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Short Title

Clinical Assessment of a HYDRAGLYDE® Regimen

Long Title

Clinical Assessment of a Regimen of AIR OPTIX® plus HYDRAGLYDE® Silicone Hydrogel Lenses and HYDRAGLYDE® Containing Lens Care Solutions

Protocol Number:	LCW773-P001 / NCT03026257
Study Phase:	N/A
Sponsor Name and Address:	Alcon Research, Ltd. 6201 South Freeway Fort Worth, Texas 76134-2099
Test Product:	Air Optix® plus HydraGlyde® CLEAR CARE® PLUS/AOSEPT® PLUS with HydraGlyde® Cleaning and Disinfecting Solution OPTI-FREE® PureMoist® Multi-Purpose Disinfecting Solution
US IND# / EudraCT	N/A
Indication Studied:	Contact Lens Wear and Care
Investigator Agreement:	I have read the clinical study described herein, recognize its confidentiality, and agree to conduct the described trial in compliance with Good Clinical Practice (GCP), the ethical principles contained within the Declaration of Helsinki, this protocol, and all applicable regulatory requirements. Additionally, I will comply with all procedures for data recording and reporting, will permit monitoring, auditing, and inspection of my research center, and will retain all records until notified by the Sponsor.

Principal Investigator:

Signature Date

Name:

Address:

1 SYNOPSIS

Sponsor:	Alcon Research, Ltd. 6201 South Freeway Fort Worth, Texas 76134-2099	**Protocol Number:**
Test Product:	AIR OPTIX plus HYDRAGLYDE (AOHG) CLEAR CARE Plus/AOSEPT Plus with HYDRAGLYDE (CCP) OPTI-FREE PUREMOIST (OFPM)	**Study Phase:** ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☒ N/A
Active Ingredient:	N/A	
Protocol Title:	Clinical Assessment of a Regimen of AIR OPTIX PLUS HYDRAGLYDE Silicone Hydrogel Lenses and HYDRAGLYDE Containing Lens Care Solutions	
Investigator(s)/ No. of Sites:	Approximately 8 sites	
Center Location(s)/	United States (US), Germany, Canada	
Duration of Treatment:	30 days (-0,+3 days)	
No. of Subjects	Planned approximately 256 randomized (64/habitual lens type) to achieve required 240 completed subjects. Approximately 14-50 subjects per site will be randomized. Randomization will be stratified by habitual lens type and by tear film status at screening.	
Study Population:	Volunteer adult subjects with normal eyes who are habitual silicone hydrogel (SiHy) lens wearers (Biofinity, Vita, Ultra, and Oasys) and habitual multi-purpose solution (MPS) users [redacted]	
Objective(s):	Primary Objective: To demonstrate that worn AOHG lenses cleaned and disinfected with HYDRAGLYDE containing lens solutions (HGLC), 1) OFPM and 2) CCP, for the recommended replacement period will have less cholesterol uptake compared to each of the control habitual SiHy lenses (Biofinity, Vita, Ultra, and Oasys) cleaned and disinfected with habitual MPS (HMPS).	

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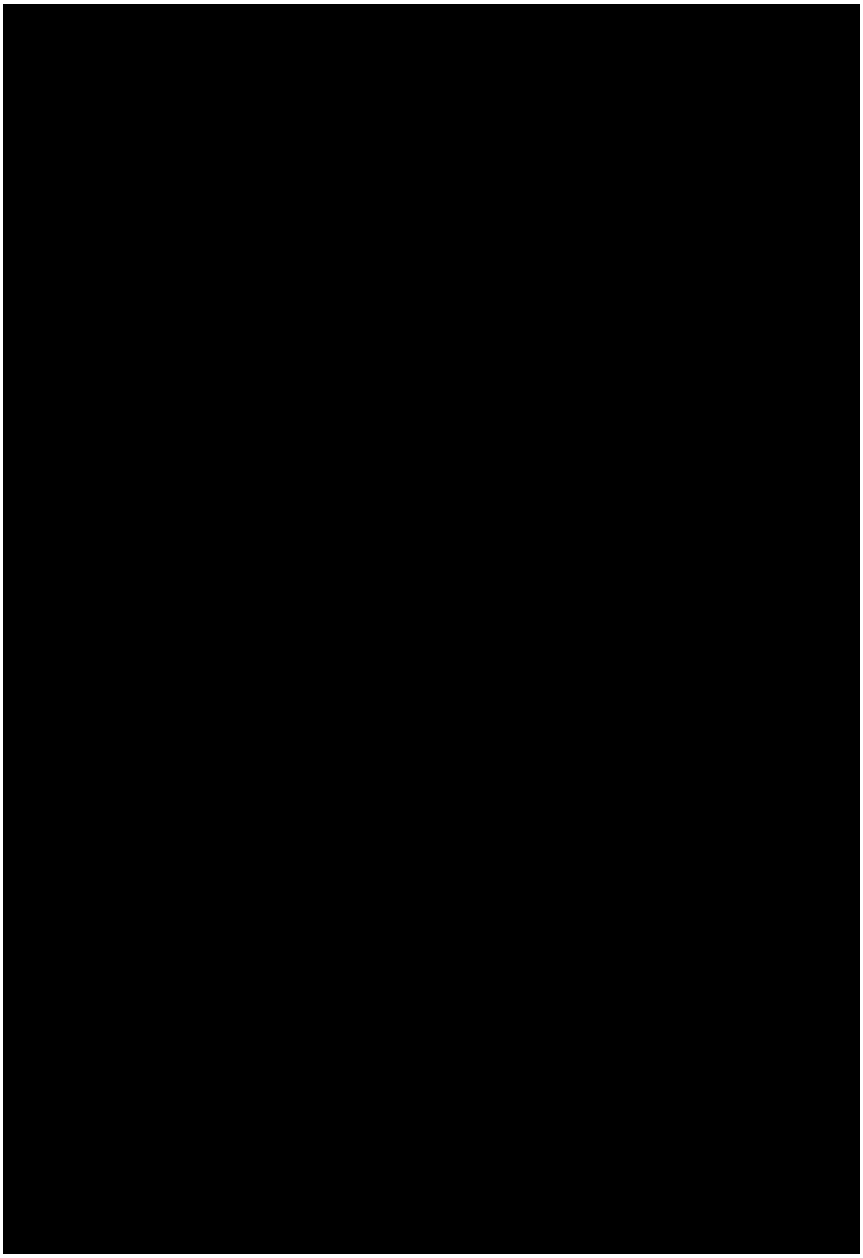

Safety:

Collect and describe Biomicroscopy findings, adverse events (AEs), and device deficiencies.

Methodology:	Multi-center, prospective, randomized, controlled, parallel-group, observer-masked and quasi-subject-masked study.
Treatments:	**Test Products:** AOHG spherical contact lenses

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	Route of Administration:	Lenses will be dispensed by the unmasked study staff member so that the subject does not see the lens label and remains masked to the details of the lens. Subjects to use the lenses as instructed by the study coordinator, according to the instructions for use.
	Duration of Treatment:	Subjects will wear the lenses bilaterally for a total duration of 30 (+3) days under a daily wear modality. The lenses will be removed every night during the study.
	Parameters:	Lenses will be available in the following parameters: Material: Lotrafilcon B, 33% water content with plasma surface treatment Base curve: 8.6 millimeters (mm) Diameter: 14.2 mm Power range: +8.00 Diopters (D) to -12.00 D (0.50 D steps above +6.00 D and -10.00) Lenses will be worn daily wear and cared for (up to 32 cleaning and disinfecting cycles) with CCP or OFPM as randomized. Bausch + Lomb (B&L) Sensitive Eyes® Plus Saline will be provided as a rinsing solution to those randomized to CCP. Test lens care solutions will be over labeled to mask the brand. See the Manual of Procedures (MOP) for detailed instructions for use of test lens care products.

Sponsor:	Alcon Research, Ltd. 6201 South Freeway Fort Worth, Texas 76134-2099	**Protocol Number:**
	Control Products:	Habitual Spherical SiHy Lenses: Bausch + Lomb ULTRA™ Contact Lenses with MoistureSeal™ Technology (Samfilcon A) (Ultra) Material: samfilcon A, 46% water content Base curve: 8.5 mm Diameter: 14.2 mm Power range: +6.00 D to -12.00 D (0.50 D steps above -6.00 D) Johnson & Johnson ACUVUE® VITA™ Brand Contact Lenses (Vita)Material: senofilcon C, 41% water content Base curve: 8.4, 8.8 mm Diameter: 14.0 mm Power range: +8.00 D to -12.00 D (0.50 D steps above +/-6.00 D) Johnson & Johnson ACUVUE® OASYS® Brand 2-Week with HYDRACLEAR® PLUS (Oasys) Material: senofilcon A, 38% water content Base curve: 8.4, 8.8 mm Diameter: 14.0 mm Power range: +8.00 D to -12.00 D (0.50 D steps above +/-6.00 D) Biofinity Material: comfilcon A, 48% water content Base curve: 8.6 mm Diameter: 14.0 mm Power range: +8.00 D to -12.00 D (0.50 D steps after +/-6.00 D)
	Route of Administration:	Lenses will be dispensed by the

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		unmasked study staff member(s) so that the subject does not see the lens label and will remain masked to the details of the lens. Subjects will use the lenses as instructed by the coordinator, according to the instructions for use.
	Duration of Treatment:	Subjects will wear the lenses bilaterally for a total duration of 30 days (-0, +3 days). Oasys lenses will be replaced (masked dispensing) at Day 15 ±1 day. The lenses will be removed every night during the study.
	Parameters:	The lenses will be available in the powers offered by each brand that are inclusive of the powers offered by AOHG (+8.00 D to -12.00 D). The lenses will be worn as daily wear and cared for with subject's HMPS (up to 32 cleaning and disinfection cycles). The HMPS will be purchased by the subject (confirmed by the site) or purchased by the site and used in the commercial packaging according to the product's instructions for use.
Subject Selection:	**Inclusion Criteria:** 1. Subjects must be at least 18 years of age and sign the inform consent document 2. Subjects' vision must be correctable to 0.1 (logMAR) or better in each eye at distance with habitual lenses at Visit 1. 3. Manifest cylinder (at screening) less than or equal to 0.75 D in each eye and spectacle add < +0.50 D in each eye. 4. Current full-time wearer (during the past 1 month for a minimum of 5 days per week and 6 hours per day) of spherical samfilcon A, comfilcon A, or senofilcon C	

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monthly replacement lenses or senofilcon A 2-week replacement lenses within the power range of lens powers available for the test AOHG spherical lenses.
5. Current user (for the past 1 month) of an MPS (excluding OFPM) to care for their lenses.
6. Willing to answer text messages on a daily basis during the study.
7. Willing to discontinue artificial tears during the study and rewetting drops on the days of study visits.
8. Uses digital devices (eg, smart phone, tablet, laptop computer, or desktop computer) for 20 consecutive minutes at least twice a week and willing to continue the same pattern for the duration of the study.

