Study Protocol

Clinical Investigation of Rotational Stability of the TECNIS® Toric II Intraocular Lens

NCT Number: **NCT04327518**

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Clinical Investigation of Rotational Stability of the TECNIS® Toric II Intraocular Lens

PROTOCOL NUMBER: NXGT-202-QROS

SPONSOR: Johnson & Johnson Surgical Vision, Inc.
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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; ISO 14155 and all other applicable regulations; conditions of approval imposed by the reviewing Institutional Review Board (IRB); Ethics Committee (EC); FDA and 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, EC 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
Sub-Investigator Printed Name	Signature	Date
Sub-Investigator Printed Name	Signature	Date

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Protocol Change History

Version	Section(s)	Page(s)	Description of Change(s)	Rationale for Change(s)
1.0	N/A	N/A	Original	N/A
2.0	Sponsor Personnel	4	Added Medical Safety Officer	Updated sponsor personnel to include Medical Safety Officer
	1 Synopsis: Clinical Hypothesis	10	Changed the primary endpoint timepoint from 3-months to 1-week and specified that the requirement for preoperative astigmatism is corneal astigmatism	Updated to align with the planned timepoint for analysis for the primary endpoint and provided clarification preoperative astigmatism requirement.
	1 Synopsis: Number of Subjects; 8 Study Population	11, 19	Changed the timepoint for the target to achieve approximately 100 bilaterally-implanted subjects available for analysis from 3-months to 1-week. Number of subjects was changed from approximately 20 subjects to approximately 15 subjects.	Updated to align with the planned timepoint for analysis for the primary endpoint and the planned number of subjects to be enrolled per site.
	1 Synopsis: Evaluation Criteria	12	Added the word “the” in the first sentence and changed the primary endpoint timepoint from 3-months to 1-week	Grammatical change and updated to align with the planned timepoint for analysis for the primary endpoint
	1 Synopsis & 8.1 Inclusion Criteria	11, 19	Pre-existing corneal astigmatism of one diopter or greater;	Corrected error with the inclusion criteria
	1 Synopsis: Exclusion Criteria; 8.2 Exclusion Criteria	12, 20	Added planned monovision as an exclusion criterion.	To clarify the refractive requirements for the study.
	1 Synopsis: Data Analysis	12-13	Changed the primary endpoint timepoint from 3-months to 1-week. Provided clarification that the percent of eyes with misalignments will also be reported for all other postoperative timepoints (1-day and 3-months)	Updated to align with the planned timepoint for analysis for the primary endpoint and provided clarification for other endpoint data at other postoperative timepoints.
	5. Acronyms	14-15	Added ADE, BSS, UADE and USADE. Corrected spelling error for HIPAA.	ADE, BSS, UADE and USADE were missing from the list of Acronyms and the acronym for HIPAA was incorrect.
	6 Study Objectives and Endpoints; 6.1 Primary Endpoint; 6.2 Other Endpoints	15-16	Changed the primary endpoint timepoint from 3-months to 1-week. Provided clarification that the 3-month visit will be the key timepoint for visual acuity, manifest refraction and patient and investigator reported outcomes questionnaire evaluations and that other timepoints will be provided as supportive analysis. Changed Percentage of eyes that achieve UCDVA of 0.3, 0.2, 0.1 & 0.0 logMAR to 20/40,	Updated to align with the planned timepoint for analysis for the primary endpoint and provided clarification for other endpoint data at other postoperative timepoints.

Version	Section(s)	Page(s)	Description of Change(s)	Rationale for Change(s)
			20/32, 20/25 & 20/20. Changed Percentage of eyes with lens axis misalignments < 5º to ≤ 5º.	
2.0	7.1 Table 1 Intraocular lens	18	Table 1 revised	Table 1 revised to match DFU
	9.3 Investigator Approval	22-23	Deleted Clinical Investigator Brochure Signature Page and Hospital/Ambulatory Surgery Center Clinical Study Acknowledgement from the list of documents to be signed and returned to JJSV.	The Clinical Investigator Brochure is not a requirement for this study since the IOLs are marketed product. The Directions for Use is applicable for this study. Also removed Hospital/Ambulatory Surgery Center Clinical Study Acknowledgement to reflect current practice.
	10.1 Experimental Plan, Overview	23	Grammatical changes to 2nd and 3rd paragraph. Also deleted slit lamp from the procedures that will be done at the operative visit.	To correct grammatical changes and to reflect revised protocol requirements for procedures to be done at the operative visit.
	10.2 Visit Schedule	23	Deleted foot note “a” from the 3-month visit.	Foot note “a” was initially referenced at the 3-month visit in error. This deletion corrects the error.
	10.3 Preoperative Procedures	23-25	• Deleted Uncorrected Distance Visual Acuity from the procedures that should be done at the Preoperative Visit and provided clarification regarding additional preoperative information that should be collected. Made correction to IOL model (from ZCT to ZCU);	To correct typo in original version
	10.6 Operative Procedures	26-28	• Provided clarification regarding additional procedures that can’t be performed during surgery. Also referenced Appendix for instructions for capturing photographs through the surgical microscope. Implant Instrument Used – added implant instruments that are approved to be used in the study. Specified that BSS will be collected on the case report form.	Some of the implant instruments that are approved for use in the study were inadvertently not included in Version 1.0 of the protocol. Also clarified that BSS solution used will be recorded in the case report form.
	10.7 Postoperative Procedures	29-31	• Provided clarification regarding postoperative procedures for uncorrected distance visual acuity testing, manifest refraction, best corrected distance visual acuity and biomicroscopic slit lamp photographs and lens axis orientation. • Provided clarification regarding training requirements for individuals performing slit lamp exams and photography.	To provide clarity for the testing requirements for uncorrected distance visual acuity, best corrected distance visual acuity and manifest refraction at the postoperative visits.

Version	Section(s)	Page(s)	Description of Change(s)	Rationale for Change(s)
			• Added the requirement for the Investigator Satisfaction Questionnaire to be completed at the 1-week visit. • Updated letters for the Appendix references to reflect the updated appendices. • Added details regarding handling secondary surgical interventions in the study Added details regarding the use of M&S System for uncorrected distance visual acuity, best corrected distance visual acuity and manifest refraction testing.	
2.0	10.8 Exit of Subjects	32	• Added slit lamp photographs of IOL position to the list of data that may be collected at an unscheduled visit. Also, clarified that fundus exam can be dilated or undilated. • Provided clarification regarding the procedures that are required to be completed if a greater degree of rotation is noted since last study visit and IOL repositioning is required. Clarified instructions for handling surgical complications and discontinued subjects.	To clarify subject exit procedures and requirements.
	10.9 Unscheduled Visits	33	• Added slit lamp photographs of IOL position to the list of data that may be collected at an unscheduled visit. Also, clarified that fundus exam can be dilated or undilated. • Provided clarification regarding the procedures that are required to be completed if lens axis orientation had changed since last study visit and IOL repositioning is required. Updated the method of estimating the amount of rotation and clarified requirements for completing an unscheduled visit for a second eye 1-day or 1-week visit if the first eye is examined.	To provide clarity regarding the requirements for estimating the amount of rotation and completion of unscheduled visits for a second eye 1-day or 1-week visit if the first eye is examined.
	10.10 Protocol Deviations	33	Updated to reflect that protocol deviations will be documented in the Clinical Trial Management System.	Corrected to reflect the planned process for handling protocol deviations.
	11.1 Adverse Event Definitions	34	Updated letters for the Appendix references to reflect the updated appendices.	To provide the correct Appendix references.

Version	Section(s)	Page(s)	Description of Change(s)	Rationale for Change(s)
2.0	23 Statistical Methods	43-45	Updated the timepoint for the rotational stability endpoint and specified that the 3-month timepoint is the key timeframe for other endpoints.	Updated to align with the planned timepoint for analysis for the primary endpoint and provided clarification for other endpoint data at other postoperative timepoints.
	23.1 Analysis Population	44	Provided clarification regarding the analysis population and available axis data. Also provided clarification on how data will be handled if a repositioning or lens removal procedure is required.	To provide clarity regarding the analysis population and situational data.
	23.2 Primary study endpoint	44	Updated the timepoint from 3-months to 1-week for the primary endpoint	Updated to align with the planned timepoint for analysis for the primary endpoint
	23.3 Other Endpoint	45	Updated to reflect the revised timeframes for other endpoint data.	Updated to align with the planned timepoint for analysis for the other endpoint data
	Appendix A	46	Updated to reflect that pupil size will be collected at all postoperative visits, complications/adverse events will also be collected at preoperative visits, and the Investigator Satisfaction Questionnaire will be completed at the 1-week visit.	Updated to align with study procedures per the revised protocol.
	Appendix B	47	Equipment list. This appendix was formerly Slit Lamp Exam Ratings.	Added to provide clarity regarding study equipment.
	Appendix C	48	Instructions for capturing photos through the surgical microscope. This appendix was formerly Slit Lamp Retroillumination Photographs.	Added to provide instructions for capturing photographs through the surgical microscope.
	Appendix D	49	Instructions for Using the M&S System. This appendix was formerly American Academy of Ophthalmology Task Force Consensus Statement on Adverse Events for Intraocular Lenses	Added to provide instructions for using the M&S System.
	Appendix E	50	Instructions for Distance Visual Acuity Testing. This appendix was formerly Instructions for adverse event and complaint reporting	Added to provide instructions for performing distance visual acuity testing.
	Appendix F	51	Maximum Plus Manifest Refraction Technique with Cylinder Refinement. This appendix was formerly Patient Satisfaction Questionnaire (PSQ)	Added to provide instructions for maximum plus manifest refraction technique with cylinder refinement
	Appendix G	52	Refraction Adjustments. This appendix was formerly Investigator Satisfaction Questionnaire (ISQ)	Added to provide instructions for refraction adjustments.

Version	Section(s)	Page(s)	Description of Change(s)	Rationale for Change(s)
2.0	Appendix J	57	Instructions for Lens Axis Measurement with Slit Lamp Updated appendix letter to reflect the appendix number in this revision of the protocol and updated the process for axis measurement.	Simplified the instructions for axis measurement estimation.
	Appendix B, C, D, E, F, G, H, I, J, K, L, M, N	47-61	Updated letters of each appendix to reflect additional appendices.	To provide the correct Appendix letters in order.
3.0	Sponsor Personnel	4	Added Head of Global Clinical Science; updated title for Director, Clinical Operations, Surgical Vision	Updated sponsor personnel to include Head of Global Clinical Science and to clarify title for Director, Clinical Operations, Surgical Vision
	1 Synopsis: Overall Study Design	13	Updated number of sites to up to 8 sites; clarified that refractive target outcomes will be emmetropia for each eye enrolled in the study; updated visit schedule to address either bilateral or unilateral subjects.	Updated to align with the study design change to allow for unilateral or bilateral enrollment.
	1 Synopsis: Study Population Characteristics	14-15	Updated to allow for unilateral or bilateral enrollment in the study; updated the total number of subjects to be enrolled in the study, percentage of eyes from unilateral and bilateral subjects, and the expected number of subjects per site; updated the inclusion criteria to allow for unilateral or bilateral enrollment; updated the exclusion criteria to exclude enrollment of eye designated for near correction in subjects with planned monovision correction.	Updated to align with the study design change to allow for unilateral or bilateral enrollment.
	1 Synopsis: Study Visits and Procedures	16	Included clarification that the ICF will include designation as to whether one or both eyes are to be included in the study; clarifies that PSQ is only for bilaterally implanted subjects.	Updated to align with the study design change to allow for unilateral or bilateral enrollment.
	4 Study Design	17	Updated number of sites and total number of subjects to be enrolled in the study for unilateral or bilateral cataract surgery.	Updated to align with the study design change to allow for unilateral or bilateral enrollment.
	6.2 Other Endpoints	19	Clarifying that PSQ is only administered to bilateral subjects.	Updated procedures due to study design change.
	8 Study Population	22	Updated number of sites, total number of subjects to be enrolled in the study, percentage of eyes from unilateral and bilateral subjects, and the expected number of subjects per site; updated that subjects will be included for unilateral or bilateral cataract surgery.	Updated to align with the study design change to allow for unilateral or bilateral enrollment.

