BAUSCH + LOMB

Clinical Investigation Plan
Technolas TENEO 317 Model 2 Excimer Laser

Study #884

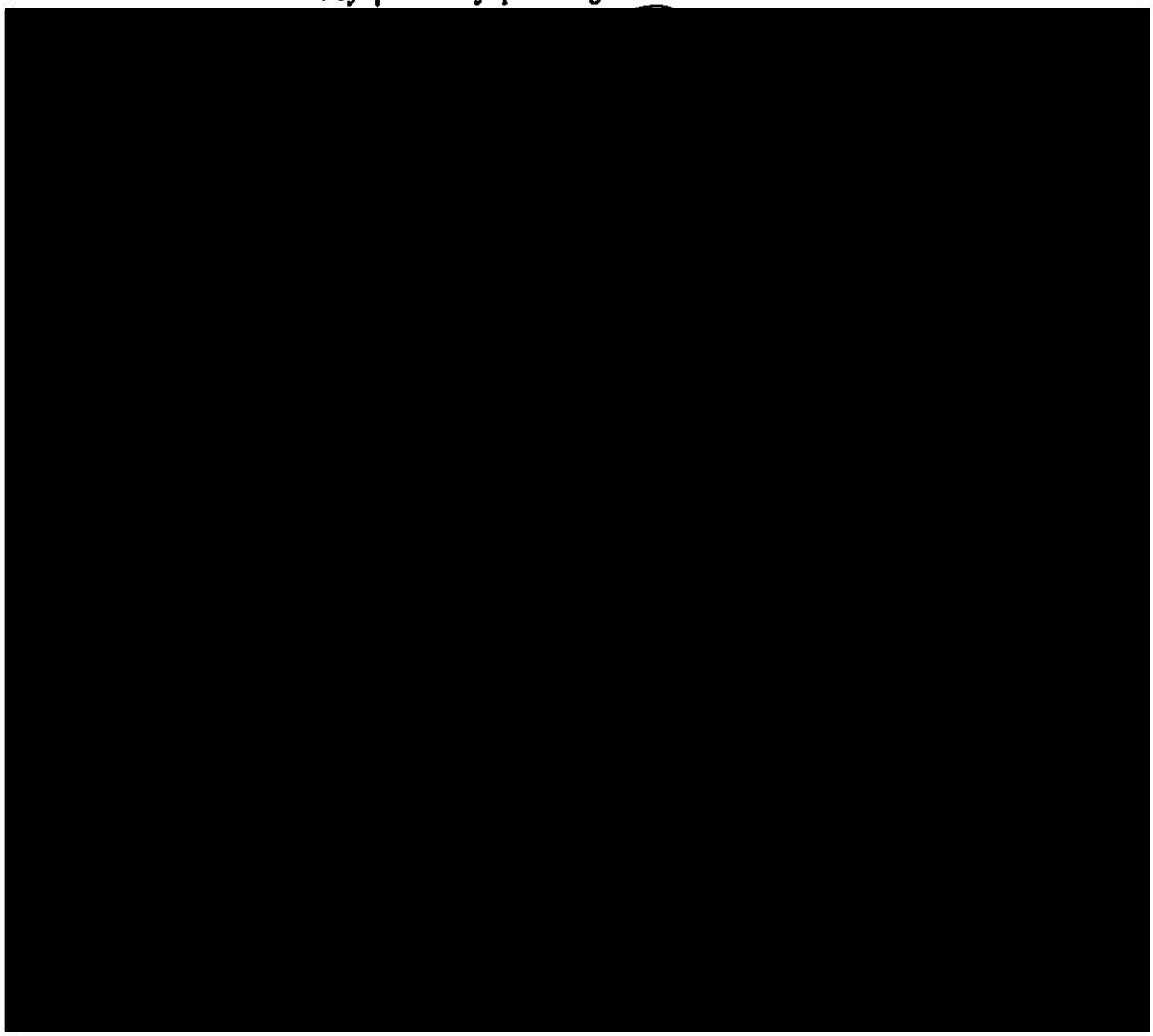
A Study to Investigate the Safety and Effectiveness of the Technolas® TENEO 317 Model 2 Excimer Laser for Laser In Situ Keratomileusis (LASIK) Surgery to Treat Myopia or Myopic Astigmatism

Developmental phase of study:	Pivotal IDE Clinical Trial
Study design:	Multicenter, open label, non-randomized safety and effectiveness study
Date:	November 15, 2018 (Version 1.0) January 28, 2019 (Version 2.0) February 20, 2019 (Draft version 3.0) February 25, 2019 (Draft version 3.1) April 24, 2019 (Version 4.0) August 26, 2019 (Version 5.0) March 4, 2020 (Version 6.0) July 15, 2020 (Version 7.0) November 19, 2020 (Version 8.0)
Sponsor	Bausch & Lomb Incorporated A division of Bausch Health Companies 1400 North Goodman Street Rochester, [redacted]

This clinical investigation is being conducted in accordance with 21 CFR Parts 11, 50, 54, 56 and 812; ISO 14155 (2011 (E)) Clinical Investigation of Medical Devices for Human Subjects (ISO GCP); and elements of ANSI Z80.11-2012 (R2017) Laser Systems for Corneal Reshaping; and applicable local regulations. The confidential information in the following document is provided to you, as an Investigator or consultant, for review by you, your study personnel, and the applicable IRB/EC. By accepting this document, you agree that the information contained herein will not be disclosed to others without written authorization from Bausch & Lomb Incorporated, except to the extent necessary to obtain consent from those persons who participate in this study.

Protocol Review and Approvals

A Study to Investigate the Safety and Effectiveness of the Technolas® TENEO 317 Model 2 Excimer Laser for Laser In Situ Keratomileusis (LASIK) Surgery to Treat Myopia or Myopic Astigmatism



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Reviewed and approved:

Personnel Responsible for Conducting the Study

A Study to Investigate the Safety and Effectiveness of the Technolas® TENEO 317 Model 2 Excimer Laser for Laser In Situ Keratomileusis (LASIK) Surgery to Treat Myopia or Myopic Astigmatism

Contract Research Organization / Medical Monitor

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Principal Investigator Protocol Agreement Page

COMMITMENTS OF THE INVESTIGATOR:

I agree to conduct the study in accordance with the relevant, current protocol(s) and will only make changes in a protocol after being notified by the Sponsor, except when necessary to protect the safety, rights, or welfare of subjects. I agree to comply with all requirements regarding the obligations of clinical investigators and all other pertinent requirements in 21 CFR Part 812.

I agree to personally conduct or supervise the described investigation. I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study are adequately trained and qualified to fulfill their responsibilities and are informed about their obligations in conducting the study.

I agree to inform any patients that the device is being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent in 21 CFR Part 50 and institutional review board (IRB) review and approval in 21 CFR Part 56 are met.

I agree to report to the Sponsor adverse experiences that occur in the course of the investigation(s) in accordance with 21 CFR Part 812.150.

I agree to disclose to the Sponsor accurate financial information to allow the Sponsor to submit complete and accurate certification or disclosure statements required under 21 CFR Part 54. I agree to promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.

I agree to maintain adequate and accurate records in accordance with 21 CFR Part 812.140 and to make those records available for inspection in accordance with 21 CFR Part 812.145 and if I transfer custody of the records to any other person I will notify the Sponsor.

I will be responsible for the control of devices under investigation and will ensure that the investigational device is used only with subjects under my supervision. Upon completion or termination of the clinical investigation, I will either return all investigational devices to the Sponsor or dispose of the device as instructed by the Sponsor.

I will ensure that an IRB that complies with the requirements of 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to report to the IRB all deviations in the research activity and all unanticipated problems involving risks to human subjects or others, per IRB requirements. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

I have never been disqualified as an Investigator or had a research study terminated by the FDA, IRB/IEC or a Sponsor for noncompliance of an investigator agreement, investigational plan, IRB/IEC requirements or the requirements of 21 CFR Part 50, 21 CFR Part 54, 21 CFR Part 56, or 21 CFR Part 812. If an investigation or other research was terminated, I will provide an explanation of the circumstances that led to termination.

A current Curriculum Vitae has been provided to the Sponsor to demonstrate education, training, and experience that qualifies me to conduct clinical research as an expert in the field related to the device under investigation.

_____

Principal Investigator, Printed Name

_____ _____

Principal Investigator, Signature Date

Upon signing, provide a copy of this page to Bausch + Lomb and retain a copy for your files.

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LIST OF ABBREVIATIONS

Abbreviation/Acronym	Term
AE	Adverse event
ANSI	American National Standards Institute
BSCVA	Best Spectacle Corrected Visual Acuity
CFR	Code of Federal Regulations
COVID-19	Coronavirus infectious disease 2019
CRF	Case report form
cpd	Cycles per degree
CRO	Contract Research Organization
CV	Curriculum vitae
D	Diopter
DHHS	Department of Health and Human Services
FDA	Food and Drug Administration
Form 3455	Financial Disclosure by Clinical Investigators
GCP	Good Clinical Practice (ISO 14155) for medical devices
IDE	Investigational Device Exemptions
IEC	Independent Ethics Committee
IOP	Intraocular pressure
IRB	Institutional Review Board
ISO	International Organization for Standardization
ISO/IEC	ISO/International Electrotechnical Commission
LASIK	Laser-assisted *in situ* keratomileusis
MRSE	Manifest Refraction Spherical Equivalent
msec	Milliseconds
OOW	Out of window
OSDI	Ocular Surface Disease Index
OZ	Optical zone
PI	Principal Investigator
PMAA	Premarket authorization application
POQ	Post-operative PROWL questionnaire
PRK	Photoreactive keratectomy
PRQ	Pre-operative PROWL questionnaire
PROWL	Patient reported outcome in laser-assisted in situ keratomileusis
SE	Spherical equivalent
SW	Software
UCNVA	Uncorrected near visual acuity
UDVA	Uncorrected distance visual acuity
UADE	Unanticipated adverse device effect
Z80.11	ANSI Standard – Laser Systems for Corneal Reshaping

NOTE: The first occurrence of some abbreviations is not spelled out in the document (e.g., units of measure).

2. SYNOPSIS

Bausch + Lomb Study #884	
Title:	A Study to Investigate the Effectiveness of the TENEO 317 Model 2 (1.28 US) Excimer Laser for Laser In Situ Keratomileusis (LASIK) Surgery to Treat Myopia or Myopic Astigmatism
Phase of study:	Pivotal IDE Study for Effectiveness
Number of study centers and subjects:	Up to twelve (12) clinical centers in the United States. Approximately 334 subject eyes will be treated with a target of 300 operative (study) eyes completing the study.
Objectives:	To evaluate the effectiveness of the TENEO 317 Model 2 (1.28 US) Excimer Laser in Laser In Situ Keratomileusis (LASIK) surgery for myopia or myopic astigmatism
Indications for use:	Myopia: -1.00 to -10.00 D Astigmatism: 0.0 D to −3.0 D MRSE Treated: -1.0 D to −11.50 D
Study design:	This will be a multicenter, prospective, open label, non-randomized, single arm study evaluating the safety and effectiveness of the Technolas TENEO 317 Model 2 (version 1.28 US software) Excimer Laser when used in LASIK surgery to treat myopia or myopic astigmatism. Both eyes of a subject may be enrolled so long as both eyes meet all inclusion/exclusion requirements. The study purpose, procedures, and subject responsibilities will be explained to the potential participant. The subject's willingness and ability to meet the follow-up requirements will be determined. When it has been established that the subject appears to be eligible and willing to participate, written informed consent (which includes consent to have photo and video recordings of the eye surgery made) will be obtained. Written informed consent will be obtained from each study subject prior to performing any study specific procedures which include items which are NOT part of the Investigator's routine standard of care. In addition, written informed consent must be obtained prior to the day of surgery. A complete ophthalmic examination will be done at the Pre-Operative Visit scheduled within 60 days prior to surgery. All enrolled subject eyes that meet eligibility criteria will be seen according to the following schedule:

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	• Visit 1: Pre-operative (1 to 60 days prior to treatment) • Visit 2: Operative (Day 0) • Visit 3: Initial Post-Op (Day 1) • Visit 4: One Week (Day 5-9) • Visit 5: One Month (3 to 5 weeks post-op) • Visit 6: 3 Months (10 to 14 weeks post-op) • Visit 7: 6 Months (21 to 26 weeks post-op) • Visit 8: 9 Months (35 to 43 weeks post-op) A 180-Day premarket approval (PMA) supplement will be submitted to the US Food and Drug Administration (FDA) when all subjects have exited the study.
Number of Subject Eyes Planned	Sponsor intends to treat approximately 334 eyes, with anticipation to have 300 eyes after a 10% dropout rate evaluable for safety and effectiveness post-LASIK surgery at the time refractive stability is achieved[1] . It is planned to have ≥ 20 subject eyes per dioptric bin (i.e., per column and row for presentation of preoperative refractive error by sphere and cylinder) over the spherical correction range to be studied and ≥30 subject eyes per dioptric bin over the cylinder correction range to be studied. Of the subjects in the -0.25 to -1.0 D astigmatism range, at least 30 eyes are planned in each of the -0.25 to -0.5 D and the -0.5 to -1.0 D astigmatism ranges. (See also **Section 5.2**)
Inclusion Criteria	This study will include subjects who meet all of the following inclusion criteria: 1. Are 22 years of age or older. 2. Have read, understood, and signed an informed consent form (ICF). 3. Have demonstrated stable refraction (i.e., a change of ≤ ± 0.5 D in sphere and cylinder) for a minimum of 12 months prior to surgery verified by consecutive refractions, medical records or prescription history.

[1] Refractive stability for the study cohort is defined as a minimum of 95% of eyes that should have a change of ≤ 1.00 D of manifest refraction spherical equivalent between two refractions performed at least 3 months apart.

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	4. Have myopic refractive error with or without astigmatism; sphere -1.0 D up to -10.00 D, cylinder between 0.0 D and -3.0 D; with a manifest refraction spherical equivalent (MRSE) between -1.0 D and -11.50 D. 5. Have uncorrected distance visual acuity (UDVA) of 20/40 or worse 6. Have manifest, distance best spectacle corrected visual acuity (BSCVA) of 20/25 (logMAR 0.1) or better in an operative eye. 7. Have equal to or less than 0.50 D spherical equivalent (SE) difference between cycloplegic and manifest refractions at Visit 1 (Pre-operative). 8. Have normal corneal topography as determined by the Investigator. 9. Have discontinued use of contact lenses for at least 2 weeks (for hard or toric lenses) or 3 days (for soft contact lenses) prior to the pre-operative examination, and through the day of surgery. 10. All contact lens wearers must demonstrate a stable refraction (within ± 0.5 D), as determined by MRSE, on two consecutive examinations at least 1 week apart, in an eye to be treated and the axis of cylinder should not differ by more than 15 degrees from the baseline cycloplegic refraction. 11. Have the ability to lie flat without difficulty. 12. Are willing and able to comply with the schedule for all post-surgery follow-up visits.
Exclusion Criteria	This study will exclude subjects who meet any of the following exclusion criteria: 1. Subjects for whom the combination of their baseline corneal thickness and the planned operative parameters for the LASIK procedure would result in treatment depth less than 250 microns from corneal endothelium. 2. Eyes for which the baseline manifest subjective refraction exhibits a difference greater than 0.50 D in sphere power, or a difference greater than 0.50 D in cylinder power, or a difference in cylinder axis of more than 15 degrees compared to the baseline cycloplegic subjective

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	refraction. For manifest cylinder of less than 0.50 D, the difference in cylinder axis will not be taken into consideration. 3. Subjects for whom the pre-operative assessment of the cornea indicates that one or both eyes are not suitable candidates for treatment based upon the Investigator's medical judgment. 4. Have evidence of retinal vascular disease. 5. Have a history of or have active corneal disease or infection (e.g., recurrent corneal erosion syndrome, herpes simplex or herpes zoster keratitis, etc.) in either eye. 6. Have a known sensitivity to any study medication. 7. Have central corneal scars affecting visual acuity or unstable keratometry with irregular mires in an eye considered for eligibility. 8. Have keratoconus, subclinical or forme fruste keratoconus, corneal dystrophy or other corneal irregularity (e.g., irregular astigmatism). 9. Have visually significant or progressive cataract in an eye considered for eligibility. 10. Had previous intraocular or corneal surgery in an eye considered for eligibility that might confound the outcome of the study or increase the risk to the subject. 11. Use chronic medications by any administration route that may increase risk to the subject or may confound the outcome of the study, including those known to affect wound healing (e.g., corticosteroids, antimetabolites, etc.). 12. Are known to have acute or chronic disease or illness (e.g., dry eye, cataract, glaucoma, immuno-compromised, rheumatoid arthritis, clinically significant atopic disease, acne rosacea, etc.) that would increase operative risk or confound the results of the study. 13. Are taking medications contraindicated with LASIK such as isotretinoin (Accutane) or amiodarone hydrochloride (Cordarone). 14. Are known to be pregnant, lactating, or who plan to become pregnant during the course of the study.

