Study to Evaluate Safety and Effectiveness of the Boston Orthokeratology (oprifocon A) Shaping Lens in the Arise Orthokeratology Lens Design with Non-spherical Posterior Peripheral Curves

CLINICAL STUDY PROTOCOL

STUDY #918

Sponsor: Bausch & Lomb Incorporated

This clinical investigation is being conducted in accordance with 21 Code of Federal Regulations (CFR) Parts 11, 50, 54, 56, and 812; 42 CFR Part 11 – Clinical Trials Registration and Results Information Submission; EN ISO 14155:2020 *Clinical investigation of medical devices for human subjects – Good clinical practice*; Medical Device Regulation (MDR) (EU) 2017/745; International Council for Harmonization (ICH) Good Clinical Practice; the Declaration of Helsinki and applicable local regulations. Additional information on the investigational test article(s) is presented in the Investigator's Brochure for the Boston Orthokeratology (oprifocon A) Shaping Lens, Arise Orthokeratology Lens Design.

Revision Chronology:

Amendment 5, Version 6.0	-	30 Nov 2023
Amendment 4, Version 5.0	-	04 Aug 2023
Amendment 3, Version 4.0	-	14 July 2023
Amendment 2, Version 3.0	-	26 May 2023
Amendment 1, Version 2.0	-	09 Feb 2023
Original, Version 1.0	-	23 Jan 2023

Key design elements of this protocol will be registered on www.clinicaltrials.gov as required by current regulations and, if applicable, other public databases as required by local country regulations. In addition, results of this study will be made publicly available on www.clinicaltrials.gov regardless of outcome as required by current regulations and, if applicable, in other public databases as required by local country regulations. The identity of the subjects who participated in the study will be maintained confidential.

SPONSOR APPROVAL PAGE

Study to Evaluate Safety and Effectiveness of the Boston Orthokeratology (oprifocon A) Shaping Lens in the Arise Orthokeratology Lens Design with Non-spherical Posterior Peripheral Curves

PROTOCOL - STUDY #918

[redacted]

[redacted] _____ _____

[redacted] Broese, Director, Global Device Complaint Management Date
Bausch & Lomb Incorporated

INVESTIGATOR STATEMENT OF APPROVAL

Study to Evaluate Safety and Effectiveness of the Boston Orthokeratology (oprifocon A) Shaping Lens in the Arise Orthokeratology Lens Design with Non-spherical Posterior Peripheral Curves

STUDY #918

I have read this clinical study protocol and concur that it contains all information necessary to conduct the study and agree to abide by all provisions set forth therein.

I agree to conduct this study in accordance with 21 CFR Parts 11, 50, 54, 56 and 812; 42 CFR Part 11 – Clinical Trials Registration and Results Information Submission; EN ISO 14155:2020 *Clinical investigation of medical devices for human subjects – Good clinical practice*; Medical Device Regulation (MDR) (EU) 2017/745; International Council for Harmonization (ICH) Good Clinical Practice; the Declaration of Helsinki and applicable local regulations.

I will not initiate the study until I have obtained written approval by the appropriate IRB/EC and have complied with all financial and administrative requirements of the governing body of the clinical institution and the Sponsor. I agree to obtain written informed consent from each study subject prior to performing any study specific procedures.

I understand my obligation as the Principal Investigator to supervise all testing of the investigational products used in this study involving human subjects and to ensure that the investigational product is dispensed as per protocol.

I understand my obligation as the Principal Investigator to ensure that all study personnel assisting in the conduct of the study are qualified and are properly trained to conduct their assigned tasks and obligations during the entire course of the trial. I agree to maintain adequate and accurate records in accordance with government regulations and to make those records available for inspection.

I testify that I have never been disqualified as an Investigator by any Regulatory Authority and have never been involved in a study or other research that was terminated due to misconduct or fraudulent activity.

I understand that my signature on this document indicates my agreement to this Clinical Investigational Plan/Protocol and to review and, if appropriate, sign the clinical study report. I understand that my signature on electronic case report forms indicates that the data therein has been reviewed and accepted by me.

I understand that this document and related information is subject to confidentiality terms found in my signed Confidentiality or Clinical Services Agreement. I agree to protect the confidentiality of my patients when allowing the Sponsor of this clinical investigation, and/or relevant regulatory authorities and IRBs, direct access to my medical records for study subjects.

_____ _____

Principal Investigator, Signature Date

Print Principal Investigator Name and Address below:

_____

_____

_____

PERSONNEL AND FACILITIES

NOTE: The information on this page is subject to change. All changes will be provided under separate cover.

Function	Organization
Study Sponsor: protocol, investigational product supply and distribution, safety monitoring and reporting to FDA, study oversight, regulatory, and auditing	Bausch & Lomb Incorporated 1400 North Goodman Street Rochester, NY 14609 USA Main telephone number: 585-338-5306
Manufacturer of Investigational Test Article(s)	Bausch & Lomb Incorporated 6 Lancaster Parkway Lancaster, NY 14086
Statistical Analysis and Data Management	[redacted]
Medical Monitor	[redacted]
Electronic Data Capture (EDC)	[redacted]
Clinical Study Management, Monitoring, and Safety Monitoring	[redacted]
Investigative Clinical Sites	An up-to-date Protocol 918 Investigator Contact List[1] of Investigators, investigation sites, involved with this clinical investigation will be maintained by the Sponsor in a separate document.

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APPENDICES

GLOSSARY OF TERMS

Adverse device effect (ADE)	Adverse event related to the use of an investigational medical device. Note 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. Note 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.
Adverse event (AE)	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 and whether anticipated or unanticipated. Note 1: This definition includes events related to the investigational medical device. Note 2: This definition includes events related to the procedures involved. Note 3: For users or other persons, this definition is restricted to events related to the use of investigational medical devices.
Anticipated serious adverse device effect (ASADE)	Anticipated serious adverse device effect is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.
Device deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance. Note 1: Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling. Note 2: This definition includes device deficiencies related to the investigational medical device.
Investigational medical device	A medical device being assessed for clinical performance, effectiveness, or safety in a clinical investigation. Note 1: This includes medical devices already on the market that are being evaluated for new intended uses, new populations, new materials or design changes. Note 2: This includes medical devices already on the market that are being evaluated within their intended use in a post-market clinical investigation (interventional or non-interventional). Note 3: The terms “investigational medical device” and “investigational device” are used interchangeably.
Life-threatening adverse event	An adverse event is considered “life-threatening” if, in the view of either the Investigator or Sponsor, its occurrence places the patient or subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.

Malfunction	Failure of a medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical investigation plan.
Medical device	An instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific purpose(s) of: – diagnosis, prevention, monitoring, treatment or alleviation of disease; – diagnosis, monitoring, treatment, alleviation of or compensation for an injury; – investigation, replacement, modification, or support of the anatomy or of a physiological process; – supporting or sustaining life; – control of conception; – disinfection of medical devices; providing information by means of in vitro examination of specimens derived from the human body; and does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.
Product complaints	Any oral, electronic, or written communication that alleges deficiencies related to the identity (labeling), quality, durability, reliability, safety, effectiveness, or performance of a marketed product, including failure of the product, labeling or packaging to meet specifications, whether or not the product is related to or caused the alleged deficiency. A complaint may allege that an adverse event or medical device malfunction has occurred.
Serious adverse device effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Serious adverse event (SAE)	An adverse event that led to any of the following outcomes: • Death • Serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following: – a life-threatening illness or injury, or – a permanent impairment of a body structure or a body function including chronic diseases, or – in-patient or prolonged hospitalization, or – medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment to a body structure or a body function. • Fetal distress, fetal death, a congenital abnormality, or birth defect including physical or mental impairment.
Serious health threat	Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects,

	users or other persons, and that requires prompt remedial action for other subjects, users or other persons. Note 1: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.
Treatment-emergent adverse event (TEAE)	A treatment-emergent adverse event is defined as any event not present prior to the initiation of the treatments or any event already present that worsens in either intensity or frequency following exposure to the treatments.
Unanticipated adverse device effect (UADE)	Unanticipated adverse device effect is any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. [FDA, 21CFR 812.3]
Unanticipated serious adverse device effect (USADE)	Unanticipated serious adverse device effect is a serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the current risk assessment. [EN ISO 14155:2020]
Use error	User action or lack of user action while using the medical device that leads to a different result than that intended by the manufacturer or expected by the user. Note 1: Use errors includes slips, lapses and mistakes. Use error includes the inability of the user to complete a task. Note 2: Use errors can result from a mismatch between the characteristics of the user, user interface, task or use environment. Note 3: Users might be aware or unaware that a use error has occurred. Note 4: An unexpected physiological response of the patient is not by itself considered a use error. Note 5: A malfunction of a medical device that causes an unexpected result is not considered a use error.
Vulnerable subject	Individuals who are unable to fully understand all aspects of the investigation that are relevant to the decision to participate, or who could be manipulated or unduly influenced as a result of a compromised position, expectation of benefits or fear of retaliatory response.

LIST OF ABBREVIATIONS

Abbreviation /Acronym	Term
AE	adverse event
ADE	adverse device effect
BSCVA	best spectacle-corrected visual acuity
CFR	Code of Federal Regulations
CI	confidence interval
eCRF	electronic case report form
D	diopter
EC	ethics committee
EDC	electronic data capture
FAS	Full Analysis Set
FDA	United States Food and Drug Administration
GCPs	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICF	informed consent form
ICH	International Council for Harmonisation
ID	identification
IDE	Investigational Device Exemption
IRB	Institutional Review Board
ISO	International Organization for Standardization
logMAR	logarithm of the minimum angle of resolution
MCMC	Markov Chain Monte Carlo
MRSE	Manifest Refractive Spherical Equivalent
OD	right eye
OS	left eye
OU	both eyes
PAL	product accountability log
RGP	rigid gas permeable
SAE	serious adverse event
SOP	standard operating procedure
TEAE	Treatment-emergent adverse event
UADE	unanticipated adverse device effect
UDVA	uncorrected distance visual acuity
US	United States
USAN	United States Adapted Name
VA	visual acuity

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

SYNOPSIS

Bausch & Lomb Incorporated Study #918	
Title:	Study to Evaluate Safety and Effectiveness of the Boston Orthokeratology (oprifocon A) Shaping Lens in the Arise Orthokeratology Lens Design with Non-spherical Posterior Peripheral Curves
Name of Test Article:	Arise Orthokeratology Lens
Number of Study Centers Planned:	Approximately 6-10 Investigative sites in the United States
Number of Subjects Planned:	Approximately 90 subjects will be enrolled.
Background:	The Bausch + Lomb Vision Shaping Treatment VST is based on a reverse geometry orthokeratology design that includes a base curve/treatment curve, a reverse curve, alignment curves and peripheral curves. The base curve is used to only flatten the cornea and is not considered a fitting curve. The parameters of the Arise Orthokeratology Lens are controlled to be within the bounds determined by the spherical posterior curves of other lens designs prescribed for the Bausch + Lomb Vision Shaping Treatment. The term peripheral curves excludes the base curve and includes the zones defined as the reverse curve, alignment curves and peripheral curves. Peripheral curves are designed to help control centration of the lens. When there are elevation differences between the flat and steep meridians on the cornea (e.g., corneal toricity), spherical peripheral curves, including the reverse curve, alignment curves and peripheral curves, may not align completely to the cornea and can result in a lens with sub-optimal centration. Aspheric curves and toric (e.g., dual axis) peripheral curves on reverse geometry lenses for overnight orthokeratology have been available in the US market for more than 10 years for fitting lenses. The intent of the Arise Orthokeratology Lens is to provide a stable and centered lens that helps ensure the treatment zone of the lens is well positioned in relation to the pupil and is shaping the central portion of the cornea for optimal results.
Objective(s):	The objective of this orthokeratology study is to evaluate the safety and effectiveness of the Arise Orthokeratology Lens with non-spherical posterior peripheral curves.
Study Design:	Approximately 90 subjects will be enrolled in this multi-center, single-arm, open-label study. All subjects will be seen for a Screening Visit at which informed consent will be obtained and eligibility assessed. If subjects satisfy all eligibility criteria, they will be enrolled in the study. Subjects will be seen to assess the treatment effect of overnight orthokeratology over a 3-month period.
Diagnosis and Main Criteria for Inclusion:	To be eligible for entry into the study, the subject must: 1. Be 12 years or older on the date the Informed Consent Form (ICF) is signed and, as subject or parent or legal guardian of a minor subject, have capacity to read, understand and provide written voluntary informed consent on the IRB-approved ICF and provide authorization as appropriate for local privacy regulations. 2. Be orthokeratology lens naïve. 3. Spherical refractive error between plano and -5.00D. 4. Astigmatism no greater than 1.50D. 5. Corneal topography sagittal height differential of ≥ 30 microns between the two main meridians (flat and steep) at an 8mm chord. 6. Has keratometric readings from 39.00 to 48.00D. 7. Has a clear and undistorted Mire Reflex. 8. Be willing and able to comply with all treatment and follow-up study visits and

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	procedures. 9. Must be willing to refrain from wearing habitual soft contact lenses during the study period. 10. Subjects must be correctable through spherocylindrical refraction to 42 letters (0.1 logMAR) or better (distance, high contrast) in each eye.
Main Criteria for Exclusion:	The subject is ineligible for entry into the study if the subject meets any of the following criteria: 1. Subject is considered by the Investigator, to not be a suitable candidate for participation or it is not in the best interest of the subject to participate in the study. 2. Subjects who have worn rigid gas permeable (RGP) contact lenses within the last 30 days or who have worn polymethylmethacrylate (PMMA) lenses within the last three months. 3. Prior eyelid, strabismus, intraocular, or refractive surgery. 4. Keratoconus or an irregular cornea. 5. Subjects with any systemic disease currently affecting ocular health or in the Investigator's opinion may have an effect on ocular health during the course of the study. 6. Subjects using any systemic or topical medications that will, in the Investigator's opinion, affect ocular physiology or lens performance. 7. A known allergy to fluorescein, benoxinate, or proparacaine. 8. A history of corneal hypoesthesia (reduced corneal sensitivity), corneal ulcer, corneal infiltrates, ocular viral or fungal infections or recurrent ocular infections. 9. Subjects with an active ocular disease or who are using any ocular medication. 10. Subjects with any Grade 2 or greater finding during the slit lamp examination. Subjects with corneal infiltrates, of ANY GRADE, are NOT eligible. Refer to Appendix B: Methods of Clinical Evaluation. 11. Subjects with any "Present" finding during the slit lamp examination that, in the Investigator's judgement, interferes with contact lens wear. Refer to Appendix B: Methods of Clinical evaluation. 12. Subjects with any scar or neovascularization within the central 6mm of the cornea. Subjects with minor peripheral corneal scarring (that does not extend into the central area), that in the Investigator's judgement, does not interfere with contact lens wear, are eligible for this study. 13. Subjects participating in any drug or device clinical investigation within 2 weeks prior to entry into this study (Screening Visit) and/or planning to do so during the period of study participation. 14. Subjects who are amblyopic. 15. Immediate family or close relative is a member of the office staff, including the Investigator(s). 16. Females of childbearing potential (those who are not surgically sterilized or postmenopausal) if they meet any one of the following: – They are currently pregnant – They plan to become pregnant during the study – They are breastfeeding
Investigational Product, Dose and Mode of Administration:	The Investigator will fit each qualifying subject according to Appendix D: Fitting Guide. The study lenses will be ordered specifically for each subject after fitting is assessed. Subjects will return approximately 15 days later to have the lenses dispensed.

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	Each subject will wear the study lenses in both eyes overnight for approximately 3 months.
Duration of Treatment:	The study will consist of seven visits. Visit 1 will take approximately 30 minutes and Visits 2 through 7 will take approximately one hour each. The subject treatment will be approximately 3 months.
Statistical Methods:	Continuous data will be summarized using descriptive statistics: number of non-missing observations (n), mean, standard deviation, median, minimum and maximum. Categorical data will be summarized using frequencies and percentages. The proportion of subjects who achieve monocular uncorrected distance visual acuity (UDVA) of 20/40 or better in both eyes at the 3-Month Follow-up Visit will be presented.
Criteria for Evaluation:	The primary safety outcome is the rate of serious adverse events at the subject and eye levels. [redacted] The primary effectiveness outcome is the proportion of subjects who achieve monocular UDVA of 20/40 or better in both eyes at the 3-Month Follow-up Visit. [redacted]

INTRODUCTION

The Bausch + Lomb Vision Shaping Treatment VST is based on a reverse geometry orthokeratology design that includes a base curve/treatment curve, a reverse curve, alignment curves and peripheral curves. The base curve is used to only flatten the cornea and is not considered a fitting curve. The parameters of the Arise Orthokeratology Lens are controlled to be within the bounds determined by the spherical posterior curves of other lens designs prescribed for the Bausch + Lomb Vision Shaping Treatment.

The reverse curve, alignment curves and peripheral curves are designed to help control centration of the lens. When there are elevation differences between the flat and steep meridians of the cornea (e.g., corneal toricity), spherical peripheral curves, including the reverse curve, alignment curves and additional peripheral curves, may not align completely to the cornea and can result in a lens with poor centration. Throughout the protocol the term "peripheral curves" excludes the Base Curve and includes the zones defined in the Bausch + Lomb Vision Shaping Treatment as the Reverse Curve, Alignment Curves and Peripheral Curves.

