Study Protocol

A PROSPECTIVE STUDY TO EVALUATE THE SAFETY AND EFFECTIVENESS OF WAVEFRONT-GUIDED PRK CORRECTION OF MYOPIC REFRACTIVE ERRORS WITH THE IDESIGN ADVANCED WAVESCAN STUDIOSYSTEM AND THE STAR S4 IR EXCIMER LASER SYSTEM

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PROPRIETARY
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A PROSPECTIVE STUDY TO EVALUATE THE SAFETY AND EFFECTIVENESS OF WAVEFRONT-GUIDED PRK CORRECTION OF MYOPIC REFRACTIVE ERRORS WITH THE IDESIGN ADVANCED WAVESCAN STUDIO SYSTEM AND THE STAR S4 IR EXCIMER LASER SYSTEM

PROTOCOL NUMBER: STAR-115-MIPS

SPONSOR: Abbott Medical Optics Inc.
510 Cottonwood Drive
Milpitas, CA 95035

Investigator Agreement

As an Investigator, I agree to:

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

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

Investigator Printed Name	Signature	Date
Subinvestigator Printed Name	Signature	Date

Acknowledged By:

Signature of Sponsor's Representative	Date

Printed Name and Title

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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	Personnel and Facilities	iv	Updated contact information	Changes reflect a change in personnel and contact information
	1.0, 3.0, 6.1, 6.2, 8.0, 8.2, 10.3, 10.5, 11.3, 19, 20.5, Appendices C, E, H, L	1, 4, 9, 10, 11, 34, 35, 44, 46, 49, 54	Formatting, minor clarifications and typographical errors	
	1.0, 4.0, 6.2, 8.0, 10.6, 20.6, Appendices A, B, C, G, N	2, 4, 8, 9, 18, 19, 20, 22, 37, 39, 40, 41, 42, 48, 56	Contrast sensitivity sub-study added to protocol	Sub-study added based on FDA feedback
	1.0, 3.0	1, 4, 7	Rates of serious adverse events changed to specify only those that are device related	Adverse event reporting SOP has been changed to clarify serious AE that are device related.
	1.0, 8.2	4, 13	Exclusion criteria #5 updated to also specifically exclude subjects with ocular hypertension (without glaucomatous changes)	Clarification
	1.0, 6.2, 10.1, 10.3, 10.9, 20.2, 20.3, Appendices A, C, H, I,	16-21, 23, 25, 27, 28, 37, 40, 42, 43, 51, 53, 55	Updates to evaluations, procedures, order of exams and statistical updates to the study design including: OSDI, NEI-RQL-42, Schirmer I Tear Test, satisfaction questionnaires, keratometry and video recording. Clarification of PRVSQ version name.	Additional procedures added to the protocol to respond to FDA feedback and to improve the overall study design.
	2.0	7	Updated background to include that study G120151 received PMA approval	The section now reflects the current status of ongoing clinical studies.
	5.0, 6.1, 20.1, 20.2	8, 9, 35	NEI removed as a secondary endpoint.	No longer seeking claims based on the NEI
	8.0	12	Specify that the protocol will enroll only those subjects eligible for military medical benefits.	Added based on FDA feedback on study population
	1.0,8.2	4, 13	Added clarification to Exclusion criteria #5 that subjects will be excluded for severe dry eye syndrome or symptoms.	Added based on updated iDesign labeling.

Version	Section(s)	Page(s)	Description of Change(s)	Rationale for Change(s)
2.0 cont'd.	11.1	25	Removed the word "Serious" from the title of Study Specific Adverse Events to Clarify that events listed are not automatically considered serious adverse events. Updated criteria for determining adverse events of halo, glare and dry eye.	Criteria were added based on FDA feedback and guidance documents. Serious removed as anticipated events are not automatically considered serious.
	11.1	26	Specified what determines "Foreign Body Sensation", "Pain" and "Ghost/double images" to be recorded as study specific complications	Clarification
	20.2	36	Added an alpha level to poolability analysis	Clarification
3.0	20.1	35	Updated the significant number of missing data when ITT analyses are to be performed	Corrected to match the statistical analysis plan
	6.2, 10.3, 10.6 and 20.3 Appendices C, N	9, 18, 22, 37, 42, 56-57	Updated spatial frequencies for mesopic contrast sensitivity testing	Updated based on FDA feedback on contrast sensitivity

1. SYNOPSIS

PROTOCOL: A prospective study to evaluate the safety and effectiveness of wavefront-guided PRK correction of myopic refractive errors with the iDesign Advanced WaveScan Studio System and STAR S4 IR Excimer Laser System.

Protocol Number: STAR-115-MIPS

STUDY TREATMENTS: Investigational Product: iDesign Advanced WaveScan Studio System (software version 1.3, international configuration) and STAR S4 IR Excimer Laser System (Abbott Medical Optics, CA)

Control Product: None

STUDY OBJECTIVE: The purpose of this clinical study is to evaluate the safety and effectiveness of wavefront-guided Photorefractive Keratectomy, commonly referred to as PRK, performed with the iDesign Advanced WaveScan Studio System and STAR S4 IR Excimer Laser System (Abbott Medical Optics, CA) for the correction of myopic refractive errors with and without astigmatism.

CLINICAL HYPOTHESIS: The results of this trial will demonstrate that wavefront-guided PRK correction with the iDesign Advanced WaveScan Studio System and STAR S4 IR Excimer Laser System is safe and effective for the treatment of myopia with and without astigmatism by meeting the primary safety and effectiveness study endpoints including specific criteria for UCVA outcomes, predictability of MRSE, refractive stability, maintenance of BSCVA, induced refractive cylinder, corneal haze, and rates of serious, device-related adverse events.

OVERALL STUDY DESIGN:

Structure: Prospective, multicenter, bilaterally-treated, open-label, non-randomized clinical trial.

Number of sites: Up to 7 sites in USA

Duration: 12 months

Administration: Surgeons will perform wavefront-guided PRK for the treatment of myopic refractive errors based upon measurements obtained with the iDesign System using the STAR S4 IR laser.

Visit Schedule: There will be 9 scheduled study visits: preoperative, operative, 1 day, 1 week, and 1, 3, 6, 9 and 12 months.

STUDY POPULATION CHARACTERISTICS:

Condition: Stable myopic refractive error, with or without astigmatism

Number of Subjects: Up to 334 subjects will be enrolled to achieve a minimum of 334 treated eyes (in approximately 167 bilaterally treated subjects), resulting in at least 300 evaluable eyes at the point of refractive stability. Subjects will be treated bilaterally.

Each site should treat a minimum of 20 eyes, and no site may treat more than 25% of eyes.

A distance-corrected contrast sensitivity substudy will also be conducted with at least 65 eyes from a single site.

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

1. Signed informed consent and HIPAA authorization
2. At least 18 years of age at enrollment (date informed consent signed)
3. The refractive error, based on the iDesign displayed refraction selected for treatment ("4.0 Rx calc" at 12.5 mm), must be myopia with or without astigmatism with sphere up to -8.00 D, and cylinder between 0.00 D and -4.00 D with a maximum spherical equivalent (SE) of -10.00 D.
4. Anticipated residual stromal bed thickness of at least 250 microns as calculated by the iDesign system
5. Distance Best Spectacle Corrected Visual Acuity (BSCVA) of 20/20 or better
6. BSCVA ≥2 lines (≥10 letters) better than distance Uncorrected Visual Acuity (UCVA)
7. Less than or equal to 0.75 D difference between cycloplegic and manifest refraction sphere.
8. A stable refractive error (based on a previous exam, medical records, lensometry, or prescription at least 12 months prior to the preoperative manifest refraction), as defined by a change of ≤1.00 D in MRSE.
9. Any subject eye with a history of contact lens wear within the last 4 weeks must demonstrate refractive stability according to the following:
    - Rigid contact lenses (toric or spherical) must be removed for at least 4 weeks and soft contact lenses (toric or spherical) for at least 2 weeks prior to the first refraction used to establish stability.
    - Two consecutive manifest refractions and keratometry readings must be conducted at least 7 days apart.
    - Refractive stability is defined as a change of not more than 0.50 D in manifest refractive sphere and cylinder as well as keratometry meridian (either axis) between measurements.

- If the subject/eye meets the refractive stability criteria, contact lens wear is not permitted prior to surgery

10. Agreement between manifest refraction (adjusted for optical infinity) and iDesign System refraction chosen for treatment, as follows:
    - Spherical Equivalent: Magnitude of the difference is less than 0.625 D.
    - Cylinder: Magnitude of the difference is less than or equal to 0.5 D.
    - Cylinder Axis Tolerance: If either the manifest cylinder entered into the iDesign System or the iDesign cylinder selected for treatment is less than 0.5 D, there is no requirement for axis tolerance. When both cylinders have a magnitude of at least 0.5 D, the axis tolerance as determined by the iDesign system is linearly reduced from 15° (0.5 D) to 7.5° (7.0 D) based on the average magnitude of both cylinders. Note: If the axis tolerance is not in the calculated range, the iDesign system will produce a warning and this exam may not be used for treatment planning.
11. Willing and capable of complying with follow-up examinations for the duration of the study.

Exclusion Criteria (all criteria apply to each eye):

1. Women who are pregnant, breast-feeding, or intend to become pregnant, or not using an adequate method of birth control [examples are any form of barrier contraception (such as condom or diaphragm with contraceptive cream/jelly), birth control pills, hormonal implant, IUD, abstinence or surgical sterilization (tubal ligation, hysterectomy or vasectomy)]. Note: Women who were pregnant or nursing may not be enrolled until 6 months after either delivery or have stopped nursing and there is documented refractive stability.
2. Concurrent use of systemic (including inhaled) medications that may impair healing, including but not limited to: antimetabolites, isotretinoin (Accutane®) within 6 months of treatment, and amiodarone hydrochloride (Cordarone®) within 12 months of treatment.

   NOTE: The use of inhaled or systemic corticosteroids, whether chronic or acute, is deemed to adversely affect healing and subjects using such medications are specifically excluded from eligibility.
3. History of any of the following medical conditions, or any other condition that could affect wound healing: collagen vascular disease, autoimmune disease, immunodeficiency diseases, ocular herpes zoster or herpes simplex, endocrine disorders (including, but not limited to unstable thyroid disorders and diabetes), lupus, and rheumatoid arthritis.

   NOTE: The presence of diabetes (either type 1 or 2), regardless of disease duration, severity, or control, will specifically exclude subjects from eligibility.
4. Subjects with a cardiac pacemaker, implanted defibrillator or other implanted electronic device.
5. History of prior intraocular or corneal surgery (including cataract extraction), active ophthalmic disease or abnormality (including, but not limited to, symptomatic

blepharitis, recurrent corneal erosion, severe dry eye syndrome or symptoms, neovascularization > 1 mm from limbus), retinal detachment/repair, clinically significant lens opacity, clinical evidence of trauma, corneal opacity within the central 9 mm and visible on topography, at risk for developing strabismus, or with evidence of glaucoma or propensity for narrow angle glaucoma.

NOTE: Subjects with ocular hypertension (without glaucomatous changes) or open angle glaucoma, regardless of medication regimen or control, or an IOP greater than 21 mmHg at screening, are specifically excluded from eligibility.

6. Evidence of keratoconus, corneal dystrophy or irregularity, or abnormal topography.
7. Known sensitivity or inappropriate responsiveness to any of the medications used in this study.
8. If either eye does not meet all inclusion criteria
9. Desire to have monovision.
10. Participation in any other clinical study, with the exception of the fellow eye in this study.

EVALUATION CRITERIA:

The purpose of this clinical study is to evaluate the safety and effectiveness of the iDesign Advanced WaveScan Studio System and STAR S4 IR Excimer Laser System (Abbott Medical Optics, CA). The primary safety endpoints include the percentages of eyes with losses of BSCVA, induced astigmatism and serious adverse events. The primary efficacy endpoints include percent of eyes achieving refractive stability, percent of eyes with UCVA of 20/40 or better, and the predictability of MRSE outcomes. Other endpoints include contrast sensitivity, binocular UCVA, manifest cylinder, keratometry, iDesign measurements, intraocular pressure, anterior segment evaluation, non-directed ocular visual symptoms, patient reported outcomes (PRO) measures (OSDI, PRVSQ for PRK/LASIK, NEI-RQL-42, exploratory Satisfaction) and Schirmer I Tear Test (with anesthetic).