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	15. Have known sensitivity to medications used for standard LASIK. 16. Have the presence of systemic disease likely to affect wound healing, e.g., autoimmune disease, systemic connective tissue disease, diabetes, or severe atopic disease. 17. Are participating in any other ophthalmic clinical trial within 30 days of screening or during this clinical trial. 18. Have an ocular muscle disorder including a strabismus or nystagmus, or other disorder affecting fixation. 19. Have a history of or evidence of glaucoma or are a glaucoma suspect. 20. Eyes with mesopic pupil size > 7.0 mm. 21. Have a Schirmer's pre-operative test without anesthesia < 4 mm/5 minutes
Planned Study Period and Duration of Treatment	Enrolled subject eyes will undergo LASIK surgery and will be followed for approximately nine months after surgery.
Test Medical Device	Technolas TENEO 317 Model 2 excimer laser is a scanning excimer laser that operates at 193 nm ultraviolet wavelength to photoablate corneal tissue in order to achieve a refractive change.
Study Effectiveness Endpoints	• The percentage of eyes that achieve predictability (attempted versus achieved) of MRSE within ± 0.50 D • The percentage of eyes that achieve predictability (attempted versus achieved) of MRSE within ± 1.00 D • The percentage of eyes targeted for emmetropia that achieve a UDVA of 20/40 or better
Statistical Methods	Continuous measures will be summarized by the mean, standard deviation, median, minimum, and maximum. Categorical and incidence measures will be summarized by both count and percentage. Following multiple imputations of missing data, each primary endpoint will be compared to a corresponding null proportion using a binomial test.
Sample Size Calculation	The study will involve an evaluation of approximately 334 treated eyes at up to 12 investigational sites. A final sample size of at least 300 evaluable study eyes at the final visit (Visit 8, Month 9) will be analyzed. ANSI Z80.11-2012 (R2017) recommends a sample size of

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	300 treated eyes when there is a change to the indication (treatment range); the additional 34 study eyes will allow for losses up to 10% due to early subject discontinuation.

This study will be performed in compliance with ISO 14155, including the archiving of essential study documents. This investigational plan follows guidelines outlined in the U.S. Food and Drug Administration (FDA) guidance entitled *Checklist of Information Usually Submitted in an Investigational Device Exemptions (IDE) Application for Refractive Surgery Lasers dated October 1996*, and elements of the international ANSI standard Z80.11-2012 (R2017) entitled *Laser Systems for Corneal Reshaping* and the ANSI, IEC, and ISO standards referenced therein. All data furnished to the investigator and his/her staff, and all data obtained through this study, will be regarded as confidential and proprietary in nature and will not be disclosed to any third party, except for the FDA or other regulatory body, without written consent from the Sponsor.

3. INTRODUCTION

The Technolas Teneo 317 Model 2 (ver. 1.28 US software [SW]) excimer laser is a scanning excimer laser that operates at the 193 nm ultraviolet wavelength to photoablate corneal tissue and employs a proprietary aspheric ablation profile rather than a conventional "Munnerlyn" ablation profile. By scanning a small diameter beam (1 mm in diameter), the Teneo 317 Model 2 (ver. 1.28 US SW) excimer laser offers the following advantageous features:

- Flexible treatment patterns for the treatment of myopia
- Wide ablation zones (up to 7 mm), and
- A smooth ablation surface

3.1 Epidemiology of Myopia and Myopic Astigmatism and Treatment

Myopia and myopic astigmatism are recognized as serious public health problems, with approximately 2.5 billion people expected to be myopic by the year 2020. [1] There are a number of treatments available for treating myopia and myopic astigmatism, including eyeglasses, contact lenses, surgery, pharmaceutical treatments, and, within the past 25 years in the United States, wide use of refractive surgery (notable, laser in situ keratomileusis [LASIK] surgery). Although anisometropia, predominantly myopia, may occur in young children as early as age 6, refractive surgery in the pediatric population is generally discouraged and LASIK surgery in the United States (US) is not approved by the US Food and Drug Administration for people 18 years of age or younger. The FDA also warns that LASIK surgery may not be appropriate for people in their 20s and younger. [2]

A number of epidemiological studies and clinical studies have reported the demographics of myopia patients. It is recognized that comparisons of data for myopia patients globally is influenced by a number of factors including age, country, sex, race, ethnicity, occupation, environment, life style, and complex genetic factors. [3] The statements in this section are consequently not comprehensive and only intended to indicate general trends that have been seen in selected papers and reviews.

Global studies of myopia patients show some similarities in various regions. In the US, Western Europe, and Australia, the prevalence of myopia of at least -1.0 D in a survey of 29,281 persons 40 years of age and older was estimated as 25.4%, 26.0%, and 16.4% in 2000. [1] In the same survey, patients with at least -5.0 D of myopia (higher myopes) represented 4.5%, 4.6%, and 2.8% of patients. [1] A survey of the prevalence of refractive errors in occupants of Singapore in the Singapore Epidemiology of Eye Disease (SEED) Study, a multiethnic Asian population, gave rates among adults 40 years of age and older similar to that seen for the US, Western Europe, and Australia: 38.9% for myopia, 8.4% for high myopia, and 58.8% for astigmatism. [4]

The gender distribution of myopia patients or myopia patients undergoing LASIK surgery generally favors a similar number of women and men, [4-6] with some reviews contrarily suggesting a preponderance of women over men by prevalence or by patients undergoing LASIK surgery. [1,7] With regards to ethnicity, a 2009 review of Americans between the ages of 12 and 54 years undergoing revealed Asians had the highest prevalence of myopia (18.5%), followed by Hispanics (13.2%), African-Americans (6.6%) and Caucasians (4.4%). [8]

Refractive LASIK surgery patients in large retrospective clinical trials were relatively young in studies done in the UK (mean age 35.6 years), [5] Israel (mean age 29.9 years), [6] and Iran (mean age 29.4 years). [7] There also is a trend for younger myopia patients in the US and Singapore, with myopia rates dropping by decade for both men and women in multiple ethnic groups analyzed. [1,4] However, a necessary condition for refractive surgery is stable refraction, which typically does not occur until 18-22 years of age,[9] which suggests a lower age limit for LASIK patients to be the onset of adulthood.

Most myopia patients undergoing LASIK surgery will likely have some degree of astigmatism ≥ -0.25 cylinder error). In a retrospective study in Iran, 11550 cases of compound myopic astigmatism (≥ -0.25 sphere, ≥ -0.25 cylinder error) were noted, while there were only 827 cases of simple myopia (≥ -0.25 sphere, no cylinder error).[7] In other data on myopic astigmatism, there were increases over time in rates of myopia and astigmatism in the SEED study, [4] with 72% of the increase in the rate of astigmatism due to myopic astigmatism.

In summary, the epidemiology and demographics from large retrospective studies of myopia and myopic astigmatism indicate that LASIK patients in the US are equally likely to be men or women, include adult age groups, and are likely to have both sphere and cylinder refractive error. Although minority populations have a higher rate of myopia in the US, their possible under-representation or even over-representation in this study cannot be predicted without a proper understanding of the demographics of patients serviced by the clinical sites and recruited as subjects for this study. Nevertheless, the present study does not have an adequate sample size to power analyses at this level of demographic stratification.

3.2 History of LASIK:

The first approach to myopic keratomileusis was developed by Barraquer in the 1960s.[10,11] A corneal lenticule was harvested with a microkeratome and then frozen. The frozen lenticule was then reshaped into the desired refractive lenticule with a cryolathe, thawed and sutured in place with an eight-bite anti-torque suture.[11,12] This microkeratome required a great deal of experience to get reproducible results and freezing the lenticule caused death of the keratocytes and in some cases haze in the tissue. Irregular astigmatism and the

potential for a lost lenticule were also problems with the technique.[12,13] Krumeich later attempted a non-freeze keratomileusis but this technique also had variable results and poor predictability.

The development of the automated microkeratome by Luis Ruiz using a non-freeze technique brought reproducibility to the procedure. The technique involved creating two keratectomies. The first keratectomy created a planar cap, which was initially excised from the cornea but later was left hinged to prevent inadvertent loss of the cap. The second keratectomy was also planar and was performed with the same microkeratome by changing the interchangeable plates and adjusting the diameter of the second cut. When the cap was put back in place, it essentially sank into the depression created by the second keratectomy, creating a flatter corneal curvature. This technique is referred to as Automated Lamellar Keratomileusis or ALK.[11,14] The cornea remained clear but there were technical difficulties with the refractive cut. Variability in the refractive keratectomy (second cut) thickness, diameter and centration led to overcorrection, undercorrection, or irregular astigmatism. To achieve the proper refractive keratectomy, the intraocular pressure needed to be above 65 mmHg, otherwise a poor quality keratectomy was achieved. Other variables included microkeratome blade quality, sharpness and width that also affected the predictability of the result.

In 1983, Photorefractive Keratectomy (PRK) using an Argon Fluoride (ArF) Excimer Laser was first suggested by Trokel and Srinivasan.[15-18] In 1992, Burrato used an Excimer Laser in conjunction with ALK by harvesting a cap with the automated microkeratome and treating the stromal surface of the cap with an Excimer Laser and replacing it without the use of sutures.[19,20] In 1994, Brint used Burrato's technique, treating the cap with an Excimer Laser, and in four eyes the ablation was performed in situ.[21] They reported minimal corneal haze, good visual acuity and more predictable results than with a mechanical refractive cut.

In 1991, Pallikaris coined the term LASIK, an acronym which stands for 'Laser In-Situ Keratomileusis', and reported using an excimer laser for LASIK of high myopes.[22] In 1994, he compared the LASIK technique with surface photorefractive keratectomy (PRK) and found in a small series that LASIK created less corneal haze, was more stable and had greater predictability than PRK.[23] Irregular astigmatism was noted in most of the LASIK eyes in the first two weeks but subsided by one month. LASIK also appeared to have the advantage over PRK with visual stabilization occurring earlier, with lesser tendency for regression. The PRK subjects required topical steroids for three months while the LASIK group required them for one month.

In 1992, the scanning spot excimer laser technique for the delivery of laser radiation for photoablation of corneal tissue began to appear in the literature.[24] Results from preclinical tissue studies demonstrated that optical scanning delivery of excimer laser energy produces

smooth and gradual ablations without step-like transition zones, and without thermal damage.[25-28] The FDA approved the first broad-beam excimer laser system for laser assisted in-situ keratomileusis (LASIK) treatment of myopia/myopic astigmatism in 1998,[29] followed by the first scanning spot laser for PRK in 1999 [30] and the first scanning spot laser for LASIK in 2000.[31] Today, virtually all excimer lasers systems used to perform LASIK surgery rely on computer-controlled scanning spot technology.

3.3 Risk/Benefit Analysis of LASIK

The risks of performing LASIK on sighted eyes include improper correction, decrease in BSCVA, glare, halo, foreign body sensations, corneal scarring, corneal ulceration or perforation, intraocular infection, corneal decompensation, persistent corneal edema, hyphema, hypopyon, endophthalmitis, microbial keratitis,[32] cataract, epithelium in the interface, lost / misplaced / misaligned flap, dry eye, or melting of the flap.

Steps taken to mitigate the risks associated with this protocol include

- enlisting only Investigators with prior training and experience in corneal refractive surgery, including experience with: (a) the use of femtosecond laser "flap makers" and (b) laser-assisted in situ keratomileusis (LASIK) ensuring that Investigators review and understand this investigational protocol; and
- monitoring the study for adherence to the protocol and verifying all incidences of adverse effects are reported. During the period when study procedures and/or study sites are interrupted by the COVID-19 pandemic (see Section **7.4.1.1**), monitoring may occur remotely.

The principle benefit of an aspheric LASIK procedure is the potential freedom from or reduced dependence on spectacles (glasses) and/or contact lenses for the correction of refractive error. LASIK may be safer than contact lens wear in the long term.[23] Additional potential benefits include rapid visual recovery and stabilization of refraction, and reduced risk of iatrogenic corneal stromal irregularity due to scanning of small overlapping beam.

4. OBJECTIVE

The primary objective of this clinical investigation is to collect safety and effectiveness data for the Technolas Teneo 317 Model 2 excimer laser for Laser Assisted In-Situ Keratomileusis (LASIK) correction of myopia and myopic astigmatism. It is intended that the results of the study will be submitted to the U.S. Food and Drug Administration (FDA) in a 180-Day premarket approval application (PMA) supplement.

5. STUDY DESIGN

5.1 Justification of Study Design

The TENEO 317 Model 2 excimer laser workstation received CE Mark status in Europe in 2017 and is currently running version 1.28 software (SW). The difference between the EU version 1.28 and the version 1.28 US SW is that the version 1.28 US SW will have software treatment capabilities other than myopic LASIK with or without astigmatism that will be disabled on all Technolas TENEO 317 Model 2 systems to be used in this myopia/myopic astigmatism study.

A retrospective post-CE Mark chart review provides evidence of the safety and effective performance of the TENEO 317 Model 2 excimer laser running PROSCAN ver. 1.27.2 SW for completing LASIK surgeries on myopic eyes with or without astigmatism through 1 month of follow-up with 518 eyes treated at 10 sites in Europe, Middle East and Africa.[33] Of the 518 eyes enrolled in the chart review, 72 eyes had spherical myopia and 446 eyes had myopic astigmatism.

In the chart review report, 93% of subject eyes were 20/20 or better at $\geq$ 1 mo, and 99% were 20/32 or better at $\geq$ 1 mo. Further, 100% of subject eyes had uncorrected distance visual acuity of 20/40 or better post-surgery.

The Technolas TENEO 317 Model 2 aspheric ablation PROSCAN version 1.27.2 software was the subject of a post-market study that demonstrated excellent results for spherical correction and showed a slight under-correction for cylinder. As a result, the laser's internal cylinder conversion factor for the PROSCAN version 1.27.2 software was increased to compensate for cylindrical under-correction, while the spherical correction component remained unchanged. The resulting revised aspheric ablation PROSCAN version 1.28 US software is the subject of this study.

5.2 Description of Study Design

The design of this clinical study is a prospective, open-label, multicenter, non-randomized clinical investigation, where the effects of LASIK in correcting myopia and myopic astigmatism are evaluated by comparing post-operative refraction and visual acuity to standard guidelines. The study treatment range (indication for use) includes up to MRSE -11.50 D.

The study will involve an evaluation of approximately 334 treated eyes at up to 12 investigational sites, with a final sample size of at least 300 study eyes evaluable at the final visit. Every effort will be made to enroll approximately the same number of eyes at each investigational site. The additional 34 study eyes will allow for losses up to 10% due to early subject discontinuation. Both eyes of a subject may be enrolled. Subjects will be permitted to have both eyes enrolled so long as both eyes meet all inclusion/exclusion

requirements. Analyses will include all enrolled eyes treated with the TENEO 317 laser. Enrollment will be limited to subject eyes with sphere of -1.0 D up to -10.00 D, cylinder between 0.0 D and -3.0 D; with a manifest refraction spherical equivalent (MRSE) between -1.0 D and -11.50 D.

Enrolled subjects can possibly attend up to 8 study visits. It is planned to enroll and treat approximately 334 subject eyes, with an expectation that approximately 300 study eyes will complete post-surgical follow-up for 9 months. All subjects, regardless of the time of individually achieving refractive stability, will be followed up until the last study visit (Visit 8) which is Month 9 post-operatively.

For completed subjects, it is planned to have ≥ 20 eyes per each diopter (see Dioptric Bins, **Table 1**) of spherical correction to be studied and ≥ 30 eyes per dioptric bin of cylinder correction to be studied. Of the eyes in the -0.25 to -1.0 D astigmatism range, at least 30 eyes are planned to be in each of the -0.25 to -0.5 D and the -0.5 to -1.0 D astigmatism ranges (see **Table 1**, Bin Table).

A 180-Day PMA supplement application will be submitted to the FDA when the enrolled study cohort has completed approximately 9 months of safety and effectiveness assessments post-surgery (cf. **Appendix A**).

Table 1. LASIK Preoperative "Dioptric Bin" Enrollment Plan

Refractive Error Stratified by Manifest Sphere and Cylinder						
		Cylinder (in minus notation				
	0 Cylinder (Sphere Only)	−0.25 to −0.5 D	−0.51 to −1 D	−1.01 to −2 D	−2.01 to −3 D	Total
Sphere (in minus notation)	n	n	n	n	n	n
−1 to −2 D	> 0	> 0	> 0	> 0	> 0	≥ 20
−2.01 to −3 D	> 0	> 0	> 0	> 0	> 0	≥ 20
−3.01 to −4 D	> 0	> 0	> 0	> 0	> 0	≥ 20
−4.01 to −5 D	> 0	> 0	> 0	> 0	> 0	≥ 20
−5.01 to −6 D	> 0	> 0	> 0	> 0	> 0	≥ 20
−6.01 to −7 D	> 0	> 0	> 0	> 0	> 0	≥ 20
−7.01 to −8 D	> 0	> 0	> 0	> 0	> 0	≥ 20
−8.01 to −9 D	> 0	> 0	> 0	> 0	> 0	≥ 20
−9.01 to −10 D	> 0	> 0	> 0	> 0	> 0	≥ 20
Total	≥3 0	≥ 30	≥ 30	≥ 30	≥ 30	≥ 300

5.2.1 Fellow Eye Treatments

Because unilateral enrollment would result in subjects with a significant degree of anisometropia, and the safety and effectiveness of the TENEO 317 Model 2 excimer laser (ver. 1.28 US SW) specific to the treatment of myopia or myopic astigmatism are supported by retrospective data, bilateral LASIK treatments will be permitted in this study. Both eyes may be enrolled for efficacy and safety assessments if the subject is fully informed that the surgical risks apply equally to each eye. If an intraoperative complication or adverse event occurs in the first eye, treatment must be abandoned in the second eye. Each eye treated according to this protocol for an enrolled subject will be reported on separately and included in the data analysis.

5.2.2 Enhancement and Retreatment Procedures

If the treated eye remains under-corrected and/or corneal haze or vision regression decreases to UDVA of 20/30 or worse, then an enhancement or retreatment may be performed. No enhancement or retreatment may be performed before a subject exits the study.