Version	Section(s)	Page(s)	Description of Change(s)	Rationale for Change(s)
3.0	8.1 Inclusion Criteria	23	Updated to allow for unilateral or bilateral enrollment	Updated to align with the study design change to allow for unilateral or bilateral enrollment.
	8.2 Exclusion Criteria	24	Updated to exclude enrollment of eye designated for near correction in subjects with planned monovision correction.	Updated to align with the study design change to allow for unilateral or bilateral enrollment.
	10.1 Experimental Plan Overview	26-27	Updated number of sites and total number of subjects to be enrolled in the study for unilateral or bilateral cataract surgery; percentage of eyes from unilateral and bilateral subjects; corrected the analysis time point to 1-week; clarified that PSQ is only administered to bilateral subjects.	Updated to align with the study design change to allow for unilateral or bilateral enrollment.
	10.2 Visit Schedule	27-28	Updated to account for bilateral or unilateral subjects: for bilateral subjects, 3-month visit window is based on the 2nd eye operative date; added footnote to Table 2 to clarify instructions on bilateral 3-month visit.	Updated to align with the study design change to allow for unilateral or bilateral enrollment.
	10.3 Preoperative Procedures	29-30	Clarifying that preoperative procedures are to be performed for each enrolled eye; removed restriction for monovision.	Updated to align with the study design change to allow for unilateral or bilateral enrollment.
	10.6 Operative Procedures	30	Updated to allow for MIGS (minimally invasive glaucoma surgery) following consultation with the medical monitor.	Allowing for more standard of care procedures to be done with consultation with medical monitor.
	10.7 Postoperative Procedures	33, 35	Clarifying that Binocular UCDVA should be done for bilateral subjects only; clarifying that PSQ is only administered to bilateral subjects.	Updated to align with the study design change to allow for unilateral or bilateral enrollment.
	21 Statistical Methods	47	Adding that data from other study visits other than key timeframe may be reported for supportive analysis.	Updated to align with the study design change to allow for unilateral or bilateral enrollment.
	21.1 Analysis Population	48	Updated analysis to reflect changes due to unilateral or bilateral enrollment.	Updated to align with the study design change to allow for unilateral or bilateral enrollment.
	21.5 Sample Size calculation	49	Updated text to reflect sample size was calculated for 1-week instead of 3-months.	Updated to align with time frame for primary endpoint.
	Appendix A	50	Updated footnotes to specify which procedures are applicable only in subjects bilaterally implanted with the study lens (binocular UCDVA and PSQ).	Updated to align with the study design change to allow for unilateral or bilateral enrollment.

Version	Section(s)	Page(s)	Description of Change(s)	Rationale for Change(s)
	Appendix B	51	Updated equipment list to allow for a loan of a slit lamp compatible with slit-lamp camera.	To reflect current sites' equipment needs.
3.0	Appendix F	55	Removed Snellen and added M&S System to study Manifest Refraction procedure instructions.	Correction to procedure instructions as M&S System will be utilized to collect study Manifest Refraction.
	Appendix J	61	Updated instructions for lens axis measurement with slit lamp to use the limbus as a reference mark rather than the pupil.	Correction made to align with practical methods used by sites as pupil sizes may not be equal between each eye.

1. SYNOPSIS

PROTOCOL: Clinical Investigation of Rotational Stability of the TECNIS® Toric II Intraocular Lens

Protocol Number: NXGT-202-QROS

STUDY LENS: TECNIS Toric II – One-Piece Aspheric Acrylic Monofocal Posterior Chamber IOL (Model ZCU).

STUDY OBJECTIVE: The purpose of this clinical study is to evaluate the rotational stability of the TECNIS Toric II IOL.

CLINICAL HYPOTHESIS: TECNIS Toric II IOL will demonstrate excellent rotational stability by demonstrating ≤ 5º of axis misalignment from the intended IOL axis of orientation in 90% of eyes at the 1-week postoperative visit, in patients with preoperative corneal astigmatism.

OVERALL STUDY DESIGN:

Structure: Prospective, multi-center, single-arm, open-label

Number of sites: Up to 8 sites

Duration: Three months

Indication: The TECNIS Toric II 1-Piece posterior chamber lenses are indicated for the visual correction of aphakia and pre-existing corneal astigmatism of one diopter or greater in adult patients with or without presbyopia in whom a cataractous lens has been removed by phacoemulsification and who desire improved uncorrected distance vision, reduction in residual refractive cylinder, and increased spectacle independence for distance vision. The device is intended to be placed in the capsular bag.

Administration: Refractive target outcomes will be emmetropia for each eye enrolled in the study. Surgeons will perform standardized, small-incision, cataract surgery and implant the study lenses using a JJSV-validated insertion system qualified for use with TECNIS Toric II lenses as specified in the Directions for Use (DFU).

Visit Schedule: Subjects will be implanted with the study lens in one or both eyes; in bilateral subjects the second eye is to be implanted within one-month of the first eye surgery. All eyes of all subjects will undergo a minimum of 5 to a maximum of 8 scheduled visits: Preoperative for both eyes; Operative each eye, 1-day each eye, and 1-week visits for each eye; and a 3-month visit for one or both eyes.

STUDY POPULATION CHARACTERISTICS:

Condition: Unilateral or bilateral cataracts with corneal astigmatism of approximately 1.0 D to 6.0 D.

Models ZCU 1.50, 2.25, 3.00, 3.75, 4.50, 5.25. 6.00

Number of Subjects: Up to 192 subjects will be enrolled to achieve 200 evaluable eyes at the 1-week visit with a target of 75% of the eyes coming from bilateral subjects and 25% of the eyes coming from unilateral subjects.

Each site should enroll approximately 24 subjects and no site may enroll more than 25% of the enrollment total.

Inclusion Criteria

1. Minimum 22 years of age;
2. Unilateral or Bilateral cataracts for which cataract extraction and posterior chamber IOL implantation have been planned;
3. Pre-existing corneal astigmatism of one diopter or greater;
4. Predicted residual refractive cylinder based on toric IOL calculator, considering surgically induced astigmatism (SIA) and posterior corneal astigmatism (PCA) must be ≤0.50 D;
5. Potential for postoperative BCDVA of 20/30 Snellen or better;
6. Clear intraocular media other than cataract in each eye;
7. Availability, willingness and sufficient cognitive awareness to comply with examination procedures and study visits;
8. Signed informed consent form (ICF) and health insurance portability and accountability act (HIPAA) authorization;
9. Ability to understand and respond to a questionnaire in English.

Exclusion Criteria:

1. Irregular corneal astigmatism;
2. Any corneal pathology/abnormality other than regular corneal astigmatism or corneal instability due to contact lens wear;
3. Previous corneal or intraocular surgery;
4. Inability to focus or fixate for prolonged periods of time (e.g., due to strabismus, nystagmus, etc.);
5. Any pupil abnormalities (non-reactive, fixed, or abnormally shaped pupils);
6. Dilated pupil size of < 6.0 mm;

7. Recurrent severe anterior or posterior segment inflammation or uveitis;
8. Subjects with conditions associated with increased risk of zonular rupture, including capsular or zonular abnormalities that may lead to IOL decentration, including pseudoexfoliation, trauma, or posterior capsule defects;
9. Known ocular or systemic disease that, in the opinion of the investigator, may affect visual acuity or require surgical intervention during the course of the study, [macular degeneration, cystoid macular edema, proliferative diabetic retinopathy (severe), uncontrolled glaucoma, irregular corneal astigmatism, choroidal hemorrhage, concomitant severe eye disease, extremely shallow anterior chamber, microphthalmos, non-age related cataract, severe corneal dystrophy, severe optic nerve atrophy, etc.];
10. Use of systemic or ocular medications (e.g., Flomax) that may affect vision including prior, current, or anticipated use during the course of the study 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);
11. Patient is pregnant, plans to become pregnant, is lactating or has another condition associated with the fluctuation of hormones that could lead to refractive changes;
12. Concurrent participation or participation within 30 days prior to the preoperative visit in any other clinical study.
13. Planned monovision correction (eye designated for near correction)

NOTE: *Physicians considering enrolling a patient with one or more of the conditions listed under the warning or precaution in the final approved labeling of the device should weigh the potential risk/benefit ratio before enrollment.*

EVALUATION CRITERIA:

The purpose of this clinical study is to evaluate the rotational stability of the TECNIS® Toric II IOL. Rotational stability of the IOL will be evaluated by measuring axis misalignment, which is defined as the absolute difference between intended IOL axis of orientation (immediately at the end of the surgery) and follow-up visit(s) as measured by a photographic based method.

PRIMARY ENDPOINT

The primary outcome for the study is the percentage of eyes with ≤ 5º axis misalignment from the intended IOL axis of orientation at the 1-week visit.

DATA ANALYSIS:

Rotational stability of the IOL will be evaluated by measuring axis misalignment, which is defined as the absolute difference between intended IOL axis of orientation (immediately at the end of the surgery) and follow-up visit(s) as measured by a photographic based method. For the primary endpoint the percentage of eyes with ≤ 5º of axis misalignment from the intended IOL axis of orientation at the 1-week postoperative visit along with the 95% confidence interval will be

reported. The percent of eyes with misalignments ≤ 5º, < 10º, < 20º and >30º will also be reported for all other postoperative timepoints (1-day and 3-months).

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For visual acuity and refractive data, descriptive statistics will include the mean, standard deviation, median, minimum and maximum. For visual acuity, the frequency and proportion of eyes achieving each acuity line will also be reported. The frequency and proportion of eyes within 0.5 D and within 1.0 D of intended values will also be determined for postoperative refractive cylinder and spherical equivalent.

For questionnaire data, the frequency and proportion with each rating for each item will be reported. In addition, the frequency and proportion of eyes with medical findings, lens findings, complications and adverse events will also be reported.

STUDY VISITS AND PROCEDURES:

Subject eligibility will be assessed at the preoperative visit according to the inclusion/exclusion criteria. The ICF and HIPAA must be signed by any patients who agree to participate in the study prior to undergoing any study-specific procedures. This will include designation as to whether one or both eyes are to be included in the study. Those subjects who meet the inclusion/exclusion criteria and agree to participate will be implanted in one or both eyes with the study lens. All subjects are intended to have either unilateral or bilateral cataract surgery with the second-eye surgery occurring no more than 30 days after the first eye surgery.

Key preoperative data include ocular health and history, pupil measurement, visual acuities, keratometry, intraocular pressure (IOP), biomicroscopic slit lamp findings, fundus exam findings and biometry. The operative visit will include standard procedures for cataract surgery and IOL implantation as well as photographic image of the IOL position, slit lamp exam, complications and adverse event assessment. Key postoperative data include photographic image of the IOL position, manifest refraction, uncorrected distance visual acuity (UCDVA), best-corrected distance visual acuity (BCDVA), Slit Lamp findings, non-directed visual symptoms, 2-item Patient Satisfaction Questionnaire (PSQ), 3-item Investigator Satisfaction Questionnaire (ISQ) and adverse events. The PSQ will only be administered on subjects bilaterally implanted with the study lens.

2. BACKGROUND/INTRODUCTION

Approximately a third of patients presenting for cataract surgery are likely to have at least 1.0 D of corneal astigmatism.[1] Patients with astigmatism that desire spectacle independence after cataract

[1] Hoffmann PC, Hütz WW. Analysis of biometry and prevalence data for corneal astigmatism in 23,239 eyes. J Cataract Refract Surg. 2010;36(9):1479-1485.

surgery will need a method to eliminate or reduce corneal cylinder. Kessel et. Al., compared the two most commonly available options to reduce astigmatism and noted that the most effective way to reduce astigmatism is by implanting a toric IOL.[2] For toric IOLs to be effective, IOL rotation after implantation must be minimal; it has been noted that as little as 1 degree of rotation can result in 3.3% reduction in the toric lens effectiveness in reducing astigmatism.