Aspheric curves and toric (e.g., dual axis) peripheral curves on reverse geometry lenses for overnight orthokeratology have been available in the U.S. market for more than 10 years for fitting lenses. The intent of the Arise Orthokeratology Lens is to provide a stable and centered lens that helps ensure the treatment zone of the lens is well positioned in relation to the pupil and is shaping the central portion of the cornea for optimal results.

1. BACKGROUND, RATIONALE AND OBJECTIVES

2.1 Intended Purpose of Device

The Arise Orthokeratology Lens is intended for use in the reduction of myopic refractive error in non-diseased eyes.

2.2 Target Population

The Arise Orthokeratology Lens is for use in the reduction of myopic refractive error, regardless of gender or ethnicity and who do not have contraindications for the device.

2.3 State of the Art

Further information regarding the relevance of this study in the context of state-of-the-art clinical practice such as background information, summary of relevant literature, mechanism of action, intended clinical performance, and a summary of existing relevant clinical data of the investigational device can be found in the Investigator Brochure for this study, Study 918, *Boston Orthokeratology (oprifocon A) Shaping Lens Arise Orthokeratology Lens Design*[2], Section 5 Existing Data.

2.4 Objective of Study

The objective of this overnight orthokeratology study is to evaluate the safety and effectiveness of the Arise Orthokeratology Lens with non-spherical posterior peripheral curves.

2.5 Minimization of Bias and Confounding Factors

The Sponsor will avoid improper influence on any parties participating in, or contributing to, the clinical investigation or the induction thereof. The selection and treatment of subjects and evaluation of clinical investigation data are potential sources of bias. Methods that are incorporated within the clinical investigation design to minimize potential bias include, but are not limited to, screening subjects to confirm eligibility with defined inclusion/exclusion criteria prior to enrollment; maintaining a log of all subjects screened and enrolled; collecting demographics and medical ocular history at baseline to later assess possible characteristics that may influence endpoints; standardizing data collection requirements and clinical investigation procedures; requiring a Financial Disclosure by Investigators; using standardized training materials for all trial personnel; and by scheduling regular monitoring visits to be conducted to verify adherence to the clinical investigation plan and source data. Compensation of the Investigators is not dependent on the study outcomes.

2. STUDY DESIGN

This is a multi-center, single-arm, open-label, bilateral clinical trial.

3.1 Description of Study Design

This is a single-treatment study evaluating the safety and effectiveness of the Arise Orthokeratology Lens with non-spherical posterior peripheral curves.

Approximately 90 subjects (180 eyes) will be enrolled in this 3-month, multi-center, single-arm, open-label study at approximately 6-10 investigative sites in the United States (US).

All subjects will be seen for a Screening Visit at which informed consent will be obtained and eligibility assessed. If subjects satisfy all eligibility criteria, they will be enrolled in the study. Subjects will be seen to assess the treatment effect of overnight orthokeratology over a 3-month period. All subjects will be assigned a subject identification (ID) number in sequential order by the Electronic Data Capture (EDC) system. At the Screening Visit, if a subject is eligible, study lenses will be ordered specifically for that subject. Eligible subjects will come back approximately 2 weeks after the Screening Visit for a Dispensing Visit. Each subject will also be dispensed Boston SIMPLUS Multi-Action Solution, including a study lens case, and Boston Rewetting Drops. These solutions will be replenished during the study as needed. Subjects must NOT use ANY other cleaning and disinfecting solution or rewetting drops during the study unless the Investigator transitions individual subjects to a different Boston Lens Care System. Subjects will be required to wear their study lenses for a minimum of eight (8) hours on an overnight wear basis for approximately 3 months, with scheduled in-office follow-up visits at 1-day, 1-week, 1-month, 2-months and 3-months. These follow-up visits must be conducted within 2 hours of the subject removing the study lenses.

Daily disposable soft contact lenses (Bausch + Lomb Biotrue ® ONEday (nesofilcon A) Contact Lenses known as “maintenance lenses”) will be dispensed to provide supplemental visual correction during the day as needed for the orthokeratology lens adaptation period.

3.2 Informed Consent Process

Voluntary written informed consent must be obtained from every subject prior to the initiation of any study-related activities. The Investigator must have a defined process for obtaining consent. Subjects must be given ample time to read, understand, and ask questions, in order to consider voluntary participation. The subject must indicate voluntary consent by providing a written signed and dated informed consent form (ICF). A copy of the signed and dated ICF must be provided to the subject and the original document must be filed in the subject's study records. A representative ICF for each investigative site is maintained in the Study Master File.

The ICF must meet all applicable local laws and be written in language that the subject understands. Subjects must be informed that their participation in the study is voluntary and that their decision to withdraw from participation at any time during the study will not impact any aspect of their standard care. Subjects will be provided with contact information for the appropriate individuals should questions or concerns arise after signing the ICF during the clinical study.

Subjects must also be informed that their records may be accessed by appropriate authorities and Sponsor-designated personnel. The Investigator must ensure all procedures and practices are in place to protect the privacy and the best interest of the subject.

3.3 Selection of Study Population

Recruitment for the study may start at any point after the Investigator agrees, in writing, to participate in the study. Written informed consent, including Health Insurance Portability and Accountability Act (HIPAA), enrollment in the study, or dispensing of study products cannot begin until the Investigator has received Institutional Review Board (IRB) and Sponsor approval to conduct the study. The Sponsor and IRB must approve any advertising used to recruit subjects prior to use of that advertising.

All consented subjects must be accounted for, whether or not they participate in the study. The Sponsor will record information for each potential study subject who signs an ICF. Once a potential subject is consented, their information will be recorded on the screening log and the Investigator should proceed with screening procedures.

Potential subjects will be classified as eligible or "Screen Failures." A subject deemed a Screen Failure cannot participate in the study since he/she has not met the study inclusion criteria or has met the exclusion criteria. Electronic case report forms (eCRFs) must be completed for screen failure subjects and a copy of their signed ICF, and any information collected as part of screening (e.g., source documents, etc.) must be kept in their medical records.

Once a subject is enrolled, a subject is considered active and must be accounted for at every visit until exited (completed or discontinued) from the study, even if they are not dispensed study materials. Refer to Section 3.3.4 for subjects determined to be lost to follow-up.

3.3.1 Eligibility

Any person who satisfies all eligibility criteria, and in the opinion of the Investigator, is suitable for rigid gas permeable (RGP) overnight orthokeratology contact lens wear may

be entered into the study. Subjects must agree to wear lenses on an overnight wear basis (every night). There are no restrictions as to the subject's gender or occupation. Subjects of legal age must have the legal capacity to volunteer and must agree to sign an Informed Consent Form. Subjects not of legal age must agree to sign an Assent Form and their parent/guardian must sign the Informed Consent Form.

3.3.1.1 Inclusion Criteria

The subject is eligible for entry into the study if the subject meets all of the following criteria:

1. Be 12 years or older on the date the Informed Consent Form (ICF) is signed and, as subject or parent or legal guardian of a minor subject, have capacity to read, understand and provide written voluntary informed consent on the IRB-approved ICF and provide authorization as appropriate for local privacy regulations.
2. Be orthokeratology lens naïve.
3. Spherical refractive error between plano and -5.00D.
4. Astigmatism no greater than 1.50D.
5. Corneal topography sagittal height differential of ≥ 30 microns between the two main meridians (flat and steep) at an 8mm chord.
6. Has keratometric readings from 39.00 to 48.00D.
7. Has a clear and undistorted Mire Reflex.
8. Be willing and able to comply with all treatment and follow-up study visits and procedures.
9. Must be willing to refrain from wearing habitual soft contact lenses during the study period.
10. Subjects must be correctable through spherocylindrical refraction to 42 letters (0.1 logMAR) or better (distance, high contrast) in each eye.

3.3.1.2 Exclusion Criteria

The subject is ineligible for entry into the study if the subject meets any of the following criteria:

1. Subject is considered by the Investigator, to not be a suitable candidate for participation or it is not in the best interest of the subject to participate in the study.
2. Subjects who have worn rigid gas permeable (RGP) contact lenses within the last 30 days or who have worn polymethylmethacrylate (PMMA) lenses within the last three months.
3. Prior eyelid, strabismus, intraocular, or refractive surgery.
4. Keratoconus or an irregular cornea.
5. Subjects with any systemic disease currently affecting ocular health or in the Investigator's opinion may have an effect on ocular health during the course of the study.

6. Subjects using any systemic or topical medications that will, in the Investigator's opinion, affect ocular physiology or lens performance.
7. A known allergy to fluorescein, benoxinate, or proparacaine.
8. A history of corneal hypoesthesia (reduced corneal sensitivity), corneal ulcer, corneal infiltrates, ocular viral or fungal infections or recurrent ocular infections.
9. Subjects with an active ocular disease or who are using any ocular medication.
10. Subjects with any Grade 2 or greater finding during the slit lamp examination. Subjects with corneal infiltrates, of ANY GRADE, are NOT eligible. Refer to Appendix B: Methods of Clinical Evaluation.
11. Subjects with any "Present" finding during the slit lamp examination that, in the Investigator's judgement, interferes with contact lens wear. Refer to Appendix B: Methods of Clinical Evaluation.
12. Subjects with any scar or neovascularization within the central 6mm of the cornea. Subjects with minor peripheral corneal scarring (that does not extend into the central area), that in the Investigator's judgement, does not interfere with contact lens wear, are eligible for this study.
13. Subjects participating in any drug or device clinical investigation within 2 weeks prior to entry into this study (Screening Visit) and/or planning to do so during the period of study participation.
14. Subjects who are amblyopic.
15. Immediate family or close relative is a member of the office staff, including the Investigator(s).
16. Females of childbearing potential (those who are not surgically sterilized or postmenopausal) if they meet any one of the following:
    - They are currently pregnant
    - They plan to become pregnant during the study
    - They are breastfeeding

If a subject meets all of the inclusion criteria, and does not exhibit any of the exclusion criteria, he or she is eligible for entry into the study. Any subject enrolled in the study, who later is found to have had any of the exclusion criteria present at entry (Screening Visit or Dispensing Visit) will be discontinued at the Sponsor's request.

3.3.2 Subject Completion

The subject has completed the study after completion of the Exit Visit procedures at the 3-Month Follow-up Visit. Subjects who require further follow-up for an adverse event (AE) will be followed according to Section 6.1.12.

3.3.3 Subject Discontinuation

A subject MAY be discontinued (at the discretion of the Investigator, the Sponsor, and/or the IRB) prior to the final study visit for a variety of reasons, including, but not limited to:

1. An adverse event (AE) occurring during the course of the study, which precludes continued treatment or follow-up
2. Persistent Grade 3 or 4 slit lamp findings (must be reported to the Sponsor within 24 hours)
3. Persistent study-related symptoms/complaints

A subject MUST be discontinued prior to the final study visit for any of the following reasons:

1. Voluntary withdrawal
2. Death
3. Investigator decision that it is not in the best medical interest of the subject to continue participation in the investigation
4. Ineligible at Screening Visit – a subject who was enrolled but was later found to have not met the eligibility criteria
5. Inability to maintain recommended wearing schedule
6. Continued failure to follow subject instructions
7. Lack of motivation
8. Lost to follow-up (refer to Section 3.3.4)
9. Misses the Dispensing, 1-Day, or 1-Week Visit
10. Misses more than one of the 1-Month, 2-Month or 3-Month Visits
11. Instillation of non-medically indicated solution not specified in the protocol
12. Unacceptable lens performance
13. Becomes pregnant during the study

Prior to discontinuing a subject, every effort should be made to contact the subject, schedule a final study visit, obtain as much follow-up data as possible, and retrieve all study materials. Adverse events will be followed as described in Section 6.1.12.

Subject discontinuations will be documented clearly on the source document and applicable electronic case report form (eCRF). The Investigator should indicate the PRIMARY (one) reason that the subject was discontinued for each eye. Subjects who voluntarily withdraw from the study are not required to provide a reason for their decision but should be encouraged to share this information.

Exit Visit assessments should be completed for early discontinued subjects, if possible.

At the final study visit, all study subjects should be examined to ensure that their ocular health is consistent with pre-study, baseline conditions. Any adverse effects determined to have been reasonably caused by participation in the study will be followed per the

standard of care. Participation in the study will not impact post-study choices of study subjects for correcting their vision using marketed products (e.g., contact lenses and contact lens care solutions).

Whether a subject completes or is discontinued from the study, they will be directed by the Investigator for their appropriate method of vision correction.

3.3.4 Lost to Follow-Up

Subjects who do not return for scheduled follow-up visits, as defined by the visit window and could not be contacted via 2 telephone calls and 1 letter with delivery confirmation, are to be considered lost to follow-up. All follow-up attempts should be documented and kept with the subject's source documentation, and the applicable eCRFs will be completed. If the Investigator determines that a subject has been lost to follow-up, the "study exit date" should be recorded as the date of last visit to the clinic as a study subject. Just prior to database lock, the database will be reviewed for all lost to follow-up entries to confirm, once again, that the contact with the subject was never made. A study subject may withdraw from the study at any time for any reason.

3.4 Investigators

The study will be conducted at approximately 6 investigative sites located in the US by Investigators who are determined by Bausch + Lomb to be suitably qualified by training and experience to conduct this study. This will include appropriate current state licensing and study-specific training. Principal Investigators will sign the Device Investigator Agreement form prior to the start of the study.

Each Investigator will attempt to enroll approximately 11-12 subjects. In the event that selected sites do not meet full enrollment, the Sponsor may decide to increase enrollment as needed at other currently active sites and/or additional site(s) may be added to satisfy the enrollment requirements of the study.

The Study 918 List of Investigative Sites identifies the names of the Principal Investigators, the address and contact information for each investigative site. For the purposes of this study, the Sponsor will not specify a Coordinating Investigator. The roles and responsibilities of the Principal Investigators are defined in the Clinical Trial Agreement, Device Investigator Agreement, and the Investigator Statement of Approval on Page 3 of this study protocol.

3.5 Finances

The study will be financed through Bausch + Lomb Corporate Research & Development. A Clinical Trial Agreement will be executed between Bausch + Lomb and each Investigator prior to their participation in the clinical trial. The agreement will include the responsibilities of each party, payment and reimbursement procedures and requirements, intellectual property and publication terms, insurance and indemnification, and coverage for subject injury. Investigator and subject compensation are outlined in the Investigator's Clinical Trial Agreement. Compensation will not be dependent on the study outcomes.

3.6 Study Duration

The study will consist of seven visits. Visit 1 will take approximately 30 minutes and Visits 2 through 7 will take approximately one hour each. The clinical investigation will take approximately 14 weeks for each subject to complete. Refer to Appendix A: Schedule of Visits and Procedures).

Subjects will be followed for approximately 3 months (unless discontinued, lost to follow-up) from the initial Screening Visit and must adhere to the following schedule:

SCHEDULED FOLLOW-UP VISITS		
Visit	**Target**	**Acceptable Visit Range**
V1: Screening Visit	N/A	N/A
V2: Dispensing Visit	N/A	N/A
V3: 1-Day Follow-up Visit	Day 1	+1 day
V4: 1-Week Follow-up Visit	Day 7	±2 days
V5: 1-Month Follow-up Visit	Day 30	± 3 days
V6: 2-Month Follow-up Visit	Day 60	± 3 days
V7; 3-Month Follow-up Visit	Day 90	± 3 days

3. STUDY MATERIALS

Bausch + Lomb will provide the Investigator all orthokeratology contact lenses, anesthetic drops and lens care products required for the study.

The following care system for study lenses will be provided prior to the start of study:

- Boston SIMPLUS® Multi-Action Solution for cleansing, rinsing, disinfecting, and storing the lenses.
- Boston® Rewetting Drops for rewetting lenses.
- NOTE: Investigators have the option of dispensing any Boston Lens Care System if, in their judgement, Boston SIMPLUS is not the preferred regimen (e.g., not the subject's habitual Boston Lens Care System, or is not performing satisfactorily).

Although the majority of subjects may not require maintenance lenses, Bausch + Lomb will provide each investigative site a supply of Bausch + Lomb Biotrue® ONEday (nesofilcon A) Contact Lenses in representative powers of -0.50, -1.00, -1.50, -2.00, -2.50, and -3.00D for use as needed during the orthokeratology lens adaptation phase.

Use of habitual soft contact lenses and lens care products other than those provided for this study is not allowed during the study period.

Conformity to general safety and performance requirements to protect the health and safety of the subjects for the investigational test article are addressed in the design verification-design review process referenced in BL SOP 20-D022-3, *Investigational Material Release for Bausch Health Companies R&D Activities.*[3]

4.1 Description of Test Article (Test)

The Test lens to be used in this study is the Arise Orthokeratology (oprifocon A) Lens. The Arise Orthokeratology Lens is a lathe cut contact lens with a spherical or aspherical

base curve and non-spherical posterior peripheral curves. The posterior curve is selected to properly fit an individual eye for orthokeratology and the anterior curve is selected to provide the necessary optical power for a temporary reduction of myopia. A peripheral curve system on the posterior surface allows tear exchange between the lens and the cornea. The Arise Orthokeratology Lens is manufactured by Bausch & Lomb Incorporated, Lancaster, NY and shipped in Boston SIMPLUS Multi-Action Solution.

A Fitting Guide for Arise Orthokeratology Lens is provided in Appendix D: Fitting Guide.

4.2 Description of Comparator (Comparator)

Not Applicable; this is a single-treatment study evaluating safety and effectiveness of the Arise Orthokeratology Lens.