5.2.3 Description for Use of Pre-vs-Post Subjective Patient Questionnaire (PROWL)[34-37]

The pre-operative and post-operative PROWL (Patient Reported Outcomes with LASIK) questionnaires were developed and validated to sample patient impressions of LASIK surgery adequacy for improved vision and activities such as night driving, sports, etc. dependent on good patient vision. Select PROWL questions and domains will be analyzed for this study, not the PROWL-PRQ and PROWL-POQ questionnaires in their entirety. However, the entire PROWL questionnaires are included in this study since they were validated as such.[36,37] PROWL questions and domains relating to subject subjective preoperative and postoperative impressions of their LASIK surgery[36,37] (including clusters of questions or domains for vision clarity, far vision, near vision, patient satisfaction with vision and with surgery, and quality of life) and patient-perceived safety assessments (i.e., driving, dry eye [OSDI domains 1 and 3],[38,39] and the frequency, severity, and bothersomeness of visual symptoms) will be analyzed as described in **Section 8.5** and **Section 9.6.3.3.1** and by the methods and respective scoring methodologies for each of the above domains as detailed in the study Statistical Analysis Plan. The PROWL questionnaires[34, 35] should be completed by the study subject in a secluded area, free of directions from clinical staff.

5.3 Selection of Study Population

5.3.1 Eligibility[40, 41]

5.3.1.1 Inclusion Criteria:

1. Are 22 years of age or older.
2. Have read, understood, and signed an informed consent form (ICF).
3. Have demonstrated stable refraction (i.e., a change of ≤ 0.5 D in sphere and cylinder) for a minimum of 12 months prior to surgery, verified by consecutive refractions and/or medical records or prescription history.
4. Have myopic refractive error with or without astigmatism; sphere between -1.0 D and -10.00 D, cylinder between 0.0 D and -3.0 D; with a manifest refraction spherical equivalent (MRSE) between -1.0 D and -11.50 D.
5. Have uncorrected distance visual acuity (UDVA) of 20/40 or worse.
6. Have manifest best spectacle corrected distance visual acuity (BSCVA) of 20/25 (logMAR 0.1) or better in an operative eye.
7. Have less than or equal to 0.50 D spherical equivalent (SE) difference between cycloplegic and manifest refractions at Visit 1 (Pre-operative).
8. Have normal corneal topography as determined by the Investigator.
9. Have discontinued use of contact lenses for at least 2 weeks (for hard or toric lenses) or 3 days (for soft contact lenses) prior to the pre-operative examination, and through the day of surgery.
10. All contact lens wearers must demonstrate a stable refraction (within ± 0.5 D), as determined by MRSE, on two consecutive examinations at least 1 week apart, in an eye to be treated and the axis of cylinder should not differ by more than 15 degrees.
11. Have the ability to lie flat without difficulty.
12. Are willing and able to comply with the schedule for all post-surgery follow-up visits.

5.3.1.2 Exclusion Criteria:

1. Subjects for whom the combination of their baseline corneal thickness and the planned operative parameters for the LASIK procedure would result in treatment depth less than 250 microns from corneal endothelium.
2. Eyes for which the baseline manifest subjective refraction exhibits a difference greater than 0.50 D in sphere power, or a difference greater than 0.50 D in cylinder power, or a difference in cylinder axis of more than 15 degrees compared to the baseline cycloplegic subjective refraction. For manifest cylinder of less than 0.50 D, the difference in cylinder axis will not be taken into consideration.

3. Subjects for whom the pre-operative assessment of the cornea indicates that one or both eyes are not suitable candidates for treatment based upon the Investigator's medical judgment.
4. Have evidence of retinal vascular disease.
5. Have a history of or have active corneal disease or infection (e.g., recurrent corneal erosion syndrome, herpes simplex or herpes zoster keratitis, etc.) in an eye.
6. Have a known sensitivity to any study medication.
7. Have central corneal scars affecting visual acuity or unstable keratometry with irregular mires in an eye considered for eligibility.
8. Have keratoconus, subclinical or forme fruste keratoconus, corneal dystrophy or other corneal irregularity (e.g., irregular astigmatism).
9. Have visually significant or progressive cataract in an eye considered for eligibility.
10. Had previous intraocular or corneal surgery in an eye considered for eligibility that might confound the outcome of the study or increase the risk to the subject.
11. Use chronic medications by any administration route that may increase risk to the subject or may confound the outcome of the study, including those known to affect wound healing (e.g., corticosteroids, antimetabolites, etc.).
12. Are known to have acute or chronic disease or illness (e.g., dry eye, cataract, glaucoma, immuno-compromised, rheumatoid arthritis, clinically significant atopic disease, acne rosacea, etc.) that would increase operative risk or may confound the results of the study.
13. Are taking medications contraindicated for LASIK such as isotretinoin (Accutane) or amiodarone hydrochloride (Cordarone).
14. Are known to be pregnant, lactating, or who plan to become pregnant during the course of the study.
15. Have known sensitivity to medications used for standard LASIK.
16. Have the presence of systemic disease likely to affect wound healing, e.g., autoimmune disease, systemic connective tissue disease, diabetes, or severe atopic disease.
17. Are participating in any other ophthalmic clinical trial within 30 days of screening or during this clinical trial.
18. Have an ocular muscle disorder including a strabismus or nystagmus, or other disorder affecting fixation.
19. Have a history of or evidence of glaucoma or are a glaucoma suspect.
20. Have eyes with mesopic pupil size > 7.0 mm.
21. Have a Schirmer's pre-operative test without anesthesia < 4 mm/5 minutes

Subjects failing to meet eligibility criteria prior to scheduling of surgery are considered screen failures.

5.3.2 Subject Enrollment

The subject must satisfy all eligibility criteria prior to enrollment. The subject is considered enrolled in the study at the time they sign the informed consent form (which includes consent to have photo and video recordings of the eye surgery made), with the study eye selected by the Investigator at the first study visit (Pre-operative). It is understood the number of subject eyes enrolled at the first study visit may be slightly more than the target number of 334 treated eyes.

5.3.3 Subject Completion

The subject has completed the entire study when the LASIK refractive surgery has been completed and the Sponsor receives completed eCRF documentation for all required visits and a study exit eCRF. Subjects who require further follow-up for an AE will be followed until the AE has resolved or remitted, **regardless of whether they have completed all study visits.**

A Study Exit eCRF must be completed for all subjects who complete or are early discontinued from the clinical investigation.

5.3.4 Subject Discontinuation

A subject MAY discontinue prior to the final study visit due to an AE occurring during the study which requires further medical intervention. A subject MUST be discontinued prior to the final study visit if they voluntarily withdraw for any reason, it is the Investigator's decision that it is not in the best medical interest of the subject to continue participation in the study, or in the event of death of the subject.

Prior to discontinuing a subject who voluntarily withdraws, every effort should be made to contact the subject, schedule a final study visit, and obtain as much follow-up data as possible. Regardless of the patient voluntary withdrawal, adverse events should continue to be followed by the investigator until they have resolved or remitted. Subject withdrawals will be documented clearly on the source document and applicable eCRF.

Discontinued subjects who withdraw consent should be followed outside of the study protocol according to the Investigator's normal post-operative standard of care.

A Study Exit eCRF must be completed for all subjects who discontinue from the clinical investigation. The reasons for subject withdrawal and discontinuation of any subject will be documented clearly on the applicable eCRF and recorded.

Subjects who discontinue the study prior to the surgical procedure will be considered screen failures and will not be recorded on the eCRF. Subjects who are discontinued during/after study LASIK surgery will not be replaced.

5.3.5 Lost to Follow-up

Subjects who do not return for the final visit, as defined by the visit window, and cannot be contacted, may be considered lost to follow-up. Subjects who do not return for the final visit will have at least 2 documented attempts made to contact the subject by telephone or email. If all other attempts fail, a certified, return receipt requested letter will be sent to the last known address.

All follow-up attempts will be documented and documentation will be kept with the subject's source documents, and the applicable eCRFs will be completed. Documentation of the contact attempts and, if appropriate, a copy of the certified letter will be maintained in the subject's study file. It is expected that lost to follow-up subjects will comprise < 10% of all study eyes.

The exit date for subjects who are lost to follow-up will be the date of the last study visit (scheduled or unscheduled) attended by the subject.

5.4 Investigators

The clinical trial will be conducted at up to 12 investigational sites located in the US. The study will be conducted by Investigators who are determined by the Sponsor to be suitably qualified by training and experience to conduct this study. Such training and experience should comply with the international standard ISO 14155-2011 "Clinical Investigation of Medical Devices for Human Subjects - Good Clinical Practice" (ISO GCP) and FDA/CDRH Medical Device Regulations.

A TPV Engineer in conjunction with the Bausch & Lomb Training Team, will conduct Physician and staff training at each site on the operation and use of the TENEO 317 Laser. In addition, the Training team will be on site for the initial few surgeries to guide and support the PI and study staff on the use of the equipment. Training will be conducted as per TPV specifications, in line with the TENEO 317 model 2 user manual and a technical and medical In-Service checklist, and culminating with a Certificate of Training, with training recorded on the Site Training Log. The Physician and staff also will be trained through the Study Reference Manual which speaks to training on procedures, subject discontinuation, reporting of AEs and protocol deviations.

In addition, the Sponsor reserves the right to temporarily suspend or prematurely discontinue this study either at a single site or at all sites at any time and for any reason. If such action is taken, Sponsor will discuss this with the investigator (including the reasons for taking such action) at that time. Sponsor will promptly inform all other investigators and/or institutions conducting the study if the study is suspended or terminated for safety reasons and will also inform the regulatory authorities of the suspension or termination of the study and the reason(s) for the action. If required by applicable regulations, the investigator must inform the IRB/IEC promptly and provide the reason for the suspension

or termination. Each investigative site should enroll a minimum of 20 subject eyes and no more than 15% of total enrollment. Efforts will be made by the Sponsor and the administrating CRO to ensure approximately the same number of eyes will be enrolled at each clinical site.

5.5 Study Duration

Eligible subject eyes that are enrolled into the study will be seen for approximately 9 months after LASIK refractive surgery.

5.6 Protocol Amendments and Follow-up of the Protocol

The content and data of this protocol have been reviewed and accepted by the Sponsor. If an amendment is needed, this will be added by the Sponsor. All amendments will be recorded with the justification of changes to the protocol.

6. STUDY MATERIALS

6.1 Description of Test Medical Device

Like its parent device (Technolas 217z Excimer Laser System), the TENEO 317 Model 2 (ver. 1.28 US SW) Excimer Laser Workstation is an ophthalmologic system based on excimer laser technology used for refractive surgery that offers very precise pre-programmed ablation patterns to reshape the cornea of the human eye. The TENEO 317 Model 2 (ver. 1.27.2 SW EU) received CE Mark approval in Europe in 2017. The TENEO 317 Model 2 (ver. 1.28 US SW) excimer laser employs optical scanning technology operating at 193 nm ultraviolet wavelength to photo-ablate corneal tissue and imparts a proprietary aspheric ablation profile. The TENEO 317 Model 2 system employs a small laser spot (1 mm diameter), a randomized laser spot targeting pattern at 500 Hz, and a beam fluence of 200 mJ/cm^2. Three different auxiliary lasers are used in the TENEO 317 Model 2 in order to assist the surgeon in aiming the treatment beam correctly on the eye to be treated. Since the excimer laser emits in the invisible UV range at a wavelength of 193 nm, an aiming laser (aiming beam) consisting of a red diode laser is coupled coaxially with the treatment beam. Additionally, there is a fixation laser which is a red flashing laser diode that provides a fixation target for the subject eye during the surgery. A focusing laser which is generated by a green diode laser serves to align the treatment level. Other main features of TENEO 317 Model 2 (ver. 1.28 US SW) excimer laser are:

- Flying Spot technology provided by scanner systems for maximum flexibility in personalized treatment profiles.
- Short treatment times by 500 Hz technology with 1 mm laser spots.
- Precision for positioning of the laser pulse due to state of the art dynamic rotational eye tracking and z-axis tracking.

- Standard treatment with an asphericity algorithm taking into account the pre-operative asphericity of the cornea and the surgically induced spherical aberration.

Other hardware modifications have been made to the TENEO 317 Model 2 Excimer Laser System as compared to the approved Technolas 217z Excimer Laser System and these modifications have been tested and verified in a series of non-clinical studies conducted to verify design output meets the design input requirements.

6.2 Instructions for Use and Administration

The TENEO 317 Model 2 (ver. 1.28 US SW) excimer laser will be used to perform all myopia and myopic astigmatism LASIK procedures during this study and use instructions are described in detail in **Appendix C** of this investigational plan. The graphical user interface (GUI) for the investigational 1.28 US SW can only present treatments for spherical myopia and myopic astigmatism indications. All other indications for use are disabled, are not visible as potential treatment options, and cannot be enabled by an end user.

The TENEO 317 Model 2 (ver. 1.28 US SW) excimer laser system alignment verification for laser spot accuracy and cylinder axis alignment will be done upon installation of the TENEO 317 Model 2 excimer laser and again at intervals detailed in the Instructions for Use for the laser system found in **Appendix C**.

All Investigators will be provided with detailed instructions on configuring the laser system; control of environmental conditions during LASIK surgery including humidity and temperature parameters and control; specification of auxiliary surgical devices to be used (see Section 6.3 and **Appendix B**); and pre-operative measurements to be taken to develop the customized treatment plan for each subject. All in-clinic pre-operative procedures, operative procedures (including LASIK surgeries), and post-operative procedures during the COVID-19 pandemic will be conducted in accordance with medical guidance to reduce risk of COVID-19 transmission between study staff and subjects (available at **www.aao.org/covid-19**). Local, state, and federal public health guidances also will be followed during the COVID-19 pandemic (see Sections **7.1.3.5**, **7.1.4**, **7.1.5**, **7.4.1.1**, and **7.4.1.2** for additional information related to trial conduct changes during the COVID-19 pandemic to be implemented to insure subject safety and well-being as well as data integrity).

Note: Measurements also will be taken upon the device installation to ensure that illumination levels that reach the retina (i.e., due to aiming beams, fixation lights, microscope illumination, or secondary radiation from the treatment beam) are held as low as possible. Illumination levels for the operation microscope shall conform to the limits set

by ISO 10936-2 and for other illumination sources to the limits for non-exempt instruments set by ANSI standard Z80.36.

6.3 Other Materials

6.3.1 Essential Equipment Supplied by the Clinical Site

6.3.1.1 Any commercially available femtosecond laser may be used to create corneal flaps prior to performing the LASIK procedure with the TENEO 317 Model 2 (ver. 1.28 US SW) excimer laser. The method of flap production and the make and model of the system used will be recorded in the CRFs.

6.3.1.2 Investigators may use any commercially available corneal topographer to obtain corneal curvature, asphericity and pachymetry measurements of subject eyes. The make and model of the system used will be recorded in the CRFs.

6.3.2 Materials Provided by the Sponsor

6.3.2.1 ETDRS Charts for manifest refraction and visual acuity testing at 40 cm and 4 meters for left and right eyes will be provided by the Sponsor if the Investigator does not have these charts.

6.3.2.2 Specular microscopes will be provided by the Sponsor to three or more clinical sites if an Investigator does not have one. The same make and model of specular microscope will be used for an endothelial cell density sub-study at each of the three or more clinical sites.

6.3.2.3 A commercially available contrast sensitivity measurement device capable of evaluating binocular mesopic (3.0 ± 2.0 cd/m^2) contrast sensitivity with and without glare at spatial frequencies of 1.5, 3, 6, and 12 cycles per degree (cpd) will be provided by the Sponsor to three or more clinical sites

6.3.2.4 Pupillometer capable of measuring photopic and mesopic pupil size by infrared means. A Colvard or Neuroptics infrared pupillometer is preferred

7. STUDY METHODS

7.1 Study Visits

All subjects will be followed for approximately 9 months unless the subject is discontinued early from the investigation. **Appendix A** provides a chart identifying the examination schedule and required parameters for assessment. Subject visits are scheduled to occur at the following intervals:

Visit 1 (Pre-operative Visit) Days -60 to -1

Visit 2 (Operative Visit)	Day 0
Visit 3	Day 1 post-operative
Visit 4	One Week (Day 5 to 9 post- operative)
Visit 5	One Month (Week 3-5 post-operative)
Visit 6	3 Months (Week 10-14 post-operative)
Visit 7	6 Months (Week 21-26 post-operative)
Visit 8	9 Months (Week 35-43 post-operative)

If the subject should return at any time other than the protocol-prescribed scheduled visits, the visit will be documented as an unscheduled visit. All visits, scheduled or unscheduled, must be reported to the Sponsor on the appropriate Case Report Forms (CRF).

7.1.1 Pre-operative Visit 1 – Day -60 to -1

Following identification of a potential subject, the Investigator (or designee) will explain the purpose of the study, study procedures, risks/benefits, and study responsibilities to the potential subject. The subject's willingness and ability to meet the follow-up requirements of the study will be determined. Patients that appear to be eligible will be approached for study participation and sign a written Informed Consent Form (ICF) prior to the commencement of study related procedures. The written ICF includes an addendum section that provides subject consent to have photo and video recordings of the eye surgery made. Written informed consent will be obtained prior to the Investigator performing study specific procedures that are NOT part of his/her routine standard of care.

The subject or his/her legal representative and the person obtaining written consent will sign and date the IRB/IEC approved ICF. The original signed document will be retained in the subject records, and a copy will be provided to the subject. Subjects will be given ample time to review the ICF before signing it.

In addition, the applicable privacy regulation requirements must be met (e.g. Health Insurance Portability and Accountability Act [HIPAA] authorization). Research subjects treated at clinical sites located in areas that have additional local requirements will be provided with the required additional local information (e.g. local Bill of Rights).

