acrylic material, which is a variant of the hydrophobic acrylic SENSAR material that is used for the material/mechanical 1-piece parent, the JJSV 1-Piece IOL Model AAB00, on which the TECNIS 1-piece monofocal IOL lens model ZCB00 is also based. The ZFR00V lens has the same overall geometry/dimensions (13 mm overall length and 6 mm optic diameter) as the material/mechanical 1-piece parent monofocal IOL models. The investigational ZFR00V lens also has the same TECNIS modified prolate (aspheric) design on the anterior optic surface as TECNIS diffractive multifocal and extended range of vision IOLs to reduce spherical aberration.

Control IOL Model ZCB00

The control IOL Model ZCB00 (**Figure 2**) shares the same material, general dimensions, geometry, and one-piece soft acrylic lens platform as the SENSAR 1-Piece IOL, Model AAB00, which is the mechanical parent of the ZFR00V IOL.

Figure 1: Drawing and Photograph of TECNIS IOL Model ZFR00V

Figure 2: Drawing and Photograph of TECNIS IOL Model ZCB00



Like all of JJSV's 1-piece soft acrylic IOLs, investigational IOL Model ZFR00V and the control IOL Model ZCB00 have a surface treatment of polyethylene glycol (PEG) to reduce tackiness of the lens surface and include a ProTEC 360° barrier edge, the stability of Tri-Fix 3-point design, and a frosted-edge treatment.

INDICATIONS FOR INVESTIGATIONAL IOL

The Model ZFR00V is indicated for primary implantation for the visual correction of aphakia in adult patients with or without presbyopia, with less than 1 diopter of pre-existing corneal astigmatism, in whom a cataractous lens has been removed. The lens mitigates the effects of presbyopia by providing improved intermediate and near visual acuity, while maintaining distance visual acuity comparable to that of an aspheric monofocal IOL. The lens provides a full range of vision and increased spectacle independence. The lens is intended for capsular bag placement only.

INDICATIONS FOR CONTROL IOL

The TECNIS monofocal IOL Model ZCB00 is indicated for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed by extracapsular cataract extraction. These devices are intended to be placed in the capsular bag.

STORAGE AND DISTRIBUTION

Consignments of the investigational study lens model will be supplied to the investigative sites. All study lenses should be stored in the original packaging and kept in a dry place. Lenses should not be stored in direct sunlight or at temperatures greater than 45° C (113°F). Each lens is packaged in a lens tray and sealed in a peel-pouch. The lens is sterile as long as the package has not been opened or damaged and the shelf-life

expiration date has not been exceeded. The Principal Investigator is responsible for ensuring that the investigational lenses are used only for subjects enrolled in this study.

COMPARISON CHART

Table 1 describes the dimensional and optical similarities between the study lenses and other associated JJSV lenses.

Table 1: Comparison of Design Features

	SENSAR 1-PIECE IOL, MODEL AAB00	TECNIS OPTIBLUE 1-PIECE IOL, MODEL ZCB00V	TECNIS MULTIFOCAL IOL, MODEL ZM900	TECNIS SYMFONY EXTENDED RANGE OF VISION IOL, MODEL ZXR00	INVESTIGATIONAL IOL, MODEL ZFR00V
	(MECHANICAL / MATERIAL PARENT)	(MONOFOCAL ANALOG)	(OPTICAL CO-PARENT)	(OPTICAL CO-PARENT)	(SUBJECT DEVICE)
LENS DESIGN	1-piece acrylic lens with spherical anterior surface	1-piece acrylic lens with aspheric anterior surface	3-piece silicone lens with aspheric anterior surface	1-piece acrylic lens with aspheric anterior surface	1-piece acrylic lens with aspheric anterior surface
LENS MATERIAL	Surface-treated SENSAR® soft acrylic	Sensar-UV[2] soft acrylic	Polysiloxane	Same as AAB00	Same as ZCB00V
DIMENSIONAL FEATURES					
OVERALL DIAMETER	13.0 mm	Same as AAB00	12.0 mm	Same as AAB00	Same as AAB00
OPTICAL CENTER THICKNESS	0.7 mm (20D lens)	Same as AAB00	1.13 mm (20D lens)	Same as AAB00	Same as AAB00
HAPTIC ANGLE	No angulation, but offset from optic body	Same as AAB00	5°	Same as AAB00	Same as AAB00
OPTIC BODY DIAMETER	6.0 mm	Same as AAB00	Same as AAB00	Same as AAB00	Same as AAB00
HAPTIC MATERIAL	Same as optic	Same as AAB00	Polyvinylidene fluoride	Same as AAB00	Same as AAB00
HAPTIC WIDTH	0.39 mm	Same as AAB00	0.18 mm	Same as AAB00	Same as AAB00
HAPTIC THICKNESS	0.46 mm	Same as AAB00	0.18 mm	Same as AAB00	Same as AAB00
HAPTIC STYLE	C-Loop	Same as AAB00	Cap C	Same as AAB00	Same as AAB00
OPTICAL FEATURES					
OPTIC SHAPE	Biconvex	Same as AAB00	Same as AAB00	Same as AAB00	Same as AAB00
ANTERIOR OPTIC PROFILE	Spherical	Aspheric	Aspheric	Aspheric	Aspheric
POSTERIOR OPTIC PROFILE	Spherical monofocal	Same as AAB00	Spherical diffractive	Spherical diffractive	Modified spherical diffractive
OPTIC EDGE DESIGN	PROTEC 360° squared edge	Same as AAB00	Same as AAB00	Same as AAB00	Same as AAB00
DIOPTER POWER RANGE	+6.0 to +30.0D in 0.5D increments	+5.0 to +34.0D in 0.5D increments	Same as ZCB00V[1]	Same as ZCB00V[1]	Same as ZCB00V[1]
REFRACTIVE INDEX	1.470 (35° C)	1.471 (35°C)	1.46 (37° C)	Same as AAB00	Same as AAB00
ADD POWER	N/A	N/A	+4 D	N/A[2]	N/A[3]
RANGE OF VISION	N/A	N/A	N/A	Through 2.0 D[2]	Through 3.0 D[3]

[1] Only IOLs from +14.0 D to +26.0 D will be used in the clinical study.
[2] There is no distinct add power. Clinically, the range of binocular visual acuity 0.2 LogMAR or better approximates 2.0 D in the negative defocus range.
[3] There is no distinct add power.

7.2 IOL IMPLANTATION SYSTEMS

The investigational TECNIS IOL Model ZFR00V and the control TECNIS IOL Model ZCB00 lenses are to be implanted using the UNFOLDER Platinum-1 Series Implantation System (DK7796 handpiece with the UNFOLDER Platinum-1 Series cartridge, Model 1MTEC30) or the ONE SERIES Ultra Implantation System (DK7786 or DK7791 handpiece with the One Series Ultra cartridge, Model 1VIPR30).

8. STUDY POPULATION

All study subjects will be enrolled from the normal surgical cataract population at up to 15 sites in the U.S.A. Up to 300 subjects will be enrolled to achieve approximately 270 bilaterally implanted subjects, resulting in approximately 244 evaluable subjects (122 subjects per lens group) at 6 months. This allows for a screen failure rate of approximately 10% and a drop-out rate of approximately 10% for implanted subjects. Each site should implant a minimum of 20 subjects, and no site may implant more than 25% of the enrollment total.

This study will include only subjects undergoing bilateral primary cataract extraction and IOL implantation and who meet all of the study inclusion and exclusion criteria in both eyes. Subjects who meet the eligibility criteria will be offered enrollment in the study. Eligibility criteria may not be waived by the investigator. Any questions regarding patient eligibility are to be discussed with JJSV prior to subject enrollment. Those subjects who meet the eligibility criteria and agree to participate will be randomized to receive either the investigational IOL Model ZFR00V or the control IOL Model ZCB00 in both eyes. Subjects will be enrolled at each site sequentially until the overall study recruitment goals are met or the site limit is reached.