4.3 Instructions for Use and Administration

Each subject will be assigned a subject number. Eligible subjects will be dispensed lenses at the Dispensing Visit. Subjects will be required to wear their study lenses for a minimum of 8 hours overnight for 3 months. Subjects will be instructed to wear their lenses to the 1-Day Follow-up Visit (Visit 3). Subjects will not wear their study lenses to subsequent Follow-up Visits (Visits 4, 5, 6 and 7).

The Investigator or designee will instruct all subjects to adhere to the Subject Instructions provided at the Dispensing Visit. Refer to Appendix C: Subject instructions.

4.3.1 Storage Requirements

All study lenses and solutions provided by the Sponsor must be stored in a secure location and maintained at ambient room temperature.

4.3.2 Subject Instructions

All subjects must be given Subject Instructions for the study lenses (Appendix C: Subject instructions). Subjects must comply with the instructions provided to them. Subject Instructions will be supplied to the Investigator by Bausch + Lomb for distribution to the subject.

The Investigator or other designee must review, with the subject, the Subject Instructions and the precautions and warnings for lens wear, lens care, handling, cleaning, and disinfecting, and return of study materials.

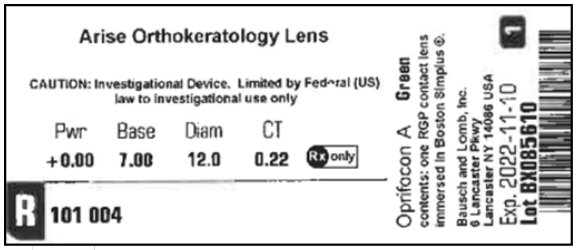
Any subject who does not follow instructions to a degree that, in the Sponsor or Investigator's opinion, jeopardizes the subject's well-being or the validity of the study should be discontinued.

4.4 Packaging and Labeling

4.4.1 Lenses

The study lenses will be packaged and labeled in a manner consistent with the study design.

Sample of label:



R Right or Left eye designation

101 004 6-digit unique identifier
(3 digit site ID + 3 digit subject ID)

The Arise Orthokeratology Lenses used in this study will be packaged in polycarbonate vials containing Boston SIMPLUS Multi-Action Solution with investigational labels. The labels will contain the following information:

- Lens power
- Base curve
- Lens diameter
- CT (Center thickness)
- Eye (R or L)
- Subject identifier (101 004: Investigative site 101 and Subject 004)
- Lens color (right lenses are green, left lenses are blue)
- Expiration date (denotes 30 days after lens was packaged for shipment)
- Lot number
- Manufacturer's name and location
- Investigational Device Caution Statement

4.4.2 Study Supplies

The Sponsor will provide the following study supplies for each subject:

- Pair of study lenses
- Bottle of Boston SIMPLUS Multi-Action Solution
- Bottle of Boston Rewetting Drops
- Study Lens Case
- Subject Instructions

4.4.3 Other Study Supplies

A back-up pair of study lenses will be kept at the investigative site for each subject in the event a replacement is needed.

Each investigative site will be provided with a Slit Lamp Filter Kit (Kodak Wratten #12 yellow filter) and extra of the following supplies in the event a subject requires replenishment:

- Boston SIMPLUS Multi-Action Solution
- Boston Rewetting Drops
- Study Lens Cases

4.5 Accountability

Designated site staff will be responsible to keep current and accurate records of study materials during the study. The records will include receipt and acknowledgement of all study lenses, and other supplies as identified in Section 4.4.2 and Section 4.4.3. Each Arise Orthokeratology Lens will be identified and traced by a unique Lot Number. The disposition of study lenses dispensed and returned by the subjects will be recorded on study product accountability logs. The study lenses are to be dispensed only to subjects enrolled in the study, in accordance with the conditions specified in this protocol.

Upon completion of the study, a Clinical Monitor will review and verify the Investigator's accountability logs.

Following verification, and as directed by the Sponsor, all worn/unworn study lenses must be returned. Worn lenses should be placed in a study lens case dry and shipped along with unused lenses to the Sponsor at the address below using the study supplied pre-printed FedEx labels:

4.6 Masking/Unmasking

Not applicable; this is an open-label study.

4.7 Product Replacement

If a subject requires lens(es) to be replaced, an unscheduled visit can be performed for product replacement only. Each subject will have a back-up pair of lenses stored at the investigative site in the event replacement is needed. Refer to Section 6.1.11.

4. SAFETY AND EFFECTIVENESS VARIABLES

Safety and effectiveness variables are presented below. A full list and description of all safety and effectiveness variables and study procedures are provided in Appendix A: Schedule of Visits and Procedures and Appendix B: Methods of Clinical Evaluation. A summary of the planned statistical analyses is presented in Section 8. Product risks are also described in the Study 918 Investigator's Brochure[1], *Section 6.1 Benefit-Risk Profile, Table 16 Benefits and Risks*.

5.1 Safety Variables

The primary safety outcome is the rate of serious adverse events at the subject and eye levels.

[redacted]

5.2 Effectiveness Variables

The primary effectiveness outcome is the proportion of subjects who achieve monocular UDVA of 20/40 or better in both eyes at the 3-Month Follow-up Visit.

[redacted]

5.3 Risk Assessment and Mitigation

Information concerning potential risks associated with the investigational device (as well as possible interactions with concomitant medical treatments and risk-to-benefit ratio) can be found within the Investigator's Brochure for the study. Risks are also summarized within the Informed Consent Form. The assessments required for the study are routinely performed and are standard of care for contact lens wearers. The subjects will be informed of any potential study-specific risks in the ICF or if new risks become apparent during the study. Upon review of the clinical and preclinical data no additional risks were identified over the standard of contact lens and care solution use. Risk mitigation includes periodic assessments of ocular health by vision care specialists throughout the study, oversight by the study Sponsor, its representatives and Medical Monitor, and well-defined procedures for the management of adverse events, should they occur.

Anticipated serious adverse device effects are presented in Section 7.1.4.1. Additional descriptions of the risks and benefits to subject safety associated with wearing contact lenses, use of contact lens care products is presented in the package insert.

5. STUDY METHODS

6.1 Study Visits

Refer to Appendix A: Schedule of Visits and Procedures and the methods of clinical evaluation.

Following identification of a potential subject, the Investigator (or designee) will explain the purpose of the study, procedures, risks/benefits, and subject responsibilities to the potential subject. The subject's willingness and ability to meet the follow-up requirements of the study will be determined. If the subject chooses to participate in the investigation, written informed consent will be obtained. The subject and the person obtaining written consent, will sign and date the IRB -approved ICF. Both the Investigator and subject must keep the signed ICF document. The Investigator should retain the signed original document in the subject's medical record and provide a copy to the subject. In addition, the applicable privacy regulation requirements (Health Insurance Portability Accountability Act; HIPAA) authorization must be met.

6.1.1 Screening (Visit 1)

A Screening Log will be provided by the Sponsor to track all consented subjects who the Investigator interviews regarding the study. Once all available lines on the Screening Log have been completed, or the Investigator has fulfilled his/her quota of subjects, the Investigator will sign and date the log to verify that all the subjects who interviewed for the study have provided informed consent and HIPAA authorization.

After obtaining written informed consent, prospective subjects will be screened to determine whether they meet the entry criteria for the study.

The screening visit will proceed as follows:

a. Collect subject's demographics such as age, gender, etc.

b. Current type of vision correction: none, spectacles, contact lenses.

c. Collect the following contact lens use history information:

- Average number of days per week worn
- Average daily wearing time, hours per day
- Average hours of comfortable wear per day
- Hours lenses worn on the day of this visit
- Current lens brand and lens wear modality
- Current lens care products
- Habitual rewetting drop use

d. Collect ocular medical history (within 1 year of signing the ICF) and concomitant ocular medications. Concomitant ocular medications (as defined for this study) are any medications taken for ocular conditions within 30 days previous to signing the ICF (or) any medications taken for ocular AEs during the course of the study.

e. For subjects with a habitual correction perform high-contrast distance visual acuity with their habitual correction.

f. Perform high-contrast uncorrected distance visual acuity (UDVA) for each eye.

g. Perform the following assessments (without lenses) using a phoropter:
   - Spherocylindrical refraction
   - Distance high-contrast BSCVA

h. Perform corneal topography and record:
   - Sag differential (Screening visit only)
   - Mire reflex (central 3mm of Placido rings)
   - Keratometry readings
   - HVID (Screening Visit only)
   - Pupil size (Screening Visit only)

i. Perform a slit lamp examination (without lenses) and record:
   - Any slit lamp findings including ungraded finding marked as “Present”
   - Any corneal scars
   - Any neovascularization within the central 6mm of the cornea
   - Any corneal staining
   - Any corneal infiltrate (record details of corneal infiltrates according to Section 2.0: Slit-Lamp Examination of Appendix B: Methods of Clinical Evaluation)
   - Record and sketch any scars and slit lamp findings greater than Grade 2 in the subject’s source document.

j. Collect/assess all AEs/ADEs, including serious or significant non-serious AEs.

k. Confirm eligibility by indicating on the Screening Log whether the subject is a "Screen Pass" or "Screen Fail". "Screen Fail" subjects are ineligible and cannot be dispensed in the study. The reason for screen failure must be documented in the eCRF and in the subject medical record and must be maintained with a copy of their ICF. Only "Screen Pass" subjects should be dispensed in the study.

l. Provide subject with a copy of the signed ICF.

m. Based on the measurements obtained, order two pairs of lenses by following instructions in the Lens Order Instructions Form.

n. Complete the relevant Screening Visit eCRFs.

6.1.2 Dispensing (Visit 2)

Dispensing visit is scheduled based upon the delivery date of the lenses (Approximately 15 days) and should proceed as follows:

a. Ensure the correct lenses for the subject have been received prior to dispensing the first lens.

   - Site designee will handle preparation of the lenses: After receipt of the study lenses and prior to the Study Lens Dispensing Visit, perform the following cleaning procedure:

   Soak the lenses for at least 4 hours in Boston SIMPLUS Multi-Action Solution. Rub both sides of the lenses carefully with 4 drops of Boston SIMPLUS Multi-Action Solution in the palm of the hand for 20 seconds. Rinse for approximately 5 seconds with a steady stream of Boston SIMPLUS Multi-Action Solution. The lens is ready for placement on the eye.

b. Record changes in concomitant ocular medications.

c. Perform uncorrected high-contrast distance visual acuity (UDVA) for each eye.

d. Perform the following assessments(without lenses) using phoropter:

   - Spherocylindrical refraction
   - Distance high-contrast BSCVA

e. Perform a slit lamp examination (without lenses) and record:

   - Any slit lamp findings including ungraded finding marked as "Present"
   - Any corneal scars
   - Any neovascularization within the central 6mm of the cornea
   - Any corneal staining
   - Any corneal infiltrate (record details of corneal infiltrates according to Section 2.0: Slit-Lamp Examination of Appendix B: Methods of Clinical Evaluation)
   - Record and sketch any scars and slit lamp findings greater than Grade 2 in the subject's source document

f. Insert a drop of anesthetics in each eye prior to lens insertion.

g. Evaluate the study lenses on the eye and record the following lens fit assessments:
   - Lens centration
   - Lens movement

h. The study lenses will then be removed. The subject must disinfect and clean their lenses prior to insertion that evening.

i. Collect/assess all AEs/ADEs, including serious or significant non-serious AEs.

j. Following lens assessment, have the subject take the lenses with them. Instruct the subject that the lenses should be worn overnight for at least eight (8) hours each night.

k. Dispense maintenance lenses, as needed.

l. Give the subject a copy of the Subject Instructions and dispense Boston SIMPLUS Multi-Action Solution or other approved Boston Lens Care System and Boston Rewetting Drops. Review the lens and solution instructions with the subject.

m. Remind subject that they must return the next day for their 1-Day Follow-up Visit with the lenses still on the eye from overnight wear period.

n. Schedule the subject to return for their 1-Day Follow-up Visit within 2 hours of awakening.

o. Complete the relevant Dispensing Visit eCRFs.

6.1.3 1-Day Follow-up (Visit 3)

The subject must return for the 1-Day Follow-up Visit one day (visit window of +1 day) after the Dispensing Visit.

a. Ensure that the subject arrives at the clinic while wearing the study lenses.

b. Record any changes in concomitant ocular medications.

c. Collect the following lens wear parameters:
   - Hours of lens wear the previous night
   - Frequency of rewetting drops use

d. Evaluate the study lenses on the eye and record the following lens fit assessments:
   - Lens centration
   - Lens movement

e. Remove the lens from the subject's eye.

f. Collect Symptoms/Complaints.

g. Collect Lens Performance ratings using 0-100 scales.

h. Perform monocular uncorrected high-contrast distance visual acuity (UDVA) for each eye.

i. Perform the following assessments (without lenses) using a phoropter:

- Spherocylindrical refraction. Explain any induced refractive astigmatism greater than 1.00D compared to the Dispensing Visit (Visit 2).
- Distance high-contrast BSCVA. Explain any loss of BSCVA of 2 or more lines compared to the Dispensing Visit (Visit 2).

j. Perform corneal topography (within 30 minutes of lens removal) and record:
   - Topography reading
   - Mire reflex
   - Keratometry readings

k. Perform a slit lamp examination (without lenses) and record:
   - Any slit lamp findings including ungraded finding marked as "Present"
   - Any new corneal scars
   - Any neovascularization within the central 6mm of the cornea
   - Any increase in grading of corneal staining
   - Any corneal infiltrate (record details of corneal infiltrates according to Section 2.0: Slit-Lamp Examination of Appendix B: Methods of Clinical Evaluation)
   - Record and sketch any scars and slit lamp findings greater than Grade 2 in the subject's source document

l. Collect/assess all AEs/ADEs, including serious or significant non-serious AEs.

m. Following lens assessment, have the subject take the lenses with them. Instruct the subject that the lenses should be worn overnight for at least eight (8) hours each night.

n. Schedule the subject to return for their 1-Week Follow-up Visit within 2 hours of the subject removing the lenses.

o. Instruct the subject to soak and clean their lenses prior to insertion each evening.

p. If the lens fit is unacceptable, order two lenses if refitting one eye (or two pairs of lenses if refitting both eyes) by following the instructions for lens refitting in the Lens Order Instructions Form. New lens(es) will be made and sent to the Investigator for dispensing. The subject should suspend wearing study lenses while the new lens(es) are being made.

   Upon receipt of the new lens(es), schedule an Unscheduled Visit for dispensing due to refinement of lens fit, and reset the sequence of follow-up visits on a subject basis starting with the 1-Day Follow-up Visit followed by a 1-Week Follow-up Visit, etc.

   Note: Each eye can only be refit one time, either at the 1-Day Follow-up Visit or the 1-Week Follow-up Visit.

q. Complete the relevant Follow-up Visit eCRFs.

6.1.4 1-Week Follow-up (Visit 4)

The subject must return for the 1-Week Follow-up Visit on day 7 (± 2 days).

a. Record any changes in concomitant ocular medications.

b. Collect the following lens wear parameters:

- Hours since lens removal
- Number of nights of lens wear
- Average nightly wearing time, hours per night
- Frequency of rewetting drops use

Note: Do not perform any ophthalmic examinations with the maintenance lenses in place (if any).

c. Collect Symptoms/Complaints.

d. Collect Lens Performance ratings using 0-100 scales.

e. Perform uncorrected high-contrast distance visual acuity (UDVA) for each eye.

f. Perform the following assessments (without lenses) using a phoropter:

- Spherocylindrical refraction. Explain any induced refractive astigmatism greater than 1.00D compared to the Dispensing Visit (Visit 2).
- Distance high-contrast BSCVA. Explain any loss of BSCVA of 2 or more lines compared to the Dispensing Visit (Visit 2).

g. Perform corneal topography and record:

- Topography reading
- Mire reflex
- Keratometry readings

h. Perform a slit lamp examination (without lenses) and record:

- Any slit lamp findings including ungraded finding marked as “Present”
- Any new corneal scars
- Any neovascularization within the central 6mm of the cornea
- Any increase in grading of corneal staining
- Any corneal infiltrate (record details of corneal infiltrates according to Section 2.0: Slit-Lamp Examination of Appendix B: Methods of Clinical Evaluation)
- Record and sketch any scars and slit lamp findings greater than Grade 2 in the subject’s source document

i. Collect/assess all AEs/ADEs, including serious or significant non-serious AEs.

j. Remind the subject that it is recommended that the lenses be worn overnight for at least eight (8) hours each night.

k. If the lens fit is unacceptable, order two lenses if refitting one eye (or two pairs of lenses if refitting both eyes) by following the instructions for lens refitting in the Lens Order Instructions Form. New lens(es) will be made and sent to the Investigator for dispensing. The subject should suspend wearing study lenses while the new lens(es) are being made.

   Upon receipt of the new lens(es) schedule an Unscheduled Visit due to refinement of lens fit and reset the sequence of follow-up visits on a subject basis starting with the 1-Day Follow-up Visit followed by a 1-Week Follow-up Visit, etc.

   Note: If the lens fit is not acceptable, refinement to the lens can be made at this visit only if a lens refit was not ordered at the 1-Day Follow-up Visit.

l. Schedule the subject to return for 1-Month Follow-up Visit within 2 hours of the subject removing the lenses.

m. Complete the relevant Follow-up Visit eCRFs.