Exclusion Criteria:

1. Habitual lens wear in an extended wear modality (routinely sleeping in lenses overnight for 1 or more nights per week).
2. Unstable tear film with a NIKBUT < 6 seconds in either eye without lenses.
3. Any anterior segment infection, inflammation, disease or abnormality that contraindicates contact lens wear as determined by the Investigator (within 7 days of enrollment, or current).
4. History of herpetic keratitis, corneal surgery or irregular cornea.
5. Prior refractive surgery (eg, laser assisted in situ keratomileusis and photorefractive keratectomy).
6. Any use of systemic or ocular medications for which contact lens wear could be contraindicated as determined by the Investigator.
7. Subjects who are currently using or have not discontinued Restasis®, Xiidra™ and/or topical steroids within the past 7 days.
8. Use of mechanical eyelid therapy or eyelid scrubs within 14 days before Visit 1 and not willing to discontinue during the study.
9. Biomicroscopy findings that are abnormal or graded moderate (Grade 3) or severe (Grade 4) at Visit 1.
10. Monocular subjects (only one eye with functional vision) or subjects fit with only one lens.
11. Known pregnancy or lactating.

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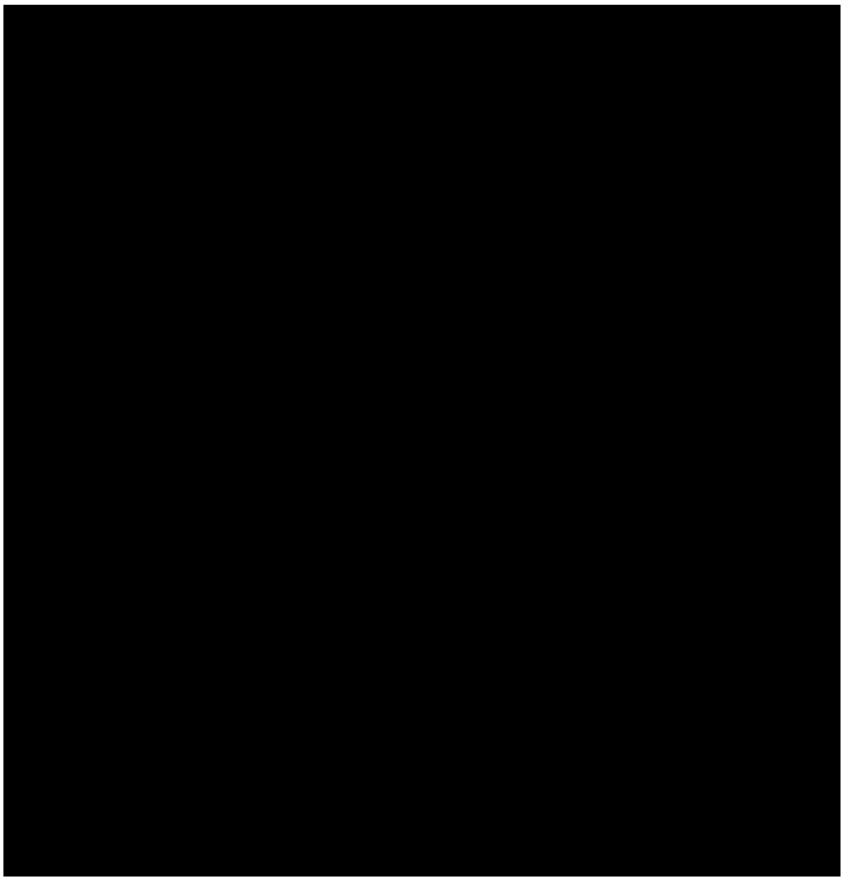
12. Enrollment of site staff or family/household members of the site staff who are listed on the study personnel log as having a role in the execution of this study.
13. Participation in any clinical study within 30 days of Visit 1.

Assessments:

Primary Efficacy:

- Total Cholesterol Uptake to be assessed on worn right (OD) lenses collected at Day 30



Safety:

- Biomicroscopy
- AEs
- Device Deficiencies

Statistical Methods: Planned Analysis

Three analysis sets will be defined, Safety, Full, [redacted]. The Safety Analysis Set will include all

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subjects/eyes exposed to any test or control products evaluated in this study. The Full Analysis Set (FAS) will consist of all subjects randomized and exposed. [redacted] The FAS will serve as the primary analysis dataset for all efficacy evaluations.

All data from evaluable subjects will be included in the efficacy analysis; no imputation for missing values will be performed.

To address the primary efficacy objective, planned analyses are summarized below:

Endpoint	Comparison	Statistical Method
PRIMARY		
Ex vivo total cholesterol uptake (Day 30)	AOHG/OFPM and AOHG/CCP vs Ultra, Biofinity, Vita, and Oasys Superiority	[redacted]

[redacted]

A sequential gatekeeping strategy will be implemented to control multiplicity, by testing the primary efficacy hypotheses first for both HYDRAGLYDE regimen comparisons; [redacted]

[redacted]

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[redacted]

Safety

Each safety variable will be summarized descriptively. AEs will be classified as treatment-emergent or pre-treatment. Counts and percentages will be provided by relationship to regimen, and separate tables will be generated for ocular and nonocular AEs. Counts and percentages in each grade category will be presented for each biomicroscopy parameter. Device deficiencies will also be tabulated. Supporting subject listings describing details of each safety variable will be provided. No inferential testing will be performed for safety analysis.

Sample Size Justification

Sample size calculations for attaining the specified power at one-sided α=0.05 for each of the relevant efficacy endpoints are summarized below:

Endpoint	Assumptions	Power	N
PRIMARY			
Ex vivo total cholesterol uptake	Expected difference = 3.26 Common standard deviation (SD) = 3.12	97%	25 /group (based on t-test of equal means)

[redacted]

1.1 Glossary of Terms for Safety

Adverse Event (AE)	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 (test article). *Note: For subjects, this definition includes events related to the test article, the control article, or the procedures involved. For users or other persons, this definition is restricted to events related to the test article.*
Adverse Device	Adverse event related to the use of an investigational medical device (test article) or control article. *Note: This definition*

Effect (ADE)	*includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation; any malfunction; and use error or intentional misuse of the test article or control article.*
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. *Note: This definition includes malfunctions, use errors, and inadequate labeling.*
Malfunction	Failure of a medical device to meet its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the labeling of the device. The intended performance of the device refers to the intended use for which the device is labeled or marketed.
Product Complaint	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.
Non-serious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.
Serious Adverse Event (SAE)	Adverse event that led to any of the following: • Death. • A serious deterioration in the health of the subject that either resulted in: a) a life-threatening illness or injury. Note: Life-threatening means that the individual was at immediate risk of death from the event as it occurred, ie, it does not include an event which hypothetically might have caused death had it occurred in a more severe form. b) any potentially sight-threatening event or permanent impairment to a body structure or a body function. c) in-patient hospitalization or prolonged hospitalization. Note: Planned hospitalization for a pre-existing condition, without serious deterioration in health, is not considered a serious adverse event. In general, hospitalization signifies that the individual remained at the hospital or emergency

	ward for observation and/or treatment (usually involving an overnight stay) that would not have been appropriate in the physician's office or an out-patient setting. Complications that occur during hospitalization are adverse events. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred, the event should be considered serious. d) a medical or surgical intervention to prevent a) or b). e) any indirect harm as a consequence of incorrect diagnostic test results when used within manufacturer's instructions for use. • Fetal distress, fetal death, or a congenital abnormality or birth defect. Refer to Section 12 for additional SAEs.
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Serious Public Health Threat	Any event type which results in imminent risk of death, serious deterioration in state of health, or serious illness that requires prompt remedial action. This would include: Events that are of significant and unexpected nature such that they become alarming as a potential public health hazard, eg, human immunodeficiency virus or Creutzfeldt-Jacob Disease.
Use Error	Act or omission of an act that results in a different medical device response than intended by manufacturer or expected by user. Note: This definition includes slips, lapses, and mistakes. An unexpected physiological response of the subject does not in itself constitute a use error.

2 OVERVIEW OF STUDY PLAN

	Visit 1	Visit 2	Visit 3	Visit 4 / Exit	USV
Procedure/ Assessment	**Screening**	**Day 1- Insertion** 1-7 days from Visit 1. *No lenses worn on day of the visit*	**Day 1: 8hrs (± 30 min)**	**Day 30 (+3 days): 8hrs (± 30 min)/Exit**	**Unscheduled Visit**
Informed Consent	✓				
Demographics	✓				
Medical History	✓				
Concomitant Medications	✓	✓	✓	✓	✓
Inclusion/Exclusion	✓				
[redacted]					
Biomicroscopy (Note: conjunctival staining conducted at designated sites only)	[redacted]				
Randomize Eligible Subjects	✓				
Dispense assigned study lenses in a masked manner		✓[g]			(✓)
[redacted]					
Collect lenses for shipping and analyses				✓	(✓)
Exit Form	(✓)	(✓)	(✓)	✓	(✓)
Assess Adverse Events	✓[d]	✓	✓	✓	✓

(Both observed and reported)					
Assess Device Deficiencies		✓	✓	✓	✓
[redacted]					

[redacted] [c] Without lenses at baseline to determine eligibility [redacted] [d] AEs are collected from the time of informed consent. [redacted] [g] Lenses also dispensed at Day 15±1 in office for subjects assigned to continue wearing Oasys.