8.1 INCLUSION CRITERIA

Note: All criteria apply to each eye

- Minimum 22 years of age
- Bilateral cataracts for which posterior chamber IOL implantation has been planned
- Preoperative best-corrected distance visual acuity (BCDVA) of 20/40 Snellen or worse with a glare source or 20/40 Snellen or worse without a glare source
- Potential for postoperative BCDVA of 20/30 Snellen or better
- Corneal astigmatism:
  - Normal corneal topography
  - Predicted postoperative corneal astigmatism of less than 1.00 D in both eyes, including posterior corneal astigmatism (PCA)
- Clear intraocular media other than cataract in each eye
- Availability, willingness and sufficient cognitive awareness to comply with examination procedures and study visits

- Signed informed consent and HIPAA authorization or equivalent documentation necessary to comply with applicable privacy laws pertaining to medical treatment in the governing countries
- Ability to understand and respond to a questionnaire in English

8.2 EXCLUSION CRITERIA

Note: All criteria apply to each eye

- Requiring an intraocular lens power outside the available range of +14.0 D to +26.0 D
- Any clinically-significant pupil abnormalities (non-reactive, fixed pupils, or abnormally-shaped pupils)
- Inability to focus or fixate for prolonged periods of time (e.g., due to strabismus, nystagmus, etc.)
- Prior corneal refractive (LASIK, LASEK, RK, PRK, etc.) or intraocular surgery, Including prophylactic peripheral iridotomies and peripheral laser retinal repairs
- Corneal abnormalities such as stromal, epithelial or endothelial dystrophies (e.g., any observed guttata) that are predicted to cause visual acuity losses to a level worse than 20/30 Snellen during the study
- Irregular corneal astigmatism
- Inability to achieve keratometric stability for contact lens wearers (as defined in Section 10.3 Preoperative Procedures)
- Recent ocular trauma or ocular surgery that is not resolved/stable or may affect visual outcomes or increase risk to the subject
- Subjects with diagnosed degenerative visual disorders (e.g., macular degeneration or other retinal disorders) that are predicted to cause visual acuity loss to a level worse than 20/30 Snellen during the study
- Subjects with conditions associated with increased risk of zonular rupture, including capsular or zonular abnormalities that may lead to IOL decentration or tilt, such as pseudoexfoliation, trauma, or posterior capsule defects
- Use of systemic or ocular medications that may affect vision
- Prior, current, or anticipated use during the course of the 6-month study of tamsulosin or silodosin (e.g., Flomax, Flomaxtra, Rapaflo) that may, in the opinion of the investigator, confound the outcome or increase the risk to the subject (e.g., poor dilation or a lack of adequate iris structure to perform standard cataract surgery)
- Poorly-controlled diabetes
- Acute, chronic, or uncontrolled systemic or ocular disease or illness that, in the opinion of the investigator, would increase the operative risk or confound the outcome(s) of the study (e.g., immunocompromised, connective tissue disease, suspected glaucoma, glaucomatous changes in the fundus or visual field, ocular inflammation, etc.). Note: controlled ocular hypertension without glaucomatous changes (optic nerve cupping and visual field loss) is acceptable.
- Known ocular disease or pathology that, in the opinion of the investigator,
  - may affect visual acuity
  - may require surgical intervention during the course of the study (macular degeneration, cystoid macular edema, diabetic retinopathy, uncontrolled glaucoma, etc.)

  - may be expected to require retinal laser treatment or other surgical intervention during the course of the study (macular degeneration, cystoid macular edema, diabetic retinopathy, etc.)
- Pregnancy, planned pregnancy, presently lactating, or another condition associated with hormonal fluctuation that could lead to refractive changes
- Concurrent participation or participation within 60 days prior to preoperative visit in any other clinical trial
- Desire for monovision correction

9. INVESTIGATOR SELECTION

9.1 INVESTIGATOR QUALIFICATIONS

JJSV will select ophthalmic surgeons who have completed a residency in ophthalmology (or its documented equivalent) and are licensed to practice medicine and perform surgery at his/her investigative site. Each site will have one designated principal investigator; some sites may have additional implanting sub-investigators/surgeons.

Investigators will be selected from surgeons who are experienced in small-incision surgery and have implanted TECNIS 1-piece IOLs in cataract patients. Investigators should have established personalized A-constants for the TECNIS 1-piece IOL Model ZCB00. All sites are required to have adequate staff support for reporting and subject follow-up, as well as the necessary instrumentation to conduct study testing.

9.2 INVESTIGATOR OBLIGATIONS

Investigators are required to fulfill the following obligations:

- Conduct the study in accordance with the relevant and current protocol. Investigator will make changes to a protocol only after notifying and obtaining approval from JJSV, the FDA and the Investigational Review Board (IRB), except when necessary to protect the safety, rights or welfare of subjects
- Personally conduct and supervise the study
- Maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties
- Be responsible for protecting the rights, safety and welfare of subjects under the investigator's care and be responsible for the control and documentation of the devices under investigation
- Inform patients that the device(s) are being used for investigational purposes and that requirements relating to obtaining informed consent and IRB approval are met according to 21CFR50, 21CFR56, 21CFR812 and all other applicable laws and regulations
- Maintain confidentiality as required by HIPAA or similar laws and regulations
- Shall not obtain written informed consent from any subject to participate or allow any subject to participate before obtaining FDA and IRB approval

- Document in each subject's case history that informed consent was obtained prior to participation in the study as required by 21CFR812
- Report to JJSV and the reviewing IRB any adverse experiences that occur during the course of the study in accordance with applicable laws and regulations
- Maintain adequate and accurate records in accordance with applicable laws and regulations and make available all study documents and subject medical records for inspection by either JJSV, duly authorized regulatory agencies (e.g., FDA, PMDA, Health Canada, MOH, etc.) and/or the IRB
- Submit progress reports on the investigation to JJSV and the reviewing IRB at regular intervals, but no less often than yearly as required by 21CFR812.150
- Ensure the IRB that is responsible for initial and continuing review of the study complies with applicable laws and regulations
- Report all changes in research activity and all unanticipated problems involving risks to patients to the IRB and JJSV
- Supervise and permit investigational device use and disposition in accordance with applicable regulations and protocol requirements. Upon completion of enrollment or termination of the study or the investigator's part of the study, or at JJSV's request, return to JJSV any remaining supply of the investigational device
- Provide sufficient accurate financial information to JJSV to allow JJSV to submit complete and accurate certification or disclosure statements as required by 21CFR54. Promptly update this information if any relevant changes occur during the course of the investigation or for up to one year following completion of the study
- Comply with all other obligations of clinical investigators and requirements according to all applicable FDA regulations (e.g., 21CFR812), all other applicable laws and regulations, and all conditions of approval imposed by the reviewing IRB and the FDA
- Ensure that all associates, colleagues and employees assisting in the conduct of the study are adequately informed about the protocol, the investigational device, their study-related duties and functions and agree to fulfill their obligations in meeting the above commitments.

Investigators shall provide adequate time and resources to conduct and report on the study. The Investigator, or delegate, shall notify JJSV of any change in the conduct of the study including changes in study personnel assigned to the study project, location of the investigational device(s), or maintenance of study records, etc.

9.3 INVESTIGATOR APPROVAL

It is the responsibility of the investigator to obtain prospective approval of the study protocol, protocol amendments or changes, informed consent forms and other relevant documents (e.g., advertisements) from the IRB. All correspondence with the IRB should be retained in the Investigator Study Files/Notebook. Copies of IRB submissions and approvals should be forwarded to JJSV. Study sites will obtain IRB approvals and fulfill any other site-specific regulatory requirements. The investigator is required to report to

JJSV within five working days any withdrawal of approval by the reviewing IRB for his/her participation in the investigation.

Prior to the start of subject enrollment, the following documents must be signed and returned to JJSV:

- Confidentiality Agreement
- Clinical Study Agreement
- Investigator Agreement/Protocol Signature page
- Clinical Investigator Brochure Signature page
- Financial Disclosure form
- Signed and dated copy of investigator's current curriculum vitae
- Copy of the investigator's current medical license
- Hospital/Ambulatory Surgery Center Clinical Study Acknowledgement, if required

By signing the study documents, the investigator agrees to conduct this study according to the obligations above and all other applicable regulatory and legal requirements.

10. EXPERIMENTAL PLAN

10.1 OVERVIEW

This study will be conducted in accordance with U.S. Code of Federal Regulations, the Declaration of Helsinki, ISO 14155:2011 and all other applicable laws and regulations. The study will not begin until regulatory and IRB approvals have been obtained.

This study will be a prospective, multicenter, bilateral, comparative, three-way masked (Sponsor, subject and evaluator), randomized clinical investigation conducted at up to 15 sites. Up to 300 subjects will be enrolled to achieve approximately 270 bilaterally implanted subjects, resulting in approximately 244 evaluable subjects (122 per lens group) at 6 months. After informed consent is obtained and confirmation that all eligibility criteria are met, the eye(s) may be treated according to randomization.

After signing the informed consent form, subjects meeting all eligibility criteria will be randomized in a masked fashion to a treatment group: either the investigational IOL Model ZFR00V or the control IOL Model ZCB00. Prior to randomization, the investigator will choose which eye to operate on first for each subject at his/her discretion based on his/her standard clinical practice (e.g., the eye with the worse cataract, poorer best-corrected distance vision and/or more severe optical/visual complaints). All subjects are intended to have bilateral cataract surgery with the second-eye surgery occurring after the 1-week postoperative exam for the first eye, but no more than 30 days after the first eye surgery. All subjects will be examined through 6 months postoperatively according to the visit schedule described in **Section 10.2**, Visit Schedule.

Study evaluators responsible for conducting all vision testing will remain masked to which lenses were implanted through the 6-month study visit. Because differences between the investigative and control lenses may be discernible upon slit-lamp examination, special care must be taken to maintain masking of subjects and study technicians. As such, it is recommended that only the investigator, sub-investigator or other designated and trained clinician perform all biomicroscopic slit-lamp exams. To maintain consistency, as well as masking, it is recommended that a single individual (study technician or coordinator designated by the investigator) conduct all postoperative study-related vision testing, although a back-up person should also be designated and trained. The subject should also remain masked to the randomized treatment throughout the study.