6.1.5 1-Month Follow-Up (Visit 5)

The subject must return for the 1-Month Follow-up Visit on day 30 (± 3 days).

a. Record any changes in concomitant ocular medications.

b. Collect the following lens wear parameters:

   - Hours since lens removal
   - Average number of nights per week worn
   - Average nightly wearing time, hours per night
   - Frequency of rewetting drops use

   Note: At the 1-Month Follow-up Visit no additional refinement can be made to the lens design. If the lens performance is acceptable, continue with the scheduled visits. If the lens performance is unacceptable, subject should be discontinued.

   Note: Do not perform any ophthalmic examinations with the maintenance lenses in place (if any).

c. Collect Symptoms/Complaints.

d. Collect Lens Performance ratings using 0-100 scales.

e. Perform uncorrected high-contrast distance visual acuity (UDVA) for each eye.

f. Perform the following assessments (without lenses) using a phoropter:

   - Spherocylindrical refraction. Explain any induced refractive astigmatism greater than 1.00D compared to the Dispensing Visit (Visit 2).
   - Distance high-contrast BSCVA. Explain any loss of BSCVA of 2 or more lines compared to the Dispensing Visit (Visit 2).

g. Perform corneal topography and record:

   - Topography reading
   - Mire reflex

- Keratometry readings

h. Perform a slit lamp examination (without lenses) and record:
   - Any slit lamp findings including ungraded finding marked as "Present"
   - Any new corneal scars
   - Any neovascularization within the central 6mm of the cornea
   - Any increase in grading of corneal staining
   - Any corneal infiltrate (record details of corneal infiltrates according to Section 2.0: Slit-Lamp Examination of Appendix B: Methods of Clinical Evaluation)
   - Record and sketch any scars and slit lamp findings greater than Grade 2 in the subject's source document

i. Collect/assess all AEs/ADEs, including serious or significant non-serious AEs.

j. Remind the subject that it is recommended that the lenses be worn overnight for at least eight (8) hours each night.

k. Schedule the subject to return for their 2-Month Follow-up Visit within 2 hours of the subject removing the lenses.

l. Complete the relevant Follow-up Visit eCRFs.

6.1.6 2-Month Follow-Up (Visit 6)

The subject must return for the 2-Month Follow-up Visit on day 60 (± 3 days).

a. Record any changes in concomitant ocular medications.

b. Collect the following lens wear parameters:
   - Hours since lens removal
   - Average number of nights per week worn
   - Average nightly wearing time, hours per night
   - Frequency of rewetting drops use

   Note: Do not perform any ophthalmic examinations with the maintenance lenses in place (if any).

c. Collect Symptoms/Complaints.

d. Collect Lens Performance ratings using 0-100 scales.

e. Perform monocular uncorrected high-contrast distance visual acuity (UDVA) for each eye.

f. Perform the following assessments (without lenses) using phoropter:
   - Spherocylindrical refraction. Explain any induced refractive astigmatism greater than 1.00D compared to the Dispensing Visit (Visit 2).
   - Distance high-contrast BSCVA. Explain any loss of BSCVA of 2 or more lines compared to the Dispensing Visit (Visit 2).

g. Perform corneal topography and record:
   - Topography reading
   - Mire reflex
   - Keratometry readings

h. Perform a slit lamp examination (without lenses) and record:
   - Any slit lamp findings including ungraded finding marked as "Present"
   - Any new corneal scars
   - Any neovascularization within the central 6mm of the cornea
   - Any increase in grading of corneal staining
   - Any corneal infiltrate (record details of corneal infiltrates according to Section 2.0: Slit-Lamp Examination of Appendix B: Methods of Clinical Evaluation)
   - Record and sketch any scars and slit lamp findings greater than Grade 2 in the subject's source document

i. Collect/assess all AEs/ADEs, including serious or significant non-serious AEs.

j. Remind the subject that it is recommended that the lenses be worn overnight for at least eight (8) hours each night.

k. Schedule the subject to return for their 3-Month Follow-up Visit within 2 hours of the subject removing the lenses.

l. Complete the relevant Follow-up Visit eCRFs.

6.1.7 3-Month Follow-Up (Visit 7)

***Note*:** *If a subject requires further follow-up due to an ongoing AE, the subject should not be exited until the event resolves or stabilizes.*

The subject must return for the 3-Month Follow-up Visit on day 90 (± 3 days).

a. Record any changes concomitant ocular medications.

b. Collect the following lens wear parameters:
   - Hours since lens removal
   - Average number of nights per week worn
   - Average nightly wearing time, hours per night
   - Frequency of rewetting drops use

   Note: Do not perform any ophthalmic examinations with the maintenance lenses in place (if any).

c. Collect Symptoms/Complaints.

d. Collect Lens Performance ratings using 0-100 scales.

e. Perform monocular uncorrected high-contrast distance visual acuity (UDVA) for each eye.

f. Perform the following assessments (without lenses) using a phoropter:
   - Spherocylindrical refraction. Explain any induced refractive astigmatism greater than 1.00D compared to the Dispensing Visit (Visit 2).
   - Distance high-contrast BSCVA. Explain any loss of BSCVA of 2 or more lines compared to the Dispensing Visit (Visit 2).

g. Perform corneal topography and record:
   - Topography reading
   - Mire reflex
   - Keratometry readings

h. Perform a slit lamp examination (without lenses) and record:
   - Any slit lamp findings including ungraded finding marked as "Present"
   - Any new corneal scars
   - Any neovascularization within the central 6mm of the cornea
   - Any increase in grading of corneal staining
   - Any corneal infiltrate (record details of corneal infiltrates according to Section 2.0: Slit-Lamp Examination of Appendix B: Methods of Clinical Evaluation)
   - Record and sketch any scars and slit lamp findings greater than Grade 2 in the subject's source document

i. Collect/assess all AEs/ADEs, including serious or significant non-serious AEs.

j. Collect all worn/unworn study lenses from the subject.

k. Complete the relevant Follow-up eCRFs as appropriate.

6.1.8 Exit Visit

Note**:** *If a subject requires further follow-up due to an ongoing AE, the subject should not be exited until the event resolves or stabilizes.*

a. Record any changes concomitant ocular medications.

b. Perform monocular uncorrected high-contrast distance visual acuity (UDVA) for each eye.

c. Perform the following assessments (without lenses) using a phoropter:
   - Spherocylindrical refraction. Explain any induced refractive astigmatism greater than 1.00D compared to the Dispensing Visit (Visit 2).
   - Distance high-contrast BSCVA. Explain any loss of BSCVA of 2 or more lines compared to the Dispensing Visit (Visit 2).

d. Perform corneal topography and record:
   - Topography reading
   - Mire reflex

- Keratometry readings

e. Perform a slit lamp examination (without lenses) and record:
   - Any slit lamp findings including ungraded finding marked as "Present"
   - Any new corneal scars
   - Any neovascularization within the central 6mm of the cornea
   - Any increase in grading of corneal staining
   - Any corneal infiltrate (record details of corneal infiltrates according to Section 2.0: Slit-Lamp Examination of Appendix B: Methods of Clinical Evaluation)
   - Record and sketch any scars and slit lamp findings greater than Grade 2 in the subject's source document

f. Collect/assess all AEs/ADEs, including serious or significant non-serious AEs.

g. Collect all worn/unworn study lenses from the subject, if not already done.

h. Complete the Exit Visit eCRF as appropriate.

6.1.9 Unscheduled Visits

Additional visits may be scheduled, as necessary, to ensure the safety and well-being of subjects. All additional exams should be fully documented in the source documents and on Unscheduled Visit eCRFs, as appropriate. Visits intended to fulfill scheduled visit requirements that fall outside the designated scheduled visit range, are not Unscheduled Visits. In these cases, the visit data will be collected and transcribed to the appropriate intended scheduled visit eCRF.

If a subject is seen for multiple visits during a given visit timeframe, the data from the visit that is intended to meet the protocol requirements for the scheduled visit should be captured on the visit eCRF. Where such a determination cannot be made, the first visit within the scheduled visit interval will be used for completion of the protocol required scheduled visit eCRF. Data from any additional visits within a scheduled visit interval will be captured on an Unscheduled Visit eCRF.

If the exclusive purpose of the visit is to dispense replacement study lens/study supplies and the subject is not experiencing any problems, refer to Section 6.1.11.

Procedures to be followed during an Unscheduled Visit will depend on the reason for the visit. Indicate the reason for the Unscheduled Visit:

- Signs and Symptoms
- Recheck
- Dispensing due to refinement of lens fit (perform all assessments under Section 6.1.2)
- 1-Day due to refinement of lens fit (perform all assessments under Section 6.1.3)

- 1-Week due to refinement of lens fit (perform all assessments under Section 6.1.4)
- Product Dispensing Only (same lens – e.g., back-up pair due to lost lens)

- Visit Out of Range for visits within a scheduled visit interval not qualifying to represent the intended protocol requirement
- Discontinued
  - Other (please explain)

If the subject is experiencing problems, assessments will be performed according to the Investigator's judgement.

a. Collect any relevant medical treatment information, including any adverse events, including whether a culture may have been taken.
b. Record any changes in concomitant ocular medications.
c. Collect the following lens wear parameters:
   - Hours since lens removal
   - Average number of nights per week worn
   - Average nightly wearing time, hours per night
   - Frequency of rewetting drops use

   Note: Do not perform any ophthalmic examinations with the maintenance lenses in place (if any).

d. Collect Symptoms/Complaints.
e. Collect Lens Performance rating using 0-100 scales.
f. Perform uncorrected high-contrast distance visual acuity (UDVA) for each eye.
g. Perform the following assessments (without lenses) using a phoropter:
   - Spherocylindrical refraction. Explain any induced refractive astigmatism greater than 1.00D compared to the Dispensing Visit (Visit 2).
   - Distance high-contrast BSCVA. Explain any loss of BSCVA of 2 or more lines compared to the Dispensing Visit (Visit 2).
h. Perform a slit lamp examination (without lenses) and record:
   - Any slit lamp findings including ungraded finding marked as "Present"
   - Any new corneal scars
   - Any neovascularization within the central 6mm of the cornea
   - Any increase in grading of corneal staining
   - Any corneal infiltrate (record details of corneal infiltrates according to Section 2.0: Slit-Lamp Examination of Appendix B: Methods of Clinical Evaluation)
   - Record and sketch any scars and slit lamp findings greater than Grade 2 in the subject's source document

   Note: Do not perform any ophthalmic examinations with the maintenance lenses in place (if any).

i. Perform corneal topography and record:
   - Topography reading

- Mire reflex
- Keratometry readings

j. Collect/assess all AEs/ADEs including serious or significant non-serious AEs.
k. If the subject needs to exit the study at this visit, complete the Exit Visit eCRF per Section 6.1.8
l. Collect the study lenses dispensed to the subject (if subject is exiting).
m. Complete the Unscheduled Visit eCRF.

6.1.10 Missed Visits

Missed visits will be handled as follows:

If a subject misses any scheduled follow-up visit as defined by visit window, the visit is considered missed. Indicate a missed visit on the eCRF for that scheduled visit. Due to the study design, the subject must attend the Dispensing Visit, 1-Day Follow-up Visit and 1-Week Follow-up Visits. If the subject misses any of these visits, they must be discontinued. In addition, if the subject misses more than one of the 1-Month, 2-Month or 3-Month Follow-up Visits, the subject must be discontinued. If the subject must be discontinued, schedule the subject for an Exit Visit as soon as possible. If the subject cannot be reached or rescheduled, the subject should be recorded as Lost to Follow-Up.

6.1.11 Product Dispensing Only Visit

If a subject is seen for resupply or replacement of study materials and the subject is not experiencing any problems, a complete exam is not required. The Product Dispensing Only form can be found within the Unscheduled Visit eCRF. If any assessment is performed, then the corresponding additional forms within the Unscheduled Visit eCRF must be completed.

If study lenses are dispensed, collect the following information in the source document for each being dispensed, and transcribe to the Product Dispensing Only eCRF form:

- Visit date
- Subject ID number
- Subject initials
- Primary reason for lens replacement

Record the lens quantity dispensed, and for which eye the lenses are being dispensed in the Accountability Log.

If back-up lenses are dispensed, order a new back-up pair of lenses by following instructions for lens re-order in the Lens Order Instructions Form.

If study lenses were replaced for any reason other than lens loss, collect the worn lenses from the subject. All worn lenses will be returned to the Sponsor in lens case(s) at the end of the study. Place the lens case(s) in a labeled zippered bag.

All study lenses must be returned to the Sponsor at the end of the study.

Note: All unworn study lenses are to be returned as directed with the materials provided. All study lenses must be accompanied by a Product Accountability Log or as directed by the Sponsor.

6.1.12 Post-study Follow-up

If a subject requires discontinuation or is completing the study, but has an ongoing AE, the subject should not be exited until the event resolves or stabilizes. This may imply that follow-up will continue via Unscheduled Visits and that additional evaluations may be requested by the Sponsor.

Investigator must schedule Unscheduled Visits, as necessary.

Note: All VA measurements MUST be made using a phoropter.

a. Remove any contact lenses the subject may be wearing. Perform a slit lamp examination. Record and sketch the ocular results and findings in the subject's source document.

b. Complete an ocular examination without lenses on the eyes, including spherocylindrical refraction and high-contrast distance BSCVA.

c. The Investigator is required to follow the subject until the condition no longer warrants further follow-up for study purposes. An Unscheduled Visit eCRF must be completed for each of these visits.

Once the AE has resolved or stabilized, the Investigator may proceed with completing the Exit Visit.

6.2 Study Completion/Early Study Terminations/Suspensions

6.2.1 Study Completion

The study is considered completed when all subjects have successfully completed the study or have been exited. Subjects who require further follow-up will be followed according to Section 6.1.12. There is no planned follow-up period after the clinical investigation is complete.

The completion of the clinical investigation shall be deemed to coincide with the last visit of the last subject and when follow-up is complete.

Bausch + Lomb will notify the Investigator when to contact the IRB to inform them that the study is complete.

6.2.2 Early Study Termination/Suspension

If during the study it becomes evident to the Sponsor that the study should be stopped prematurely or placed on hold, appropriate notification will be given to the Investigator(s), IRBs, and FDA, as applicable. Bausch + Lomb will instruct the Investigators to stop/restart dispensing study materials and will arrange for study closeout, if applicable, at each site.

6.3 Subject Concomitant Medications/Therapy

Ocular medications or systemic or topical medications that, in the Investigator's opinion, could potentially affect ocular physiology or lens performance are prohibited, unless medically necessary during the course of the study.

6.4 Treatment Compliance

Treatment compliance will be assessed using lens wear parameter data.

6.5 Protocol Deviations

A deviation from the protocol is an unintended and/or unanticipated departure from the procedures and/or processes approved by the Sponsor and the IRB and agreed to by the Investigator. It is a Sponsor expectation that Investigators will follow the protocol and procedures as written. The Sponsor will not grant protocol waivers for this study. The Investigator may implement a deviation from the protocol to eliminate an immediate hazard to study subjects without prior IRB approval. As soon as possible after such an occurrence, the implemented deviation, as well as the reasons for it should be submitted to the IRB for review and approval. It should also be submitted to the Sponsor for agreement, and to the regulatory authorities, if required.

In the event a protocol deviation occurs, the date of and reason for deviations must be documented in all cases. Significant or major protocol deviations impacting the rights or safety of the subject, or the integrity of the study must be reported by the Investigator to the IRB and Medical Monitor immediately. Reporting of all other protocol deviations must adhere to the requirements of the governing IRB. Unless the protocol deviations put the subject at risk or the subject's condition requires that they be discontinued from the study, subjects may continue to participate until the end of the study.

Site Corrective Action Plans will be developed and completed as deemed necessary by the Sponsor, Sponsor designee (e.g., CRO) for sites or Investigators who deviate from this protocol in a way that adversely affects the rights, safety, or well-being of the subject(s) and/or the quality or integrity of data. The Site Corrective Action Plan will outline the deviation and the site's corrective and/or remedial actions. Decisions regarding critical deviations that merit Investigator disqualification and site closure will be made by the Sponsor and documented in the Trial Master File.

6. ADVERSE EVENTS

7.1 Introduction to Adverse Event Definitions

Adverse events, serious AEs (SAEs), significant non-serious AEs, non-significant non-serious AEs, adverse device effects (ADEs), anticipated serious adverse device effects (ASADEs), and unanticipated adverse device effects (UADEs) are defined in this section and in the protocol's glossary.

An AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device, comparator, or the procedures involved. For users or other persons, this definition is restricted to events not related to investigational medical devices.

7.1.1 Serious Adverse Event (SAE) Definitions

An AE that (related or not related to the investigational test articles, comparator products or study procedures):

- Led to death.

- Led to serious deterioration in the health of the subject, that resulted in:
  - A life-threatening illness or injury; or
  - A permanent impairment of a body structure or a body function (e.g., blindness); or
  - Inpatient or prolonged hospitalization; or
  - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.
- Led to fetal distress, fetal death, or a congenital abnormality or birth defect.

NOTE: A planned hospitalization for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered an SAE.

Serious adverse events may include but are not limited to any hazardous, sight-threatening conditions occurring after exposure to the investigational test article including, but not limited to, the following:

- A presumed infectious ulcer (defined as a progressive erosion of the corneal tissue). For the purposes of reporting, this includes:
  - Central or para-central location
  - Penetration of Bowman's membrane
  - Infiltrate ≥2mm diameter
  - Associated with iritis
  - Associated with any increase in intraocular pressure
  - Culture positive for microorganisms
  - Increasing size or severity at subsequent visits

NOTE: Signs of a presumed infectious corneal ulcer may include irregular focal infiltrates, active lesions with raised edges, significant diffuse infiltration, anterior corneal to mid-stromal involvement, erosion with overlying staining, conjunctival and lid edema, anterior chamber reaction (iritis), and severe bulbar and limbal redness. Symptoms associated with a presumed infectious ulcer (microbial keratitis) may include pain of rapid onset, severe redness, purulent or mucopurulent discharge, tearing, and photophobia.