3 ABBREVIATIONS

Abbreviation	Definition
ADE	Adverse device effect
AE	Adverse event
ANOVA	Analysis of variance
AOHG	AIR OPTIX plus HYDRAGLYDE
[redacted]	[redacted]
B&L	Bausch + Lomb
[redacted]	[redacted]
Biofinity	CooperVision® Biofinity® Contacts
CCP	CLEAR CARE Plus/AOSEPT Plus with HYDRAGLYDE
CE	*Conformité Européene*
CI	Confidence interval
CL	Confidence limit
CRF	Case report form
CSR	Clinical study report
D	Diopters
DEP	Deviations and evaluability plan
eCRF	Electronic case report form
EDC	Electronic data capture
EOBO	Polyoxyethylene -polyoxybutylene
[redacted]	[redacted]
[redacted]	[redacted]
FDA	US Food and Drug Administration
fl. Oz.	Fluid ounces
GCP	Good Clinical Practice
HGLC	HYDRAGLYDE containing lens solutions
HMPS	Habitual multipurpose solution
Hrs	Hours
IEC	Independent ethics committee
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ID	Identification
IRB	Institutional review board
[redacted]	[redacted]
[redacted]	[redacted]
LCS	Lens care system
[redacted]	[redacted]
MedDRA®	Medical Dictionary for Regulatory Activities
Min	Minute(s)
ml	Milliliter
mm	Millimeters
MOP	Manual of procedures
MPS	Multipurpose Solution

Abbreviation	Definition
N/A	Not applicable
[redacted]	[redacted]
[redacted]	[redacted]
Oasys	Johnson & Johnson ACUVUE® OASYS® Brand 2-Week with HYDRACLEAR® PLUS
OD	Right eye
OFPM	OPTI-FREE PUREMOIST
OS	Left eye
[redacted]	[redacted]
Rx	Prescription
SADE	Serious adverse device effect
SAE	Serious adverse event
SD	Standard deviation
SiHy	Silicon hydrogel
SMS	Short message service
[redacted]	[redacted]
Ultra	Bausch + Lomb ULTRA™ Contact Lenses with MoistureSeal™ Technology (Samfilcon A)
US	United States
[redacted]	[redacted]
VA	Visual acuity
[redacted]	[redacted]
Vita	Johnson & Johnson ACUVUE® VITA™ Brand Contact Lenses

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5 INTRODUCTION

5.1 Study Rationale and Background

HYDRAGLYDE (polyoxyethylene-polyoxybutylene), developed by Alcon Laboratories, Inc., is a proprietary surfactant with a large hydrophilic component that brings moisture to lens surfaces. HYDRAGLYDE technology is used in premium lens care solution products from Alcon, including OPTI-FREE PUREMOIST MULTI-PURPOSE DISINFECTING SOLUTION, and AOSEPT PLUS with HYDRAGLYDE Cleaning and Disinfecting Solution (marketed as CLEAR CARE PLUS with HYDRAGLYDE Moisture Matrix in the US). These lens care products are specially designed to improve the wettability of reusable SiHy lenses; which are particularly prone to surface de-wetting (Keir 2013).

The AIR OPTIX brand of SiHy contact lenses (lotrafilcon B with plasma surface technology) has been shown to resist lipid deposition better than other SiHy contact lenses and maintain good surface wettability even after 30 days of wear (Nash 2014). However, switching to HYDRAGLYDE containing lens care products has been shown to significantly improve patient-reported comfortable lens wear time when used to clean and disinfect AIR OPTIX Aqua contact lenses (TDOC-0051197 CSR for Protocol LCD913-P001 and TDOC-0013454 CSR for Protocol C-09-074).

In order to provide the benefits of this surfactant on the first day of wear, HYDRAGLYDE (0.04% EOBO-41 polyoxyethylene-polyoxybutylene) has been added to the packaging solution of AIR OPTIX Aqua lenses. The addition of HYDRAGLYDE to the packaging solution of AIR OPTIX plus HYDRAGLYDE lenses has shown to interact with the lens surface and significantly improve the wetting substantivity of the lens (Lemp 2016), providing a longer lasting moisture effect.

The overall objective of this clinical study is to compare the on-eye performance of a HYDRAGLYDE regimen of lenses and lens care with a regimen of marketed SiHy lenses and marketed multipurpose solutions that do not contain HYDRAGLYDE.

[redacted] Multipurpose solutions are commonly used disinfection systems in the marketplace and are included in most private label solutions; therefore, they are a reasonable control to the test solutions in this study, which are a hydrogen peroxide based solution and a POLYQUAD/ALDOX preserved MPS both containing HYDRAGLYDE for longer lasting lens surface wettability to further reduce lipid deposition and promote tear film stability.

5.2 Known and Potential Risks

Safety information on AOHG, OFPM, and CCP may be found in the products' labeling. The Investigator should advise subjects of the following general warnings and precautions with contact lens wear, including the following:

- Serious eye injury, scarring of the cornea and loss of vision may result from problems associated with wearing contact lenses and using lens care products.
- Eye problems, including infection, corneal ulcers, corneal neovascularization, or iritis can develop rapidly and lead to loss of vision if left unattended.
- Smoking and/or swimming increases the risk of corneal ulcers with contact lens wear, especially when lenses are worn overnight or while sleeping.
- The risk of ulcerative keratitis has been shown to be greater among users who wear their lenses overnight compared to those who do not wear them overnight.

The risks with contact lens wear are increased with a pre-existing or active ocular infection or inflammation, improper lens fit, and/or noncompliance with regimen. The AOHG contact lenses are for daily use and are to be cared for with CCP or OFPM at the end of each day. Subjects who fail to follow the instructions for replacing and caring for their contact lenses could experience an eye infection of the cornea or injury. A corneal ulcer could develop rapidly and lead to loss of vision. An improperly fitted contact lens may affect corneal curvature and result in vision fluctuations upon lens removal.

Potential serious complications with contact lens wear are usually accompanied by 1 or more of the following signs or symptoms:

- Moderate to severe eye pain not relieved by removing the lens
- Foreign body sensation
- Excessive tearing/ocular secretions including mucopurulent discharge
- Ocular hyperemia

- Photophobia
- Burning, stinging, itching, or other pain associated with the eyes
- Comfort is less compared to when the lens was first placed on the eye
- Poor VA/blurred vision
- Rainbows or halos around objects
- Feeling of dryness

Subjects should be instructed to remove the lenses if any of the above signs or symptoms are noticed. A serious condition such as a corneal ulcer, infection, or iritis may be present, and may progress rapidly. Less serious reactions such as abrasions, infiltrates, and bacterial conjunctivitis must be managed to avoid more serious complications. In addition, the Investigator should advise subjects of possible ocular dryness, increased lens awareness/intolerance, and visual changes with concomitant medications or during pregnancy.

It is important for OFPM and CCP users to follow directions and all labeling instructions for proper use, including use of the lens case. Subjects who are noncompliant and fail to follow the instructions for cleaning, storage, and disinfection of their contact lenses could experience an eye infection or injury. Contact lens wearers unfamiliar with a hydrogen peroxide solution (CCP) could inadvertently use the peroxide solution as a lubricating/rewetting drop or rinse their contact lenses prior to insertion, resulting in chemical burn due to the unneutralized peroxide solution. Additionally, using the wrong lens cup, overfilling the lens cup with peroxide solution or disinfecting the lenses for less than the specified time can result in incomplete neutralization of the peroxide solution. In such cases, adverse ocular effects such as discomfort, burning, stinging, pain, inflammation or irritation as well as chemical burn or irritation to the fingers may occur. These adverse effects are usually temporary, and users should be instructed to immediately flush the eyes or fingers with saline or water should this occur. Overall, the potential risks associated with use of the subject's Habitual SiHy/MPS, AOHG/OFPM, and AOHG/CCP are similar when used as indicated.

5.3 Potential Benefits

Contact lenses may offer improved peripheral vision and the convenience of not wearing spectacles. Proper use of lens care solutions can promote safe and comfortable lens wear. Material properties and design characteristics of contact lenses and lens care solutions used in this study are features consistent with the successful contact lens wear.

6 ETHICS

This clinical study will be conducted in accordance with the principles of the Declaration of Helsinki, and in compliance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) E6 GCP Consolidated Guideline and other regulations as applicable. The Investigator and all clinical study staff will conduct the clinical study in compliance with the protocol. The Investigator will ensure that all personnel involved in the conduct of the study are qualified to perform their assigned responsibilities through relevant education, training, and experience.

Before clinical study initiation, this protocol, the informed consent form (and assent form, if applicable), any other written information given to subjects, and any advertisements planned for subject recruitment must be approved by an Independent Ethics Committee/Institutional Review Board (IEC/IRB). The Investigator must provide documentation of the IEC/IRB approval to the Sponsor. The approval must be dated and must identify the applicable protocol, amendments (if any), informed consent form, assent form (if any), all applicable recruiting materials, written information for subject, and subject compensation programs. The IEC/IRB must be provided with a copy of the Investigator's Brochure, any periodic safety updates, and all other information as required by local regulation and/or the IEC/IRB. At the end of the study, the Investigator will notify the IEC/IRB about the study's completion. The IEC/IRB also will be notified if the study is terminated prematurely. Finally, the Investigator will report to the IEC/IRB on the progress of the study at intervals stipulated by the IEC/IRB.

Voluntary informed consent will be obtained from every subject (and/or legal representative, as applicable) prior to the initiation of any screening or other study-related procedures. The Investigator must have a defined process for obtaining consent. Specifically, the Investigator, or designee, will explain the clinical study to each potential subject and the subject must indicate voluntary consent by signing and dating the approved informed consent form. The subject must be provided an opportunity to ask questions of the Investigator, and if required by local regulation, other qualified personnel. The Investigator must provide the subject with a copy of the consent form written in a language the subject understands. The consent document must meet all applicable local laws and will provide subjects with information regarding the purpose, procedures, requirements, and restrictions of the study, along with any known risks and potential benefits associated with the investigational product, the available compensation, and the established provisions for maintaining confidentiality of personal, protected health information. Subjects will be told about the voluntary nature of participation in the study and will be provided with contact information for the appropriate individuals should questions or concerns arise during the study. The subject also will be told that their

records may be accessed by appropriate authorities and Sponsor-designated personnel. The Investigator must keep the original, signed copy of the consent and must provide a duplicate copy to each subject.

7 PROTOCOL AMENDMENTS

Modification of the protocol is prohibited without prior written agreement in the form of a protocol amendment. All amendments will be created by the Sponsor and must be approved by the IEC/IRB prior to implementation except when required to mitigate immediate safety risks or when the changes involve only logistical or administrative revisions.

