a Novartis company

Short Title

Assessing Fitting Guides in Alcon Multifocal Contact Lenses

Long Title

Assessing Fitting Guides in Alcon Multifocal Contact Lenses

Protocol Number:	CLK027-P001 / NCT03118934
Study Phase:	N/A
Sponsor Name and Address:	Alcon Research, Ltd. 6201 South Freeway Fort Worth, Texas 76134-2099
Investigational Products:	1. AIR OPTIX AQUA® Multifocal (AOA MF) Contact Lens 2. DAILIES® AquaComfort Plus® Multifocal (DACP MF) Contact Lens 3. DAILIES TOTAL1® Multifocal (DT1 MF) Contact Lens
US IND# / EudraCT	N/A
Indication Studied:	Contact lens wear
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:** **CLK027-P001**
Investigational Products:	1. AIR OPTIX AQUA Multifocal (AOA MF) Contact Lens 2. DAILIES AQUACOMFORT PLUS Multifocal (DACP MF) Contact Lens 3. DAILIES TOTAL1 Multifocal (DT1 MF) Contact Lens	**Study Phase:** ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☒ N/A
Active Ingredient:	N/A	
Protocol Title:	Assessing Fitting Guides in Alcon Multifocal Contact Lenses	
Investigator(s)/ No. of Sites:	Multicenter; Approximately 20 sites	
Center Location(s)/	US, Canada, EU	
No. of Subjects	Required: 160, Planned: 180 [9 per site (6 weekly/monthly wearers and 3 daily disposable wearers); approximately 60 in each test lens brand; [redacted]	
Duration of Treatment:	10 ± 3 days	
Study Population:	Current soft contact lens wearers needing presbyopia-correction, with a near spectacle ADD of +0.50 to +2.50 D (inclusive)	
Objective(s):	**Primary Objective** • To demonstrate noninferiority of the alternative fitting guide compared to the current fitting guide as determined by the mean number of trial lenses needed to fit each eye at the Screening/Fitting visit for all Alcon MF lenses combined	

[redacted]

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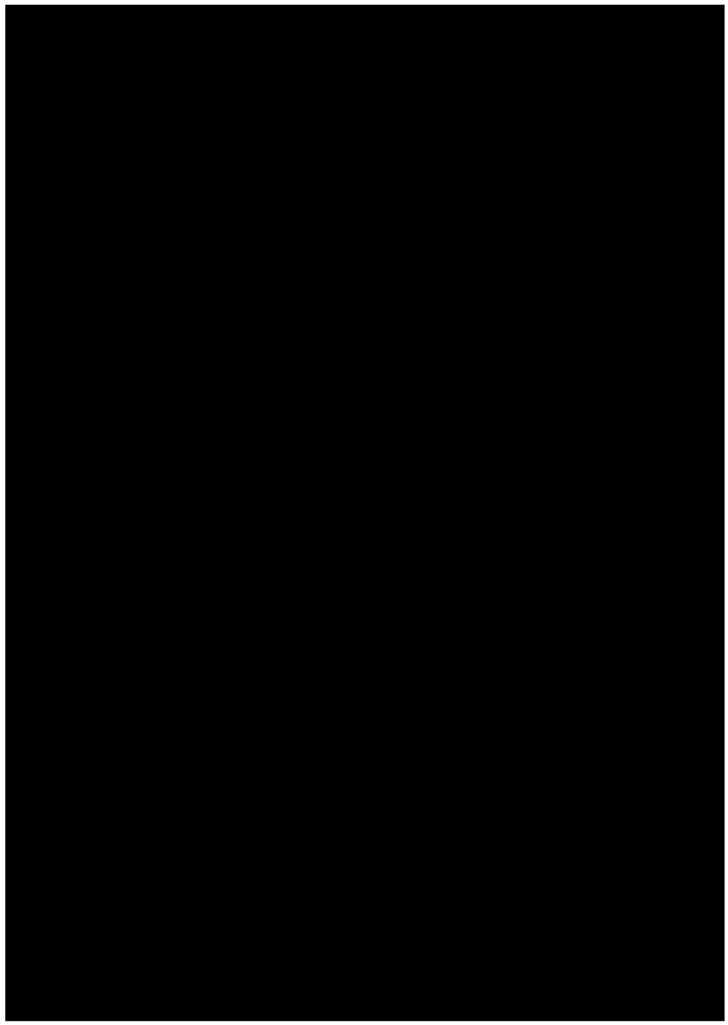

Safety Objective

- Assess and describe adverse events (AEs), biomicroscopy findings, and device deficiencies.

Methodology: This is a multi-center, subject-masked, prospective, randomized, stratified, parallel group study.

Treatments:

Investigational Product: AIR OPTIX AQUA Multifocal Contact Lens

Route of Administration: Lenses will be dispensed to habitual weekly/monthly wearers by qualified study staff according to the randomization plan. Test contact lenses will be worn bilaterally.