DATA ANALYSIS:

All endpoints will be evaluated at the refractive stability time point. The safety population will be the primary analysis population for all endpoints and includes all eyes that receive study treatment. However, if there are greater than 10% of eyes with missing study exams at the stability time point, an intent-to-treat (ITT) population will be used as the primary analysis population for the primary effectiveness endpoints.

STUDY VISITS AND PROCEDURES:

The STAR S4 IR Excimer Laser System and the iDesign Advanced WaveScan Studio System will be used to perform wavefront-guided PRK treatments. Inclusion and exclusion qualifications will be assessed at the preoperative visit according to the

inclusion/exclusion criteria. Both eyes of subjects are intended to be treated in the study on the same day.

Key preoperative and postoperative data include iDesign measurements, visual acuities, manifest refraction, keratometry (iDesign and auto/manual), pachymetry, biomicroscopic slit-lamp findings, intraocular pressure, contrast sensitivity, iDesign measurements, Schirmer I Tear Test (with anesthetic), adverse events and complications, non-directed ocular visual symptoms and patient reported outcomes (PRO) assessments of visual functioning and directed ocular visual symptoms (using the NEI-RQL-42, OSDI and PRVSQ for PRK/LASIK instruments). Ocular health and history are also assessed preoperatively. A chart summary of procedures required at each study visit is provided in **Appendix A**.

2. BACKGROUND/INTRODUCTION

Photorefractive Keratectomy, commonly referred to as PRK, is a procedure that uses excimer laser energy, after removal of the corneal epithelium, to create a superficial lamellar keratectomy in the corneal stroma that is of a shape designed to correct or ameliorate a refractive condition. PRK is a popular surgical treatment option for patients with thin corneas and the absence of any flap-related complications is a benefit as compared to LASIK. This benefit is particularly important to the US Armed Forces, where 80% of the refractive surgeries performed are PRK.

This will be the first study of wavefront-guided PRK using the iDesign System in conjunction with the STAR S4 IR Excimer laser for treatment of myopia with or without astigmatism. Currently no excimer lasers are approved for this indication in the US.

The PRK technique was studied extensively in the 1990's by VISX, Incorporated (now Abbott Medical Optics Inc., herein referred to as AMO) and was granted approval for non-wavefront guided PRK for the STAR Excimer Laser system to treat low to moderate myopia (PMA# P930016) in March, 1996.

In 2003, VISX, Incorporated received FDA approval for its first indication of wavefront-guided LASIK treatments using the STAR S4 IR Excimer Laser System with the WaveScan System aberrometer. Currently, the STAR S4 IR Excimer Laser System with the WaveScan System aberrometer is FDA approved in the United States and used internationally for wavefront-guided LASIK treatment of myopia, myopic astigmatism, mixed astigmatism, hyperopia, and hyperopic astigmatism.

Following FDA approval of wavefront-guided LASIK treatment, wavefront-guided PRK was studied in an investigator-sponsored IDE #G030141. This prospective evaluation of the safety and effectiveness of the Star S4 IR laser and the WaveScan System was conducted by the US Navy (lead by investigator Capt. Steven Schallhorn, M.D.).

Although VISX did not submit a PMA for the PRK indication, the study, which completed in 2007, showed good results. Of the 597 eyes treated, (397 in the primary efficacy cohort), there were no eyes with losses of ≥2 lines of best spectacle corrected visual acuity (BSCVA), no eyes with BSCVA worse than 20/40 at any visit, no eyes with an increase in postoperative cylinder of ≥ 2.00 D, and there were no outstanding or unresolved adverse events or safety concerns at the time of study completion (12 months).

In addition, there have been published reports of wavefront-guided PRK using the STAR and WaveScan System. Manche and Haw, 2011 conducted a prospective study of wavefront-guided PRK versus wavefront-guided LASIK using the STAR S4 IR Excimer

Laser system and WaveScan system and concluded that both wavefront guided PRK and LASIK are safe and effective at treating myopia[1].

Recently, AMO has developed a new aberrometry system, the iDesign Advanced WaveScan Studio System (referred to herein as the iDesign System). This aberrometer incorporates a higher density Hartmann-Shack sensor than the earlier AMO aberrometer (WaveScan System). The iDesign System creates treatment tables that are transferred to the STAR S4 IR Excimer Laser System for refractive treatments.

The iDesign Advanced WaveScan Studio system is currently under investigation in two IDE clinical studies for different laser assisted in situ keratomileusis (LASIK) indications: mixed astigmatism (G120162) and hyperopia with or without astigmatism (G120164). A third study of myopia with or without astigmatism (G120151) has been completed and received FDA approval on May 6, 2015. Prior to initiating the US iDesign studies, a treatment study in Canada using the iDesign system in conjunction with the STAR S4 IR Excimer laser was conducted for the same three LASIK indications.

For myopia, the results of the Canadian study and the US IDE study showed that device performance was acceptable and exceeded effectiveness target values. To improve outcomes, the results from the Canadian study were used to identify physician adjustments to optimize the treatment plans for the USA IDE clinical investigation. The results of the US study showed that an additional adjustment would further improve outcomes. The updated adjustments based on outcomes of the US IDE study are now automated in iDesign software version 1.3.

3. CLINICAL HYPOTHESIS

The results of this trial will demonstrate that wavefront-guided PRK correction with the iDesign Advanced WaveScan Studio System and STAR S4 IR Excimer Laser System is safe and effective for the treatment of myopia with and without astigmatism by meeting the primary safety and effectiveness study endpoints including specific criteria for UCVA outcomes, predictability of MRSE, refractive stability, maintenance of BSCVA, induced refractive cylinder, corneal haze, and rates of serious, device related adverse events.

4. STUDY DESIGN

This study is a 12-month, prospective, multi-center, bilateral, open-label, non-randomized clinical trial.

[1] Manche, E. and W. Haw. (2011). Wavefront-Guided Laser in Situ Keratomileusis (Lasik) versus Wavefront-Guided Photorefractive Keratectomy (Prk): A Prospective Randomized Eye-to-Eye Comparison. Trans Am Ophthalmol Soc. 2011 Dec; 109: 201–220

Up to 334 subjects will be enrolled to achieve a minimum of 334 treated eyes (of approximately 167 bilaterally-treated subjects), resulting in at least 300 evaluable eyes at the point of refractive stability. Twenty or more eyes are intended to be treated per dioptric bin across both sphere and cylinder treatment ranges.

The study will be conducted at up to 7 sites in the USA. Each site should enroll a minimum of 20 eyes, and no site may treat more than 25% of eyes.

A distance-corrected contrast sensitivity substudy will also be conducted with at least 65 eyes from a single site.

JUSTIFICATION OF STUDY DESIGN

The study is being conducted for USA regulatory purposes to expand the STAR S4 IR Excimer Laser system indications to include wavefront-guided PRK for the treatment of myopia. The study design is based on the American National Standard for Ophthalmics for Laser Systems for Corneal Reshaping, ANSI Z80.11.2012.

5. ACRONYMS

The following acronyms are used throughout the document:

- UCVA: Uncorrected visual acuity (distance)
- BSCVA: Best spectacle corrected visual acuity (distance)
- MR: Manifest refraction
- MRSE: Manifest refraction spherical equivalent
- MRS: Manifest refractive sphere
- MRC: Manifest refractive cylinder
- IDSE: iDesign spherical equivalent
- IDS: iDesign sphere
- IDC: iDesign cylinder
- PRK: Photorefractive Keratectomy
- LASIK: Laser assisted in situ keratomileusis
- D: diopters

6. STUDY OBJECTIVES AND ENDPOINTS

The purpose of this clinical study is to evaluate the safety and effectiveness of PRK, performed with the iDesign Advanced WaveScan Studio™ System and STAR S4 IR Excimer Laser System (Abbott Medical Optics, CA) for the correction of myopic refractive errors with and without astigmatism.

6.1 PRIMARY ENDPOINTS

Effectiveness

1. MONOCULAR UCVA
   - Success criteria: ≥ 85% of eyes will achieve UCVA of 20/40 or better
2. MRSE WITHIN 0.50 D OF TARGET
   - Success criteria: ≥ 50% of eyes will have MRSE within 0.50 D of intended correction.
3. MRSE WITHIN 1.00 D OF TARGET
   - Success criteria: ≥ 75% of eyes will have MRSE within 1.00 D of intended correction
4. REFRACTIVE STABILITY
   - Success criteria: ≥ 95% of eyes achieve refractive stability. *Note: Additional criteria for determining the time point for achievement of refractive stability are provided in* ***Section 6.3****.*

Safety

1. MAINTENANCE OF BSCVA-LINES LOST
   - Success criteria: <5% of eyes with a loss of >2 lines of BSCVA from preoperative
   - Success criteria: <1% of eyes with haze beyond 6 months with loss >2 lines of BSCVA
2. MAINTENANCE OF BSCVA-PRESERVATION 20/40
   - Success criteria: <1% of eyes with a BSCVA of 20/20 or better preoperatively will have BSCVA of worse than 20/40 postoperatively
3. INDUCED MANIFEST REFRACTIVE ASTIGMATISM
   - Success criteria: <5% of eyes will have induced manifest refractive astigmatism >2.00 D
4. SERIOUS, DEVICE-RELATED ADVERSE EVENTS
   - Success criteria: <1% of eyes with serious, device-related adverse events

6.2 OTHER ENDPOINTS:

1. Monocular mesopic distance corrected contrast sensitivity with and without glare at spatial frequencies of 1.5, 3 , 6, and 12 cpd
2. Monocular photopic distance corrected contrast sensitivity without glare at spatial frequencies 3, 6, 12 and 18 cpd
3. Binocular UCVA
4. Manifest cylinder analyses (vector and non-vector)
5. iDesign aberrometry measurements (including higher order aberrations)
6. Keratometry (iDesign and auto/manual)
7. Intraocular pressure via applanation tonometry

8. Anterior segment evaluation (biomicroscopic slit-lamp exam) for determination of medical findings including re-epithelialization, corneal clarity, complications, etc.
9. Visual symptoms via the patient reported outcomes (PRO) instrument Patient Reported Visual Symptom Questionnaire (PRVSQ for PRK/LASIK)
10. Ocular/visual symptoms (from non-directed responses obtained from the open-ended question “are you having any difficulties with your eyes or vision?”)
11. National Eye Institute Refractive Error Quality of Life – 42 (NEI-RQL) questionnaire results for all 13 sub-scales: dependence on correction, satisfaction with correction, activity limitations, far vision, clarity of vision, expectations, near vision, diurnal fluctuations, glare, symptoms, worry, suboptimal correction, and appearance
12. Ocular Surface Disease Index (OSDI) questionnaire
13. Schirmer I Tear Test (with anesthetic)
14. Exploratory satisfaction questionnaires non-validated questionnaires designed to collect patient satisfaction data prior to and following refractive corneal surgery

6.3 DEFINITION OF THE TIME POINT OF REFRACTIVE STABILITY

The critical time point for analysis of safety and effectiveness is based on achievement of refractive stability. The criteria for determination of the point of refractive stability are as follows (per ANSI Z80.11-2012):

- At least 95% of the treated eyes have a change ≤1.00 D of MRSE and MRC between refractions performed at 1 month and 3 months after surgery or any two refractions performed at least 3 months apart
- The mean rate of change in MRSE and MRC, as determined by a paired analysis, is ≤0.5 D per year (0.04 D/month) over the same time period
- The mean rate of change in MRSE and MRC decreases monotonically over time, with a projected asymptote of zero or a rate of change attributable to normal aging
- The 95% confidence interval for the mean rate of change includes zero or a rate of change attributable to normal aging
- Stability is confirmed at least 3 months after the stability time point by a statistically adequate subgroup.