Amendments may necessitate that the informed consent form and other study-related materials be revised. If the informed consent form is revised, all subjects currently enrolled in the study may be required by the IRB to sign the approved, revised informed consent form.

There are no amendments, as this is the original version of protocol LCW773-P001.

8 SUBJECT POPULATION

The study population includes approximately 256 subjects to be randomized at approximately 8 sites, with approximately 14 to 50 subjects randomized per site. To participate in the study, subjects must be 18 years old or older, current full-time wearer [redacted] of samfilcon A, comfilcon A, senofilcon C monthly replacement or senofilcon A 2-week replacement spherical lenses within the power range of lens powers available for the test AOHG, and currently using (during the past 1 month) a MPS (excluding OFPM) to care for their lenses. Approximately 64 subjects per habitual lens type will be randomized and recruitment of brands by sites will be competitive.

Subjects must sign the informed consent form. Subjects must be willing to discontinue artificial tears during the study and rewetting drops on the days of study visits. [redacted] The complete inclusion and exclusion criteria are presented in Section 1.

The enrollment for the study is planned for approximately 8 weeks. The expected duration of subject participation in the study is up to 40 days and treatment will be 30 (+3) days for all subjects [redacted]

An advertisement may be used to aid recruitment. If an advertisement is required, the advertisement will be submitted to the IRB for approval.

9 TREATMENTS ADMINISTERED

Upon signing the informed consent, subjects will be considered enrolled in the study and a subject identification (ID) number will be assigned by entering the subject into the electronic data capture (EDC) system by a designated staff member at the investigational site(s). The qualified subject will be randomized and assigned to either AOHG or Habitual SiHy lenses in a 1:1 ratio. Subjects in the AOHG lens group will be further randomized and assigned to either OFPM or CCP in a 1:1 ratio.

[redacted]

Throughout the study, the designated unmasked site personnel will be responsible for the accounting of all study products and will ensure that the study products are not used in any unauthorized manner.

9.1 Identity of Study Treatments

Test Products:	AIR OPTIX plus HYDRAGLYDE (AOHG)
	OPTI-FREE PUREMOIST (OFPM)
	CLEAR CARE Plus/AOSEPT Plus with HYDRAGLYDE (CCP)
Control Products:	Johnson & Johnson ACUVUE® OASYS® Brand 2-Week with HYDRACLEAR® PLUS (Oasys)
	Johnson & Johnson ACUVUE® VITA™ Brand Contact Lenses (Vita)
	Bausch + Lomb ULTRA™ Contact Lenses with MoistureSeal™ Technology (Samfilcon A) (Ultra)
	CooperVision® Biofinity® Contacts (Biofinity)
	Habitual MPS (HMPS)

The study lenses will be procured by the investigational site(s). All study lenses are *Conformité Européene* (CE)-marked, FDA and Health Canada approved, and will be sourced from commercial stock, including commercial packaging and labelling. Assigned lenses will be masked to the Investigator and subject. This will be accomplished by an unmasked

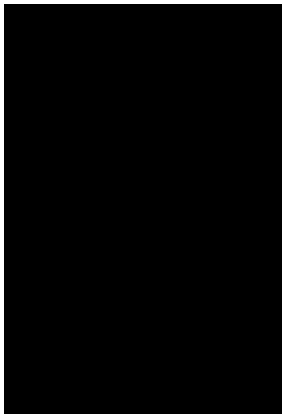
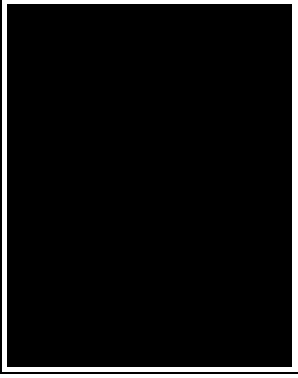
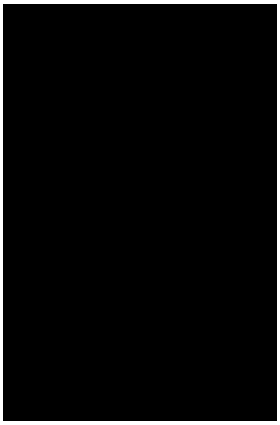
coordinator dispensing the commercially packaged study lenses assigned to the subject with the blister label removed.

OFPM will be supplied in sterile 10 fl. Oz. (300 mL) filled bottles with investigational labelling. A new lens case will be supplied with each bottle.

CCP will be supplied in sterile 12 fl. Oz. (355 mL) filled bottles with investigational labelling. A new lens case will be supplied with each bottle.

Table 9-1 Study Treatment OFPM and CCP

Properties	**OFPM (Test product)**	**CCP (Test product)**	**HMPS (Control product)**
Administration	Subjects will use OFPM to store and disinfect their contact lenses as instructed by the study site personnel, dispensing the solution according to the instructions for use.	Subjects will use CCP to store and disinfect their contact lenses as instructed by the study site personnel, dispensing the solution according to the instructions for use.	Subjects will use their HMPS to store and disinfect their contact lenses as instructed by the study site personnel, dispensing the solution according to the instructions for use.
Duration of Treatment	The subject will wear their assigned lenses in a daily wear modality for 30 (+3) days using OFPM daily to care for their lenses.	The subject will wear their assigned lenses in a daily wear modality for 30 (+3) days using CCP daily to care for their lenses.	The subject will wear their assigned lenses in a daily wear modality for 30 (+3) days using their HMPS daily to care for their lenses.
Quantity/Dosage	Up to 32 cleaning and disinfecting cycles will be used for the study.	Up to 32 cleaning and disinfecting cycles will be used for the study.	Up to 32 cleaning and disinfecting cycles will be used for the study.
Supply	OFPM will be supplied sterile, in 10- fl. Oz. (300 mL) filled bottles with	CCP will be supplied sterile, in 12 fl. Oz. (355 mL) filled bottles with investigational	HMPS will either be: 1) Purchased by the subject and reimbursed. The

	investigational labelling. A new lens case will be supplied with each bottle. The product is manufactured by Alcon Laboratories in Fort Worth, Texas. The study kit will contain one bottle of the test solution (bottle will be re-labeled), and green and white screw top case. 	labelling. A new lens case will be supplied with each bottle. The product is manufactured by Alcon Laboratories in Fort Worth, Texas. The study kit will contain one bottle of the test solution (bottle will be re-labeled), and the lens cup that contains platinum disk for neutralization of the solution. Marketed sterile saline (B&L SENSITIVE EYES PLUS SALINE in commercial packaging) will be provided separate from the kit by the unmasked study coordinator to each subject to use for rinsing lenses and cases as needed. 	unmasked site personnel must confirm at Visit 2 that the solution purchased by the subject was the HMPS identified during screening and that is not expired. 2) Purchased by the site according to the HMPS identified during screening and dispensed to the subject for use during the study. HMPS will be dispensed/used in commercial packaging. The manufacturer information for each product can be found in the package insert. 

		[redacted]	

OFPM and CCP will be provided in the commercial bottle but will be re-labeled in local language. Included on the investigational labels for the randomized product will be the kit number, protocol number, fill volume, storage conditions, the indicator "Disinfecting Solution" and a statement that the product is for investigational use only. OFPM and CCP should be stored at room temperature or below.

Additionally, the following warning will be included on the investigational label for CCP: "IMPORTANT: Misuse will result in burning and stinging. Use only lens case provided. Do not remove lenses from the lens case for at least 6 hours. The solution needs time to neutralize. Never rinse lens with product prior to insertion. Red snap cap means product is not for direct use on eye."

More information on the OFPM, CCP, or HMPS can be found in the Product Labeling. Refer to the MOP for product labels for OFPM and CCP.

The new label will be sufficient to mask the OFPM and CCP, thus maintaining the subject masking to brand. A designated unmasked staff member (other than the Investigator) at the site will be assigned to dispense the sealed test kit and the HMPS to ensure Investigator masking. Unmasked site personnel cannot conduct study specific procedures.

9.2 Usage

The subjects will use the study lenses bilaterally according to the Instructions for Use provided by the product manufacturer, as instructed by the designated site personnel. All study lenses will be dispensed by a trained, unmasked staff member and provided to the subjects.

The subjects will wear the assigned lenses (AOHG or Habitual SiHy) [redacted]. Subjects assigned to the senofilcon A 2-week replacement lenses will be asked to return to the site to be dispensed in a masked manner [redacted]. All unplanned lens replacements must be documented in EDC.