- Any central or paracentral (within the central 6mm of cornea) corneal event that results in permanent opacification (such as corneal scar or vascularization)
- Any serious adverse ophthalmic events including hypopyon and/or hyphema
- Any neovascularization within the central 6mm of the cornea
- Permanent loss of ≥2 lines of BSCVA
- All cases of iritis

7.1.2 Significant Non-Serious Adverse Event Definitions

A significant non-serious adverse event is an AE that does not meet the serious criteria, is considered significant by the Sponsor, and requires expedited reporting to the Sponsor (see Section 7.3.1). These events include but are not limited to:

- Peripheral non-progressive non-infectious corneal ulcers
- All symptomatic corneal infiltrative events
- All cases of corneal staining greater than or equal to Grade 3
- A temporary loss of two or more lines of BSCVA (for greater than or equal to 2 weeks)
- Neovascularization cases Grade 2 or greater (if not within the central 6mm of the cornea)
- Any ocular event that necessitates temporary lens discontinuation of greater than or equal to 2 weeks

7.1.3 Non-Significant Non-Serious Adverse Events Definitions

A non-significant non-serious adverse event may include but is not limited to the following and does not require expedited reporting:

- Bacterial conjunctivitis
- Viral conjunctivitis
- Allergic conjunctivitis
- Corneal edema
- Contact lens related papillary conjunctivitis
- Loss of contrast sensitivity

7.1.4 Adverse Device Effect (ADE) Definitions

An adverse device effect is an AE that is assessed to be related to the use of an investigational medical device. This definition includes AEs resulting from insufficient or inadequate instructions for use; deployment, implantation, installation, or operation; or any malfunction of the investigational medical device. This definition also includes any event resulting from use error or from intentional misuse of the investigational medical device.

7.1.4.1 Anticipated Serious Adverse Device Effect (ASADE) Definition

An anticipated serious adverse device effect (ASADE) is an ADE that first meets the serious criteria (see Section 7.1.1) and which, by its nature, incidence, severity, or outcome, has been previously identified in the investigational plan or application (including a supplementary plan or application) and/or in the risk analysis report. ASADEs include but are not limited to:

- Corneal ulcer (infectious or non-infectious)
- Keratitis

- Sensitivity to light (photophobia)
- Excessive eye secretions including mucopurulent discharge
- Blurred vision, rainbows, or halos around objects
- Poor visual acuity (reduced sharpness of vision)
- Moderate to severe eye pain not relieved by removing the lens

7.1.4.2 Unanticipated Serious Adverse Device Effect (USADE) Definitions

An unanticipated serious ocular or non-ocular adverse device effect is an adverse event related to the use of an investigational medical device that has resulted in any of the consequences characteristic of a serious adverse event as described in Section 7.1.1 and which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

This definition includes but is not limited to AEs resulting from insufficient or inadequate instructions for use, deployment, or any malfunction of the investigational medical device.

This definition also includes any event resulting from use error or from intentional misuse of the investigational medical device. USADEs include but are not limited to

- Any central or paracentral (within 6 mm of cornea) corneal event that results in permanent opacification (such as corneal scar or vascularization)
- Any serious adverse ophthalmic events including hypopyon and/or hyphema
- Any neovascularization within the central 6 mm of the cornea
- Permanent loss of ≥2 lines of BSCVA
- All cases of iritis.

7.1.5 Relationship Definition: Study Device and/or Other Study Materials

- **Related:** There is at least a reasonable possibility that the AE is related to the study device and/or rewetting drops. Reasonable possibility means that there is evidence to suggest a causal relationship or association between the study device and/or rewetting drops and the AE.
- **Not related:** There is little or no reasonable possibility that the AE is related to the study device and/or rewetting drops. This assessment implies that the AE has no evidence to suggest either a causal relationship or association to the study device and/or Rewetting Drops and a more likely or certain alternative etiology exists.

7.1.6 Severity Definitions

- **Mild:** Subject awareness of a sign or symptom that is easily tolerated, requires no treatment, and does not interfere with subject's daily activities.

- **Moderate:** Subject awareness of a sign or symptom which may be a low level of concern to the subject and may interfere with daily activities but can be relieved by simple therapeutic care.
- **Severe:** A sign or symptom that interrupts the subject's daily activity and requires systemic therapy or other treatment

7.2 Procedures for Evaluating Adverse Events

Throughout the course of this study all efforts will be made to remain alert to reportable AEs. If an AE occurs the first concern will be the safety of the subject and appropriate medical intervention will be made. All SAEs, ocular and systemic, must be recorded and reported as required.

All reportable AEs occurring after signing of informed consent and through the subject's end of participation in the study must be reported. All reportable AEs must be followed until the event resolves or stabilizes. This may imply that follow-up will continue after the subject has left the study, and that additional evaluations may be requested by the Sponsor.

Ocular AEs of possible clinical significance should be photo-documented and shared with the Medical Monitor in electronic form.

When evaluating for reportable AEs, the Investigator should refer to the definitions for AEs to determine:

- Whether the event is serious (refer to Section 7.1.1 and Section 7.1.2)
- Whether the event is severe (refer to Section 7.1.6)
- Whether the event is significant (refer to Section 7.1.2 and Section 7.1.3)
- Whether the event is related to the study device (refer to Section 7.1.5)

7.3 Procedures for Reporting Adverse Events

7.3.1 Procedures for Reporting Serious or Significant Adverse Events

An AE classified as a SAE or a Significant Non-Serious Ocular AE requires expeditious handling and reporting to the Sponsor to comply with regulatory requirements, as follows:

- To ensure subject safety, all SAEs, regardless of relationship to the study device, must be immediately (i.e., within a maximum 24 HOURS after becoming aware of the event) reported to [redacted] and Sponsor. All information relevant to the SAE must be recorded on the Sponsor provided SAE report form signed by the Investigator. Within 24 hours of knowledge of a new SAE, the Investigator must enter the SAE information onto the hard copy SAE report form and send the form to the following email distribution:
  - [redacted]
- The Investigator must verify that the report was received by MedTrials and/or the Sponsor. If the Investigator is not able to verify it was successfully received by

[redacted] and/or Sponsor, the Investigator must call the CRO clinical study manager by phone to follow-up. The CRO will forward the documentation to the medical monitor and the sponsor for review.

- Investigators should not wait to receive additional information to fully document the event before initially notifying [redacted] and Sponsor of an SAE or a Significant Non-Serious AE. Additional relevant information such as hospital records and autopsy reports should be provided to [redacted] and Sponsor as soon as they are available.
- The Investigator should take all appropriate measures to ensure the safety of the subjects: notably, he/she should follow a subject with an SAE or Significant Non-Serious AE until the event has resolved or the condition has stabilized. This may imply that follow-up will continue after the subject has left the study, and that additional evaluations may be requested by the Sponsor.
- Ensure that the subject's identity is protected and the subject's identifiers in the clinical trial are properly mentioned on the form.
- BEGIN TREATMENT OF THE AE IMMEDIATELY BY A SUITABLY LICENSED EYE CARE PROFESSIONAL.
- Continue to update the paper SAE or Significant Non-Serious AE Report Form, if applicable, each time the subject is seen during the management of the event and at resolution of the event. All updated report forms should be submitted by the site to [redacted] and the Sponsor within 24 hours. Whenever possible, it is suggested that the Investigator take photographs of all ocular AEs of possible clinical significance and forward them to [redacted] and the Sponsor.
- Events requiring medical treatment will be evaluated by the Sponsor. Upon review of the medical treatment, Bausch + Lomb Clinical Operations representatives may contact the Investigator to request further information concerning the treatment.
- Report all USADEs to the reviewing IRB within 10 working days following awareness of the USADE or according to the established reporting procedures of the IRB, whichever is shorter.
- Submit all bills, prescription receipts, and culture reports/fees related to the AE to the Bausch + Lomb Clinical Operations. Expense incurred for study related medical treatment will be paid by Bausch + Lomb Clinical Operations.

7.3.2 Procedures for Reporting Off-Site Unanticipated Serious Adverse Device Effects

When participating in multicenter clinical investigations, Investigators may receive off-site USADE reports. These are Sponsor reports of USADEs which occurred at other clinical sites for the same trial, or in different trials using the same investigational test article or comparator, that met the criteria for reporting to a regulatory agency. These should be reported to the reviewing IRB within 10 working days or per their established reporting procedures, whichever is shorter.

7.3.3 Device Deficiencies: Definition and Reporting Procedures

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 any complaints/deficiencies or malfunctions experienced with the study lens during this trial to the Medical Monitor promptly using the Device Deficiency Report and provide all source documents and eCRFs that will assist with evaluation of risk to subject safety (e.g. symptoms/complaints, lens performance ratings, VA, topography, mire reflex, slit lamp, etc.). The Sponsor and Medical Monitor shall review all device deficiencies, and, upon the Sponsor's request, Investigators must supply any additional information related to the safety reporting of a particular event.

Report device deficiencies **within 24 hours** of knowledge to:

- [redacted]

The Medical Monitor will distribute, within 24 hours of knowledge, all device deficiencies to the Sponsor.

The Sponsor shall review all device deficiencies and determine and document in writing whether they could have led to an SAE. In the event of a disagreement between the Sponsor and the Investigator(s), the Sponsor shall communicate both opinions to the reviewing IRB per their established reporting procedures and the health authority.

7.3.4 Procedures for Reporting and Culturing of Corneal Ulcer or Suspected Ocular Infection

For purposes of this study, the Sponsor requests that cultures should be obtained in cases of corneal ulcer or suspected ocular infection, unless medically contraindicated. Cultures should be taken from the cul-de-sac, lower eyelid margin, and the corneal lesion (if applicable). The required culturing techniques are outlined in Appendix B.

When a culture is obtained, the contact lenses and contact lens cases which were being utilized by the subject at the time of the AE should be collected from the subject for culturing and processing by the local clinical laboratory designated by the site.

Microbial data generated from returned subject supplies (e.g., lenses, lens cases, and/or lens case solutions) are for information only. Because microbes may be introduced into subject supplies during use, recovery of microbes from returned subject supplies cannot be presumed to indicate etiology or direction of organism transmission.

The ocular cultures, along with the associated contact lenses and contact lens cases, will be sent to the local clinical laboratory designated by the site for analysis. The clinical laboratory will report the culture results to the Investigator who will record the results in the eCRF.

7.3.5 Guidelines for Reporting Pregnancies

During the study, all female subjects of childbearing potential should be instructed to contact the Investigator immediately if they suspect they might be pregnant (e.g., missed, or late menstrual period). Female subjects who become pregnant during the study will be

followed until completion of pregnancy. Every effort will be made to obtain the health status of the mother and infant or fetus (in cases of miscarriage or therapeutic abortion) at term. Pregnancy itself is not considered an AE.

All confirmed pregnancies must be reported on a Pregnancy Report and submitted to the Medical Monitor via facsimile or email transmission within 24 hours of the Investigator's awareness of the pregnancy. The Medical Monitor will distribute the completed report to the Sponsor as per the distribution listed below.

All pregnancies will be followed until outcome even after study closure. The outcome of all pregnancies will be reported on a paper Pregnancy Outcome Report and submitted to the Medical Monitor via facsimile or email transmission once the outcome is learned. The Medical Monitor will distribute the completed report to the Sponsor as per the distribution listed below.

Although pregnancy occurring in a clinical study is not considered to be an AE or SAE, any pregnancy complication, spontaneous abortion, or elective termination of a pregnancy, for medical reasons, will be recorded as an SAE. Any serious complication or event resulting from the pregnancy should be reported to the Medical Monitor within 24 hours on the SAE or Significant Non-Serious AE Report Form along with the Pregnancy Report Form.

The contact for reporting pregnancies and pregnancy outcomes are:

- [redacted]

7. STATISTICAL METHODS

Changes to these statistical plans will be documented in protocol amendments and/or the statistical analysis plan.

8.1 Study Endpoints

8.1.1 Primary Safety Outcomes

The primary safety outcome is the rate of serious adverse events at the subject and eye levels.

[redacted]

8.1.3 Primary Effectiveness Outcomes

The primary effectiveness outcome is the proportion of subjects who achieve high-contrast monocular UDVA of 20/40 or better in both eyes at the 3-Month Follow-up Visit.

[redacted]

8.2 Hypotheses

No statistical hypotheses will be tested.

8.3 Sample Size

The FDA recommended a sample size of 50 completed subjects. The sample size is not based on statistical hypothesis tests. Enrollment of 70 subjects will allow for early discontinuation of up to 28% of the subjects to achieve a final sample size of 50 subjects.

8.4 Randomization

There will be no randomization in this single treatment study.

8.5 Study Populations

8.5.1 Full Analysis Set (FAS)

The FAS will consist of all dispensed subjects for subject level summaries and, for eye level summaries, both of their eyes.

8.5.2 Per Protocol (PP) Set

The PP Set will consist of all FAS subjects without important protocol deviations that could affect the primary effectiveness endpoint. The membership of the PP Set will be determined prior to database lock.

8.5.3 Safety Set

The FAS will be used to evaluate safety outcomes.

8.6 Statistical Analysis

8.6.1 Methods of Analysis

General Methods

Continuous data will be summarized using sample size (n), mean, standard deviation (SD), median, minimum, and maximum. Categorical data will be presented using the total counts for each category and corresponding percentages. The denominator for each percentage will be the number of subjects or eyes with non-missing data unless otherwise indicated.

Data from the FAS will be used for analysis unless otherwise specified.

For each assessment, the baseline value will be defined as the last observation before the first insertion of the study lenses. Change from baseline will be computed as follow-up value minus baseline value.

As customary for contact lens trials, eyes will be treated as independent sampling units in eye level analyses unless otherwise noted.

Listings of data will be produced in addition to tables of summary statistics.

The proportion of subjects with non-missing monocular UDVA data for both eyes at the 3-Month Visit who achieved monocular UDVA of 20/40 or better in both eyes at the 3-Month Follow-up Visit will be presented.

As a sensitivity analysis, the summary will be produced using the PP Set.

8.6.2 Adverse Events

All AEs occurring during the study will be recorded and classified on the basis of MedDRA terminology. Descriptions of AEs will include the date of onset, the date the AE ended, the severity of the AE, the relationship to the study device, the action taken to treat the AE, and the outcome. All reported treatment—emergent AEs (TEAEs) will be summarized by the number of subjects (or eyes, as appropriate) reporting AEs, system organ class, severity, seriousness, and relationship to study device. TEAEs are those AEs with and onset on or after the date of the first study device use.

Serious adverse events will be summarized at the subject and eye levels.

Adverse events will be summarized by severity. Each subject (or eye, as appropriate) will be counted only once within a system organ class or a preferred term by using the AEs with the highest severity within each category.

Adverse events will be summarized by relationship to study device. Each subject (or eye, as appropriate) will be counted only once within a system organ class or a preferred term by using the AEs with the greatest relationship within each category.

All information pertaining to AEs noted during the study will be listed by subject, detailing verbatim given by the Investigator, preferred term, system organ class, start

date, stop date, severity, action taken, and device relatedness. The AE onset will also be shown relative (in number of days) to the day of initial use of the study device.

Serious adverse events (SAEs) will be tabulated.

In addition, a list of subjects who discontinued from the study and a list of subjects who experienced SAEs will also be provided.

8.6.3 Subject Demographics and Baseline Characteristics

Demographics and baseline characteristics will be summarized descriptively for the FAS and PP Set.

8.6.4 Subject Discontinuation

The reasons for study discontinuation will be summarized for the FAS.

8.6.5 Protocol Deviations

Important (major) protocol deviations will be summarized by category for the FAS in a table.

Categories of important protocol deviations leading to exclusion from the PP Set will include the following:

- Ineligibility at screening but treated
- Not dispensed study treatment
- Use of medications that could potentially affect the primary effectiveness endpoint
- Errors in the assessment of the primary effectiveness endpoint
- Compliance with study treatment of less than 80%

Additional important protocol deviation categories may be added prior to database lock.

8.6.6 Treatment Compliance

Lens wear parameters (average number of nights worn per week and average nightly wearing time, in hours) will be summarized using continuous and categorical summary statistics by visit. The overall average number of nights per week, overall average nightly wearing time, and overall compliance (%), estimated for each subject based on visit dates and reported lens wear parameters, will also be summarized. Compliance will be based on an expected wearing time of eight hours per day.

8.6.7 Treatment Exposure

Treatment exposure (days), defined as the difference between the last date of lens wear and the first date of lens wear + 1, will be summarized using continuous summary statistics.

8.6.8 Missing Data

Missing data will not be imputed.

8.6.9 Multiplicity Issues

Multiplicity issues do not pertain to this study because there is no hypothesis testing.

8.6.10 Interim Analyses

No interim analyses are planned.

8. DATA QUALITY ASSURANCE

9.1 Subject Confidentiality

All personal subject data collected and processed for the purposes of this trial will be maintained by the Investigator and his/her staff with adequate precautions as to ensure that the confidentiality of the data is in accordance with local, state, and federal laws and regulations.