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	Duration of Treatment:	The total duration of treatment will be 10 ± 3 days per dispensed lens. Lenses will be worn on a daily wear basis and cared for with their habitual lens care solution.
	Dosage:	The lenses will be available from +6.00 D to -10.00 D (0.25 D steps) for sphere and near ADD will be +0.5 D to +2.50 D.
	Investigational Product:	DAILIES AQUACOMFORT PLUS Multifocal Contact Lens
	Route of Administration:	Lenses will be dispensed to habitual weekly/monthly wearers by qualified study staff according to the randomization plan. Test contact lenses will be worn bilaterally.
	Duration of Treatment:	The subjects will wear the lenses for 10 ± 3 days per dispensed lens under a daily wear daily disposable modality. The subjects will remove and discard the study lenses every night and use a new pair of study lenses every morning.
	Dosage:	The lenses will be available from +6.00 D to -10.00 D (0.25 D steps) for sphere and near ADD will be +0.5 D to +2.50 D.
	Investigational Product:	DAILIES TOTAL1 Multifocal Contact Lens
	Route of Administration:	Lenses will be dispensed to all habitual daily disposable lens wearers by qualified study staff. Test contact lenses will be worn bilaterally.
	Duration of Treatment:	The subjects will wear the lenses for 10 ± 3 days per dispensed lens under a daily wear daily disposable modality. The subjects will remove

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		and discard the study lenses every night and use a new pair of study lenses every morning.
	Dosage:	The lenses will be available from +6.00 D to -10.00 D (in 0.25 D steps) for sphere and near ADD will be +0.5 D to +2.50 D.

Subject Selection:

Inclusion Criteria:

1. Subjects with normal eyes who are not using any ocular medications, aged 40-65 and must sign the informed consent.
2. Requires a near spectacle ADD of +0.50 D to +2.50 D (inclusive).
3. Current full-time soft contact lens wearers (during the past 1 month for a minimum of 5 days per week, 6 hours per day) needing presbyopia correction within the power range of lens powers available for the test lenses.
4. Cylinder equal to or lower than - 0.75 D in both eyes.
5. Best corrected VA to 0.18 logMAR (Snellen equivalent 20/30) or better in each eye at distance (as determined by manifest refraction at screening).
6. Willing to wear lenses for a minimum of five days per week, six hours per day, and attend all study visits.
7. Uses digital devices (eg, uses a smart phone, tablet, laptop computer, or desktop computer for at least 2 hours/day and 5 days/week) and willing to continue the same pattern for the duration of the study.

Exclusion Criteria:

1. Any use of systemic or ocular medications for which contact lens wear could be contraindicated as determined by the Investigator.
2. Current Alcon MF contact lens wearers.
3. Monocular subjects (only one eye with functional vision) or subjects fit with only one lens.
4. Anterior segment infection, inflammation or abnormality.
5. Any active anterior segment ocular disease that would contraindicate contact lens wear.
6. Biomicroscopy findings observed during the Visit 1 slit-lamp examination that are moderate (Grade 3) or higher and/or corneal vascularization that is mild (Grade 2)

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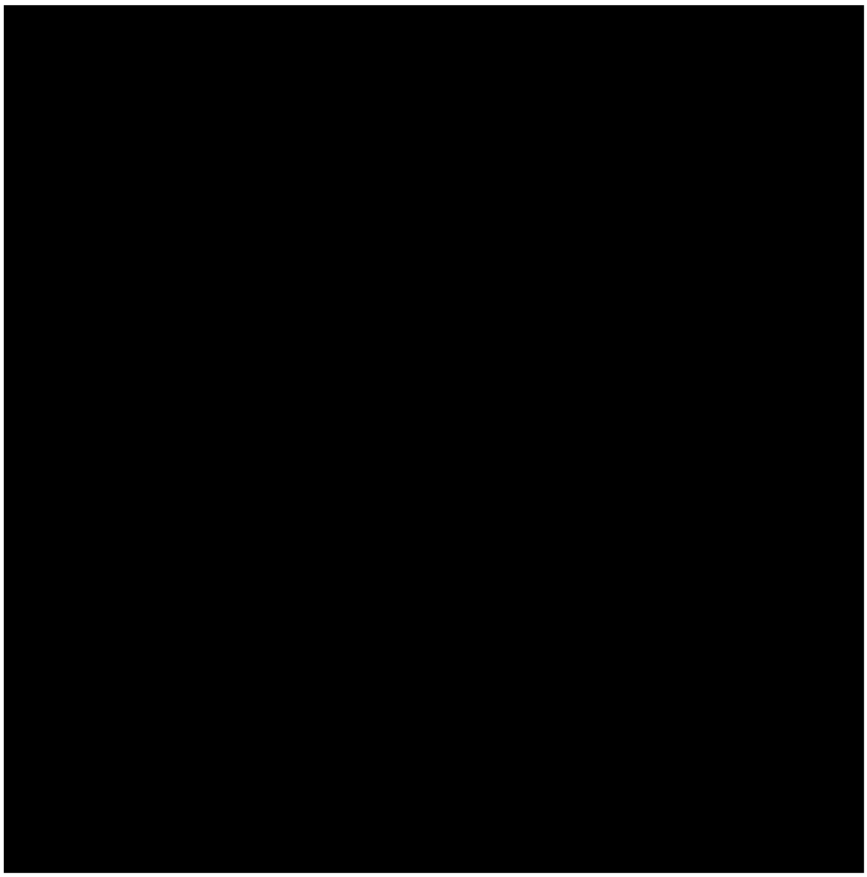
or higher in either eye at screening.

