Title

Multifocal Visual Performance Study - Seamless transition with Precision Profile MF lenses

Protocol Number:	CLT792-P001/ NCT03757039
Development Stage of Project:	Product Support
Sponsor Name and Address:	Alcon Research, Ltd. and its affiliates ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099
Test Products:	○ AIR OPTIX® plus HydraGlyde® (lotrafilcon B) Multifocal (AOHG MF) contact lenses ○ DAILIES TOTAL1® (delefilcon A) Multifocal (DT1 MF) contact lenses ○ DAILIES® AquaComfort Plus® (nelfilcon A) Multifocal (DACP MF) contact lenses

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, all applicable regulatory authority regulations, and conditions of approval imposed by the reviewing IRB or regulatory authority.
- I will supervise all testing of the device involving human subjects and ensure that the requirements relating to obtaining informed consent and IRB review and approval are met in accordance with applicable local and governmental regulations.
- I have read and understand the appropriate use of the investigational product(s) as described in the protocol, current Investigator's Brochure, product information, or other sources provided by the Sponsor.
- I understand the potential risks and side effects of the investigational product(s).
- I agree to maintain adequate and accurate records in accordance with government regulations and to make those records available for inspection.
- I agree to comply with all other requirements regarding the obligations of clinical Investigators and all other pertinent requirements of the Sponsor and government agencies.
- I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed of their obligations in meeting the above commitments.

Have you ever been disqualified as an Investigator by any Regulatory Authority? ☐ No ☐Yes
Have you ever been involved in a study or other research that was terminated? ☐ No ☐Yes If yes, please explain here:

Principal Investigator:

Signature Date

Name and professional position:

Address:

Table of Contents

List of Tables

[redacted]

List of Figures

1 GLOSSARY OF TERMS

Names of Test Product(s)	Throughout this document, test product(s) will be referred to as: - AOHG MF - DT1 MF - DACP MF
Name of Control Product(s)	Progressive addition lens spectacles (PALs)
Adverse Device Effect	Adverse event related to the use of an investigational medical device (test product) or control product. *Note: This definition 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 product or control product.*
Adverse Event	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 product). *Note: For subjects, this definition includes events related to the test product, the control product, or the procedures involved. For users or other persons, this definition is restricted to events related to the test product.* Requirements for reporting Adverse Events in the study can be found in Section 11.
Anticipated Serious Adverse Device Effect	Serious adverse device effect which by its nature, incidence, severity, or outcome has been identified in the risk management file.
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.* Requirements for reporting Device Deficiencies in the study can be found in Section 11.
Enrolled Subject	Any subject who signs an informed consent form for participation in the study.
Interventional Clinical Trial	A research trial that prospectively assigns, whether randomly or not, human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes, and/or a research trial in which diagnostic or monitoring procedures beyond standard of care

	are conducted and generate outcomes for use in analysis of data.
Investigational Product	Is defined as a preventative (vaccine), a therapeutic (drug or biologic), device, diagnostic, or palliative used as a test or control product in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the authorized form, or when used for an unauthorized indication, or when used to gain further information about the authorized form.
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.
Non-serious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.
Postmarketing/Post-authorization study	Any study conducted within the conditions laid down in product labelling and other conditions laid down for the marketing of the product or under normal conditions of use. A postmarketing study falls either within the definitions of an interventional or a non- interventional study and may also fall within the definition of a post-approval study.
Product Complaints	Any oral, electronic, or written communication that alleges deficiencies related to the identity (labeling), quality, durability, reliability, safety, effectiveness, or performance of a marketed product, including failure of the product, labeling or packaging to meet specifications, whether or not the product is related to or caused the alleged deficiency. A complaint may allege that an adverse event or medical device malfunction has occurred.
Randomized Subjects	Any subject who is assigned a randomized treatment.
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Serious Adverse Event (SAE)	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 11 for additional SAEs.*
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 (HIV) or Bird Flu.

Significant Non-Serious Adverse Event	Is a symptomatic, device-related, non-sight threatening adverse event that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks. *Refer to Section 11 for additional Significant Non-Serious AEs.*
Unanticipated Serious Adverse Device Effect (USADE)	Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the risk management file.
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 LIST OF ACRONYMS AND ABBREVIATIONS

Table 2–1 List of Acronyms and Abbreviations Used in This Protocol

Abbreviation	Definition
ADD	Addition
ADE	Adverse device effect
AE	Adverse event
AOHG MF	AIR OPTIX plus HydraGlyde Multifocal contact lenses
BCVA	Best corrected visual acuity
CFR	Code of Federal Regulations
CL	Contact lens
cm	Centimeter
COL	Clinical Operations Lead
CRF	Case report form
CSM	Clinical Site Manager
D	Diopter(s)
DACP MF	DAILIES AquaComfort Plus Multifocal contact lenses
DT1 MF	DAILIES TOTAL1 Multifocal contact lenses
eCRF	Electronic case report form
EDC	Electronic data capture
FAS	Full analysis set
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
HIV	Human immunodeficiency virus
ICF	Informed consent form
ICH	International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent ethics committee
IP	Investigational product
IRB	Institutional review board
IRT	Interactive response technology
ISO	International Organization for Standardization
logMAR	Logarithm of the minimum angle of resolution
m	Meter
MF	Multifocal
mm	Millimeter

Abbreviation	**Definition**
MOP	Manual of procedures
n	Number
N/A	Not applicable
NI	Noninferiority
OD	Right eye
OS	Left eye
OU	Both eyes
PAL	Progressive addition lens spectacles
PP	Per protocol analysis set
SAE	Serious adverse event
SADE	Serious adverse device effect
SD	Standard deviation
US	United States
USADE	Unanticipated serious adverse device effect
VA	Visual acuity

3 PROTOCOL SUMMARY

Investigational product type	Device
Study type	Interventional
Investigational products	Test Products: • AIR OPTIX plus HydraGlyde (lotrafilcon B) Multifocal (AOHG MF) contact lenses • DAILIES TOTAL1 (delefilcon A) Multifocal (DT1 MF) contact lenses • DAILIES AquaComfort Plus (nelfilcon A) Multifocal (DACP MF) contact lenses Control Product: • Progressive addition lens spectacles (PALs)
Purpose and rationale	The purpose of this trial is to demonstrate noninferiority in functional visual performance of Alcon´s Precision Profile MF contact lenses compared to PALs in a presbyopic population.
Objective(s)	The overall objective is to demonstrate noninferiority of multifocal (MF) contact lenses versus PALs in the transition time [redacted] The primary objective is to demonstrate noninferiority in transition time between distance and intermediate vision with MF contact lenses compared to PALs. [redacted]
Endpoint(s)	Primary effectiveness endpoint: • Average transition time during alternate distance (4 m) and intermediate (80 cm) viewing

Safety

- Adverse events (AEs)
- Biomicroscopy findings
- Device deficiencies

Assessment(s)	Effectiveness [redacted] Safety • AEs • Biomicroscopy • Device deficiencies

Study Design	This is a prospective, randomized, parallel group study measuring the average transition time during alternate distance (4 m) and intermediate (80 cm) viewing. Habitual contact lens wearers will be randomized to either AOHG MF, DACP MF, or DT1 MF contact lenses. This will be a double-masked trial for the contact lens group. PAL wearers will not be masked. Subjects will be expected to attend 1or 2 office visits (Visit 2 may be performed on the same day immediately following Visit 1). All study contact lenses will be dispensed according to the subject's prescription and fitted using the Alcon MF fitting guide. PAL wearers will wear their habitual spectacles.
Subject population	Presbyopic subjects aged ≥ 38 and ≤ 58 years with normal eyes (other than correction for refractive error), whose habitual correction is either any MF contact lens (with a preference for Alcon Precision Profile Design wearers) with a LO or MED ADD (or equivalent to an ADD of max +2.00 D) or progressive addition lens spectacles. Wear of habitual correction must be at least 5 days per week and at least 6 hours per day. Planned number of subjects enrolled: ~ 60 Required number of completed subjects: 48 (12 per group)
Key inclusion criteria (See Section 8.1 for a complete list of inclusion criteria)	Presbyopic subjects aged ≥ 38 and ≤ 58 years with normal eyes (other than correction for refractive error), whose habitual correction is either any MF contact lens (with a preference for Alcon Precision Profile Design wearers) with a LO or MED ADD (or equivalent to an ADD of max +2.00 D) or progressive addition lens spectacles. Wear of habitual correction must be at least 5 days per week and at least 6 hours per day.
Key exclusion criteria (See Section 8.2 for a complete list of exclusion criteria)	Monocular subjects or subjects fit with only one contact lens. Known pregnancy or lactating. History of or planned refractive surgery or irregular cornea in either eye.

