1.0 TITLE PAGE

A Study to Evaluate the Safety and Effectiveness of a
Silicone Hydrogel Custom Contact Lens

PROTOCOL

STUDY #886

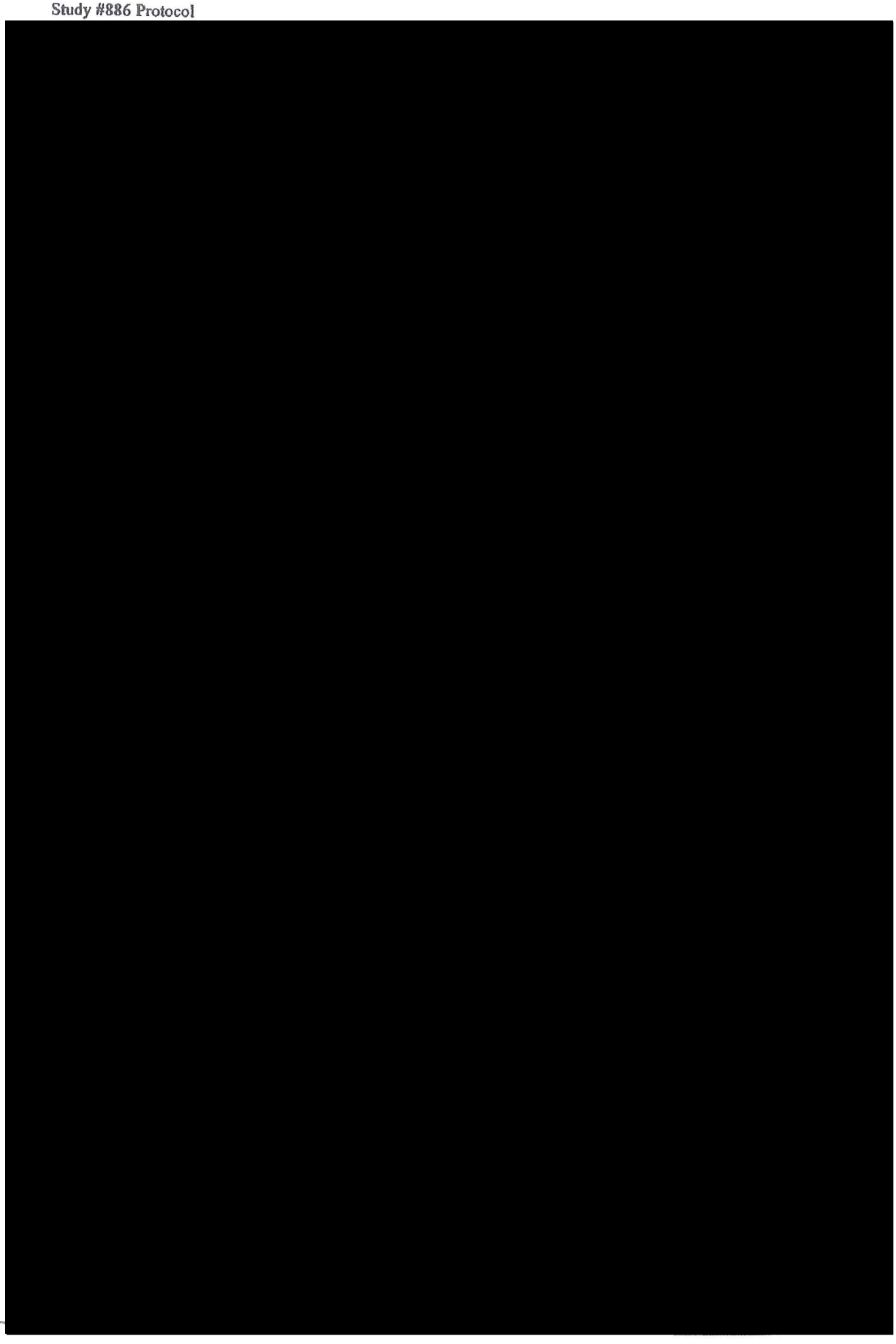
Sponsor:

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. The protocol was developed with consideration of the provisions in: International Organization for Standardization (ISO) 14155-1:2011 Clinical investigation of medical devices for human subjects – Part 1: General requirements; 14155-2:2011 Part 2: Clinical investigation of medical devices for human subjects – Part 2: Clinical investigational plan; ISO 11980:2012 Ophthalmic Optics – Contact lenses and contact lens care products – Guidance for clinical investigations; International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) and applicable local regulations. The Sponsor intends to register this clinical trial with the public database https://ClinicalTrials.gov.

Revision Chronology:

Original	1.0	November 2, 2018
Revision	2.0	December 12, 2018
Revision	3.0	January 25, 2019



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3.0 INVESTIGATOR STATEMENT OF APPROVAL

A Study to Evaluate the Safety and Effectiveness of a
Silicone Hydrogel Custom Contact Lens

PROTOCOL

STUDY #886

I have read the attached document, 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 Code of Federal Regulations (CFR) Parts 11, 50, 54, 56, and 812. The protocol was developed with consideration of the provisions in: International Organization for Standardization (ISO) 14155-1:2011 Clinical investigation of medical devices for human subjects – Part 1: General requirements; 14155-2:2011 Part 2: Clinical investigation of medical devices for human subjects – Part 2: Clinical investigational plan; ISO 11980:2012 Ophthalmic Optics – Contact lenses and contact lens care products – Guidance for clinical investigations, International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) 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 will obtain written informed consent from each study subject prior to performing any study specific procedures.

I understand that my signature on a case report form 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 IRB/ECs, direct access to my medical records for study subjects.

_____

Principal Investigator, Printed Name

_____ _____

Principal Investigator, Signature Date

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

4.0 PERSONNEL AND FACILITIES RESPONSIBLE FOR CONDUCTING STUDY

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

Sponsor	**CRO**
Bausch & Lomb Incorporated 1400 North Goodman Street Rochester, NY 14609	Promedica International 3100 Bristol Street, Suite 250 Costa Mesa, CA 92626
[redacted]	[redacted]

5.0 TABLE OF CONTENTS

TABLES

APPENDICES

6.0 LIST OF ABBREVIATIONS

Abbreviation	Term
ADE	adverse device effect
AE	adverse event
ANOVA	analysis of variance
BSCVA	best spectacle-corrected visual acuity
CFR	Code of Federal Regulations
eCRF	electronic Case Report Form
D	diopter
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ID	identification
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	intent-to-treat
logMAR	logarithm of the minimum angle of resolution
MCMC	Markov chain Monte Carlo
MedDRA	Medical Dictionary for Regulatory Activities
MPS	multi-purpose solution
OD	Doctor of Optometry
PP	per-protocol
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	standard deviation
UADE	unanticipated adverse device effect
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 (eg, units of measure).

7.0 INTRODUCTION

Bausch + Lomb is evaluating the safety, efficacy, and product performance of an investigational silicone hydrogel contact lens. Silicone hydrogel contact lenses offer the advantage of high oxygen transmissibility compared to non-silicone hydrogel soft contact lenses, promoting the level of health of the eye.

8.0 OBJECTIVE

The objective of this study is to evaluate the safety and efficacy of a custom silicone hydrogel contact lens when worn on a daily basis by currently adapted soft contact lens wearers.

9.0 STUDY DESIGN

9.1 Description of Study Design

This is a multicenter, randomized 2:1, parallel, bilateral, double-masked study at 7 to 10 investigative sites in the United States (US) comparing the Bausch + Lomb custom samfilcon B (test) lens with the hioxifilcon D, 54% water, Alden Optical® HP Sphere (control) lens.

Approximately 84 subjects will be enrolled in this 3-month study.