7. History of herpetic keratitis, corneal surgery or irregular cornea.
8. Prior refractive surgery (eg, LASIK, PRK).
9. A pathological dry eye that precludes contact lens wear.
10. Use of mechanical eyelid therapy or eyelid scrubs within 14 days before Visit 1 and not willing to discontinue during the study.
11. Enrollment of more than 1 member of the same household in the study.
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.

Endpoints:

Primary Effectiveness

- Mean number of trial lenses needed to fit at Screening/Fitting



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[redacted]

Safety

- AEs
- Biomicroscopy
- Device deficiencies

Statistical Methods:

Planned Analysis

Three analysis sets will be defined: Safety, Full, and Per Protocol (PP). The Safety Analysis Set will include all subjects/eyes exposed to study lenses evaluated in this study, except for those used for trial fit at Visit 1. The Full Analysis Set (FAS) will consist of subjects randomized or assigned to study lenses as applicable, and exposed to study lenses including trial fit at Visit 1. The PP Analysis Set is a subset of the FAS and excludes data which meet any of the critical deviation or non-evaluable criteria as specified in the Deviations and Evaluability Plan (DEP). The FAS will serve as the primary analysis dataset for all effectiveness evaluations

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

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Effectiveness

To address the primary effectiveness objective, planned analysis is summarized below:

Endpoint	Comparison	Statistical Method
PRIMARY		
Number of lenses for fitting at Visit 1	Alternative vs Current Noninferiority	Mixed effect repeated measures model NI margin = 0.5

[redacted]

Safety

Each safety variable will be summarized descriptively. AEs will be classified as treatment-emergent, based upon treatment-specific exposure, or pre-treatment. Count and percentage will be provided by relationship to device, 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 analyses.

Sample Size Justification

When the sample size in each group is 80 (160 eyes), a two-group t-test will have 83% power to demonstrate noninferiority with a margin of 0.5 (one-sided α=0.05), assuming that the expected difference in means is 0.25 and the common standard deviation is

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0.6 [redacted]

2 OVERVIEW OF STUDY PLAN

	Visit 1	Visit 2 Dispense 1 / Visit 2 Dispense 2	Visit 3 Follow-up 1 / Visit 3 Exit	USV
Procedure/ Assessment	**Screening and Fitting**	**Dispensing 0-7 days from Visit 1**	**Day 10 ± 3 – Follow-up / Exit**	**Unscheduled Visit**
Randomization • Site to Fitting Guide	✓ *			
Informed Consent	✓			
Demographics	✓			
Medical History	✓			
Concomitant Medications/ Changes in Concomitant Medications	✓	✓	✓	✓
Subjective (Manifest) refraction	✓	(✓)	(✓)	(✓)
BCVA † (with manifest refraction)	✓	(✓)	(✓)	(✓)
[redacted]				
Study contact lens parameters optimization and fitting †	✓			
[redacted]				
[redacted]				
Inclusion/Exclusion	✓			
Randomization Weekly/Monthly Subject to study lens	✓ **			
Dispense study lenses		✓ **		
[redacted]				

	Visit 1	Visit 2 Dispense 1 / Visit 2 Dispense 2	Visit 3 Follow-up 1 / Visit 3 Exit	USV
Procedure/ Assessment	**Screening and Fitting**	**Dispensing 0-7 days from Visit 1**	**Day 10 ± 3 – Follow-up / Exit**	**Unscheduled Visit**
[redacted]				
Biomicroscopy	✓	✓	✓	✓
[redacted]				
Assess optimal prescription			✓ [e]	(✓)
Assess AEs	✓ [f]	✓	✓	✓
Assess device deficiencies	✓	✓	✓	✓
[redacted]				
Exit Form	(✓)	(✓)	✓	(✓)

AE = Adverse Event; BCVA = Best Corrected Visual Acuity; logMAR = logarithmic Minimum Angle of Resolution; USV = Unscheduled Visit; VA = Visual Acuity

[redacted]

[e] If subject needs a new prescription, perform Visit 2 Dispense 2 and Visit 3/Exit

[f] AEs are collected from the time of informed consent

[redacted]

(✓) as needed, or if a 2-line change in contact lens corrected VA is observed (Manifest refraction and BCVA only)

* Prior to Visit 1

** per randomization scheme, if weekly/monthly lens wearers

[redacted]