<table>
<tr><td>Data analysis and sample size justification</td><td>
Planned Analysis
To address the primary effectiveness objective, planned analysis is summarized below:
<table>
<tr><td>Endpoint</td><td>Comparison</td><td>Statistical Method</td></tr>
<tr><td>Primary</td><td></td><td></td></tr>
<tr><td>Average transition time between distance and intermediate</td><td>MF lenses vs PALs</td><td>Generalized linear model
NI margin = 0.5 second</td></tr>
</table>
[redacted]
No inferential testing will be performed for the safety analyses.
Sample Size Justification
Sample size calculation for the primary effectiveness endpoint (one-sided $\alpha = 0.05$) is summarized below:
<table>
<tr><td>Primary Endpoint</td><td>Assumptions</td><td>Power</td><td>N/group</td></tr>
<tr><td>Average transition time between distance and intermediate</td><td>Common SD = 0.456
NI margin = 0.5</td><td>80%</td><td>12</td></tr>
</table>
</td></tr>
<tr><td>Key words</td><td>Presbyopic, multifocal</td></tr>
<tr><td>Associated materials</td><td>Lubrication/re-wetting drops will not be permitted within 2 hours prior to study Visit 2.</td></tr>
</table>

Table 3–1 Schedule of Study Procedures and Assessments

	ALL SUBJECTS	MULTIFOCAL CONTACT LENS WEARERS	PROGRESSIVE ADDITION LENS SPECTACLE WEARERS	ALL SUBJECTS
Visit	**Visit 1/ Screening**	**Visit 2/ Exposure/Exit**	**Visit 2/ Exposure/Exit**	**Unscheduled Visit**
Procedure/Assessment	**Day 1 (May be performed same day as Visit 2)**	**0-14 Days from Visit 1**	**0-14 Days from Visit 1**	
Informed Consent	✓			
Demographics	✓			
Medical History	✓	✓	✓	✓
Concomitant Medications	✓	✓	✓	✓
Inclusion/Exclusion	✓	✓	✓	
Randomize		✓		
Habitual correction (type/brand, power)		✓	✓	
[redacted]		[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]
Dispense study contact lenses in a masked manner		✓		
[redacted]		[redacted]	[redacted]	

	ALL SUBJECTS	MULTIFOCAL CONTACT LENS WEARERS	PROGRESSIVE ADDITION LENS SPECTACLE WEARERS	ALL SUBJECTS
Visit	**Visit 1/ Screening**	**Visit 2/ Exposure/Exit**	**Visit 2/ Exposure/Exit**	**Unscheduled Visit**
Procedure/Assessment	**Day 1 (May be performed same day as Visit 2)**	**0-14 Days from Visit 1**	**0-14 Days from Visit 1**	
[redacted]				
[redacted]		■	■	
[redacted]		■	■	
[redacted]		■	■	
[redacted]		■		
[redacted]		■	■	
[redacted]		■		
[redacted]		■	■	
[redacted]		✓		
Transition time during alternate distance (4 m) and intermediate (80 cm) viewing		✓	✓	

	ALL SUBJECTS	MULTIFOCAL CONTACT LENS WEARERS	PROGRESSIVE ADDITION LENS SPECTACLE WEARERS	ALL SUBJECTS
Visit	**Visit 1/ Screening**	**Visit 2/ Exposure/Exit**	**Visit 2/ Exposure/Exit**	**Unscheduled Visit**
Procedure/Assessment	**Day 1 (May be performed same day as Visit 2)**	**0-14 Days from Visit 1**	**0-14 Days from Visit 1**	
[redacted]		■	■	■
[redacted]		■	■	■
[redacted]		■	■	■
[redacted]		■	■	■
AEs	✓	✓	✓	✓
Device deficiencies	✓	✓		(✓)
Exit form†	(✓)	✓	✓	(✓)

(✓) assessment performed as necessary, eg, decrease of VA by 2 lines or more with investigational product (IP)
*source only; † must be performed as a screening assessment and prior to study exit

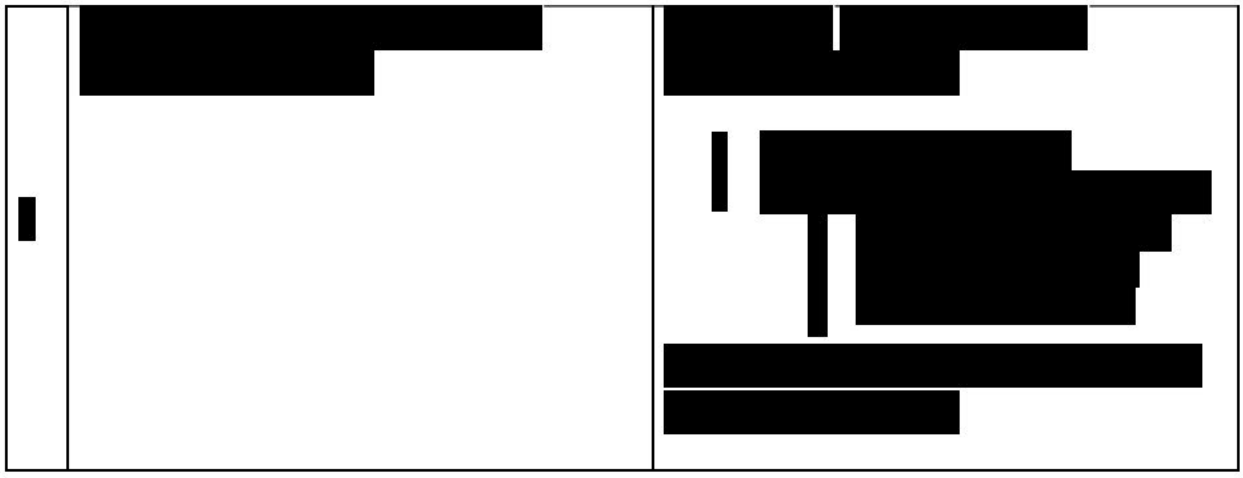
4 PROTOCOL AMENDMENTS

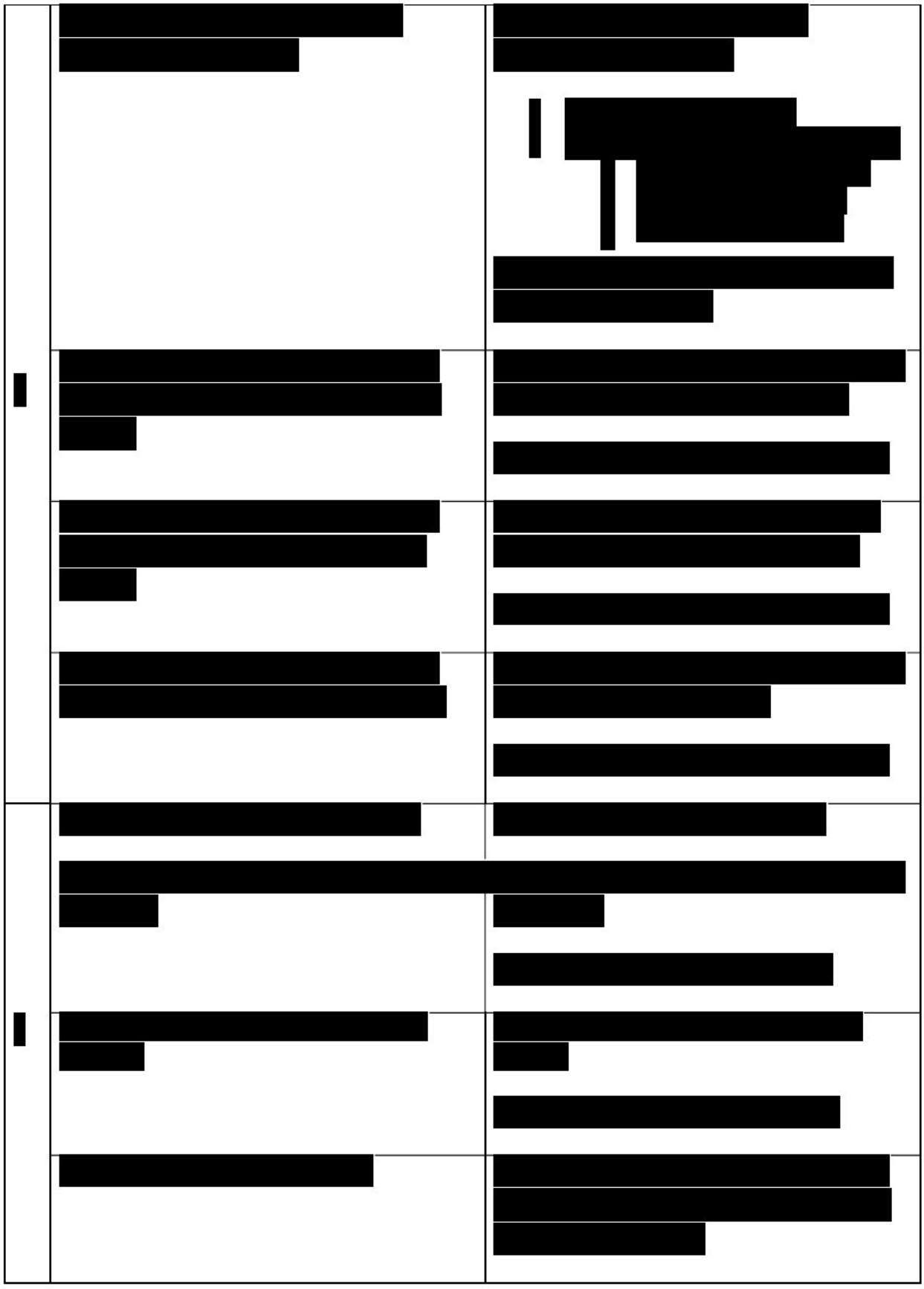
Modification of the protocol is prohibited without prior written agreement in the form of a protocol amendment. All amendments must be created by the Study Sponsor and must be approved by the IRB/IEC and global and regional Health Authorities, as applicable, prior to implementation except when required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