JJSV has developed a new IOL platform designed to minimize rotation to ≤ 5º within the first week after implantation. The TECNIS® Toric II 1-Piece lens is an ultraviolet light-absorbing posterior chamber intraocular lens (IOL) that compensates for corneal spherical aberrations and corneal astigmatism. The benefits of aspheric compensation for corneal spherical aberrations are contingent upon full refractive correction of sphere and cylinder. The IOLs incorporate a proprietary wavefront-designed toric aspheric optic with a squared posterior optic edge designed to provide a 360º barrier. The edge of the optic has a frosted design to reduce potential edge glare effects. In addition, compared to the TECNIS Toric 1-Piece IOL, the haptics of the TECNIS Toric II 1-Piece IOLs have a squared and frosted design. The anteriorly located cylinder axis marks denote the meridian with the lowest power and is to be aligned with the steep corneal meridian.

3. CLINICAL HYPOTHESIS

TECNIS Toric II IOL will demonstrate excellent rotational stability by demonstrating ≤ 5º of axis misalignment from the intended IOL axis of orientation in 90% of the eyes at the 1-week postoperative visit.

4. STUDY DESIGN

This is a prospective, multicenter, single-arm, open-label clinical study of the commercially available TECNIS Toric II IOL. The study will be conducted in up to 192 subjects needing unilateral or bilateral cataract surgery in up to 8 sites in United States (US). The subjects will be followed for up to 3-months postoperatively.

5. ACRONYMS

The following acronyms are used throughout this document:

- ADE: adverse device effect
- AK: astigmatic keratotomy
- BCDVA: best-corrected distance visual acuity
- BSS: balanced salt solution
- CRF: case report form

[2] Kessel L, Andresen J, Tendal B, Erngaard D, Flesner P, Hjortdal J. Toric Intraocular Lenses in the Correction of Astigmatism During Cataract Surgery: A Systematic Review and Meta-analysis. Ophthalmology. 2016;123(2):275-286.

- CRI: corneal relaxing incisions
- D: diopters
- DFU: directions for use
- EDC: electronic data capture
- GCP: good clinical practice
- HIPAA: health insurance portability and accountability act
- ICF: informed consent form
- IOL: intraocular lens
- IOP: intraocular pressure
- IRB: institutional review board
- ISQ: investigator satisfaction questionnaire
- LASIK: laser-assisted in-situ keratomileusis
- LASEK: laser epithelial keratomileusis
- LRI: limbal relaxing incisions
- OCCI: opposite clear corneal incisions
- OR: operating room
- PRK: photorefractive keratectomy
- PSQ: patient satisfaction questionnaire
- SAE: serious adverse events

- UCDVA: uncorrected distance visual acuity
- UADE: unanticipated adverse device effect
- USADE: unanticipated serious adverse device effect

6. STUDY OBJECTIVES AND ENDPOINTS

The purpose of this clinical study is to evaluate the rotational stability of the TECNIS® Toric II IOL. Primary endpoint is percentage of eyes with ≤ 5º axis misalignment from the intended IOL axis of orientation at the 1-week postoperative visit.

The final 3-month visit will be the key timepoint for visual acuity, manifest refraction and patient and investigator reported outcomes questionnaire evaluations. Other timeframes will be provided as supportive analysis.

6.1 PRIMARY ENDPOINT

The primary endpoint for the study is the percentage of eyes with ≤ 5º axis misalignment from the intended IOL axis of orientation at the 1-week postoperative visit. Rotational stability of the IOL will be evaluated by measuring axis misalignment, which is defined as the absolute difference between intended IOL axis of orientation (immediately at the end of the surgery) and follow-up visit(s) as measured by a photographic based method.

6.2 OTHER ENDPOINTS

- Residual mean manifest cylinder and spherical equivalent for all eyes
- Percentage of eyes that achieve UCDVA of 20/40, 20/32, 20/25 & 20/20
- Percentage of eyes that achieve accuracy of cylinder (to target):
  - within: ± 0.50 D and ± 1.00 D
- Analysis of lens axis misalignment (compared to target) including:
  - Mean absolute and signed value of the misalignment
  - Percentage of eyes with lens axis misalignments ≤ 5º, < 10º, < 20º and >30º
- Medical findings/Lens findings/Complications
- Subject responses on Patient Satisfaction Questionnaire (PSQ)

  NOTE: Should be administered only in subjects who have been implanted with the study lens bilaterally
- Investigator responses on Investigator Satisfaction Questionnaire (ISQ)
- Adverse event rates including the rate of IOL repositioning and/or IOL exchange primarily due to IOL misalignment.

7. STUDY PRODUCTS

7.1 INTRAOCULAR LENSES

The TECNIS® Toric II IOL (study lens), Models ZCU150, ZCU225, ZCU300, ZCU375, ZCU450, ZCU525, and ZCU600 are posterior chamber, 1-piece, aspheric, hydrophobic acrylic foldable IOLs and are to be implanted in the capsular bag following cataract extraction. It is designed to minimize the occurrence of large rotations (greater than 10°) following implantation.

The TECNIS Toric II is a UV light-absorbing posterior chamber lens that compensates for corneal spherical aberrations and corneal astigmatism. The benefits of aspheric compensation for corneal spherical aberrations are contingent upon full correction of spherical (defocus) and cylindrical (astigmatic) refractive error.

The TECNIS Toric II incorporates an aspheric optic with a squared posterior optic edge designed to provide a 360° barrier for reducing the incidence of posterior capsular opacification (PCO). The visual benefits of the proprietary wavefront-designed aspheric optic have been clinically assessed using the TECNIS Z9000 IOL (under Investigational Device Exemption G960221). As featured in the currently marketed TECNIS Toric (ZCT Series) design, the edge of the optic is frosted to reduce potential for edge glare effects.

The TECNIS Toric II IOLs have two sets of four axis orientation marks 180° apart in the outer periphery of the anterior optic surface to indicate the meridian of the lowest power (flat meridian). These axis orientation marks are for proper alignment of the flat meridian of the IOL with the steep meridian of the corneal curvature.

The ZCU150, ZCU225, ZCU300, ZCU375, ZCU450, ZCU525, and ZCU600 lens models are intended for cataract patients with pre-existing corneal astigmatism that, when taking surgically induced astigmatism into account, have approximately 0.75 D to 4.75 D of predicted corneal astigmatism to be corrected **(Table 1)**.

TABLE 1: TECNIS® Toric II Models ZCU, IOL Astigmatism Correction Range

	Cylinder Powers (D)						
IOL Model	**ZCU150**	**ZCU225**	**ZCU300**	**ZCU375**	**ZCU450**	**ZCU525**	**ZCU600**
IOL Plane (Labeled)	1.50	2.25	3.00	3.75	4.50	5.25	6.00
Corneal Plane*	1.03	1.54	2.06	2.57	3.08	3.60	4.11

*The corresponding cylinder values at the corneal plane have been calculated based on the average pseudophakic eye.

Table 2 lists the general design characteristics of the TECNIS Toric II IOLs.

TABLE 2: Lens Characteristics of the TECNIS® Toric II Model ZCU

CHARACTERISTICS	TECNIS Toric II IOL (Model ZCU)
Lens Design	1-piece acrylic biconvex monofocal IOL with aspheric toric anterior curvature
Lens Material	Surface-treated SENSAR® soft acrylic (acrylic with covalently bound UV absorber), AMOS3225
Overall Diameter	13.0 mm
Optical Center Thickness	0.722 mm (20.0 D Lens)
Haptic Angle	No angulation, but offset from the optic body
Optic Body Diameter	6.0 mm
Haptic Material	Same as optic
Haptic Width	0.39 mm
Haptic Thickness	0.46 mm
Haptic Style	C-loop
Other features	Axis orientation marks
Optic Shape	Biconvex
Anterior Optic Profile	Aspheric with a maximum and a minimum radii of curvature perpendicular to each other
Posterior Optic Profile	Spherical
Optic Edge Design	PROTEC™ squared edge
Dioptric Power Range	+5.0 to +34.0 D in 0.50 D increments
Cylinder Power Range	1.50 D, 2.25 D, 3.00 D, 3.75 D, 4.50 D, 5.25 D, and 6.00 D (at the IOL plane)
Refractive Index	1.470 (35° C)

CHARACTERISTICS	TECNIS Toric II IOL (Model ZCU)
Asphericity of Lens	-0.27 um
Theoretical A-constant[a]	118.8 for ultrasound biometry, 119.3 for optical biometry

[a] For lens power calculations, the investigator's personalized A-Constant for the TECNIS Toric ZCU IOLs are to be used.

INDICATION

The TECNIS® Toric II 1-Piece posterior chamber lenses are indicated for the visual correction of aphakia and pre-existing corneal astigmatism of one diopter or greater in adult patients with or without presbyopia in whom a cataractous lens has been removed by phacoemulsification and who desire improved uncorrected distance vision, reduction in residual refractive cylinder, and increased spectacle independence for distance vision. The device is intended to be placed in the capsular bag.

7.2 IMPLANTATION SYSTEMS

JJSV recommends using The UNFOLDER® Platinum 1 Series Implantation System (the 1MTEC30 Cartridge and the DK7796 inserter). Alternate validated insertion systems that can be used to insert the TECNIS Toric II 1-Piece lens include the UNFOLDER® EMERALD-AR Series Implantation System (with the 1CART30 Cartridge), the ONE SERIES Ultra Insertion System (the 1VPR30 Cartridge and the DK7786 or DK7791 inserters) or any other Johnson & Johnson Surgical Vision, Inc.-qualified insertion system. Only insertion instruments that have been validated and approved for use with this lens should be used. Please refer to the DFU for the insertion instrument or system for additional information.

8. STUDY POPULATION

All study subjects will be enrolled from the normal surgical cataract population at up to 8 sites in the U.S. Up to 192 subjects (116 bilateral and 76 unilateral) will be enrolled to achieve approximately 200 eyes available for analysis at 1-week with a target of 75% of the eyes coming from bilateral subjects and 25% of the eyes coming from unilateral subjects. This accounts for screen failures, drop-out rate and unanalyzable photographs for toric IOL rotation analysis. Each site should implant approximately 24 subjects and no site may implant more than 25% of the enrollment total.

This study will include subjects undergoing unilateral and bilateral primary cataract extraction and IOL implantation and who meet all the study inclusion and exclusion criteria in one or 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 receive the TECNIS Toric II IOL Model ZCU in one or 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

1. Minimum 22 years of age;
2. Unilateral or Bilateral cataracts for which cataract extraction and posterior chamber IOL implantation have been planned;
3. Pre-existing corneal astigmatism of one diopter or greater;
4. Predicted residual refractive cylinder based on toric IOL calculator, considering surgically induced astigmatism (SIA) and posterior corneal astigmatism (PCA) must be ≤0.50 D;
5. Potential for postoperative BCDVA of 20/30 Snellen or better;
6. Clear intraocular media other than cataract in each eye;
7. Availability, willingness and sufficient cognitive awareness to comply with examination procedures and study visits;
8. Signed informed consent form (ICF) and health insurance portability and accountability act (HIPAA) authorization;
9. Ability to understand and respond to a questionnaire in English.