At the Screening Visit, approximately two-thirds of the eligible subjects will be randomized to receive the test lens (custom samfilcon B lenses) and the other one-third eligible subjects will be randomized to receive the control lens (Alden Optical HP Sphere). Both groups will wear their assigned lenses on a daily wear basis throughout the study with visits planned for Screening (Visit 1), Dispensing (Visit 2), 1 Week (Visit 3), 1 Month (Visit 4), 2 Months (Visit 5), 3 Months (Visit 6) and/or a final Exit Visit.

Subjects will be randomized sequentially by the randomization system as they are enrolled. Subjects will be dispensed product according to their assigned treatment and will remain masked during the entire study period.

Subjects will be provided with test or control lenses as part of the dispensing package along with instructions for the use and care of the lenses.

Subjects will be provided with ReNu MultiPlus® Lubricating and Rewetting Drops for use as needed during the study.

Subjects will store their worn study lenses in a lens case filled with Bausch + Lomb Biotrue® multi-purpose solution (MPS).

9.2 Selection of Study Population

Written informed consent, enrollment in the study, or dispensing of study products cannot begin until the Investigator has received Institutional Review Board (IRB) 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 they participate in the study or not. Bausch + Lomb will provide a Screening Log on which to enter information for each

subject who signs an Informed Consent Form (ICF). All screened subjects must be entered onto the Screening Log, in the order in which they were consented, where they will be assigned a sequential subject identification (ID) number. Once a potential subject is consented and their initials are entered onto the Screening Log, the Investigator should proceed with Screening procedures.

Potential subjects are deemed either "Screen Pass" or "Screen Fail." "Screen Fail" subjects are subjects who have not met the study inclusion criteria or have met the exclusion criteria and cannot be randomized into the study.

"Screen Pass" subjects have met all of the study inclusion criteria and have not met any of the exclusion criteria. Only "Screen Pass" subjects can be randomized to receive the study lenses and can be assigned a subject identification (ID) number from the randomization system.

Once a subject is randomized, 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 9.2.4 for subjects determined to be lost to follow-up.

9.2.1 Eligibility

9.2.1.1 Inclusion Criteria

1. Subjects must be 18 to 40 years old on the date the ICF is signed and have the capacity to provide voluntary informed consent.
2. Subjects must be able to read, understand, and provide written informed consent on the IRB-approved ICF and provide authorization as appropriate for local privacy regulations.
3. Subjects must have clear central corneas and be free of any anterior segment disorders in each eye.
4. Subjects must be myopic, require contact lens correction from -1.00 diopter (D) to -6.00 D, and wear contact lenses in each eye.
5. Subjects must be correctable through spherocylindrical refraction to 47 letters (0.0 logarithm of the minimum angle of resolution [logMAR]) or better (distance, high-contrast) in each eye.
6. Subjects must be able and willing to comply with all treatment and follow-up/study procedures.
7. Subjects must be adapted soft contact lens wearers and agree to wear their study lenses on a daily wear basis for approximately 3 months.

9.2.1.2 Exclusion Criteria

1. Subjects participating in any drug or device clinical investigation within 2 weeks prior to entry into this study and/or during the period of study participation.
2. Subjects who are women of childbearing potential (those who are not surgically sterilized or postmenopausal) are excluded from participation in the investigation if they meet any one of the following conditions:

- She is currently pregnant.
- She plans to become pregnant during the study.
- She is breastfeeding.

3. Subjects who have worn gas permeable lenses in either eye within the last 30 days or who have worn polymethylmethacrylate lenses in either eye within the last 3 months.
4. Subjects with any systemic disease currently affecting ocular health or which in the Investigator's opinion may have an effect on ocular health in either eye during the course of the study.
5. Subjects using any systemic or topical medications that will, in the Investigator's opinion, affect ocular physiology or lens performance.
6. Subjects with an active ocular disease in either eye or who are using any ocular medication.
7. Subjects who currently wear monovision, multifocal, or toric contact lenses in either eye.
8. Subjects with an ocular astigmatism >1.00 D in either eye.
9. Subjects with anisometropia (spherical equivalent) >2.00 D.
10. Subjects with any Grade ≥2 finding in either eye during the slit lamp examination (refer to APPENDIX B for methods of clinical evaluation). Subjects with corneal infiltrates in either eye, of ANY GRADE, are not eligible to participate in this study.
11. Subjects with any "Present" finding during the slit lamp examination in either eye (refer to APPENDIX B for methods of clinical evaluation) that, in the Investigator's judgment, interferes with contact lens wear.
12. Subjects with any scar or neovascularization within the central 6 mm of the cornea in either eye. Subjects with minor peripheral corneal scarring (that does not extend into the central area), that in the Investigator's judgment, does not interfere with contact lens wear, are eligible to participate in this study.
13. Subjects who are aphakic in either eye.
14. Subjects who are amblyopic in either eye.
15. Subjects who have had any corneal surgery (eg, refractive surgery) in either eye.
16. Subjects who are allergic to any component in the study care products.
17. Subjects who meet any of the following criteria:
    - The subject is an employee of the investigative site.
    - The subject, or a member of the subject's household, is an ophthalmologist, an optometrist, an optician, or an ophthalmic assistant/technician.
    - The subject, or a member of the subject's household, is an employee of a manufacturer of contact lenses or contact lens care products (eg, Alcon, Bausch + Lomb, Ciba Vision, CooperVision, Johnson & Johnson, etc.)
    - The subject, or a member of the subject's household, is an employee of a market research firm.

If a subject meets all the inclusion criteria and does not exhibit any of the exclusion criteria, the subject is eligible for entry into the study. Ineligible subjects MUST NOT be enrolled in this study and are considered a "Screen Fail". Any subject enrolled in the study who later is found to have not met the eligibility criteria at entry will be discontinued.

9.2.2 Subject Completion

The subject has completed the study when the 3-Month Visit is concluded. Subjects who require further follow-up will be followed according to the Adverse Event or Unscheduled Visit Section.

9.2.3 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:

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

A subject MUST be discontinued prior to the final study visit (3-Month Visit [Visit 6]) for any of the following reasons:

- Voluntary withdrawal
- Death
- Investigator decision that it is not in the best medical interest of the subject to continue participation in the investigation
- Ineligible after randomization – a subject who was enrolled but was later found to have not met the eligibility criteria in the protocol
- Inability to maintain recommended wearing schedule
- Continued failure to follow subject instructions
- Misses more than one consecutive follow-up visit
- Lack of motivation
- Lost to follow-up (refer to Section 9.2.4)
- Instillation of non-medically indicated solution not specified in the protocol
- Other eye is discontinued
- Becomes pregnant during the study

Prior to discontinuing a subject, every effort should be made to contact the subject, schedule an Exit Visit, obtain as much follow-up data as possible, and retrieve all study materials. Adverse events will be followed as described in Section 13.0. Subject

discontinuations will be documented clearly on the source document and applicable eCRF. The Investigator should indicate the PRIMARY (one) reason that the subject was discontinued for each eye. Subjects who are discontinued from the study following randomization will not be replaced.

Exit Visit assessments should be completed for discontinued subjects.

9.2.4 Lost to Follow-Up

Subjects who do not return for scheduled follow-up visits, as defined by the visit window and cannot be contacted, are to be considered lost to follow-up. All attempts to contact the subject should be documented and kept with the subject's source documentation, and the applicable eCRFs will be completed. The exit date will be the date of the subject's last visit to the clinic as a study subject.

9.3 Investigators

The study will be conducted at approximately 7-10 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. Principal Investigators and Sub-Investigators will be identified on the Device Investigator Agreement Form.

Each Investigator will attempt to enroll approximately 8-12 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.