Amendments may necessitate that the informed consent and other study-related material be revised. If the consent form is revised, all subjects currently enrolled in the study must sign the approved, revised informed consent (re-consent), as required by the IRB/IEC.

4.1 Amendments

[redacted]





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	[redacted]	[redacted]
	[redacted]	[redacted]
	[redacted]	[redacted]
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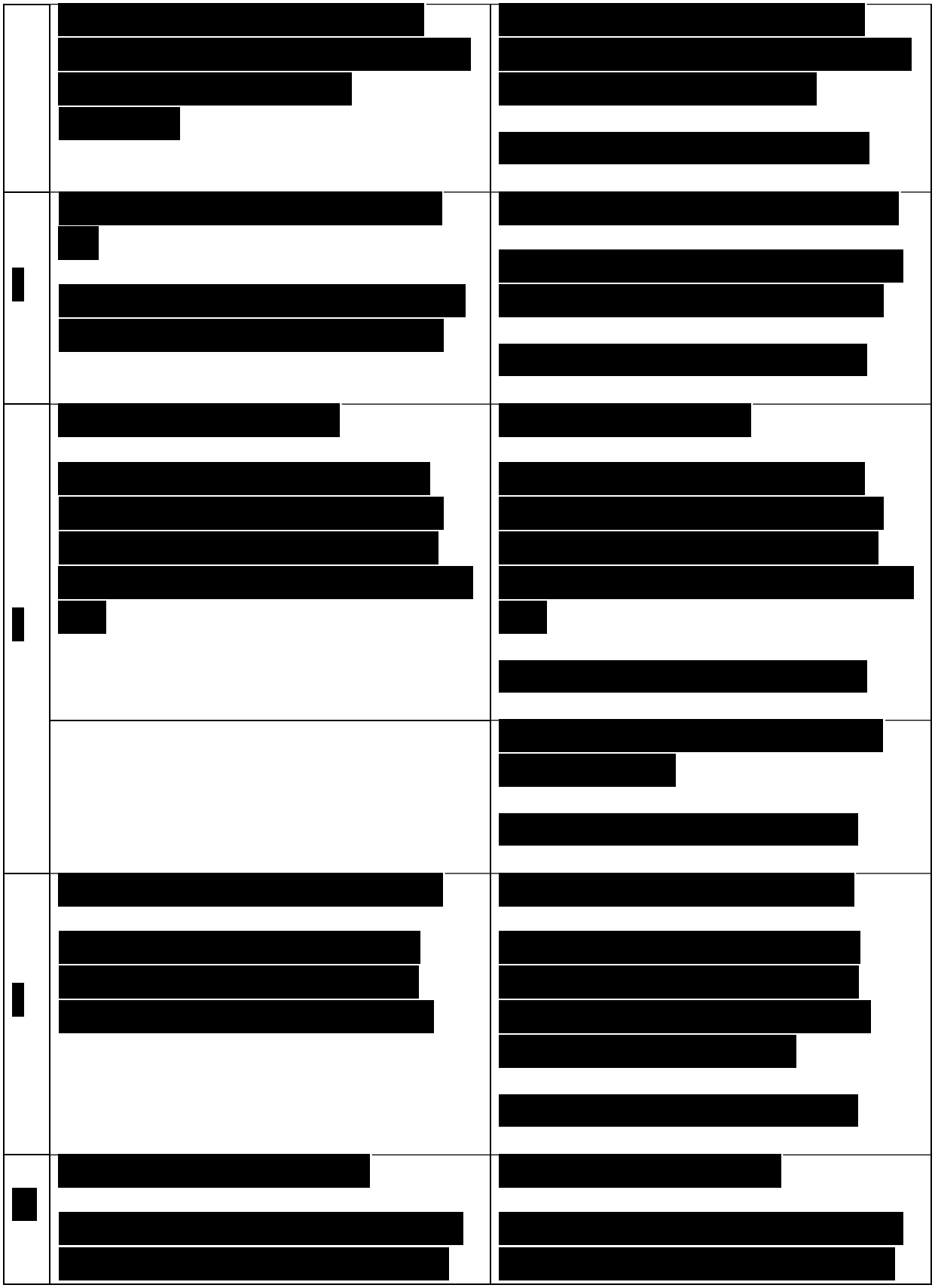
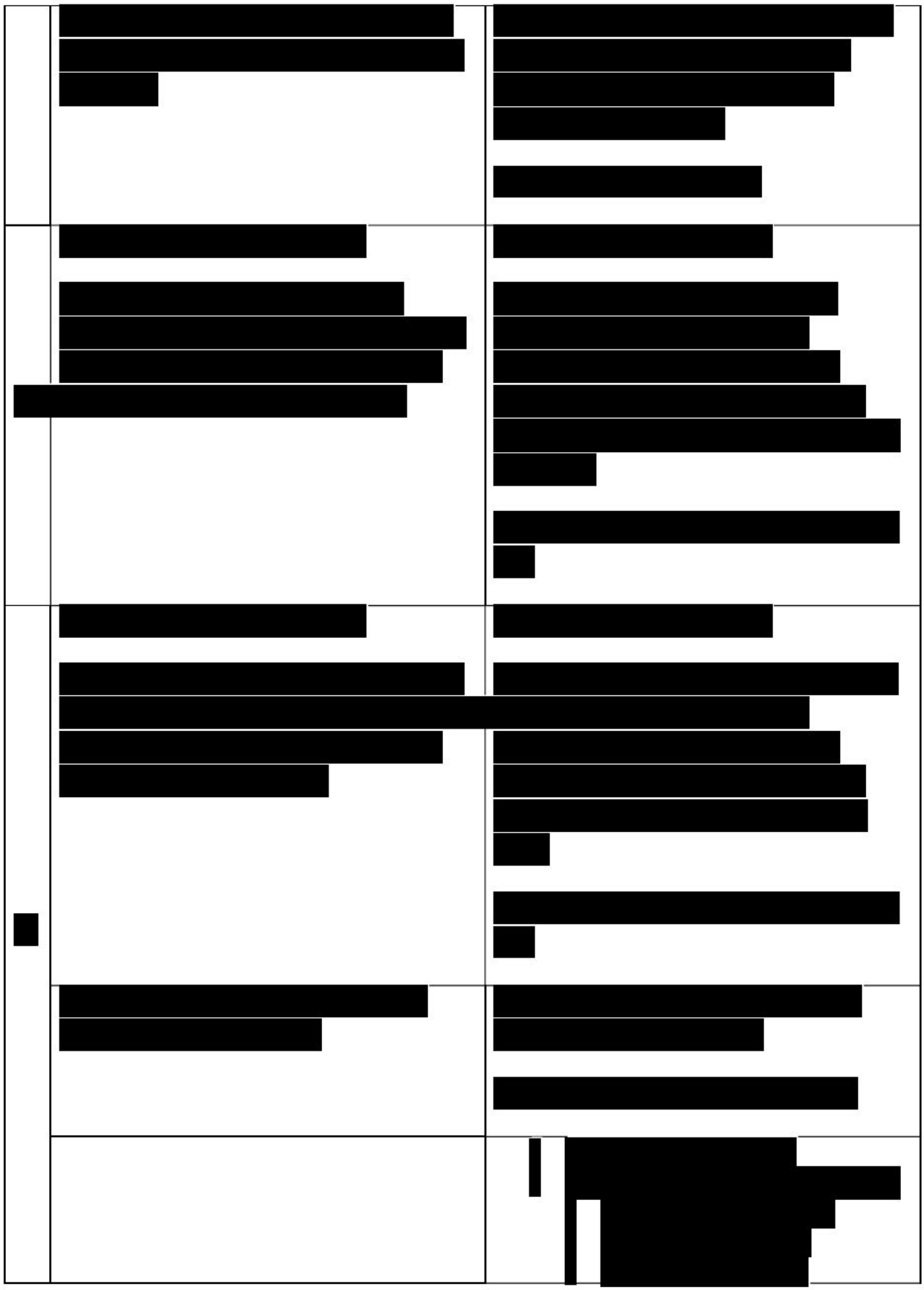