Key preoperative data include ocular health and history, visual acuities, manifest refraction, keratometry, topography, biomicroscopic slit-lamp findings, ocular symptoms and biometry. The operative visit will include standard procedures for cataract surgery and IOL implantation. Key postoperative data collection includes monocular and binocular uncorrected and distance-corrected visual acuities, contrast sensitivity, defocus curve, slit-lamp findings, non-directed visual symptoms, questionnaires and adverse events. A chart summary of all examination procedures required at each study visit is provided in **Appendix A**. If needed, specific equipment necessary to perform the required procedures may be supplied for the duration of the study (**Appendix B**).

10.2 VISIT SCHEDULE

The study visit schedule for all study subjects is outlined in **Table 2**.

All subjects are intended to have bilateral cataract surgery with the second eye surgery occurring after the 1-week exam for the first eye but no more than 30 days after the first eye surgery. After each surgery, the operative eye will be examined at 1 day (1-2 days) and 1 week (7-14 days) postoperative. Based on the date of the second-eye surgery, both eyes will be evaluated at 1 month (30-60 days) and 6 months (120-180 days) postoperative. Unscheduled visits may be conducted as necessary at the discretion of the investigator for medically-indicated follow-up.

TABLE 2: Visit Schedule

VISIT	EYES EVALUATED	EXAM	VISIT WINDOW
1	Both Eyes	Preoperative Exam	Within 60 days prior to 1st surgery
2	First Eye	Operative	0-60 days after preoperative exam
3	First Eye	1 day	1-2 days postoperative
4	First Eye	1 week[a]	7-14 days postoperative
5	Second Eye	Operative[a]	No more than 30 days after 1st eye surgery
6	Second Eye	1 day	1-2 days postoperative
7	Second Eye	1 week	7-14 days postoperative
8	Both Eyes	1 month	30 - 60 days postoperative from 2nd eye surgery[b]
9	Both Eyes	6 months	120 - 180 days postoperative from 2nd eye surgery[b]

[a] The 1-week exam for the first eye should be completed prior to implanting the second eye.

[b] If for any reason the second eye is not implanted, the first eye should be examined for the 1-month study visit 37 to 67 days following the first eye surgery and for the 6-month study visit 127 to 210 days following the first eye surgery.

10.3 PREOPERATIVE PROCEDURES

All subjects treated in the study must sign the current IRB-approved informed consent form and meet the eligibility criteria. The informed consent form must be signed before any study-specific examinations are performed, and this must be documented in the source documents. An Authorization for Use/Disclosure of Health Information Form (HIPAA authorization) or similar medical treatment privacy law documentation must also be signed.

All preoperative testing for the study must be completed within 60 days prior to the first surgery. Data from routine (non-study-specific) preoperative cataract examinations performed prior to the informed consent process may be included, provided these tests are conducted no more than 60 days prior to the first-eye surgery and the test date(s) are documented on the preoperative Case Report Form (CRF). If a test/exam is required by the protocol, but is not part of the routine testing the investigator performs for the cataract evaluation, that test/exam is considered study-specific and is not to be done until after the informed consent form has been signed by the subject. Following the informed consent process, completion of the preoperative study exam, determination that the subject meets all the required entrance criteria (including lens power determination), and documentation by the study investigator of the first eye to be

implanted, the subject may be scheduled for surgery and randomized to a treatment group.

As the Informed Consent Form is signed at the beginning of the preoperative study exam, some subjects may not qualify after study-specific testing is performed. Subjects will be considered screen-failures if they do not qualify, or if they qualify but decide not to participate further in the study, or if they decide not to proceed with surgery. These subjects will be exited from the study.

Preoperative testing to be performed for each eye includes the following:

POTENTIAL DISTANCE VISUAL ACUITY

The subject must be capable of achieving Snellen 20/30 or better best-corrected distance vision in each eye after cataract extraction and IOL implantation. The surgeon may use his/her judgment, the Potential Acuity Meter (PAM), or other methods (e.g., pinhole, laser interferometer, etc.) to estimate the subject's potential postoperative acuity.

BEST-CORRECTED DISTANCE VISUAL ACUITY AND MANIFEST REFRACTION

Preoperative manifest refraction is required. Monocular, best-corrected distance visual acuity (BCDVA) is to be measured using a standard Snellen chart or equivalent and must be Snellen 20/40 or worse with a glare source or 20/40 Snellen or worse without a glare source.

KERATOMETRY

Predicted postoperative corneal astigmatism, based on measurements by keratometry, should be less than 1.00 D. No irregular astigmatism should be present preoperatively. If the preoperative keratometric astigmatism is greater than 0.50 D, assess the impact of posterior corneal astigmatism (PCA) on predicted residual astigmatism by using a calculator that accounts for PCA (e.g., J&J TECNIS Toric Calculator, Barrett Toric Calculator, etc.).

CONTACT LENS WEAR AND CORNEAL STABILITY

For contact lens wearers, keratometric corneal stability following cessation of contact lens wear must be verified before surgery. PMMA contact lenses are not to be worn for at least 6 months; rigid gas-permeable contact lenses are not to be worn for at least 1 month; and extended-wear or daily-wear soft contact lenses are not to be worn for at least 1 week prior to the preoperative visit. Corneal stability must be verified for any subject who has worn PMMA lenses within 5 years or any other type of contact lenses within 6 months prior to the preoperative visit. To verify stability, repeat the keratometric measurements at least 1 week after the initial preoperative baseline keratometric

measurement. Corneal curvature is considered to be stable if the difference in keratometric cylinder (vertical vs. horizontal keratometric readings) between the two timepoints does not exceed 0.50 D. Additionally, the difference between the two horizontal readings as well as the difference between the two vertical readings must be no more than 0.50 D. Changes in keratometric axis must be no more than ±15°. If a change exceeding these criteria is noted, surgery is to be postponed until keratometric stability is demonstrated. Final biometry measurements and surgery should not take place until keratometric stability is achieved. Note: if this method of determining corneal stability is not a standard procedure in your practice, the subject must sign the informed consent form prior to starting the stability procedure.

IOL POWER AND TARGETED REFRACTION

Axial length and anterior chamber depth (ACD) must be measured to determine the appropriate lens power to implant using an A-Constant. IOLMaster, Lenstar or immersion biometry methods are preferred; however, surgeons should use the biometry method with which they have the most experience and that which was used in the determination of personalized A-Constants for TECNIS IOLs.

Power calculations for a given subject must be completed for both lens groups prior to randomization. For investigational lens Model ZFR00V, IOL power should be determined with calculations using the labeled A-Constant of 119.3. For control lens Model ZCB00, the investigator may use the labeled A-Constant of 119.3 or use their personalized A-Constant for the Model ZCB00 monofocal lens.

Lens powers should be calculated to achieve emmetropia at distance in both eyes, and the IOL power that is predicted to result in the least amount of ametropia should be selected for implantation. Intentional over- or under-correction should NOT be planned for either eye; however, surgeons may adjust the targeted refraction for the second eye only as necessary to achieve emmetropia based on a subject's first-eye outcome.

QUESTIONNAIRES

Questionnaires will be administered preoperatively to collect information regarding spectacle usage, visual symptoms, visual quality, and subject satisfaction. Two questionnaires will be used in this study:

1) Patient-Reported Visual Symptoms Questionnaire (PRVSQ, **Appendix M**)
2) Patient-Reported Spectacle Independence Questionnaire (PRSIQ, **Appendix N**)

ADDITIONAL PREOPERATIVE INFORMATION TO BE COLLECTED:

- Informed consent
- Subject demographic information

- Planned surgery dates for each eye
- Ocular history, including presence of ocular pathology for each eye
- Intraocular pressure for each eye
- Cataract type and density for each eye
- Fundus exam results for each eye
- Medical findings from a biomicroscopic slit-lamp exam for each eye
- Ocular symptoms for each eye
- Ocular and systemic medications

10.4 RANDOMIZATION AND STUDY MASKING

A randomization list will be created by the J biostatistician for each investigative site and the randomization code will be uploaded into the electronic data capture system (EDC). Subjects will be randomized to the investigational lens Models ZFR00V and the control lens Model ZCB00. Unmasked study personnel at the site will be trained to the randomization process through the EDC system and will randomize subjects after the subject has signed the informed consent form, has met all eligibility criteria and the investigator has documented which eye will be implanted first.

For the duration of this study, the subjects and study staff who conduct study vision testing and/or collect study vision data will be masked to the treatment group to which a given subject was randomized. For this reason, care must be taken such that subjects and masked evaluators are not informed of the implanted lenses. In addition, key Sponsor personnel will be masked during the study, as necessary.

As part of the informed consent process, the investigator or delegate will explain to the subject the requirements of a randomized study and the differences expected between the two lens models in the study: the investigational lens Model ZFR00V and the control lens Model ZCB00. .

Only the surgeon and the operative staff will know which lens type is implanted and will be unmasked throughout the study. There may also be site coordinators and other site study staff, such as those performing slit-lamp exams, who will be unmasked. Unmasked study staff and study subjects will be instructed not to disclose the lens type the subject received or to talk about the lens to any subjects or masked evaluators.

The subjects and the study technicians performing the postoperative vision tests are to be masked through study completion. To maintain subject/technician-masking through the 6-month study exams, a masking plan will be tailored for each site to detail how lens assignment information will be concealed from masked technicians. Recommended steps to maintain masking include ensuring that all items pertaining to lens group assignment and lens implantation records are kept separately from all other study documents and subject medical records until after completion of the final study visit. For

example, lens stickers (indicating the lens model implanted) may be kept in the study product accountability notebook until completion of the final study visit, at which time they may be placed in the subject medical charts. In the meantime, temporary lens stickers (without lens model designations) may be used in the subject's medical chart.