9.4 Study Duration

Subjects will be followed for 3 months after dispensing (unless discontinued or lost to follow-up) and must adhere to the following schedule:

Table 1. Schedule of Visits

Visit Number	Visit Name	Target	Acceptable Visit Range
1	Screening Visit	None	Day -30 to Day-7
2	Dispensing Visit	Day 1	Not applicable
3	1-Week Visit	Day 8	Day 5 – 9
4	1-Month Visit	Day 31	Day 27 – 35
5	2-Month Visit	Day 61	Day 54 – 68
6	3-Month Visit	Day 92	Day 91* – 101

CRITICAL NOTE: The 3-Month Visit must occur no earlier than Day 91.

The visit range is based on the date test lenses are initially dispensed (Dispensing Visit). A visit scheduling table will be provided in the initial study shipment to aid the Investigator in scheduling follow-up visits.

9.5 Treatments

Approximately 56 subjects (112 eyes) will be randomized to receive Bausch + Lomb investigational custom samfilcon B lenses and approximately 28 subjects (56 eyes) will be randomized to receive Alden Optical HP Sphere contact lenses. Subjects will be assigned randomization numbers, according to the randomization system.

Subjects will wear their lenses on a daily wear basis for 3 months.

NOTE: Use of other contact lenses is not allowed during the study.

10.0 STUDY MATERIALS

Bausch + Lomb will provide all study materials at no charge to the Investigator. All study materials will be provided to the site for each subject prior to the start of the study. Refer to Section 10.8 for ordering replacement test or control product in the case of loss or damage.

10.1 Description of Test Article

The Bausch + Lomb investigational custom samfilcon B contact lens (test) is an investigational silicone hydrogel contact lens which will be provided in the following parameters:

- Sphere Power: -1.00 to -6.00 D in steps of 0.25 D
- Diameter: 14.2 mm
- Base Curve: 8.6 mm
- Material: samfilcon B, 41% water

10.2 Description of Comparator Product

The Alden Optical HP Sphere contact lens (control) is a hydrogel contact lens which will be provided in the following parameters:

- Sphere Power: -1.00 to -6.00 D in steps of 0.25 D
- Diameter: 14.2 mm Visibility tint
- Base Curve: 8.3 mm
- Material: hioxifilcon D, 54% water

10.3 Instructions for Use and Administration

New study lenses will be dispensed at the Dispensing Visit. Lenses will be worn on a daily basis for 3 months. Subjects must wear their study lenses to all follow-up visits.

10.3.1 Storage Requirements

All test and control lenses provided by the Sponsor must be stored in a secure location accessible only to study personnel and maintained at room temperature.

10.3.2 Subject Instructions

a. All subjects must be given Subject Instructions (see APPENDIX D) for use of the study lenses. 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.

b. All subjects must refer to the Bausch + Lomb Biotrue Multi-Purpose solution package insert for care instructions, precautions, and warnings related to contact lens wear.

c. The Investigator or other designee must review instructions and warnings for lens wear, lens care, handling, cleaning, and disinfecting with the subject.

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

10.3.3 Fitting Guide

The Investigator should refer to the Fitting Guide (see APPENDIX E) for fitting the test and control lenses.

10.4 Other Materials

10.4.1 Care System

All subjects will be dispensed the following care products for use during the study:

- Biotrue Multi-Purpose solution for daily rinsing, cleaning, disinfecting, and storing their lenses in lens cases. All commercially available Biotrue bottles include a green lens case.
- ReNu MultiPlus Lubricating and Rewetting Drops for use as needed during the study

Investigators will be provided Biotrue Multi-Purpose solution and lens cases for return of study lenses to the Sponsor at the end of the study.

NOTE: Use of other contact lens care products is not allowed during the study.

10.5 Packaging and Labeling

The test lenses (custom samifilcon B) used in this study will be packaged in glass vials with investigational labels. The labels will contain the following information:

- Lens power
- Base curve
- Lens diameter
- Lot number
- Expiration date
- Manufacturer's name and location
- Caution statement

The control lenses (Alden Optical HP Sphere) used in this study will be provided in the glass vials. The labels will contain the following information:

- Lens power
- Base curve
- Lens diameter
- Lot number
- Expiration date
- Manufacturer’s name and location

10.6 Accountability

The unmasked designee will be responsible for keeping current and accurate records of the amount of study test lenses received and dispensed, and its disposition. The study lenses must be stored under the appropriate conditions in a secure area and are to be dispensed only to subjects enrolled in the study, in accordance with the conditions specified in this protocol. During the course of the study, the unmasked designee must maintain an inventory of all lenses dispensed to or returned by the subject, including subject identifiers. A Product Accountability Log will be provided to the sites to maintain records of the study lenses assigned to each enrolled subject.

At time points throughout the study and/or upon completion of the study, the Sponsor/Sponsor's representative will review and verify the Investigator's Product Accountability Logs. Following verification, and as directed by the Sponsor, all worn and unworn lenses must be returned to the Clinical Trial Materials Supply Management at the address listed on the Personnel and Facilities page.

10.7 Masking/Unmasking

This study is double-masked; therefore, the Investigator/site staff, subjects, and Bausch + Lomb personnel or designee(s) involved in the collection of study data will be masked to the study lenses. Each site must have an unmasked designee that will be responsible for dispensing and accountability. This designee shall not participate in study assessments that may cause bias to the study data. Study Monitors will become unmasked during site visits when they perform product accountability.

Lens markings on both products are not product-specific. Markings and lens tints are similar between products and are indistinguishable.

Randomization will be produced prior to study enrollment by an unmasked statistician not otherwise involved in the trial. An unmasked designee will be responsible for dispensing the test and control lenses according to the randomization system. Investigators will not have access to the randomization system information and lenses will be dispensed directly to the subject, thereby maintaining Investigator masking. In an effort to ensure that both the Investigator and subject remain masked, the unmasked designee MUST dispense the study lenses and MUST remove lenses from their glass vials out of the Investigator’s and subject’s sight immediately prior to dispensing. Subjects will not be given additional replacement lenses to take home, thereby

maintaining subject masking. A reserve pair will remain at the site if a replacement is needed.

The Investigator should contact the Medical Monitor prior to unmasking of study lenses. In an emergency situation, however, where knowledge of the study lenses is critical to subject safety, the code may be broken by requesting the allocated treatment for that subject from the unmasked designee.

The Investigator must notify the Sponsor as soon as possible after unmasking. In addition, the Investigator must record the date, time, and reason for unmasking the study treatment in the source documentation.

10.8 Replacement Lenses

Replacements are permitted for damage, satisfaction, and vision at the discretion of the Principal Investigator. All lens replacements need to be tracked for reason and date and must also be rechecked for fit.

A reserve pair of study lenses for each dispensed subject should be retained in-office at all times in case a non-scheduled lens replacement is required. If the reserve is used, an immediate replacement order is required. Any additional/replacement of test or control products (in the case of loss or damage) must be ordered through Clinical Trial Materials using the Replacement Lens Order Form for Study #886. Do not order through Bausch + Lomb Customer Service. The form can be scanned to [redacted]

10.9 Risk Assessment

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.

10.10 Methods of Assigning Subjects to Treatment Groups

10.10.1 Treatment Allocation

Randomized treatment assignments will be allocated to eligible subjects sequentially using the next available assignment in the randomization schedule.

10.10.2 Randomization Method

Randomization will be provided to the sites via the randomization system. When it is time to randomize an eligible subject, the unmasked designee will use the randomization system to obtain the subject's treatment assignment.

11.0 EFFECTIVENESS AND SAFETY VARIABLES

11.1 Primary Effectiveness Variable

The primary effectiveness endpoint will be statistical non-inferiority with respect to mean distance high-contrast logMAR lens VA for each eye between the test and control lenses.

11.2 Secondary Effectiveness Variables

Not applicable.

11.3 Safety Variables

The primary safety endpoint will be statistical non-inferiority with respect to the proportion of eyes with any slit lamp findings Grade >2 at any follow-up visit between the test and control lenses.