		[redacted]
	[redacted]	[redacted]
	[redacted]	[redacted]

5 INTRODUCTION

5.1 Rationale and Background

Presbyopia is an age-related vision condition in which the crystalline lens gradually loses its ability to change shape when acted upon by the ciliary muscle. It typically becomes evident by 40 to 45 years of age and it is expressed by a reduction in the ability to define letters or objects at near distance. The condition can be corrected by the use of single-vision or bifocal spectacles, PALs, or MF contact lenses.

Alcon manufactures three MF contact lenses (lotrafilcon B, nelfilcon A, and delefilcon A) with the same Precision Profile optical design that allows for the same fitting process with all three lenses. The AOHG MF soft contact lenses are made of a lens material that is approximately 33% water and 67% lotrafilcon B, a fluoro-silicone containing hydrogel which is surface-treated. These lenses may be prescribed for daily wear or extended wear for up to 6 nights of continuous wear with removal for disposal, or cleaning and disinfection prior to reinsertion, as recommended by the eye care professional.

The DACP MF daily disposable, soft contact lens is made up of 69% water and 31% nelfilcon A polymer (polyvinyl alcohol partially acetalized with N-formylmethyl acrylamide). DT1 MF (delefilcon A) daily disposable, soft contact lenses feature a unique water gradient composition from a silicone-rich highly breathable core (33% water) to an ultrasoft hydrophilic surface gel (> 80% water at the lens surface).

The goal of this study is to demonstrate seamless transition [redacted] vision in presbyopes using Precision Profile Design MF contact lenses.

5.2 Purpose of the Study

The purpose of this postmarket study is to generate 'real world' visual performance data to demonstrate a fast transition time when reading from digital devices [redacted] using Alcon's Precision Profile Design contact lenses. The Alcon MF lenses will be compared to PALs. [redacted]

At the end of the study, a clinical study report will be prepared in accordance with applicable regulatory requirements and standards.

[redacted]

5.3 Risks and Benefits

A summary of the known and potential risks and benefits associated with AOHG MF, DACP MF, and DT1 MF contact lenses can be found in their respective package inserts. Safety information about AOHG MF, DACP MF, and DT1 MF contact lenses may be found in their respective product labeling.

There may also be unknown risks to use of AOHG MF contact lenses, DT1 MF contact lenses, or DACP MF contact lenses. Any risk to subjects in this clinical study will be minimized by compliance with the eligibility criteria and study procedures, clinical oversight, and monitoring. In this study, the duration of the planned clinical exposure of the currently marketed MF contact lenses is up to 3 hours. Site personnel will educate subjects on proper hygiene and lens care, handling, and compliance with use of the study contact lenses, as applicable. Site personnel will advise the subjects to remove contact lenses and/or alert site staff for prompt follow-up if there are symptoms such as ocular discomfort, foreign body sensation, excessive tearing, vision changes, or hyperemia.

Refer to the product label for additional information.

6 STUDY OBJECTIVES

6.1 Primary Objective(s)

Table 6–1 Primary Objective(s)

Objective(s)	Endpoint(s)

The primary objective is to demonstrate noninferiority in transition time between distance and intermediate vision with MF contact lenses compared to PALs.	Average transition time during alternate distance (4 m) and intermediate (80 cm) viewing

6.2 Secondary Objective(s)

Not Applicable.

[redacted]

6.4 Safety Objective(s)

Table 6–3 Safety Objective(s)

Objective(s)	Endpoint(s)
Demonstrate the safety profile of the study products.	• Adverse events (Any AEs and device deficiencies for non-study marketed devices/products will be considered and processed as spontaneous (following the post-market vigilance procedures) and should be communicated to the device's/product's manufacturer as per local requirements.) • Biomicroscopy findings • Device deficiencies

7 INVESTIGATIONAL PLAN

7.1 Study Design

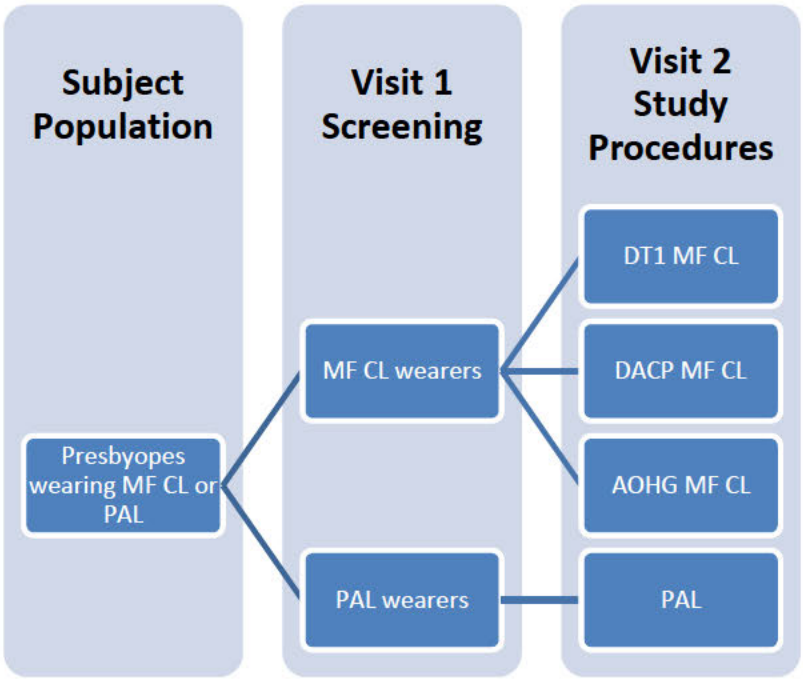
This is a prospective, randomized parallel group study measuring the average transition time

Habitual contact lens wearers will be randomized to either AOHG MF, DACP MF, or DT1 MF contact lenses. This will be a double-masked trial for the contact lens group. The PAL wearers will not be randomized and will wear their habitual PALs during the study. This group will not be masked. Investigators will be masked to the brand and type of PAL for habitual PAL wearers.

Subjects will be expected to attend 1 to 2 office visits (Visit 2 may be performed on the same day immediately following Visit 1). All study contact lenses will be prescribed according to the subject's prescription and fitted using the Alcon MF fitting guide. PAL wearers will wear their habitual spectacles. Subjects are expected to complete the study in approximately 2 to 3 hours.

The study is expected to be completed in approximately 8 weeks.

Figure 7-1 Study Design



7.2 Rationale for Study Design

In this study, the visual performance of the current marketed AOHG MF, DACP MF, and DT1 MF contact lenses will be assessed in a prospective, double-masked (for the contact lens group) design with up to 3 hours of exposure to the study lenses. The MF contact lens performance will be compared to the visual performance of PAL. The study design and the exposure duration of the study lenses is supported by the MF fitting guidelines for the Precision Profile Design contact lenses.

7.3 Rationale for Duration of Treatment/Follow-Up

The duration of exposure to the contact lenses was chosen to address the objective of this study, and is aligned with MF fitting guidelines for initial fit assessment following lens insertion.

7.4 Rationale for Choice of Control Product

PALs were chosen as the control product to address the study objectives. PALs are an alternative to MF contact lenses for the correction of presbyopia.