† Source only

3 ABBREVIATIONS

3.1 List of Abbreviations

Abbreviation	Definition
ADD	Additional power
ADE	Adverse device effect
AE	Adverse event
AOA MF	AIR OPTIX AQUA Multifocal
BCVA	Best corrected visual acuity
D	Diopter
DACP MF	DAILIES AQUACOMFORT PLUS Multifocal
DEP	Deviations and evaluability plan
DT1 MF	DAILIES TOTAL1 Multifocal
ECP	Eye care practitioners
eCRF	Electronic case report form
EDC	Electronic data capture
EU	European Union
FAS	Full Analysis Set
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICF	Informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent ethics committee
IP	Investigational product
IRB	Institutional review board
LASIK	Laser-assisted in situ keratomileusis
logMAR	Logarithmic minimum angle of resolution
MF	Multifocal
MOP	Manual of procedures
N/A	Not applicable
NI	Noninferiority
OD	Right eye
OS	Left eye
OU	Both eyes
PI	Principal Investigator
PP	Per protocol analysis set
PRK	Photorefractive keratectomy
pt	Point

Abbreviation	Definition
SADE	Serious adverse device effect
SAE	Serious adverse event
UCL	Upper confidence limit
US	United States
USV	Unscheduled visit
VA	Visual acuity

3.2 Glossary of Terms

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 Effect (ADE)	AE related to the use of an investigational medical device (test article) or control article. *Note: This definition includes AEs 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 AE or medical device malfunction has occurred.
Non-serious Adverse Event	AE that does not meet the criteria for a serious AE.
Serious Adverse Event (SAE)	AE 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 SAE. 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 AEs. 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 7 for additional SAEs.*
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a SAE.
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.*

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5 INTRODUCTION

5.1 Study 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, progressive addition lenses, or multifocal (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 AIR OPTIX AQUA MF (AOA 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 DAILIES AQUACOMFORT PLUS MF (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). DAILIES TOTAL1 MF (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).

Some eye care practitioners (ECPs) hesitate offering their presbyopic patients MF contact lenses due to the perceived impression of the added time it takes to fit these lenses. The goal of this study is to collect data on 2 fitting guides in a population of current soft contact lens wearers needing presbyopia correction so that a recommendation can be made on one global fitting guide that will reduce the amount of time needed to fit the lenses by the ECPs and will optimize patient outcomes.

5.2 Known and Potential Risks

A summary of the known and potential risks and benefits associated with AOA MF, DACP MF, and DT1 MF can be found in their respective package inserts.

Safety information about AOA MF, DACP MF, and DT1 MF Control lenses may be found in their respective product labeling. The Investigator should advise subjects of the following general warnings and precautions with contact lens wear:

- 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
- Non-compliance with lens care instructions may increase the risk of developing a serious eye infection
- 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 with those who do not

The risks with contact lens wear are increased with a pre-existing or active ocular infection or inflammation, improper lens fit, and noncompliance with regimen. Subjects will be instructed to wear both lenses as daily wear according to instructions for use and/or following the instructions from the Investigator. Subjects who fail to follow the instructions for replacing their contact lenses could experience an eye infection of the cornea or an eye 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.

DACP MF and DT1 MF are not intended for use with a disinfecting solution, and the biocompatibility with lens care solutions and any associated clinical effects are unknown.

Potential serious complications with contact lens wear are usually accompanied by one 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 with when the lens was first placed on the eye
- Poor visual acuity (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 is 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, or visual changes with concomitant medications or during pregnancy.

The vision with multifocal contact lenses compared to spectacles may be less sharp or different, which may be more noticeable under low illumination (dimly lit room), reduced visibility (fog or heavy rain), or isolated sources of very bright light (headlights of oncoming vehicle). In addition, the PI should advise subjects of possible ocular dryness, increased lens awareness/intolerance, or visual changes with some concomitant medications or during pregnancy.

The PI must assess for ocular changes to determine whether to discontinue or restrict lens wear. Examples include the following:

- Ocular infections
- Tarsal papillary changes
- Local or generalized corneal edema
- Epithelial microcysts
- Epithelial staining
- Infiltrates
- Neovascularization
- Endothelial polymegathism
- Conjunctival injection
- Iritis

5.3 Risk Minimization

During the clinical study, qualified investigational site personnel will verify that the dispensed study lens power meets individual subject needs and the study lenses demonstrate adequate centration and movement on the eye. Trained investigational site personnel will educate subjects on proper hygiene and study lens handling, and compliance with the use of

the study MF contact lenses. Subjects should be instructed not to wear study lenses while sleeping or during water activities like swimming. Trained investigational site personnel will also advise subjects to remove study lenses and return for prompt follow-up of symptoms, such as ocular discomfort, foreign body sensation, excessive tearing, vision changes, or hyperemia.

Trained investigational site personnel will monitor for AEs from study lens exposure via examination and VA testing. Trained investigational site personnel will manage the occurrence of AEs as appropriate with study lens discontinuation, study lens administration, and continued follow-up.