7. STUDY PRODUCTS

7.1 IDESIGN ADVANCED WAVESCAN STUDIO SYSTEM

The iDesign Advanced WaveScan Studio System (or iDesign System) incorporates iDesign Measurement System hardware and iDesign Treatment Planning Software. The iDesign Measurement System measures lower order and higher-order wavefront aberrations of the human eye using a high density Hartmann-Shack wavefront sensor. In addition, the instrument measures keratometry, pupil diameter, and corneal

topography. The Treatment Planning Software calculates treatment profiles from iDesign wavefront measurements using a Fourier based algorithm.

In this study, all eyes will be targeted for emmetropia and "Surface PRK" treatments will be calculated using iDesign software version 1.3, in international configuration with no physician adjustments.

The Principal Investigator is responsible for ensuring that the iDesign System is only used to treat subjects enrolled in this study.

7.2 STAR S4 IR EXCIMER LASER SYSTEM

The STAR S4 IR Excimer Laser System is a Class III ophthalmic surgical laser designed to create a superficial lamellar keratectomy on exposed corneal tissue. Corneal tissue is removed by a process known as ablative photodecomposition. Ablative photodecomposition occurs when far-ultraviolet radiation reacts with organic molecules, resulting in the photochemical breakdown of the molecular bonds without a significant thermal effect. The source of the far-ultraviolet photons is a high efficiency, gas-discharge excimer laser that electronically excites a combination of argon and fluorine, producing an ultraviolet wavelength of 193 nm. The STAR S4 IR Excimer Laser System combines submicron precision of tissue removal by an excimer laser with a sophisticated computer controlled delivery system.

In the USA, the STAR S4 IR Excimer Laser System is approved for wavefront-guided LASIK, Conventional (manifest refraction based) LASIK, and Conventional PRK. The system is also approved for phototherapeutic keratectomy (PTK). In this study, the STAR S4 IR Excimer Laser will be used in conjunction with the iDesign treatment plans for wavefront-guided PRK.

8. STUDY POPULATION

All study subjects will be enrolled from the normal myopic patient population at up to 7 sites in the U.S.A. Up to 334 subjects will be enrolled to achieve a minimum of 334 treated eyes (in approximately 167 bilaterally treated subjects), resulting in at least 300 evaluable eyes at the point of refractive stability. Each site should treat a minimum of 20 eyes, and no site may treat more than 25% of the enrollment total.

This study will include only subjects who qualify for and intend to have bilateral PRK for the treatment of myopia with or without astigmatism and who meet all of the study inclusion and exclusion criteria in both eyes. After signing the informed consent, subjects meeting all inclusion and exclusion criteria will be offered treatment in the study until either the dioptric bin allotment is full or the study/site limit is reached. Eligibility criteria may not be waived by the investigator. Any questions regarding patient eligibility

are to be discussed with AMO prior to subject enrollment. Subjects must be eligible for military medical benefits.

8.1 INCLUSION CRITERIA

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

1. Signed informed consent and HIPAA authorization
2. At least 18 years of age at enrollment (date informed consent signed)
3. The refractive error, based on the iDesign displayed refraction selected for treatment ("4.0 Rx calc" at 12.5 mm), must be myopia with or without astigmatism with sphere up to -8.00 D, and cylinder between 0.00 D and -4.00 D with a maximum spherical equivalent (SE) of -10.00 D
4. Anticipated residual stromal bed thickness of at least 250 microns as calculated by the iDesign system
5. Distance Best Spectacle Corrected Visual Acuity (BSCVA) of 20/20 or better
6. BSCVA ≥2 lines (≥10 letters) better than distance Uncorrected Visual Acuity (UCVA)
7. Less than or equal to 0.75 D difference between cycloplegic and manifest refraction sphere.
8. A stable refractive error (based on a previous exam, medical records, lensometry, or prescription at least 12 months prior to the preoperative manifest refraction), as defined by a change of ≤1.00 D in MRSE.
9. Any subject eye with a history of contact lens wear within the last 4 weeks must demonstrate refractive stability according to the following:
    - Rigid contact lenses (toric or spherical) must be removed for at least 4 weeks and soft contact lenses (toric or spherical) for at least 2 week prior to the first refraction used to establish stability.
    - Two consecutive manifest refractions and keratometry readings must be conducted at least 7 days apart.
    - Refractive stability is defined as a change of not more than 0.50 D in manifest refractive sphere and cylinder as well as keratometry meridian (either axis) between measurements.
    - If the subject/eye meets the refractive stability criteria, contact lens wear is not permitted prior to surgery
10. Agreement between manifest refraction (adjusted for optical infinity) and iDesign System refraction chosen for treatment, as follows:
    - Spherical Equivalent: Magnitude of the difference is less than 0.625 D.
    - Cylinder: Magnitude of the difference is less than or equal to 0.5 D.
    - Cylinder Axis Tolerance: If either the manifest cylinder entered into the iDesign System or the iDesign cylinder selected for treatment is less than 0.5 D, there is no requirement for axis tolerance. When both cylinders have a magnitude of at least 0.5 D, the axis tolerance as determined by the iDesign system is linearly reduced from 15° (0.5 D) to 7.5° (7.0 D) based on the average magnitude of both

cylinders. Note: If the axis tolerance is not in the calculated range, the iDesign system will produce a warning and this exam may not be used for treatment planning.

11. Willing and capable of complying with follow-up examinations for the duration of the study.

8.2 EXCLUSION CRITERIA:

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

1. Women who are pregnant, breast-feeding, or intend to become pregnant, or not using an adequate method of birth control [examples are any form of barrier contraception (such as condom or diaphragm with contraceptive cream/jelly), birth control pills, hormonal implant, IUD, abstinence or surgical sterilization (tubal ligation, hysterectomy or vasectomy)]. Note: Women who were pregnant or nursing may not be enrolled until 6 months after either delivery or have stopped nursing and there is documented refractive stability.
2. Concurrent use of systemic (including inhaled) medications that may impair healing, including but not limited to: antimetabolites, isotretinoin (Accutane®) within 6 months of treatment, and amiodarone hydrochloride (Cordarone®) within 12 months of treatment.

   NOTE: The use of inhaled or systemic corticosteroids, whether chronic or acute, is deemed to adversely affect healing and subjects using such medications are specifically excluded from eligibility.
3. History of any of the following medical conditions, or any other condition that could affect wound healing: collagen vascular disease, autoimmune disease, immunodeficiency diseases, ocular herpes zoster or herpes simplex, endocrine disorders (including, but not limited to unstable thyroid disorders and diabetes), lupus, and rheumatoid arthritis.

   NOTE: The presence of diabetes (either type 1 or 2), regardless of disease duration, severity, or control, will specifically exclude subjects from eligibility.
4. Subjects with a cardiac pacemaker, implanted defibrillator or other implanted electronic device.
5. History of prior intraocular or corneal surgery (including cataract extraction), active ophthalmic disease or abnormality (including, but not limited to, symptomatic blepharitis, recurrent corneal erosion, severe dry eye syndrome or symptoms, neovascularization > 1 mm from limbus), retinal detachment/repair, clinically significant lens opacity, clinical evidence of trauma, corneal opacity within the central 9 mm and visible on topography, at risk for developing strabismus, or with evidence of glaucoma or propensity for narrow angle glaucoma.

   NOTE: Subjects with ocular hypertension (without glaucomatous changes) or open angle glaucoma, regardless of medication regimen or control, or an IOP greater than 21 mmHg at screening, are specifically excluded from eligibility.
6. Evidence of keratoconus, corneal dystrophy or irregularity, or abnormal topography.

7. Known sensitivity or inappropriate responsiveness to any of the medications used in this study.
8. If either eye does not meet all inclusion criteria
9. Desire to have monovision.
10. Participation in any other clinical study, with the exception of the fellow eye in this study.

9. INVESTIGATOR SELECTION

9.1 INVESTIGATOR QUALIFICATIONS

AMO will select ophthalmic surgeons who have completed a residency in ophthalmology (or its documented equivalent), are licensed to practice medicine and perform refractive surgery at his/her investigative site.

Investigators will be selected from surgeons who are experienced in refractive surgery with the STAR system for CustomVue treatments. 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. Each site will have one designated principal investigator; some sites may have additional surgical sub-investigators.

9.2 INVESTIGATOR OBLIGATIONS

Investigators are required to fulfill the following obligations:

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

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

9.3 INVESTIGATOR APPROVAL

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

investigator is required to report to AMO 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 AMO:

- Confidentiality Agreement
- Cooperative Research and Development Agreement (CRADA)
- Investigator Agreement/Protocol Signature page
- Clinical Investigator Brochure Signature page
- Financial Disclosure form
- Signed and dated copy of investigator's current curriculum vitae
- Copy of the investigator's current medical license
- IRB approval documents

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

10. EXPERIMENTAL PLAN

10.1 OVERVIEW

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

This study will be a 12-month, prospective, multicenter, open-label, bilateral, non-comparative, non-randomized 1-year clinical investigation conducted at up to 7 sites. Up to 334 subjects will be enrolled to achieve a minimum of 334 treated eyes (in approximately 167 bilaterally treated subjects), resulting in at least 300 evaluable eyes at the point of refractive stability. After signing the informed consent, subjects meeting all inclusion and exclusion criteria for both eyes will be offered treatment in the study until either the dioptric bin allotments are full or the study/site limit is reached. Both eyes are intended to be treated on the same day. The follow-up visit schedule will be the same for each operative eye, as described in Section 10.2, Visit Schedule.

Although the study is not masked, to maintain consistency, study technicians conducting study-related vision testing (and qualified backups) should be designated by the investigator for all study-related vision testing. It is recommended that these technicians remain consistent throughout the study.

Key data collection includes iDesign measurements, distance visual acuities, manifest refraction, keratometry (iDesign and auto/manual), pachymetry, biomicroscopic slit-lamp findings, intraocular pressure, contrast sensitivity, Schirmer I Tear Test (with anesthetic),

adverse events, non-directed ocular visual symptoms and PRO assessments of visual functioning and directed ocular visual symptoms (NEI-RQL-42, OSDI, and PRVSQ for PRK/LASIK) as well as the satisfaction questionnaires. Ocular health and history are also assessed preoperatively. A chart summary of procedures required at each study visit is provided in **Appendix A**. If needed, specific equipment necessary to perform the required procedures will be supplied for the duration of the study (**Appendix B**).

10.2 VISIT SCHEDULE

All eyes will be examined preoperatively and postoperatively based on the following visit schedule outlined in **Table 1**. Unscheduled visits may be conducted as necessary at the discretion of the investigator for medically-indicated follow-up.

Table 1: Visit Schedule

VISIT	EXAM	VISIT WINDOW
1	Preoperative Exam	Within 120 days prior to surgery
2	Operative	0-120 days after preoperative exam
3	1 day	1-2 day postoperative
4	1 week	5-8 days postoperative
5	1 month	3-6 weeks postoperative
6	3 months	10-14 weeks postoperative
7	6 months	20-26 weeks postoperative
8	9 months	35-43 weeks postoperative
9	12 months	44-60 Weeks postoperative

Note: 1 month = 4 weeks, 1 week = 7 days

10.3 PREOPERATIVE PROCEDURES

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

Following the informed consent process, completion of the preoperative study exam and determination that both eyes of the subject meet all of the required inclusion/exclusion criteria, the subject's eyes may be treated in the study unless the dioptric bin(s) is(are) full or the study/site limit is reached.

As the Informed Consent Form is signed prior to beginning study specific procedures, 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 proceed with surgery, do not undergo surgery because the dioptric bin(s) is(are) full, or site/study enrollment is complete. These subjects will be exited from the study.

The following preoperative procedures must be completed within 120 days prior to surgery (see also **Appendix A**). General descriptions and requirements of the various tests are provided in the manual of testing procedures (**Appendix C)**. Non-directed responses to the open-ended question "Are you having any difficulties with your eyes or vision?", followed by all patient reported outcome questionnaires, followed by the iDesign measurement are to be administered first before any other study-specific ocular examinations. All non-contact procedures (e.g. topography and keratometry) will be performed before contact assessments (e.g. IOP and pachymetry). If required, cycloplegic refraction/fundus exam will be the final procedures performed at the study visits.

The preoperative visit is unique in that some procedures (such as the pachymetry) may have been performed as part of a standard of care visit, prior to informed consent. If the subject returns for examination on a separate day the order above should be adhered to for the procedures being conducted on that day.