7.5 Data Monitoring Committee

Not applicable.

8 STUDY POPULATION

The study population consists of male or female subjects aged ≥ 38 and ≤ 58 with presbyopia. The aim is to enroll approximately 60 subjects at approximately 2 sites; 1 in the United Kingdom and 1 in the United States (US), with a target of 48 total subjects completed. Each site is expected to enroll approximately 30 subjects with a target of 24 completed (approximately 6 subjects per group at each site). Site-specific targets may vary based upon individual site capabilities. Estimated time needed to recruit subjects for the study is approximately 6 to 8 weeks. Because a 20% screening failure and/or discontinuation rate is expected, approximately 60 subjects are expected to be enrolled.

8.1 Inclusion Criteria

Written informed consent must be obtained before any study specific assessment is performed. Upon signing informed consent, the subject is considered enrolled in the study.

Subjects eligible for inclusion in this study must fulfill **all** of the following criteria:

1. Subject must be able to understand and sign an IRB/IEC approved Informed Consent form.

2. Willing and able to attend all scheduled study visits as required per protocol.

3. Subjects must be ≥ 38 and ≤ 58 years of age.

4. Current contact lens wearers (during the past 3 months for a minimum of 5 days per week and 6 hours per day) of any MF contact lens (with a preference for Alcon

Precision Profile Design wearers) with a LO or MED ADD (or equivalent to an ADD of max +2.00 D).

OR

Current PAL wearers (wearing spectacles for a minimum of 5 days per week and 6 hours per day) with a prescription check in the last 12 months and spectacles up to date based on the prescription check with an ADD no higher than +2.00 D and a spherical refractive error between -0.50 and -6.50 D.

5. Contact lens wearers: manifest cylinder (at screening) less than or equal to 0.75 D in each eye and a spherical refractive error (vertex distance 10-14mm) between -0.50 and -6.50 D

6. Subjects' BCVA vision with manifest refraction must be 0.1 (logMAR) or better in each eye at distance at Visit 2.

7. Willing to discontinue artificial tears and rewetting drops within approximately 2 hours prior to or during study Visit 2.

8.2 Exclusion Criteria

Subjects fulfilling **any** of the following criteria are not eligible for participation in this study.

1. Any anterior segment infection, inflammation, or abnormality or disease (including systemic) that contraindicates contact lens wear, as determined by the Investigator

2. Any use of systemic or ocular medications for which contact lens wear could be contraindicated, as determined by the Investigator.

3. History of refractive surgery or plan to have refractive surgery during the study or irregular cornea in either eye.

4. Ocular or intraocular surgery (excluding placement of punctal plugs) within the previous 12 months or planned during the study.

5. Biomicroscopy findings at screening that are moderate (Grade 3) or higher and/or corneal vascularization that is mild (Grade 2) or higher, and/or any infiltrate.

6. Current or history of pathologically dry eye in either eye that, in the opinion of the Investigator, would preclude contact lens wear.
7. Current or history of herpetic keratitis in either eye.
8. Eye injury in either eye within 12 weeks immediately prior to enrollment for this trial.
9. Current or history of intolerance, hypersensitivity or allergy to any component of the study products.
10. Any use of topical ocular medications and artificial tear or rewetting drops that would require instillation during contact lens wear.
11. The Investigator, his/her staff, family members of the Investigator, family members of the Investigator's staff, or individuals living in the households of the aforementioned persons may not participate in the study.
12. Participation of the subject in a clinical trial within the previous 30 days or currently enrolled in any clinical trial.
13. Monocular subjects (only one eye with functional vision) or subjects fit with only one contact lens.
14. Known pregnancy or lactating.

8.3 Rescreening of Subjects

Rescreening of subjects is not allowed in this study.

9 TREATMENTS ADMINISTERED

9.1 Investigational Product(s)

Test Product(s):

- AIR OPTIX plus HydraGlyde (lotrafilcon B) Multifocal (AOHG MF) contact lens
- DAILIES TOTAL1 (delefilcon A) Multifocal (DT1 MF) contact lens
- DAILIES AquaComfort Plus (nelfilcon A) Multifocal (DACP MF) contact lens

Control Product(s) (If applicable): Progressive addition lens spectacles

Table 9–1 Test Products

Test Product	AIR OPTIX plus HydraGlyde (lotrafilcon B) Multifocal – AOHG MF contact lens	DAILIES TOTAL1 (delefilcon A) Multifocal – DT1 MF contact lens	DAILIES AquaComfort Plus (nelfilcon A) Multifocal – DACP MF contact lens
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA		
Indication for use and intended purpose in the current study	The intended use of these contact lenses is for vision correction.		
Product description and parameters available for this study	Material: Lotrafilcon B Water content: 33% Power range: -0.50 to -6.00 D in 0.25 D steps Add: LO, MED Base curve (mm): 8.6 mm Diameter (mm): 14.2 mm	Material: Delefilcon A Water content: 33% core, > 80% surface Power range: -0.50 to -6.00 D in 0.25 D steps Add: LO, MED Base curve (mm): 8.5 mm Diameter (mm): 14.1 mm	Material: Nelfilcon A Water content: 69% Power range: -0.50 to -6.00 D in 0.25 D steps Add: LO, MED Base curve (mm): 8.7 mm Diameter (mm): 14.0 mm
Formulation	Information can be found in the associated package insert		
Study Usage	Wear:	Wear:	Wear:

	Daily Wear Bilateral Replacement period: N/A Exposure: approximately 2-3 hours Lens Care: N/A	Daily Wear Bilateral Replacement period: N/A Exposure: approximately 2-3 hours Lens Care: N/A	Daily Wear Bilateral Replacement period: N/A Exposure: approximately 2-3 hours Lens Care: N/A
Number/ Amount of product to be provided to the subject	One pair of study lenses will be provided to each subject in the contact lens group according to their randomization assignment. Replacement lenses will be available if needed. Multiple lenses may be used to fit the subject per the Alcon MF Fitting guide or investigator's discretion.		
Packaging description	Blister foil pack		
Labeling description	Commercial labeling		
Storage conditions	Refer to the package insert		
Supply	Each Site will procure study contact lenses. Refer to the MOP, Section 10.3, for additional details		

Table 9–2 Control Product

Control Product(s)	Progressive addition lens spectacles
Manufacturer	N/A
Indication for Use	Subjects will use their habitual progressive addition lens spectacles as instructed by their eye care professional.

Product description and parameters available for this study	Progressive addition lens spectacles
Formulation	N/A
Usage	N/A
Number/Amount of Product to be Provided to the subject	N/A
Packaging description	N/A
Labeling description	N/A
Storage conditions	N/A
Additional identifying information	N/A
Supply	Subject will provide their own habitual progressive addition spectacles

The study lenses must be maintained within specified environmental condition, per the labeling.

More information on the test products can be found in the Package Inserts, Directions for Use.

9.2 Other Medical Device or Medication Specified for Use During the Study

No other medical devices or medications are required to be used in conjunction with the treatments during the clinical study.

9.3 Treatment Assignment / Randomization

Habitual contact lens wearing subjects will be randomized in a 1:1:1 ratio to receive AOHG MF, DT1 MF, or DACP MF, respectively. Habitual PALs wearing subjects will not be randomized.

Only after signing the ICF, a subject will be assigned a subject number by the electronic data capture system.

A randomization list will be generated using a validated system that automates the random assignment of treatment arms to randomization numbers in the specified ratio. Subjects will be assigned treatment according to the randomization list uploaded in the IRT system. The randomization list will be generated and maintained by the Study Sponsor.

At Visit 2, all eligible subjects in the contact lens group will be randomized via the EDC/IRT integration system to one of the treatment arms. The unmasked study coordinator will access the respective system after confirming that the subject meets all the eligibility criteria. A randomization number will be automatically assigned to the subject according to the subject randomization list but will not be communicated to the site user. The EDC/IRT integration system will inform the site user of the treatment assignment to be dispensed to the subject.

9.4 Treatment masking

The contact lens group in this study is double-masked, with contact lens group subjects randomized to use AOHG MF, DT1 MF or DACP MF lenses for the study visit. Investigators will be masked to the type and brand of PAL.