To maintain subject masking, a temporary IOL implant identification card will be issued to the subject at the time of surgery. Following completion of the final study exam, each subject will be given the permanent IOL implant identification card.

10.5 STUDY LENS SUPPLY

The investigational lenses will be obtained from a site consignment that is supplied by the Sponsor following IRB approval for a given site. Two lenses should be available for each case, a primary lens and a back-up lens. Unused back-up lenses are to be returned to the site consignment. At the completion of study enrollment, any remaining consignment lenses will be shipped back to the Sponsor following reconciliation of investigational lens inventory by a Sponsor CRA. At all times, the storage, access and use of all investigational lenses must be controlled and complete lens accountability maintained (See **Section 15.2** Lens Accountability).

Control lenses for the study will be sourced from each site's routine commercial lens inventory or sponsor-provided consignment.

10.6 OPERATIVE PROCEDURES

The investigator should use his or her standard, small-incision, cataract extraction surgical technique. Lenses should be folded for implantation and inserted into the capsular bag using one of the Sponsor-validated insertion systems described in **Section 7.2**.

Investigators should manage surgical outcomes to ensure that the total postoperative refractive astigmatism is as minimal as possible. The total postoperative astigmatism, including surgically-induced astigmatism and PCA, should be targeted to be less than 1.0 D. Astigmatism may be managed by incision type and placement only. **No additional refractive procedures are to be performed during the operative procedure or throughout the postoperative study period (e.g., LRI, OCCI, CRI, AK, PRK, LASIK or LASEK).**

Operative case report forms will include the following information:

INCISION TYPE AND SIZE

Lenses should be inserted through an incision ranging in size from approximately 2.2-3.0 mm, per the investigator's standard technique when using the UNFOLDER Platinum-1 Series Implantation System or the ONE SERIES Ultra Implantation System.

The incision may be clear corneal, limbal or scleral tunnel at the discretion of the investigator.

CAPSULORHEXIS SIZE AND METHOD

The anterior capsulotomy should be a continuous, curvilinear capsulorhexis approximately 5.0 to 5.5 mm in diameter to allow slight overlap of the lens optic edge. The anterior capsulotomy method may be manual (rhexis) or laser-assisted.

CRYSTALLINE LENS REMOVAL

Crystalline lens removal may occur using laser fragmentation combined with phacoemulsification/aspiration or using only phacoemulsification/aspiration.

VISCOELASTIC

Viscoelastic materials should be used as is customary for each investigator and recorded on the case report form (CRF).

IMPLANT INSTRUMENTATION USED

Lenses should be folded for implantation and inserted into the capsular bag using either the UNFOLDER Platinum-1 Series Implantation System (DK7796 handpiece with the Platinum-1 Series cartridge, Model 1MTEC30) or the ONE SERIES Ultra Implantation System (DK7786 [plunger] or the DK7791 [twist] handpieces with the ONE SERIES Ultra cartridge, Model 1VIPR30).

SURGICAL COMPLICATIONS

Should a surgical complication occur, implantation of a study lens will be at the investigator's discretion. In the event of capsular bag or zonular rupture, the lens should not be implanted. Additionally, the lens is not to be implanted in the sulcus. In this case, the investigator may implant his/her choice of a back-up, non-investigational IOL. The subject should be exited from the study if a non-study lens is implanted as a result of a surgical complication during the first eye implantation; however, the eye will be followed until resolution of the complication prior to exiting the subject. Should a surgical complication occur during the second-eye surgery and result in implantation of a non-study lens, the subject will not be exited from the study; the first eye will continue to be followed per-protocol, although data may be analyzed separately, and the second eye will be followed for safety until resolution of the complication.

MEDICATIONS

Preoperative, operative and intraoperative medications should be used as is customary for each investigator and will be recorded on the CRF.

TYPE OF CLOSURE

Wound closure is left to the surgeon's discretion and will be recorded on the CRF .

ADDITIONAL OPERATIVE INFORMATION COLLECTED INCLUDES:

- Date of surgery
- Operative eye
- Lens model, power, and serial number
- Lens placement
- Other surgical procedures
- Surgical technique according to protocol
- Product complaints
- Serious and/or device-related adverse events

10.7 POSTOPERATIVE PROCEDURES

Postoperatively, subjects will be examined according to the schedule in **Section 10.2**, Visit Schedule. Only the most recently operated eye will be evaluated at the subsequent 1-day and 1-week visits after surgery.

Both eyes will be evaluated at the 1-month and 6-month visits.

Study technicians who are responsible for conducting all vision testing will be masked to study treatments. Therefore, it is recommended that only the investigator/ sub-investigator or other designated and trained clinician perform the biomicroscopic slit-lamp exams. To maintain consistency and masking throughout the study, it is recommended that a single individual (study technician or coordinator designated by the investigator) conduct all postoperative study-related vision testing, although a back-up person should also be designated and trained.

NOTE: Subjects are not to wear contact lenses postoperatively until after completion of this study. Wearing contact lenses may potentially cause corneal edema or topography changes that may influence the visual acuity results. During the study, if correction is required, spectacles should be prescribed.

A CRF will be used to collect the following postoperative information, although not all data are required at every visit (see **Appendix A**):

MANIFEST REFRACTION AND REFRACTION ADJUSTMENTS (MASKED PROCEDURE)

Postoperative manifest refractions are to be performed using the M&S System at a distance of 4.0 meters. Manifest refraction (MR) is to be performed using the Maximum Plus refraction method. Autorefractors are not recommended for use in this study.

Because 4.0 meters is not a distance that is equivalent to optical infinity, refraction adjustments are necessary to ensure proper vision testing that accounts for test distance and refraction distance. **Appendix C** lists the refraction adjustments required for various vision tests that use the manifest refraction obtained from a distance of 4.0 meters ("ETDRS Rx").

DISTANCE VISUAL ACUITY TESTING (MASKED PROCEDURE)

Distance visual acuity will be measured postoperatively under photopic lighting conditions (85 cd/m^2, 80–110 cd/m^2 acceptable) using the M&S System at a test distance of 4.0 meters. For eyes unable to achieve a postoperative BCDVA of Snellen 20/40 (i.e., LogMAR 0.3, number of letters correct 70), a reason must be specified. Instructions for using the M&S System are detailed in **Appendix D**, and for distance visual acuity testing in **Appendix E**.

INTERMEDIATE VISUAL ACUITY (MASKED PROCEDURE)

Intermediate visual acuity will be measured under photopic conditions (85 cd/m^2, 80-110 cd/m^2 acceptable) using the M&S System at a test distance of 66 cm. Instructions for using the M&S System are detailed in **Appendix D** and for intermediate vision testing in **Appendix F.**

NEAR VISUAL ACUITY (MASKED PROCEDURE)

Near visual acuity will be measured at test distances of 40 cm and 33 cm under photopic conditions (85 cd/m^2, 80-110 cd/m^2 acceptable) and at 40 cm under mesopic conditions (3 cd/m^2) using the M&S System.

Instructions for using the M&S System are detailed in **Appendix D** and for near vision testing in **Appendix G.**

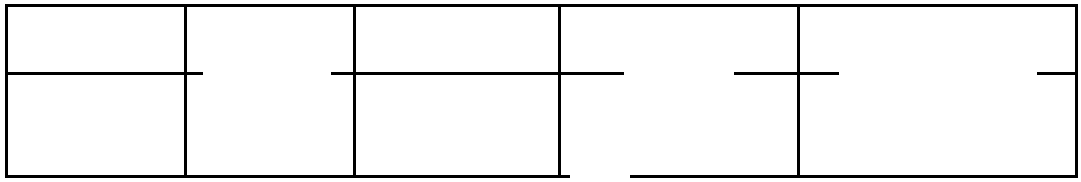
The following near visual acuity measurements are to be performed per the visit

DEFOCUS TESTING (MASKED PROCEDURE)

Binocular and monocular (first eye) best-corrected distance defocus testing will be performed on all subjects in accordance with the methodology described in Annex F of the International Standards for Ophthalmic Implants – Intraocular Lenses Part 7 (ISO 11979-7:2018). While the testing includes plus-power defocus, the study endpoint is based upon minus-power defocus results.

Defocus testing will be performed under photopic conditions (85 cd/m^2, 80-110 cd/m^2 is acceptable) using the M&S System at 4.0 meters with the ETDRS refraction in place (no adjustment necessary for test distance).

At each defocus increment, a LogMAR visual acuity is to be obtained. Further instructions for defocus testing are detailed in **Appendix H**.



PUPIL SIZE

Pupil sizes under photopic (with and without glare), and mesopic (with and without glare) lighting conditions will be measured postoperatively during the study. For consistency, the same method of measurement should be used throughout the study.