8.2 EXCLUSION CRITERIA

1. Irregular corneal astigmatism;
2. Any corneal pathology/abnormality other than regular corneal astigmatism or corneal instability due to contact lens wear;
3. Previous corneal or intraocular surgery;
4. Inability to focus or fixate for prolonged periods of time (e.g., due to strabismus, nystagmus, etc.);
5. Any pupil abnormalities (non-reactive, fixed, or abnormally shaped pupils);
6. Dilated pupil size of < 6.0 mm;
7. Recurrent severe anterior or posterior segment inflammation or uveitis;
8. Subjects with conditions associated with increased risk of zonular rupture, including capsular or zonular abnormalities that may lead to IOL decentration, including pseudoexfoliation, trauma, or posterior capsule defects;
9. Known ocular or systemic disease that, in the opinion of the investigator, may affect visual acuity or require surgical intervention during the course of the study, [macular degeneration, cystoid macular edema, proliferative diabetic retinopathy (severe),

uncontrolled glaucoma, irregular corneal astigmatism, choroidal hemorrhage, concomitant severe eye disease, extremely shallow anterior chamber, microphthalmos, non-age related cataract, severe corneal dystrophy, severe optic nerve atrophy, etc.];

10. Use of systemic or ocular medications (e.g., Flomax) that may affect vision including prior, current, or anticipated use during the course of the study 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);
11. Patient is pregnant, plans to become pregnant, is lactating or has another condition associated with the fluctuation of hormones that could lead to refractive changes;
12. Concurrent participation or participation within 30 days prior to the preoperative visit in any other clinical study;
13. Planned monovision correction (eye designated for near correction).

NOTE: *Physicians considering enrolling a patient with one or more of the conditions listed under the warning or precaution in the final approved labeling of the device should weigh the potential risk/benefit ratio before enrollment.*

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 toric IOLs in cataract patients 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 and all legal requirements for clinical trials including ISO 14155 and Good Clinical Practice (GCP). Investigator will only make changes to a protocol after notifying and obtaining approval from JJSV and the Institutional 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.
- Maintain confidentiality as required by HIPAA or similar laws and regulations.
- Shall not obtain written ICF any subject to participate or allow any subject to participate before obtaining IRB approval.
- Document in each subject's case history that informed consent was obtained prior to participation in the study.
- Report to JJSV and the reviewing IRB any adverse experiences that occur during the study in accordance with applicable laws and regulations.
- Read and understand the information in the DFU for the study.
- 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) 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.
- 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.
- Provide sufficient accurate financial information to JJSV to allow JJSV to submit complete and accurate certification or disclosure statements. Promptly update this information if any relevant changes occur during 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 U.S. regulations and all conditions of approval imposed by the reviewing IRB.
- 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 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, ICF 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
- Financial Disclosure form
- Signed and dated copy of investigator's current curriculum vitae
- Copy of the investigator's current medical license

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 the Declaration of Helsinki, ISO 14155:2011 and all other applicable laws and regulations. The study will not begin until IRB approval has been obtained.

This study will be a prospective, multicenter, single-arm, open-label clinical investigation conducted at up to 8 sites. Up to 192 subjects (116- bilateral and 76- unilateral) will be enrolled to achieve approximately 200 eyes available for analysis at 1-week with a target of 75% of the eyes coming from bilateral subjects and 25% of the eyes coming from unilateral subjects. After ICF is obtained and confirmation that all eligibility criteria are met, the eyes may be treated with the study lens.

The investigator will choose which eye to operate on first for each subject at his/her discretion and standard clinical practice (e.g., the eye with the worse cataract, poorer best-corrected distance vision and/or more severe optical/visual complaints). All bilateral subjects are intended to have bilateral cataract surgery with the second-eye surgery occurring no more than 30 days after the first eye surgery. All subjects will be examined through 3 months postoperatively according to the visit schedule described in **Section 10.2**, Visit Schedule.

To maintain consistency, 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.

Key preoperative data include ocular health and history, pupil measurement, visual acuities, keratometry, intraocular pressure (IOP), biomicroscopic slit lamp findings, fundus exam findings, and biometry.

The operative visit will include standard procedures for cataract surgery and IOL implantation as well as photographic image of the IOL position, complications and adverse event assessment.

Key postoperative data include photographic image of the IOL position, manifest refraction, UCDVA, BCDVA, slit lamp findings, non-directed visual symptoms, PSQ, ISQ and adverse events. PSQ should be administered only to subjects that undergo bilateral implantation with study lenses. 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 unilateral or bilateral cataract surgery with the study lens. In bilateral subjects the second eye surgery should occur no more than 30 days after the first eye surgery. For both unilateral and bilateral subjects, after each surgery, the operative eye should be examined at 1 day (1-2 days), 1 week (5-14 days) and 3-months (60-120 days) postoperative. For bilateral subjects, based on the date of the second-eye surgery, both eyes should be evaluated at the same 3-month postoperative visit. 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	5-14 days postoperative
5	Second Eye	Operative	No more than 30 days after 1st eye surgery
6	Second Eye	1 day	1-2 days postoperative
7	Second Eye	1 week	5-14 days postoperative[a]
8	Both Eyes	3 months	60 - 120 days postoperative from 2nd eye surgery[a,b]

[a] Subjects with a bilateral treatment, if both the 1st and 2nd eyes are within visit window, this visit may be done on the same day.

[b] If for any reason the second eye is not implanted, the first eye should be examined for the 3-month study visit 60 to 120 days following the first eye surgery.

10.3 PREOPERATIVE PROCEDURES

All subjects treated in the study must sign the current IRB-approved ICF and meet the eligibility criteria. The ICF must be signed before any study-specific examinations are performed, and this must be documented in the source documents. HIPAA authorization 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 ICF 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.

As the ICF 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 enrolled 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 VISUAL ACUITY AND MANIFEST REFRACTION

The standard manifest refraction should be performed and monocular BCDVA should be recorded using a standard Snellen chart or equivalent.

KERATOMETRY

Preoperative corneal astigmatism should be determined by biometric keratometry readings. The same method used preoperatively must also be used at the postoperative visits.

CONTACT LENS WEAR AND CORNEAL STABILITY

The surgeon should follow their routine procedures to establish keratometric corneal stability in contact lens wearers before surgery.

NOTE: *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.*

IOL POWER AND TARGETED REFRACTION

Keratometry, axial length and anterior chamber depth (ACD) must be measured to determine the appropriate lens power for implantation. Optical biometry methods (i.e., IOLMaster® or LENSTAR®) are preferred; however, surgeons should use the biometry method based on their experience and medical judgement.

The spherical equivalent lens power, as determined by the investigator's standard biometry methods, should be calculated to achieve emmetropia (± 0.50 D) at distance for all eyes. Intentional overcorrection or under-correction (i.e., outside ± 0.50 D) should NOT be planned for either eye; however, surgeons may adjust the targeted refraction as necessary to achieve emmetropia based on their surgeon factor, study subject experience and/or subject first-eye outcomes.

NOTE: *Surgeon may choose to use 119.3 or personalized A-constant for the TECNIS® Toric ZCU lens.*

ADDITIONAL PREOPERATIVE INFORMATION COLLECTED SHOULD INCLUDE:

- Informed consent
- Subject demographic information
- Planned surgery dates for each enrolled eye
- Ocular history, including presence of ocular pathology for each enrolled eye
- Dilated pupil size (measured by standard practice at the study site).
- Any medical findings from a slit lamp exam, dilated fundus exam, intraocular pressure or other assessment.
- Ocular and systemic medications

10.4 STUDY LENS SUPPLY

The principal investigator will implant lenses from their commercial TECNIS Toric II inventory.

10.5 SELECTION OF THE IOL

In order to facilitate IOL selection and axis placement, JJSV provides a web-based proprietary tool, the TECNIS Toric Calculator (www.TecnisToricCalc.com) for the surgeon. Preoperative keratometry, biometry data, incision location, spherical equivalent IOL power, and the surgeon's estimated surgically induced corneal astigmatism are used as inputs for the TECNIS Toric Calculator. These inputs are used to determine the axis of placement in the eye and the predicted residual refractive astigmatism for TECNIS Toric II 1-Piece IOL models.

NOTE: *The TECNIS Toric Calculator also provides an option for including the Posterior Corneal Astigmatism (PCA). The predetermined value for posterior corneal astigmatism must be included in the calculation by checking the box labeled "Include Posterior Corneal Astigmatism (PCA)".*

Surgeons can use their preferred Toric Calculator for determination of lens axis placement.

10.6 OPERATIVE PROCEDURES

Surgical procedures should be in accordance with your routine practice and in accordance with the labeling. The surgeons should follow the procedures as described in the DFU for appropriate alignment of the IOL axis.

NOTE: *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).*

Additional procedures such as MIGS (minimally invasive glaucoma surgery) may be allowed following consultation with the medical monitor.

Optiwave Refractive Analysis (ORA) can be used as a part of routine cataract surgery to improve accuracy of the correction. If ORA is used it will be documented in the Operative case report form.

REFERENCE AXIS

Prior to surgery the operative eye should be marked per the surgeon's routine standard of care method.

Operative case report forms should include the following information:

INCISION TYPE AND SIZE

The incision may be clear corneal, limbal or scleral tunnel at the discretion of the investigator. Lenses should be inserted per the investigator's standard technique when using the JJSV-qualified implantation system.

CAPSULORHEXIS SIZE AND METHOD

The anterior capsulotomy should be made per investigator's standard technique. The anterior capsulotomy method may be manual (rhexis) or laser-assisted.

CRYSTALLINE LENS REMOVAL

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

BALANCED SALT SOLUTION (BSS) STERILE IRRIGATING SOLUTION

BSS solution should be used as is customary for each investigator and recorded on the case report form.

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), the UNFOLDER® EMERALD-AR Series Implantation System (with the 1CART30 Cartridge), the ONE SERIES Ultra Insertion System (the 1VPR30 Cartridge and the DK7786 or DK7791 inserters), or any other Johnson & Johnson Surgical Vision, Inc.-qualified insertion system.

NOTE: *Use of capsular tension ring is not allowed.*

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 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 recorded in the source document for each subject, as appropriate. At the operative and postoperative visits, only medications required for treatment of an SAE will be recorded on the CRFs.

TYPE OF CLOSURE

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

BASELINE PHOTOGRAPH OF THE IOL POSITION

At the end of each case (regardless of whether repositioning was required), a minimum of 3 high-quality photographs should be taken through the surgical microscope showing the lens in its final position. Care should be taken to ensure clear visibility in the photo of both the scleral vessels and the lens axis marks as this will be the baseline image for all future rotation measurements. **Appendix C** provides detailed instructions for capturing photographs through the surgical microscope. If video capabilities are available, the surgeon should capture the entire surgery through the surgical microscope on video. If at the end of surgery, a high-quality image of the eye cannot be obtained for any reason, then a slit lamp photograph should be taken following surgery as a back-up.

ADDITIONAL OPERATIVE INFORMATION COLLECTED SHOULD INCLUDE:

- Date of surgery
- Operative eye
- Lens power and serial number
- Intended spherical equivalent
- Intended cylinder
- Capsular bag polishing
- Lens placement
- Surgical complications or other surgical procedures
- Difficulty of lens implantation
- Product complaints
- Serious and/or device-related adverse events
- Confirmation that surgical photos have been taken/uploaded

10.7 POSTOPERATIVE PROCEDURES

Postoperatively, subjects will be examined according to the schedule in **Section 10.2**, Visit Schedule.

To maintain consistency, it is recommended that only the investigator/ sub-investigator or other designated and trained clinician perform the slit lamp exams and slit lamp photographs, although a back-up person should also be designated and trained Also, 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 postoperative CRF will be used to collect the following postoperative information, although not all data are required at every visit:

UNCORRECTED DISTANCE VISUAL ACUITY TESTING

Monocular and binocular visual acuities will be measured using the ETDRS (Early Treatment Diabetic Retinopathy Study) chart presented on a self-calibrating monitor in the M&S system at 4 meters (13 feet) under photopic (85-110 cd/m2) conditions. Instructions for using the M&S System are detailed in **Appendix D**, and for distance visual acuity in **Appendix E**. Monocular UCDVA should be measured at 1-day, 1-week and 3-months study visits. Binocular UCDVA should be measured at the 3-month study visit only in subjects bilaterally implanted with the study lens.

NOTE: *To adjust 4.0-meter to optical infinity, +0.25 D lens must be placed in the trial frame for each eye before measuring UCDVA.*

MANIFEST REFRACTION

Postoperative manifest refractions are to be performed using the M&S System at a distance of 4.0 meters. Manifest refraction is to performed using the Maximum Plus refraction method as detailed in **Appendix F**. Also refer to **Appendix G**, Refraction Adjustments.