Table 9–3 Unmasked Individuals Associated with the Study

Unmasked Individual	**Extent of Unmasking**	**Rationale**
Unmasked Study Coordinator(s)	The Unmasked Study Coordinator(s) will manage IP inventory, as well as IP administration. This individual will have access to IP supply, accountability logs, and other documents or supplies pertaining to IP (including brand/type of PAL). The unmasked coordinator will also assist with device deficiency and adverse event reporting.	The Unmasked Study Coordinator(s) will be unmasked to allow for storage and dispensing, as well as accountability for all contact lens IP.
Clinical Operations Lead (COL)	The COL will have access to IP supply, accountability logs, and other documents or supplies pertaining to IP. This individual assists with masked and unmasked data reviews.	The COL will be unmasked to allow for oversight of the CSM, in conjunction with all IP accountability tasks.
Clinical Site Manager (CSM)	CSM will have access to IP supply, accountability logs, and other documents or supplies pertaining to IP accountability. This individual monitors unmasked and masked study data.	The CSM will be unmasked to allow for performance of IP accountability, management of device deficiencies and related AE lens returns, and any other IP related tasks.
Unmasked Data Manager(s)	The Unmasked Data Manager(s) will have access to restricted fields in eDC that would contain unmasking data.	The Unmasked Data Manager(s) will be unmasked to allow for review of all restricted data.
IRT Manager	The IRT manager will be unmasked to allow for system programming,	The IRT manager is unmasked to all aspects of

Unmasked Individual	**Extent of Unmasking**	**Rationale**
	testing, and to allow for technical oversight of the system.	the trial for system development purposes.
Randomization Specialist	The Randomization specialist will be unmasked to allow for generation of the randomization list and uploading of that list into the IRT system.	Generates and therefore has full knowledge of treatment codes but otherwise is operationally not associated with the Clinical Trial Team or any decision-making aspects related to clinical trial design, execution, or reporting.

This level of masking will be maintained throughout the conduct of the study. Unmasking will occur only after all planned study data have been validated, and the database locked.

Masked study personnel must avoid seeking information that may compromise masking. Unmasked study personnel must not disseminate information that is potentially unmasking to any masked personnel. The masked and unmasked site personnel must coordinate all study activities as necessary to protect masking and minimize bias during the study.

In the event of a medical emergency where the knowledge of subject treatment is required, an individual Investigator will have the ability to unmask the treatment assignment for a specific subject after contacting an appropriate Study Sponsor representative if time allows. Unmasking must be done according to the instructions provided for the study IRT system. Refer to Section 11.5.

9.5 Accountability Procedures

Upon receipt of the IP, the Investigator or delegate must conduct an inventory. During the study, Masked Investigator must designate unmasked staff to provide the IP to the subjects in accordance with their randomization assignment. Throughout the study, the Investigator or delegate must maintain records of IP dispensation and collection for each subject. This record must be made available to the study monitor for the purposes of verifying the accounting of IP supplies. Any discrepancies and/or deficiencies between the observed disposition and the

written account must be recorded along with an explanation. All IP must be accounted for by Study Sponsor personnel, and in no case be used in an unauthorized situation.

It is the Investigator's responsibility to ensure that:

- All study products are accounted for and not used in any unauthorized manner
- All used foils and unused supplies are returned by each subject
- All unused products are available for return to the Study Sponsor, as directed
- Any study lenses associated with a device deficiency or with any product-related adverse event (ie, ADE or SADE) are returned to the Study Sponsor for investigation, unless otherwise directed by the Sponsor. Refer to Section 11 of this protocol for additional information on the reporting of device deficiencies and AEs and the return of study products associated with these events.

The Investigator is responsible for proper disposition of all unused IPs at the conclusion of the study, according to the instructions provided in the MOP.

9.6 Changes to concomitant medications, treatments/ procedures

After the subject is enrolled into the study, the Investigator must instruct the subject to notify the study site about:

- Any new medications
- Alterations in dose or dose schedules for current medications,
- Any medical procedure or hospitalization that occurred or is planned
- Any non-drug therapies (including physical therapy and blood transfusions).

The Investigator must document this information in the subject's case history source documents.

10 STUDY PROCEDURES AND ASSESSMENTS

Subjects will be expected to attend 1-2 office visits. Visit 1/Screening visit procedures may be performed the same day as Visit 2 procedures. Visit 2 should occur 0-14 days from Visit 1.

Study randomization for the contact lens group should occur at Visit 2 if it is performed on a separate date as the Visit 1/Screening visit. All study contact lenses will be prescribed according to the subject's prescription and fitted using the Alcon MF fitting guide. A subject's participation will be terminated if the subject does not achieve a successful fit with

the Alcon Precision Profile Design study lenses according to the MF fitting guidelines or at the Investigator's discretion. PAL wearers will wear their habitual spectacles. [redacted] Used study contact lenses will be removed at the subject's exit and destroyed by the site.

10.1 Informed Consent and Screening

The Investigator or delegate must explain the purpose and nature of the study, and have the subject read, sign, and date the IRB/IEC-approved informed consent document. The subject must sign the ICF BEFORE any study-specific procedures or assessments can be performed, including study-specific screening procedures. Additionally, have the individual obtaining consent from the subject and a witness, if applicable, sign and date the informed consent document. A signed informed consent document defines the point of enrollment.

The Investigator or delegate must provide a copy of the signed document to the subject and place the original signed document in the subject's chart, or provide documentation as required by local regulations.

10.2 Description of Study Procedures and Assessments

Detailed descriptions of assessments and procedures are provided in the MOP. The Investigator is responsible for ensuring responsibilities for all procedures and assessments are delegated to appropriately qualified site personnel.

10.2.1 Demographics

Obtain demographic information including age, race, ethnicity, and sex.

10.2.2 Medical History

Collect medical history information, 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. Throughout the subject's participation, obtain information on any changes in medical health and/or the use of concomitant medications.

10.2.3 Investigational Product compliance

Review subject compliance with the IP usage and adjunct product usage and collect all used and unused IP and other products that were dispensed.

10.2.4 Adverse Event Collection: Safety Assessment

Assess and record any AEs that are observed or reported, including those associated with changes in concomitant medication dosing since the previous visit.

10.2.5 Slit-Lamp Biomicroscopy: Safety Assessment

Slit-lamp examination must be performed in both eyes prior to study exit.

10.2.6 Device Deficiencies: Safety Assessment

Assess and record any device deficiencies that are reported or observed since the previous visit. Requirements for reporting device deficiencies in the study can be found in Section 11.

10.3 Unscheduled Visits

If a subject visit occurs between any regularly scheduled visits, this visit must be documented as an Unscheduled Visit. During all unscheduled visits, the Investigator must conduct the following procedures:

- Collect AE and device deficiency information
- Assess and record changes in medical condition or concomitant medication
- Perform biomicroscopy (assessments with or without lenses as possible)
- Perform BCVA (OD, OS, logMAR distance (4 m), intermediate (80 cm), and near (40 cm) with manifest refraction)

The Investigator may perform additional procedures for proper diagnosis and treatment of the subject. The Investigator must document this information in the subject's case history source documents.

If during an Unscheduled Visit the subject is discontinuing the IP or discontinuing from the study, the Investigator must conduct Exit procedures according to Table 3–1 and Section 10.4.3, as possible.

10.4 Discontinued Subjects

10.4.1 Screen Failures

Screen failures are subjects who are excluded from the study after signing the informed consent and prior to randomization.

The Investigator must document the reason for screen failure in the subject's case history source documents.

Subject numbers must not be re-used.

10.4.2 Discontinuations

Discontinued subjects are individuals who voluntarily withdraw or are withdrawn from the study by the Investigator after signing informed consent, including screen failures.

Subject numbers of discontinued subjects must not be re-used.

Subjects may discontinue from study or study treatment at any time for any reason. Subjects may also be discontinued from study treatment at any time if, in the opinion of the Investigator, continued treatment poses a risk to their health.

For subjects discontinuing from the study, the Investigator must complete all Exit procedures according to Table 3–1 Schedule of Study Procedures and Assessments, if the subject is willing and able, and if in the opinion of the Investigator it is safe for the subject to do so.

The Investigator must document the reason for study or treatment discontinuation in the subject's case history source documents.

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

10.4.3 Schedule of Procedures and Assessments for Subjects Discontinued from Investigational Product

N/A. Any subject discontinued from IP will be discontinued from the study.

10.5 Clinical Study Termination

The Study Sponsor reserves the right to close the investigational site or terminate the study in its entirety at any time.

If the clinical study is prematurely terminated or suspended by the Study Sponsor:

- The Study Sponsor must:
    - Immediately notify the Investigator(s) and subsequently provide instructions for study termination.

- Inform the Investigator and the regulatory authorities of the termination/suspension and the reason(s) for the termination/suspension.