PREOPERATIVE PROCEDURES

- Informed consent process and documentation
- Subject demographic information
- Ocular and systemic medical history
- Ocular and systemic concomitant medication history
- Non-directed ocular/visual symptoms (from non-directed responses obtained from the open-ended question "Are you having any difficulties with your eyes or vision?").
- Binocular Subjective Questionnaires: OSDI, PRVSQ for PRK/LASIK, NEI-RQL-42 and exploratory Satisfaction Questionnaire
- iDesign System Measurement (refraction, aberrometry, topography, keratometry, pupillometry)
- Keratometry (iDesign and auto/manual)
- Corneal topography (Humphrey/Zeiss Atlas or Pentacam)
- UCVA – photopic, monocular, distance (ETDRS)
- UCVA – photopic, binocular, distance (ETDRS)
- Manifest Refraction (ETDRS)
- BSCVA – photopic, monocular, distance (ETDRS)
- Monocular distance corrected contrast sensitivity substudy
    - Mesopic with and without glare at 1.5, 3, 6, and 12cpd
    - Photopic without glare at 3, 6, 12, and 18 cpd
- Refractive stability check for contact lens wearers
- Anterior segment examination (biomicroscopic slit-lam exam)

- Schirmer I Tear Test (with anesthetic)
- Intraocular pressure (applanation tonometry)
- Pachymetry (ultrasound)
- Cycloplegic Refraction
- Dilated fundus examination
- Planned surgery date
- iDesign treatment planning and calculation
- Adverse events and complications
- Device deficiencies/complaints

Note: All eyes will be targeted for emmetropia and undergo a “Surface PRK” treatment; no physician adjustments will be used.

10.4 RANDOMIZATION AND MASKING

This is a nonrandomized study without masking.

10.5 OPERATIVE PROCEDURES

Following determination of the treatment profile using the iDesign system, wavefront-guided PRK will be performed with Star S4 IR™ laser. After anesthesia and placement of the lid speculum, an Amoils Epithelial Scrubber (Innova, Inc., Toronto, Ontario, Canada) will be used to remove the corneal epithelium. Immediately after PRK treatment, apply mitomycin C 0.01% for 15 seconds immediately then rinse the ocular surface with balanced salt solution, instill topical medications, then place a bandage contact lens (BCL). The BCL should be worn until the 1-week study visit.

Both eyes are intended to be treated on the same day. If a clinically significant complication or adverse event is observed during the treatment of the first eye, the fellow eye will not be treated until resolution of the event in the first eye.

To ensure control of environmental conditions during treatments, including temperature and humidity, all laser suites shall be equipped with air conditioning and/or heating systems, humidifiers, and environmental monitoring devices. It is important to maintain a carefully controlled surgical environment. All treatments shall be performed in surgical environments where the humidity is between 35-45% and the temperature is between 68-72° F.

All eyes will undergo the PRK procedure using the STAR SR IR™ Excimer laser to perform ablation according to the iDesign treatment plan. It is recommended that Iris Registration (IR) be used for alignment of all treatments. Refer to **Appendix K** for a detailed summary of the surgical procedure.

10.6 POSTOPERATIVE PROCEDURES

Postoperatively, each treated eye will be examined according to the schedule in **Appendix A,** Visit Schedule.

IMMEDIATE POSTOPERATIVE CARE

Subjects may experience pain during the first week following treatment. The immediate postoperative pain control regimen is left to the Investigator's discretion. All postoperative regimen components shall be recorded:

- Bandage contact lens
- Eye shield(s) during sleep (1 week)
- For all eyes, the postoperative medication regimen will consist of mitomycin C 0.01% for 15 seconds immediately after the ablation, ophthalmic antibiotic QID for 1 week, fluorometholone 0.1% for 8 weeks (QID initially and tapering 1 drop every 2 weeks starting at week 3) and analgesic as needed. Continued use beyond these guidelines is allowed if medically necessary.

EARLY POSTOPERATIVE EXAMINATION PROCEDURES (1 DAY AND 1 WEEK)

Postoperative examinations will be conducted at 1 day and 1 week after treatment. The following clinical information shall be assessed and recorded during each postoperative exam (see also **Appendix A**). General descriptions and requirements of tests are provided in **Appendix C**. Following the assessment of non-directed optical/visual symptoms, iDesign measurements are to be performed before any other ocular examinations. All non-contact procedures (e.g. topography and keratometry) will be performed before contact assessments (e.g. IOP and pachymetry).

- Ocular and systemic medical history and concomitant medications
- Bandage contact lens should be removed before ocular exams (1-week only)
- Non-directed ocular/visual symptoms (from non-directed responses obtained from the open-ended question "Are you having any difficulties with your eyes or vision?").
- iDesign System Measurement (refraction, aberrometry, topography, keratometry, pupillometry (1-week only)
- UCVA – photopic, monocular, distance (ETDRS)
- UCVA – photopic, binocular, distance (ETDRS) (1-week only)
- BSCVA – photopic, monocular, distance (ETDRS) (1-week only)
- PRVSQ for PRK/LASIK (1-week only)
- Anterior Segment Examination
- Adverse Events and Complications
- Device Deficiencies/Complaints

PERIODIC POSTOPERATIVE EXAMINATION PROCEDURES

Periodic examinations will be conducted at 1, 3, 6, 9, and 12 months after treatment. In the event that extended follow-up is not needed, the follow-up period may be reduced.

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

The following data shall be assessed and recorded during the periodic examinations, although not all are required at all periodic visits (see also **Appendix A**). General descriptions and requirements of the various tests are provided in **Appendix C**. Non-directed responses to the open-ended question “Are you having any difficulties with your eyes or vision?”, followed by all patient reported outcome questionnaires, followed by the iDesign measurement, are to be administered first before any other ocular examinations. All non-contact procedures (e.g. topography and keratometry) will be performed before contact assessments (e.g. IOP and pachymetry). If required, cycloplegic refraction/fundus exam will be the final procedures performed at the study visits.

- Ocular and systemic medical history and concomitant medications
- Non- directed ocular/visual symptoms (from non-directed responses obtained from the open-ended question “Are you having any difficulties with your eyes or vision?”).
- Binocular Subjective Questionnaires: OSDI, PRVSQ for PRK/LASIK , NEI-RQL-42 and exploratory Satisfaction Questionnaire (Note: For reliability validation purposes the PRVSQ will be completed by the subject at the visit and also at home 7 days after the 3-month visit and mailed back to the site.)
- iDesign System Measurement (refraction, aberrometry, topography, keratometry, pupillometry)
- Keratometry (iDesign and auto/manual)
- Corneal Topography (Humphrey/Zeiss Atlas or Pentacam)
- UCVA – photopic, monocular, distance (ETDRS)
- UCVA – photopic, binocular, distance (ETDRS)
- Manifest Refraction (ETDRS)
- BSCVA – photopic, monocular, distance (ETDRS)
    - At 3 months or later, if there is a loss of 2 or more lines of BSCVA (≥ 10 letters) compared to the preoperative visit, a rigid contact lens over refraction should be performed to determine if the BSCVA loss is due to irregular astigmatism. If a rigid contact lens over refraction is not medically advisable, then a pin-hole acuity should be obtained
- Monocular distance corrected contrast sensitivity substudy

  - Mesopic with and without glare at 1.5, 3, 6, and 12 cpd
  - Photopic without glare at 3, 6, 12, and 18 cpd
- Anterior Segment Examination
- Schirmer I Tear Test (with anesthetic)
- Intraocular pressure (applanation tonometry)
- Pachymetry (ultrasound) (1 and 12-months only)
- Cycloplegic Refraction (6 and 12-months only)
- Dilated Fundus Examination (6 and 12-months only)
- Adverse Events and Complications
- Device Deficiencies/Complaints

10.7 RETREATMENT PROCEDURES

NON-REFRACTIVE RETREATMENTS

Non-refractive retreatments or procedures without further laser treatment (e.g., treatment of complications, recurrent corneal erosions, etc.) may be performed as deemed necessary by the investigator. If possible notify the sponsor prior to performing any non-refractive retreatments.

REFRACTIVE RETREATMENTS

Refractive retreatments are not allowed during the study.

10.8 EXIT OF SUBJECTS

An Exit Case Report Form will be completed for all subjects, either when they complete the study or if they exit early.

It is the responsibility of the investigator to provide follow-up data to AMO for each subject, and every attempt should be made to gather that complete follow-up data for subjects 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 chosen for this clinical study.

Subjects will be considered enrolled if they sign an informed consent form. A subject will be considered a screen failure if he/she does not meet the inclusion/exclusion criteria or if consent is withdrawn prior to treatment or the subject does not undergo surgery because the dioptric bin(s) is(are) full, or site/study enrollment is complete.

Following treatment, subjects will be considered “lost-to-follow-up” from the study if irretrievably lost for unavoidable reasons such as: subject moved/unable to locate, subject uncooperative/refuses further study participation, subject ill/unable to travel. In the event of subject relocation, efforts 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. A subject will be considered discontinued from the study only if the subject dies.

If a subject is exited early from the study, an Exit Case Report Form will be completed, indicating the reason for study exit. In the event of a serious adverse event, the subject may be exited from the study; however, efforts must be made by the investigator to follow the subject until resolution of the event.

If a subject terminates from the study before the 12-month visit then every attempt should be made to have a final visit with the subject and capture the procedures required at the 12-month visit as outlined in **Appendix A**. Additionally, 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 in the interim.

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 at the discretion of the investigator (based on the reason for the unscheduled visit), however, assessments that are recommended for every unscheduled visit are: UCVA, iDesign system measurement, manifest refraction, BSCVA, anterior segment exam, concomitant medication, adverse events, complications, device deficiencies and complaints as outlined in **Appendix A**. In addition, if a subject is seen at an unscheduled visit due to an ocular visual symptom complaint, the PRVSQ for PRK/LASIK and OSDI, will be administered at that visit, as well as prior to any secondary surgical intervention (e.g. epithelial debridement) for an ocular visual symptom complaint.

For unscheduled visits, the order of procedures (if performed) is to be similar to the scheduled study exams. Non-directed responses to the open-ended question "Are you having any difficulties with your eyes or vision?", followed by patient reported outcome questionnaires (if necessary),followed by the iDesign measurement (if performed) are to be administered first before any other study specific ocular examinations. All non-contact procedures (e.g. topography and keratometry) are to be performed before contact assessments (e.g. IOP and pachymetry). Cycloplegic refraction/fundus exam (if performed) are to be the final procedures.

10.10 PROTOCOL DEVIATIONS

Any departure from the protocol procedures represents a protocol deviation. Protocol deviations may be subject-based (e.g., inclusion/exclusion criteria, informed consent deviation, etc.) or procedural-based (e.g., out-of-interval visits, non-compliance with testing procedures, etc.). All protocol deviations will be documented using protocol deviation case report forms. Any deviation made to protect the life or physical well-being of a subject in an emergency as well as any use of the investigational device without obtaining informed consent must be reported to AMO within 5 working days. Protocol deviations will be monitored by AMO, and if the non-compliance is persistent or egregious, AMO may take action, including but not limited to termination of the sites participation in the study. Each Principal investigator is also responsible for informing the reviewing IRB of record 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 (following ISO 14155) as any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the study device.

Serious Adverse Event (SAE)

An adverse event is considered serious (following 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 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 or possibly related to the study device (following the guidelines in Section 11.4, Causal Relationship). A device related event is considered an adverse device effect (ADE; following ISO 14155) resulting from the use of the study device.

Study-Specific Anticipated Events

ADVERSE EVENTS

The following is a list including, but not limited to, ocular adverse events that are anticipated and must be reported to AMO for this study. Any events that are unlikely but anticipated will be reported to the FDA.