12.0 STUDY METHODS

12.1 Study Visits

Refer to APPENDIX A for a schedule of visits and parameters and APPENDIX B for 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. It is strongly preferred that the signed original document be retained in the subject's records, while a copy be provided to the subject. In addition, the applicable privacy regulation requirements must be met.

12.1.1 Screening Visit (Visit 1)

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

A Screening Log will be provided by the Sponsor to track all consented subjects that 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 form to verify that all the subjects who interviewed for the study have provided informed consent and Health Insurance Portability Accountability Act (HIPAA) authorization and any other applicable state requirements. The Investigator will send a copy of the Screening Log to the Sponsor. The Investigator will retain the original document for his/her records.

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

Screening will proceed as follows:

a. Enter the subject information on the next available line of the Screening Log.

b. Collect subject's medical history

c. Collect the following lens history information from the subject:

- 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

d. Collect demographic and baseline information and perform the following baseline assessments (without lenses) and record in the subject's source document:
   - Spherocylindrical refraction
   - Distance best spectacle-corrected visual acuity (BSCVA)
   - Keratometry

e. Perform a slit lamp examination (remove the lenses if the subject wore lenses to the visit). Record and diagram the results and findings in the subject's source document and appropriate eCRF:
   - Any ungraded finding marked as "Present"
   - Any corneal scars
   - Any neovascularization within the central 6 mm of the cornea
   - Any corneal staining
   - Any corneal infiltrate (record details on the Corneal Infiltrates Evaluation Form [APPENDIX C])
   - any other graded slit lamp findings Grade 2 or greater

f. Indicate on the Screening Log whether the subject is a "Screen Pass" or "Screen Fail."
   - "Screen Fail" subjects are ineligible and cannot be randomized in the study. The reason for screen failure must be documented on the Screening Log and in the subject record and must be maintained with a copy of their ICF.
   - Only "Screen Pass" subjects should be randomized in the study.

g. If the subject is eligible, collect Symptoms/Complaints and Subjective Assessment information from the subject regarding their habitual lenses.

h. Assign subject numbers based on the randomization system. The unmasked designee will determine the subject's randomized lens by using the randomization system and record on the Screening Log.

i. Assess BSCVA to determine subject prescription. The prescription determined from this fitting assessment will be used to dispense/order test or control lenses according to the lens to which the subject is randomized.

j. Record the lens parameters to be dispensed/ordered based on the diagnostic fitting.

k. For each subject, use the lens order form to order the appropriate study contact lenses (test or control). Schedule the subject for their Dispensing Visit within 30 days.

l. Collect/assess all AEs, including serious or significant non-serious AEs, since consent was signed.

m. For female subjects, re-emphasize the exclusion criterion stating that if the subject is of childbearing potential and is pregnant and or breast feeding, she is ineligible to be a part of the study.

12.1.2 Dispensing Visit (Visit 2)

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

b. Perform a slit lamp examination (remove the lenses if the subject wore lenses to the visit). Record all slit lamp findings and, at a minimum, sketch the following in the subject's source document:

- any ungraded finding marked as "PRESENT"
- any new corneal scars
- any neovascularization within the central 6 mm of the cornea
- any corneal staining
- any corneal infiltrate (record details on the Corneal Infiltrates Evaluation Form [APPENDIX C])
- any other graded slit lamp findings Grade 2 or greater

c. Dispense study lens, record sphere power, record in Product Accountability Log. In an effort to ensure that both the Investigator and subject remain masked, the unmasked designee MUST dispense the study lenses and MUST remove lenses from their glass vials out of the Investigator's and subject's sight immediately prior to dispensing.

d. Subject inserts pair of the study lenses in his/her eyes.

NOTE: Study lenses should be allowed to equilibrate a minimum of 3 minutes on the eye.

e. After a minimum of 3 minutes, perform the following assessments:

- Collect Symptoms/Complaints and Subjective Assessment information
- Distance high-contrast logMAR lens VA
- Over-refraction and distance VA
- Lens wettability, centration, movement
- Lens deposits

For each eye, compare the distance high-contrast logMAR lens VA to the distance BSCVA obtained at the Screening visit. If the VA has decreased by ≥5 letters (0.1 logMAR), explain.

f. Dispense lens case. Instruct the subject to store their study lenses in the lens case filled with Bausch + Lomb Biotrue MPS according to the Subject Instructions (APPENDIX D).

g. If the subject is discontinued or exited at this visit, complete the Exit Visit eCRF.

h. For female subjects, re-emphasize the exclusion criterion stating that if the subject is of childbearing potential and is pregnant and or breast feeding, she is ineligible to be a part of the study.

12.1.3 1-Week, 1-Month, 2-Month, and 3-Month Visits (Visits 3, 4, 5, and 6)

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

NOTE: If all scheduled visits are performed on time and the subject completed the 3-Month Visit, the Exit Visit will be done at the same time.

NOTE: Study lenses should not be dispensed at this visit unless replacement lenses are required. Lenses worn to this visit should be returned to the subject for use until the next scheduled visit.

NOTE: If the subject does not come to a visit wearing lenses due to requiring a replacement and is not experiencing any problems, it is preferred to do an Unscheduled Visit for Product Dispensing Only and reschedule the current visit within the visit window. Refer to Unscheduled Visit, Section 12.1.4.

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

b. Collect the following lens information from the subject:

- 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

c. Collect Symptoms/Complaints and Subjective Assessment information from the subject regarding their study lenses.

d. Evaluate the lenses (while on eye), and record the following assessments:

- Distance high-contrast logMAR lens VA
- Over-refraction and distance VA
- Lens wettability, centration, movement
- Lens deposits

For each eye, compare:

- The distance high-contrast logMAR lens VA at this visit to the distance high-contrast logMAR lens VA obtained at the Dispensing Visit.
- The distance high-contrast logMAR lens VA at this visit to the distance BSCVA obtained at the Screening Visit
- If the VA has decreased by ≥10 letters (0.2 logMAR), explain.

e. Perform a slit lamp examination (remove the lenses if the subject wore lenses to the visit) and note the following:

- Any ungraded finding marked as “Present”
- Any new corneal scars
- Any neovascularization within the central 6 mm of the cornea
- Any corneal staining

- Any corneal infiltrate (record details on the Corneal Infiltrates Evaluation Form – APPENDIX C)
- Any other graded slit lamp findings Grade >2

f. For female subjects, re-emphasize the exclusion criterion stating that if the subject is of childbearing potential and is pregnant and or breast feeding, she is ineligible to be a part of the study.

12.1.4 Exit Visit

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

NOTE: If a subject requires further follow-up on an AE/SAE upon discontinuation or completion of 3-Month Visit, the Investigator must schedule Unscheduled Visits to follow up as necessary. At these unscheduled follow-up visits, the subject should remove contact lenses s/he may be wearing. At a minimum, a slit lamp examination, keratometry, spherocylindrical refraction, and distance BSCVA should be completed. 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 follow-up visits.

a. Indicate status of the subject on the Subject Exit Form. If the status is "Discontinued" or "Non-dispensed," indicate the PRIMARY exit reason for each eye on the Subject Exit Form.

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

c. Collect study lens from subject and record in Product Accountability Log.

d. For all subjects, complete an exit ocular examination without lenses on the eyes. Collect the following assessments at the 3-Month Visit or at the Exit Visit:

- Spherocylindrical refraction
- Distance BSCVA
- Keratometry

e. For each eye, compare the final visit distance BSCVA to the distance BSCVA obtained at the Screening Visit. If the VA has decreased by ≥10 letters (0.2 logMAR), explain.

f. For each eye, compare the final visit keratometry readings to the Screening Visit keratometry readings. If there is a change of ≥1.00 D, explain.

g. The Subject Exit eCRF should be completed.