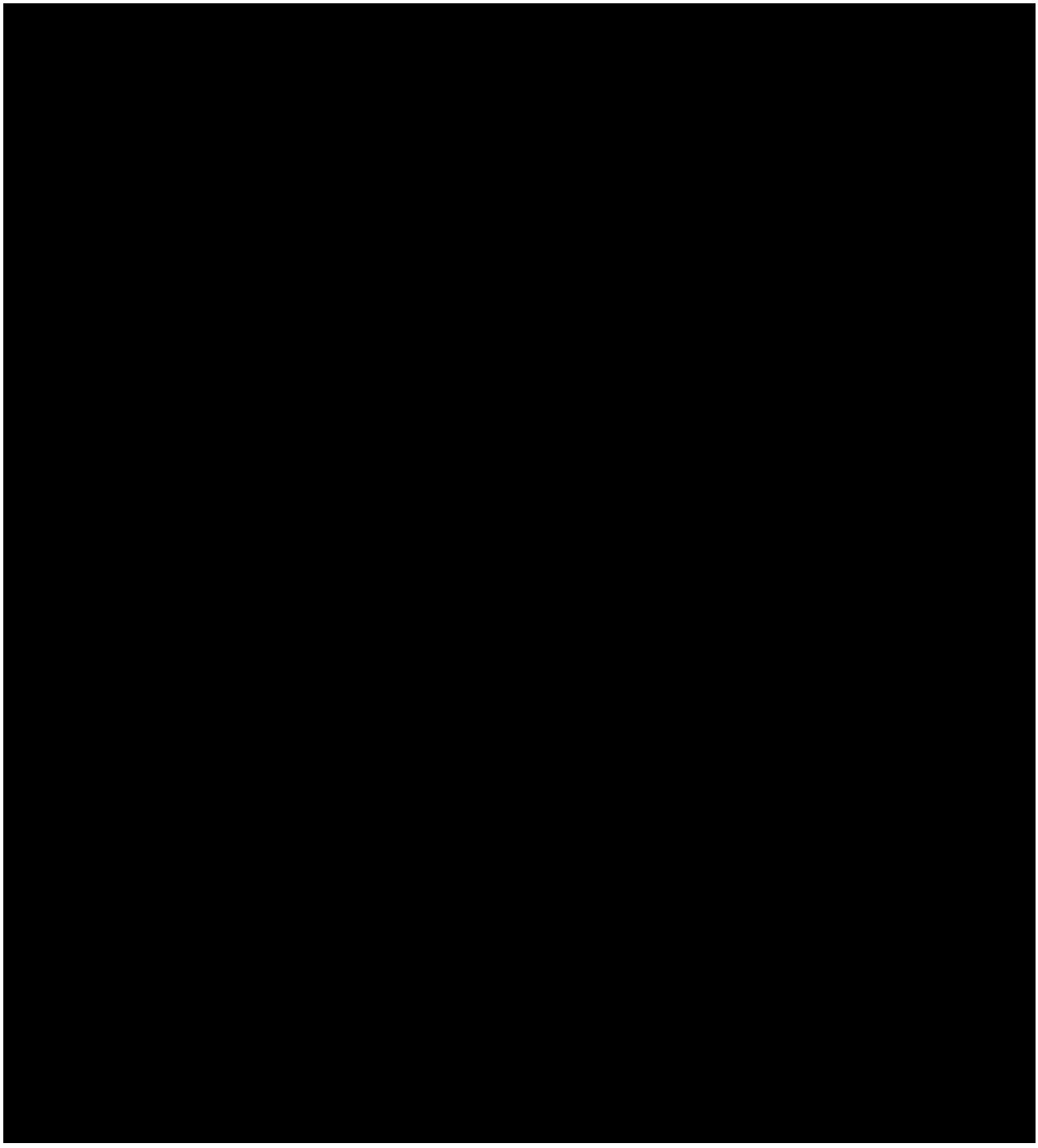
Subjects assigned to the AOHG lenses will be instructed to care for the lenses daily using either OFPM or CCP, according to randomized assignment of product. Subjects assigned CCP will be provided with B&L SENSITIVE EYES PLUS SALINE as a rinsing solution. AOHG lens care solutions will be provided by the Sponsor. Subjects assigned to the Habitual

SiHy lenses will be instructed to care for the lenses daily using their HMPS according to the products' instructions for use. A new bottle of the HMPS to be used for the study will either be purchased by the subjects and confirmed by the masked investigational site personnel or purchased by the site.

[redacted]

[redacted]

[redacted]



10 STUDY PROCEDURES

10.2 Visits and Examinations

10.2.1 Visit 1 – Screening

	Note: Potential subjects should be instructed to attend Visit 1 (Screening) wearing their habitual contact lenses and to bring their HMPS (used or unused bottle).
1	Have the subject or legally authorized representative read, sign, and date the IEC-approved informed consent document. Additionally, have the individual obtaining consent from the subject and a witness, if applicable, sign and date the informed consent document. Provide a photocopy of the signed document to the subject and place the original signed document in the subject's chart.
2	Enter the subject into EDC in order to obtain their 5-digit subject ID number. *Note*: Obtain subject ID number for all subjects who signed an informed consent form (including screen failures).

3	Obtain demographic information, contact lens and lens care history, and medical history, including information on all medications used within the past 30 days. Include herbal therapies, vitamins, and all over-the-counter as well as prescription medications.
4	[redacted]
5	[redacted]
6	
7	
8	[redacted]
9	Perform biomicroscopy assessment using slit-lamp examination scales. For details and order of staining procedures, refer to MOP.
10	Assess and record any AEs that are observed or reported from the time of informed consent (see Section 12).

11	Review inclusion/exclusion criteria to determine if the subject qualifies to be randomized in the study. The unmasked site personnel must confirm randomization by entering applicable details of eligibility in the EDC system and obtain assignment of study lens/lens care treatment group.
12	Schedule Visit 2 (Day 1 Insertion) within 1-7 days of Visit 1 (Screening).
13	Remind subjects that spectacles or habitual contact lenses/lens care solutions can continue to be used until the day prior to Visit 2. Habitually worn lenses can be returned or a new pair dispensed. [redacted] Subjects randomized to habitual SiHy/MPS must have a new bottle of the HMPS, identified during screening, ready for dispensing at Visit 3. This can be accomplished in two ways for the study: 1) The subject purchases a new bottle of the HMPS and brings it to Visit 2. In this case the subject will be reimbursed for their purchase. The unmasked coordinator must confirm the solution purchased was the HMPS identified during screening and that it is not expired. The unmasked coordinator will dispense the purchased HMPS at Visit 3. 2) The site purchases the subject's HMPS and the unmasked coordinator dispenses to the subject at Visit 3.

10.2.2 Visit 2 (1-7 Days from Visit 1) – Day 1 Insertion Visit

1	Obtain information on any changes in medical health and/or the use of concomitant medications since previous visit.
2	Perform biomicroscopy assessment using slit-lamp examination scales with no conjunctival/corneal staining procedures. Refer to MOP for details.
3	[redacted]

4	Unmasked coordinator to dispense randomized study lenses. Record time of lens insertion.
5	[redacted]
6	[redacted]
7	[redacted]
8	
9	[redacted]
10	Assess and record any AEs that are observed or reported (see Section 12).

11	Record any Device Deficiencies that are observed or reported (see Section 12).
12	[redacted]

10.2.3 Visit 3 - Day 1: after approximately 8 hrs (± 30 mins)

	Note: Subjects must respond to the 8 hrs text message questionnaire prior to proceeding with Visit 3.
1	Obtain information on any changes in medical health and/or the use of concomitant medications since previous visit.
2	[redacted]
3	Perform biomicroscopy assessment with lenses on the eye using slit-lamp examination scales with no conjunctival/corneal staining procedures. Refer to MOP for details.
4	[redacted]

5	[redacted]
6	Unmasked coordinator to assign and dispense study lens care solutions - Ensure test solutions are provided per randomized group assignment - masked label to subjects. - HMPS to be purchased by subject or provided by site. Subject/site will be reimbursed. Site to confirm correct unexpired HMPS dispensed if subject is purchasing the HMPS. - Review product instructions for use with subjects. Educate subjects assigned to CCP product and B&L SENSITIVE EYES PLUS SALINE on the use of correct lens case with the product.
7	Assess and record any AEs that are observed or reported (see Section 12).
8	Record any Device Deficiencies that are observed or reported (see Section 12).
9	Unmasked coordinator to instruct subjects assigned the 2-week replacement lenses to return to site on Day 15 (±1 Day). Schedule lens replacement in office. Collect initial 2-week lenses. Refer to MOP for details. Unmasked coordinator to dispense replacement 2-week lenses. [redacted]

10	[redacted]

10.2.4 Visit 4 - Day 30 (+3 days): 8 hrs (±30 min)/Exit

	Note: Ensure subjects answered the 6 hrs text message questionnaire based on lenses worn during Day 30 prior to proceeding with Visit 4.
1	[redacted]
2	Obtain information on any changes in medical health and/or the use of concomitant medications since Visit 3.
3	[redacted]
4	[redacted]
5	[redacted]

6	[redacted]
7	[redacted]
8	Assess and record any AEs that are observed or reported (see Section 12).
9	Record any device deficiencies that are observed or reported (see Section 12).
10	Collect worn study lenses for shipment and analysis. Record time of lens removal. Refer to MOP for details.
11	Exit the subject from the study.

[redacted]

[redacted]

10.4 Discontinued Subjects

Discontinued subjects are those who withdraw or are withdrawn from the study after being randomized. Subjects may discontinue from the study at any time for any reason. Subjects may also be discontinued from the study at any time if, in the opinion of the Investigator, their continued participation poses a risk to their health. Discontinued subjects will not be replaced (ie, their subject numbers will not be re assigned/re-used).

If a subject is identified not to fulfill the eligibility criteria for study inclusion during the Screening visit [redacted], the subject will be screen failed and will not participate any further in the study. The EDC system will be updated to confirm the subject is a screen failure. The Investigator will explain to the subject the reason(s) why eligibility was not met and provide appropriate information/treatment, if required. The Exit form will be completed for all discontinued subjects and screen failures.

Should a subject exhibit any clinically relevant signs, symptoms, or other clinical observations that possibly could be associated with suspected sensitivity or intolerance to one of the study treatments, the Investigator must document those observations on an AE Form. Observations must also be reported for occurrences not associated with any study treatment (see Section 12.3, Procedures for Recording and Reporting AEs and SAEs).

Any subject who exits early from the study should undergo all procedures outlined at [redacted]/Exit. Additionally, the Exit Form must be completed and the reason for discontinuation must be identified and captured in EDC.

Finally, to ensure the safety of all subjects who discontinue early, Investigators should assess each subject and, if necessary, advise them of any therapies and/or medical procedures that might be needed to maintain their health.

10.5 Clinical Study Termination

If the clinical study is prematurely terminated or suspended, the Sponsor will inform the Investigator and the regulatory authorities of the termination/ suspension and the reason(s) for the termination/suspension. The Investigator should promptly notify the IEC/IRB of the termination or suspension and of the reasons. The Sponsor reserves the right to close the investigational site or terminate the study in its entirety at any time, for reasonable cause. Reasons for the closure of an investigational site or termination of a study may include:

- Successful completion of the study
- The study's enrollment goals are met
- The Investigator fails to comply with the protocol or GCP guidelines
- Safety concerns
- Sufficient data suggesting lack of efficacy
- Inadequate recruitment of subjects by the Investigator

The Investigator also may terminate the study at his/her site for reasonable cause. If the Sponsor terminates the study for safety reasons, it will immediately notify the Investigator(s) by telephone and subsequently will provide written confirmation of and instructions for study termination.

11 ANALYSIS PLAN

11.1 Subject Evaluability

The final subject evaluability will be determined prior to breaking the code for masked treatment assignment and locking the database.

11.2 Analysis Data Sets

11.2.1 Safety Data Set

Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis. The safety analysis set will include all subjects/eyes exposed to the study lens and/or the study lens care system (LCS) evaluated in this study as a regimen. For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual lens or regimen exposed.