- Corneal infiltrate or ulcer
- Any persistent corneal epithelial defect at 1 month or later
- Corneal edema at 1 month or later
- IOP with increase >10 mmHg above baseline on two consecutive examinations or an IOP greater than 30 mmHg on two consecutive examinations
- Haze beyond 6 months with loss of ≥2 lines (≥10 ETDRS letters) of BSCVA
- Decrease in BSCVA of ≥2 lines (≥10 ETRDS letters) not due to irregular astigmatism as shown by hard contact lens refraction (or pin hole acuity if hard contact lens refraction is not medically advisable) at 3 months or later
- Retinal detachment
- Retinal vascular accidents
- Ocular penetration
- At 3 months or later:
  - Severe halos, based on subject response of both “Extremely bothered” to questions 1e and “Yes” to question 1f on the PRVSQ for PRK/LASIK
  - Severe glare, based on subject response of both “Extremely bothered” to questions 2e and “Yes” to question 2f on the PRVSQ for PRK/LASIK
  - Dry eye based on subject score of ≥ 33 on the OSDI in combination with a Schirmer score of ≤ 5 mm.
- Corneal melt
- Glaucoma or ocular hypertension
- Severe allergic reaction to study medication

COMPLICATIONS

The following events are considered refractive surgery complications (not an all-inclusive list):

- Corneal edema between 1 week and 1 month after the procedure
- Peripheral corneal epithelial defect at 1 month or later
- Recurrent corneal erosion at 1 month or later
- Foreign body sensation at 1 month or later per the non-directed assessment of ocular visual symptoms, “are you having any difficulties with your eyes/vision?”
- Pain at 1 month or later per the non-directed assessment of ocular visual symptoms, “are you having any difficulties with your eyes/vision?”
- Ghost/double images based on subject response to question 5 on the PRVSQ for PRK/LASIK

- Transient light sensitivity syndrome

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

Any UADE (USA 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. Product complaints can pertain to any marketed AMO device being used in the study as well as the investigational device. The investigator is to assess whether the deficiency could have led to a serious adverse event without suitable action or intervention or under less fortunate circumstances.

11.3 ADVERSE EVENT AND COMPLAINT REPORTING REQUIREMENTS

All adverse events and any complaint encountered using any AMO product, regardless of severity and whether or not attributed to the study device(s), are to be reported to AMO 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. Specific instructions on notification procedures to AMO are included in **Appendix L**, Adverse Event Reporting.

Reporting of adverse events shall follow the USA Code of Federal Regulations (21CFR812) and ISO 14155. General guidelines are provided below:

Adverse Event Reporting

An adverse event that is not serious or device-related is to be reported to AMO 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 AMO in a timely manner. Notification of complaints/device deficiencies will occur by either recording

complaints on the CRF when the complaint occurred (e.g. operative form) or by a phone call to the Sponsor. 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 48 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

Serious and/or device-related events (ADEs) are to be documented using the Detailed Adverse Event CRF. In the event of a serious adverse event (SAE), which may or may not be related to use of the study device, AMO must be notified immediately (no later than 48 hours after detection). Any SAE is to be reported by phone and by submitting the completed Detailed Adverse Event CRF. The SAE 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 study device-related and was not previously expected in nature, severity, or degree of incidence, the investigator is to report the UADE/USADE to AMO within 48 hours, and to the investigator's IRB as soon as possible, but no later than 10 working days, after learning of the event 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. An attempt should be made in every case to determine if the event may be device-related.

The following definitions are to be used as guidelines in determining the relationship between the event and the study device and/or procedure.

Definitely related:	There is a definite causal relationship 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.
Possibly related:	The adverse event has not been determined to be related to the device or use of the device, but no other cause has been definitively 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 study device

	could exist, but the adverse event is most likely explained by causes other than the device and/or the use of the study device.
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

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

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. Obtain and maintain in the subject's files all pertinent medical data relating to the event including the subject's medical records and 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 AMO closely informed as to the outcome of serious and/or device-related adverse events, thereby allowing AMO to comply with the appropriate regulatory reporting requirements. A Detailed Adverse Event Update CRF should be completed each time the subject returns to the investigator or other specialist(s) for follow-up of serious and/or device-related adverse event until resolution of the event. Any subject who is exited from the study due to a serious and/or device-related adverse event will be followed until the outcome is determined.

12. PROTOCOL CHANGES/AMENDMENTS

If the investigator desires to modify any procedure and/or the design of the study, he or she must contact and obtain consent from AMO regarding the proposed changes prior to implementation. Any modifications (including additional data collection beyond the protocol or outside the normal standard of care) require approval by the FDA and all other appropriate regulatory agencies, as well as approval of the governing IRBs prior to implementation.

13. ETHICS REVIEW AND PATIENT WELFARE

13.1 INSTITUTIONAL REVIEW BOARD (IRB)

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

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

13.2 INFORMED CONSENT

The current version of the IRB-approved study informed consent must be signed by each study subject prior to any study-specific examinations being performed. The IRB-approved informed consent is to be signed and dated by the subject as well as by the person who conducted the informed consent discussion. The signed informed consent 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 AMO 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 21CFR812 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.

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. However, 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 AMO:

- Subject's name
- Study identification number
- Subject's contact information
- Study protocol number and the Sponsor name (AMO)
- A statement that informed consent was obtained prior to participation in the study (including the date)

- Dates of all subject visits and surgeries throughout the duration of the study
- Concurrent medications
- Corrected and uncorrected distance visual acuity (NOTE: ETDRS visual acuity score cards are considered source documentation and are to be retained by the site in the subject chart)
- Manifest refraction
- Occurrence and status of any operative complications, postoperative medical 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 AMO 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 (EDC) 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 AMO.

14.4 STUDY SUMMARY

A final investigator's summary will be provided to AMO and the reviewing IRB within 3 months after termination or the completion of the study or the investigator's part of the investigation.

15. MONITORING

AMO 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, AMO will follow specific data monitoring procedures. Following review of EDC data, requests for data clarification will be handled through the EDC data system. To minimize data omissions and inconsistencies on clinical reports and to ensure that data are accurately transcribed to computer data files, AMO 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 on the case report forms at the investigative site and in the data management system at AMO. Ongoing data review for clinical data monitoring will be conducted and will include evaluation of outliers for visual acuity and refractions as well as review of adverse event listings.

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 centralized and 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 (e.g., key cards), subjects, and forms can be traced and will allow monitoring of the study site progress and compliance.

Device Accountability

Use of the iDesign study device, the STAR-S4-IR laser and the STAR-S4-IR key cards used in this study will be tracked by the investigative site and AMO. Key card accountability will be maintained at the investigative on a site log to track disposition/return to AMO. During periodic investigative site monitoring visits AMO will review investigative site records and logs.

Site Monitoring Plan

Prior to performing any study treatments, 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 AMO or have undergone significant changes, or have not been visited in the past year. A study initiation visit will be conducted for all sites prior to or at the time of the first treatment.

Throughout the duration of the study, site visits to monitor compliance to this protocol will be made at each investigative site. During a routine site monitoring visit, AMO 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 AMO products have been reported in a timely fashion.

AMO will also review source documents to verify that all required items have been documented in the subject medical charts. Refer to Section 14.1, Source Documents, for a list of items that are required for source documentation. In addition to subject files, study logs will be checked and conformance to lighting levels for visual acuity tests will be verified. Training on study-specific procedures may also be conducted during monitoring visits as necessary.

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

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

15.3 SAFETY MONITORING

The medical monitor will review results throughout the clinical trial as necessary to ensure the continued safety of the device and to ensure that no subjects are exposed to unreasonable risk. The medical monitor will be available to answer 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 AMO, shall also review any interim progress reports, as applicable.

16. PUBLICATIONS

Refer to the Cooperative Research and Development Agreement (CRADA) for information regarding AMO publication policies.

17. RISK ANALYSIS

POTENTIAL RISKS AND RISK MANAGEMENT

The safety and effectiveness of an iDesign System guided PRK treatment with the STAR Excimer Laser System, as well as long-term effects of PRK surgery in general, have not been fully determined. Unexpected complications or side effects may occur. As with any surgery or investigational procedure, all potential risks cannot be identified.

There may be complications and adverse events during or following the surgery which may be temporary or permanent. These may include pain, infection, foreign body sensation, dryness, fluctuation or decreased vision, change in visual quality, glare, halos, double vision, photophobia, transient light sensitivity syndrome, haze, corneal scarring and other medical findings, over- or under-correction, irregular astigmatism, corneal transplant, or blindness. Additional medications or surgeries may be required to treat these complications/adverse events.

RISK MANAGEMENT

Subjects will be closely monitored thought the trial duration. The occurrence of adverse events and complaints will be assessed at each study visit and reported to AMO according to Section 11.0, Adverse Events and Product Complaints. Additionally, AMO 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

PRK treatment using the iDesign system in conjunction with the STAR S4 IR Excimer laser is expected to provide improved uncorrected distance visual acuity and accurate and stable refractive outcomes. Additionally, it is expected that the general clinical outcomes in this iDesign PRK study for the treatment of myopia with or without astigmatism will be similar to results obtained for the iDesign LASIK study for treatment of myopia with or without astigmatism, which has been submitted as a panel-track PMA supplement (P930016/S044).

CONCLUSION

The hazards/risks associated with Advanced CustomVue Treatment using the iDesign Advanced WaveScan Studio System in conjunction with the STAR S4 IR Excimer laser are acceptable and expected to be similar to those of LASIK treatment using the iDesign System and STAR S4 IR Excimer laser. The potential clinical benefits of PRK treatment using the iDesign Advanced WaveScan Studio System in conjunction with the STAR S4 IR Excimer laser outweigh the residual risks when the device is used as intended.

18. RECORDS RETENTION

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

The investigator must maintain and have access to the following essential documents until notified by the Sponsor. Note: This may be for a minimum of 15 years after completion of the study unless country-specific requirements are longer. AMO requires notification if the investigator wishes to relinquish ownership of the data so that mutually agreed-upon arrangements can be made for transfer of ownership to a suitably qualified, responsible person.

- All case report forms
- All adverse event information (adverse event forms, follow-up letters, etc.)
- Investigational supply records/inventory
- IRB and regulatory approval documentation
- Study correspondence
- Study agreements
- Site visit documentation
- Protocol(s) and the reason for any deviations from the protocol
- Subject log(s)
- Clinical Investigator's Brochure
- Completed subject informed consent forms and medical privacy forms (e.g., Authorization for Use/Disclosure of Health information or equivalent documentation necessary to comply with applicable privacy laws pertaining to medical treatment in the governing countries)
- Subject medical chart/clinic notes

19. TERMINATION OF THE INVESTIGATION

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

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

Additionally, the investigator, or AMO, may stop a subject's participation at any time. AMO may also stop the study at any time for reasons it determines appropriate. If refractive stability is established prior to the 12-month visit, the study may be terminated before all subjects reach the final 12 month visit. However, no suspension of the study would be made to disadvantage the study subjects. In the event of an early termination of the investigation, the sponsor will notify study sites, IRBs and appropriate regulatory bodies of the termination. Subjects will be followed as appropriate.

20. STATISTICAL METHODS

This section highlights the analyses for the primary and secondary study endpoints as well as the key safety endpoints. All endpoints will be evaluated at the refractive stability time point. Visual acuities will be converted to logMAR.

20.1 ANALYSIS POPULATION

The safety population will be the primary analysis population for all endpoints and includes all eyes that receive study treatment. However, if there are a significant number of missing values (>5% eyes with missing data at the time point of stability), an intent-to-treat (ITT) population will be used as the primary analysis population for the primary effectiveness endpoints. In this case, missing data will be imputed.

20.2 PRIMARY STUDY ENDPOINTS

All primary effectiveness and safety endpoints will be evaluated at the stability time-point.

PRIMARY EFFECTIVENESS ENDPOINTS

MONCULAR UCVA

The proportion of eyes achieving the target of 20/40 or better will be at least 85%. The frequency, proportion and 95% confidence intervals of eyes with each acuity line of UCVA will be summarized at each study exam.

MRSE PREDICTABILITY (WITHIN 0.50 D AND 1.00 D OF TARGET)

The proportion of eyes with MRSE within 0.50 D of intended correction will be at least 50%. In addition, the proportion of eyes with MRSE within 1.00 D of intended correction at the stability time-point will be at least 75%. The frequency, proportion and 95% confidence intervals of eyes with achieved MRSE within 0.50 D and 1.00 D of intended will be summarized over time.