12.1.5 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 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.

12.1.5.1 Product Dispensing Only (Part of the Unscheduled Visit - used only if lens replacement is needed)

If a subject is only seen for an unscheduled lens replacement, a complete exam is not required as long as the subject is not experiencing any problems. In an effort to ensure the Investigator remains masked, an unmasked designee MUST dispense the lens(es) to the subject. Record lenses dispensed in the Product Accountability Log.

12.1.5.1.1. If study lenses are dispensed, collect the following information in the source document and transcribe to the Product Dispensing Only eCRF Form:

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

12.1.5.2 If any assessment is performed, then an Unscheduled Visit Form must be completed instead of a Product Dispensing Only Form.

NOTE: All worn study lenses are to be returned to the Sponsor at the end of the study as directed with the materials provided. Worn lenses will be dry stacked in lens cases and returned to Bausch and Lomb. All contact lenses must be accompanied by a CTM Product Accountability Log.

If a subject is experiencing problems, complete the following:

a. Indicate the reason for the Unscheduled Visit.

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

c. Collect Symptoms/Complaints and Subjective Assessment information.

d. Evaluate the lenses (while on eye) and record the following assessments in the source documentation and eCRF:

   - Distance high-contrast logMAR lens VA
   - Over-refraction and distance VA
   - Lens wettability, centration and movement
   - Lens deposits

   For each eye, compare the distance high-contrast logMAR lens VA to the distance BSCVA obtained at the Screening Visit. If the VA has decreased by ≥10 letters (0.2 logMAR), record in the subject's source document and explain.

e. Perform the following assessments without lenses and record in the subject's source document: spherocylindrical refraction, distance BSCVA, and keratometry.

f. Perform a slit lamp examination (without lenses). Record all slit lamp findings and, at a minimum, sketch the following in the subject's source document:

   - Any ungraded finding marked as "PRESENT"
   - Any new corneal scars
   - Any neovascularization within the central 6 mm of the cornea
   - Any corneal staining
   - Any corneal infiltrate (record details on the Corneal Infiltrates Evaluation Form [APPENDIX C])
   - Any other graded slit lamp findings Grade ≥2

g. For female subjects, re-emphasize the exclusion criterion stating that if the subject is of childbearing potential and is pregnant and or breast feeding, she is ineligible to be a part of the study.

h. If the subject is discontinued or exited at this visit, the Exit Visit Form should also be completed.

12.1.6 Missed Visits

If a subject misses any scheduled follow-up visit and cannot be seen prior to the start of the visit range for the next scheduled follow-up visit, the visit is considered missed. Indicate a missed visit on the eCRF for that scheduled visit.

12.2 Study Completion

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

12.2.1 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) and IRBs, and US Food and Drug Administration (FDA) or Local Health Authority, as applicable. Bausch + Lomb Global Clinical Operations will instruct the Investigators to stop/restart dispensing study materials and will arrange for study closeout, if applicable, at each site.

12.3 Concomitant Medications/Therapy

Other contact lenses/solutions are not allowed to be used by subjects during the study.

Ocular medications or systemic or topical medications that, in the Investigator's opinion, could potentially affect ocular physiology or lens performance are also prohibited, unless medically necessary during the course of the study. If used during the course of the study, these medications must be reported in the source and the appropriate eCRF.

12.4 Treatment Compliance

The Investigator or other designee will review instructions and warnings for lens wear, lens care, handling, cleaning, and disinfecting with the subject. 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 must be discontinued.

12.5 Protocol Deviations

The date of and reason for deviations will be documented in all cases. Significant or major protocol deviations impacting the safety of the subject or the integrity of the study must be reported by the Investigator to the IRB immediately. Reporting of all other protocol deviations must adhere to the requirements of the governing IRB.

Subjects may continue to participate until the end of the study, unless the protocol deviations put the subject at risk or the subject's condition requires that they be discontinued from the study.

13.0 ADVERSE EVENTS

13.1 Adverse Event Definitions

For the purposes of this study, AEs include ocular AEs in the study eye(s), all ocular and non-ocular serious adverse events (SAEs), adverse device effects (ADEs), and unanticipated adverse device effects (UADEs). AEs, SAEs, ADEs, and UADEs are defined as follows:

13.1.1 Adverse Events

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

Throughout the course of this study, all efforts will be made to remain alert to possible AEs. The term "AEs" includes both SAEs and significant non-serious AE. Each are defined below.

If an AE occurs, the first concern will be the safety of the subject and appropriate medical intervention will be made. All AEs (SAEs and significant non-serious AEs) that occur will be reported in this study.

AEs should be differentiated into device related and non-device related. Any corneal infiltrate, ulcer, neovascularization, etc. shall be presumed to be device related, in the absence of an alternative explanation.

All AEs occurring after signing of informed consent and through the subject's end of participation in the study must be reported. All AEs must be followed until the event resolves or stabilizes.

All AEs should be photo documented and communicated to the CRO and Sponsor in electronic form.

13.1.2 Adverse Device Effect

An adverse device effect (ADE) is an AE 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.

13.1.3 Anticipated Serious Adverse Device Effect

An anticipated serious adverse device effect (ASADE) is a serious adverse device effect 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 may 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

13.1.4 Unanticipated Adverse Device Effect

An unanticipated adverse device effect (UADE) 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.

13.1.5 Serious Adverse Events (SAE)

- Serious adverse event is an AE that:
    - 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 (eg, 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: 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 are those events that result in, or have potential to cause, either permanent impairment of an ocular function or damage to an ocular structure and may necessitate medical or surgical intervention.

Serious adverse events may include any hazardous, **sight-threatening conditions** occurring after exposure to the test article, including 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 ≥2 mm diameter;
    - Associated with iritis Grade ≥2;
    - 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 6 mm of cornea) corneal event that results in permanent opacification (such as vascularization);
- Any serious adverse ophthalmic events including hypopyon and hyphema;
- Any neovascularization within the central 6 mm of the cornea;
- Permanent loss of ≥2 lines of BSCVA;
- All cases of iritis.

13.1.6 Significant Non-Serious Adverse Events

Significant non-serious AEs should include:

- Peripheral non-progressive non-infectious corneal ulcers;
- All symptomatic corneal infiltrative events;
- All cases of corneal staining Grade ≥3;
- A temporary loss of ≥2 lines of BSCVA (for ≥2 weeks);
- Neovascularization cases Grade ≥2.

Any ocular event that necessitates temporary lens discontinuation of ≥2 weeks

13.1.7 Non-Significant Non-Serious Adverse Events

Non-significant non-serious AEs may include but are not limited to:

- Bacterial conjunctivitis;
- Viral conjunctivitis;

- Allergic conjunctivitis;
- Corneal edema;
- Contact lens–related papillary conjunctivitis; and,
- Loss of contrast sensitivity.

13.2 Adverse Event Treatment and Culturing

With any AE, treat the subject as appropriate to prevent further complications and to potentially resolve the event consistent with the standard of care.

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 culturing techniques are outlined in APPENDIX F.

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 clinical lab designated by the site.

Microbial data generated from returned subject supplies (eg, 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 clinical laboratory designated by the site for analysis. The clinical laboratory will report the culture results to both the Investigator and to the Sponsor.

13.2.1 Medical Treatment Including Non-Adverse Events

In the event that a subject requires medical treatment (prescription medication) for an ocular condition, treat the subject as appropriate to prevent further complications and to potentially resolve the event.

13.3 Evaluations

When evaluating AEs, the Investigator must determine if the event is serious (refer to Section 13.1.5 for criteria) and assess the severity of symptoms and the relationship of the event to the study device using the following guidelines:

13.3.1 Severity

- **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.