After providing written informed consent, prospective subjects will be screened to determine whether they meet the entry criteria for the study. Ocular medications used for the study eyes will be documented in the subject source document and the appropriate eCRF, and demographic information will be collected. The pre-operative clinical evaluation will consist of a complete ophthalmic examination conducted at least one but no more than 60 days prior to surgery and will consist of the following:

- Informed Consent Form completion
- Review of inclusion/exclusion criteria

- Pre-operative PROWL questionnaire [34]
- Subject demographics
- Subject medical history
- Subject ocular history
- History of contact lens wear
- Pupil size (mesopic)
- Manifest refraction (sphere/cylinder/axis)
- Keratometry
- Specular microscopy (endothelial cell density sub-study)
- Corneal topography
- Uncorrected Near Visual Acuity (UCNVA), photopic conditions
- Uncorrected Distance Visual Acuity (UDVA), photopic conditions
- Distance Best Spectacle-Corrected Visual Acuity (BSCVA), photopic conditions
- Slit lamp examination
- Contrast sensitivity sub-study, mesopic conditions
- Schirmer's test without anesthesia
- Pachymetry
- Manifest refraction under cycloplegia
- Intraocular pressure (Tonometry)
- Dilated fundus exam (vitreous, optic nerve, retina, macula, cup/disc)

7.1.2 Operative Visit 2 – Day 0

Subjects will return to the clinic and be reassessed to confirm eligibility (i.e., confirm that there have been no changes since the Pre-Operative Visit that would make the subject ineligible). If the subject is no longer eligible or is unable to attend Operative Visit 2 within specified visit interval due to the impact of the COVID-19 pandemic, the subject must be discontinued (refer to **Section 5.3.4** and **Section 7.4.1.2**). If the subject is eligible, surgery will be performed using the surgical procedure described in **Appendix C**. If Operative Visit 2 was impacted by COVID-19, the subject may be rescreened for eligibility so long as the inclusion/exclusion requirements of **Section 5.3.1.1** and **Section 5.3.1.2** are met.

7.1.2.1 Ocular Medications

Ocular medications used for eyes of enrolled subjects and any AEs must be documented in the subject source document and reported as appropriate.

7.1.2.2 Surgical Technique

Eligible subjects will undergo a LASIK surgical procedure with the TENEO 317 Model 2 (ver. 1.28 US SW) excimer laser device on one or both eyes. In no case should a concurrent bilateral procedure be attempted if there are problems or complications during the surgical procedure for the initial subject eye. The minimum diameter of the optical zone, the degree

of myopia and the magnitude and axis of the astigmatic correction are all determined by the surgeon based on the subjective manifest refraction and mesopic pupil size. The typical optical zones used for TENEO 317 Model 2 (1.28 US) laser treatments of myopia or myopic astigmatism performed outside of the US have been approximately between 6.0 mm and 7.0 mm; however, the 1.28 US software will permit treatments of mesopic pupil sizes within the range of 4.5 mm to 7.0 mm. Operator attempts to enter an OZ size outside this range results in a prompt, "out of range". **If the corneal flap created is smaller than the treatment zone size, the procedure will be cancelled.** The default treatment parameters (K = 43.3 D, Q = -0.20), not the measured pre-operative keratometry (K) and asphericity (Q) values, will be manually entered into the Teneo 317 Model 2 (ver. 1.28 US SW) excimer laser system. This information is used to develop a laser ablation pattern that removes tissue based on an aspheric algorithm, and additional peripheral tissue removal necessary to achieve the desired post-operative corneal surface asphericity.

Treatment plans for all eyes undergoing LASIK surgery are strongly recommended to be targeted for emmetropia

For expected residual postoperative cylindrical refractive error of ≥ 1.0 D or spherical refractive error of ≥ 2.0 D, the subject should be given the opportunity to experience his/her best spectacle vision with anticipated correction only and be willing to proceed with the surgery.

Details of the surgical technique are described in **Appendix C**.

7.1.2.3 Operative Report

The following information is to be obtained intraoperatively and recorded for all enrolled eyes (i.e., first or both eyes):

- Operative eye
- Treatment type
- Targeted refractive outcome
- Optical zone
- LASIK ablation (anticipated residual corneal thickness following LASIK surgery)
- Central and maximum ablation depth
- Type of femtosecond laser, anticipated flap thickness and diameter
- Operative lamellar / ablation complications
- Procedure aborted (if applicable)
- Recording of adverse events

7.1.2.4 Immediately Post-Surgery

The treated eyes are managed with medications (e.g., topical antibiotics, analgesic and anti-inflammatory drops, and any other medicines prescribed at the physician's discretion),

bandage contact lens, and/or punctal plugs as per the treating physician's usual regimen. The subject is instructed to return in 24 hours to begin post-operative evaluations.

7.1.3 Post-operative Visits – Days 1 to Month 9

Subjects will be followed for six (6) post-operative visits. Recording of ocular medications used for subject eyes enrolled and any AEs or complications/possible AEs in the subject source document and appropriate eCRF must be continued throughout the course of the study. Each eye that is enrolled is examined independently.

The following measures are to be included at the follow-up in-clinic examinations for all treated eyes of participating subjects. If a subject cannot receive timely safety assessments due to the COVID-19 pandemic, protocol deviations will occur and the processes described in **Section 7.1.3.5** and **Section 7.4.1.2** are to be followed until such time as the subject can be seen at an in-clinic visit and planned examinations can occur within the appropriate visit windows (see **Appendix A**):

7.1.3.1 Day 1 Post-operative **– Visit 3**

- AE and complication/possible AE recording, all treated eyes
- Any change in Concomitant Medications
- UCNVA and UDVA, photopic conditions
- Slit lamp examination

7.1.3.2 Week 1 Post-operative (all enrolled eyes) **– Visit 4**

- AE and complication/possible AE recording, all treated eyes
- Any change in Concomitant Medications
- Manifest refraction (sphere/cylinder/axis)
- UCNVA, UDVA and BSCVA, photopic conditions
- Slit lamp examination

7.1.3.3 Month 1 Post-operative (all enrolled eyes) **– Visit 5**

- AE and complication/possible AE recording, all treated eyes
- Any change in Concomitant Medications
- Corneal topography
- Manifest refraction (sphere/cylinder/axis)
- UCNVA, UDVA and BSCVA, photopic conditions
- Slit lamp examination
- Tonometry

7.1.3.4 Months 3, 6, 9 Post-operative (all enrolled eyes) – Visits 6, 7, and 8[2]

- Post-operative PROWL questionnaire [35]
- AE and complication/possible AE recording, all treated eyes

[2] Further details for the study visits and procedures can be found in **Appendix A** and **Appendix B**.

- Any change in Concomitant Medications
- Manifest refraction (sphere/cylinder/axis)
- Specular microscopy sub-study (only at Month 6)[3]
- Corneal topography
- Mesopic pupil size
- UCNVA, UDVA and BSCVA, photopic conditions
- Slit lamp examination
- Contrast sensitivity sub-study, mesopic conditions (only at Month 6)[3]
- Schirmer's test without anesthesia (only at Month 6)
- Pachymetry (only at Month 6 as needed)
- Tonometry
- Dilated fundus examination (only required if loss of BSCVA from pre-op BSCVA)

7.1.3.5 Mitigation of COVID-19 Related Disruption to In-Clinic Visits

Due to the impact of the COVID-19 pandemic on clinical trial conduct (see Section **7.4.1.1** for description), a Telephone Contact is to be instituted by the practice if possible to collect any relevant safety data on health and medication changes in the event the subject was unable to visit the office for a scheduled follow-up visit. The option of using telemedicine contacts during an in-window period for a subject rather than a clinic visit will be with the best judgment of an Investigator in light of prioritizing subject safety as well as adherence to local, state, and federal guidelines related to COVID-19 and guidance from national professional ophthalmic organizations including the American Academy of Ophthalmology and the American Society of Cataract and Refractive Surgeons.

The Telephone Contact acts as a substitution for the in-clinic protocol visit when there is a COVID-19 related disruption inhibiting standard visit completion. The Telephone Contact will limit the remote data collection to safety oversight and medication changes and will be recorded on the Protocol Specific Visit eCRF.

All subjects who have had a recent Telephone Contact in-window (for a visit that would have been missed due to COVID-19 disruption), will be notified to visit the site, albeit OOW, to complete their missed visit assessments if possible. When possible, the above assessments will be conducted out of window at a clinical site (due to the COVID-19 pandemic disruption) as though they were in window, so long as they occur prior to the opening of the window of the next planned study visit. If an out of window visit due to the COVID-19 pandemic cannot occur before the next study visit window, the study visit will be considered missed (see **Section 7.1.5**).

This OOW study visit to complete the missed assessments will now be recorded as an Unscheduled Visit (see Section **7.4.1.2** for further explanation about conduct and recording of out of window study visits during the COVID-19 pandemic). In the event an OOW

[3] Preoperative and Month 6 (Visit 7), conducted at three or more sites.

Unscheduled Visit is completed while COVID-19 restrictions were in place, there will not be a requirement for a Telephone Contact.

All subjects, regardless of the time of individually achieving refractive stability, will be followed up until the last study visit (Visit 8) which is Month 9 post-operatively. Upon completion of Visit 8, all subjects will be exited from the study.

7.1.4 Unscheduled Visits

Additional visits may be scheduled, as necessary, to ensure the safety and well-being of subjects. If the subject should return at any time other than the protocol prescribed reporting intervals, the visit will be documented as an Unscheduled Visit. All additional eye examinations should be fully documented in the source documents and on Unscheduled Visit eCRFs, as appropriate. Data from any additional visits within a scheduled visit interval will be captured on Unscheduled Visit eCRFs.

Visits intended to fulfill scheduled visit requirements that fall outside the designated scheduled visit interval, including those due to COVID-19 related disruption, are considered Unscheduled Visits and will be collected and transcribed on the unscheduled visit eCRFs.

7.1.5 Missed Visits

If a subject misses any scheduled follow-up visit and cannot be seen prior to the start of the visit interval for the next scheduled follow-up visit, the visit is considered missed. A visit would be considered a Missed Visit if neither a Telephone Contact nor an OOW Visit to complete the assessments was performed.

7.2 Study Completion

Bausch + Lomb or its representative will notify the Investigators when to contact the IRB to inform them that the study is complete.

7.2.1 Early Study Termination

If during the study the Sponsor determines that the study should be stopped prematurely, the study will be terminated or suspended, and appropriate notification will be given to the Investigator(s), IRB and FDA, as applicable. Bausch + Lomb or its representative will instruct the Investigators to stop the study treatment, to assure appropriate therapy and follow-up for the subjects, and to arrange for study closeout at each site as appropriate.

7.3 Concomitant Medications/Therapy

The Investigator may use any medications or treatment that is judged necessary, appropriate, and beneficial to the subject.

Documentation of all medications used by the subject during this study for the treatment of operative eyes (with the exception of the surgeon's standard regimen for pre-, intra- and post-operative medications) will be made on the appropriate sections of the eCRFs.

7.4 Protocol Deviations

As required under §21 CFR 56.108(a)(3)&(4), an Investigator should notify the Sponsor and reviewing IRB of any deviation from the investigational plan intended to protect the life or physical well-being of a subject in an emergency. The date of and reason for protocol deviations will be documented in all cases. Significant or major protocol deviations affecting the safety, rights, and welfare of the subject or the integrity of the study must be reported by the Investigator to the IRB immediately. Reporting of all other protocol deviations must adhere to the requirements of the governing IRB.

Protocol assessments will continue until the end of the study, unless the protocol deviations put the subject at risk or the subject's condition requires that he/she should be discontinued from the study.

7.4.1 Protocol Deviations During COVID-19 National Health Emergency

7.4.1.1 Introduction

On January 31, 2020, the United States Secretary for the Department of Health and Human Services (DHHS) declared a public health emergency because of the global spread of coronavirus SARS-CoV-2 infections, also known as the coronavirus infectious disease 2019 (COVID-19). On March 11, 2020, the World Health Organization declared COVID-19 to be a pandemic. Shortly thereafter, on March 13, 2020, the President of the United States declared a National Health Emergency because of the COVID-19 pandemic. The US Food and Drug Administration issued guidance for the conduct of clinical trials during the COVID-19 pandemic and on March 19, 2020, the American Academy of Ophthalmology recommended that all ophthalmologists only provide urgent or emergent care.

On March 24, 2020, the study CRO at the request of the Sponsor sent a letter to all clinical sites to stop enrollment for the 884 study. The letter notified the clinical site Investigators that the Sponsor is suspending #884 study enrollment and asked the Investigators to cancel any pending treatments until further notice. For site questions regarding currently-enrolled and treated subjects, the site staff was made aware the Sponsor was available to support them, as was the Medical Monitor. For study subjects already treated, the Investigators were asked to keep detailed documentation, including annotation of the subjects' medical record and case report form, when connecting with study subjects and following reporting requirements of any protocol deviation related to COVID-19 (see Section **7.4.1.2**).

7.4.1.2 Guidance for Protocol Deviations Related to COVID-19 Pandemic

Because all study #884 clinics paused study-related activities for 7 weeks or more following guidance from the US government relating to the COVID-19 pandemic, the Sponsor provided:

- guidance to the study Investigators on how to handle the halt in enrollment and management of in-clinic study visits and an alternative if a subject is unable to visit the clinic.
- an addendum for how to complete the eCRF in response to the limited data collection or visits impacted by the COVID-19 pandemic,
- a unique template for telephone contacts during the COVID-19 pandemic,
- an example for completing the protocol deviation form with COVID-19 disruption information, and
- subject contact verification log to record the confirmed contact method and date to inform all active subjects of the COVID-19 impact on the study.

The Sponsor will require that all out of window visits as described in Section 7.1.4 make use of the above tools and be reinterpreted to account for any delayed Visits and in office assessments due to the COVID-19 pandemic disruption according to the following guidance:

- If the patient is unable to visit the practice in the designated protocol window, a Telephone Contact (TC) will be made if possible to collect health changes and medication changes. A TC status form will be initiated, and a Protocol Deviation will be filled out for the TC with the reason being due to COVID-19 disruption if applicable.
- Visits intended to fulfill protocol visit requirements that fall outside the designated scheduled visit interval due to the inability of the patient to be seen in the office will now be collected and all assessments that were intended to be completed in-window will be done and the data transcribed on the Unscheduled Visit eCRF.
- The Telephone contact will limit the remote data collection to safety oversight and medication changes and will be recorded on the Protocol Specific Visit eCRF A Protocol Deviation will no longer be recorded for the Unscheduled Visit (with the reason being “due to COVID-19 disruption” if applicable). All out of window visit data (COVID related and otherwise) will now be recorded on the Unscheduled Visit eCRF.

Any out of window study visits occurring during the COVID-19 pandemic and after the clinic of an Investigator is allowed to reopen for non-essential study visits and surgery according to the current rules and regulations of the Investigator’s state, the FDA, and the DHHS will be processed as described in Sections 7.1.3-7.1.5 and associated protocol

deviations during the COVID-19 pandemic will be processed as described in Section 7.4 or this Section as appropriate.

8. ADVERSE SAFETY EVENTS

Each eye treated must be examined for the presence or absence of adverse safety events at all visits, whether scheduled or not. The collection of safety events begins at the time the subject signs the informed consent form. Refer to Table 2 for instructions on events that require expedited reporting to the Sponsor.

For the purposes of this study, adverse safety events are defined broadly to include a range of events encompassing four hierarchical categories of risk, Adverse Events (AE), Unanticipated Adverse Device Effects (UADE), Complications/Potential Adverse Events, and Symptoms, each having an associated level of required CRF/IRB/Sponsor/FDA reporting (See **Table 2**Table 2. Safety Event Reporting, "Safety Event Reporting").

The first category, AEs, represents the key safety events that are surveilled during the study (**Section 8.1**). The second category (**Section 8.2**), UADEs, represent rare unanticipated safety events directly attributable to the device.

Table 2. Safety Event Reporting

	Symptoms	Complications/ Possible AEs	Adverse Events	UADEs
Required Action	Recorded in Subject Questionnaires	Recorded in Postoperative CRFs	Record in AE CRF within 48 hours	Record in AE CRF and on UADE form within 48 hours
			Investigator Reports to IRB per IRB policy	Investigator reports to IRB within 10 working days or per IRB policy, whichever is shorter
				Sponsor reports to FDA, all IRBs and all Investigators within 10 working days of Sponsor notification

.

Tertiary safety events include anticipated Complications/Possible Adverse Events known to occur following laser refractive surgery (**Section 8.4**), and subjective Symptoms reported by subjects (**Section 8.5**).

A representative list of safety events that are associated with each risk category are summarized in **Sections 8.1–8.5** below:

8.1 Adverse Events

An adverse event (AE) as defined in ISO standard 14155 is "*any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device*."

The following AEs are the key safety events surveilled during the study. Each occurrence of these AEs must be reported to the Sponsor by recording in the AE CRF within 48 hours, and in addition, must be reported to the IRB per IRB policy (See **Table 2**).

- Loss of > 2 lines (10 letters) BSCVA
- BSCVA worse than 20/40
- BSCVA worse than 20/25 if 20/20 or better preoperatively
- Haze ≥ trace with loss of BSCVA > 2 lines (10 letters)
- Increased manifest refractive astigmatism > 2.0 D
- Corneal epithelial defect involving the keratectomy at one month or later
- Melting of the flap
- Miscreated flap (lost, incomplete, too thin)
- Diffuse lamellar keratitis (Grade 3 or above) [42]
- Corneal infiltrate or ulcer
- Any persistent corneal epithelial defect at one month or later
- Epithelium in the interface with loss of 2 lines (10 letters) or more best spectacle corrected visual acuity (BSCVA)
- Intraocular Pressure (IOP) with increase of >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 or greater (≥ 10 letters ETDRS) of BSCVA
- Decrease in BSCVA of greater than or equal to 2 lines (≥ 10 letters ETDRS) not due to irregular astigmatism as shown by rigid contact lens refraction at 3 months or later
- Retinal detachment
- Corneal Edema at 1 month or later
- Retinal vascular accidents
- Any other vision-threatening event
- Ocular penetration

8.2 Unanticipated Adverse Device Effects (UADE)

UADEs are considered to be rare, unanticipated events and have a serious effect on health or safety or represent any life-threatening problem or death caused by the device, if the event has not previously been identified in the investigational plan or in **Section 8.1** or **Section 8.4**. Each occurrence of an UADE must be recorded in both the AE & UADE CRFs within 48 hours of occurrence. Investigators have 10 working days to report the occurrence of a UADE to the Sponsor (via UADE CRF), and thereafter the Sponsor has 10 working days to report the UADE to the FDA, the IRB and all study Investigators. (see **Table 2**Table 2. Safety Event Reporting**,** "Safety Event Reporting") as described in 21 CFR 812.150(b)(1). UADEs may include, but are not limited to, the following events:

- Device related death
- Enucleation of treated eye
- Corneal transplant of treated eye

8.3 Reporting Device Deficiencies

A device deficiency is defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device deficiencies include malfunctions, use errors, and inadequate labeling.