REFRACTIVE STABILITY

Refractive stability will be evaluated for two cohorts: a “consecutive cohort” (eyes with data at two consecutive visits) and a “consistent cohort” (eyes with data at all periodic visits through the point of stability and the confirmatory time point). At least 95% of eyes will have a change ≤1.00 D of MRSE and MRC between refractions performed at 1 month and 3 months after surgery or any two refractions performed at least 3 months apart. The frequency, proportion and 95% confidence intervals of eyes with MRSE and MRC changes ≤1.00 D, as well as ≤0.50 D, between visits will be presented.

Additionally, the mean change (paired differences) in MRSE and MRC between visits will be calculated to evaluate the additional refractive stability criteria. The mean rate of change in MRSE and MRC is to be ≤0.50 D per year (≤0.04 D/month). The mean rate of change in MRSE and MRC should decrease monotonically over time. At the point of stability, the 95% confidence intervals of the mean rate of change in MRSE and MRC between visits should include zero. Lastly, stability is to be confirmed at least 3 months after the stability time point by a statistically adequate subgroup using the same refractive stability criteria.

PRIMARY SAFETY ENDPOINTS

MAINTENANCE OF BSCVA

The proportion of eyes with a loss of >2 lines of BSCVA from preoperative will be <5%, the proportion of eyes with haze beyond 6 months with a loss > 2 lines of BSCVA will be <1%, and the proportion of eyes with BSCVA of 20/20 or better preoperatively and BSCVA 20/40 or worse postoperatively will be <1%. The frequency, proportion and 95% confidence intervals of eyes with BSCVA acuity line changes and eyes with each acuity line of BSCVA will be summarized at each study exam.

INDUCED MANIFEST REFRACTIVE ASTIGMATISM

The proportion of eyes with induced manifest refractive astigmatism of >2.00 D will be <5%. The frequency, proportion and 95% confidence intervals of eyes with absolute changes in manifest refractive cylinder will be summarized at each periodic study visit.

SERIOUS, DEVICE-RELATED ADVERSE EVENTS

The proportion of eyes with serious, device-related adverse events will be <1% cumulatively. The number and proportion of eyes with serious, device-related adverse events throughout the study will be summarized.

Site Poolability

Baseline demographic data (age, gender, race, and contact lens wear) and baseline iDesign refractions (IDS, IDC and IDSE) will be reported by site. To assess the poolability of the sites, a one-way ANOVA will be used for continuous variables and the Chi-square test or Fisher's Exact tests will be used for categorical variables. An alpha level of 0.15 will be used to assess the site poolability.

Outcome Stratification

To evaluate the consistency of results, the primary effectiveness and safety points will be stratified by key factors at the stability point. These factors will include age group, gender, race, site, preoperative contact lens wear, preoperative iDesign spherical equivalent, preoperative iDesign sphere, preoperative iDesign cylinder, wavefront capture diameter, iris registration status, and clinically significant protocol deviations.

For comparisons across categories, a Mantel-Haenszel chi-square test for ordinal data and a Cochran-Mantel-Haenszel test for non-ordinal data will be used to compare the observed percentages across categories. Additionally, the results for each category will be compared to the target criterion for each study endpoint using chi-square goodness-of-fit test. All statistical tests and p-values will be reported as 2-sided and a significance level of 0.15 will be used to assess homogeneity of the primary safety and effectiveness endpoints for baseline and demographic variables.

Handling of Missing Data for Primary Effectiveness Endpoints

Missing data for ITT analyses of the primary endpoints will be imputed using multiple imputation methods[2] using the MI and MIANALYZE procedures in SAS. Sensitivity analyses including worst-case analyses will also be performed for the primary effectiveness endpoints.

20.3 ADDITIONAL ENDPOINTS

Results for mesopic contrast sensitivity with and without glare (1.5, 3, 6, and 12 cpd) and photopic contrast sensitivity without glare (3, 6, 12, and 18 cpd) will be reported using nonparametric analyses. The frequencies and proportions of eyes with each acuity line changes of binocular UCVA will be reported over time. Mean MRSE, MRS and MRC outcomes, as well as the accuracy of MRS and MRC, will be presented over time. MRC will be analyzed using both non-vector and vector methods. Keratometric analyses will include mean average keratometry, stability of average keratometry, and keratometric cylinder analyses. Mean iDesign aberrometry measurements (HOA) and changes in HOAs will be presented. The mean change in Schirmer I Tear Test (with anesthetic) measurements will be evaluated. The change in intraocular pressure over time will also be evaluated. The frequency and proportion of biomicroscopic slit-lamp findings, including corneal clarity, will be reported over time. The frequency and proportion of eyes with spontaneously reported ocular visual symptoms (non-directed) as well as analyses of the PRVSQ for PRK/LASIK PRO for subjective visual symptoms will be presented. All 13 sub-scales of the NEI-RQL will be analyzed and reported over time. Additionally, mean scores for the OSDI PRO will be analyzed and reported over time. The frequency and proportion of patient satisfaction about the study procedure from the non-validated questionnaires designed to collect patient satisfaction data prior to and following refractive corneal surgery will be summarized. The numbers and proportions of eyes with complications and adverse events and retreatment procedures will be summarized.

Results from the PRSVQ questionnaires completed following the 3-month study visit will be used for reliability validation purposes for the PRSVQ only and will not be analyzed in this study or used for AE reporting.

20.4 VISUAL ACUITY CONVENTIONS AND GENERAL STATISTICS

Visual acuity data will be converted to LogMAR values prior to analysis and adjusted for the test distance used if it is not the standard distance for the chart. Manifest and cycloplegic refractive data will be adjusted for optical infinity and converted to minus cylinder format for presentation and analyses.

[2] Little, R.J.A. and Rubin, D.B. (2002) *Statistical Analysis with Missing Data*. J. Wiley & Sons, New York

Descriptive statistics will typically include sample size (N), mean, standard deviation (SD), median, minimum (Min) and maximum (Max) as appropriate for continuous variables. For continuous variables, statistical tests (e.g., t-test) assuming normality will generally be used. For categorical data, the frequency and proportion will be reported and Fisher's exact test or Chi-square test will generally be applied.

20.5 INTERIM REPORTS

Interim Analyses

Up to four interim analyses may be conducted to determine the point of refractive stability, when 90% of treated subjects have reached the 3, 6, 9 and 12 month visits, respectively. These analyses will only include refractive stability criteria evaluation. Interim analyses will not be disseminated to investigators/site personnel.

20.6 SAMPLE SIZE CALCULATIONS

OVERALL STUDY SAMPLE SIZE

Per ANSI Z80.11-2012, Annex E, the sample size calculation is to be based on the probability of observing an adverse event at a rate greater than or equal to the expected rate but less than or equal to an acceptable target. This study will be powered to detect the percentage of eyes losing 2 or more lines of BSCVA at 3 months. In the approved indication for the original STAR S4 IR System Myopia clinical study (PMA P930016-S016, approved 05/23/03), the percentage of eyes losing 2 or more lines of BSCVA at 3 months was 0.3% (1/318, 95% exact CI (0.00%, 1.7%)). The target rate will be chosen to assure that the proposed study will be able to detect at least the upper limit of the exact 95% confidence interval.

The hypothesis is

$\boldsymbol{H_0}$: $p_{trt} \leq p_{\text{target}}$

$\boldsymbol{H_1}$: $p_{\text{trt}} > p_{\text{target}}$

where

p_{trt} = Estimate of the percentage of eyes losing 2 or more lines of BSCVA at 3 months using the STAR S4 IR and iDesign System

p_{target} = Expected percentage of eyes losing 2 or more lines of BSCVA at 3 months per previously approved PMA P930016-S016

Using the binomial distribution with an alpha of 0.05, 80% power and a sample size of n=300 eyes, a rate of at least 1% can be detected. Adding 15% for loss due to attrition yields a sample size of 340 eyes. Adding 10% for loss due to attrition yields a sample size of 334 eyes (167 subjects) to be treated in order to achieve 300 evaluable eyes at

the point of refractive stability. Adding an additional 50% to account for screen failures allows approximately 334 subjects to be enrolled.

CONTRAST SENSITIVITY SUBSTUDY SAMPLE SIZE

The sample size calculation for the sub-study is based on ANSI guidance (ANSI Z80.11) using non-inferiority approach. With a sample size is 65, a paired t-test with a 0.05 one-sided significance level will have over 90% power to detect the paired difference in mean contrast sensitivity is no less than 0.15 below zero when the expected mean difference is 0, assuming the non-inferiority margin equals 0.15 and the the standard deviation of the differences is 0.40.

APPENDIX A SUMMARY OF PROCEDURES REQUIRED AT EACH VISIT

Examination **Note:** 1 month = 4 weeks, 1 week = 7 days	**Preop** Days -120 to 0[1]	**Op** Day 0	**1 Day** Days 1-2	**1 Wk** Days 5-8	**1 Mo** Weeks 3-6	**3 Mo** Weeks 10-14	**6 Mo** Weeks 20-26	**9 Mo** Weeks 35-43	**12 Mo/ET** Weeks 44-60	**Unsched.**[3]
Informed consent	X									
Demographics	X									
Ocular and systemic medical history and concomitant medications	X	X	X	X	X	X	X	X	X	X
Inclusion/Exclusion criteria	X									
Ocular/Visual Symptoms (Non-directed)[8]	X	X	X	X	X	X	X	X	X	X
PRVSQ, OSDI, NEI-RQL-42 and Satisfaction[7] PRO Questionnaires	X			X[9]	X	X[9]	X	X	X	X[3]
iDesign System Measurement of refraction, aberrometry, topography, keratometry, pupillometry	X				X	X	X	X	X	X (after 1 week)
Keratometry (iDesign and auto or manual)	X				X	X	X	X	X	X
Corneal topography (Humphrey/ Zeiss Atlas or Pentacam)	X				X	X	X	X	X	X
UCVA-photopic, monocular, distance (ETDRS)	X		X	X[6]	X	X	X	X	X	X (after 1 week)
UCVA-photopic, binocular, distance (ETDRS)	X			X[6]	X	X	X	X	X	
Manifest Refraction (ETDRS)	X				X	X	X	X	X	X
BSCVA- photopic, monocular, distance (ETDRS)	X				X	X[2]	X[2]	X[2]	X[2]	X[2]
Contrast sensitivity substudy (monocular distance corrected)	X					X	X	X	X	X
Refractive stability assessment for contact lens wearers	X									
Anterior segment exam (biomicroscopic slit-lamp exam)	X		X	X	X	X	X	X	X	X
Schirmer I Tear Test (with anesthetic)	X				X	X	X	X	X	X
Intraocular pressure (applanation tonometry)	X				X	X	X	X	X	X
Pachymetry (ultrasound)	X				X				X	X
Cycloplegic refraction	X						X		X	X
Bilateral PRK Surgery		X								
Dilated fundus exam	X						X		X	X
Complications[5]	X	X	X	X	X	X	X	X	X	X
Adverse events (Ocular[2]/Non-Ocular)	X[4]	X	X	X	X	X	X	X	X	X
Device deficiencies/complaints	X	X	X	X	X	X	X	X	X	X

[1] All screening assessments should be performed prior to surgery. The screening period is the 120 days before surgery, up to and including the day of surgery.
[2] At 3 months or later, if there is a loss of 2 or more lines of BSCVA (≥ 10 letters) compared to the preoperative visit, a rigid contact lens over refraction (or pin hole acuity if rigid contact lens over refraction is medically inadvisable) should be performed to estimate the best poss ble corrected visual acuity.
[3] At the investigator's discretion for unscheduled visits based on the reason for the unscheduled visit. Subject seen at an unscheduled visit due to an ocular visual symptom complaint should complete the PRVSQ, OSDI, and NEI-RQL.
[4] Adverse event collection begins after informed consent.
[5] As determined by slit lamp findings and patient reported outcomes questionnaires.
[6] Examinations should be performed after removal of the bandage contact lens (if re-epithelized).
[7] Two exploratory Satisfaction PROs will be administered (Pre-Op and then all other time points).
[8] Non-directed responses are obtained from asking the open-ended question "Are you having any difficulties with your eyes or vision?"
[9] For instrument validation purposes the PRVSQ will be the only PRO conducted at week 1. At M3 the PRVSQ will be given a second time at 3M + 7 days for reliability validation.
Note: Non-directed responses to the open-ended question "Are you having any difficulties with your eyes or vision?", followed by all patient reported outcome questionnaires, followed next by the iDesign measurement are to be obtained first in that order before any other ocular examinations. All non-contact procedures (e.g. topography and keratometry) are to be performed before contact assessments (e.g. IOP and pachymetry). Cycloplegic refraction/fundus exam are to be the final procedures.