Monitors, auditors, and other authorized representatives of CRO, the Sponsor, the IRB approving this trial, the FDA, the Department of Health and Human Services, other domestic government agencies, and other foreign regulatory agencies will be granted direct access to the trial subject's original medical and trial records for verification of the data and/or clinical trial procedures. Access to this information will be permitted to the aforementioned individuals to the extent permitted by law.

A report of the results of this trial may be published or sent to the appropriate health authorities in any country in which the product may ultimately be marketed, but the subject's identity will not be disclosed in these documents.

Suspected data breaches involving Personal Health Information will be escalated to Bausch + Lomb Data Privacy representative per [redacted]

9.2 Study Monitoring

Bausch + Lomb Clinical Operations 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 Clinical Operations.

Prior to the start of the study, member(s) of the Bausch + Lomb Clinical Operations, Clinical Affairs will review the protocol, eCRF, 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 rights and well-being of subjects are protected
- Tthe conduct of the investigation is in compliance with the currently approved protocol/amendment, 21 CFR Parts 11, 50, 54, 56 and 812; 42 CFR Part 11 – Clinical Trials Registration and Results Information Submission; EN ISO 14155:2020 *Clinical investigation of medical devices for human subjects – Good clinical practice*; Medical Device Regulation (MDR) 2017/745; International

Council for Harmonization (ICH) Good Clinical Practice; the Declaration of Helsinki and applicable local regulations

- the integrity of the data, including adequate study documentation
- the facilities remain acceptable
- the Investigator and site personnel remains qualified and able to conduct the study investigational test article accountability

During the course of the study, if the Sponsor determines that an Investigator is non-compliant with the protocol and/or applicable regulatory requirements, the Sponsor 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 the Sponsor's actions.

Plans for monitoring study sites, designated to ensure compliance with GCPs, study-specific procedures, human rights and applicable regulations, are described in the Monitoring Plan.[5]

9.3 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 his/her participation in the study.

Examples of source documents include hospital records, clinical and office charts, laboratory notes, memoranda, signed ICFs, evaluation checklists, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, and information initially recorded in an electronic format. Source documentation worksheets may be provided by the Sponsor to record pertinent information.

Subject completed forms are also considered source data. In no instance, should an Investigator or study site personnel record any data or make changes to subject completed forms. The Investigator or designee should review subject completed forms during study visits for completeness and accuracy. If an entry is found to be illegible or a mistake is found (e.g., incorrect year was recorded), the subject should be instructed to edit the entry by drawing a single line through the original entry, entering the new information, and dating and initialing the change.

Subjects should be provided the rating scales (separate document) to use while responding to the lens performance assessments being collected. Enter rating from 0-100 (e.g., 90).

9.4 Case Report Forms and Data Verification

Subject data required by this protocol are to be transferred from source to the eCRFs. The Investigator and his/her 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 required on the eCRFs needs to be supplied, including subject identification, date(s), assessment values, etc., and any

omission or discrepancy will require explanation. All information on eCRFs must be traceable to source documents.

A Clinical Monitor will be responsible for reviewing and verifying 100% of the data recorded on the eCRFs, utilizing the original source documentation and will query discrepant findings. The Investigator and study site personnel will be responsible for answering all queries. The eCRF data will be reviewed for completeness, accuracy, consistency, and medical sense. Programmed edit checks will be used to reduce data entry errors and identify unusual data for verification prior to statistical analysis.

A copy of the eCRF data will be retained at the conclusion of the study by the Investigator, who must ensure that it is stored in a secure place.

9.5 Recording of Data and Retention of Documents

Subject data recorded on eCRFs during the study will be documented to maintain subject confidentiality. The subject will only be identified by the subject ID. Confidentiality of subject records must be maintained to ensure adherence to applicable local privacy regulations.

The Investigator has to retain records for 2 years after the investigational product is approved by the FDA. 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/EC approvals for the study protocol, all amendments, ICF(s), and advertisements
- IRB/EC annual study review
- IRB/EC correspondence and reports (e.g., AE reports, protocol deviations, and safety updates)
- Regulatory documents (e.g., financial disclosure and delegation of authority forms)
- All source documents
- eCRFs
- Subject's signed ICF(including HIPAA)
- Device Investigator 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 study records are transferred to another location, the Investigator will provide notice of such transfer in writing to Bausch + Lomb Clinical Operations.

9.6 Auditing Procedures

Audits of clinical research activities in accordance with the Sponsor's internal Standard Operating Procedures (SOPs) 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/EC, the Investigator must inform the Sponsor immediately that this request has been made.

9.7 Institutional Review Board/Ethics Committee Approval

The Investigator should ensure that the following are approved by their institution's IRB, or if not using their institution's IRB/EC, approved by the reviewing central IRB prior to entering any subjects in the study:

- The protocol
- The Investigator's participation in the study
- Subject recruitment materials (written information or materials including web pages, radio advertisements, television spots or written text developed to encourage subject enrollment)
- The ICF to be used in this study

Documentation of IRB/EC approval of the study protocol and informed consent must be provided to the Sponsor prior to initiation of the study. In addition, the Investigator must ensure that the reviewing IRB/EC 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/EC prior to implementation as directed.

9.8 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 Bausch + Lomb products and activities receive fair, accurate, and reasonable presentation.

9. REFERENCES

10.1 Global and Regional Regulatory References:

EN ISO 14155:2020 *Clinical investigation of medical devices for human subjects – Good Clinical Practice*

EN ISO 11980:2012 *Ophthalmic Optics – Contact Lenses and contact lens care products – Guidance for clinical investigations*

21 CFR Part 11 – Electronic Records; Electronic Signatures

21 CFR Part 50 – Protection of Human Subjects

21 CFR Part 54 – Financial Disclosure by Clinical Investigators

21 CFR Part 56 – Institutional Review Boards

21 CFR Part 812 – Investigational Device Exemptions

42 USC 282(j)

REGULATION (EU) 2017/745 (also called European Medical Device Regulation MDR) – Regulation of the European Union on medical devices

10.2 Literature References

[1]Study 918 Investigator Contact List

[2] Study 918 - Boston Orthokeratology (oprifocon A) Shaping Lens, Arise Orthokeratology Lens Design Investigator Brochure

[3]B&L SOP No 20-D022-3 Investigational Material Release for Bausch Health Companies R&D Activities

[4]B&L SOP No. CLN 035 – Privacy of Clinical Data and Related Information

[5]Study 918 Monitoring Plan

APPENDIX A: SCHEDULE OF VISITS AND PROCEDURES

All study tasks should be performed by qualified study site personnel as indicated on the delegation of authority log under the supervision of the Principal Investigator. **(Refer to important footnote at the bottom of the table)**

PROCEDURES/ASSESSMENTS		Screening Visit 1	Dispensing Visit 2	1-Day Visit 3	1-Week Visit 4	1-Month Visit 5	2-Month Visit 6	3-Month Visit 7	Exit Visit
Informed Consent/HIPAA Authorization		X							
Demographics		X							
Contact lens use history		X							
Ocular medical history and concomitant ocular medications		X							
Changes in Concomitant ocular medications			X	X	X	X	X	X	X
Eligibility		X							
Dispense Study Materials			X						
Collect Study Materials								X	X
Monocular high-contrast distance VA with habitual correction		X							
Anesthetic drops prior to lens insertion			X						
To be performed with study lenses	Lens fit assessment		X	X[a]					
To be performed without lenses	Monocular UDVA (each eye)	X	X	X	X	X	X	X	X
	Spherocylindrical refraction	X	X	X	X	X	X	X	X
	Distance high-contrast BSCVA	X	X	X	X	X	X	X	X
	Topography	X		X	X	X	X	X	X
	Biomicroscopy	X	X	X	X	X	X	X	X
	Compare refractive astigmatism to Dispensing Visit			X	X	X	X	X	X
	Compare BSCVA to Dispensing Visit			X	X	X	X	X	X

APPENDIX A: SCHEDULE OF VISITS AND PROCEDURES (CONTINUED)

Lens wear parameters			X	X	X	X	X	
Adverse Events	X	X	X	X	X	X	X	X
Symptoms/Complaints			X	X	X	X	X	
Lens Performance Ratings			X	X	X	X	X	

[a] The 1-Day Follow-up visit will be conducted within 2 hours of awakening and topography will be performed within 30 minutes of lens removal

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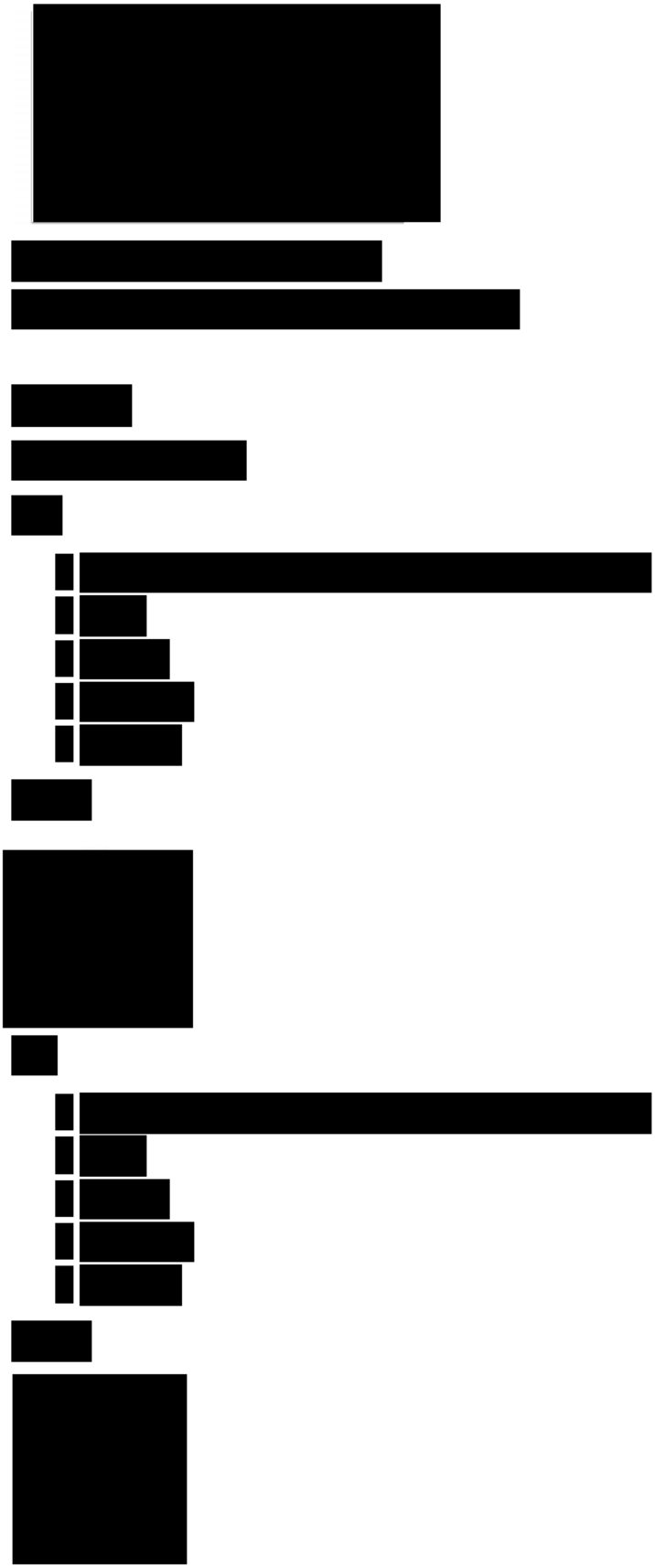

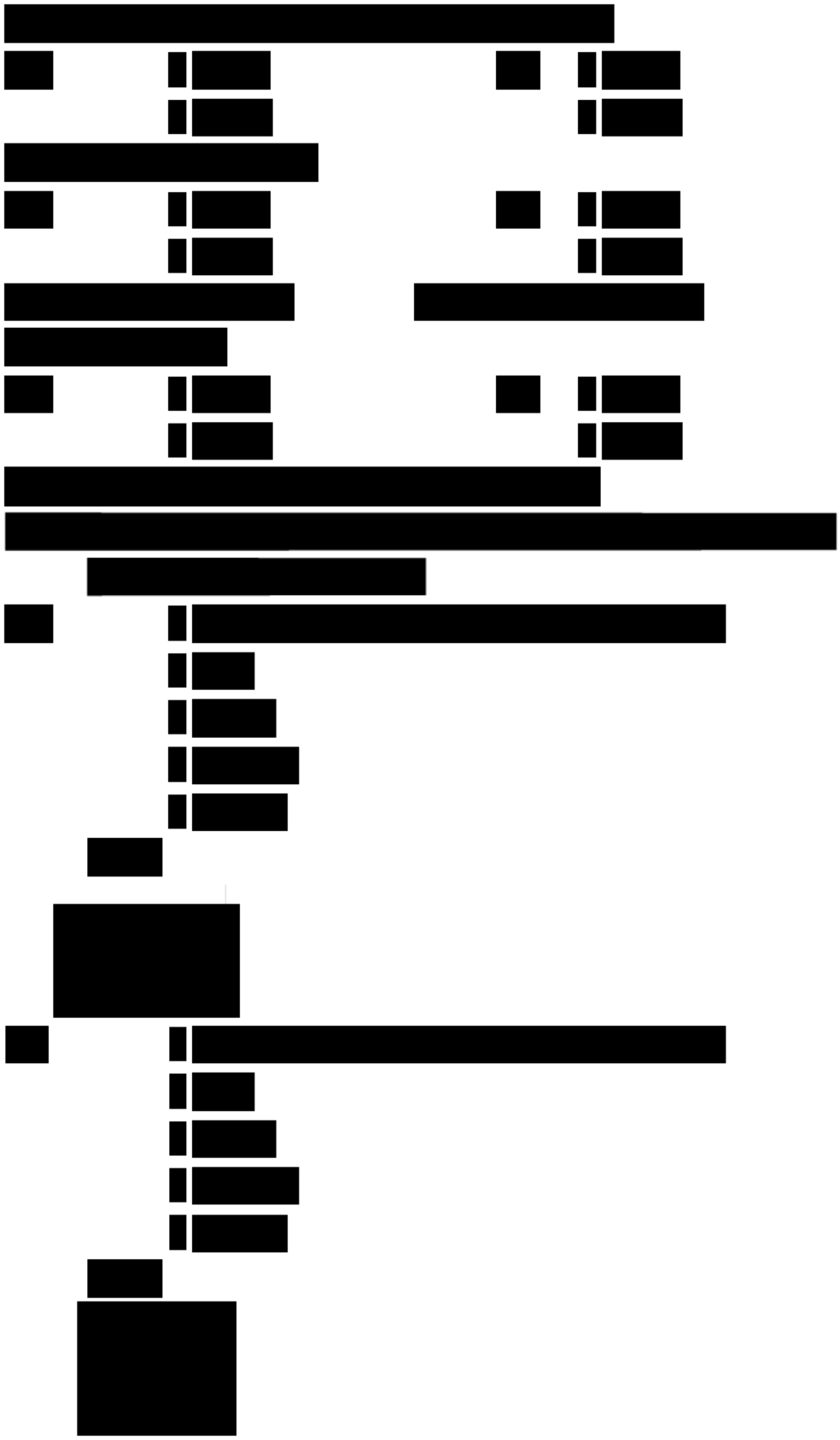

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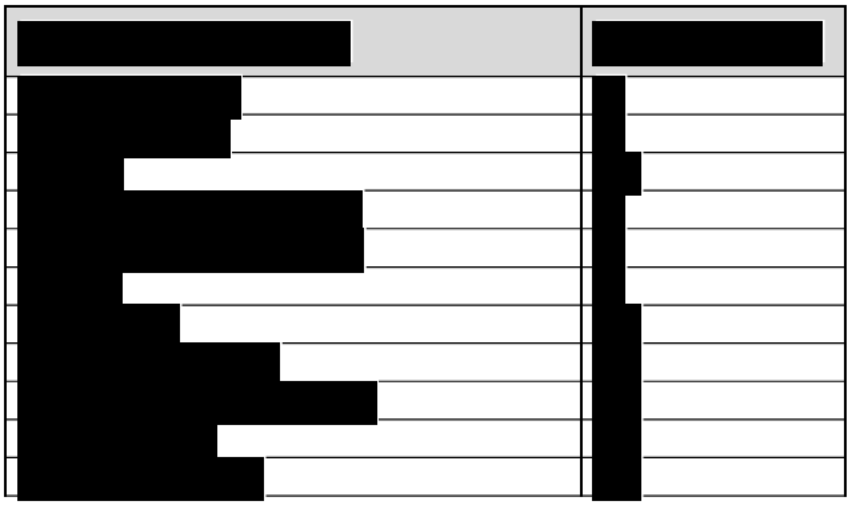

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APPENDIX C: SUBJECT INSTRUCTIONS

INTRODUCTION

You will participate in this study designed to evaluate the product performance of the investigational Arise Orthokeratology Lens. Study lenses will be dispensed at the Dispensing Visit. It is very important that you do not use any other contact lenses other than those dispensed to you during the study.

During the initial week(s) of treatment, some patients may experience changes in vision that may require temporary alternate corrective eyewear. This should be discussed with your study doctor.

You are cautioned to carefully follow the wearing schedule recommended by your study doctor regardless of how comfortable your lenses feel. The lenses are intended for overnight wear. Lenses should be removed each morning for disinfecting and cleaning. If the lenses continue to be well tolerated, they may be re-inserted each night.