11.2.2 Full Analysis Data Set

The FAS is the set of all randomized subjects who are exposed to a study lens on Day 1 or a study regimen (lens and LCS) thereafter.

[redacted]

11.3 Demographic and Baseline Characteristics

Demographic information (age, sex, ethnicity, race) will be summarized on the safety, full, [redacted]

11.4 Efficacy Analyses

This study defines one primary endpoint [redacted]. All efficacy evaluations will use the FAS as the primary analysis set. [redacted]

[redacted]

11.4.1 Primary Efficacy

The primary objective of this study is to demonstrate less cholesterol uptake with each of the test regimens (AOHG/OFPM, AOHG/CCP) compared to each of the control regimens (Biofinity/HMPS, Vita/HMPS, Ultra/HMPS, Oasys/HMPS).

The corresponding endpoint is the cholesterol uptake (deposits) measured from worn lenses at Day 30 (2-week wear of Oasys and 30-day wear for other), for each of the test and control regimens. OD lenses from approximately 25 subjects per regimen will be analyzed for the *ex vivo* analysis.

[redacted]

[redacted]

[redacted]

11.4.2 Secondary Efficacy

No secondary efficacy objective is defined for this study.

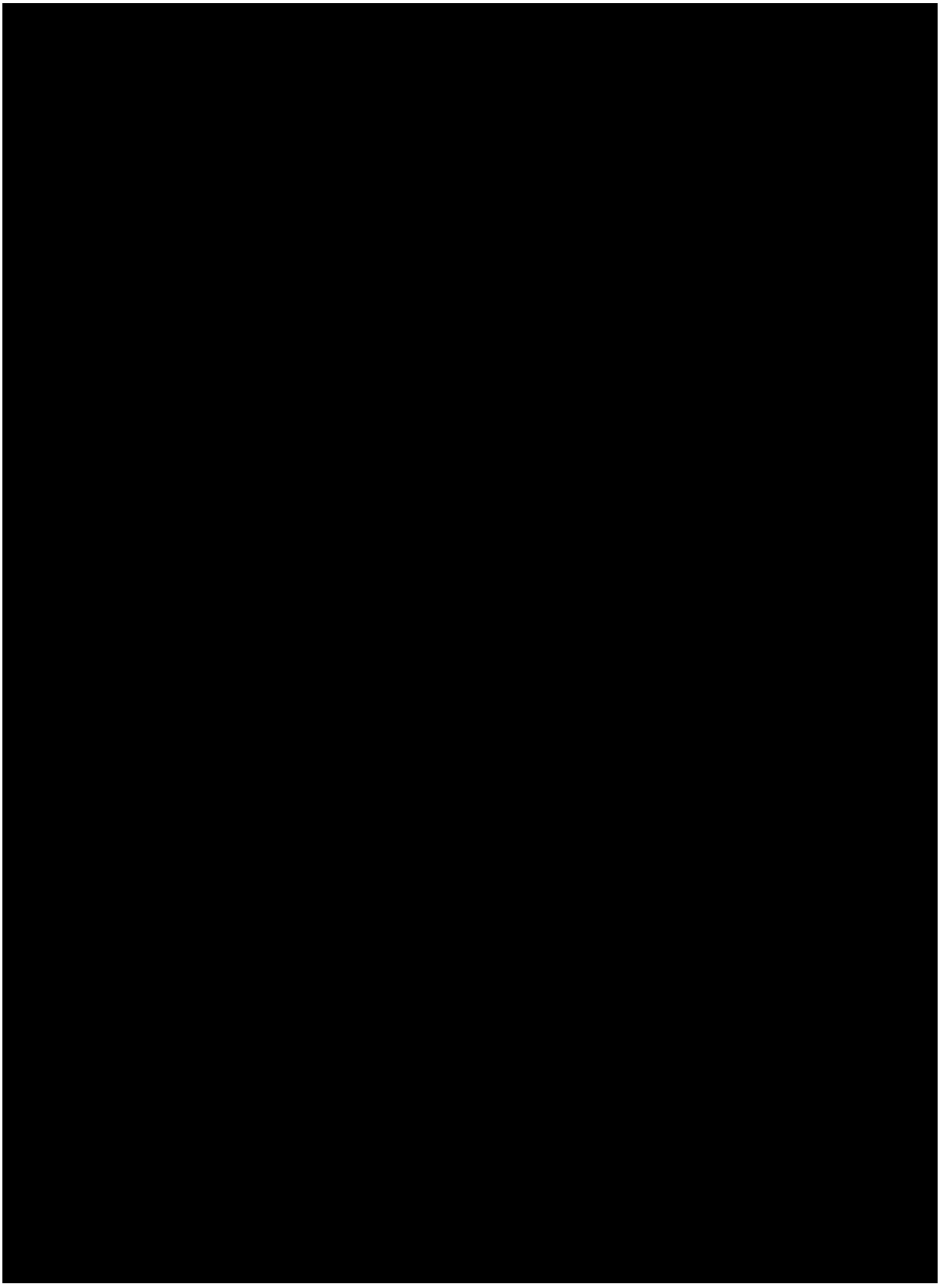
11.4.2.1 Statistical Hypotheses

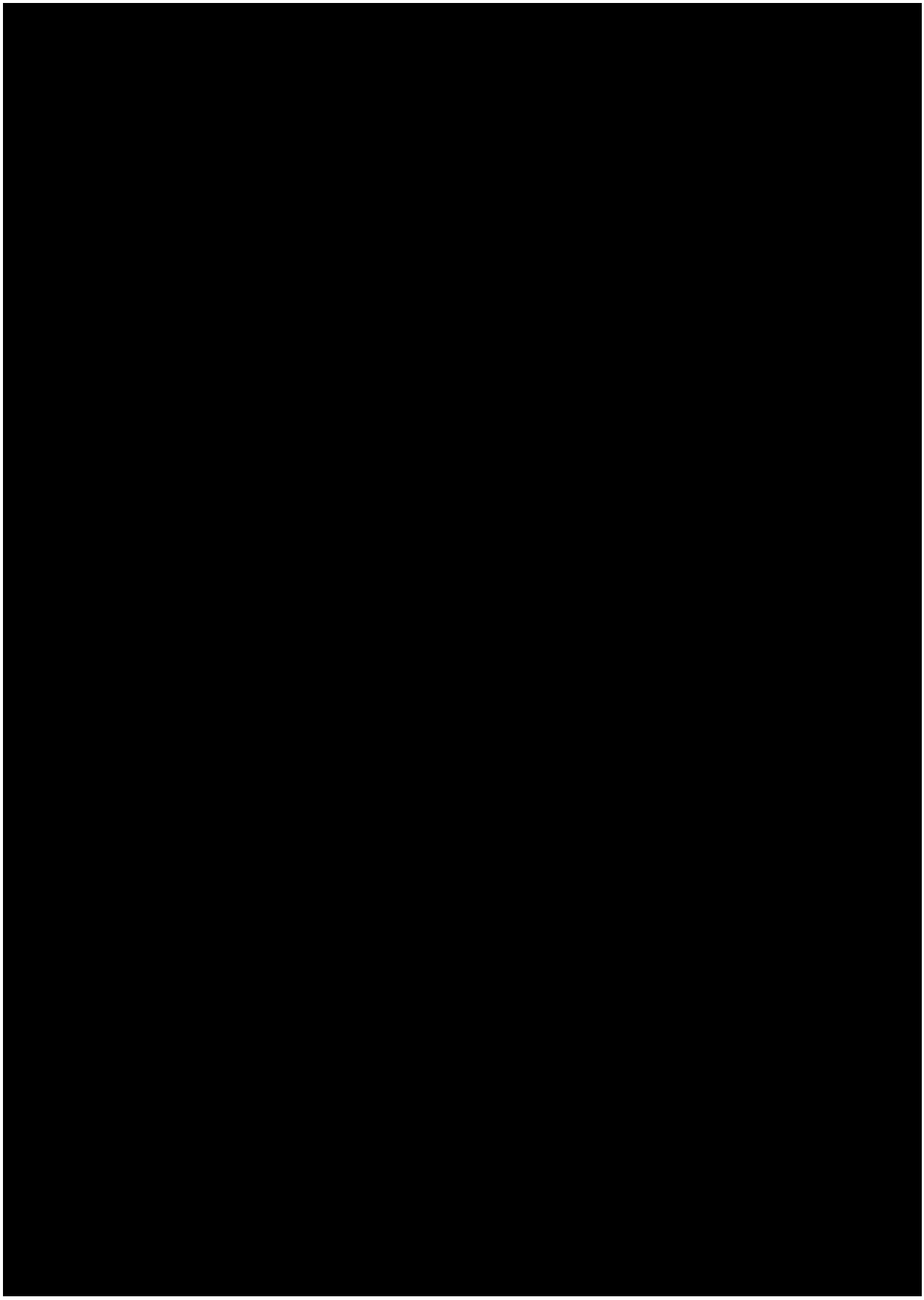
Not applicable.