BEST-CORRECTED DISTANCE VISUAL ACUITY

Monocular visual acuities will be measured using the M&S System at 4 meters (13 feet) under photopic (80-110 cd/m2) conditions. Instructions for using the M&S System are detailed in **Appendix D**, and for distance visual acuity in **Appendix E**.

KERATOMETRY

Corneal astigmatism should be determined by biometry keratometric readings. The same method used preoperatively must also be used at the postoperative visit (1-week and 3-month).

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.

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 H**.

BIOMICROSCOPIC SLIT LAMP PHOTOGRAPHS AND LENS AXIS ORIENTATION

Study subjects are to have their pupils dilated to approximately 6 mm or more at each postoperative visit in order to take slit lamp photographs that capture limbal vessels and iris detail with precise focus, while also capturing the lens fiducial marks with reasonable focus (the cameras focal plane should be anterior to the IOL fiducials; see **Appendix I**).

The lens orientation should also be measured by the investigator, or other study personnel, by rotating the slit lamp beam to match the IOL axis orientation and reading the axis to the nearest degree from the scale (see **Appendix J**).

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 3-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 3-month visit to evaluate retinal status and fundus visualization. Examinations may be done dilated with ophthalmoscopy.

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 subjects report any issues, they should be recorded, and the level of severity determined (mild, moderate or severe) as appropriate.

MEDICATIONS

Postoperative ocular medications should be used as is customary for each investigator and recorded in the source document for each subject, as appropriate. Only medications required for treatment of a serious adverse event (SAE) will be recorded on the case report forms.

PATIENT SATISFACTION QUESTIONNAIRE (PSQ)

The 2-item questionnaire will be administered at the 3-month visit to collect information regarding spectacle usage, and subject satisfaction (**Appendix K**). PSQ should be administered only to subjects that undergo bilateral implantation with study lenses.

INVESTIGATOR SATISFACTION QUESTIONNAIRE (ISQ)

This 3-item questionnaire is self-administered and should be completed by the PI or sub-PI examining the subject. The purpose of this questionnaire is to collect investigator satisfaction with the clinical outcomes (e.g., rotational stability, uncorrected distance visual acuity) of the eyes implanted with the study lens. At the 1-week and 3-month visits, investigator feedback from the 3-item ISQ will be collected for each implanted eye (**Appendix L**).

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 and **Appendix M** for further information.

Secondary Surgical Interventions

Secondary surgical interventions due to refractive error and/or medical complications are serious adverse events. Secondary surgical interventions have become the standard of care in some cases and are considered to be in the subject's best interest. The clinical protocol will allow for secondary surgical interventions in the following categories:

- IOL repositioning due to a significant axis misalignment resulting in a visual outcome that is unsatisfactory, providing the axis misalignment is rotationally correctable.
- IOL exchange due to incorrect spherical power resulting in a significant decrease in uncorrected visual acuity.
- IOL exchange due to surgical or postoperative medical complications or adverse events.

If IOL repositioning procedure is required, the investigator should collect dilated slit lamp photograph showing IOL position prior to reposition.

NOTE: *If a toric IOL is repositioned, the subject will continue to be followed through study completion for safety. If a toric IOL is exchanged for a non-toric IOL, the subject should be followed until resolution of the serious adverse event/adverse device effect.*

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 surgery, implantation in the first eye is aborted due to a surgical complication, or the subject dies prior to first-eye treatment.

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.

Subjects will be "discontinued" from the study if the subject does not undergo surgery; or if both study lenses 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:

- Manifest refraction (using standard Snellen Chart)
- Uncorrected and best-corrected Snellen distance visual acuity
- Intraocular pressure
- Slit lamp examination for medical and/or lens findings

- Slit lamp photographs of IOL position
- Dilated or undilated fundus exam
- Ocular symptoms
- Adverse events
- Medications

If in the opinion of the investigator, IOL misalignment is suspected to be the cause of subjects' visual complaint at an unscheduled visit, the investigator should collect UCDVA, manifest refraction, BCDVA, Keratometry, non-directed visual symptoms, dilated slit lamp photographs **(Appendix I)** and lens axis orientation measurement **(Appendix J)**.

NOTE: *In the opinion of the investigator, if the estimated lens axis orientation remains unchanged since the last study visit, slit lamp photographs need not be repeated.*

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.

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 in the Clinical Trial Management System. Any deviation made to protect the life or physical well-being of a subject in an emergency 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 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 N**.

- 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 N** (i.e., *BCDVA of 20/40 or worse at 1 month or later; and Grade 1+ uveitis/iritis persists for greater than 3 months after surgery*). Raised IOP, according to the guidelines listed in **Appendix N** will be considered serious if present at the last study visit (60-120 days after second eye).

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. 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 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 US Code of Federal Regulations (21CFR 812) for sites in the USA. Specific instructions on notification procedures to JJSV are included in **Appendix M**. 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 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, ICF 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 ICF must be signed by each study subject prior to any study-specific examinations being performed. The IRB-approved ICF is to be signed and dated by the subject as well as by the person who conducted the informed consent discussion. The signed ICF 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
- Concurrent medications
- Corrected and uncorrected distance visual acuity
- 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 study, 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.

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 to ensure compliance with study procedures.

Additional training on study-specific procedures may also be conducted during monitoring visits.

Upon study completion, a final close-out 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.

16. MEDICAL 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 study reports.

17. PUBLICATIONS

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

18. RISK ANALYSIS

POTENTIAL RISKS AND RISK MANAGEMENT

RISKS OF THE TECNIS® TORIC II INTRAOCULAR LENS

The acrylic 1-piece IOL TECNIS Toric II (ZCU Series) is designed to have improved rotational stability relative to the currently marketed TECNIS Toric 1-piece IOL (ZCT Series). The lenses are made from the same SENSAR soft acrylic material that is used in marketed TECNIS 1-piece lenses. Its aspheric anterior surface is intended to compensate for corneal spherical aberration.

The risk documentation for the currently marketed TECNIS 1-piece lenses, ZCB00 and ZCT Series, is applicable. For ZCB00 and ZCT lenses, current risk documentation concludes that all risks are identified as low or medium and deemed acceptable.

An additional risk assessment for the TECNIS Toric II was conducted to analyze potential hazardous situations resulting from the design differences compared to the ZCB00 and ZCT designs. With the implementation of a Risk Control Plan under this risk assessment, no additional

safety issues have been identified for the study products for their intended use in the proposed clinical investigation.

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 JJSV according to **Section 11.0**, Adverse Events and Product Complaints. Additionally, JJSV 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 TECNIS Toric II is expected to be similar to the TECNIS Toric ZCT lens series. The primary benefit from implantation of the TECNIS Toric II is the correction of astigmatism following removal of the natural crystalline lens due to cataract.

CONCLUSION

The hazards/risks associated with the TECNIS Toric II are acceptable and within those of JJSV's currently marketed IOLs. The potential clinical benefits of the TECNIS Toric II IOL outweigh the residual risks when the devices are used as intended.

19. 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 15 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 within the EDC system
- 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)
- Study lens supply records/inventory
- IRB approval documentation
- Study correspondence
- Study agreements
- Site visit documentation
- Protocol(s) and the reason for any deviations from the protocol
- Subject log(s)
- Completed subject ICFs and HIPAA authorizations
- Subject medical chart/clinic notes

20. TERMINATION OF THE INVESTIGATION

JJSV can suspend or terminate the clinical investigation at any time for reasons it determines appropriate. Additionally, the investigator, or JJSV, may stop a subject's participation at any time. 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.

21. STATISTICAL METHODS

This section highlights the analyses to be performed for key study endpoints. 1-Week postoperative visit will be the key timeframe for rotational stability. The final 3-month postoperative visit will be the key timeframe for visual acuity, refraction and questionnaire. Data from other study visits (other than key timeframe) may be reported for supportive analysis. All complications and adverse events will be evaluated at all visits.

Descriptive statistics will typically include mean, standard deviation, median, minimum, maximum for continuous data with frequency and proportion reported for categorical data.

21.1 ANALYSIS POPULATION

For monocular endpoints, all eyes implanted with a study toric IOL (model ZCU150 through ZCU600) will be pooled together for analysis; which include both study eyes from bilaterally implanted subjects and one study eye from unilaterally implanted subjects. For binocular endpoints (i.e., binocular visual acuity and patient satisfaction questionnaire), only bilaterally

implanted subjects will be included for analysis. Available data will be used for analysis (i.e., no data imputation for missing data).

For the rotational stability endpoint, the primary analysis population will be all eyes implanted with a study toric IOL (model ZCU150 through ZCU600) and with available valid axis data at the 1-week visit.

21.2 PRIMARY ENDPOINT

PROPORTION OF EYES WITHIN 5 DEGREES OF ABSOLUTE IOL ROTATION

The primary endpoint for this study is the amount of absolute axis rotation from operative axis to the 1-week visit as measured by the photographic axis method. The proportion of eyes with less than or equal to 5 degrees of absolute rotation at 1-week will be reported along with the 95% confidence interval for this proportion.

The clinical success criterion will be that 90% of eyes will have lens rotation of 5 degrees or less at 1-week using the photographic measurement method.

The primary study endpoint is based on objective analysis of study photographs by designated sponsor personnel.

21.3 OTHER ENDPOINTS

Rotational Stability

In addition to the absolute axis rotation at 1-week, data will also be reported at 1 day and 3 months. The proportion of eyes within 5º for all postoperative visits as well as the proportion of eyes with less than 10º, 20º and greater than 30º of rotation will be reported. Mean absolute rotation will also be reported for all visits using descriptive statistics.

Visual Acuity

For visual acuity, the values will be converted to LogMAR prior to analysis. Descriptive statistics for all eyes will be reported for mean LogMAR monocular uncorrected and best corrected distance

visual acuity. The frequency and proportion of eyes achieving each acuity line will also be reported for uncorrected and best corrected distance visual acuity.

Residual Refraction

Descriptive statistics will be reported for mean refractive cylinder, cylinder vs intended cylinder, spherical equivalent and spherical equivalent vs intended and for percent reduction in cylinder for all eyes. In addition, the frequency and proportion of eyes within 0.50 D and within 1.00 D of intended values will be reported for refractive cylinder and spherical equivalent.

Adverse Events

The frequency and proportion of eyes with medical/lens findings or adverse events will also be reported.

Other Findings

Enrollment data, demographic data, accountability data and operative complications/ procedures will be reported using descriptive statistics.

Patient Satisfaction and Investigator Satisfaction Questionnaires

For questionnaires, the frequency and proportion with each response will be reported for the individual items on the questionnaire.

21.4 INTERIM REPORTS

Multiple interim study analyses may be conducted during the study.

21.5 SAMPLE SIZE CALCULATIONS

With 200 eyes, the two-sided 95% confidence interval for the proportion of eyes within 5 degrees of absolute rotation at 1-week will extend within 3.0% from the observed proportion assuming an expected proportion of 95% or higher.