13.3.2 Relationship to Study Device and/or Rewetting Drops

- **Related:** There is at least a reasonable possibility that the AE/SAE 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. Also referred to as an ADE.
- **Unrelated:** There is little or no reasonable possibility that the AE/SAE is related to the study device and/or Rewetting Drops. This assessment implies that the AE/SAE 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.

13.4 Procedures for Reporting Serious Adverse Events, Unanticipated Adverse Device Events, and Significant Non-Serious Adverse Events

Events classified as SAE/UADE or significant non-serious AEs require expeditious handling and reporting to the Sponsor or designee to comply with regulatory requirements, as follows:

- Must be immediately reported to the Medical Monitor within 24 hours of knowledge of the event using the Sponsor-provided form (SAE/UDE reporting form) by emailing the completed form to [redacted]. The Medical Monitor will email a copy of the form to: [redacted]; [redacted] upon receipt. The Medical Monitor will email/fax a copy of the form immediately (within 24 hours) for SAEs only to [redacted] upon receipt.
- Investigators should not wait to receive additional information to fully document the event before notifying the medical monitor and Sponsor/designee of an SAE/UADE/significant non-serious AE. If only limited information is initially available, follow-up reports are required. Additional relevant information such as hospital records and autopsy reports should be provided to the Sponsor/designee 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/UADE/significant non-serious AEs 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.

In the case of an AE (serious and significant non-serious) or medical treatment (non-AE), the Investigator must:

- Report the AE or medical treatment to the Medical Monitor and Sponsor/designee within 24 hours of knowledge of the event using the Sponsor-provided form (SAE/UADE Report Form) by emailing the completed form to the Medical Monitor and Sponsor/designee.
- Indicate on the Initial SAE/UADE Report Form whether the SAE/UADE is presumed to be not study related, lens related, solution related, or both lens/solution related.

- 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.
- Enter the SAE/UADE/significant non-serious AE into the eCRF within 3 business days of submitting the Initial SAE/UADE Report Form.
- Continue to update the eCRF, if applicable, each time the subject is seen during the management of the incident and at resolution of the incident. Whenever possible, it is suggested that the Investigator take photographs of all AEs and forward them to the Sponsor.
- Cases 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.
- Submit all bills, prescription receipts, and culture reports/fees related to the AE to Bausch + Lomb Clinical Operations. Expenses incurred for study-related medical treatment will be paid by Bausch + Lomb Clinical Operations.

Actions required by Investigators for reporting non-serious ocular AEs in the study eye(s) are summarized below.

Table 2. Non-serious Adverse Events

Non-serious ocular AEs in the study eye(s)	**Non-device-related**	**Device-related**
Required action	Recorded on AE CRF only; No expedited report to Sponsor; No report to IRB	

Actions required by Investigators for reporting all SAEs in the study eye(s) and/or non-study eye are summarized below.

Table 3. Serious Adverse Events, Unanticipated Device Adverse Events and Significant Non-Serious Adverse Events

SAEs (ocular and non-ocular), UADE, significant non-serious AE	Non-device-related	Device-related	
		Anticipated	Unanticipated
Required action	Recorded on SAE/UADE Report Form and AE CRF ⇩ Investigator submits expedited report to Sponsor and its representative within 24 hours; Report to IRB, if required per IRB policy		Recorded on SAE/UADE Report Form and AE CRF ⇩ Investigator submits expedited report to Sponsor and its representative within 24 hours; Investigator reports to IRB within 10 working days or per IRB policy, whichever is shorter
			Sponsor conducts evaluation ⇩ Sponsor or its representative reports to FDA, all IRBs, and all Investigators within 10 working days

13.4.1 On-Site Serious Adverse Event and Unanticipated Adverse Device Effect Reporting

The site must report any SAE or UADE on a SAE/UADE report form and any available documents 24 hours of becoming aware of an event.

The contacts for reporting SAEs/UADEs are:

[redacted]

and

[redacted]

The site must also report UADEs to the reviewing IRB within 10 working days following awareness of the UADE or according to the established reporting procedures of the IRB, whichever is shorter. The site should also complete applicable CRFs within 3 working days of event identification. The Sponsor or its representative will report the UADE to the FDA, all other IRBs, and all Investigators within 10 working days after first being informed by the Investigator.

13.4.2 Off-Site Unanticipated Adverse Device Effect Reporting

When participating in multicenter clinical investigations, Principal Investigators may receive off-site UADE reports. These are Sponsor reports of UADEs which occurred at other clinical sites for the same trial, or in different trials using the same test article, 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.

13.4.3 Reporting Device Deficiencies

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

Investigators must evaluate, record, and report via applicable forms any complaints/ deficiencies or malfunctions experienced with a test or control lens during this trial to the Sponsor and its representative promptly. The Sponsor 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.

The contact for reporting device deficiencies is:

[redacted]

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.

13.4.4 Guidelines for Reporting Pregnancies

All female subjects of childbearing potential must use an effective method of birth control during the study, to include 2 weeks after last visit, in a manner such that risk of contraceptive failure is minimized. Abstinence is allowed as a birth control method.

During the study, all female subjects of childbearing potential should be instructed to contact the Investigator immediately if they suspect they might be pregnant (eg, 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 to the medical monitor and CRO via confirmed facsimile or email transmission and must be submitted on a Pregnancy Report Form to the Sponsor or designee within 24 hours of the Investigator's awareness of the pregnancy.

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 Sponsor within 24 hours on a SAE/UADE Report Form along with the Pregnancy Report Form.

The contacts for reporting pregnancies are:

[redacted]

and

[redacted]

[redacted]

14.0 STATISTICAL METHODS

14.1 Study Endpoints

14.1.1 Primary Effectiveness Endpoint

The primary effectiveness endpoint will be statistical non-inferiority with respect to mean distance high-contrast logMAR lens VA for each eye between the test and control lenses. For each eye, distance high-contrast logMAR lens VA will be averaged over all scheduled visits as the primary endpoint. A non-inferiority upper bound of 0.06 (3 letters) will be used to assess the difference (test – control) in mean logMAR lens VA.

14.1.2 Primary Safety Endpoint

The primary safety endpoint will be statistical non-inferiority with respect to the proportion of eyes with any slit lamp findings Grade >2 at any follow-up visit between the test and control lenses. A non-inferiority upper bound of 0.10 will be used to assess the difference (test – control) in proportions of slit lamp outcomes.

14.2 Hypotheses

14.2.1 Primary Effectiveness Endpoint

The null hypothesis (H_0) for the primary effectiveness endpoint is that the difference between the test mean (μ_T) and the control mean (μ_C) in distance high-contrast logMAR lens VA averaged over all scheduled visits is ≥0.06. The alternative hypothesis (H_1) is that the difference is <0.06.

$$H_0: \mu_T - \mu_C \geq 0.06$$

$$H_1: \mu_T - \mu_C < 0.06$$

14.3 Primary Safety Endpoint

The null hypothesis (H_0) for the primary effectiveness endpoint is that the difference between the test (π_T) and the control (π_C) in the proportion of eyes with any slit lamp findings Grade >2 at any follow-up visit is ≥0.10. The alternative hypothesis (H_1) is that the difference is <0.10.

$$H_0: \pi_T - \pi_C \geq 0.10$$

$$H_1: \pi_T - \pi_C < 0.10$$

14.4 Sample Size

Sample size calculation inputs (eg, standard deviations [SDs] and expected percentages) were estimated based on the results of a previous clinical trial evaluating the test lens.[1]

14.4.1 Primary Effectiveness Endpoint

When the sample sizes in the groups are 100 eyes and 50 eyes, a 2-group 0.05 one-sided t-test will have 99% power to reject the null hypothesis that the test lens is inferior to the

control lens (the difference in means, μ_T - μ_C, is ≥0.060) in favor of the alternative hypothesis that the test lens is non-inferior to the control lens, assuming that the expected difference in means is 0.000 and the common SD is 0.076.