5.4 Potential Benefits

Contact lenses may offer correction of ametropia, improved peripheral (side) vision, the convenience of not wearing spectacles, a non-permanent device application, and a perceived improvement of cosmetic appearance. Material properties and design characteristics of contact lenses used in this study are features consistent with successful contact lens wear. There is no intended clinical benefit to the subjects who participate in this study; however, subjects will receive study visit assessments free of change (that will not substitute for a regular eye exam).

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 Good Clinical Practice (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, 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, 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 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 and other study-related material be revised. If the consent form is revised, all subjects currently enrolled in the study may be required by the IEC/IRB to sign the approved, revised informed consent form.

8 SUBJECT POPULATION

The study population includes approximately 180 subjects to be enrolled at approximately 20 sites, with approximately 9 subjects enrolled per site. To participate in the study, subjects must be current soft contact lens wearers needing presbyopia-correction, with a near spectacle ADD of +0.50 D to +2.50 D (inclusive).

The expected duration of subject participation in the study is 10 ± 3 days (7 days minimum) and up to 33 days (maximum) for all subjects with a minimum of 2 scheduled visits and a maximum of 5 scheduled visits, depending on the necessity to optimize the subject's prescription.

The complete inclusion and exclusion criteria are presented in Section 1.

Each site will enroll approximately 9 subjects (6 will be monthly/weekly habitual lens wearers and 3 will be daily disposable habitual lens wearers). [redacted]

9 TREATMENTS ADMINISTERED

Upon signing the informed consent form, subjects will be considered enrolled in the study and will be assigned a number in the appropriate numerical sequence. Subject numbers will be assigned by the electronic data capture (EDC) system at each investigational site.

Randomization for this study will be implemented in 2 parts. First, each site will be randomized to one fitting guide and will fit all subjects at their site using the assigned fitting guide (current or alternative). The purpose of this strategy is to reduce the likelihood that errors will be made in fitting the trial lenses if trying to use two similar fitting guides. Randomization of the fitting guide will be stratified by region.

Secondly, subjects who currently wear monthly/weekly contact lenses will be randomized to either AOA MF or DACP MF contact lenses (1:1 randomization). Subjects who currently wear daily disposable contact lenses will be fitted with DT1 MF contact lenses.

The study lenses will be dispensed in an unmasked manner by a trained study staff member. Subjects are unmasked to the study lenses that are dispensed, but will be masked to the fitting guides used to fit each eye for all study lenses.

Throughout the study, the Investigator will be responsible for the accounting of all study materials and will ensure that the study products are not used in any unauthorized manner.

9.1 Identity of Study Treatments

Investigational Product: AIR OPTIX AQUA Multifocal Contact Lens
Investigational Product: DAILIES AQUACOMFORT PLUS Multifocal Contact Lens
Investigational Product: DAILIES TOTAL 1 Multifocal Contact Lens

All study lenses (AOA MF, DACP MF, and DT1 MF) will be procured by the investigational site(s). All study lenses are *Conformité Européene* (CE)-marked and FDA/Health Canada approved, and will be sourced from commercial stock, including commercial packaging and labelling. No over-labelling is required for the test lenses. Storage conditions of the test lenses can be found documented in the respective AOA MF, DACP MF, and DT1 MF packaging and labeling.

9.2 Usage

The subjects will use the study lenses according to the Instructions for Use provided by the product manufacturer, in addition to following instructions from the designated site

personnel. All study lenses will be prepared by a trained study staff member and dispensed to subjects. All test lenses will be worn bilaterally.

The total duration of lens wear for **AIR OPTIX AQUA Multifocal Contact Lenses** will be 10 ± 3 days (7 days minimum) and up to 26 days (maximum) depending on necessity of refit dispensing and follow-up visits. The lenses will be available from +6.00 D to -10.00 D (0.25 D steps) for sphere and near ADD will be +0.5 D to +2.50 D. Lenses will be worn on a daily wear basis and cared for with their habitual lens care solution.

The total duration of lens wear for **DAILIES AQUACOMFORT PLUS Multifocal Contact Lenses** will be 10 ± 3 days (7 days minimum) and up to 26 days (maximum) depending on necessity of refit dispensing and follow-up visits. The lenses will be worn under a daily wear daily disposable modality. The subjects will remove and discard the study lenses every night and use a new pair of study lenses every morning. The lenses will be available from +6.00 D to -10.00 D (0.25 D steps) for sphere and near ADD will be +0.5 D to +2.50 D.

The total duration of lens wear for **DAILIES TOTAL 1 Multifocal Contact Lenses** will be 10 ± 3 days (7 days minimum) and up to 26 days (maximum) depending on necessity of refit dispensing and follow-up visits. The lenses will be worn under a daily wear daily disposable modality. The subjects will remove and discard the study lenses every night and use a new pair of study lenses every morning. The lenses will be available from +6.00 D to -10.00 D (in 0.25 D steps) for sphere and near ADD will be +0.5 D to +2.50 D.