APPENDIX A: SUMMARY OF PROCEDURES REQUIRED AT EACH VISIT

Examination	Preop Both eyes	Op 1st & 2nd eyes	1 day 1st & 2nd eyes	1 Wk 1st & 2nd eyes	3M Both eyes
Informed consent, ocular history, inclusion/exclusion criteria potential visual acuity, targeted refraction, IOL power calculations and biometry	X				
Lens power/serial number, operative procedures		X			
Manifest refraction	X			X	X
UCDVA – photopic, monocular			X	X	X
UCDVA - photopic, binocular					X[a]
BCDVA - photopic, monocular	X			X	X
Surgical microscope photographs		X			
Keratometry	X			X	X
Intraocular pressure	X		X	X	X
Slit lamp exam	X		X	X	X
Pupil Size (Dilated)	X		X	X	X
Slit lamp retroillumination photographs (dilated)		X[b]	X	X	X
Slit lamp lens axis measurement (dilated)			X	X	X
Fundus exam	X		X[c]	X[c]	X
Ocular/visual symptoms (non-directed)	X		X	X	X
Patient Satisfaction Questionnaire (PSQ)					X[a]
Investigator Satisfaction Questionnaire (ISQ)				X	X
Complications/Adverse Events	X	X	X	X	X

[a] Only in subjects bilaterally implanted with the study lens
[b] In cases, where good quality photographs are unattainable through surgical microscope or per PI discretion
[c] Fundus exam required only if medically indicated

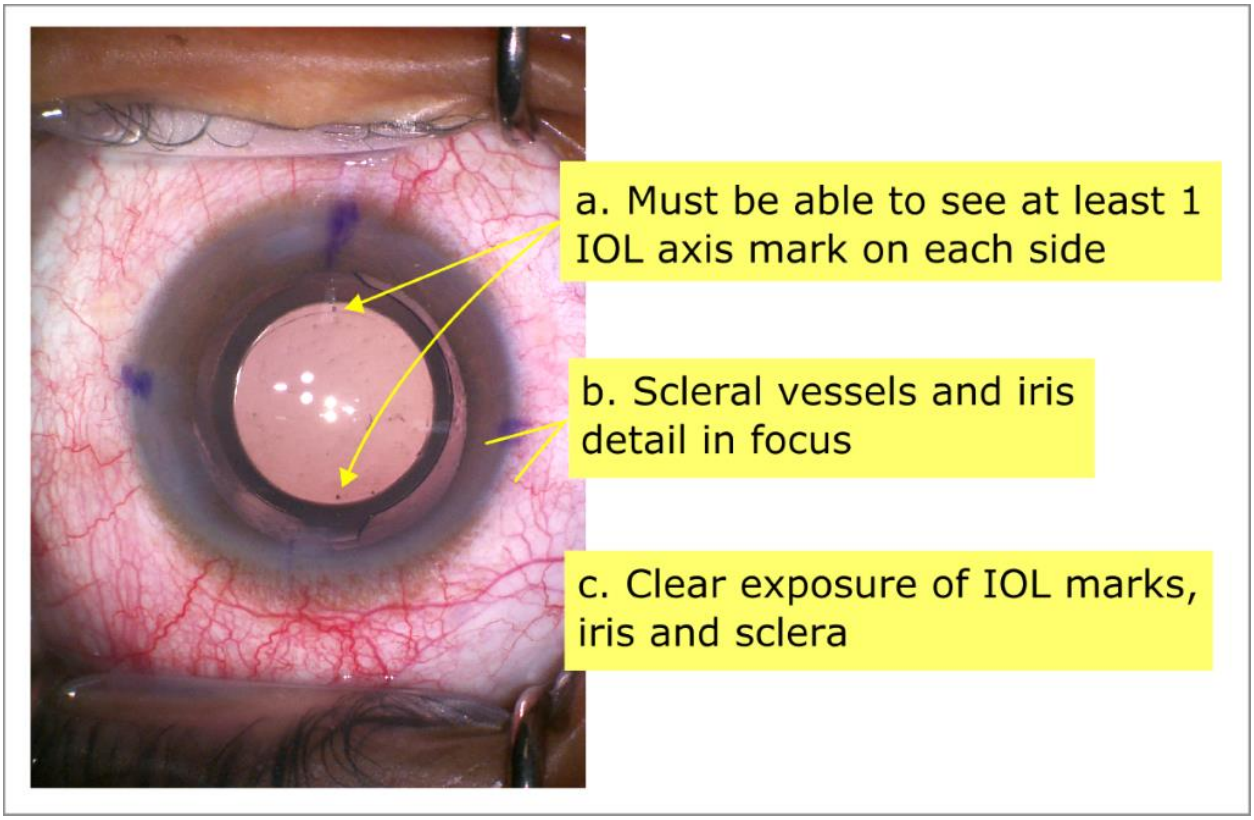
APPENDIX B: EQUIPMENT LIST

The following equipment will be supplied to an investigative site for the duration of the study provided that the site does not already have such equipment available for use. This equipment loan will be documented in the Clinical Study Agreement, which indicates that the equipment is to be returned to JJSV at the completion of the study.

- M&S Technologies CTS-1000 Smart System© Computerized Vision Testing System, including laptop computer, tablet, near chart overlays, and glare bracket ("M&S System")
- Digital slit-lamp camera
- Surgical microscope camera
- Slit lamp compatible with slit-lamp camera

APPENDIX C: INSTRUCTIONS FOR CAPTURING PHOTOS THROUGH THE SURGICAL MICROSCOPE

1) Take photos at the end of surgery when the IOL is in its final position.
2) Pupil should be dilated enough to see IOL dots on both sides of the lens. Make sure wound sealing / corneal ink marking do not obscure the IOL dots.
3) Eye should be centered in frame with sclera visible through 360°.
4) Eye should be looking directly towards camera.
5) Camera should be focused on iris and limbal features.
6) The IOL dots will be slightly posterior to (behind) the focal plane, i.e. they may be slightly out of focus.
7) Ensure you can see IOL axis alignment marks on both sides, magnification shows sclera on both sides, iris and scleral vessels are in focus.
8) Press 'FREEZE/FLASH' button, review image and save good quality images. Make sure to capture ***three*** good quality images per eye.



APPENDIX D: INSTRUCTIONS FOR USING M&S SYSTEM

Distance visual acuity testing will be performed using the ETDRS chart presented in the M&S System. The ETDRS is a LogMAR chart with proportionally spaced Sloan letters at 100% contrast for high contrast visual acuity. Each presentation is randomized and is consistent and repeatable. The system is calibrated for test distance to subject and pixels/inch so that optotypes precisely follow ANSI Z80.21-2010 and ISO 8596:2000 with regard to size, spacing between optotypes and spacing between lines.

Example of LogMAR 4.0 meter chart screen

The M&S System background screen luminance is automatically calibrated to 85 cd/m^2 (range of 80-110 cd/m^2 is acceptable) for photopic testing. Room lights should be off, and any other necessary lighting should be dim or dark (to levels lower than the illumination from the laptop screen) to maximize pupil size. No surface (including reflective surfaces) within the subject's field of vision should be brighter than the chart background in luminance. The room lighting and screen luminance will be verified each time the computer is turned on using the JJSV-provided, auto-adjusting, monitor-calibration system to ensure light levels are appropriate.

The M&S System will be set up to perform required visual tests in a specific order, with prompts on the screen to allow the technician to set up the subject for monocular or binocular testing, refraction adjustments as needed and uncorrected or best-corrected testing. Letters on all charts will appear randomly, with the technician controlling movement through charts based on subject responses.

As a subject completes a visual acuity line, the technician will select the total number of letters correctly read for that line on the handheld controller, press "Enter" and then confirm the number of letters correct at the next prompt. The M&S System will then advance to the next line of testing and the process will repeat. The system will end the test when the subject no longer has any correct responses. The number of letters correctly read will be displayed on the laptop screen, along with the LogMAR value and Snellen acuity. Record the total number of letters read. Once a test is completed, follow the prompts on the computer screen to start the next test.

Test results are stored in the M&S computer and a hard copy will be printed and validated as a back-up.

APPENDIX E: INSTRUCTIONS FOR DISTANCE VISUAL ACUITY TESTING

For distance visual acuities, the M&S System laptop should be placed at a test distance of 4.0 meters from the subject. A laptop setting may be used to reverse charts for rooms that require "folding" via a mirror to reach a distance of 4.0 meters. Whether standard or "folded", measure and record the test distance accurately. If the room set-up does not allow the computer to be placed at precisely 4.0 meters, the M&S System can be adjusted to account for the actual test distance used.

The M&S System will be set up to perform the required distance visual acuity tests in a specific order, with prompts on the screen to allow the technician to set up the subject for monocular or binocular testing, refraction adjustment as needed and uncorrected or best-corrected testing. A phoropter may be used for distance acuity and refraction testing.

Subjects should be reminded prior to testing that squinting or head-tilting is not allowed, as these can increase depth of focus by partially obstructing the pupil. The technician is to monitor the subject to prevent and ensure that the subject is not squinting or tilting his or her head forward or sideways to read letters during visual acuity testing. If either behavior is observed, the subject is to be reminded by the testing technician not to do so.

Distance visual acuity measurements are to be performed per the visit schedule in **Appendix A**. To test subjects monocularly, occlude the second eye in the phoropter or with an occluder if trial lenses are used.

Visual acuity measurements are based on the total number of correctly read letters. Subjects should be persuaded to read the smallest letters possible even if they must guess. Follow the testing process listed in **Appendix D** and refraction adjustments listed in **Appendix G**. At the end of the test, the number of letters correctly read will be displayed on the laptop screen, along with the LogMAR value and Snellen acuity. Record the total number of letters read in the EDC system.

APPENDIX F: MAXIMUM PLUS MANIFEST REFRACTION TECHNIQUE WITH CYLINDER REFINEMENT

Manifest refraction testing will be performed using the M&S System ETDRS chart, with the room lighting set lower than the chart lighting level.

NOTE: *Objective refraction by either retinoscopy or autorefraction can be used as a starting point for the Manifest Refraction. Always ensure that the endpoint of refraction is maximum plus (or minimum minus) power that yields best visual acuity.*

1) Occlude the fellow eye.

2) SPHERE: Starting with the objective refraction, refine the sphere to yield best visual acuity.

   NOTE: *Add plus power (or reduce minus) until subject demonstrates at least a 1-line loss from best visual acuity (fogging). Then step down to the most plus (or least minus) sphere power until visual acuity and clarity show no improvement.*

3) CYLINDER AXIS: Refine cylinder with a cross-cylinder and the objective cylinder refraction as the starting point. Refine axis first and power second, since the correct axis can be found with an incorrect power, but the correct power cannot be found with an incorrect axis.

   a. Direct the subject's attention to 1 line above (larger letters) the best visual acuity. With the trial cylinder (axis and power) in the phoropter, introduce cross-cylinder for axis refinement. When asking the subject which cross-cylinder axis position is better, "one or two?", remind the subject to look at different letters on the line and report preference based on the overall clarity of the letters.

   b. Refine the axis based on the subject's responses, using small steps (less than five degrees), until the subject reports no difference in the two choices.

   c. Cylinder axis may be further confirmed by bracketing: Slowly rotate the trial cylinder in one direction until the subject reports blurring and note the axis. Rotate the trial cylinder in the opposite direction past the presumed axis until the subject reports blurring, again noting the axis. The average of the two noted axes can be taken as the final astigmatism axis.

4) CYLINDER POWER: Set the cross cylinder to refine cylinder power and present choices to the subject, reminding the subject to look at different letters on the line and report preference based on overall clarity of the letters. Reduce or increase trial cylinder power accordingly.

   a. Maintain the spherical equivalent throughout cylinder power refinement by adjusting the sphere once for every two clicks of cylinder power change.

5) SPHERE CHECK: Introduce plus sphere with approximately 0.75 D to 1.00 D so the subject reports and demonstrates a reduction in visual acuity. Then reduce sphere power in 0.25 D steps until visual acuity and clarity show no improvement.

APPENDIX G: REFRACTION ADJUSTMENTS FOR VISUAL ACUITY TESTING

Postoperative study manifest refractions are to be performed using the M&S System at a distance of 4.0 meters. 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 differences between the test distance and refraction distance. The adjustment required (in diopters) is 1/test distance (in meters). To adjust a 4.0-meter refraction to optical infinity, -0.25 D is to be added to the sphere of the refraction to obtain a true distance (infinity) correction. On the other hand, to adjust optical infinity to a 4.0-meter test distance, +0.25 D is to be given. In the case where the refraction distance (4.0 meters) and the vision test distance (4.0 meters) are the same, no adjustment is necessary. The following table lists the refraction adjustments required for the various vision tests that are required for this study:

Refraction Adjustments for Visual Acuity Testing

Vision Test	Test Distance	Adjustment for Test Distance
Uncorrected distance visual acuity (UCDVA)	4.0 m	+0.25 D adjustment only
Best-corrected distance visual acuity (BCDVA)	4.0 m	No adjustment; ETDRS Rx only (phoropter)

APPENDIX H: SLIT LAMP EXAM RATINGS

A. Ratings of Aqueous Cells and Flare: For consistency across study sites, the SUN (Standardization of Uveitis Nomenclature) Working Group Grading Scheme a is to be used for grading of anterior chamber cells and flare.