Photopic pupil size measurements are to be performed under the same lighting conditions at which photopic distance visual acuity is tested. Pupil sizes under the other lighting conditions will be measured during the contrast sensitivity testing procedures. Instructions for measuring pupil size are detailed in **Appendix J.**

DISTANCE CONTRAST SENSITIVITY TESTING (MASKED PROCEDURE)

Best-corrected distance contrast sensitivity will be tested monocularly (first eye) and binocularly under mesopic with and without glare and photopic with glare conditions using the M&S System for sine-wave gratings at 1.5, 3, 6, and 12 cycles per degree (cpd) (mesopic without glare and mesopic with glare) and 3, 6, 12, and 18 cpd (photopic with glare). **The test distance is 8 feet (2.5 meters).** Best-corrected distance contrast sensitivity is to be performed with a +0.12 D refraction adjustment, added to the sphere of the manifest refraction. Detailed instructions for contrast sensitivity testing are provided in **Appendix K**.

BIOMICROSCOPIC SLIT-LAMP EXAM

A biomicroscopic slit-lamp exam must be performed at each postoperative visit to determine the presence or absence of any medical or lens findings, complications or adverse events. IOL decentration and tilt are to be determined subjectively. The center of the lens relative to the pupil can be used to determine IOL decentration, and, if present, the diffractive rings may be used as a guide to locate the center of the IOL. Note that the pupil center may not always be aligned with the visual axis of the eye; therefore, the investigator should consider deviations in pupil center from visual axis when reporting IOL decentration.

Findings of aqueous cells and flare, corneal edema, posterior capsule striae (wrinkles), posterior capsular opacification, and IOL glistenings are to be rated using standardized grading scales of 0 to +4 (0 = none, +4 = severe) during the slit-lamp biomicroscopy. The specific grading scales are provided in **Appendix L**.

ND:YAG CAPSULOTOMY

If a Nd:YAG capsulotomy is necessary, it is recommended that the procedure be performed at least 1 week prior to a study exam; this is particularly important for the 6-month study visit, as this is the key study exam for evaluation of safety and effectiveness.

FUNDUS EXAM

A fundus exam is to be performed at the 6-month visit to evaluate retinal status and fundus visualization. Examinations may be done dilated with ophthalmoscopy or undilated with an imaging system that allows for undilated views of the peripheral retina (e.g., Optomap). The same fundus examination method that was used preoperatively should be used for the 6-month study visit.

INTRAOCULAR PRESSURE

Intraocular pressure (IOP) is to be measured using the investigator's usual method. It is recommended that the same method be used for all study subjects at the site for the duration of the study.

OCULAR SYMPTOMS (NON-DIRECTED; SPONTANEOUS)

Subjective ocular symptoms are to be assessed at each postoperative visit by asking "Are you having any difficulties with your eyes/vision?" Subjects should not be prompted for specific responses; however, if a subject reports halos, glare or starbursts, the level of severity should be determined (mild, moderate or severe).

MEDICATIONS

Postoperative ocular medications should be used as is customary for each investigator and recorded in the source document for each subject. Medications will be recorded on a medication log CRF as applicable.

ADVERSE EVENTS

Subjects should be assessed at each visit for occurrence of and/or change in status of any adverse events, particularly serious and/or device-related adverse events. See **Section 11.0**, Adverse Events, for further information.

QUESTIONNAIRES

Questionnaires will be administered at the 1-month and 6-month visits to collect information regarding spectacle usage, visual symptoms, visual quality, and subject satisfaction. Two questionnaires will be used in this study:

1) Patient-Reported Visual Symptoms Questionnaire (PRVSQ, **Appendix M**)
2) Patient-Reported Spectacle Independence Questionnaire (PRSIQ, **Appendix N**)

In order to minimize any effect the doctor-patient relationship may have on a subject's responses on the questionnaire, the study questionnaires will be self-administered by the subjects. The questionnaires are to be administered at the start of the 1-month and 6-month study visits, prior to any visual acuity testing.

In addition, if a subject is seen after the 1-month postoperative visit for an unscheduled visit due to an optical/visual symptom complaint, the PRVSQ will be administered at that visit, as well as prior to any secondary surgical intervention for an optical/visual symptom complaint. If additional unscheduled visits and/or a secondary surgical intervention due to the same optical/visual symptom complaint occur within 2 weeks of each other, it is not necessary to complete the PRVSQ a second time.

The optical visual symptom complaints that trigger the need for the PRVSQ to be administered at an unscheduled visit include any of the seven symptoms from the

PRVSQ: halos, glare, starbursts, sensitivity to light, occlusions, multiple or double vision or poor low light vision.

10.8 EXIT OF SUBJECTS

An Exit CRF will be completed for each subject that completes the study or exits the study before completing all scheduled visits.

It is the responsibility of the investigator to provide complete follow-up data to JJSV for each subject, and every attempt should be made to gather that complete follow-up data for all subjects enrolled, as missing data can have a negative effect on the study results. Patients who would be traveling, relocating or otherwise unavailable for postoperative follow-up visits should not be enrolled in this clinical study.

A subject will be considered a "screen failure" if he/she does not meet the eligibility criteria, consent is withdrawn prior to randomization or surgery, implantation in the first eye is aborted due to a surgical complication, or the subject dies prior to first-eye treatment.

Subjects will be "discontinued" from the study if the subject is randomized but does not undergo surgery; or if one study lens (if implanted unilaterally) or both study lenses (if implanted bilaterally) are removed; or if the subject dies.

If a subject receives at least one study lens, he/she is to be followed according to the schedule in Table 2 (**Section 10.2**) for visit windows.

Subjects will be considered “lost-to-follow-up” from the study only if irretrievably lost for unavoidable reasons such as: subject moved/unable to locate, subject ill/unable to travel, subject uncooperative/refuses further study participation. In the event of subject relocation, effort must be made by the investigator to secure follow-up information (i.e., slit-lamp findings and general visual acuity, etc.) from the subject’s new physician.

If a subject is exited early from the study, the investigator must indicate the reason for study exit on the CRF. In the event of a lens removal or other serious adverse event, the subject may be exited from the study; however, effort must be made by the investigator to follow the subject until resolution of the adverse event before exiting the subject from the study.

All study subjects are to be instructed to undergo regular eye examinations at least yearly and also to return to their doctor if any eye complications are experienced.

10.9 UNSCHEDULED VISITS

During the study period, if a non-protocol-required visit is done for the purpose of medically-indicated follow-up for a study eye, data from this visit should be reported using the Unscheduled Visit CRF. The need for unscheduled visits is at the investigator's discretion. Specific examinations to be performed at unscheduled visits are also at the discretion of the investigator (based on the reason for the unscheduled visit) and data are to be recorded in the appropriate section of the CRF.

Data to be collected may include:

- Snellen manifest refraction
- Uncorrected and best-corrected distance visual acuity using a Snellen chart
- Intraocular pressure
- Slit-lamp examination for medical and/or lens findings
- Fundus exam
- Ocular symptoms
- Adverse events
- Medications

If, prior to the second-eye surgery, the fellow eye is re-examined (e.g., at a first eye, 1-day visit) and there are clinically significant changes from the preoperative exam, data are to be reported using the Unscheduled Visit CRF. If there are no changes or non-clinically significant changes from the original preoperative exam, an Unscheduled Visit CRF is not required.

At a second-eye 1-day or 1-week visit (or a 1-month visit, if the visit intervals for the first and second eyes do not overlap), if the first eye is examined and there are medical and/or lens findings and/or a subject has an optical/visual symptom complaint, data are to be reported using the Unscheduled Visit CRF.

Conditions found postoperatively, but previously documented at the preoperative visit, do not trigger an unscheduled visit report. However, if the severity of the condition increases from the preoperative visit, an Unscheduled Visit CRF is needed.

In addition, if a subject is seen after the 1-month postoperative visit for an unscheduled visit due to an optical/visual symptom complaint, the PRVSQ must be administered, a mesopic pupil size measurement obtained, and monocular contrast sensitivity under mesopic (with and without glare) conditions at that visit. These must be done prior to any secondary surgical intervention for an optical/visual symptom complaint. If additional unscheduled visits and/or a secondary surgical intervention due to the same optical/visual symptom complaint occur within 2 weeks of each other, it is not necessary to complete the PRVSQ, mesopic pupil size, or monocular contrast sensitivity measurements a second time.

The optical visual symptoms that, when reported at an unscheduled visit, trigger the need for PRVSQ administration include any of the seven symptoms listed in the PRVSQ: halos, glare, starbursts, sensitivity to light, occlusions, multiple or double vision or poor low light vision.

10.10 PROTOCOL DEVIATIONS

Any departure from the protocol procedures represents a protocol deviation. Protocol deviations may be subject-based (e.g., inclusion/exclusion criteria, informed consent deviation, etc.) or procedural-based (e.g., out-of-interval visits, non-compliance with testing procedures, etc.). All protocol deviations will be documented using the protocol deviation CRF. Any deviation made to protect the life or physical well-being of a subject in an emergency as well as any use of the investigational device without obtaining informed consent must be reported to JJSV within 5 working days. Protocol deviations will be monitored by the Sponsor, and if the non-compliance is persistent or egregious, Sponsor may take action, including but not limited to termination of the investigator's participation in the study. The investigator is also responsible for informing the reviewing IRB of instances of protocol non-compliance in accordance with the IRB requirements.