Please keep all appointments and follow these instructions thoroughly. If you have any questions or problems, call your study doctor at _____.

Your study doctor or staff will schedule your 1-Day Follow-up appointment for within 2 hours of your awakening the day after you sleep in your lenses for the first time. It is important that you **wear your lenses to this appointment**. Unless your study doctor finds it necessary to refine the fit of your lens, this will be the only appointment that you will need to wear your lenses to an appointment. The remaining appointments will be scheduled for within 2 hours of removing lenses from your eyes in the morning.

PATIENT LENS CARE DIRECTIONS

Your study doctor or staff will review instructions for the care of your contact lenses.

To ensure proper disinfecting, all steps listed below must be followed:

1. Wash your hands with mild soap. (Caution – pump soaps may contain oil-based suspension agents.)
2. Place lenses in empty lens case and fill to top ridges with fresh Boston SIMPLUS Multi-Action Solution. Soak lenses for at least 4 hours before wearing.
3. Wash hands with mild soap before cleaning (rubbing) lenses. After soaking, remove lenses from lens case and rub both sides of the lenses carefully with 4 drops of Boston SIMPLUS Multi-Action Solution in the palm of your hand for 20 seconds.
4. Rinse for approximately 5 seconds with a steady stream of Boston SIMPLUS Multi-Action Solution to eliminate loosened surface deposits and insert lenses.
5. Discard solution from lens case after each use. For lens rewetting and lubrication, use Boston® Rewetting Drops.

If your study doctor recommends a different lens care regimen, appropriate instructions will be provided and reviewed with you.

INSERTION AND REMOVAL OF CONTACT LENSES

Preparing the Lens for Wearing

It is essential that you learn and use good hygienic methods in the care and handling of your contact lenses. Cleanliness is the first and most important aspect of proper contact lens care. Hands should be clean and free of any foreign substances when you handle your lenses.

The procedures are:

- Always wash, rinse and dry hands thoroughly before handling your contact lenses.
- Avoid soaps containing cold cream, lotions or oily cosmetics prior to handling your lenses. These substances can adhere to the surface of the lens and be difficult to remove.
- Handle lenses with the fingertips, avoiding use of fingernails that can scratch or chip lenses.
- Always start with the same lens first to avoid mix-ups.
- Remove the lens from its storage case and examine it. Be sure it is clean, moist and free of any nicks or cracks.

Placing the Lens on the Eye

- Prepare the lens for placement by following Step 3 (rubbing) and Step 4 (rinsing) in the Patient Lens Care Directions above.
- Place lens on the top of index finger of dominant hand.
- With other hand, hold down lower lid and lift upper lid up. Gently place lens on the center of your eye. It is not necessary to press the lens on the eye.
- Gently release lids and blink. The lens should center automatically.
- Use the same technique to insert the other lens.

There are other methods of lens placement. If this method proves too difficult for you, discuss alternatives with your study doctor.

Note: if vision is blurred after insertion, check for the following conditions:

- Lens is not centered (refer to section below on “Centering a Lens”)
- If lens is centered, remove and check for any of the following:
  a. Cosmetics or oil on the lens. Clean, rinse, disinfect and replace on eye.
  b. The lens may be on the wrong eye.

If you find your vision is still blurred after checking the possibilities as listed above, remove both lenses and consult your study doctor.

Centering the Lens

Very rarely, a lens that is on the cornea will displace onto the white portion (sclera) of the eye during lens wear. This can also occur during insertion or removal of your lens if proper technique is not utilized. To center a lens, follow one of the procedures below or one recommended to you by your study doctor.

- Close your eyelids and gently massage the lens into place through the closed lids.

OR

- Gently push the off-centered lens onto the cornea while the eye is open using finger pressure on the upper or lower lid next to the edge of the lens.

Removing the Lens

Before attempting to remove your lens, it is very important that you verify the lens is moving. The lens is designed to be worn overnight and may be slightly stuck in place on the eye in the morning. Apply two to three drops of Boston Rewetting Drops to your eyes in the morning and wait until the lens begins to move freely with the blink before you attempt to remove it.

It is recommended that you have the following items available when you are ready to remove your lenses:

- A lens storage case
- Solution for cleaning and storing your lenses
- A clean towel

Always remove the same lens first to avoid confusion. Wash, rinse and dry your hands thoroughly.

There are two suggested methods of lens removal:

TWO FINGER METHOD

1. Place a towel on the counter to catch the lens.
2. Place the tip of the forefinger of one hand on the middle of the upper lid margin and the forefinger of the other hand on the middle of the lower lid margin.
3. Press the lid margin inward and then together. The lens should be wedged out of your eye and onto your hand or the towel.
4. The lens may come out but remain on your eyelid or be de-centered onto the white part of your eye. If the latter occurs, re-center the lens onto your cornea before repeating the removal process.

BLINK METHOD

Seat yourself at a table covered with a clean towel and lean over until you are looking at the surface.

1. Place your index finger at the outer junction of your upper and lower lids; stretch the skin outward and slightly upward. Do not allow your lid to slide over the lens.
2. Blink briskly. The lens will be pinched by the pressure of your eyelids and pop out onto the clean surface of the towel, or you may catch the lens in the palm of your hand.

Note: If these methods for removing your lens are difficult for you, your study doctor can provide you with alternatives.

IMPORTANT SAFETY INFORMATION

- Always follow the product directions for use. Failure to follow product directions may lead to vision loss.
- Always wash and dry hands before handling lenses.
- Do not use tap water, bottled water or saliva with lenses or lens case.
- Only use fresh solution to clean and disinfect contact lenses.
- Always discard any remaining solution in your lens case after each disinfection cycle.
- Saline solution or rewetting drops will not disinfect your lenses.
- Always replace your solutions, lenses, and lens case(s) as directed.
- To avoid contamination, do not touch tip of container to any surface. Replace cap after using.
- Not for use with heat (thermal) disinfection.

WARNINGS

You should be aware of and fully discuss with your study doctor the following warnings pertaining to contact lens wear:

- Problems with contact lenses could result in serious injury to your eye. It is essential that you follow your study doctor's direction and all labeling instructions for proper use of lenses. Eye problems, including corneal ulcers, can develop rapidly and lead to loss of vision.
- If you experience eye discomfort, excessive tearing, vision changes, or redness of the eye, you should immediately remove lenses and promptly contact your study doctor.
- Strict compliance with your wearing restrictions, wearing schedule, and follow-up visit schedule should be followed.

Arise Orthokeratology Lenses are to be worn overnight with removal during all or part of each following day. Wearing the lenses continuously (extended wear) presents increased risk, which increases with the number of consecutive days that the lenses are worn between removals. Although the process prescribes only overnight wear with the removal during waking hours, and although the safety risks of overnight wear with removal upon awakening may not be as great as with uninterrupted extended wear, there is still increased risk beginning with the first overnight period.

The risk of ulcerative keratitis has been shown to be greater among wearers of extended wear lenses than among wearers of daily wear lenses. The risk among extended wear lens wearers increases with the number of consecutive days that lenses are worn between removals, beginning with the first overnight use. This risk can be reduced by carefully following directions for routine lens care, including cleaning the storage case. Additionally, smoking increases the risk of ulcerative keratitis for contact lens wearers.

ADVERSE EFFECTS

You should be informed that the following problems might occur:

- Eyes stinging, burning, itching (irritation), or other eye pains.
- Comfort is less than when lens was first placed on eye.
- Feeling of something in the eye, such as a foreign body or scratched area.
- Excessive watering (tearing) of the eyes.
- Unusual eye secretions.
- Redness of the eyes.
- Reduced sharpness of vision (poor visual acuity).
- Blurred vision, rainbows, or halos around objects.
- Sensitivity to light (photophobia).
- Dry eyes.

If you notice any of the above, **IMMEDIATELY REMOVE YOUR LENSES**.

- If the discomfort or problem stops, then look closely at the lens.
- If the lens is in any way damaged, DO NOT put the lens back on your eye. Place the lens in the storage case and contact your study doctor.
- If the lens has dirt, an eyelash, or other foreign objects on it, or the problem stops, and the lens appears undamaged, you should thoroughly clean, rinse and disinfect the lens; then reinsert it. Do not use a tap water rinse, use the approved conditioning solution as a rinsing agent.
- If the problem continues, you should IMMEDIATELY remove the contact lens and consult your study doctor.

When any of the above problems occur, a serious condition such as infection, corneal ulcer, neovascularization, iritis, persistent stromal edema or GPC (giant papillary conjunctivitis) may be present. You should be instructed to keep the lens off the eye and seek immediate professional identification of the problem and prompt treatment to avoid serious eye damage.

CARE FOR A STICKING (NON-MOVING) LENS

Observe your lenses with a mirror to confirm that they move freely upon blinking before you attempt to remove them. If a lens sticks (stops moving/cannot be removed), you should apply two to three drops of Boston Rewetting Drops directly to the eye and wait until the lens begins to move freely on the eye before removing it. If non-movement continues after 5 minutes, re-instill rewetting drops and compress the lid margin above or below the lens to release the suction. If non-movement persists, do not attempt to remove the lens but immediately contact your study doctor.

APPENDIX D: FITTING GUIDE

IMPORTANT

This Fitting Guide has been developed to provide study doctors with information covering characteristics of the investigational orthokeratology contact lens and to illustrate fitting procedures. Please read carefully and keep this information for future use.

PRODUCT DESCRIPTION

Arise Orthokeratology (oprifocon A) Lenses are a lathe cut gas permeable contact lens. The posterior curve is selected to properly fit an individual eye for orthokeratology and the anterior curve is selected to provide the necessary optical power for a temporary reduction of myopia. A peripheral curve system on the posterior surface allows tear exchange between the lens and the cornea.

Arise Orthokeratology Lenses are made of oprifocon A polymer with a water content of less than 1 percent that contains an ultraviolet absorber, Uvinul D-49. The blue tinted lenses for the right eye contain D&C Green #6 as a color additive. The green tinted lenses for the left eye contain D&C Green #6 and C.I. Solvent Yellow #18.

DETAILED DESCRIPTION

Arise Orthokeratology Lenses have a design known as reverse geometry. This means that the secondary curve on the posterior surface, next to the base curve, has a radius of curvature that is steeper (shorter radius) than the base curve (central curve). This curve is referred to as the “Fitting Curve” or the “Reverse Curve”.

The Fitting Curve is surrounded by a flatter intermediate zone that is approximately equal in radius to the flat keratometer reading of the central cornea. This zone is referred to as the “Alignment Zone” or the “Alignment Curve.” In this way the geometry of the secondary curves are in the opposite relationship to the base curve, as occurs with standard GP contact lenses. Outside the Alignment Zone, at the edge of the lens, is a peripheral curve that allows for tear exchange under the lens to take place. The function of the steep Fitting Curve, on the Arise Orthokeratology Lenses, is to allow the base curve to be fit in a flat relationship to the central cornea and still maintain lens stability on the cornea. With a regular GP contact lens design that is fitted flat on the cornea there is only one support point for the contact lens, which occurs at the center of the lens. This lens will tend to rock and de-center on the cornea. With the Arise Orthokeratology Lens, there is support for the lens at both the central cornea and in the area of the Alignment Zone. This will reduce lens rocking and aid in centering.

LENS PARAMETERS AVAILABLE

Chord Diameter	9.6mm to 11.6mm
Center Thickness	
For Low Minus Lens	0.20mm to 0.32mm
For Plus Lenses	0.20mm to 0.32mm
Base Curve	7.30mm to 10.15mm

Reverse Curve	5.0mm to 9.0mm Steeper than the base curve in proportion to the amount of correction
Alignment Curve 1	7.0mm to 9.0mm Steeper than the base but flatter than the reverse curve. Generally equal to the Flat K of the cornea being fit
Alignment Curve 2	7.25mm to 9.25mm Steeper than the base curve but flatter than AC1 and reverse curve
Peripheral Curves	9.00mm to 15.00mm
Back Vertex Power	+1.50 Diopters to -5.00 Diopters

HOW THE LENS WORKS (ACTIONS)

Arise Orthokeratology Lenses produces a temporary reduction of myopia by changing the shape (flattening) of the cornea, which is elastic in nature. Flattening the cornea reduces the focusing power of the eye, and if the amount of corneal flattening is properly controlled, it is possible to bring the eye into correct focus and completely compensate for myopia.

The posterior surface of regular contact lenses generally aligns with the central cornea and rests directly on the corneal tear layer. Regular contact lenses are designed to cause little or no effect on the cornea but Arise Orthokeratology Lenses are designed to purposely flatten the shape of the cornea by applying slight pressure to the center of the cornea when the patient is asleep.

After the lens is removed, the cornea retains its altered shape for all or most of one's waking hours. The lenses are designed to be worn overnight with removal during the following day. The Arise Orthokeratology Lenses must be worn at night on a regular schedule to maintain the orthokeratology effect, or myopia will revert to the pretreatment level.

INDICATIONS

Arise Orthokeratology Lenses are indicated for use in the reduction of myopic refractive error in non-diseased eyes. The lenses are indicated for overnight wear for the temporary reduction of myopia up to 5.00 diopters in eyes having astigmatism up to 1.50 diopters. The lenses may only be disinfected using a chemical disinfection system.

Note: To maintain the Orthokeratology effect of myopia reduction, overnight lens wear must be continued on a prescribed schedule. Failure to do so can affect daily activities (e.g., night driving),visual fluctuations and changes in intended correction.

CONTRAINDICATIONS (REASONS NOT TO USE)

DO NOT USE Arise Orthokeratology Lenses when any of the following conditions exist:

- Acute and subacute inflammation or infection of the anterior chamber of the eye.
- Any eye disease, injury, or abnormality that affects the cornea, conjunctiva, or eyelids.

- Severe insufficiency of tears (dry eyes).
- Corneal hypoesthesia (reduced corneal sensitivity).
- Any systemic disease which may affect the eye or be exacerbated by wearing contact lenses.
- Allergic reactions of ocular surfaces or adnexa which may be induced or exaggerated by wearing contact lenses or use of contact lens solutions.
- Allergy to any ingredient, such as mercury or thimerosal, in a solution which is to be used to care for your Arise Orthokeratology Lenses.
- Any active corneal infection (bacterial, fungal, or viral).
- If eyes become red or irritated.

WARNINGS

After a thorough eye examination, including appropriate medical background, subjects should be fully apprised by the study doctor of all the risks with contact lens wear. Subjects should be advised of the following warnings pertaining to contact lens wear:

- Incorrect use of contact lenses and lens care products can result in serious injury to the eye. It is essential that subjects follow the study doctor's directions and all labeling instructions for proper use of contact lenses and lens care products.
- Eye problems, including corneal ulcers, can develop rapidly and lead to loss of vision. If the subject experiences eye discomfort, excessive tearing, vision changes, loss of vision or redness of the eye, immediately remove the lenses and do not wear them until instructed to do so by the study doctor.
- All study subjects must see their study doctor according to the schedule given to them.
- Arise Orthokeratology Lenses are to be worn overnight with removal during all or part of each following day. Wearing the lenses continuously (extended wear) presents increased risk, which increases with the number of consecutive days that the lenses are worn between removals. Although the Arise Orthokeratology process prescribes only overnight wear with removal during waking hours, and although the safety risks of overnight wear with removal upon awakening may not be as great as with uninterrupted extended wear, there is still increased risk beginning with the first overnight period. The risk of ulcerative keratitis has been shown to be greater among wearers of extended wear lenses than among wearers of daily wear lenses. The risk among extended wear lens wearers increases with the number of consecutive days that lenses are worn between removals, beginning with the first overnight use. The risk can be reduced by carefully following directions for routine lens care, including cleaning the storage case. Additionally, smoking increases the risk of ulcerative keratitis for contact lens wearers.

ADVERSE EFFECTS

The subject should be informed that the following problems may occur:

- Eyes stinging, burning, itching (irritation), or other eye pain.
- Comfort is less than when lens was first placed on eye.
- Feeling of something in the eye, such as foreign body or scratched area.
- Excessive watering (tearing) of the eyes.
- Unusual eye secretions.
- Redness of the eyes.
- Reduced sharpness of vision (poor visual acuity).
- Blurred vision, rainbows, or halos around objects.
- Sensitivity to light (photophobia).
- Dry eyes.

If the subject notices any of the above, he or she should be instructed to **IMMEDIATELY REMOVE THE LENSES.**

- If the discomfort or problem stops, then look closely at the lens.
- If the lens is in any way damaged, DO NOT put the lens back on the eye. Place the lens in the storage case and contact the study doctor.
- If the lens has dirt, an eyelash, or other foreign body on it, or the problem stops and the lens appears undamaged, the subject should thoroughly clean, rinse and disinfect the lens; then reinsert it. Do not use tap water rinse, use the approved conditioning solution as a rinsing agent.
- If the problem continues, the subject should **IMMEDIATELY** remove the contact lenses and consult the study doctor.

When any of the above problems occur, a serious condition such as infection, corneal ulcer, neovascularization, iritis, persistent stromal edema or GPC (giant papillary conjunctivitis) may be present. The subject should be instructed to keep the lens off the eye and seek immediate professional identification of the problem and prompt treatment to avoid serious eye damage including corneal scarring, opacification, blindness or loss of eye.