- The Investigator must:
  - Promptly notify the IRB/IEC of the termination or suspension and of the reasons.
  - Provide subjects with recommendations for post-study treatment options as needed.

The Investigator may terminate the site's participation in the study for reasonable cause.

10.5.1 Follow-up of subjects after study participation has ended

Following this study, the subject will return to their eye care professional for their routine eye care.

11 ADVERSE EVENTS AND DEVICE DEFICIENCIES

11.1 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 11–1 Categorization of All Adverse Events

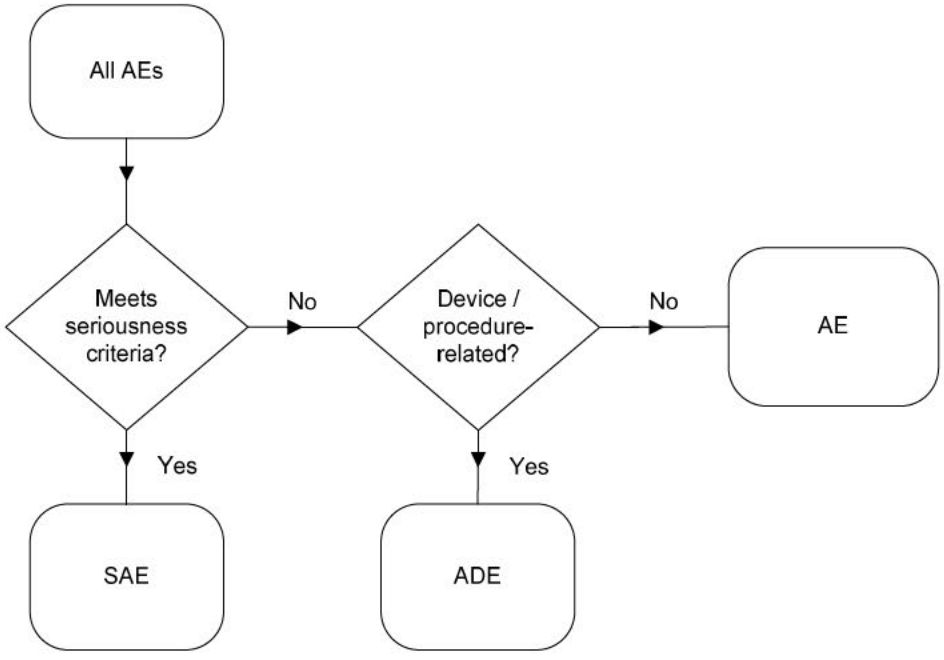
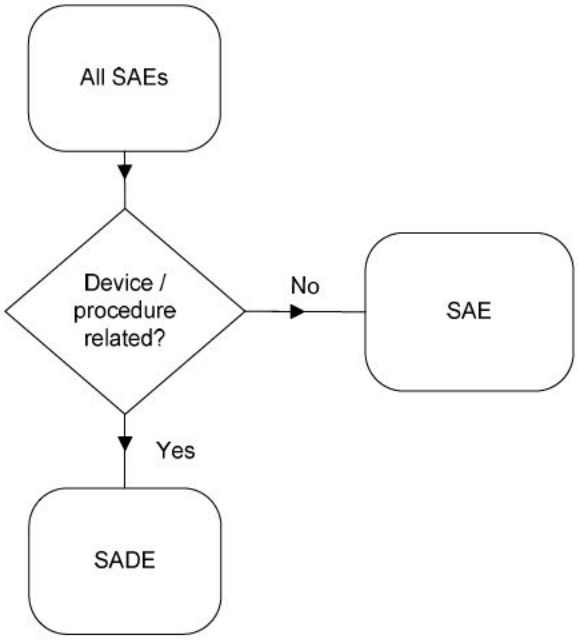


Figure 11–2 Categorization of All Serious Adverse Events



Device Deficiencies

A device deficiency may or may not be associated with subject harm (ie, ADE or SADE); however, not all ADEs or SADEs are due to a device deficiency. The Investigator should determine the applicable category for the identified or suspect device deficiency and report any subject harm separately.

11.2 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 *any protocol-specific parameters and/or questionnaires* evaluated during the study are to be reviewed by the Investigator. Any untoward (unfavorable and unintended) change in *a protocol-specific parameter or questionnaire response* 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.

11.3 Procedures for Recording and Reporting

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 reported or observed 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
- 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 faxed or emailed to the Study Sponsor at 1-817-302-1927 or msus.safety@alcon.com 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 (ie, habitual multifocal contact lenses 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 Manual of Procedures 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.

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.

11.4 Return product analysis

Study Sponsor representatives and their contact information are provided in the Manual of Procedures 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.

11.5 Unmasking of the Study Treatment

Masked information on the identity of the assigned medical device should not be disclosed during the study (refer to Section 9.4). 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.

11.6 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.

11.7 Pregnancy in the Clinical Study

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

12 ANALYSIS PLAN

Continuous variables will be summarized using the number of observations, mean, standard deviation (SD), median, minimum and maximum, as well as confidence intervals or confidence limits where applicable. Categorical variables will be summarized with counts and percentages from each category. Any deviations to the analysis plan will be updated during the course of the study as part of a protocol amendment or will be detailed in the clinical study report.

12.1 Subject Evaluability

Final subject evaluability must be determined prior to breaking the code for masked treatment assignment and locking the database, based upon the Deviations and Evaluability Plan.

12.2 Analysis Sets

12.2.1 Safety Analysis Set

Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis. As such, the safety analysis set will include all subjects/eyes exposed to any study product evaluated in this study, except for the lenses used at Visit 2 for the purpose of parameter optimization and fitting as they are not intended for the assessment of safety. For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study product exposed.

12.2.2 Full Analysis Set

The full analysis set (FAS) is the set of all subjects assigned to PALs or randomized to the contact lens group who are exposed to any study product evaluated in this study, except for the lenses used for optimization and fitting.

12.2.3 Per Protocol Analysis Set

The per protocol (PP) analysis set is a subset of FAS and excludes all data/subjects which have met any of the critical deviation or evaluability criteria identified in the Deviations and Evaluability Plan.

12.3 Demographic and Baseline Characteristics

Demographic and baseline characteristics will be summarized by lens and overall. Counts and percentages will be presented for categorical variables such as sex, age group, race, and ethnicity. Number of observations, mean, SD, median, minimum, and maximum will be presented for continuous variables such as age.

12.4 Effectiveness Analyses

This study defines 1 primary, [redacted] All effectiveness evaluations will use the FAS as the primary analysis set. [redacted] analyses of the primary [redacted] will be conducted using the PP Analysis Set only if the number of subjects excluded from the PP Analysis Set exceeds 5% of the FAS.

A sequential gatekeeping strategy will be used to control testing of multiple effectiveness endpoints. Therefore, the overall Type I error will be maintained at one-sided 0.05 with the following testing order:

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

12.4.1 Analysis of Primary Effectiveness Endpoint(s)

The primary objective of this study is to demonstrate noninferiority in transition time between distance and intermediate with MF contact lenses compared to PALs. The primary endpoint is the average transition time, calculated from a maximum of 3 readings, recorded in seconds, during alternate viewing from distance (4 m) to intermediate (80 cm) and vice versa.

12.4.1.1 Statistical Hypotheses

The null and alternative hypotheses are formulated in terms of the predefined margin of 0.5 for noninferiority:

H_0: $\mu_{(MF)} - \mu_{(PAL)} \geq 0.5$
H_a: $\mu_{(MF)} - \mu_{(PAL)} < 0.5$

where $\mu_{(MF)}$ and $\mu_{(PAL)}$ denote the mean of average transition time between distance and intermediate viewing for MF contact lenses and PALs, respectively.

12.4.1.2 Analysis Methods

A generalized linear model will be utilized to test these hypotheses, with a term for treatment (4 levels: AOHG MF, DT1 MF, DACP MF, and PAL). Difference between MF (pooling all 3 MF groups) and PAL and the corresponding one-sided 95% upper confidence limit (UCL) will be computed. Noninferiority in transition time will be declared if the UCL is less than 0.5. Furthermore, subsequent superiority will be declared if UCL is less than 0.

[redacted]

[redacted]

[redacted]

12.5 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 primary and secondary effectiveness analyses.

12.6 Safety Analyses

The safety endpoints are:

- AEs
- Biomicroscopy findings
- Device deficiencies

There are no safety hypotheses planned in this study. The focus of the safety analysis will be a comprehensive descriptive assessment of occurrence of AEs as well as the other listed parameters.