11. ADVERSE EVENTS AND PRODUCT COMPLAINTS

11.1 ADVERSE EVENT DEFINITIONS

Adverse Event (AE)

An adverse event is defined (per ISO 14155) as 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 study device.

Serious Adverse Event (SAE)

An adverse event is considered serious (per ISO 14155) if it is an untoward occurrence which may or may not be related to use of the study device that

- is sight- or life-threatening,
- results in death,
- requires inpatient hospitalization or prolongation of hospitalization (a planned hospitalization for a pre-existing condition without a serious deterioration in health is not considered a serious adverse event),
- results in permanent impairment of a body structure or body function,
- necessitates medical or surgical intervention to prevent permanent impairment to a body structure or function, or
- results in fetal distress, fetal death or a congenital abnormality or birth defect

Device-Related Adverse Event/Adverse Device Effect (ADE)

A device-related adverse event is defined as any adverse event that is believed to be definitely, probably, possibly or unlikely to be related to the study device (following the guidelines in Section 11.4, Causal Relationship). A device-related event is also considered an adverse device effect (ADE; following ISO 14155) resulting from the use of the study device that may result from user error, insufficiencies or inadequacies in the instructions for use, deployment, implantation, installation, operation of any malfunction of the device.

Anticipated Study-Specific Serious Adverse Events

The following is a list including, but not limited to, ocular serious adverse events (SAE) that are anticipated and must be reported to JJSV for this study. Any events that are unlikely but anticipated (i.e., endophthalmitis) will be reported to the FDA and other appropriate regulatory agencies. Adverse event definitions in accordance with the American Academy of Ophthalmology Task Force Consensus Statement are included in **Appendix O**.

- Endophthalmitis/intraocular infection
- Hypopyon
- Hyphema
- IOL dislocation
- Cystoid macular edema
- Pupillary block
- Retinal detachment/tear
- Corneal edema
- Chronic anterior uveitis/iritis
- Raised IOP that persists (i.e., is present at the last study visit)
- Toxic anterior segment syndrome
- Visual symptoms requiring secondary surgical intervention (e.g., lens removal)
- Tilt and decentration requiring secondary surgical intervention (e.g., repositioning)
- Residual refractive error resulting in a secondary surgical intervention
- Retained lens material resulting in secondary surgical intervention

NOTE 1: Wound “burps” during the first week postoperatively, suture removal, planned blepharoplasty, and Nd:YAG capsulotomy (for PCO) are not considered adverse events for this study.

NOTE 2: Corneal edema, and chronic anterior uveitis/iritis will be considered serious according to the guidelines listed in **Appendix O** (i.e., corneal edema resulting in BCDVA of 20/40 or worse at 1 month or later; and Grade 1+ uveitis/iritis longer than 3

months). Raised IOP, according to the guidelines listed in **Appendix O** will be considered serious if present at the last study visit (120-180 days after second eye implant).

Unanticipated Adverse Device Effect (UADE)/Unanticipated Serious Adverse Device Effect (USADE)

Any UADE (21CFR 812.3(s)) or USADE (ISO 14155) is defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan (i.e., this protocol), application (including a supplementary plan or application), or risk assessment, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

11.2 PRODUCT COMPLAINT/DEVICE DEFICIENCY DEFINITION

A product complaint/device deficiency is defined (21 CFR 820.3(b) and ISO 14155) as any alleged deficiency related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device. This may include malfunctions, use error, and inadequacies in labeling. Product complaints can pertain to any marketed JJSV device being used in the study as well as the investigational device. The investigator is to assess whether the deficiency could have led to a serious adverse event without suitable action or intervention or under less fortunate circumstances.

11.3 ADVERSE EVENT AND COMPLAINT REPORTING REQUIREMENTS

All adverse events and any complaint encountered using any JJSV product, regardless of severity and whether or not attributed to the study device(s), are to be reported to JJSV and recorded on the case report form corresponding to the visit during which awareness of the event occurred. Adverse events are also to be reported to the reviewing IRB as per the IRB's reporting requirements. If required, adverse events will be reported to the appropriate regulatory agencies (e.g., FDA) according to all applicable laws and regulations.

Reporting of adverse events shall follow the USA Code of Federal Regulations (21CFR 812) for sites in the USA. General guidelines are provided below:

Adverse Event Reporting

An adverse event that is not serious or device-related is to be reported to JJSV in a timely manner. Notification of non-serious and non-device related adverse events will occur by recording events on the CRF when noted. Such adverse events are also to be reported to the reviewing IRB per their reporting requirements.

Complaints/Device Deficiency Reporting

A general product complaint or device deficiency is to be reported to JJSV in a timely manner. Notification of complaints/device deficiencies will occur by recording complaints on the CRF at the visit the complaint occurs (e.g., operative visit) and/or by a phone call/email to JJSV.

Any device deficiency that could have led to a serious adverse event without suitable action or intervention, or under less fortunate circumstances, must be reported to the sponsor immediately (no later than 24 hours after detection). Device deficiencies that could have led to a serious adverse event should also be reported to the investigator's IRB per their reporting requirements.

Serious and/or Device-Related Adverse Event Reporting

SAEs and/or ADEs are to be documented using the Serious Adverse Event/Adverse Device Effect (SAE/ADE) CRF. In the event of an SAE, JJSV must be notified immediately (no later than 48 hours after detection). Any SAE/ADE is to be reported to JJSV by phone, email and/or by submitting the completed SAE/ADE CRF. Any SAE or device-related AE should also be reported to the investigator's IRB per their reporting requirements.

Unanticipated Adverse Device Effect (UADE)/Unanticipated Serious Adverse Device Effect (USADE) Reporting

If during the study, a serious adverse event occurs that may reasonably be regarded as device-related and was not previously expected in nature, severity, or degree of incidence, the investigator is to report the UADE/USADE to JJSV within 48 hours, and to the investigator's IRB as soon as possible (and no later than 10 working days after learning of the event for sites in the USA as required by 21CFR812).

11.4 CAUSAL RELATIONSHIP

The investigator should always be alert to adverse events that may be related to the study device or the use of the study device (i.e., the procedure specific to the initial application of the device). An attempt should be made in every case to determine the causality of the event. The following definitions are to be used as guidelines in determining the relationship between the event and the study device and/or use of the device.

Definitely related:	If the event is associated with the device and/or the use of the device beyond a reasonable doubt, a causal relationship exists

	between the adverse event and the device and/or the use of the study device.
Probably related:	There is a reasonable possibility of a causal relationship between the adverse event and the device and/or the use of the study device and/or the adverse event cannot be reasonably explained by another cause.
Possibly related:	The adverse event has not been determined to be related to the device or the use of the device, but no other cause has been identified and the device and/or the use of the study device cannot be ruled out as a possible cause.
Unlikely to be related:	The possibility of a potential causal relationship between adverse event and the device and/or the use of the device could exist, but the adverse event can be reasonably explained by another cause.
Not related:	There is no possibility of a causal relationship between the adverse event and the device and/or the use of the study device and/or the adverse event can be attributed to another cause.

If an adverse event is believed to be definitely, probably or possibly related to the study device and/or the use of the device, the event will be considered related to the study device and/or the use of the device.

11.5 ADVERSE EVENT FOLLOW-UP

For every adverse event, appropriate measures should be undertaken to treat and/or monitor the subject until resolution occurs. The subject's files are to include all pertinent medical data relating to the event including the subject's medical records, medical reports and/or judgments from colleagues or outside specialists who assisted in the treatment and follow-up of the subject. The investigator should keep JJSV closely informed as to the outcome of serious and/or device-related adverse events, thereby allowing JJSV to comply with the appropriate regulatory reporting requirements. An SAE/ADE CRF should be completed each time the subject returns to the investigator or other specialist(s) for follow-up of a serious and/or device-related adverse event until resolution of the event. Any subject who is to be exited from the study due to a serious and/or device-related adverse event should be followed until the outcome is determined prior to being exited from the study.

12. PROTOCOL CHANGES/AMENDMENTS

If the investigator wishes to modify any procedure and/or the design of the study, he or she must contact and obtain consent from JJSV regarding the proposed changes prior to implementation. Any modifications (including additional data collection) require approval

by the FDA and all other appropriate regulatory agencies, as well as approval of the governing IRBs prior to implementation.

13. ETHICS REVIEW AND PATIENT WELFARE

13.1 INSTITUTIONAL REVIEW BOARD (IRB)

It is the responsibility of the investigator to obtain prospective approval of the study protocol, protocol amendments or changes, informed consent forms and other relevant documents (e.g., advertisements) from the IRB. All correspondence with the IRB should be retained in the Investigator Study Files/Notebook. Copies of IRB submissions and approvals should be forwarded to JJSV.

The investigator is responsible for notifying the IRB of reportable adverse events as well as any other circumstance in which additional procedures outside the protocol were conducted to eliminate apparent hazards to subjects.

13.2 INFORMED CONSENT

The current version of the IRB-approved study informed consent form must be signed by each study subject prior to any study-specific examinations being performed. The IRB-approved informed consent form is to be signed and dated by the subject as well as by the person who conducted the informed consent discussion. The signed informed consent form will be maintained by the investigator as a permanent part of the subject's medical records. A copy of the signed and dated form is to be provided to the subject. The investigator will provide JJSV written acknowledgement on the preoperative case report form that a signed agreement of informed consent has been obtained and is in the investigator's possession for each subject. As required by 21CFR 812 Part G, the site shall document in the source documents that informed consent was obtained prior to participation in the study for each subject enrolled.