9.3 Accountability Procedures

Upon receipt of the IP, the Investigator or designee will conduct an inventory. Designated study staff will prepare (removal of blister label) and provide the study lenses to the subjects in accordance with their assigned subject ID number. During the study, the staff designee 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 clinical supplies. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded along with an explanation. Study contact lens associated with a device deficiency or with any product-related AEs (eg, adverse device effects [ADEs]/serious adverse device effects [SADEs]) must be returned to the Sponsor. Refer to Section 12 of this protocol for additional information on the reporting of device deficiency or product-related AEs.

9.4 Subject Confidentiality and Methods Used to Minimize Bias

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 Sponsor will collect a copy of the enrollment log without any identifying subject information. All documents submitted to the Sponsor will identify the subjects exclusively by number and demographic information. No other personally identifying information should be transmitted to the Sponsor.

This study is subject-masked. Subjects are masked only to the MF fitting guides, and will be wearing study lenses for 10 ± 3 days (7 days minimum) and up to 26 days (maximum) depending on necessity of refit dispensing and follow-up visits.

Sites will be assigned a fitting guide associated with a random number from the fitting guide randomization list, stratified by region. Each site will receive an envelope, next available in ascending random number, that contains a card listing the respective fitting guide to use. Subsequently, habitual weekly/monthly lens wearing subjects will also be randomly assigned to study lenses (AOA MF or DACP MF) in numerical order; the randomization schedule will be blocked to ensure a balance of study lens allocations within investigational sites. The randomization schemes will be generated and maintained by the Sponsor. Only once all study data have been verified, validated, and the database locked, will individual subjects be unmasked. Refer to Section 12 of this protocol for information on the reporting of AEs.

9.5 Study Entry

Participants will be recruited from the Investigators' patient population, referrals, or IEC/IRB approved recruitment materials. Patients who appear to be eligible subjects will be approached for study participation and sign an informed consent form (ICF) prior to the commencement of study related procedures.

The PI or designee will explain the study purpose, procedures, and subject responsibilities to the potential participant. The subject must be given the opportunity to ask questions and allowed time to consider the information provided. The subject's willingness and ability to meet the follow-up requirements will be determined. When it has been established that the subject may be eligible for possible participation in the study, written informed consent will be obtained. Upon signing the ICF, the subject will be enrolled into the study and study procedures performed to determine eligibility for randomization if required.

The original signed copy of the informed consent form will be retained with the subject's medical records, and a copy will be provided to the subject.