All AEs occurring from the time a subject signs informed consent to study exit will be accounted for in the reporting. Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis. Descriptive summaries (counts and percentages) for ocular and nonocular AEs will be presented by Medical Dictionary for Regulatory Activities Preferred Terms. AEs leading to study discontinuation, significant nonserious AEs, and SAEs will be identified. Individual subject listings will be provided, as necessary.

Individual subject listings will be provided for AEs that occur after signing informed consent but prior to exposure to IP.

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 (last assessment prior to study lens exposure) to any subsequent visit within the same period will be presented. A supportive listing will be generated which will include all biomicroscopy data from all visits within the same period for those eyes experiencing the increase.

Two listings for device deficiencies, prior to exposure of study contact lenses and treatment-emergent, will be provided. Additionally, each device deficiency category will be tabulated.

No inferential testing will be done for safety analysis.

12.7 Interim Analyses and Reporting

There are no plans to conduct an interim analysis and no criteria by which the study would be terminated early based upon statistical determination

12.8 Sample Size Justification

Sample size calculation is based on published results regarding response time for distance and near visual acuity, with high and low contrast.

To demonstrate noninferiority (margin = 0.5 seconds) as a one-tailed hypothesis with $\alpha = 0.05$, and using a common standard deviation of 0.456, 80% power can be attained with a sample size of 48 (12 per group). For a comparison using a 3:1 ratio, required sample sizes for 80% power are 24:8 (test:control).

13 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

13.1 Subject Confidentiality

The Investigator must ensure that the subject's anonymity is maintained throughout the course of the study. In particular, the Investigator must keep an enrollment log with confidential identifying information that corresponds to the subject numbers and initials of each study participant. At the end of the clinical study, the Study Sponsor will collect a copy of the enrollment log ***without any identifying subject information***. All documents submitted to the Study Sponsor will identify the subjects exclusively by number and demographic information. No other personally identifying information will be transmitted to the Study Sponsor.

The Study Sponsor may release anonymized study data to external researchers for purposes of future research directly related to the study objectives, or future research that is beyond the scope of the current study objectives. The Informed Consent Form explains this to study subjects. Anonymization means that all identifiable information will be removed from the dataset and all links to the subjects in the study will be removed. Anonymization of the data will maintain confidentiality of the subjects who participate in the study so that they cannot be identified by external researchers. The anonymized data set will contain records from all

of the subjects in the current study, but the anonymization process might change the data set in some ways, so external researchers will be informed that they might not be able to duplicate some of the results from this study.

13.2 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, and all discrepancies shall be appropriately documented via the query resolution process. Site monitors are appointed by the Study Sponsor and are independent of study site staff.

If electronic records are maintained, the method of verification must be determined in advance of starting the study.

At a minimum, source documents 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
- IP 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 study 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.

Only designated individuals at the site will complete the CRFs. The CRFs must be completed at regular intervals following the clinical study visit schedule. It is expected that all data reported have corresponding entries in the source documents. The Principal Investigator is responsible for reviewing and certifying that the CRFs are accurate and complete. The only

subject identifiers recorded on the CRFs will be subject number, and subject demographic information.

13.3 Data Review and Clarifications

A review of CRF data to the subject's source data will be completed by the site monitor to ensure completeness and accuracy. After the CRFs have been completed, additional data clarifications and/or additions may be needed as a result of the data cleaning process. Data clarifications are documented and are part of each subject's CRF.

13.4 Sponsor and Monitoring Responsibilities

The Study Sponsor will designate a monitor to conduct the appropriate site visits at the appropriate intervals according to the study monitoring plan. The clinical investigation will be monitored to ensure that the rights and well-being of the subjects are protected, the reported data are accurate, complete, and verifiable from the source documents, and the study is conducted in compliance with the current approved protocol (and amendments[s], if applicable), with current GCP, and with applicable regulatory requirements.

The site may not screen subjects or perform the informed consent process on any subject until it receives a notification from an appropriate Study Sponsor representative that the site may commence conducting study activities. Monitoring will be conducted periodically while the clinical study is ongoing. Monitoring methods may include site visits, telephone, written and fax correspondence. Close-out visits will take place after the last visit of the last subject at the site.

A Coordinating Investigator may be identified by the Study Sponsor to review and endorse the final study report. In cases where a Coordinating Investigator is engaged, the Study Sponsor will select the Coordinating Investigator based upon their experience, qualifications, active study participation, and their willingness and availability to take on this role.

13.5 Regulatory Documentation and Records Retention

The Investigator is required to maintain up-to-date, complete regulatory documentation as indicated by the Study Sponsor and the Investigator's files will be reviewed as part of the ongoing study monitoring. Financial information is to be kept separately.

Additionally, the Investigator must keep study records and source documents consistent with the terms of the clinical study agreement with the Study Sponsor. If the Investigator retires, relocates, or for any other reason withdraws from responsibility of keeping the study records, then the Study Sponsor must be notified and suitable arrangements made for retention of

study records and source documents needed to comply with national and international regulations.

13.6 Quality Assurance and Quality Control

The Study Sponsor will secure agreement from all involved parties to ensure direct access to all study related sites, source data and documents, and reports for the purpose of monitoring and auditing by the Study Sponsor, and inspection by domestic and foreign regulatory authorities. Quality control will be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly. Agreements made by the Study Sponsor with the Investigator/Institution and any other parties involved in the clinical study will be provided in writing as part of the protocol or as a separate agreement.

14 ETHICS

This clinical study must be conducted in accordance with the ethical principles contained within:

- The Declaration of Helsinki, and in compliance with the ICH E6 GCP Consolidated Guideline, ISO 14155:2011, and the applicable US FDA 21 CFR Regulations.
- SOPs of the Study Sponsor and contract research organizations participating in the conduct of the clinical study and all other applicable regulations.
- Notifications and timelines for reporting protocol deviations should be based upon applicable Ethics Committee requirements

The Investigator must ensure that all personnel involved in the conduct of the study are qualified to perform their assigned responsibilities through relevant education, training, and experience. The Investigator and all clinical study staff must conduct the clinical study in compliance with the protocol. Deviations from this protocol, regulatory requirements and/or GCP must be recorded and reported to the Sponsor prior to database lock. If needed, corrective and preventive action should be identified, implemented, and documented within the study records. Use of waivers to deviate from the clinical protocol is prohibited.

Before clinical study initiation, this protocol, the informed consent form , any other written information given to subjects, and any advertisements planned for subject recruitment must be approved by an IRB/IEC. The Investigator must provide documentation of the IRB/IEC approval to the Study 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

IRB/IEC must be provided with a copy of the Package Insert, any periodic safety updates, and all other information as required by local regulation and/or the IRB/IEC. At the end of the study, the Investigator must notify the IRB/IEC about the study's completion. The IRB/IEC also must be notified if the study is terminated prematurely. Finally, the Investigator must report to the IRB/IEC on the progress of the study at intervals stipulated by the IRB/IEC.

Voluntary informed consent must be obtained in writing from every subject and the process shall be documented before any procedure specific to the clinical investigation is applied to the subject. The Investigator must have a defined process for obtaining consent. Specifically, the Investigator, or their delegate, must 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 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 IP and the study, 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 must be provided with contact information for the appropriate individuals should questions or concerns arise during the study. The subject also must 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 (file in subject's medical records) and must provide a duplicate copy to each subject according to local regulations.

The Study Sponsor assures that the key design elements of this protocol will be registered on www.clinicaltrials.gov as required by current regulations and, if applicable, other public databases as required by local country regulations. In addition, results of this study will be made publicly available on www.clinicaltrials.gov regardless of outcome as required by current regulations and, if applicable, in other public databases as required by local country regulations.

15 REFERENCES

15.1 References applicable for all clinical studies

- ISO 11980:2012 Ophthalmic optics - Contact lenses and contact lens care products - Guidance for clinical investigations
- ISO 14155:2011 Clinical investigation of medical devices for human subjects - Good clinical practice

15.1.1 US references applicable for clinical studies

- 21 CFR Part 11 - Electronic Records; Electronic Signatures
- 21 CFR Part 50 - Protection of Human Subjects
- 21 CFR Part 56 - Institutional Review Boards
- 21 CFR Part 812 - Investigational Device Exemptions
- 21 CFR Part 54 - Financial Disclosure by Clinical Investigators
- The California Bill of Rights

15.2 References for this clinical study

Not applicable. There are no references.

Date/Time (mm/dd/yyyy GMT):	Signed by:	Justification:
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]