NOTE: The informed consent process also includes obtaining the subject's signature on an Authorization for Use/Disclosure of Health Information for Research Form or equivalent documentation necessary to comply with applicable privacy laws pertaining to medical treatment in the governing countries.

NOTE: The sponsor will secure appropriate insurance for study subjects prior to study start.

14. DOCUMENTATION

14.1 SOURCE DOCUMENTS

Source documents must be kept for all study subjects. Source documents may include a subject's medical records, hospital charts, clinic charts, the investigator's subject study

files, as well as results of any diagnostic tests or procedures such as topographies or laboratory tests with photographs or instrument printouts.

Each site is expected to adhere to the clinic's own standard documentation requirements for medical charts/clinic notes. For the purposes of this clinical study, the medical charts/clinic notes must also include, at a minimum, the following data that will be considered source data and will be reviewed by the Sponsor:

- Subject's name and study identification number
- Subject's contact information
- Study protocol number and the Sponsor name (JJSV)
- A statement that informed consent was obtained prior to participation in the study (including the date)
- Evidence of subject eligibility
- Dates of all subject visits and surgeries throughout the duration of the study
- Implant serial number identification (NOTE: This is masked information, and may only be reviewed by unmasked study staff)
- Concurrent medications
- Corrected and uncorrected distance visual acuity (NOTE: M&S electronic data are considered source documentation and are to be retained by the site. A paper copy of the M&S results will be printed and validated by the site)
- Manifest refraction
- Occurrence and status of any operative complications, postoperative medical or lens findings and adverse events
- Occurrence and status of any subject complaints, e.g., ocular/visual symptoms
- The date the subject exited the study, and a notation as to whether the subject completed the study or reason for early exit.

14.2 SUBJECT CONFIDENTIALITY

Subjects will be assigned a site/subject number to maintain subject confidentiality. Subject names may possibly be disclosed to JJSV or regulatory agencies during inspection of medical records related to the study, but reasonable precautions will be taken to maintain confidentiality of personal information to the extent permitted by applicable laws and regulations.

14.3 CASE REPORT FORM COMPLETION

This study will use an electronic data capture system. All study staff responsible for entering data into the system must complete certification prior to using the system. The investigator is responsible for ensuring that data are properly recorded on each subject's case report forms and related documents. Prior to database lock, the investigator will verify completeness and accuracy of data submitted to the Sponsor.

14.4 STUDY SUMMARY

A final investigator's summary (study close-out) will be provided to the reviewing IRB after termination or the completion of the study or the investigator's part of the investigation, as directed by the Sponsor.

15. MONITORING

The Sponsor will perform three types of monitoring to ensure compliance with regulations: data monitoring, administrative monitoring, and safety monitoring.

15.1 DATA MONITORING

In order to ensure a well-controlled clinical trial, the Sponsor will follow specific data monitoring procedures, routinely generate reports and periodically review safety and effectiveness data. To avoid bias, any analyses generated prior to site closures will not be disseminated to any of the investigative sites.

An electronic data capture system (EDC) will be used to transmit case report forms from the investigative site to the Sponsor. Requests for data clarification will be handled through this same system.

To minimize data omissions and inconsistencies on clinical reports and to ensure that data are accurately transcribed to computer data files, the Sponsor will follow internal data processing procedures that include automated and manual quality control checks to identify any data discrepancies. Any such items will be resolved and documented as needed in EDC.

Prevention of Missing Data

Methods used to safeguard against missing data that can have deleterious effects on the study integrity and reliability of its outcomes will include training study staff with WebEx/Skype, centralized and/or on-site programs. In addition, subjects will be encouraged at the time of informed consent to avoid missing study visits, as missing data may affect the study reliability and diminish the scientific value of their contribution to the study.

15.2 ADMINISTRATIVE MONITORING

Administrative monitoring procedures will ensure that study devices, subjects, and forms can be traced and will allow monitoring of investigator progress and compliance. Accountability and traceability of study devices will be monitored by trained Sponsor personnel.

Device Accountability

Complete accountability of the investigational lenses will be maintained at the investigative site by maintaining records of all study lenses (Model ZFR00V) received from and returned to the Sponsor. A site log will be used to track all investigational lenses for date of receipt, eye implanted, serial number, lens power, use and disposition/return to the Sponsor; in addition, serial numbers will be recorded for all implanted control lenses. This site log and any other study lens information will be maintained in the operating room study binder. During periodic investigative site monitoring visits, Sponsor personnel will review site lens inventory records and logs to ensure IOL accountability compliance and investigational lens traceability.

Site Monitoring Plan

Prior to performing any study implants, the requirements of the study and reporting mechanisms will be explained to each investigator either personally at the investigative site or at a formal study investigator meeting. When necessary, a pre-study site qualification visit may be performed to assess the adequacy of the site to perform the study for sites that have not previously worked with the Sponsor or have undergone significant changes or have not been visited in the past year. An initial site visit will be conducted prior to the first implant for all sites.

Throughout the duration of the study, site visits to monitor compliance to this protocol will be made at each investigative site. During interim site monitoring visits, the Sponsor will review informed consent documents and subject eligibility, and the data on study case report forms will be verified against subject charts and other source documents to ensure complete and accurate reporting. The subject files will also be reviewed to assure that all adverse events and any issues encountered with JJSV products have been reported in a timely fashion.

The Sponsor will also review source documents to verify that all required items have been documented in the subject medical charts. Refer to **Section 14.1**, Source Documents, for a list of items that are required for source documentation. In addition to subject files, study logs will be checked and conformance to lighting levels for visual acuity tests will be verified.

Additional training on study-specific procedures may also be conducted during monitoring visits. A training/monitoring visit specific to this study is likely to occur just prior to or during the first of the 1-month and 6-month visits, wherein the most extensive vision testing occurs.

Upon study completion, a site visit will be made to each site to monitor the last of the subject data records and finalize any outstanding study issues.

A separate Study Monitoring Plan will be established prior to study start that will define the type and frequency of monitoring visits and frequency of record monitoring.

15.3 SAFETY MONITORING

The medical monitor will review results throughout the clinical trial as necessary to ensure the continued safety of the device and to ensure that no subjects are exposed to unreasonable risk. The medical monitor will be available to answer all questions from investigators. The medical monitor will review and assess any reports of serious and/or device-related adverse events as well as device deficiencies that could have led to a serious adverse event and discuss these with the reporting investigator(s) as necessary. The medical monitor, as well as any other qualified personnel designated by the Sponsor, shall also review any interim progress reports, as applicable.

16. PUBLICATIONS

Refer to the Clinical Trial Agreement for information regarding JJSV publication policies.

17. RISK ANALYSIS

POTENTIAL RISKS AND RISK MANAGEMENT

Investigational IOL Model ZFR00V

The investigational IOL Model ZFR00V is designed to provide far vision and a range of intermediate to near vision; however, glasses may still be needed to improve distance vision and/or to have better vision for certain intermediate or near tasks. Some visual symptoms, particularly dysphotopsias such as halos, glare, starbursts, etc., may be expected. Dysphotopsias may become less noticeable over time; however, the IOL may be removed if necessary. There may be a reduction in contrast sensitivity under certain conditions compared to a monofocal lens although contrast sensitivity is expected to be similar to that of TECNIS Multifocal IOLs. Due to the diffractive optic design, the ability to perform some eye treatments (e.g., retinal photocoagulation) may be affected, and caution should be used when interpreting results of autorefractors or wavefront aberrometers that utilize infrared light, or when performing a duochrome test. These risks are not unlike those for other diffractive technology IOLs, but the use of these instruments is not recommended for use in this study.

General Risks of Cataract Surgery and IOL Implantation

There are risks and complications associated with cataract surgery and IOL implantation in general. These can include worsening of vision, hemorrhage, loss of corneal clarity, inflammation, infections, retinal detachment, pupil changes, glaucoma, etc. Complications can result in poor vision, loss of vision or loss of the eye.

Risk Management

Subjects will be closely monitored throughout the trial duration. The occurrence of adverse events and complaints will be assessed at each study visit and reported to the Sponsor according to **Section 11.0**, Adverse Events and Product Complaints. Additionally, the Sponsor will monitor incoming data following the procedures outlined in **Section 15.0**, Monitoring. The Medical Monitor will ensure subjects are not exposed to additional risks by monitoring serious adverse events, device-related adverse events, and device-deficiencies that could have led to serious adverse events (**Section 15.3**, Safety Monitoring).

POTENTIAL BENEFITS

The general clinical performance of the investigational IOL Model ZFR00V is expected to be similar to the TECNIS Model ZCB00 IOL regarding distance visual acuity and safety outcomes. Improved vision in the intermediate to near range, as well as functionality for certain tasks, may be achieved with the investigational IOL Model ZFR00V compared to the control IOL.

CONCLUSION

The hazards/risks associated with the investigational IOL Model ZFR00V are acceptable and within the range of those of other advanced-optic IOLs from JJV. The potential clinical benefits of the investigational IOL Model ZFR00V outweigh the residual risks when the device is used as intended.