14.4.2 Primary Safety Endpoint

With 50 eyes in the control group and 100 eyes in the test group, the upper limit of the observed 1-sided 95% confidence interval will be expected to be <0.100 with 99% power when the control proportion, π_C, is 0.012 and the test expected proportion, π_T, is 0.012; results are based on 10000 simulations using the Newcombe-Wilson score method to construct the confidence interval.[2]

14.4.3 Overall Power and Sample Size

Assuming independence of the primary endpoints, the overall power of the study to show non-inferiority for both endpoints is 98%. Accounting for up to 10% losses, approximately 168 eyes (84 subjects) should be enrolled.

14.5 Randomization

Subjects will be randomized to 1 of 2 treatment arms in a 2:1 ratio (test:control), wearing either test or control lenses in both eyes for the duration of the study. Randomization will be stratified by investigational site.

Subjects will be randomized, after they are deemed eligible to participate, according to subject-specific randomization information provided by the randomization system.

14.6 Study Populations

14.6.1 Intent-to-Treat Population

The intent-to-treat (ITT) population will consist of all randomized eyes. Eyes will be included in treatment groups according to the treatments to which they were randomized for ITT population summaries.

14.6.2 Per-Protocol Population

The per-protocol (PP) population will consist of all randomized eyes without the following important protocol deviations:

- Ineligible when randomized
- Not dispensed study lenses
- Use of an incorrect lens type (eg, due to improper randomization, erroneous dispensing, return to habitual lens brand, etc.)
- Use of a lens care system other than the lens care system dispensed
- Failure to wear the assigned lenses at least 80% of the expected days
- Failure to provide non-missing distance high-contrast logMAR lens VA data at all of the scheduled visits (Dispensing Visit and 1-Week, 1-Month, 2-Month, and 3-Month Visits)

Additional important protocol deviations may be identified prior to unmasking of the treatment assignments

14.6.3 Safety Population

The safety population will consist of all dispensed eyes. Eyes will be included in treatment groups according to the treatments that were actually dispensed to them for safety population summaries. If an eye uses both lens types, then the eye will be included in the test lens group for safety population summaries.

14.7 Statistical Analysis

A full declaration of planned statistical analyses will be documented in a formal statistical analysis plan (SAP). Any deviations from the SAP will be documented in the final study report.

14.7.1 Methods of Analysis

14.7.1.1 General

In general, data will be summarized by treatment group and visit as appropriate.

Eyes will be treated as independent. In other words, the correlation between eyes within subjects will be ignored.

Summaries for continuous variables will include the sample size, mean, SD, median, minimum, and maximum. Means and medians will be presented with 1 more decimal place than the recorded raw data. Standard deviations will be presented with 2 more decimal places than the recorded raw data. Minima and maxima will be presented with the same number of decimal places as the recorded raw data. Values with magnitude <1 will be presented with a leading zero to the left of the decimal (eg, 0.123 or 0.123).

Categorical data will be summarized using frequencies and percentages. Percentages will be presented with 1 decimal place. Percentages may not be presented when the count is 0. Unless otherwise specified, the denominator for percentages will be the number of non-missing values within the group being presented.

14.7.1.2 Primary Effectiveness Analysis

Monocular distance high-contrast logMAR lens VA will be assessed at each scheduled visit (Dispensing Visit and 1-Week, 1-Month, 2-Month, and 3-Month Visits). VA will be converted to logMAR units. For each eye, logMAR VA will be averaged over all scheduled visits resulting in 1 value of “All Study” logMAR lens VA per eye.

“All Study” logMAR lens VA will be presented using continuous summary statistics for the PP population by treatment group in a table at the eye level. A 2-sided 90% confidence interval for the difference (test – control) in “All Study” logMAR lens VA will be constructed using an analysis of variance (ANOVA) model with fixed factors of treatment and site. If the upper limit of the confidence interval is ≤0.06 then the null hypothesis will be rejected and the test lens will be statistically successful in this outcome.

The previous analysis will also be completed using the ITT Population as a sensitivity analysis. For this sensitivity analysis, missing logMAR VA values will be imputed 25

times using the Markov chain Monte Carlo (MCMC) method. The seed used to generate the imputations will be 1187871241. The results of analyses (as described above for the PP population) by imputation will be combined to produce a 2-sided 90% confidence interval for the difference between treatments.

14.7.1.3 Primary Safety Analysis

Graded slit lamp findings will be assessed at each scheduled follow-up visit (1-Week, 1-Month, 2-Month, and 3-Month Visits) and, optionally, at unscheduled visits. Each eye will be classified with respect to having 1 or more observations with Grade >2 (Yes, No) at any follow-up visit, including unscheduled visits.

The number and percentage of eyes with findings Grade >2 at any follow-up visit will be presented for the safety population by treatment group in a table. A 2-sided 90% confidence interval for the difference (test – control) between treatment groups will be constructed using the Newcombe-Wilson score method. If the upper confidence limit ≤10% (0.10) then the null hypothesis will be rejected and the test lens will be statistically successful in this outcome. If both treatment groups have 0 eyes with a slit lamp finding Grade >2, then the confidence interval will not be calculable, the null hypothesis will be rejected, and the test lens will be statistically successful in this outcome.

14.7.2 Multiple Comparisons

Adjustment for multiple comparisons will not be necessary because statistical success will require success in both primary endpoints.

14.7.3 Interim Analyses

No interim analyses are planned.

14.7.4 Missing Data

Missing data will be imputed for the ITT population sensitivity analysis of the primary effectiveness endpoint as described above. Unless otherwise specified, missing data will not be imputed.

15.0 DATA QUALITY ASSURANCE

15.1 Study Monitoring

Bausch + Lomb Global 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 the Bausch + Lomb Global Clinical Operations Department.

Prior to the start of the study, member(s) of the Bausch + Lomb Global Clinical Operations Department (or designees) 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.

- This clinical investigation is being conducted in accordance with 21 CFR Parts 11, 50, 54, 56, and 812. The protocol was developed with consideration of the provisions in: ISO 14155-1:2011 Clinical investigation of medical devices for human subjects – Part 1: General requirements; 14155-2:2011 Part 2: Clinical investigation of medical devices for human subjects – Part 2: Clinical investigational plan; ISO 11980:2012 Ophthalmic Optics – Contact lenses and contact lens care products – Guidance for clinical investigations; ICH GCP and applicable local regulations. The Sponsor intends to register this clinical trial with the public database https://ClinicalTrials.gov.
- The integrity of the data, including adequate study documentation.
- The facilities remain acceptable.
- The Investigator and site personnel remain qualified and able to conduct the study.
- Test article accountability

During the course of the study, if the Sponsor determines that an Investigator is not 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.

15.2 Source Documentation

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

Examples of source documents include hospital records, clinical and office charts, laboratory notes, memoranda, signed ICF, 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 to be source data. Only subjects are to record information on subject-completed forms. 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 (eg, 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.

15.3 Case Report Forms and Data Verification

Subject data required by this protocol are to be transferred from the 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 by providing an electronic signature. All information requested on the eCRFs needs to be supplied, including subject identification and initials, date(s), assessment values, etc., and any omission or discrepancy will require explanation. All information on eCRFs must be traceable to source documents.

The study monitor will be responsible for reviewing and verifying the data recorded on the eCRFs per the study Monitoring Plan, utilizing the original source documentation and will query discrepant findings. The Investigator and study site personnel will be responsible for answering all queries.

The eCRFs will be submitted to Bausch + Lomb Global Clinical Operations for quality assurance review and statistical analysis.

A copy of the eCRFs will be provided to the Investigator at the conclusion of the study, who must ensure that it is stored in a secure place.