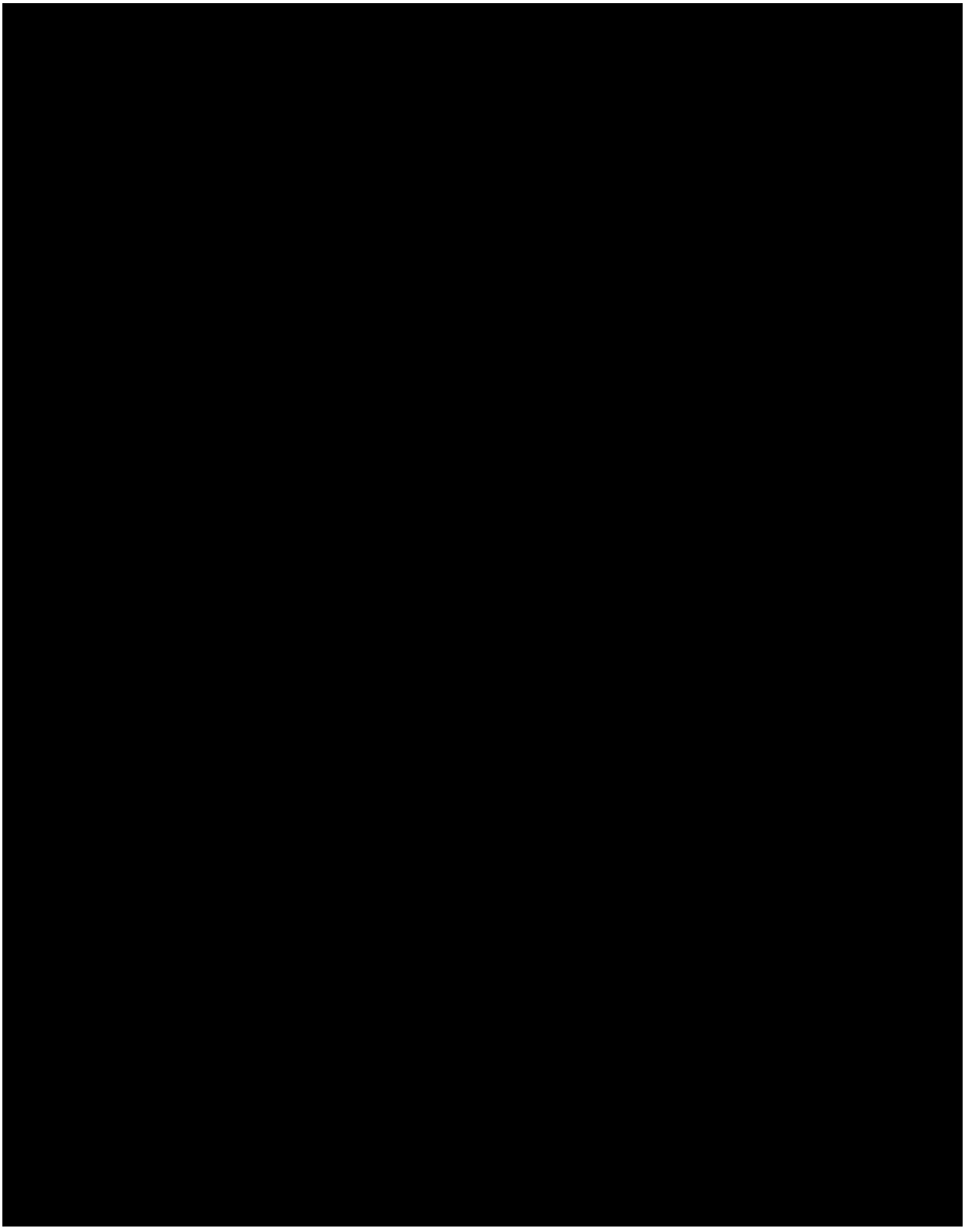
11.4.2.2 Analysis Methods

Not applicable.

[redacted]







11.5 Handling of Missing Data

All data obtained in evaluable subjects/eyes will be included in the analysis. No imputation for missing values will be carried out for the efficacy analysis.

11.7 Safety Analysis

The safety endpoints for this study are AEs, biomicroscopy findings, and device deficiencies. Data will be presented by regimen, T/C and T1/T2/C1/C2/C3/C4.

Descriptive summaries (counts and percentages) for ocular and nonocular AEs will be presented by Medical Dictionary for Regulatory Activities (MedDRA) Preferred Terms. In addition to an overall presentation of AEs, relationship to regimen (lens and/or LCS) will be identified. Serious AEs will also be tabulated separately. Individual subject listings will be provided, as necessary.

Additionally, individual subject listings will be provided for AEs that occur after signing informed consent but prior to exposure to study regimens (lens and/or LCS).

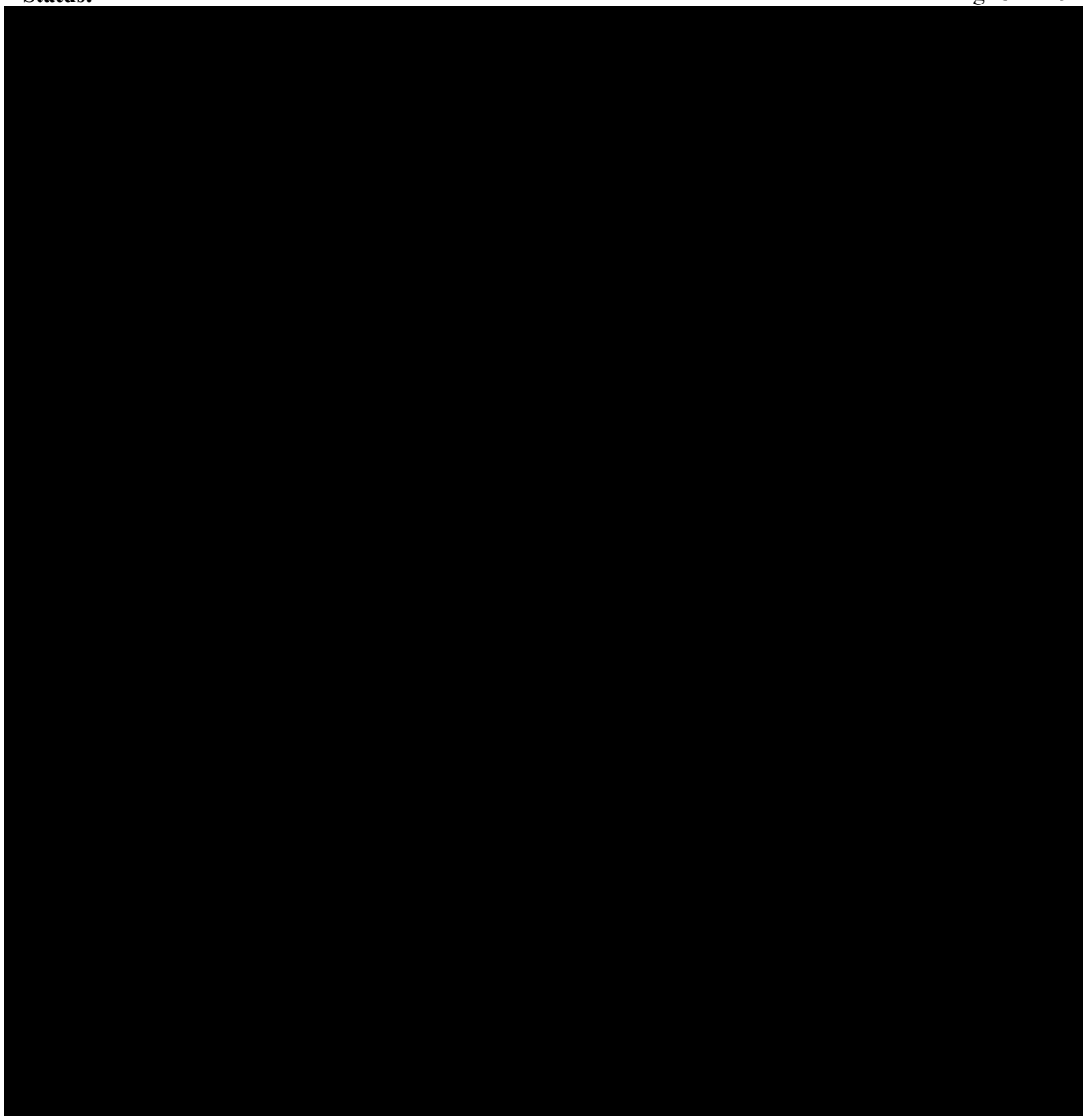
Each biomicroscopy parameter will be tabulated by its grade. For each biomicroscopy parameter, counts and percentages of eyes that experience an increase of ≥ 2 grades from baseline (Visit 1) to any subsequent visits will be presented. A supportive listing will be generated which will include all biomicroscopy data from the affected visit for those eyes experiencing the increase of ≥ 2 grades, with the following variables: regimen, Investigator, subject, age, sex, visit, eye, parameter, baseline value, and value at the visit.

Frequency counts will be tabulated for each device deficiency category. Additionally, 2 listings will be provided: prior to exposure to study regimens (lens and/or LCS) and treatment-emergent.

No inferential testing will be done for safety analysis.

11.8 Health Economics

Not applicable.



12 ADVERSE EVENTS

12.1 General Information

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 (test article). Refer to the Glossary of Terms for categories of AEs and SAEs.

Figure 12–1 Categorization of All Adverse Events

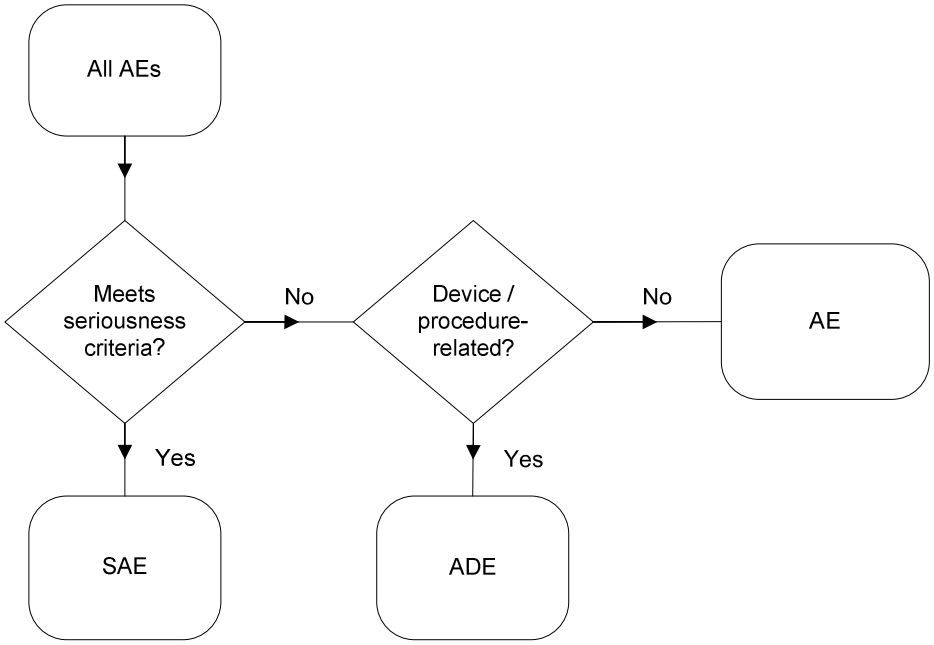
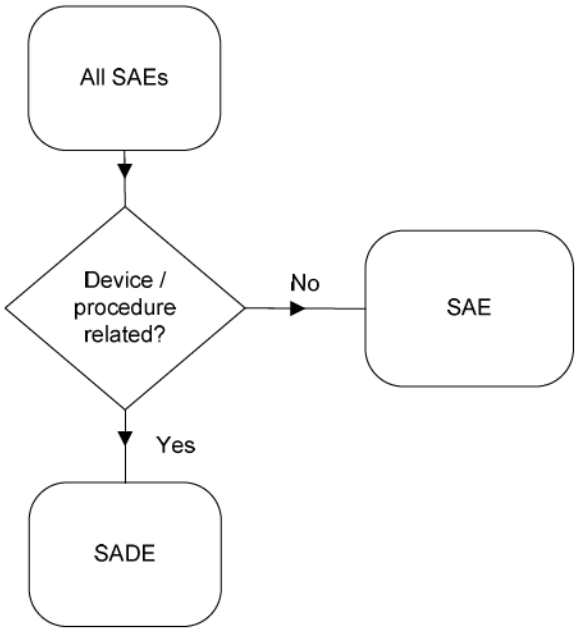


Figure 12-2 Categorization of All Serious Adverse Events



12.2 Monitoring for Adverse Events

At each visit, after the subject has had the opportunity to spontaneously mention any problems, the Investigator should inquire about AEs by asking the standard questions:

- "Have you had any health problems since your last study visit?"
- "Have there been any changes in the medicines you take since your last study visit?"