10 STUDY PROCEDURES

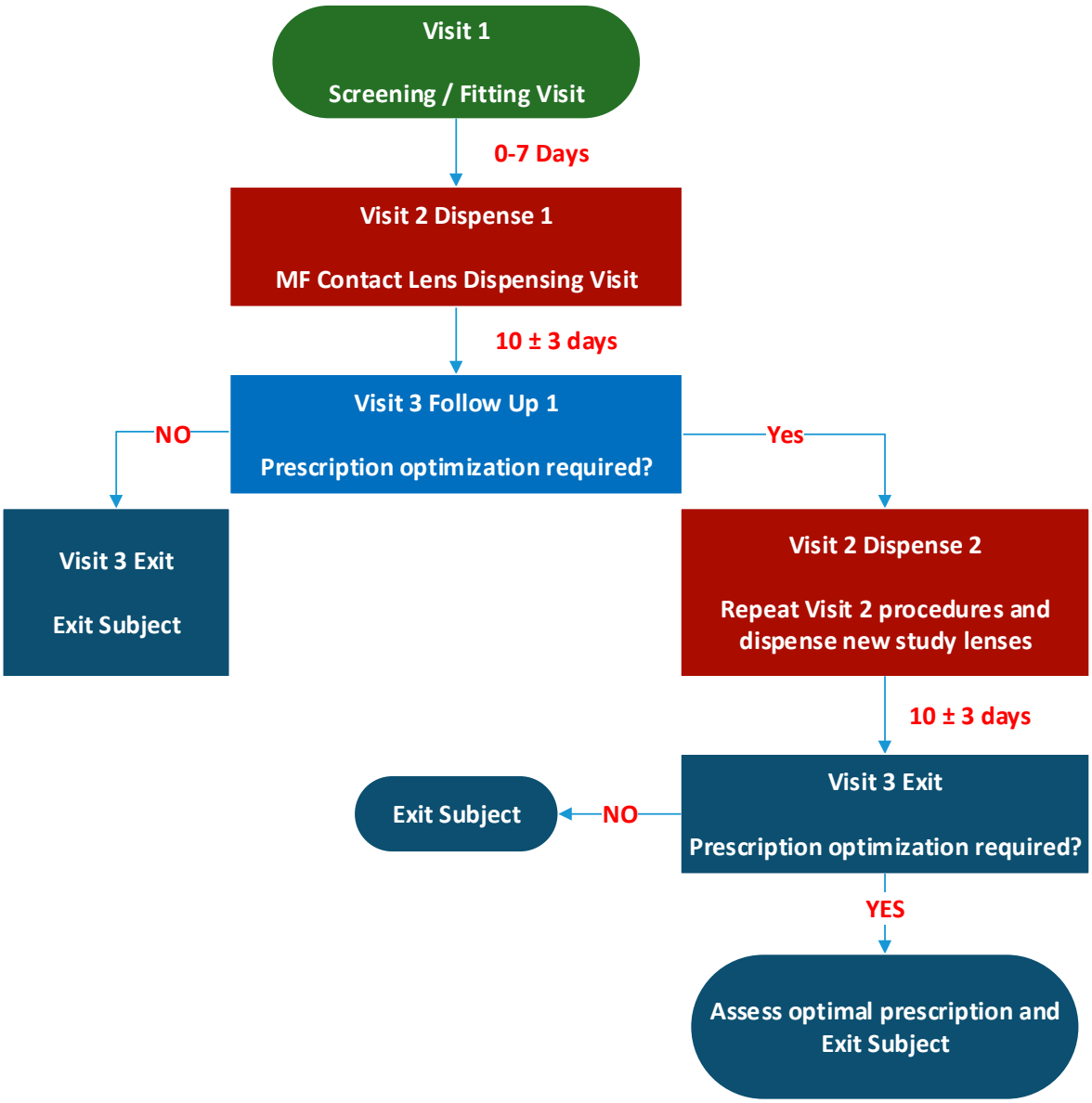
10.1 Outline of Study

This is a multicenter, subject-masked, randomized, parallel, stratified, active-controlled evaluation to compare the fitting success (determined by the mean number of trial lenses needed to successfully fit each eye) using the current MF fitting guide compared to the alternative MF fitting guide for all three of the Alcon MF contact lenses (AOA MF, DACP MF, and DT1 MF).

Approximately 180 subjects will be enrolled at approximately 20 sites, with approximately 9 subjects enrolled per site. To participate in the study, subjects must be current soft contact lens wearers needing presbyopia-correction, with a near spectacle ADD of +0.50 D to +2.50 D (inclusive).

The expected duration of subject participation in the study is 10 ± 3 days (7 days minimum) and up to 33 days (maximum) for all subjects with a minimum of 2 scheduled visits, up to 5 scheduled visits, depending on necessity of refit dispensing and follow-up visits.

Figure 10–1 Study Design



10.2 Visits and Examinations

10.2.1 General Summary of Study Visits

The general study design dictates that subjects will be screened and their eligibility confirmed at Visit 1. Subjects who are qualified to participate in the study will have their lens parameters optimized and their prescription determined at Visit 1 based upon the fitting guide assigned to the site prior to site activation.

Study lenses from the fitting set may be dispensed to the subject at Visit 1 if a sufficient number of lenses are available in the noted prescription. Otherwise, study lenses may be ordered for dispensing to subject at 'Visit 2 Dispense 1'.

For Visit 2 Dispense 1, subjects will return to the site 0-7 days from Visit 1 at which time study lenses will be dispensed based upon the prescription determined at Visit 1. A series of ophthalmic assessments will be conducted on the subjects with study lenses inserted, [redacted] Subjects will be scheduled to return to the site for their 'Visit 3 Follow-up 1' after 10 ± 3 days of lens wear in study lenses.

[redacted] A series of ophthalmic examinations will be conducted on the subject at Visit 3, and their optimal prescription assessed.

- If the subject is determined to have a successful fit following the optimal prescription assessment, the subject may be exited from the study. In this case, Visit 3 Follow-up 1 will function as Visit 3 Exit.
- If the subject is determined NOT to have a successful fit, and requires a new prescription, the subject is to be refit based upon the fitting guide assigned to the site. A new pair of study lenses will be dispensed.

For subjects who do NOT exit at Visit 3, 'Visit 3 Follow-up 1' will function as 'Visit 2 Dispense 2'. Repeat the procedures conducted at Visit 2 on the subject and dispense a new pair of study lenses with the new prescription. Schedule the subject to return to the site for 'Visit 3 Exit' after 10 ± 3 days of lens wear in study lenses

For Visit 3 Exit, conduct the same ophthalmic assessments that were conducted for the subject's Visit 3 Follow-up 1, [redacted] Assess the subject's optimal prescription following completion of ophthalmic assessments.

- If the subject is determined to have a successful fit following the optimal prescription assessment, the subject may be exited from the study.
- If the subject is determined NOT to have a successful fit with the re-dispensed lenses, a re-assessment of optimal prescription is to be conducted on the subject. However, no additional lenses are to be dispensed following the re-assessment of prescription. The subject is then exited from the study and considered NOT to have had a successful fit.