Investigators must evaluate, record, and report via applicable forms any complaints/deficiencies or malfunctions experienced with Test Device during this trial to the Sponsor or its representative promptly. The Sponsor shall review all device deficiency reports and, upon the Sponsor's request, Investigators must supply any additional information related to the safety reporting of a particular event.

The contact for reporting device deficiencies is:

[redacted]

8.4 Complications / Possible Adverse Events

Complications / possible adverse events are known to potentially occur in association with laser refractive surgery and include the safety events listed below. Each occurrence of these safety events will be recorded in the postoperative CRFs only and will not be reported to the Sponsor or the IRB (See **Table 2**Table 2, "Safety Event Reporting"):

- Allergic conjunctivitis
- Blepharitis
- Conjunctivitis
- Corneal abrasion
- Corneal edema between 1 week to less than 1 month after procedure
- Corneal flap lifting between 1 day to 1-month post-surgery for wrinkled flap
- Corneal haze

- Corneal scar
- Debris in the interface
- Diffuse lamellar keratitis (grade 2 or less) [42]
- Double/ghost images in operative eye
- Dry eye
- Enhancement not done due to flap fibrosis
- Epithelium at the flap edge
- Epithelium in the interface
- Flap is not of the size and shape as initially intended or resultant flap is misaligned
- Foreign body sensation at 1 month or later
- Iritis
- Loose epithelium
- Meibomian gland dysfunction
- Mucus under edge of flap
- Pain at 1 month or later
- Peripheral corneal epithelial defect at one (1) month or later
- Possible allergic reaction to plugs or eye drops
- Postoperative flap complications
- Punctal plug inserted
- Punctal plug replaced
- Rough epithelium
- Superficial punctuate keratopathy (SPK)
- Steroid induced IOP increase
- Subconjunctival hemorrhage
- Transient light-sensitivity syndrome (TLSS)
- Trace microstriae
- Trace corneal haze
- Vitreous floaters

8.5 Symptoms

Subjects will complete subject PROWL questionnaires at the preoperative visit and each scheduled study visit from the 3-month postoperative visit on. The PROWL questionnaires should be completed by the study subject in a secluded area, free of directions from clinical staff. Subjects will be asked to complete all PROWL questions to the best of their ability, and only certain PROWL domains will be analyzed for the purposes of this protocol. For domains dealing with symptoms and specifically evaluated with the PROWL questionnaire for this study, patients will grade the frequency, severity and inconvenience (bothersomeness) of their glare, halos, double images, and starburst visual symptoms as part of the PROWL symptom domain (questions 45-64 in the PROWL-PRQ[34] questionnaire and questions 42-61 in the PROWL-POQ[35] questionnaire). Results from domain 1 (visual function) and domain 3 (environmental stimuli) of the Ocular Surface Disease Index (OSDI) questionnaire [41] (questions 65-72 of the PROWL-PRQ[34] questionnaire and question 62-69 of the PROWL-POQ[35] questionnaire) also will be

evaluated pre- and post-surgery for evidence of dry eye association with LASIK surgery, as will questions related to far vision (PROWL-PRQ questions 16-18 and 28-29, and PROWL-POQ questions 10-12 and 22-23), near vision (PROWL-PRQ questions 24-27 and PROWL-POQ questions 18-21), and driving (PROWL-PRQ questions 12-18 and PROWL-POQ questions 6-12). For more detail, see **Section 9.6.3.3.1** and methods of symptom data analysis in the Statistical Analysis Plan.

Subjective results will be presented as percentages ("better" or "worse") and appropriate statistical analyses for change from baseline will be conducted as described in the study Statistical Analysis Plan, but the data will not be included in the analysis of "Incidence of Adverse Events". The subjective subject questionnaires used are:

- Pre-operative PROWL-PRQ [34]
- Post-operative PROWL-POQ [35]

9. STATISTICAL METHODS

9.1 Effectiveness Endpoints

9.1.1 Primary Effectiveness Endpoints

- The percentage of eyes that achieve predictability (attempted versus achieved) of MRSE within ± 0.50 D
- The percentage of eyes that achieve predictability (attempted versus achieved) of MRSE within ± 1.00 D
- The percentage of eyes targeted for emmetropia that achieve a UDVA of 20/40 or better

9.1.2 Secondary Effectiveness Endpoints

There are no secondary effectiveness endpoints

9.2 Hypotheses

9.2.1 Percentage of eyes that achieve predictability of MRSE within ± 0.50 D at the time of refractive stability

The null hypothesis (H_0) is that the proportion of eyes that achieve predictability within ± 0.50 D (π) is less than or equal to 0.80 (80%) at the time of refractive stability. The alternative hypothesis (H_1) is that the proportion is greater than 0.80 (80%).

$$H_0: \pi \leq 0.80$$

$$H_1: \pi > 0.80$$

9.2.2 Percentage of eyes that achieve predictability of MRSE within ± 1.00 D at the time of refractive stability

The null hypothesis (H_0) is that the proportion of eyes that achieve predictability within ± 1.00 D (π) is less than or equal to 0.90 (90%) at the time of refractive stability. The alternative hypothesis (H_1) is that the proportion is greater than 0.90 (90%).

$$H_0: \pi \leq 0.90$$
$$H_1: \pi > 0.90$$

9.2.3 Percentage of eyes targeted for emmetropia that achieve UDVA of 20/40 or better at the time of refractive stability

The null hypothesis (H_0) is that the proportion of eyes targeted for emmetropia and that achieve UDVA of 20/40 or better at the time of refractive stability (π), is less than or equal to 0.88 (88%). The alternative hypothesis (H_1) is that the proportion is greater than 0.88 (88%).

$$H_0: \pi \leq 0.88$$
$$H_1: \pi > 0.88$$

9.2.4 Statistical Success Criteria for the Study

The study will be statistically successful if all primary effectiveness endpoints in this section are analyzed successfully as described in Section **9.6.2** using data collected at the visit when refractive stability is achieved. Achievement of refractive stability for the study cohort requires a minimum of 95% of treated eyes should have a change of ≤ 1.00 D of manifest refraction spherical equivalent between two refractions performed at least 3 months apart.[40]

9.3 Sample Size

9.3.1 Assumptions

Prior clinical experience with the TENEO 317 excimer laser in Europe showed that 94.5% of eyes were within 0.50 D and 99% of eyes were within 1.00 D of targeted MRSE 1 month after surgery. In addition, 100% of eyes achieved UDVA of 20/40 or better at 1 month.[33]

9.3.2 Percentage of eyes that achieve predictability of MRSE within ± 0.50 D at the time of refractive stability

A one group χ^2 test with a 2.5% one-sided significance level will have > 99.99% power to detect the difference between the Null hypothesis proportion, π_0, of 0.80 and the Alternative proportion, π_1, of 0.945 when the sample size is 300.

9.3.3 Percentage of eyes that achieve predictability of MRSE within ± 1.00 D at the time of refractive stability

A one group χ^2 test with a 2.5% one-sided significance level will have > 99.99% power to detect the difference between the Null hypothesis proportion, π_0, of 0.90 and the Alternative proportion, π_1, of 0.99 when the sample size is 300.

9.3.4 Percentage of eyes targeted for emmetropia that achieve UDVA of 20/40 or better at the time of refractive stability

A one group χ^2 test with a 2.5% one-sided significance level will have > 99.99% power to detect the difference between the Null hypothesis proportion, π_0, of 0.88 and the Alternative proportion, π_1, of 0.99 when the sample size is 300.

9.3.5 Overall Enrollment

Approximately three hundred thirty-four eyes (334) eyes will be treated to evaluate 300 eyes at the time of refractive stability, as recommended by the ANSI Z80.11-2012 (R2017)[40] standard. This will allow for losses of up to 10%. Enrollment will be monitored to achieve the minimum marginal distribution of pre-operative refractive errors given for study eyes in

Enrollment will be successive without staging of enrollment since substantial prior clinical experience with the TENEO 317 model 2 excimer laser was obtained after the device received CE Mark status [33] (*cf.* **Section 5.1**).

9.4 Randomization, Stratification, and Masking

There will be no randomization or masking in this single treatment, open label study.

9.5 Study Population

All eyes enrolled and treated with the TENEO 317 model 2 excimer laser will constitute the Study Population.

9.6 Statistical Analysis

9.6.1 General Statistical Considerations

Continuous measures will be summarized by the mean, standard deviation, median, minimum, and maximum. Categorical and incidence measures will be summarized by both count and percentage.

Final study data will be provided in CDISC-compliant format, including SDTM and ADaM datasets, along with define files clearly defining the variables and coding schemes. The statistical programs used to produce the statistical results will also be provided in a PMA submission along with the processed study data.

9.6.2 Methods of Analysis

The primary analysis time point will be the time of achievement of refractive stability for all eyes. Achievement of refractive stability will be assessed in this study as required by ANSI standard Z80.11-2012 (R2017)[40]. By the ANSI standard, initial attainment of refractive stability is accepted at the latter of two postoperative refractions performed at least 3 months apart or at 3 months after surgery when compared with the 1-month interval, if all recommended criteria for refractive stability are met.[40]

9.6.2.1 Percentage of eyes that achieve predictability of MRSE within ± 0.50 D at the time of refractive stability

For each eye, the targeted manifest sphere and cylinder will be determined preoperatively. Postoperatively, manifest refraction will be assessed at all scheduled visits beginning with the Week 1 Visit.

For each observation, attempted MRSE and MRSE at the time of refractive stability will be computed in diopters as follows.

$$MRSE = Sphere + \frac{Cylinder}{2}$$

For each observation, the absolute difference (|ΔMRSE|) between the attempted MRSE and observed MRSE at the stability visit will be computed as follows.

$$|\Delta MRSE| = |MRSE\ at\ Stability\ Visit - Attempted\ MRSE|$$

Each observation will be classified as shown in the following example.

Condition	Classification
|ΔMRSE| ≤ 0.50 D	MRSE within ± 0.50 D
|ΔMRSE| > 0.50 D	MRSE not within ± 0.50 D

Predictability of MRSE within 0.50 D will be summarized categorically (MRSE within ± 0.50 D, MRSE not within ± 0.50 D) for the treated eyes population at the stability visit in a Table.

Prior to hypothesis testing, missing sphere and cylinder values at postoperative scheduled visits will be imputed using Markov Chain Monte Carlo (MCMC) methods. Details of the MCMC method to be used will be specified in the statistical analysis plan.

Binomial proportions and standard errors will be combined using multiple imputation analysis methods to test the statistical hypotheses. If the percentage of observations within ± 0.50 D of attempted at the time of refractive stability is statistically significantly greater than 80%, then the device will be statistically successful in this outcome.

9.6.2.2 Percentage of eyes that achieve predictability of MRSE within ± 1.00 D at the time of refractive stability

The methods described in the previous section will be employed in the evaluation of this endpoint. If the percentage of observations within ± 1.00 D of attempted at the time of refractive stability is statistically significantly greater than 90%, then the device will be statistically successful in this outcome.

9.6.2.3 Percentage of eyes targeted for emmetropia that achieve UDVA of 20/40 or better at the time of refractive stability

UDVA will be assessed at all scheduled postoperative visits using an ETDRS chart. The data entered into the case report form will be converted to logMAR UDVA.

Each observation will be classified as follows.

Condition	Classification
logMAR UDVA ≤ 0.3	UDVA 20/40 or Better
logMAR UDVA > 0.3	UDVA Worse than 20/40

UDVA will be summarized categorically (UDVA 20/40 or Better, UDVA Worse than 20/40) for the treated eyes population at the stability visit in a table. Prior to hypothesis testing, missing logMAR UDVA values at postoperative scheduled visits will be imputed using Markov Chain Monte Carlo (MCMC) methods. Details of the MCMC method to be used will be specified in the statistical analysis plan. Binomial proportions and standard errors will be combined using multiple imputation analysis methods to test the statistical hypotheses. If the percentage of observations with UDVA 20/40 or Better at the time of refractive stability is statistically significantly greater than 88%, then the device will be statistically successful in this outcome.

9.6.3 Additional Analyses

9.6.3.1 Additional Effectiveness Analyses

The following effectiveness descriptive summaries will be provided at Month 1, Month 3, Month 6, and Month 9. The summaries will be provided for all eyes, eyes treated for spherical myopia only, and eyes treated for astigmatic myopia. These key effectiveness variables will be presented as listed and also stratified by preoperative MRSE and by preoperative manifest cylinder power:

- Percentage of eyes with preoperative myopic MRSE ≤ 7.0 D and those > 7.0 D that achieve predictability of MRSE within ± 0.50 D at the time of refractive stability
- Percentage of eyes with preoperative myopic MRSE ≤ 7.0 D and those > 7.0 D that achieve predictability of MRSE within ± 1.00 D at the time of refractive stability
- Percentage of eyes with preoperative myopic MRSE ≤ 7.0 D and those > 7.0 D that achieve UDVA of 20/40 or better at the time of refractive stability
- Percentage of all eyes that achieve predictability (attempted versus achieved) of MRSE within ± 2.00 D
- Percentage of all eyes targeted for emmetropia that achieve UDVA of 20/12.5 or better, 20/16 or better, 20/20 or better, 20/40 or better
- Percentage of eyes not targeted for emmetropia that achieve UDVA of 20/20 or better and of 20/40 or better.
- Percentage of eyes that achieve accuracy of manifest spherical refraction within ± 0.50 D, ± 1.00 D, and ± 2.00 D of intended manifest spherical refraction
- Percentage of eyes with accuracy of manifest refraction astigmatism within ± 0.50 D, ± 1.00 D, and ± 2.00 D of intended residual cylinder power
- Percentage of eyes that achieve an UDVA equal to or better than preoperative BSCVA, including eyes that achieve an UDVA equal to or better than 20/40 if the preoperative BSCVA was 20/20 or better
- Change from baseline in BSCVA by study visit
- Change from baseline in UCNVA and UDVA
- Percentage of eyes that are overcorrected or under corrected by > 1.00 D or > 2.00 D
- Percentage of eyes that achieve a difference between postoperative and preoperative BSCVA of < -2 lines, - 2 lines, -1 line, 0 lines, +1 line, +2 lines, and > +2 lines
- Change in subjective Patient Reported Outcome questionnaire scores (see **Section 9.6.3.3.1**)
- Correction ratio (CR) = surgically induced refractive correction (SIRC)/intended refraction correction (IRC)
- Absolute shift in cylindrical axis at stability time point
- Eyes as a function of angle of cylindrical error:
    - Eyes with error of angle ≥ -15° and ≤ +15°
    - Eyes with error of angle greater than +15°
    - Eyes with error of angle less than -15°

9.6.3.2 Additional Refractive Stability Analyses

The following refractive stability descriptive summaries will be provided for each visit interval starting with the one to three-month interval and continuing to the 6- to 9-month interval.

- Eyes that exhibit a change of less than or equal to 0.50 D, 1.00 D, and 2.00 D of MRSE between two refractions performed at 1 months and 3 months, and between subsequent refractions performed at least 3 months apart.
- Mean overall change and change per month in MRSE between consecutive scheduled visits as determined by a paired analysis, with 95% confidence intervals around the mean rate of change
    - The mean rate of change in MRSE is expected to decrease 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 in MRSE is expected to include zero or a rate of change attributable to normal aging
- Mean (± SD) MRSE for the preoperative and each postoperative visit
- Change in MRSE between Month 1 and Month 3, between Month 3 and Month 6, and Month 6 and Month 9 and change per month as determined by a paired analysis
- Percentage of eyes that achieve a change in MRSE less than or equal to +0.50 D between Month 1 and Month 3, between Month 3 and Month 6, and Month 6 and Month 9
- Proportion of eyes undergoing astigmatic treatment achieving correction within ± 0.50 D and within ± 1.00 D of the attempted astigmatic correction by the time point of refractive stability
- Assessment of cylinder stability between two refractions performed at 1 months and 3 months, and between subsequent refractions performed at least 3 months apart for correction of spherocylindrical refractive errors, expressed as the proportion of eyes with a change in cylinder magnitude of 0.00 D, 0.01 D to 0.50 D, 0.51 D to 1.00 D, 1.01 D to 1.50 D, and > 1.51 D

9.6.3.3 Additional Safety Analyses

The following additional safety summaries will be provided with descriptive statistics by visit.

- Eyes with BSCVA worse than 20/40 among eyes that had a BSCVA of 20/20 or better before surgery at each study visit, stratified by preoperative MRSE, and stratified by preoperative cylinder
- Loss of BSCVA of 1, 2, ≥ 2, and > 2 lines
- Percentage of eyes that have an increase of manifest refractive astigmatism > 2.00 D of manifest cylinder compared to the preoperative refraction
- Eyes treated for sphere only that have a magnitude of postoperative manifest refractive astigmatism that increases from baseline cylinder by > 2.00 D at the postoperative interval at which stability has been established, and stratified by preoperative MRSE

- Incidence of adverse events by event type
- Frequency of miscreated flaps
- Incidence of complications
- Endothelial cell density changes
- Contrast sensitivity changes, mesopic conditions
- Schirmer's Test results, Preoperative Visit and Month 6 Visit
- Intraocular Pressure
- Subject symptoms and results for prespecified question domains (from PROWL questionnaire)

9.6.3.3.1 PROWL Questionnaire

The PROWL questionnaires (PROWL-PRQ[34] and PROWL-POQ[35]) will be administered and the questionnaire results will be presented using appropriate summary statistics. Results obtained both pre- and post- LASIK surgery will be assessed by treatment group for selected topic domains of near vision, far vision, eye dryness, subject symptoms, driving, and vision clarity as described in the Statistical Analysis Plan. See **Table 3** for the specific pre-operative PROWL-PRQ and post-operative PROWL-POQ questions to be analyzed for each of these topic domains. Mean values for all other questions in the PROWL-PRQ and PROWL-POQ will be summarized by treatment group and study visit without analysis.