18. RECORDS RETENTION

All study-related correspondence, subject records, consent forms, Authorization for Use/Disclosure of Health Information Forms or similar medical treatment privacy law documentation, records of the distribution and use of all study products, and original case report forms should be maintained by the investigator.

The investigator must maintain and have access to the following essential documents until notified by the Sponsor. Note: This may be for a minimum of 25 years after completion of the study. The Sponsor requires notification if the investigator wishes to relinquish ownership of the data so that mutually agreed-upon arrangements can be made for transfer of ownership to a suitably-qualified, responsible person.

- All case report forms
- All adverse event information (i.e., medical records, medical reports and/or judgments from colleagues or outside specialists who assisted in the treatment and follow-up of the subject)
- Investigational supply records/inventory
- IRB approval documentation

- Study correspondence
- Study agreements
- Site visit documentation
- Protocol(s)
- Subject log(s)
- Clinical Investigator's Brochure
- Completed subject informed consent forms and medical privacy forms (e.g., Authorization for Use/Disclosure of Health information)
- Subject medical chart/clinic notes (Not applicable for transfer of ownership to the Sponsor)

19. TERMINATION OF THE INVESTIGATION

The clinical investigation will be suspended in the event of high levels of complications and/or adverse events that are unexpected in nature and/or severity and evaluated as to causality relative to the study device. The clinical investigation may be suspended if the Medical Monitor or the IRB, upon review and evaluation of the clinical data, finds unacceptable clinical performance or the level of single or total complications and/or adverse events unacceptable for continuation of the investigation.

If causality is shown not to be related to the study device, the study may be resumed in accordance with the IRB and regulations of the FDA. The study will be terminated if causality is shown to be related to the study device.

Additionally, the investigator or the Sponsor may stop a subject's participation at any time. The Sponsor may also stop the study at any time for reasons it determines appropriate. However, no suspension of the study would be made to disadvantage the study subjects. Following suspension of the study for any reason, all study subjects who have already received treatment would continue to be followed through completion of the study visit schedule.

20. STATISTICAL METHODS

This section highlights the analyses to be performed for key study endpoints. The key study timeframe for all endpoints will be the 6-month postoperative visit; however, data will be reviewed at other time points as well.

20.1 ANALYSIS POPULATION

For the primary effectiveness endpoint (DCNVA at 40 cm) and monocular secondary effectiveness endpoints (DCIVA, DCNVA (at 33 cm) and BCDVA),

For eyes that do not have data available at the 6-month postoperative visit, data will be imputed for the mITT population analyses. For continuous variables (DCNVA, BCDVA and DCIVA), planned method to use is the MCMC full-data imputation as described in Little & Rubin[3] .

[3] Little, R. and Rubin, D. Statistical Analysis with Missing Data, John Wiley & Sons, Inc. New York, Second Edition, (2002).
[4] SAS Institute. The MI and MIANALYZE Procedures. SAS/STAT 9.2 User Guide. and SAS/STAT User Guide for the MI Procedure: Imputation Methods. Cary, N.C.

A Per-Protocol (PP) analysis will also be used for primary effectiveness and secondary endpoints. The PP population for monocular data will include eyes with a test or control lens implanted, evaluated within the proper study interval and without clinically-relevant protocol deviations (deviations that could potentially impact the primary or secondary endpoints) as determined prior to database lock. The PP population for binocular data will include subjects that do not have any of the deviations stated above in either eye. PP tables will include available data at the time of analysis.

The safety population (SP) will consist of all eyes and subjects implanted with either a test or control IOL(s) and with data available at the time of analysis (i.e., no data imputation). Reporting of cumulative complications and adverse events (occurring at any time postoperative) will include data from all study eyes implanted. For all safety endpoints and other endpoints, only safety population will be used. For BCDVA percent 20/40 or better vs. ISO SPE rate, a best-case population will also be used, consisting of eyes in the safety population without any clinically-relevant preoperative ocular pathologies or macular degeneration detected at any time.

For the primary DCNVA (at 40 cm), secondary BCDVA, DCIVA, DCNVA (at 33 cm) and spectacle wear endpoints, the mITT, sensitivity, PP and safety populations will be used for data reporting. For defocus curve secondary endpoint, only safety and PP populations will be used for data reporting. For safety endpoints and other endpoints, only the safety population will be used. The primary analysis will be based on first eye data, unless stated otherwise. However, select data such as some visual acuity variables will also be reported separately for second eyes as supportive data only. Safety (adverse events, medical and lens findings, and non-directed visual symptoms) and effectiveness endpoints (monocular DCNVA (at 40 and 33 cm), BCDVA and DCIVA) and monocular mesopic DCNVA will also be evaluated using all eyes (pooling both first and second eyes together) as supportive analysis. Descriptive statistics will be presented for analyses of all eyes.

[5] Rom D and B. Holland. (1995). A new closed multiple testing procedure for hierarchical families of hypotheses. Journal of Statistical Planning and Inference 46:265-275

[6] Rom D, R. Costello, and L. Connell. (1994). On closed test procedures for dose-response analysis. Statistics in Medicine 13:1583-1596

[7] Marcus R, E. Peritz, and K. Gabriel. (1976). On closed testing procedures with special reference to ordered analysis of variance. Biometrika 63:655-660.

[8] Huque M and A Sankoh. (1997). A reviewer's perspective on multiple endpoint issues in clinical trials. Journal of Pharmaceutical Sciences 7:545-564.

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20.4 SITE POOLABILITY ANALYSIS

For the primary effectiveness and secondary effectiveness endpoints, data will be reported by site.

. Since there are no inferential statistics for the secondary defocus curve endpoint, only graphs (defocus curve by site) will be presented for the site analysis. Baseline demographic data will also be reported by site.

20.5 VISUAL ACUITY CONVENTIONS AND GENERAL STATISTICS

Visual acuity data will be converted to LogMAR values prior to analysis and adjusted for the test distance used if it is not the standard distance for the chart. Descriptive statistics will typically include sample size (N), mean, standard deviation (SD), median, minimum (Min) and maximum (Max) as appropriate for continuous variables. For continuous variables, statistical tests (e.g., t-test) assuming normality will generally be used. For categorical data, the frequency and proportion will be reported, and Fisher's exact test or Chi-square test will generally be applied. For ordinal categorical data, the frequency and proportion will be reported with the Wilcoxon Rank-Sum test generally used.

20.6 INTERIM REPORTS

No interim study progress reports will be conducted for this study.

20.7 SAMPLE SIZE CALCULATIONS

Study sample sizes are based on the requirements for a Level B modification of a parent lens as well as the requirement for contrast sensitivity testing. The minimum requirements are 100 evaluable test subjects per lens group for Level B and 122 evaluable test subjects per lens group for contrast sensitivity. The screen failure rate is assumed at 10%, and the dropout rate is assumed at 10%. To achieve approximately 122 evaluable subjects in each IOL group at 6 months postoperative and allowing for screen failures and drop out, 150 subjects will be enrolled in each lens group to achieve approximately 135 bilaterally implanted subjects in each lens group.

1. **Monocular, Distance-corrected Near Visual Acuity (DCNVA) at 40 cm**

For monocular (first eye), distance-corrected near visual acuity (DCNVA), there is over 90% power to detect a 0.7-line or greater difference in mean visual acuity between the test and control groups (assumes one-sided testing with an alpha of 0.025 and standard deviation of 1.6 lines) with 122 subjects in each lens group.

2. **Monocular, Best-corrected Distance Visual Acuity (BCDVA)**

For monocular (first eye), best-corrected distance visual acuity (BCDVA), there is over 90% power to detect a 1-line or greater difference in mean visual acuity between the test and control groups (assumes one-sided testing with an alpha of 0.025 and standard deviation of 1.2 lines) with 122 subjects in each lens group.

3. **Spectacle Wear**

For spectacle wear, there is more than 90% power to detect a 20% difference between test and control subjects (assumes 80% for test and 60% for control, using a one-sided Fisher's Exact test with an alpha of 0.025) with 122 subjects in each lens group.

4. **Monocular Defocus Curve**

There is no statistical comparison for this endpoint; therefore, no sample size calculation is performed for this endpoint.

5. **Monocular, Distance-corrected Intermediate Visual Acuity (DCIVA)**

For monocular (first eye), distance-corrected intermediate visual acuity (DCIVA), there is over 90% power to detect a 0.7-line or greater difference in mean visual acuity between the test and control groups (assumes one-sided testing with an alpha of 0.025 and standard deviation of 1.6 lines) with 122 subjects in each lens group.

6. **Monocular, Distance-corrected Near Visual Acuity (DCNVA) at 33 CM**

For monocular, distance-corrected near visual acuity (DCNVA) at 33 cm, there is over 90% power to detect a 0.7-line or greater difference in mean visual acuity between the

test and control groups (assumes one-sided testing with an alpha of 0.025 and standard deviation of 1.6 lines) with 122 subjects in each lens group.

7. **Monocular and Binocular Contrast Sensitivity**

For contrast sensitivity, the ISO 11979-7:2018 sample size criteria for contrast sensitivity analysis are met with 122 subjects in each lens group.