APPENDIX B EQUIPMENT LIST

The following equipment may 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 Cooperative Research and Development Agreement (CRADA) CRADA, which indicates that the equipment is to be returned to Abbott Medical Optics at the completion of the study.

- iDesign Advanced WaveScan Studio System
- One Vector Vision CSV-1000 ETDRS visual acuity light box, stand
- Three Vector Vision ETDRS 4.0 meter distance charts (100% contrast)
- Vector Vision Contrast Sensitivity charts
- Light Meter
- Tape measure (meters)
- Trial lenses

APPENDIX C MANUAL OF TESTING PROCEDURES

Anterior Segment Examination shall be performed via biomicroscopic slit-lamp exam for determination of anterior segment medical findings including but not limited to the adnexa, conjunctiva, sclera, cornea, and iris. The cornea should be examined in detail and corneal clarity should be graded based on the scale in **Appendix J.** Any abnormalities such as corneal infiltrates or opacities, and degree of re-epithelialization should be recorded.

BSCVA (Best Spectacle Corrected Visual Acuity) shall be measured using the Vector Vision 100% contrast ETDRS charts with the Vector Vision self-calibration, backlit light box at a test distance of 4 meters and calibrated to a photopic luminance of 85 cd/m^2 (80-110 cd/m^2). The ambient room lighting shall be set from dim to dark illumination. BSCVA testing is to be performed with the ETDRS 4.0-meter manifest refraction in place; no refractive adjustment is necessary for BSCVA measurement. Detailed instructions for performing BSCVA testing are provided in **Appendix E**. A conversion chart for distance visual acuity testing between the number of correctly-read ETDRS and Snellen/Decimal acuity is provided in **Appendix D**.

Contrast Sensitivity shall be measured with the Vector Vision CSV 1000 at 8 feet under mesopic lighting conditions with and without glare and under photopic conditions without glare at spatial frequencies of 1.5, 3, 6, 12 and 18 cpd. See Reference **Appendix N** for full instructions.

Corneal Topography shall be measured with the iDesign System and a Scheimpflug (Pentacam) or Placido (Humphrey/ Zeiss Atlas) disk-based system. Images will be retained by the Investigator.

Cycloplegic Refraction shall be performed at least 30 minutes following installation of 1-2 drops of cyclopentolate 1% or tropicamide 1% to determine the subject's refraction without accommodation.

Dilated Fundus Examination shall be performed following installation of mydriatic agents approximately 30 minutes prior to determine the status of the ocular media, retina and lens.

iDesign Advanced WaveScan Studio System measures the refractive error and wavefront aberrations of the human eye using a Hartmann-Shack wavefront sensor. Preoperatively, a minimum of three measurements shall be taken to allow the iDesign system to select the exam for use in the generation of the treatment profile; a minimum wavefront diameter of 4.0 mm for preoperative measurements is required. Postoperatively, at least one measurement is required at designated study exams. Every

effort shall be made to obtain measurements with the largest wavefront diameter possible at each visit.

Schirmer I Tear Test (with anesthetic) is to be performed before applanation tonometry, ultrasonic pachymetry and other procedure that may irritate the cornea. See **Appendix M** for instructions on how to perform the Shirmer I Tear Test.

Intraocular pressure is to be measured using applanation tonometry and is to be performed after manifest refraction, vision tests, keratometry, topography, aberrometry, and biomicroscopy.

Keratometry (not simulated K) shall be conducted using the iDesign System and an auto or manual keratometer. The same keratometry method is to be used at each required visit, e.g., if auto keratometry was recorded at the preoperative exam, all postoperative keratometry readings should be auto K's. Do not use "sim K" from a corneal topography unit other than the iDesign system.

Lighting levels and lane calibration will be assessed by a representative of the Sponsor to ensure the lane length and lighting conditions are consistent across sites. The site or Sponsor designee will verify ambient room lighting is dim to dark illuminance with photopic chart background luminance level of 85 cd/m^2 (80-110 cd/m^2) with a light meter at least annually during the active enrollment and follow-up period. Verification of the chart luminance level will be done.

Manifest Refraction is to be performed using the phoropter or trial frames and the 100% ETDRS charts and the self-calibrating, backlit box at a distance of 4.0 meters and calibrated to a photopic luminance of 85 cd/m^2 (80-110 cd/m^2). The ambient room lighting shall be set from dim to dark illuminance. Manifest refraction is to be performed using the Maximum Plus refraction method as detailed in **Appendix E**. Because 4.0 meters is not optical infinity, refraction adjustments are necessary for some vision tests to ensure proper vision testing taking into account test distance and the ETDRS refraction distance (4 m). **Appendix G** lists the refraction adjustments required for the various different vision tests using the ETDRS 4.0-meter refraction.

Ocular Surface Disease Index (OSDI) is a 12-question patient reported outcomes (PRO) instrument designed to measure severity of dry eye symptoms.

Patient Reported Visual Symptom Questionnaire (PRVSQ) (2015 version for PRK/LASIK) is a self-administered, questionnaire designed to measure patient reported occurrence and level of bother related to ocular visual symptoms. Severity of patient reported ocular visual symptoms area also assessed under different situations including with and without correction and under mesopic conditions.

National Eye Institute Refractive Error Quality of Life Instrument – 42 (NEI-RQL-42) (2001 version) is a self-administered assessment tool designed specifically for those who through correction of refractive error have normal visual acuity, but may still be experiencing problems in vision-related functioning and well-being. The NEI-RQL questionnaire is to be administered before any other visual assessment or exam both preoperatively and at designated postoperative study exams.

Pachymetry to measure the central corneal thickness shall be performed with an ultrasonic pachymeter preoperatively and postoperatively as described in **Appendix A**.

Photopic Luminance is defined as 85 cd/m^2 (acceptable range of 80-110 cd/m^2).

Mesopic Pupil Size shall be measured using the iDesign System.

Refractive Stability (preoperative) is defined as a change of ≤1.00 D in MRSE (based on a previous exam, medical records, lensometry or prescription) at least 12 months prior to the preoperative manifest refraction.

Refractive Stability Check for Contact Lens Wearers is based on a change of not more than 0.50 D in manifest refractive sphere and cylinder as well as keratometric meridian (either axis) between 2 separate measurements at least 7 days apart with readings following cessation of contact lens wear of 4 weeks for rigid contact lenses (toric or spherical) and 2 weeks for soft contact lenses (toric or spherical).

iDesign Treatment Planning is required prior to the operative exam. All eyes will be targeted for emmetropia and undergo a “Surface PRK” treatment. The iDesign System will be used to create a treatment shape for each eye that qualifies for the study. The iDesign software used in this study is Version 1.3, in international configuration, with no physician adjustments.

UCVA (Uncorrected Visual Acuity) shall be measured using the Vector Vision 100% contrast ETDRS charts with the Vector Vision self-calibration, backlit light box at a test distance of 4 meters and calibrated to a photopic luminance (80-100 cd/m^2) The ambient room lighting shall be set from dim to dark illuminance. UCVA testing is to be performed through a +0.25 D trial lens refractive adjustment to compensate for optical infinity. Detailed instructions for performing UCVA testing are provided in **Appendix H**. A conversion chart for distance visual acuity testing between the number of correctly-read ETDRS and Snellen acuity is provided in **Appendix D**.

APPENDIX D CONVERSION CHARTS FOR VECTOR VISION CHARTS

Conversion Reference Chart for Vector Vision Distance Chart at 4.0 Meters

Standard Snellen 20/___ (Decimal)	Number of Letters Read At 4 Meters (13 Feet) (ETDRS)
10	55
10	54
11	53
12	52
12	51
13	50
13	49
14	48
14	47
15	46
16	45
17	44
17	43
18	42
19	41
20 (Decimal 1.0)	40
21	39
22 (Decimal 0.9)	38
23	37
24	36
25 (Decimal 0.8)	35
26	34
28	33
29 (Decimal 0.7)	32
30	31
32	30
33 (Decimal 0.6)	29
35	28
36	27
38	26
40 (Decimal 0.5)	25
42	24
44	23
46	22
48	21
50 (Decimal 0.4)	20
53	19
55	18
58	17
60	16
63	15
66 (Decimal 0.3)	14
69	13
73	12
76	11
80	10
83	9

Standard Snellen 20/___ (Decimal)	Number of Letters Read At 4 Meters (13 Feet) (ETDRS)
87	8
91	7
96	6
100 (Decimal 0.2)	5
105	4
110	3
115	2
121	1
126	0

APPENDIX E MAXIMUM PLUS MANIFEST REFRACTION TECHNIQUE WITH CYLINDER REFINEMENT

Manifest refraction testing will be performed using a self-illuminating light box calibrated to a photopic luminance of 85 cd/m^2 (80-100 cd/m^2) and 100% contrast ETDRS charts designed for 4.0 meters. The ambient room lighting shall be set to dim to dark illuminance. **NOTE: Objective refraction by iDesign measurement must 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 maximum visual acuity.

1) Occlude the fellow eye.
2) Place the iDesign system (4 mm Rx Calc) sphere (adjusted to 4 meters) and cylinder power and axis from the iDesign exam (vertex distance at 12.5mm) selected for treatment in the phoropter or trial frame
3) SPHERE: Starting with the objective refraction, refine the sphere to yield best visual acuity.
4) 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.
5) CYLINDER POWER: Set the cross cylinder to refine cylinder power and present choices to the subject, remind 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.
6) SPHERE CHECK: Introduce fogging lens (typically +0.75D sphere) and reduce in 0.25D steps until visual acuity shows no improvement.

APPENDIX F CYCLOPLEGIC REFRACTION TECHNIQUE

The baseline refraction and the amount of accommodation that the subject habitually employs can only be determined by refracting with and without cycloplegia. The chief benefit of cycloplegia, therefore, is that it reduces accommodation so that the examiner can make an accurate measurement of the refraction in the un-accommodative state. By comparing this result with a manifest refraction, the true refractive state of the eye and the accommodative tone can be established.

There are two pieces of information that are available from the cycloplegic examination that cannot be deduced from the manifest refraction alone:

- the magnitude of the refractive error free from the influence of accommodation and,
- the extent to which the accommodative tone influences the refractive state.

The following cycloplegic refraction technique is to be used throughout the study:

1. Instill 1-2 drops of cycloplegic agent (cyclopentolate 1% or tropicamide 1%) and wait at least 30 minutes to allow for a full cycloplegic effect.

2. Start with the Manifest Refraction (maximum plus; refined from the objective iDesign measurement).

3. Refine the sphere magnitude so the least minus yields the most letters. It is required that you do not refine the cylinder axis or the cylinder power.

APPENDIX G REFRACTION ADJUSTMENTS

Postoperative study manifest refractions are to be performed using the 100% ETDRS charts at a distance of 4.0 meters. Because 4.0 meters is not optical infinity, refraction adjustments are necessary to ensure proper vision testing taking into account test distance and refraction distance. The adjustment required (in diopters) is 1/test distance (in meters). To adjust a 4.0-meter manifest refraction to optical infinity, -0.25 D is to be added to the sphere of the refraction to obtain a true distance (infinity) correction. When testing uncorrected visual acuity at 4.0-meters a +0.25 D sphere is required. In the case where the manifest 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 in this study:

Refraction Adjustments for Vision Testing

Vision Test	Test Distance	Correction/Adjustment
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
Best corrected contrast sensitivity	8.0 ft (2.5 m)	+0.12 D added to ETDRS sphere Rx

APPENDIX H INSTRUCTIONS FOR USE OF VECTOR VISION ETDRS DISTANCE VISUAL ACUITY CHART

Distance visual acuity testing will be performed using the Vector Vision CSV-1000 retroilluminated light box and 100% contrast ETDRS (Early Treatment Diabetic Retinopathy Study) distance charts at a test distance of 4.0 meters (13 feet). All subjects will be tested both uncorrected monocularly and binocularly, it is recommended that monocular testing be completed before binocular testing.