Results for other PROWL questions will be summarized by treatment group as individual questions in a Table with summary statistics for categories of expectations of LASIK surgery, vision satisfaction, vision clarity, and satisfaction with LASIK surgery. **Table 4** describes the specific PROWL-PRQ and PROWL-POQ questions to be summarized for each if these categories. Normalization of individual or domain scores, if required, will be done as described in PROWL questionnaire references[36, 37] or relevant primary references annotated in the PROWL questionnaire references.

Table 3. PROWL Topic Domain Categories and Domain Questions to be Analyzed

Topics- Pre and Post LASIK surgery	PROWL-PRQ questions	PROWL-POQ questions
Visual functions	19 and 24-26,	13 and 18-20
Far vision	16-18 and 28-29	10-12 and 22-23
Near vision	24-27	18-21
Eye dryness	65- 72	62- 69
Subject symptoms	45- 64	42- 61
Driving	12 - 18	6- 12
Vision clarity	34- 36 a	28 – 30a

Table 4. PROWL Question Categories and Questions to be Analyzed

Topics- Table Summary with descriptive statistics	PROWL-PRQ questions	PROWL-POQ questions
Expectations of LASIK surgery	6- 11	
Vision Satisfaction	37	34
Vision Clarity	5	5
Satisfaction with LASIK surgery		71- 78

9.6.4 Multiplicity

All primary effectiveness endpoints must be successful to demonstrate statistical success. Consequently, no adjustment is required for the primary effectiveness endpoints.

9.6.5 Missing Data

Missing data will be imputed for the primary effectiveness endpoints as described in **Section 9.6.2.1** through **Section 9.6.2.3**.

9.6.6 Interim Analyses and Data Review

No interim analyses are planned. Members of the Sponsor team will review clinical data during the study.

10. DATA QUALITY ASSURANCE

10.1 Study Monitoring

Bausch + Lomb or its representatives must be allowed to visit all study site locations to assess the data, quality, and study integrity in a manner consistent with applicable health authority regulations and the procedures adopted by Bausch + Lomb. Study monitoring may be remote while monitors are not allowed to visit study sites due to local, state, and/or federal regulations or guidance during the COVID-19 pandemic.

Prior to the start of the study, member(s) of the Bausch + Lomb team (or designees) will review the protocol, eCRFs, regulatory obligations, and other material or equipment relevant to the conduct of the study with the Investigator/Sub-Investigator and relevant study site personnel.

Monitoring visits and telephone consultations will occur as necessary, or per the monitoring plan, during the course of the investigation to verify the following. The monitoring plan will be updated so monitoring may be done remotely during the period when in-clinic study procedures are interrupted by the COVID-19 pandemic:

- The rights and well-being of subjects are protected

- The conduct of the investigation is in compliance with the currently approved protocol/amendment, 21 CFR Parts 11, 50, 54, 56, and 812, and ISO 14155 (2011) Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice (ISO GCP), and IRB requirements
- The integrity of the data, including adequate study documentation
- The facilities remain acceptable
- The Investigator and site personnel remain qualified and able to conduct the study
- Test article accountability

During the course of the study, if the Sponsor (or designees) determines that an Investigator is non-compliant with the study plan and/or applicable regulatory requirements, the Sponsor (or designees) will take action to secure compliance. In addition, the Sponsor may terminate the Investigator's participation in the study if appropriate, or if the Investigator remains non-compliant despite Bausch + Lomb's actions.

The study medical monitor will be responsible for periodic evaluation of masked study data for irregular frequency or rates of safety signals across sites.

10.2 Source Documentation

All medical information obtained at each study visit must be recorded in the subject's record (source documentation) in real time as it is collected. Source documentation consists of original subject documents, as well as data and records with information relevant to the subject and their participation in the study.

10.3 Case Report Forms and Data Verification

Subject data required by this protocol are to be recorded on eCRFs. The Investigator and study site personnel will be responsible for completing the eCRFs. The Investigator is required to verify that all of the requested information is accurately recorded on the eCRFs. All information requested on the eCRFs needs to be supplied, including subject identification number, partial date of birth, date(s), assessment values, etc., and any omission or discrepancy will require explanation. All information on eCRFs must be traceable to source documents if not otherwise specified in the monitoring plan.

The study monitor will be responsible for reviewing and verifying the data recorded on the eCRFs, utilizing the original source documentation and will query discrepant findings. Remote monitoring may be done during the period of study procedure interruptions due to COVID-19 through remote review of electronic copies of source and study documents. The Investigator and study site personnel will be responsible for timely answering all queries. The eCRFs will be submitted electronically via an electronic data capture system to Bausch + Lomb for quality assurance review, data entry, and statistical analysis.

A copy of the final eCRFs (on CD, DVD, or other electronic media) will be retained by the Investigator at the conclusion of the study, who must ensure that it is stored in a secure place.

10.4 Data Management

Documentation for the study is the responsibility of the Investigator and the Sponsor. Individual subject eye treatment and follow-up will be documented using standardized CRFs designed to meet this protocol and as supplied to the Investigator by the Sponsor.

All data collected during this investigation will be reviewed for completeness and accuracy upon receipt by the Sponsor. Data elements which fall outside the range of expected norms will be queried with the Investigator for resolution.

Significant trends that adversely deviate from anticipated results will precipitate an additional review of data by the Investigator and the Sponsor. Where appropriate, such deviations will be reported to the IRB and to the FDA.

Once the study database is locked and data analysis has occurred, the data will be submitted in a 180-Day PMA supplement to the FDA.

10.5 Recording of Data and Retention of Documents

Confidentiality of subject records must be maintained to ensure adherence to applicable local privacy regulations.

The Investigator must retain essential documents for a period of time specified by local law or per the Investigator's Clinical Trial Agreement after the completion of the study, whichever is longer, unless otherwise notified by the Sponsor. The Investigator agrees to adhere to the document retention procedures when signing the protocol Investigator Statement of Approval.

Essential documents include but are not limited to the following:

- IRB approvals for the study protocol, all amendments, ICF(s), and advertisements
- IRB annual study review (if requested)
- IRB correspondence and reports (e.g., AE/UADE reports, protocol deviations, and safety updates)
- Regulatory documents (e.g., financial disclosure and delegation of authority forms)
- All source documents
- Archive of eCRFs
- Subject's signed ICF
- Investigator Clinical Trial Agreement
- Accountability records for the test article(s)
- Correspondence from and to the Sponsor

- Any other documents relevant to the conduct of the study

In the event that the Investigator withdraws from the study (e.g., retirement, relocation), study records will be transferred to a designee (e.g., another Investigator, and/or site IRB) mutually agreed upon by Investigator and Bausch + Lomb. The Investigator will provide notice of such transfer in writing to Bausch + Lomb.

10.6 Auditing Procedures

Audits of clinical research activities in accordance with the Sponsor's internal Standard Operating Procedures to evaluate compliance with the principles of GCP may take place. A regulatory authority may also wish to conduct an inspection (during the study or after its completion). If an inspection is requested by a regulatory authority and/or IRB, the Investigator must inform the Sponsor immediately that this request has been made.

10.7 Institutional Review Board

The Investigator should ensure, in accordance with 21 CFR 56, that their participation in the study, in addition to the protocol, subject recruitment materials (written information or materials including web pages, radio advertisements, television spots or written text developed to encourage subject enrollment) and the ICF to be used in this study are approved by their institution IRB, or if not using their institution's IRB, approved by the reviewing central IRB prior to entering any subjects in the study.

Documentation of IRB approval of the study protocol and informed consent must be provided to the Sponsor prior to initiation of the study. In addition to approving the 'Investigational Protocol' and 'Informed Consent' documents, a statement of IRB Approval should also contain the name(s) of approved Investigators, and the signature of the IRB Chairperson. The Investigator must ensure that the reviewing IRB has provided approval for any protocol amendments prior to implementation. If the amendment necessitates a revision to the ICF, the Investigator should ensure the revised form is also submitted to and approved by the Sponsor and the IRB prior to implementation.

10.8 Publication of Results

All study data generated as a result of this study will be regarded as confidential, until appropriate analysis and review by the Sponsor or its designee and the Investigator(s) are completed. The results of the study may be published or presented by the Investigator(s) after the review by, and in consultation and agreement with the Sponsor, and such that confidential or proprietary information is not disclosed.

Prior to publication or presentation, a copy of the final text should be forwarded by the Investigator(s) to the Sponsor or its designee, for comment. Such comments shall aim to ensure the scientific integrity of the proposed publications and/or presentations and ensure

that the data and material referring to Technolas Perfect Vision GmbH products and activities receive fair, accurate, and reasonable presentation.

11. REFERENCES

1. The Eye Diseases Prevalence Research Group. The prevalence of refractive errors among adults in the United States, Western Europe, and Australia. Arch Ophthalmol 2004; 122:495-505.
2. Food and Drug Administration. When is LASIK not for me? See https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/LASIK/ucm061366.htm
3. Yu L, Li Z-K, Gao J-K, et al. Epidemiology, genetics and treatments for myopia. Int J Ophthalmol 2011; 4:658-669..
4. Pan C-W, Zheng Y-F, Anuar AR, et al. Prevalence of refractive errors in a multiethnic Asian population: the Singapore Epidemiology of Eye Disease Study. Invest Ophthalmol Vis Sci 2013; 54:2590-2598.
5. Schallhorn SC, Venter JA. One-month outcomes of vavefront-guided LASIK for low to moderate myopia with the VISX STAR S4 laser in 32,569 eyes. J Refract Surg 2009; 25:S634-S641.
6. Pokroy R, Mimouni M, Sela T, et al. Myopic laser in situ keratomileusis retreatment; incidence and associations. J Cataract Refract Surg 2016; 42:1408-1414.
7. Hashemi H, Khabazkhoob M, Pakzad R, et al. The characteristics of excimer laser refractive surgery candidates. Eye & Contact Lens 2018; 44:S158-S162.
8. Gwiazda J. Treatment options for myopia. Optom Vis Sci 2009; 86:624-628.
9. Pärssinen O, Kauppinen M, Viljanen A. The progression of myopia from its onset at age 8-12 to adulthood and the influence of heredity and external factors on myopic progression. A 23-year follow-up study. Acta Ophthalmol 2014; 92:730-739.
10. Barraquer JI. Keratomileusis for the correction of myopia. *Arch Soc Am Optom.* 1964;5:27 (Spanish).
11. Barraquer JI, Autokeratoplasty with optical carving for the correction of myopia (Keratomileusis). *An Med Espec* 1965; 51:66-82 (Spanish).
12. Brint SJ. *J Cataract Refract Surg*-Vol 20, November 1994.
13. Krumiech JH. Indications, Techniques, and Complications of Myopia Keratomileusis. *Int Ophthalmol Clin.* 1983;23(3):75-92.
14. Arenas-Archila E, Sanchez-Thorin JC, Naranjo-URIBEJP, Hernandez-Lozano A. Myopic Keratomileusis In Situ: A Preliminary Report. *J Cataract Refract Surg*. 1991;17:424-435.
15. Trokel SL, Srinivasan R, Braren B. Excimer Laser Surgery of the Cornea. *AM J Ophthalmol.* 1983;96:710-715.

16. Marshall J, Trokel S, Rothery S, Schubert H. An Ultrastructural Study of Corneal Incisions Induced by an Excimer Laser at 193mm. *Ophthalmology.* 1985;92:749-758.
17. McDonald M, Kaufman HE, Frantz JM, et al. Excimer Laser Ablation in a Human Eye. *Arch Ophthalmol*. 1989;107:641-642.
18. Seiler T, Kriegerowski M, Schnoy N. Ablation Rate of Human Corneal Epithelium and Bowman's Layer with the Excimer Laser (193mm). *Refract Corneal Surg*. 1990;6:99-102.
19. Burrato L, Ferrari M. Excimer Laser Intrastromal Keratomileusis: Case Reports. *J Cataract Refract Surg.* 1992;18:37-41.
20. Burrato L, Ferrari M, Rama P. Excimer Laser Intrastromal Keratomileusis. *AM J Ophthalmol.* 1992;113:291-295.
21. Brint S. Six-Month Results of the Multicenter Phase I Study of Excimer Laser Myopic Keratomileusis. *J Cataract Refract Surg.* 1994;20:610-615.
22. Pallikaris I. A Corneal Flap Technique for Laser In Situ Keratomileusis. *Arch Ophthalmol*. 1991;145:1699-1702.
23. Pallikaris I. Excimer Laser In Situ Keratomileusis and Photorefractive Keratectomy for Correction of High Myopia. *Journal of Refractive and Corneal Surgery*. 1994;10:498-510.
24. Lin, J.T. A multiwavelength solid state laser for ophthalmic applications, *Society of Photo-optical Instrumentation Engineers Proceedings, Ophthalmol. Technol. II*. Vol. 1644, 1992.
25. Lin, J.T., *ARVO*, Sarasota, FL Vol. 34, No.4, May 1993. (Abstract)
26. Lin, J.T. et al., *ASCRS*, *Suppl. to Refr. & Corn. Surg*, Vol 9, March/April 1993.
27. Lin, J.T., Mini-excimer laser corneal reshaping using a scanning device, *SPIE Proc., Medical Lasers & Systems III,* Vol. 2131, 1994.
28. Castillo A, Romero F, Martin-Valverde JA, et al. Management and treatment of central steep islands after excimer laser photorefractive keratectomy. *J Refract Surg* 1996; 12:715-720.
29. Food and Drug Administration, Kremer Excimer Laser System, Premarket Approval Application P970005, July 30, 1998.
30. Food and Drug Administration, LaserScan LSX Excimer Laser System, Premarket Approval Application P980008, November 12, 1999.
31. Food and Drug Administration, TECHNOLAS 217A Excimer Laser System, Premarket Approval Application P990027, February 23, 2000.
32. Masters J, Kocak M, Walite A. Risk for microbial keratitis: comparative metaanalysis of contact lens wearers and post-laser in situ keratomileusis patients. J Cataract Refract Surg 2017; 43:67-73.
33. Engineering Report: Data analysis report of patients with preoperative only spherical myopia or myopic astigmatism, Technolas Document #100022264.

34. LASIK Pre-Operative Questionnaire (PRQ), available at https://www.fda.gov/downloads/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/LASIK/UCM528837.pdf.
35. LASIK Post-Operative Questionnaire (POQ), available at https://www.fda.gov/downloads/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/LASIK/UCM528841.pdf
36. Hays RD, Tarver ME, Spritzer KL, et al. Assessment of the psychometric properties of a questionnaire assessing patient-reported outcomes with laser in situ keratomileusis (PROWL). JAMA Ophthalmol 2017; 135:3-12.
37. Eydelman M, Hilmantel G, Tarver ME, et al. Symptoms and satisfaction of patients in the patient-reported outcomes with laser in situ keratomileusis (PROWL) studies. JAMA Ophthalmol 2017, 135:13-22.
38. Miller KL, Walt JG, Mink DR, et al. Minimal clinically important difference for the Ocular Surface Disease Index. Arch Ophthalmol. 2010;128 (1):94-101.
39. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. Arch Ophthalmol. 2000;118(5):615-621.
40. ANSI Standard Z80.11-2012 (R2017). Laser Systems for Corneal Reshaping (The Vision Council, Alexandria, VA).
41. Bower KS and Woreta F. Update on contraindications for laser-assisted in situ keratomileusis and photorefractive keratectomy. Curr Opin Ophthalmol 2014; 25:251-257.
42. Linebarger EJ, Hardten DR, and Lindstrom RL. Diffuse lamellar keratitis: diagnosis and management. J Cataract Refract Surg 2000; 26:1072-1077.
43. McCarey BE, Edelhauser HF, Lynn MJ. Review of corneal endothelial specular microscopy for FDA clinical trials of refractive procedures, surgical devices and new intraocular drugs and solutions. Cornea 2008; 27:1-16.
44. Huang J, Maram J, Tepelus TC, et al. Comparison of manual and automated analysis methods for corneal endothelial cell density measurements by specular microscopy. J Optometry 2018; 11:182-191.

Appendix A. Schedule of Visits and Parameters

All study tasks must be performed by qualified study site personnel as indicated on the delegation of authority log under the supervision of the Principal Investigator.