CELLS

Grade	**Cells in Field** (Field is a 1x1 mm slit beam)
0	<1
0.5+	1 - 5
1+	6 - 15
2+	16 - 25
3+	26 - 50
4+	>50

FLARE

Grade	Description
0	None
1+	Faint
2+	Moderate (iris and lens details clear)
3+	Marked (iris and lens details hazy)
4+	Intense (fibrin or plastic aqueous)

[a] Standardization of uveitis nomenclature for reporting clinical data. Results of The First International Workshop; The standardization of uveitis nomenclature (SUN) working group. Am J Ophthalmol 2005;140:509-516.

B. Ratings of Corneal Edema: Corneal edema should be classified according to the haziness of the epithelium, the number of microcysts observed, and the clouding of the stroma.

Amount	Grade	Description
None	**0**	Normal transparency: a. No epithelial or sub-epithelial haziness b. No microcysts c. No stromal cloudiness
Trace	**+1**	a. Barely discernible localized epithelial or sub-epithelial haziness, and/or b. 1 to 20 microcysts, and/or c. Barely discernible localized stromal cloudiness
Mild	**+2**	a. Faint but definite localized or generalized epithelial, sub-epithelial or stromal haziness/cloudiness, and/or b. 21-50 microcysts
Moderate	**+3**	a. Significant localized or generalized epithelial, sub-epithelial or stromal haziness/cloudiness and/or b. 51-100 microcysts
Severe	**+4**	a. Definite widespread epithelial or stromal cloudiness, giving dull glass appearance to cornea or numerous coalescent bullae (please note the number and location of bullae), and/or b. >100 microcysts or bullae, and/or c. Numerous striae (please note the number and location of striae or folds)

C. Posterior Capsule Striae Grading Scale: The following five-point grading scale is to be used for rating striae in the posterior capsule.

Amount	Grade	Description
None	0	None
Trace	+1	One detectable, barely noticeable striae
Mild	+2	One or two prominent striae
Moderate	+3	Three or more prominent striae, but visibility of retina is not impacted
Severe	+4	Three or more prominent striae affecting visualization of retina

D. Posterior Capsule Opacification Grading Scale: Below is the five-point grading scale to be used for PCO determination.

Amount	Grade	Description
None	0	Normal posterior capsule with no area of opacity. Red reflex bright.
Trace	+1	Some loss of transparency involving the posterior capsule. Red reflex fairly bright
Mild	+2	Mild loss of transparency with cloudiness extending through most of the posterior capsule. There may be a few Elschnig's pearls in the posterior capsule. Red reflex mildly diminished.
Moderate	+3	Moderate loss of transparency with difficulty visualizing the retina. There may be multiple Elschnig's pearls in the posterior capsule. Red reflex markedly diminished.
Severe	+4	Posterior capsule very opaque with inability to view the retina. The posterior capsule may have confluent Elschnig's pearls and fibrous scarring. Red reflex barely visible.

E. IOL Glistenings: Use the following scale to grade IOL glistenings, using a slit beam 2.0 mm wide and 10.0 mm long.

Amount	Grade	Description
None	0	No glistenings visible
Rare	+0.5	<10 glistenings visible
Trace	+1	10-19 glistenings visible
Mild	+2	20-29 glistenings visible
Moderate	+3	30-39 glistenings visible
Severe	+4	≥40 glistenings visible

APPENDIX I: SLIT LAMP RETROILLUMINATION PHOTOGRAPHS

Slit lamp photographs should be captured at each postoperative visit. Photographs will be analyzed to determine the IOL rotation from baseline orientation (operative photograph). The analysis procedure requires alignment of postoperative images based on landmarks identified on the limbus, iris and/or sclera. All photographs must meet the following guidelines in order to be analyzable. To ensure accuracy, the following procedures detail the process for taking retroillumination photographs in a manner that captures both the ***iris/sclera and the toric IOL axis markers***.

1. The goal is to obtain images with enough magnification (usually **10X is optimal**) and sufficient illumination to show sclera beyond the iris. Please take all images at the same slit lamp magnification (i.e., don't alternate between 10X and 16X magnification).
2. Pupils should be adequately dilated such that the IOL fiducial marks are visible on both sides. It is preferable to have more than one IOL axis mark visible on each side, however, at least one axis mark visible on each side of the IOL should be visible.
3. To help identify individual subject photographs, prior to the photographic session for each eye, take a photograph of the study subject photo ID information. Identification cards with this information will be provided for each study subject.
4. Use a short, intense slit beam to obtain a sufficiently bright red reflex (this is needed to visualize the IOL fiducial marks). Position the beam in such a way that the specular beam reflection does not obscure the IOL axis marks (ideally the beam should be entirely within the optic zone of the IOL). Use a second light source (such as an ophthalmoscope or LED lamp) for additional illumination to clearly visualize the iris and sclera.
5. Focus the image such that the iris and sclera are clear. The plane of best focus should be aligned with the limbal blood vessels and iris.

   NOTE: *Make sure large areas of limbus are not obscured by eyelids or from the shadow of the slit lamp beam arm*
6. The IOL axis marks should be posterior to the plane of best focus, and reasonably clear to allow for subsequent analysis.

   NOTE: *Some cameras allow you to focus the image before taking the picture by holding the shutter button slightly. If your camera allows this, first try focusing the image and then moving the slit lamp closer to/further away from the subject until the iris is in focus.*
7. If you obtain blurry images, first try to increase the amount of light on the subject's eye using a gooseneck microscope illuminator, ophthalmoscope or other secondary light source.
8. There may be some time delay between pressing the camera button and actual image capture; please ask subject to hold steady 1-2 seconds after camera click to avoid motion blur.

NOTE: *Do not use any built-in camera flash as this will not illuminate the iris and sclera and may increase the chances of obtaining a blurry image or shadows.*

9. Always capture images with your camera's maximum resolution and image quality settings.
10. Capture multiple photos at each session. Images may appear good on the camera screen but may be of inadequate quality once they are transferred to a larger screen.

    NOTE: *Three good quality photos per eye for every postoperative visit is required*

11. Store the photographs electronically on your computer and on the USB drive in the native format for your camera (e.g., jpeg, tiff or bmp – tiff or raw image format preferred). To establish the order and session in which they were taken, each photo file should be renamed using the subject's identification number, eye, visit and picture number, for example:

    31001-OD-1D-1.jpg, 31001-OD-1D-2.jpg, 31001-OD-1W-2.jpg etc.

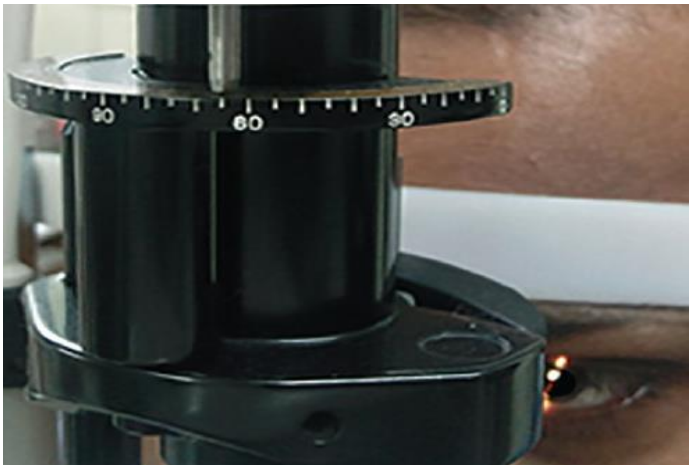
Figure 1: Examples of images with: A) Inadequate focus and exposure (poor quality) B) Adequate focus and exposure of the same eye (good quality)

A **B**

Figure 2: Examples of good quality images with adequate iris/scleral detail.

APPENDIX J: INSTRUCTIONS FOR LENS AXIS MEASUREMENT WITH A SLIT LAMP

I) After dilating the pupil, check that the subject's head plane is horizontal.
- This step will be done for every patient measurement.
- Have subject place their chin on the chin rest and forehead against the forehead strap.
- Change slit beam to thin, long and horizontal.
- Align slit beam with lower edge of the limbus of the right eye.
- Without adjusting the slit lamp height and subject continuing fixation on the same spot, move to the left eye and check if the slit beam is aligned with the lower edge of the left eye limbus.
- If the left eye limbus is not aligned with right eye limbus, then adjust subject head until reasonable alignment is achieved.
- Align the slit lamp beam to the axis of the toric IOL marks.
- Record the IOL axis orientation to the nearest degree from the slit lamp scale.



APPENDIX K: PATIENT SATISFACTION QUESTIONNAIRE (PSQ)

Instructions

- The following questions are about your far vision (more than 5 feet away) with both eyes.
- Please answer the questions based on your experience with your far vision since your last visit to the clinic.
- Please read each question carefully and answer as honestly as you can without the help of anyone.
- For each question, please mark an ☒ in the one box that is your answer.

1) How often do you feel the need to wear eyeglasses or contact lenses to improve your far vision?

None of the time	☐
A little of the time	☐
Some of the time	☐
Most of the time	☐
All of the time	☐

2) How satisfied or dissatisfied are you with your far vision WITHOUT eyeglasses or contact lenses?

Very satisfied	☐
Satisfied	☐
Undecided	☐
Dissatisfied	☐
Very dissatisfied	☐

APPENDIX L: INVESTIGATOR SATISFACTION QUESTIONNAIRE (ISQ)

Instructions

- This questionnaire is self-administered and should be completed by the investigator at the **1- week visit** and the **3-month visit** for **each eye** separately**.**
- The purpose of this questionnaire is to collect your feedback on the clinical outcomes achieved in each eye implanted with the TECNIS® Toric II IOL (study lens).
- For each question, please mark an ☒ in the one box that is your answer.

1) Please rate your overall level of satisfaction with the clinical outcomes achieved in the implanted eye.

5- Very satisfied	☐
4- Satisfied	☐
3- Undecided	☐
2- Dissatisfied	☐
1- Very dissatisfied	☐

If you marked “1- Very dissatisfied” or “2- Dissatisfied”, please specify reason.

_____

2) Please rate your level of satisfaction with the rotational stability of the study lens in the implanted eye.

5- Very satisfied	☐
4- Satisfied	☐
3- Undecided	☐
2- Dissatisfied	☐
1- Very dissatisfied	☐

If you marked “1- Very dissatisfied” or “2- Dissatisfied”, please specify reason.

_____

3) Please rate your level of satisfaction with the achieved uncorrected distance visual acuity in the implanted eye.

5- Very satisfied	☐
4- Satisfied	☐
3- Undecided	☐
2- Dissatisfied	☐
1- Very dissatisfied	☐

If you marked “1- Very dissatisfied” or “2- Dissatisfied”, please specify reason.

_____

APPENDIX M: ADVERSE EVENT AND COMPLAINT REPORTING INSTRUCTIONS

All adverse events and complaints related to using JJSV products must be reported to JJSV.