The CSV-1000 light box is self-illuminated and self-calibrates to a light level of 85 cd/m^2 (a range of 80-110 cd/m^2 is acceptable). Room lighting is to be set lower than the illumination from the light box, per the manufacturer's instructions. Ambient illuminance should be from dim to dark to maximize pupil size. No surface (including reflective surfaces) within the subject's field of vision should exceed the chart background in luminance.

The light box must be placed 4.0 meters from the subject for testing distance visual acuities. Reverse charts are available for rooms that require "folding" via a mirror to reach a distance of 4.0 meters. Whether standard or "folded," if the room set-up does not allow the chart to be placed precisely at 4.0 meters, record the actual test distance used (e.g., 3.9 meters), and visual acuity measurements will be mathematically adjusted by AMO for the actual test distance used.

Refraction adjustments should be used as necessary for the 4.0 meters visual acuity test distance. As manifest refractions are to be performed using the ETDRS chart at 4.0 meters, no adjustment is required to the refraction when testing BCDVA at 4 meters. However, as 4 meters is not optical infinity, an adjustment of +0.25 D sphere is required to test UCDVA at 4 meters (1/test distance in meters = adjustment in diopters).

To test subjects monocularly, occlude the fellow eye in the phoropter or with an occluder (if trial lenses are used). To measure visual acuity, subjects should be instructed to start with the smallest line where they can read all of the letters. If they miss any letters, go up a line until they are able to read all the letters on a line, then continue to read each subsequently smaller line. The subject should be encouraged to read as many letters possible, even if they have to guess. Testing may be stopped when it is evident that no further readings can be made. Record the total number of letters read correctly on the chart. Score sheets similar to the example below will be provided for the study. To score the visual acuity, draw a line through each letter missed (or circle letters read correctly) and then tally the total number of letters correctly read. **Scoring sheets must be used and retained as source documentation**. A conversion chart is provided on the scoring sheet for reference between the number of correctly-read ETDRS letters and Snellen equivalents. (**Appendix D**).

TO AVOID MEMORIZATION: charts will be changed between visual acuity tests.

Example of ETDRS Score Chart

ETDRS Chart #1 Line						RUNNING TOTAL	NUMBER READ
1	N	C	K	Z	O	5	
2	R	H	S	D	K	10	
3	D	O	V	H	R	15	
4	C	Z	R	H	S	20	
5	O	N	H	R	C	25	
6	D	K	S	N	V	30	
7	Z	S	O	K	N	35	
8	C	~~K~~	D	N	R	40	
9	S	~~R~~	~~Z~~	~~K~~	D	45	**41**
10	~~H~~	~~Z~~	~~O~~	~~V~~	~~C~~	50	
11	~~N~~	~~V~~	~~D~~	~~O~~	~~K~~	55	

APPENDIX I INSTRUCTIONS FOR KERATOMETRY

Every effort should be made to obtain keratometry readings from the iDesign system at every visit in addition to auto and/or manual keratometry. Keratometry must be performed prior to dilation and any contact with the cornea (e.g., tonometry or pachymetry) as follows:

1. Measure keratometry using the iDesign System and also perform an auto or manual keratometry reading. If possible use the same method at each required visit, e.g., if auto keratometry was recorded at the preoperative exam, all keratometry readings postoperatively should be auto K's in addition to those from the iDesign system.
2. **Do not use "sim K"s from a corneal topography unit.**
3. Always record the flat meridian (smaller number, e.g., 42.25) as K1. Record the steeper meridian (larger number, e.g., 43.00) as K2 along with the corresponding axis (e.g., 42.25 / 43.00 x 165).
4. Record spherical corneas by placing the corneal curvature values in both K1 and K2 and marking axes 180 attached to K2 (e.g., 44.00 / 44.00 x 180). **Spherical Ks will not be accepted with axes other than 180 (do not use 0).**

APPENDIX J SLIT-LAMP EXAM GRADING SCALE

A. Corneal Clarity

Below is the grading scale to be used for corneal clarity:

Grade	Description
0.0	Clear
0.5	Faint/trace haze
1.0	Mild haze, not affecting refraction
2.0	Moderate haze, refraction possible
3.0	Dense haze/ prevents refraction, AC visible
4.0	Dense haze/AC not visible

APPENDIX K PRK SURGICAL PROCEDURE

The following steps represent a typical PRK surgical procedure and should be used as a standard model. Both eyes will be treated on the same day provided that treatment of the first eye is without an adverse event or clinically significant surgical complication.

1. Standard preoperative preparation and intraoperative medications will be used.
2. Activate the recording device (e.g., DVD recorder) and begin video acquisition of the subjects procedure.
3. After anesthesia and placement the lid speculum, an Amoils Epithelial Scrubber (Innova, Inc., Toronto, Ontario, Canada) with a 9.0 mm brush will be used to remove the corneal epithelium prior to laser treatment.
4. Ensure magnification on the operating microscope is 1.6X. Ensure the subject's pupil is centered in the reticle as the subject is fixating on the fixation LED. Focus on the anterior stromal surface.
5. Remind patient to fixate on flashing LED, activate ActiveTrak and Iris Registration on the STAR S4 IR Excimer Laser System.
6. Confirm proper placement of the outer iris boundary (OIB).
7. After ensuring that the reticle is centered over the subject's pupil and the subject is viewing the fixation light, fully depress the foot pedal to perform the laser treatment. If necessary, stop the laser and dry the cornea if there is fluid accumulation.
8. Apply mitomycin C 0.01% for 15 seconds immediately after the ablation.
9. Rinse the stromal surface with 30 cc of balanced salt solution.
10. Instill ophthalmic antibiotic QID for 1 week, fluorometholone 0.1% for 8 weeks (QID initially and tapering 1 drop every 2 weeks starting at week 3) and analgesic as needed. Continued use beyond these guidelines is allowed if medically necessary.
11. A bandage contact lens will be placed on the operated eye.
12. Note the treatment time, whether the eye tracker lost track of the eye at any time during the procedure. Record environmental conditions (temperature and humidity.)
13. Print the STAR S4 IR Operative Report.
14. Note any adverse events or complications that occurred during treatment. Report any adverse events to the Sponsor.
15. Patients will receive antiemetics, pain medication, and lubrication at the discretion of the investigator.

APPENDIX L ADVERSE EVENT AND COMPLAINT REPORTING INSTRUCTIONS

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

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 AMO.
2. Ensure the data are submitted to AMO electronically within 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 AMO immediately (no more than 48 hours after learning of the event) as follows:
   a. Contact the following AMO personnel by phone:

      [redacted]

   b. Complete a Detailed Adverse Event Form and submit electronically to AMO

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 AMO electronically within a timely manner.

APPENDIX M SCHIRMER I TEAR TEST (WITH ANESTHETIC)

Prepare the strips while they are still in the package by folding the rounded end at the indentation, approximately 5 mm from the tip. Open the plastic package and remove the strip for the right eye, holding the strip by the square-cornered end. Instill topical anesthetic solution into both eyes, wait for a few minutes for the drops to dissipate, and then insert the strips. Ask the patient to look up, gently retract the lower lid, and insert the strip into the inferior cul-de sac, placing the fold at the lid margin. Position the strip so that it is at the lateral third of the eyelid with the longer end hanging downward over the lower eyelid. As the strip is inserted, avoid touching any part of the eye. After inserting the remaining strip into left eye, the patient may gently close the eyes. Alternatively the patient may blink as desired but should avoid forceful lid closure. Dim the lights in the room to enhance patient comfort.

Leave the strips in place for 5 minutes or until the strips are completely wet, whichever occurs first. Ask the patient to look up, remove the strips from the inferior cul-de-sac, and measure the length of each strip that has been wetted by the tears, beginning the measurement at the notch. A measuring guide is found on the Schirmer strip package. A template of the strip next to the guide allows for accurate measurement of the amount of strip wetting. Alternatively, a millimeter rule may be used to measure the length of the strip wetted by the tears.

Interpretation

A normal eye will wet between 10 and 30 mm of the strip and a severe dry eye will be wet less or equal to ≤ 5 mm in 5 minutes when the Schirmer I is performed.

Note:

Schirmer tear tests are performed before applanation tonometry or any other procedure that may irritate the cornea. If the topical ophthalmic anesthetic is not allowed to dissipate before inserting the strips, the amount of tears in the eye may be overestimated.

APPENDIX N INSTRUCTIONS FOR MONOCULAR CONTRAST SENSITIVITY TESTING USING THE VECTOR VISION SYSTEM

Monocular contrast sensitivity on the subject's first eye with the best distance correction in place (with refraction adjustment of +0.12 D added to the ETDRS refraction) will be measured using the Vector Vision self-illuminated light box and the Vector Vision Contrast Sensitivity charts, which contain a series of sine-wave gratings. The CSV-1000E chart tests four different spatial frequencies: A = 3 cycles/degree (cpd), B = 6 cpd, C = 12 cpd, and D = 18 cpd; whereas the CSV-1000-1.5CPD chart tests only one spatial frequency: E = 1.5 cpd. **The test distance is 8 feet (2.5 meters).**

Contrast sensitivity will be tested under mesopic conditions with and without glare (1.5, 3, 6 and 12 cycles per degree) and photopic conditions without glare (3, 6, 12 and 18 cycles per degree).

A trial reading with the subject should be done prior to recording the testing data to ensure subject understanding of the test procedure.

Monocular contrast sensitivity testing will be measured with the subject's best distance correction (with a refraction adjustment of +0.12 D added to the sphere of the ETDRS refraction) in front of the eye being tested with the other eye occluded.

To measure monocular contrast sensitivity using the CSV-1000E chart, subjects are to identify which circle in each vertically-aligned circle set (1-8) contains the sine-wave pattern. The reference pattern for each spatial frequency is provided under the spatial frequency designation (A, B, etc.) on the chart. A similar pattern appears in either the top or bottom of each paired circle set, getting fainter and harder to see with each subsequent circle set. Subjects should be instructed to identify whether the top circle, bottom circle, or neither circle in each circle set contains the pattern. The subject should be prompted until no difference can be determined between the two circles in each set. Any incorrect response(s) prior to no difference being detected should be retested. For example, if a subject detects no difference at number 7, but responded incorrectly at number 4, the subject should be retested starting at number 3. After retesting, the number corresponding to the last correct response in a paired circle set is the score for that spatial frequency. If the subject is unable to see the reference pattern under the letter, then the score for that spatial frequency is zero. If the subject is able to see the reference pattern under the letter, but cannot identify any pattern in circle sets 1-8, then the score for that spatial frequency is the spatial frequency designation (A, B, etc.).

Note that the circle sets on the Vector Vision CSV-1000-1.5CPD chart are oriented side-by-side instead of being vertically aligned, so subjects should be instructed to identify whether the right circle, left circle or neither circle contains the pattern for this chart.

NOTE: Spatial frequency testing is to be performed twice under each lighting condition. Score sheets must be retained as source documentation.

Mesopic testing without glare should be performed first, followed by mesopic testing with glare and lastly photopic testing without glare.

MESOPIC TESTING: Ensure room lighting is set to the proper level; typically all room lights are off or dimly lit with the exam-room door closed. In addition, the subject must view the test through the neutral density filter lenses, which will reduce the amount of illumination in the room to approximately 2.5 cd/m². After a recommended 10-minute adaptation period, mesopic testing may be performed. First use the CSV-1000-1.5CPD chart to test the spatial frequency of 1.5 cycles per degree. Then use the CSV-1000E chart to test the spatial frequencies of 3, 6 and 12 cycles per degree. (Testing at 18 cpd is not required for mesopic testing). Repeat mesopic testing without glare, and then perform and repeat mesopic testing with glare.

PHOTOPIC TESTING: Following mesopic testing, photopic testing without glare is to be performed and repeated. Room lighting should be set as low as possible with the majority of illumination from the light box. The illumination from the box is automatically calibrated at 85 cd/m2, but should be confirmed with the light meter (a range of 80-110 cd/m2 is acceptable). Continue to use only the CSV-1000E chart test face to test the spatial frequencies of 3, 6, 12 and 18 cycles per degree.