15.4 Recording of Data and Retention of Documents

Subject data recorded on eCRFs during the study will be documented in a coded fashion. The subject will only be identified by the subject number and by their initials if also required. Confidentiality of subject records must be maintained to ensure adherence to applicable local privacy regulations.

The Investigator must retain essential documents indefinitely after the completion of the study, unless otherwise notified by the Sponsor. The Investigator agrees to adhere to the document retention procedures when signing the protocol Investigator Statement of Approval.

Essential documents include but are not limited to the following:

- IRB approvals for the study protocol, all amendments, ICF(s), and advertisements
- IRB annual study review
- IRB correspondence and reports (eg, AE reports, protocol deviations, and safety updates)
- Regulatory documents (eg, financial disclosure and delegation of authority forms)
- All source documents
- Archive of eCRFs
- Subject’s signed ICF
- Device Investigator Agreement
- Accountability records for the test article
- 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 Global Clinical Operations.

15.5 Auditing Procedures

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

15.6 Institutional Review Board Approval

The Investigator should ensure their participation in the study, in addition to the protocol, subject recruitment materials (written information or materials including web pages, radio advertisements, television spots, or written text developed to encourage subject enrollment) and the ICF to be used in this study are approved by their institution IRB, or if not using their institution's IRB, approved by the reviewing central IRB prior to entering any subjects in the study. Documentation of IRB approval of the study protocol and informed consent must be provided to the Sponsor prior to initiation of the study. In addition, the Investigator must ensure that the reviewing IRB has provided approval for any protocol amendments prior to implementation. If the amendment necessitates a revision to the ICF, the Investigator should ensure the revised form is also submitted to and approved by the Sponsor and the IRB and implemented as directed.

15.7 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.

16.0 REFERENCES

1. Study 661: A Study to Evaluate the Safety and Efficacy of a New Silicone Hydrogel Contact Lens Design.

2. Newcombe RG. Interval estimation for the difference between independent proportions: comparison of eleven methods. *Statistics in Medicine* 1988; 17:873-890.

APPENDIX A: SCHEDULE OF VISITS AND PARAMETERS

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.

PROCEDURE/ASSESSMENTS	Screening Visit 1 Day -30 to -7	Dispensing Visit 2 Day 1	1-Week Visit 3 Day 5-9	1-Month Visit 4 Day 27-35	2-Month Visit 5 Day 54-68	3-Month Visit 6 Day 91-101[a]	Exit Visit
Informed consent/HIPAA authorization	X						
Demographics/baseline eye/lens characteristics	X						
Contact lens use history and use[b]	X		X	X	X	X	
Medical history	X						
Eligibility	X						
Randomization	X						
Dispense and/or return study materials		X					X
Symptoms/complaints and subjective assessments (including rewetting drops [Yes/No])	X	X	X	X	X	X	
Adverse events	X	X	X	X	X	X	X
Without lenses							
Spherocylindrical refraction	X						X
Distance BSCVA	X						X
Keratometry	X						X
Slit lamp exam	X	X	X	X	X	X	
Keratometry comparison (Exit Visit to Screening Visit)							X
With study lenses							
Distance high-contrast logMAR lens VA		X	X	X	X	X	
Over-refraction and distance VA		X	X	X	X	X	
Lens wettability/centration/movement		X	X	X	X	X	
Lens deposits		X	X	X	X	X	
VA line change comparison							
Distance high-contrast logMAR lens VA at Visit 2 to distance BSCVA at Visit 1		X					
Distance BSCVA at Exit Visit to Distance BSCVA at Visit 1							X
Distance high-contrast logMAR lens VA at Visit 3-6 to distance high-contrast logMAR lens VA at Visit 2			X	X	X	X	
Distance high-contrast logMAR lens VA at Visit 3-6 to distance BSCVA at Visit 1			X	X	X	X	

a. The 3-Month Visit MUST occur no earlier than Day 91.
b. Contact lens use history is taken at the Screening Visit and contact lens use is taken at each of the follow-up visits.

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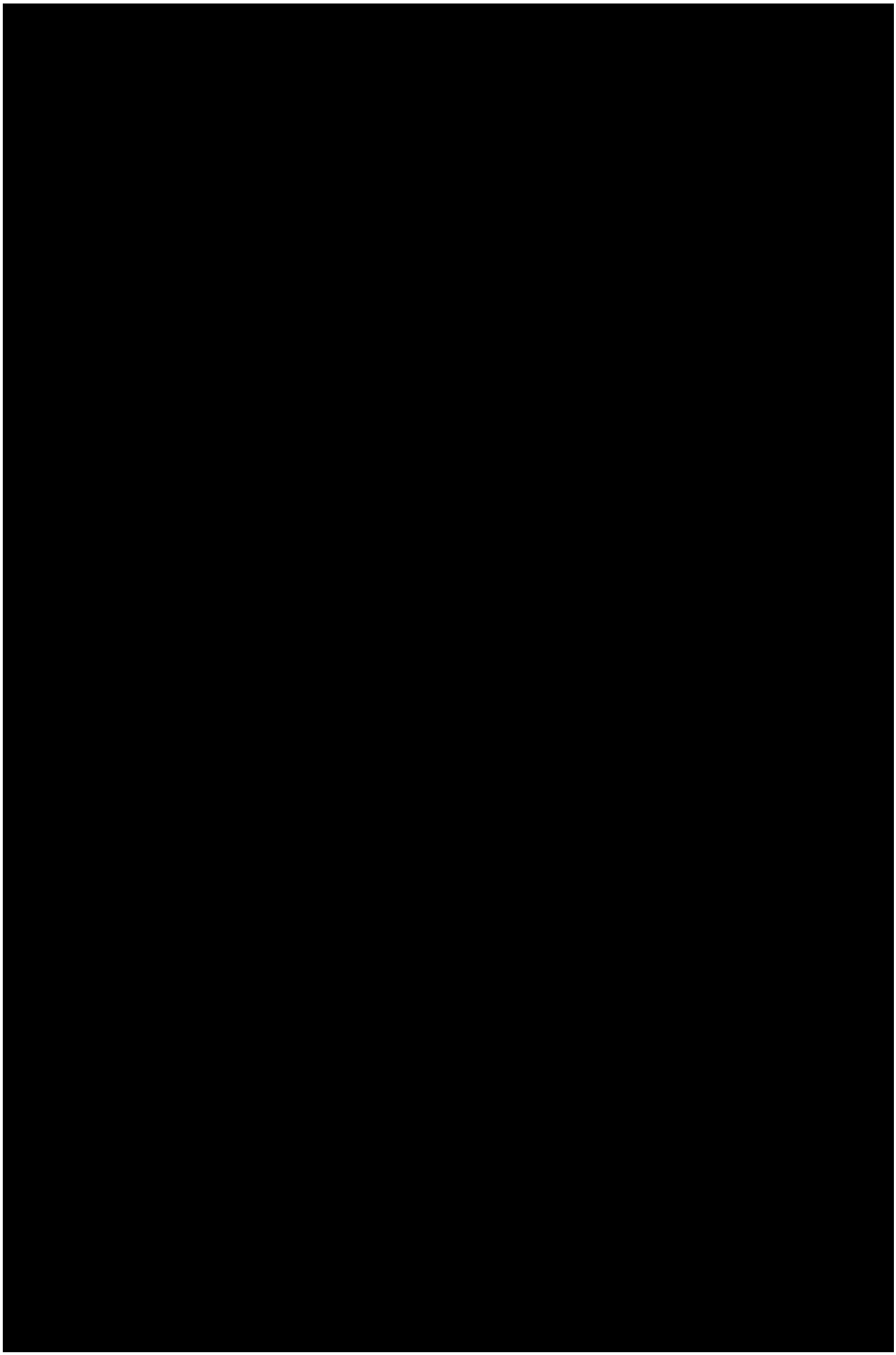

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