Test	Visit 1 Pre-Op (Day-60 to Day -1)	Visit 2 Operative Visit (Day 0)	Visit 3 Day 1[1]	Visit 4 Week 1 (Day 5-9)	Visit 5 Month 1 (Week 3-5)	Visit 6 Month 3 (Week 10-14)	Visit 7 Month 6 (Week 21-26)	Visit 8 Month 9 (Week 35-43)
Informed Consent/HIPAA	**X**							
Eligibility	**X**	X						
PROWL Questionnaire [2]	**X**					**X**	**X**	**X**
Adverse Events	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Complications		**X**	**X**	**X**	**X**	**X**	**X**	**X**
Subject Demographics	**X**							
Medical/Ocular History	**X**							
Concomitant Medications	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Schirmer's Test [3]	**X**						**X**	
LASIK Surgery, Intraoperative Events [4]		**X**						
Manifest Refraction	**X**			**X**	**X**	**X**	**X**	**X**
Keratometry [5]	**X**							
Endothelial Cell Density (ECD)[6]	**X**						**X**	
Corneal Topography	**X**				**X**	**X**	**X**	**X**
Pupil Size [7]	**X**					**X**	**X**	**X**
UCNVA [9]	**X**		**X**	**X**	**X**	**X**	**X**	**X**
UDVA [8]	**X**		**X**	**X**	**X**	**X**	**X**	**X**

[1] The same parameters are to be measured at each examination performed until re-epithelialization occurs (when applicable).
[2] The PROWL questionnaires [34, 35] should be completed by the study subject in a secluded area, free of directions from clinical staff. at Visit 6, 7 and 8.
[3] The Schirmer's test must not be conducted with anesthesia.
[4] LASIK surgery is to be conducted by a refractive surgeon adequately trained by B+L or TPV technical representatives for use of the TENEO 317 laser system and supervised by a technical representative for at least the first 4 LASIK surgeries completed by the refractive surgeon.
[5] Keratometry should be assessed only at the pre-operative study visit and as needed at a post-operative study visit to assess anomalous results in the post-operative period. Pachymetry should take place after manifest refraction has been done to avoid disturbing the cornea.
[6] Preoperative and 6 Months ECD measurements will be done at three or four clinical sites by specular microscopy.
[7] Pupil size should be assessed under mesopic conditions at the pre-operative study visit and at months 3, 6 and 9 as well as Unscheduled Visits
[8] UCNVA, UDVA and BSCVA measurements are to be taken under photopic conditions (approximately 85 cd/m^2) for each eye monocularly.

Test	Visit 1 Pre-Op (Day-60 to Day -1)	Visit 2 Operative Visit (Day 0)	Visit 3 Day 1[1]	Visit 4 Week 1 (Day 5-9)	Visit 5 Month 1 (Week 3-5)	Visit 6 Month 3 (Week 10-14)	Visit 7 Month 6 (Week 21-26)	Visit 8 Month 9 (Week 35-43)
Distance BSCVA [9]	X			X [9]	X [10]	X [10, 10]	X [10,11]	X [10,11]
Contrast Sensitivity	X						X	
Slit Lamp Examination [11]	X		X	X	X	X	X	X
Pachymetry [12]	X							
Cycloplegic Refraction	X							
Intraocular Pressure [13]	X				X	X	X	X
Dilated Fundoscopic Exam	X					X[14]	X[14]	X[14]

[9] If the visual acuity with spectacle correction is ≥ 2 lines (10 letters) below that obtained at Visit 1, a rigid contact lens over refraction should be performed to estimate the best possible corrected visual acuity.
[10] BSCVA to be completed OD and OS.
[11] The slit lamp examination should include a complete survey of the anterior segment and grading of findings as detailed in **Appendix B.**
[12] Pachymetry should be assessed only at the pre-operative study visit and as needed at post-operative study Visit 7 to assess anomalous results in the post-operative period. Pachymetry should take place after manifest refraction has been done in order to avoid disturbing the cornea.
[13] Intraocular pressure should preferably be obtained using Goldmann applanation tonometry.
[14] Dilated fundus examination (only required if loss of BSCVA occurs compared to pre-op BSCVA).

Appendix B. Description of the Investigative Device and Methods of Clinical Evaluation

1.0 TENEO 317 MODEL 2 EXCIMER LASER DESCRIPTION

The Teneo 317 Model 2 excimer laser consists of the following system components:

1.1 Excimer Laser Head:

The laser head provides the following output characteristics:

Laser medium:	ArF
Laser wavelength:	193 nm
Gas mixture:	Argon / Fluorine / Neon
Operating fill pressure:	6 bar
Repetition rate:	500 Hz
Power:	< 10.000 mW
Pulse width (duration):	8 ± 3 ns
Emergent beam size (VxH):	6 x 3 mm
Beam divergence (VxH):	51 x 27 mrad
Fluence on cornea:	200 mJ/cm^2

1.2 Laser Gas System

Included in the laser system is a gas bottle of the laser gas mixture with Argon, Fluorine and Neon. Additionally, there is another gas bottle containing Nitrogen gas, which is used for flushing the beam path and gas system for installation and service and an ongoing gas exchange inside the sealed beam path. Components of the gas system include automatic valve, pressure reducer, pressure sensors (high/low pressure section), vacuum pump, fluorine filter, computer-controlled gas delivery.

1.3 System Control

Computer and software

A computer and proprietary software are used to coordinate the control of the system, as well as determine the ablation profile and algorithm for each subject eye to be treated.

I/O (Input/Output) Board and Scanner Drivers

The I/O (Input/Output) Board receives and sends signals to the computer, as well as controlling components of the system, such as turning on and off the laser radiation, opening and closing the shutter. Furthermore, the energy delivered to the eye is monitored.

1.4 Laser Beam Delivery System

The laser beam delivery system consists of aperture, two safety shutters, focusing lens, galvanometers with scanning mirrors, and two 45°-deflection mirrors. The main functions of the beam delivery system are to shape the laser beam to the proper size and beam profile, and direct the laser pulses by the scanner to the locations on the eye determined by the computer and software.

1.5 Subject and Doctor Interface

The laser system components that comprise the subject-doctor interface include the patient bed with a joystick, operating microscope with a centration reticule, illumination light, diode-laser for fixation light, diode-laser for focus and aiming light, plume evacuator, footswitch for shutter / laser-control, computer keyboard, touchscreen, laser emission indicator, key-switch (on/off) and emergency stop, USB ports for user key and USB storage device.

1.6 System Integration

The mechanical integrity of the system is provided by a welded metal frame, with metal plates bolted to the frame. All components and sub-components are fastened to the plates and the frame. The housing of the system is used to protect the users and subjects from electric and radiation hazards. Access is only possible by using a special tool to open the covers. The electronic components are connected with shielded cable. Isolation transformers and line filters are used for the electric power lines.

1.7 Power Stability

The power stability unit consists of a closed-loop energy check system that verifies pulse energy at different control points along the sealed beam path, adjusting pulse energy throughout the treatment and maintaining consistent laser energy output from the laser head.

1.8 Electrical Safety

The Teneo 317 Model 2 excimer laser system is designed to meet the ISO/IEC standard 60601-1 (Edition 3.1): Medical Electrical Equipment – Part 1: General Requirements for Basic Safety and Essential Performance.

1.9 Radiation Disabling

Laser radiation is prevented from exiting the laser system in certain situations, such as in the following cases:
(1) The physician detects a non-optimal event, i.e., eye movement, and releases the footswitch,
(2) The Eye tracker detects eye movements out of predefined ranges,
(3) The plume evacuator failure is detected,
(4) When the energy is out of the expected range,
(5) When the surgery is completed,

(6) When the Emergency stop button is pushed, and
(7) an optional remote interlock is activated.

The shutter has been tested to be able to block the laser radiation in <50 msec. In addition, there are two shutter position sensors, one for the "open" and another for the "closed" position. If the computer receives an incorrect position signal, the laser head is shut down.

1.10 Eye Tracking

The TENEO 317 eye tracker (ET) is essentially the same as the approved 217z ET module, as both systems perform real-time (dynamic) adjustments to laser pulse positioning in response to intra-procedure eye movements. The ET for the TENEO 317 was updated to accommodate the faster repetition rate of the 317 laser (laser frequency TENEO 317: 500Hz vs. 217z: Hz100Hz; ET frequency TENEO 317: 1.740Hz vs. 217z: 240Hz), otherwise the following description applies to both ET modules.

The lateral (X/Y) eye tracker (ET) uses a co-axial infrared camera to follow movements of the pupil in order to provide positioning information to the laser system. The eye tracking system scans the image and determines the location of the center of gravity of the pupil. The center of the pupil is provided as a feedback to the computer which corrects the laser beam position to match the detected pupil center position. Should the cornea leave the predefined interval in X/Y, the laser system stops the application of pulses until the cornea is repositioned inside the acceptance range.

A second rotational/Z camera, tilted 12° to the optical axis, detects the changing angle for torsional tracking. The computer corrects the laser beam position via the scanning system to match the calculated position. Should the cornea exceed a predefined angle, the laser stops the application of pulses until the cornea rotation angle is within the accepted range.

Lastly, the ET utilizes a passive Z-tracking feature which uses information from both camera systems (X/Y) and torsional tracker to determine the position of the cornea in the axial (Z-direction) direction based on triangulation. Should the cornea leave the predefined interval in Z, the laser system stops the application of pulses until the cornea is repositioned within the accepted range.

1.11 Plume Evacuator

The Teneo 317 Model 2 excimer laser integrated plume evacuator system removes debris from a region above the surgical field and avoids the distribution of the debris into the surgery room during the ablation process. It is placed close to the ablation level to evacuate plume as effectively as possible through an integrated nozzle. If the suction nozzle is not in the treatment position, or suction flow fails during treatment the laser stops the application of pulses until the fault condition is resolved.

1.12 Slit Lamp

An optional slit lamp is integrated in the system. The slit can be adapted in width and position to be able to examine the patient's eye after flap repositioning after the excimer laser procedure has been completed.

2.0 CREATION OF THE CORNEAL FLAP FOR LASIK

The creation of the required corneal flap will be performed with a femtosecond laser. Any commercially approved femtosecond laser can be used to create the corneal flap prior to LASIK treatment.

3.0 THE PATIENT-REPORTED OUTCOMES WITH LASIK (PROWL) QUESTIONNAIRE

All subjects will complete the PROWL-PRQ Questionnaire [34] pre-operatively and all enrolled subjects will complete a separate post-operative PROWL-POQ Questionnaire [35] at several post-operative study visits. Note the entire PROWL questionnaire will be administered, mean values by question and by treatment group will be summarized, and only specific questions relating to specific patient-centric domains described in **Section 5.2.3, Section 8.5,** and/or **Section 9.6.3.3.1** will be scored and analyzed. Questionnaires will be completed independently by subjects in a private space at the beginning of each applicable visit, prior to other study assessments being performed. The PROWL-PRQ Questionnaire will be given once, at the pre-operative screening visit (Day -60 to Day -1), and the PROWL-POQ Questionnaire will be given at every study visit beginning with Visit 6 (3 months, Week 10-14) until the subject exits the study.

Subjects should be instructed to complete as many of the questions as possible by checking one box associated with each question, with an estimated completion time for each Questionnaire of about 30 minutes. Subjects will be asked to read each question carefully and answer as appropriate for how they feel – there are no right or wrong answers. Subjects will be told the test coordinator will not be present during the completion of the Questionnaire and cannot provide any guidance on how to answer any questions. If a subject is not sure of an answer, they should be encouraged to guess at an answer that seems right to them. When done, the test should be given to the study coordinator.

4.0 PACHYMETRY AND KERATOMETRY

Pachymetry and keratometry of each eye of a subject will be measured at the pre-operative Visit 1 (Screening) and not at any additional study visits unless indicated to assess anomalous results in the post-operative period. The same pachymeter and keratometer should be used for all pachymetry and keratometry measurements, respectively, on each individual eye at a clinical site.

Investigators or designated clinical staff will measure corneal thickness in both eyes of a subject using the topographer / ultrasonic device of their choice. This pachymetry measurement should be done in perpendicular alignment with the central cornea. Each eye corneal thickness will be recorded in the subject source documents and eCRFs, and the TENEO 317 excimer laser default K value of 43.3 D will be used for all eyes during LASIK surgery.

Anterior corneal curvature will be measured for each eye of a subject by keratometry. The axis and degree (in diopters) of the steep and flat axis of the cornea will be recorded.

5.0 CORNEAL TOPOGRAPHY

Corneal topography of subject eyes will be measured at Visit 1 (Screening) and at Visit 5 (Month 1) through Visit 8 (Month 9), or through the last study visit (whichever comes first). Corneal topography is to be measured prior to any study procedures requiring dilation of the eye or any procedure that requires touching the surface of the eye. The same topographer should be used for all measurements on each individual eye at a clinical site. Investigators may use any commercially available corneal topographer to obtain corneal curvature, asphericity, and pachymetry measurements of subject eyes. The make and model of the system used will be recorded in the CRFs. Each subject eye asphericity Q value provided by the topographer instrument will be recorded in the subject source documents and the eCRFs, and the TENEO 317 excimer laser default Q value of -0.20 will be used for all eyes during LASIK surgery.

6.0 PUPIL SIZE

Pupil diameter will be measured at the corneal plane to the nearest ± 0.1 mm. Pupil size will be measured under photopic conditions or in a darkened room using a handheld infrared pupillometer (preferably a Colvard pupillometer, Oasis Medical, Glendora, CA or VIP-300 pupillometer, Neuroptics, Laguna Hills, CA). If the Neuroptics VIP-300 pupillometer is used, the settings for measurement should be with the Variable Mode *On*, not *Light Off*, and data collected and entered in the EDC system using the Low Mesopic instrument reading.

Pupil measurement will be initiated only after the eye has had time to fully adapt to the testing conditions (approximately 10 minutes). The Teneo 317 Model 2 (ver. 1.28 US SW) excimer laser limits the mesopic pupil sizes that may be treated from a minimum of 4.5 mm to a maximum of 7.0 mm. Operator attempts to enter an OZ outside this range will result in a pop-up message, "out-of-range."

7.0 MANIFEST REFRACTION

It is essential that a consistent and standard procedure be used to obtain manifest refraction (MR) measurements. These measurements will be obtained by a qualified ophthalmologist, optometrist, or trained ophthalmic technician only. **At no time during the study will auto-refraction be utilized as a final endpoint refraction. Auto-refractor or lensometer readings may only be**

utilized to obtain a starting point for the refraction if necessary. The manifest refraction is considered to be the subjectively determined refraction which provides the best corrected visual acuity at a distance of optical infinity.

Each subject must be manually refracted to his/her best correction by an ophthalmologist, optometrist, or a skilled technician using the ETDRS chart at 4 meters with a phoropter or trial frame under photopic lighting conditions. All refractions will be conducted in a manner consistent with the site's standard techniques using 0.25 D steps and utilizing a Jackson cross cylinder method. The resulting manifest refraction obtained using the ETDRS chart at 4 meters is adjusted for optical infinity by subtracting 0.25 D from the sphere value. The 'Chart R' with Sloan letters will be used to obtain the manifest refraction. The manifest refraction which has been adjusted for optical infinity will be documented on the Sponsor-supplied refraction worksheet. The manifest refraction which has been adjusted for optical infinity should be used as the basis for laser refractive treatment.

The resulting manifest refraction will be placed in a trial frame and utilized to obtain BSCVA results. For testing at 4 meters, a +0.25 D must be added to the manifest refraction to correct the testing distance to optical infinity. If for some reason (e.g., dense cataract), MR cannot be obtained, the results should be documented as ND as indicated above and not entered as zeros. In the event of this occurrence, BSCVA will not be tested and the reason for ND will be required in the source document and in the eCRF.

NOTE: Contact lens wearers need to demonstrate a stable refraction (within ± 0.50 D) in the operable eye(s), as determined by MRSE on two consecutive exam dates. Stability of the refraction is determined under the following conditions:

- Lenses are not worn for at least 2 weeks (rigid or toric contact lenses) or 3 days (soft contact lenses) prior to the first refraction used to establish stability and through the day of surgery;
- The two refractions are performed at least 7 days apart.

Subjects must also be willing to discontinue contact lens wear for the duration of the study.

8.0 VISUAL ACUITY

8.1 Uncorrected Near and Distance Visual Acuity (UDVA) and Best Spectacle-Corrected Distance Visual Acuity (BSCVA) Testing

It is essential that these standard procedures be used to obtain VA measurements. The VA measurements will be obtained by a qualified ophthalmologist, optometrist, or trained ophthalmic technician. Prior to any potential subject testing, the Sponsor or its representative will certify the site is suitably staffed and equipped to conduct all necessary VA testing.

8.1.1 Testing Procedures

Testing of distance visual acuity and manifest refraction for all eyes will be conducted at 4 meters using the ETDRS charts. Testing of near visual acuity will be conducted at 40 cm.

The same testing method is to be employed for all study visits for each subject to facilitate reliable comparisons from visit to visit. The only variance in procedure being, the subject will be reading the refraction results in a trial frame for the BSCVA procedure.

If a Manifest Refraction is not obtainable, BSCVA will not be tested. The results should be documented as Not Done (ND) and not entered as zeros. The reason it was not obtainable must be recorded in the source document and in the eCRF. The Investigator should also consider whether or not failure to obtain Manifest Refraction is appropriate for recording as an AE.

First, the right eye is tested at 40 cm with an appropriate ETDRS chart scaled for near reading and then for the left eye at 40 cm with an appropriately scaled ETDRS chart. Then, the right eye is tested at 4 meters with ETDRS Chart 1, and then the left eye is tested at 4 meters with ETDRS Chart 2. A +0.25 D lens must be placed in front of the eye during testing of UDVA at 4 meters to correct for the difference between the testing distance and optical infinity; similarly, a +0.25 D lens must be added to the manifest refraction during testing of BSCVA to correct for the difference between the testing distance and optical infinity. Each chart should remain hidden from view until the eye in question is ready for testing. The subject may stand or sit for the VA test. If the subject is seated, their back should fit firmly against the back of the chair. The examiner should ensure that the subject is standing or sitting comfortably, that the head does not move forward or backward during the test, and that the subject's eyes remain at the specified distance.

The subject should be told that the chart has letters only and no numbers. If the subject forgets this instruction and reads a number, remind the subject that the chart contains no numbers and the examiner should request a letter in lieu of the number.

The subject should be asked to read slowly (at a rate not faster than about one letter per second) in order to achieve the best identification of each letter and to not proceed until the subject has given a definite response.

Examiners should never point to the chart or to specific letters on the chart or read any of the letters during the test. Each letter is scored as right or wrong. Once a subject has identified a letter with a definite single-letter response and has read the next letter, a correction of the previous letter cannot be accepted. If the subject changes a response aloud (e.g., "That was a 'C,' not an 'O'.") before the next letter is read aloud, then the change should be accepted. If the subject changes a response after beginning to read the next letter, the change is not accepted.