Changes in *biomicroscopy parameters and/or subject questionnaires* evaluated during the study are to be reviewed by the Investigator. Any untoward (unfavorable and unintended) change that is clinically relevant, in the opinion of the Investigator, is to be reported as an AE. These clinically relevant changes will be reported regardless of causality.

12.3 Procedures for Recording and Reporting AEs and SAEs

AEs are collected from the time of informed consent. Any pre-existing medical conditions or signs/symptoms present in a subject prior to the start of the study (ie, before informed consent is signed) are not considered AEs in the study and should be recorded in the Medical History section of the eCRF.

In addition, temporary lens awareness or visual changes during the fitting process are not considered AEs if the Investigator assesses that the symptom(s) can reasonably resolve within the anticipated adaptation period.

For each recorded event, the ADEs and SAEs documentation must include: date of occurrence, severity, treatment (if applicable), outcome, and assessments of the seriousness and causality. In addition, the Investigator must document all device deficiencies observed or reported with test and control articles on the Device Deficiency eCRF. The site must submit all available information on ADEs, SAEs, and device deficiencies to the Study Sponsor immediately as follows:

- All SAEs must be reported immediately (within 24 hours) of the Investigator's or site's awareness.
- ADEs that do not meet seriousness criteria and device deficiencies must be reported within 10 calendar days of the Investigator's or site's awareness.
- A printed copy of the completed ***Serious Adverse Event and Adverse Device Effect*** and/or ***Device Deficiency*** eCRF must be included with product returns. Refer to MOP for product return details.
- Additional relevant information after initial reporting must be entered into the eCRF as soon as the data become available.
- Document any changes to concomitant medications on the appropriate eCRFs.
- Document all relevant information from Discharge Summary, Autopsy Report, Certificate of Death etc., if applicable, in narrative section of the Adverse Device Effect (for related AEs) and Serious Adverse Event eCRF.

Note: Should the EDC system become non-operational, the site must complete the appropriate paper ***Serious Adverse Event and Adverse Device Effect*** and/or ***Device Deficiency*** Form. The completed form is emailed to the Study Sponsor to [redacted] according to the timelines outlined above; however, the reported information must be entered into the EDC system once it becomes operational.

Any AEs and device deficiencies for non-study marketed devices/products will be considered and processed as spontaneous (following the postmarket vigilance procedures) and should be communicated to the device's/product's manufacturer as per local requirements.

Study Sponsor representatives may be contacted for any protocol related question and their contact information is provided in the MOP that accompanies this protocol.

Further, depending upon the nature of the AE or device deficiency being reported, the Study Sponsor may request copies of applicable portions of the subject's medical records. The Investigator must also report all AEs and device deficiencies that could have led to a SADE according to the requirements of regulatory authorities or IRB/IEC.

12.4 Intensity and Causality Assessments

Where appropriate, the Investigator must assess the intensity (severity) of the AE based on medical judgment with consideration of any subjective symptom(s), as defined below:

Intensity (Severity):

Mild	An AE is mild if the subject is aware of but can easily tolerate the sign or symptom.
Moderate	An AE is moderate if the sign or symptom results in discomfort significant enough to cause interference with the subject's usual activities.
Severe	An AE is severe if the sign or symptom is incapacitating and results in the subject's inability to work or engage in their usual activities.

For every AE in the study, the Investigator must assess the causality (Related or Not Related to the medical device or study procedure). An assessment of causality will also be performed by Study Sponsor utilizing the same definitions, as shown below:

Causality:

Related	An AE classified as related may be either definitely related or possibly related where a direct cause and effect relationship with the medical device or study procedure has not been demonstrated, but there is a reasonable possibility that the AE was caused by the medical device or study procedure.
Not Related	An AE classified as not related may either be definitely unrelated or simply unlikely to be related (ie, there are other more likely causes for the AE).

The Study Sponsor will assess the AEs and may upgrade the Investigator's assessment of seriousness and/or causality. The Study Sponsor will notify the Investigator of any AEs that is upgraded from non-serious to serious or from unrelated to related.

12.5 Return product analysis

Study Sponsor representatives and their contact information are provided in the MOP that accompanies this protocol.

Alcon products associated with device deficiencies and/or product related AEs should be returned and must include the Complaint # which will be provided by Study Sponsor after the case is entered in the Study Sponsor's Global Product Complaint Management System.

12.6 Unmasking of the Study Treatment

Masked information on the identity of the assigned medical device should not be disclosed during the study (see Section 9). If the treatment code needs to be broken in the interest of subject safety, the Investigator is encouraged to contact an appropriate Study Sponsor representative prior to unmasking the information if there is sufficient time. Dependent upon the individual circumstances (ie, medical emergency), the code may be broken prior to contact with the Study Sponsor. The Study Sponsor must be informed of all cases in which the code was broken and of the circumstances involved. Additionally, the Study Sponsor may be required to unmask the information in order to fulfill expedited regulatory reporting requirements.

12.7 Follow-Up of Subjects with Adverse Events

The Investigator is responsible for adequate and safe medical care of subjects during the study and for ensuring that appropriate medical care and relevant follow-up procedures are maintained after the study.

The Investigator should provide the Study Sponsor with any new safety information (which includes new AEs and changes to previously reported AEs) that may affect the safety evaluation of the device. For AEs that are unresolved/ ongoing at time of subject exit from study, any additional information received at follow-up should be documented in the eCRFs up to study completion (ie, database lock).

All complaints received after this time period will be considered and processed as spontaneous (following the postmarket vigilance procedures) and should be communicated to the medical device's manufacturer as per local requirements.

The Investigator should also report complaints on non-Alcon products directly to the manufacturer as per the manufacturer's instructions or local regulatory requirements.

12.8 Pregnancy in the Clinical Trial

Pregnancy is not reportable as an AE; however, complications may be reportable and will be decided on a case–by-case basis.

13 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

13.1 Completion of Source Documents and Case Report Forms

The nature and location of all source documents will be identified to ensure that original data required to complete the CRFs exist and are accessible for verification by the site monitor. If electronic records are maintained, the method of verification must be determined in advance of starting the study. At a minimum, source documents should include the following information for each subject:

- Subject identification (name, sex, race/ethnicity)
- Documentation of subject eligibility
- Date of informed consent
- Dates of visits
- Documentation that protocol specific procedures were performed
- Results of study parameters, as required by the protocol
- Trial medication accountability records
- Documentation of AEs and other safety parameters (if applicable)
- Records regarding medical histories and the use of concomitant therapies prior to and during the study
- Date of trial completion and reason for early discontinuation, if applicable

It is required that the author of an entry in the source documents be identifiable. Direct access to source documentation (medical records) must be allowed for the purpose of verifying that the data recorded on the CRF are consistent with the original source data.

Electronic CRFs (eCRFs) will be provided to the sites; only designated individuals may complete the eCRFs. The eCRFs will be submitted at regular intervals based upon the clinical trial visit schedule. It is expected that all data reported will have corresponding entries in the source documents and that the Principal Investigator will review the reported data and certify that the eCRFs are accurate and complete. No subject identifiers should be recorded on the eCRFs beyond subject number, and demographic information.

Deviations from this protocol, regulatory requirements, and GCP must be recorded in the study records. An explanation of the deviation should be included, as applicable. In addition,

corrective and preventive action should be identified, implemented, and documented within the study records.

13.2 Data Review and Clarifications

The CRF data will be reviewed against the subject's source data by the study monitors to ensure completeness and accuracy. After monitoring has occurred at the clinical sites and the CRFs have been submitted, additional data clarifications and/or additions may be needed. Data clarifications and/or additions are documented and are part of each subject's CRFs.

13.3 Regulatory Documentation and Records Retention

The Investigator is required to maintain up-to-date, complete regulatory documentation as indicated by the Sponsor and the Investigator's files will be reviewed as part of the ongoing study monitoring. Financial information is not subject to regulatory inspection and should be kept separately.

Additionally, the Investigator must keep study records and source documents until the Sponsor provides written approval for their destruction. If the Investigator retires, relocates, or for any other reason withdraws from responsibility of keeping the study records, the Sponsor must be notified and suitable arrangements made for retention of study records and source documents needed to comply with national and international regulations (generally 2 years after discontinuing clinical development or after the **latest** marketing approval).

13.4 Clinical Trial Results

All data and discoveries arising out of the study, patentable or non-patentable, shall be the sole property of Alcon, Inc. Alcon reserves the right of prior review of any publication or presentation of information related to the study. Alcon may use these data now and in the future for presentation or publication at Alcon's discretion or for submission to government regulatory agencies.

14 References

Keir N, Jones L. Wettability and silicone hydrogel lenses: a review. Eye Contact Lens. 2013;39(1):100–8.

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15 APPENDIX

There are no appendices for this protocol. Please refer to the MOP.

Date/Time (mm/dd/yyyy GMT):	Signed by:	Justification:
12/15/2016 22:49:55	[redacted]	[redacted]
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