ALL ADVERSE EVENTS AND COMPLAINTS:

For events that are not considered serious or related to the study device:

1. Record the event and/or complaint on the case report form that corresponds to the visit during which awareness of the event occurred. Additionally, a complaint may be reported via a telephone call to JJSV.
2. Send the completed case report form to JJSV in a timely manner

SERIOUS ADVERSE EVENTS OR DEVICE DEFICIENCIES THAT MAY HAVE LED TO A SERIOUS EVENT

In the event of a serious event (i.e., life- or sight-threatening incident) whether or not related to the device, or a device deficiency that may have led to a serious event, the investigator shall:

1. Notify JJSV immediately (no more than 48 hours after learning of the event) as follows:
   a. Contact the following JJSV personnel by phone and/or email:

   b. Complete a Detailed Adverse Event Form and submit to JJSV

NON-SERIOUS, DEVICE-RELATED EVENTS:

For events that are not considered serious but are believed related to the study device (ADEs):

1. Complete a Detailed Adverse Event Form
2. Ensure the data are submitted to JJSV within a timely manner.

APPENDIX N: AMERICAN ACADEMY OF OPHTHALMOLOGY TASK FORCE CONSENSUS STATEMENT ON ADVERSE EVENTS FOR INTRAOCULAR LENSES

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CA); Alcon Laboratories, Inc. (Fort Worth, TX); Carl Zeiss, Inc. (Oberkochen, Germany); Oculus, Inc. (Wetzlar, Germany); Consultant and Equity Owner — AcuFocus, Inc. (Irvine, CA); ArcScan (Morrison, CO); Elenza (Roanoke, VA); Visiometrics (Barcelona, Spain).
A.G.: Consultant — Abbott Medical Optics, LensAR (Orlando, FL); Medicem (Cheshire, UK); Refocus Group (Dallas, TX); Tracey Technologies (Houston, TX); Vista Ocular (North Canton, OH); Consultant and Equity Owner — Encore Vision (Fort Worth, TX); LensGen (Irvine, CA); PowerVision (Belmont, CA).
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The American Academy of Ophthalmology Task Force for Developing Novel End Points for Premium Intraocular Lenses members include: Jack T. Holladay, MD, MSEE, Chair; Adrian Glasser, PhD, Co-Chair; Scott MacRae, MD, Co-Chair; Samuel Masket, MD; Walter Stark, MD; and the following U.S. Food and Drug Administration staff members: Malvina Eydelman, MD; Don Calogero, MS; Gene Hilmantel, OD; Eva Rorer, MD; Tieuvi Nguyen, PhD; and Michelle E. Tarver, MD, PhD.

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Special Report: The American Academy of Ophthalmology Task Force Consensus Statement on Adverse Events with Intraocular Lenses

In 1978, the US Food and Drug Administration approved the first investigational device exemption studies of intraocular lenses (IOLs). Outcomes were initially published in 1983 on pooled, publicly available data from IOL premarket approval studies that were used to support marketing approvals.[1] After publication, this "historical control" information was used as a benchmark for the assessment of the safety and effectiveness of new IOLs. These safety and effectiveness endpoints have been referred to as the "Food and Drug Administration Grid" and "Safety and Performance Endpoints" (SPEs) for IOLs. Although the SPEs were updated on the basis of additional premarket approvals in 1998, they have not been updated to reflect the development of "premium IOLs," including toric, multifocal, accommodative, and phakic IOLs.[2] Premium IOLs may present additional adverse events (AEs) to those already established for monofocal IOLs. Further, most of the AEs in the "Grid" do not have standard definitions, and the definitions used could have changed over time with advances in our understanding of ocular pathology. Considering untoward events associated with premium IOL implantation and that would be appropriate as safety endpoints in clinical studies of new premium IOLs, the American Academy of Ophthalmology's Task Force has developed consensus definitions for premium IOL SPE AEs as shown in Table 1. The AE of secondary IOL intervention has been subcategorized by the type of intervention and IOL exchange, removal, and reposition. These indications are listed and defined in Table 2 and Appendix 1.

At this time, acceptable rates for premium IOL SPE AEs have not been established. However, the definitions proposed may be used during clinical studies of new IOLs going forward to allow for the determination of appropriate SPE rates that can be applied to the assessment of new premium IOLs in the future.

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A.G.: Consultant — Abbott Medical Optics, LensAR (Orlando, FL); Medicem (Cheshire, UK); Refocus Group (Dallas, TX); Tracey Technologies (Houston, TX); Vista Ocular (North Canton, OH); Consultant and Equity Owner — Encore Vision (Fort Worth, TX); LensGen (Irvine, CA); PowerVision (Belmont, CA).
The mention of commercial products, their sources, or their use in connection with material reported herein is not to be construed as

Table 1. Postoperative Adverse Event Definitions for Intraocular Lenses

Adverse Event	Definition
Chronic anterior uveitis	Persistent anterior segment inflammation characterized by grade 1+ cell or greater using SUN criteria[3]
Clinically significant cystoid macular edema	Macular edema diagnosed by clinical examination and adjunct testing (e.g., OCT, FA) resulting in BCDVA of ≤20/40 at ≥1 mo
Corneal edema	Corneal swelling (stromal or epithelial) resulting in BCDVA of ≤20/40 at ≥1 mo
Endophthalmitis	Intraocular inflammation requiring diagnostic vitreous tap and intraocular antibiotics
Mechanical pupillary block	Shallowing of anterior chamber due to obstruction of aqueous humor flow from the posterior to anterior chamber through the pupil by the crystalline lens, vitreous face, or implanted device
Increased IOP	Elevation of IOP by ≥10 mmHg above baseline to a minimum of 25 mmHg
Rhegmatogenous RD	Partial or complete RD associated with retinal tear
Toxic anterior segment syndrome	Acute, noninfectious inflammation of the anterior segment that starts within 24 hrs after surgery, usually resulting in hypopyon and commonly presenting with corneal edema, that improves with steroid treatment
Secondary IOL intervention	
Exchange	The investigational device is replaced with the same lens model.
Removal	The investigational device is removed and replaced with a noninvestigational lens or no lens is implanted.
Reposition	The existing IOL is surgically moved to another location or rotated.

BCDVA = best-corrected distance visual acuity; FA = fluorescein angiography; IOL = intraocular lens; IOP = intraocular pressure; OCT = optical coherence tomography; RD = retinal detachment; SUN = Standardization of Uveitis Nomenclature.

Table 2. Definitions of Indications for Device Exchange, Removal, or Reposition

Indication	Definition
Capsular block syndrome	Hyper-distention of the lens capsular bag due to the IOL optic blocking egress of fluid through the anterior capsulotomy typically inducing a myopic refractive error
Cataract	Any opacification of the crystalline lens with or without reduced visual acuity
Chronic anterior uveitis	Persistent anterior segment inflammation characterized by grade ≥1+ cell using SUN criteria[3]
Endothelial cell loss	Chronic endothelial cell loss at a rate greater than that due to normal aging
Incorrect IOL power	Postoperative refractive error different from predicted and not due to a calculation or other user error
Iris pigment epithelium loss*	New or worsening iris transillumination defects or increase in pigmented cells in the anterior chamber noted after the 1-wk visit when assessed before instillation of any dilating drops
Lens optic abnormality	Unanticipated visual outcome (e.g., acuity, contrast sensitivity, symptoms) associated with opacification, vacuoles, microvacuoles, or subsurface nanoglistenings and not due to other causes
Malpositioned IOL	Decentration, tilt, or rotation of IOL requiring reoperation May include changes induced by Nd:YAG laser anterior or posterior capsulotomy
Early	If noted before 120 days postoperatively
Late	If noted at ≥120 days postoperatively
Damaged IOL	Crack of lens optic, breakage, or deformity of haptic, or other damage to the IOL May include changes induced by Nd:YAG laser anterior or posterior capsulotomy
Pupil ovalization	Progressive deformation of the pupil with elongation of the pupil in the meridian of the long axis of the IOL Documentation to be made under photopic conditions†
Pain	Graded as ≥4 on the standardized pain numeric rating scale of current pain intensity from 0 (no pain) to 10 (worst possible pain)
Peripheral anterior synechiae	Progressive closure of the anterior chamber angle due to propagation of anterior synechiae in the absence of obvious anterior uveitis
Patient-reported undesirable optical phenomena	Dysphotopsia (positive or negative or both), monocular diplopia, intolerable glare, halos, or other visual symptoms, not due to 1 of the indications listed

IOL = intraocular lens; Nd:YAG = neodymium-doped yttrium aluminium garnet; SUN = Standardization of Uveitis Nomenclature.
*If there is a transillumination defect preoperatively, then a photograph should be taken, and then at each subsequent visit, a photograph should be taken and compared with the preoperative photograph via a standardized photographic method.
†A consensus statement regarding a proposed methodology for standardizing assessment of pupil ovalization is available in Appendix 1.

The American Academy of Ophthalmology Task Force for Developing Novel Endpoints for Premium Intraocular Lenses Members include Jack T. Holladay, MD, MSEE, Chair; Adrian Glasser, PhD, Scott MacRae, MD, Samuel Masket, MD, Walter Stark, MD, and the following Food and Drug Administration staff members: Malvina Eydelman, MD, Don Calogero, MS, Gene Hilmantel, OD, Eva Rorer, MD, Tieuvi Nguyen, PhD, and Michelle E. Tarver, MD, PhD.

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Appendix 1. Oval Pupil Measurement Background and Standard Operating Procedure

Background

The only study of the oval pupil available was by Isotani et al[3] in 1995, who studied the ratio of the major to minor diameter in healthy subjects by using infrared photography. The subjects were dark adapted, so these are scotopic pupil measurements.

Standard Operating Procedure

If the clinician observes an oval or irregularly shaped pupil (dyscoria) at any visit after surgery, photographs should be taken at that visit and each subsequent visit to determine if the ovalization is progressive. The major and minor diameters of the pupil, which may not be orthogonal, are measured on the photograph, which must be taken in photopic conditions (>200 foot-candles or 2153 lux) so the pupil is maximally constricted. The pupil constriction provides the setting for pupil ovalization. For the measurement, the diameters must pass through the center of the least-squares, best-fit ellipse or centroid of the pupil perimeter. The ratio of the major to minor diameter is then calculated and reported. The photograph may be taken with any camera, including but not limited to slit-lamp cameras, topographers, and Scheimpflug devices, but the eye image must be captured under photopic conditions as specified.

References

1. Stark WJ, Worthen DM, Holladay JT, et al. The FDA report on intraocular lenses. *Ophthalmology*. 1983;90:311-317.
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3. Isotani H, Fukumoto Y, Kitaoka H, et al. Oval pupil in patients with diabetes mellitus: examination by measurement of the dark-adapted pupillary area and pupillary light reflex. *Diabetes Res Clin Pract*. 1995;29:43-48.

Special Report: American Academy of Ophthalmology Task Force Summary Statement for Measurement of Tilt, Decentration, and Chord Length

Currently, the measurement of tilt and decentration is not commercially available in an instrument or method that has been validated clinically. In lieu of a validated, commercially available instrument or method, the current statuses of 3 different approaches that have been used to measure tilt and decentration are described to help provide the basis for the future development of an instrument or technique.

Definitions

- Decentration of an intraocular lens (IOL) is the lateral horizontal and vertical displacement of an IOL relative to the visual axis as seen by the clinician through the cornea (subject-fixated coaxially sighted corneal light reflex, as described by Chang and Waring[1]).
- Tilt of an IOL is the horizontal and vertical angle from perpendicular of an IOL relative to the visual axis (subject-fixated coaxially sighted corneal light reflex, as described by Chang and Waring[1]).
- Chord length μ is the displacement (distance) between the subject-fixated coaxially sighted corneal light reflex and pupil center.[1] For some diffractive IOLs, the midpoint between pupil center and visual axis may be optimal.

Tilt, Decentration, and Chord Length μ

The goal is to measure tilt, apparent decentration through the cornea, and chord length μ on all subjects with a premium IOL.

Table 1. Ratio of IOL Toricity to Corneal Astigmatism

	Effective Lens Position					
A-constant—>	116.346	117.203	118.059	118.916	119.773	120.630
Surgeon Factor—>	0.287	0.772	1.257	1.742	2.227	2.713
ELP—>	4.000	4.500	5.000	5.500	6.000	6.500
IOL Power	Resulting Ratio of IOL Toricity to 2 D of Corneal Astigmatism					
10	1.359	1.424	1.494	1.571	1.654	1.745
22	1.277	1.330	1.387	1.450	1.519	1.595
34	1.198	1.239	1.284	1.334	1.390	1.452
46	1.121	1.151	1.185	1.223	1.267	1.316

D = diopter; ELP = effective lens position; IOL = intraocular lens.