When the subject says a letter cannot be read, the subject should be encouraged to guess. If the subject identifies a letter as one of two or more letters, ask the subject to choose one letter and, if necessary, to guess even if the next letter has already been read. If the subject does turn their head,

care must be taken to ensure that the fellow eye remains covered. When it becomes evident that no further letters can be read, despite urgings to read or guess, the examiner should stop the test for that eye.

Eyes reading 19 or fewer letters correctly at 4 meters should be tested at 1 meter. If the trial frame is to be removed when changing the test distance from 4 meters to 1 meter, the testing chart should first be removed from view to prevent the subject from reading the chart with the fellow eye.

Before testing BSCVA at 1 meter, a +0.75 D sphere should be added to the 4-meter correction already in the trial frame to compensate for the closer testing distance. Note that the 4-meter correction includes +0.25 in addition to the manifest refraction.

Before testing UDVA at 1 meter, a +1.0 D sphere should be placed in a trial frame and worn by the subject to compensate for the closer testing distance.

Where the subject may stand or sit for the 4-meter test, they must sit for the 1-meter test and *must not* move their head. (As indicated above, the subject should be seated comfortably with their back firmly placed against the back of the chair.) The avoidance of any head movement forward or backward is particularly important during the closer testing range.

The subject should be asked to read only the first six lines at 1meter distance, making 30 the maximum score attainable at that distance.

After the test of the right eye is completed, occlude the right eye. The test is then repeated for the left eye at 4 meters with standard ETDRS charts. If the subject is unable to read the chart at 4meters then move the chart closer.

8.1.2 Scoring and Recording Visual Acuity Values

The scoring and recording of visual acuity values will be done by the technician using standardized source documents for this purpose.

8.1.3 Illumination of the ETDRS Chart and Examination Room

The optimal ETDRS illumination level is approximately 85 cd/m² and all sites must ensure they are consistently as close as possible to this level through all visual acuity and refraction testing.

9.0 SLIT LAMP EXAMINATION

The slit lamp examination will be performed using a slit lamp biomicroscope and observations will be graded per the classification of slit lamp observations as described below. Additional observations/abnormalities can be reported on the eCRF and graded as appropriate.

- **Lids** – Normal / Abnormal
- **Conjunctiva** – Normal / Abnormal
  - **Bulbar Conjunctival Hyperemia**

  0 None – normal, no tissue changes

  1 Mild – trace levels of hyperemia, no clinical action required

  2 Moderate – light diffuse vessel engorgement, clinical action may be required

  3 Severe – florid vessel engorgement, clinical action usually required

  4 Very Severe – vessel engorgement accompanied by other clinical signs or symptoms of significant ocular irritation, action urgently required

- **Cornea**
  - **Clarity**

  0 Normal clarity. There is no difference in the clarity between the central treatment zone and the peripheral non-treated areas. Normal corneal stroma has a diffuse ground glass appearance. Iron lines (Hudson-Stahli lines) are considered within physiologically normal limits and should not be considered corneal haze.

  1 Trace. Defined as faint corneal haze that is easily seen by indirect broad oblique illumination but not evident with broad direct illumination. Trace haze may be diffuse and evenly spread throughout the treatment zone or may have a lacy or reticular appearance.

  2 Mild. Defined as discrete haze that is visible with difficulty by direct focal slit examination. With broad oblique illumination, mild haze has a more granular confluent pattern than trace haze.

  3 Moderate. Defined as a moderately dense corneal opacity that partially obscures iris details in direct illumination. Areas of clumped confluent haze are frequently seen for this grading level. It is easily identified by direct focal illumination.

4 Marked. Defined as a severely dense opacity that completely obscures iris details. This is the only haze-grading category that can be identified by gross examination. With slit lamp illumination, it appears as a dense gray-white corneal opacity that may demonstrate some thickness or elevation.

- **Superficial Punctate Keratitis (SPK)**

0 None – no punctate staining with fluorescein

1 Mild – less than 1/3 of cornea area stains with fluorescein

2 Moderate - 1/3 to 2/3 of cornea area stains with fluorescein

3 Severe – greater than 2/3 of cornea area stains with fluorescein

- **Corneal Edema**

0	None	No evidence of corneal swelling with normal transparency
1	Mild	Mild corneal swelling
2	Moderate	Moderate corneal swelling
3	Severe	Definite widespread cloudiness or haziness giving dull ground glass appearance to cornea, or numerous coalescent bullae

- **Corneal Epithelium**

Normal	No evidence of corneal defect, superficial punctate keratitis (SPK), or other abnormality; i.e., no corneal staining evident.
Pannus	Invasion of bulbar conjunctival blood vessels beyond limbal border into superficial cornea. May be either blood-filled or ghost vessels.
Other	Epithelial abnormalities that do not properly fall in the above three categories.

- **Corneal Stroma**

0 Normal. No evidence of corneal swelling with normal transparency.

1 1 + Edema. Minimal corneal swelling; barely discernible haziness.

2 2 + Edema. Mild corneal swelling with faint but definite localized or generalized haziness.

3 3 + Edema. Moderate corneal swelling; some corneal striae may be visible.

4 4 + Edema. Severe corneal swelling, definite widespread cloudiness or haziness giving dull ground glass appearance to cornea, or numerous coalescent bullae. Corneal striae are often present.

5 Stromal Scar. Focal or diffuse area of corneal scarring/opacity which may appear as dense haziness.

99 Other, specify: Other stromal abnormalities that do not properly fall in the above six categories.

- **Corneal Flap**

0 Normal. Smooth, homogenous, flattened appearance to corneal flap with no evidence of wrinkles or other surface irregularities. Presents with normal crisp light reflex.

1 1 + Folds. Barely discernible wrinkling of corneal flap; focal or more wide-spread. Light reflex may be slightly distorted in area of fold or wrinkle.

2 2 + Folds. Folds or wrinkles those are evident with some degree of apparent elevation above corneal bed. Light reflex definitely broken or distorted.

3 3 + Folds. Marked folds or wrinkles in flap easily visible upon gross observation. Light reflex severely broken or distorted.

4 Flap Edema. The presence of ANY severity of edema in the stroma of the flap above the level of the flap interface. **Epithelial edema is not considered to be flap edema.**

- **Corneal Interface**

0 Clear. No evidence of cells or debris in interface, i.e., completely clear and transparent.

1 Debris. Any foreign (non-cellular) material present between flap and stromal bed.

2 Epithelial cells. Single or multiple epithelial cells, located either focally or dispersed in interface.

3 Epithelial cysts. Nest or clump of aggregated epithelial cells not obviously contiguous with peripheral corneal epithelium.

4 Epithelial in-growth. Invasion of epithelial cells from the keratectomy junction/peripheral cornea that have migrated into the interface, and are contiguous with the peripheral corneal epithelium.

5 Non-epithelial cells. Any non-epithelial cells (red blood cells, white blood cells) present in the interface.

- **DLK (Diffuse lamellar keratitis,[57] interface inflammation)**

0 Normal. Absence of DLK or interface inflammation.

1 Stage 1. Defined by the presence of white granular cells in the periphery of the lamellar flap, outside the visual axis.

2 Stage 2. Defined by the presence of white granular cells in the center of the flap, involving the visual axis, in the flap periphery, or both.

3 Stage 3. Defined by the aggregation of more dense, white, and clumped cells in the center visual axis, with relative clearing in the periphery.

4 Stage 4. This is the rare result of severe lamellar keratitis with stromal melting, permanent scarring, and associated visual morbidity.

- **Anterior Chamber**
  - **Cell**

Grade	Cells in Field
0	0
0.5 +	1-5
1 +	6-15
2 +	16-25
3 +	26-50
4 +	>50

  - **Flare**

Grade		Description
0	None	
1 +	Faint	
2 +	Moderate	Iris/lens detail clear
3 +	Marked	Iris/lens details hazy
4 +	Intense	Fibrin/plastic aqueous

- **Iris / Pupil** – Normal / Abnormal

10.0 ENDOTHELIAL CELL DENSITY (SPECULAR MICROSCOPY SUB-STUDY)

Pre-operative and post-operative (Month 6) corneal endothelial cell densities will be measured by specular microscopy for both eyes (regardless whether one or both eyes are treated) of up to approximately 90 subject eyes undergoing LASIK surgery at two or more clinical sites. Specular microscopes that will be used in the sub-study must first be certified by the central reading center prior to their use for study purposes. At least two study staff members at a clinical site that will be obtaining ECD images and using the specular microscope as delegated by the principal investigator must be trained and certified by central reading center to ensure proper and consistent imaging prior to capturing study subject images. Documentation of such training and qualifications will be maintained in the site files. The ECD technicians should be delegated as a primary or back-up technician, with the primary ECD technician obtaining ECD images whenever possible and the back-up technician obtaining ECD images as necessary in lieu of the primary technician.

Clinical sites are to use their specular microscopes in accordance with the manufacturer's and reading center's recommendations and procedures. Calibration of specular microscopes will be documented and filed at each clinical site.

Standardized central corneal ECD imaging and counting methods,[43, 44] including for cell density, coefficient of variation, and hexagonality, will be implemented according to the central reading center Standard Operating Procedures and will be used to minimize variability. The measurement of the ECD in the central cornea will be performed preoperatively and at six months postoperatively (Visit 7) using a non-contact Specular Microscope (approved by or supplied by the Sponsor). Three images from the central part of the cornea will be obtained for each applicable subject visit and forwarded to the central reading center according to the center's instructions.

To determine ECD, sites will submit all preoperative and Month 6 postoperative images to the reading center (which will be masked) for image analysis. The reading center will determine the mean ECD based on the three images.

11.0 CONTRAST SENSITIVITY

At least approximately 50 patients will have their eyes enrolled in a sub-study to have monocular and binocular contrast sensitivity testing performed, testing which will be conducted at three or more clinical sites. The patients in this sub-study may be, although are not required to be, any of the subjects in the specular microscopy testing sub-study. Testing will be conducted using a commercially available contrast sensitivity instrument of the same make and model at each of the two or more clinical sites. Each instrument will be calibrated according to the manufacturer and capable of conducting binocular mesopic (approximately 3.0 ± 2.0 cd/m^2) contrast sensitivity measurements with and without glare at spatial frequencies of 1.5, 3, 6, and 12 cpd. The contrast sensitivity measurements will be made at the optimal distance recommended by the instrument manufacturer.

Subjects will practice the contrast sensitivity test once at each of two randomly selected spatial frequencies under mesopic conditions without glare before beginning tests for recorded data. Contrast sensitivity will be assessed twice for each subject at each test condition, and results will be reported as graphs of mean contrast sensitivity (± SD) vs spatial frequency at each study visit.

12.O SCHIRMER'S TEST

Appropriate commercial paper strips for conducting a Schirmer's test without anesthesia is placed in the inferior fornix extending outward of both eyes and subjects are instructed to close their eyes for 5 minutes. The test strips are then removed and the migration distance of strip wetness is measured in mm. No topical anesthetic may be used.

13.0 INTRAOCULAR PRESSURE (TONOMETRY)

The measurement of eye pressure is part of a routine eye examination in which the IOP is determined. Goldmann applanation tonometry is the most accurate method and as such is the preferred method for study subjects. However, if an alternative method (e.g., Tonopen) is required at any site, it will be allowed. In any event, the same testing method is to be employed for all study visits for each subject to facilitate reliable comparisons from visit to visit. If cycloplegic refraction is measured the same day as IOP, the intraocular pressure should be measured following the refraction to avoid disturbing the corneal surface.

14.0 CYCLOPLEGIC REFRACTION

The subject should be seated comfortably and lean their head back. One drop of Cyclopentolate 1% is added in the lacrimal sac of the eye intended to undergo LASIK surgery, repeated again 3-5 minutes later, and then the standard method for manifest refraction, and collection and recording of the refraction data, should be conducted no sooner than 20 minutes after the second drop of cyclopentolate 1% has been instilled. This procedure should be performed only after examinations and procedures not requiring pupil dilation have been completed at the relevant (i.e., the first and last) study visit. Subjects should be cautioned following cycloplegic refraction to wear sunglasses, avoid excessive sun exposure, and avoid tasks that require near vision for 6-12 hours.

15.0 DILATED FUNDUS EXAMINATION

Using an ophthalmoscope and the Investigator's preferred lens, light is shone into the eye, allowing the retina and the optic nerve to be examined. Any "abnormal" findings will be thoroughly documented and, as appropriate, rated in severity. The Investigator will classify findings as follows:

- **Optic Nerve** – Normal / Abnormal
- **Vitreous** – Normal / Abnormal
  - **Vitreal Opacities (Floaters)**

0	**None**
1	Mild
2	Moderate
3	Severe

Any further abnormalities are to be specified.

- **Macula** – Normal / Abnormal
  - **Macular Degeneration**

0	**None**
1	Mild
2	Moderate
3	Severe

Any further macular abnormalities are to be specified.

- **Retina** – Normal / Abnormal
  Any abnormalities are to be specified.

Appendix C. Instructions for Surgical Use of the TENEO 317 Model 2 (ver. 1.28 US SW) Excimer Laser System

1.0 TENEO 317 MODEL 2 EXCIMER LASER SYSTEM STORAGE AND USE CONDITIONS

For the TENEO 317 model 2 laser storage and use conditions, the temperature and humidity ranges given below will be followed, with collection of temperature and humidity values in the laser suite monthly. For these and any other environmental conditions specified in the user instructions, the TENEO 317 model 2 laser system shall conform to all safety, optical, and mechanical requirements under the environmental conditions specified in the user instructions for clinical use. **Real time evidence of temperature or humidity excursions outside of the following operating ranges requires no surgeries are to be done until TENEO 317 model 2 laser operation can safely be conducted within these ranges.**

Temperature range for storage:	-10° C to +55° C (+14° F to +131° F)
Humidity range for storage:	10% to 95% relative humidity (non-condensing)
Temperature range for operating:	+18° C to +24° C (+64° F to +75° F)
Humidity range for operating:	30% to 50% relative humidity (non-condensing)

2.0 LASIK SURGICAL TECHNIQUE

The surgical technique consists of ablating tissue from the stroma after having created a flap of corneal tissue with a femtosecond laser. The flap is folded back exposing the central cornea where the excimer laser will ablate the stromal tissue. The shape of the ablated area for myopia is achieved by allowing more laser pulses to strike the central than the peripheral portion of the ablation area. The shape of the ablated area for astigmatism is achieved by allowing more laser pulses to strike the flatter axis of the cornea. The surgery performed, and particularly the size of the optical zone, will be determined by needed refractive correction of the patient, the pupil size, the central pre-operative corneal thickness (as measured by pachymetry), flap thickness and amount of residual corneal tissue (residual corneal thickness should be no less than 250 microns).

3.0 CORNEAL FLAP PREPARATION

The subject is given topical and systemic medication (e.g., antibiotic, analgesic, and/or sedative) at the physician's discretion prior to the procedure. The subject is properly positioned on the excimer laser operating platform directly under the operating microscope. A topical anesthetic is instilled in the first or only eye to be treated and the non-operative eye is covered with an occlusive patch. The surgeon prepares the operative eye for the procedure and makes the adjustments necessary to insure that the operative eye is properly positioned for the keratectomy.

An optical zone marker may be used to ink the cornea to provide a reference mark. A lid speculum is put into place and adjusted for ease of viewing and subject control. A suction ring is then placed centrally to the cornea.

If the corneal flap is created with a femtosecond laser, a suction ring is placed centrally to the cornea, the femtosecond laser with an attached patient interface is prepared, and the subject is moved upwards to insert the patient interface into the suction clip. After complete docking, the femtosecond laser application will be performed based on the physician's assessment of the eye to be treated.

4.0 EXCIMER LASER REFRACTIVE SURGERY

The laser is programmed based on the subject's MRSE and astigmatism such that the optical zone is equal to or greater than the mesopic pupil size. Corneal topography data for each eye of a subject will be collected at the pre-operative study visit and recorded on the TENEO model 2 excimer laser; these data will be source data for the LASIK surgery. The subject is properly positioned on the excimer laser operating platform directly under the operating microscope. A speculum is placed so the laser ablation zone is constantly exposed and the subject is cautioned to not move. The Investigator may apply one or more medications to the eye while the subject is under the excimer laser. Once the surgical field is within focus, the surgeon engages the eye tracker system to track the lateral (X/Y) shift of the pupil center by the lateral (X/Y) tracker and the torsional misalignment by the rotation tracker. The corneal flap is lifted up and folded to one side exposing the stromal surface. The surgeon superimposes the two intersecting laser focus beams to ensure that the surgical field is within focus. With the subject fixating on the fixation light, and the eye tracker 'locked-on' to the subject's pupil, the excimer laser surgery is performed.

If unacceptable subject movement occurs and pupillary centration is lost, the TENEO 317 laser X/Y Eye Tracker will automatically pause the procedure. The surgeon may also halt the procedure at any time by removing their foot from the laser engagement pedal. The procedure can be resumed at the exact point where the pause occurred once the eye tracker detects pupillary centration and the surgeon depresses the foot pedal again.

After the treatment, the corneal flap is repositioned in place. Topical medications are applied, including antibiotic, steroid, and non-steroidal anti-inflammatory solutions, at the surgeon's discretion. The surgeon carefully smooths the corneal flap and wicks away excess fluid at the edges of the corneal flap and on the flap surface with sterile sponges, then wait approximately 30 to 60 seconds for flap adhesion before removing the lid speculum. The subject is instructed to close the eye, and excess fluid is absorbed from the skin with a sterile pad. The subject is then instructed to open the eye and blink a few times, to insure flap stability.

Surgery on the fellow eye may proceed immediately in a similar manner if there have been no complications. It is also possible, at the discretion of the Investigator, to create the corneal flaps

on both eyes before the LASIK surgery is conducted on either eye. Once surgery is completed, the subject may be examined at a slit lamp to insure good flap position. The subject is then given post-operative instructions and discharged from the facility.