SELECTION OF SUBJECTS

Patients are selected who have a demonstrated need and desire for a refractive reduction by orthokeratology with gas permeable contact lenses and who do not have any of the contraindications described above. Arise Orthokeratology Lenses are indicated for myopic patients who desire to have time periods during the day in which they do not need to wear their contact lenses, but still need to see clearly. Arise Orthokeratology Lenses are primarily intended for patients who are within the following parameters:

Refractive error: -1.00 diopters to -5.00 diopters with up to 1.50 diopters of astigmatism.

Keratometry: 40.00 diopters to 46.00 diopters.

FITTING CONCEPT

Arise Orthokeratology Lenses are designed to be fit so that they flatten the central cornea and thereby reduce myopia. This goal is accomplished by the lens design and the manner in which the lens is fitted. The goal in fitting is a well-centered lens having a base curve that is flatter than the flattest meridian of the cornea by at least the attempted treatment power in that meridian. A well-fit lens will have the proper sagittal depth to prevent vaulting off the central corneal apex and prevent excessive bearing in the alignment zone(s). There should be adequate edge lift to allow for proper tear exchange.

FITTING PROCEDURE

1. Screening Visit Examination

A screening subject history and examination are necessary to:

- determine whether a subject is a suitable candidate for orthokeratology contact lenses (consider subject hygiene and mental and physical state),
- make ocular measurements for initial contact lens parameter selection, and
- collect and record baseline clinical information to which post-fitting examination results can be compared.

A screening examination should include spherocylindrical refraction and high-contrast distance BSCVA, corneal topography, and biomicroscopic examination. See Section 6.1.1, Screening Visit.

2. Initial Lens Selection

The initial lens will be based on the subject's spectacle refraction and corneal topography map file. The Investigator should complete the Arise Orthokeratology Lens Order Instruction Form and follow the instructions on the form to order the initial lenses for the subject.

The following information will be required for the initial lens order:

- Subject ID (6 digit):
- Investigator Name:
- Account ID: 0ARISE
- Category: New Order
- Pre-treatment topography map file for OD and OS
    - File should be sent pre-populated with:
        - Subject ID (first name = type the word "SUBJECT", last name = 6-digit subject ID)
        - Subject date of birth
        - Subject spectacle refraction.

3. Initial Lens Evaluations (Dispensing Visit)

- Insert a drop of anesthetics in each eye prior to lens insertion.

- Evaluate the study lenses on the eye and record the following lens fit assessments:
  - lens centration
  - lens movement
- Fluorescein Pattern Interpretation:

  The fluorescein pattern should show a lens with definite central touch, approximately 4.0mm to 6.0mm in diameter with a surrounding area of pooling. The pattern should show alignment in the mid-periphery and there should be normal clearance at the edge.

  The area of pooling near the transition between the base curve and secondary curve serves as a reservoir for tears and as a potential space for corneal shifting during the flattening process of orthokeratology. The cornea adapts by flattening in the central area, which reduces the space near the transition reservoir. The size of the transition reservoir, as observed from the fluorescein pattern, is a good indicator not only of the initial fit of the lens but also of the progress of corneal flattening over time as the lens is worn.

  The fluorescein pattern provides a good method for monitoring the fit of the contact lens over time. As the cornea flattens, the area of pooling at the transition becomes less.

  The presence of the UV-absorber in the Arise Orthokeratology Lenses may require equipment enhancement to visualize fluorescein patterns adequately. A simple, inexpensive approach is the use of an auxiliary yellow Kodak Wratten #12 filter in conjunction with the cobalt blue filter of the biomicroscope.

Slit Lamp Application:

1. All customary light intensities and filter settings (Cobalt Blue) are left in place.
2. The Kodak Wratten Filter #12* (yellow) is secured on the patient side of the slit lamp microscope with the Slit Lamp Filter Kit.

ORTHO-K PROBLEM SOLVING

Low Riding Lens:

A slight low riding lens is the ideal position upon dispensing. The lens will then center with the eye closed. Do not make a change unless the lens is chronically low riding with eyelid closed (as demonstrated by topography) or if unacceptable ghosting persists.

Cause: The cornea becomes flatter from the apex to the periphery. This degree of corneal flattening is different for everyone, with some corneas having a greater or lesser degree of flattening. If the flattening is too great, the alignment curves will be too steep.

Loose Lens:

Cause: Generally caused by a low amount of flattening of the peripheral cornea or from an asymmetrical corneal shape.

High Riding Lens:

Cause: The high riding lens is usually caused either from the lens being too loose or from an asymmetrical corneal shape.

Lateral Riding Lens:

Cause: Generally caused by a very spherical cornea or a cornea with against the rule cylinder.

Vaulting:

Vaulting occurs when excessive bearing is present in the peripheral regions causing reduced central bearing. This will be seen as central pooling or increased fluorescein under the center of the lens.

Cause: The major cause of central vaulting is an alignment curve that is too steep. The more peripheral one goes from the corneal apex, the more difficult it is to predict the rate of corneal flattening. When the alignment curve is too steep, the central portion of the lens will rise up, preventing it from applying compression to the center of the cornea. A fitting curve that is too steep can also cause central vaulting but is much less common.

Under-Responders:

An under-responder is a patient whose myopia does not reduce as anticipated. An example is a -3.00, which was reduced to -1.00 after one month of wear and has not changed for 3 weeks. You will be able to refract the patient, without the lenses in, to 20/20 or better.

Cause: Typically, the under-responder will have vaulting in the center. Some patients will, however, respond slower than others perhaps due to different cell structure of the cornea. You do not want to rush into making a change if the exam figures are correct.

Central Islands:

Central islands are areas of distortion in the visual axis that are observed with corneal topography. This condition differs from the under-responder in that you will not be able to refract the patient, without the lenses in, to 20/20.

Cause: Generally caused by the fitting curve being too steep, causing the Base curve to lift off too much from the central cornea. Another cause is excessive astigmatism. With corneal astigmatism present, there are unequal bearing areas where the fitting curve comes into contact with the cornea.

Central Staining:

This is a complication due to either mechanical irritation or physiological problems.

Cause: One major cause of central staining is a coated lens. Because of the steep Fitting Curve, it is difficult to clean the central posterior surface of the lens. This will create an irritating surface, which in turn causes the staining and a tendency for lens adherence. If the BC is too flat, the reduced mechanical pressure can also

cause irritation. Reduced oxygen availability can also cause central staining, but this is a rare occurrence.

Solution: The first thing is to make sure the posterior surface of the lens is clean. Review the cleaning procedure being used by the subject. Make sure there are no dry spots.

Air Bubbles:

Air bubbles are a common occurrence and typically disappear after wear. Only when staining occurs under a persistent air bubble does the lens need to be changed.

Cause: Air bubbles form when not enough solution is under the fitting curve. Usually the upper lids will compress the lens to the cornea and the bubbles will disappear in the morning. The fitting curve has a steep configuration, which is sometimes difficult to fill with tears. Occasionally, the resultant air bubble can encompass 270 degrees around the FC. Any staining present is due to the air bubble where the cornea is not getting the lubrication or oxygen that it needs.

Solution: If the air bubble is less than 45 degrees in length upon insertion, just monitor the next day to see if any staining occurs. If the air bubble is greater than 45 degrees, have the patient remove the lens and fill the concave surface with solution and have the patient reinsert while looking down. If a large air bubble persists, monitor the next day to see if still present and if staining is present. If staining is present, monitor for three days to see if the bubble and staining recedes. Air bubbles look bad but are usually a self-limiting condition.

Reduced Holding Time:

This is when the unaided visual acuity does not hold an acceptable amount of time.

Cause: Generally caused by a lens that is not centered, with the steep area almost touching the visual axis. When the cornea normally regresses, the visual axis is impacted sooner because there is less distance between the visual axis and the edge of the peripheral steep ring. If some vaulting has occurred, there will be a smaller central visual zone with a corresponding wider concentric steep ring. The cornea can only undergo a limited amount of change. Usually, the more induced change, the faster the cornea will regress. Therefore, if you have reduced -5.00 diopters of myopia, you should not expect the unaided visual acuity to hold all day. As a general rule, the lower the starting amount of myopia, the greater chance of holding all waking hours. The Arise Orthokeratology Lenses are not recommended for reducing myopia greater than -5.00 diopters.

Ghosting at Night:

Night ghosting is a normal observation. This usually recedes with time but may always be present to some extent.

Cause: The main cause of ghosting is when the reduced illumination at night causes the pupil to become larger than the central correction area of the cornea. This might occur even with a well-centered lens. Patients with smaller pupils will not experience this to the extent of patients with very large pupils. Another cause

is a decentered lens. This can also cause ghosting during the day. Central islands can also give the same subjective complaints as ghosting.

Solution: Time is the answer for normal ghosting.

4. Follow-up Care

From the day of dispensing, the following schedule is required for this study.

- 1-Day Follow-up Visit
  - The 1-Day Follow-up Visit will be conducted within 2 hours of awakening and topography will be performed within 30 minutes of lens removal.
  - Ensure that the subject arrives for their appointment wearing the study lenses.
- 1-Week Follow-up Visit
- 1-Month Follow-up Visit
- 2-Month Follow-up Visit
- 3-Month Follow-up Visit

5. Maintenance Lenses

Daily disposable soft contact lenses (Bausch + Lomb Biotrue ONEday (nesofilcon A) Contact Lenses, known as "maintenance lenses") will be dispensed at the 1-Day Follow-up Visit as needed to provide supplemental visual correction during the day as needed for the orthokeratology lens adaptation period.

Although the majority of subjects may not require maintenance lenses, Bausch + Lomb will provide each investigative site a supply of Bausch + Lomb Biotrue ONEday (nesofilcon A) Contact Lenses in representative powers of -0.50, -1.00, -1.50, -2.00, -2.50, and -3.00D for use as needed during the orthokeratology lens adaptation phase.

6. To Refine Lens Fit

Note: Each eye can only be refit one time, either at the 1-Day Follow-up Visit or the 1-Week Follow-up Visit.

If the lens fit is unacceptable, order two lenses if refitting one eye (or two pairs of lenses if re-fitting both eyes) by following the instructions for lens refitting in the Lens Order Instructions Form.

The following information will be required for lens refitting:

- Subject ID (6 digit):
- Investigator Name:
- Account ID: 0ARISE
- Category: Refitting
- Topography map file for OD and/or OS, taken after overnight wear of previously dispensed study lenses

- File should be sent pre-populated with:
  - Subject ID (first name = type the word “SUBJECT”, last name = 6-digit subject ID)
  - Subject date of birth
  - Subject spectacle refraction.

- Reason for refitting (indicate either OD or OS, if only applies to one):
  - Lens is Vaulting
  - Lens is riding High
  - Lens is riding Low
  - Lens has Lateral Displacement
  - Undercorrection or overcorrection of treatment with the following refraction data (without lens):
- OD/OS sphere, cylinder, axis, visual acuity
  - Other reason(s) – please specify, e.g., lens discomfort

7. Patient Education

During the initial week(s) of treatment, some subjects may experience changes in vision that may require temporary alternate corrective eyewear. Daily disposable soft contact lenses (Bausch + Lomb Biotrue ONEday (nesofilcon A) Contact Lenses, known as “maintenance lenses”) will be dispensed to provide supplemental visual correction during the day as needed for the orthokeratology lens adaptation period. These lenses are to be worn on a daily disposable basis and replaced daily as needed during the initial week(s) of treatment. It is important to educate the subject of the occurrence of this potential change in vision and instruct them on the proper wear and care of maintenance lenses used during this period.

WEARING SCHEDULE

Subjects will be required to wear their study lenses for a minimum of eight (8) hours on an overnight wear basis (and worn every night).

Note: To maintain the Orthokeratology effect of myopia reduction, overnight lens wear must be continued on a prescribed schedule. Failure to do so can affect daily activities (e.g., night driving), visual fluctuations and changes in intended correction.

HANDLING OF LENSES

When lenses are dispensed, the subject should be provided with appropriate and adequate instructions and warnings for lens handling. The Investigator should recommend appropriate and adequate procedures for each individual subject in accordance with the lens-wearing schedule.

PATIENT LENS CARE DIRECTIONS

The study doctor or staff will review the instructions for lens care with each subject.

To ensure proper disinfecting, all steps listed below must be followed:

1. Wash your hands with mild soap. (Caution - pump soaps may contain oil-based suspension agents.)
2. Place lenses in empty lens case and fill to top ridges with fresh Boston SIMPLUS Multi-Action Solution. Soak lenses for at least 4 hours before wearing.
3. Wash hands with mild soap before cleaning (rubbing) lenses. After soaking, remove lenses from lens case and rub both sides of the lenses carefully with 4 drops of Boston SIMPLUS Multi-Action Solution in the palm of your hand for 20 seconds.
4. Rinse for approximately 5 seconds with a steady stream of Boston SIMPLUS Multi-Action Solution to eliminate loosened surface deposits and insert lenses.
5. Discard solution from lens case after each use. For lens rewetting and lubrication, use Boston® Rewetting Drops.

If the study doctor recommends a different lens care regimen, appropriate instructions will be provided and reviewed with the subject.

Preparing the Lens for Wearing

It is essential that you learn and use good hygienic methods in the care and handling of your contact lenses. Cleanliness is the first and most important aspect of proper contact lens care. Hands should be clean and free of any foreign substances when you handle your lenses.

The procedures are:

- Always wash, rinse and dry hands thoroughly before handling your contact lenses.
- Avoid soaps containing cold cream, lotions or oily cosmetics prior to handling your lenses. These substances can adhere to the surface of the lens and be difficult to remove.
- Handle lenses with the fingertips, avoiding use of fingernails that can scratch or chip lenses.
- Always start with the same lens first to avoid mix-ups.
- Remove the lens from its storage case and examine it. Be sure it is clean, moist and free of any nicks or cracks.

Placing the Lens on the Eye

- Prepare the lens for placement by following Step 3 (rubbing) and Step 4 (rinsing) in the Patient Lens Care Directions above.
- Place lens on the top of index finger of dominant hand.
- With other hand, hold down lower lid and lift upper lid up. Gently place lens on the center of your eye. It is not necessary to press the lens on the eye.
- Gently release lids and blink. The lens should center automatically.
- Use the same technique to insert the other lens.

There are other methods of lens placement. If this method proves difficult for you, discuss alternatives with your study doctor.

Note: if vision is blurred after insertion, check for the following conditions:

- Lens is not centered (refer to section below on "Centering a Lens")
- If lens is centered, remove and check for any of the following:
  - Cosmetics or oil on the lens. Clean, rinse, disinfect and replace on eye.
  - The lens may be on the wrong eye.

If you find your vision is still blurred after checking the possibilities as listed above, remove both lenses and consult your study doctor.

Centering the Lens

Very rarely, a lens that is on the cornea will displace onto the white portion (sclera) of the eye during lens wear. This can also occur during insertion or removal of your lens if proper technique is not utilized. To center a lens, follow one of the procedures below or one recommended by your study doctor.

- Close your eyelids and gently massage the lens into place through the closed lids.

OR

- Gently push the off-centered lens onto the cornea while the eye is open using finger pressure on the upper or lower lid next to the edge of the lens.

Removing the Lens

Before attempting to remove your lens, it is very important that you verify the lens is moving. The lens is designed to be worn overnight and may be slightly stuck in place on the eye in the morning. Apply two to three drops of Boston Rewetting Drops to your eyes in the morning and wait until the lens begins to move freely with the blink before you attempt to remove it.

It is recommended that you have the following items available when you are ready to remove your lenses:

- A lens storage case
- Solution for cleaning and storing your lenses
- A clean towel

Always remove the same lens first to avoid confusion. Wash, rinse and dry your hands thoroughly.

There are two suggested methods of lens removal:

TWO FINGER METHOD

1. Place a towel on the counter to catch the lens.
2. Place the tip of the forefinger of one hand on the middle of the upper lid margin and the forefinger of the other hand on the middle of the lower lid margin.

3. Press the lid margin inward and then together. The lens should be wedged out of your eye onto your hand or the towel.
4. The lens may come out but remain on your eyelid or be de-centered onto the white part of your eye. If the latter occurs, re-center the lens onto your cornea before repeating the removal process.

BLINK METHOD

Seat yourself at a table covered with a clean towel and lean over until you are looking down at the surface.

1. Place your index finger at the outer junction of your upper and lower lids; stretch the skin outward and slightly upward. Do not allow your lid to slide over the lens.
2. Blink briskly. The lens will be pinched by the pressure of your eyelids and pop out onto the clean surface of the towel, or you may catch the lens in the palm of your hand.

Note: If these methods for removing your lenses are difficult for you, your study doctor can provide you with alternatives.

CARE FOR A STICKING (NON-MOVING) LENS

If a lens sticks (stops moving/cannot be removed), the subject should be instructed to apply one to three drops of Boston Rewetting Drops directly to the eye and wait until the lens begins to move freely on the eye before removing it. If non-movement continues after 5 minutes, re-instill re-wetting drops and compress the lid margin above or below the lens to release the suction. If non-movement persists do not attempt to remove the lens but immediately contact the study doctor.

HOW SUPPLIED

Primary and backup lenses will be provided individually in a polycarbonate vial containing Boston SIMPLUS Multi-Action Solution.

The label will include the following information:

- Lens power
- Base curve
- Lens diameter
- CT (Center Thickness)
- Eye (R or L)
- Subject identifier (101 004: investigative site 101 and subject 4)
- Lens color (Right lenses are Green, Left lenses are Blue)
- Expiration date (denotes 30 days after lens was packaged for shipment)
- Lot number
- Manufacturer’s name and location
- Investigational Device Caution statement