10.2.2 Study Visit Procedures

10.2.2.1 Visit 1 – Screening/ Fitting Visit

1	• Review the IRB/IEC-approved informed consent and Health Insurance Portability and Accountability Act document (where applicable) with the subject. • Explain the purpose and nature of the study, and have the subject read, sign, and date the IRB/IEC-approved informed consent document. • 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. • Familiarize yourself with the fitting guide assigned to your site that will be used to fit all subjects during enrollment. Be sure to use only the fitting guide assigned to your site when fitting study subjects.
2	Obtain demographic information, [redacted], 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.
3	Conduct an ophthalmic examination of both eyes consisting of the following assessments: • Perform the screening slit-lamp biomicroscopic exam to evaluate the following: o Limbal hyperemia o Bulbar hyperemia o Other findings
4	[redacted]
5	
6	Perform a manifest refraction. ***Note:*** *Subject must be able to be fit with lenses within the available contact lens power - near spectacle ADD of +0.50 D to +2.50 D (inclusive) in both eyes. Manifest astigmatism must be less than or equal to 0.75 D at screening. Record only in source document.*
7	Perform distance BCVA with manifest refraction • OD • OS ***Note:*** *Distance BCVA must be 0.18 logMAR (Snellen equivalent 20/30) or better in each eye for the subject to qualify for the study. Record only in source document.*

8	[redacted]
9	
10	Review inclusion/exclusion criteria to determine if the subject qualifies to be entered into the study. Randomize ONLY those habitual weekly/monthly wearing subjects who qualify to be included in the study and record the subject randomization in EDC. Qualified daily disposable lens wearers will also be entered into EDC after confirming all eligibility requirements are met. If the subject does not meet inclusion and exclusion criteria, exit the subject from the study within EDC. ***Note:*** *The site must assign subject numbers for ALL subjects that sign the informed consent document (including screening failures). If the subject does not meet study entry criteria, the subject will be considered a screen failure. The minimum data entry requirements for a screen failure must be entered into the EDC.*
11	Determine study contact lens parameters optimization and fitting using the fitting guide which was assigned to your site. ***Note:*** *Record only in source document*
12	Record the prescription of each study lens placed on each eye (ie, by eye).
13	The PI will assess and record any AEs and device deficiencies reported or observed during the study visit. ***Note:*** *AEs and device deficiencies must be recorded for all enrolled subjects from the time of signature of informed consent regardless of their enrollment status (screen failure or randomized).*
14	Schedule Visit 2 Dispense 1, to take place 0-7 days after Visit 1.

10.2.2.2 Visit 2 – (0-7 days after Visit 1) Dispense 1 / Dispense 2 (if necessary) Visit

1	Obtain information on any changes in medical health and/or the use of concomitant medications.
2	Record any AEs or device deficiencies that are observed or reported, including those associated with changes in concomitant medication dosing.

3	Conduct an ophthalmic examination of both eyes consisting of the following assessments: • Perform a slit-lamp biomicroscopic exam to evaluate the following: o Limbal hyperemia o Bulbar hyperemia o Other findings ***Note:*** *Visit 2 Slit-lamp exam does NOT need to be conducted if study lenses were dispensed at Visit 1, or if new study lenses are being dispensed (on the day of Visit 2 Dispense 2) as a result of refit from the Visit 3 Follow-up 1 visit.*
4	Dispense study contact lens according to randomization scheme, if applicable.
5	[redacted]
6	
7	Perform distance logMAR BCVA for each eye with manifest refraction (*as necessary*). • OD • OS ***Note: Perform only as necessary****, ie, decrease of VA by 2 lines or more with IP. Record only in source document.*
8	[redacted]
9	
10	The PI will assess and record any AEs and device deficiencies reported or observed during the study visit.
11	Schedule Visit 3 Follow-up 1/Exit Visit, to take place after 10 ± 3 days of lens wear in study lenses.

10.2.2.3 Visit 3 – (10 ± 3 days after Visit 2) Follow-up 1 / Exit Visit

1	Obtain information on any changes in medical health and/or the use of concomitant medications.
2	Record any AEs or device deficiencies that are observed or reported, including those associated with changes in concomitant medication dosing.
3	[redacted]
4	
5	Perform distance BCVA for each eye with manifest refraction (*as necessary*). • OD • OS ***Note: Perform only as necessary**, ie, decrease of VA by 2 lines or more with IP. Record only in source document.*
6	[redacted]
7	
8	
9	

10	Conduct an ophthalmic examination of both eyes consisting of the following assessments: • Perform a slit-lamp biomicroscopic exam to evaluate the following: o Limbal hyperemia o Bulbar hyperemia o Other findings
11	[redacted]
12	Assess optimal prescription. If subject needs a new prescription, then conduct Visit 2 Dispense 2 (Section 10.2.2.2) using your assigned fitting guide.
13	Exit the subject from the study if a new prescription is not needed. If subject is NOT being exited from the study, schedule subject to return for Visit 3 Exit Visit after 10 ± 3 days of lens wear in re-dispensed study lenses. No additional dispensation of study lenses will be allowed after 1 refit.
14	[redacted]

10.3 Unscheduled Visits

Any visit that occurs between the regularly scheduled visits must be documented in the Unscheduled Visit pages of the electronic Case Report Form (eCRF). It is possible a subject may have removed their lenses prior to attending an unscheduled visit. During all unscheduled visits, the following procedures should be conducted:

1. Obtain an update on general health and any changes in concomitant medications since the previous visit.
2. Perform BCVA with manifest refraction (*as necessary*)
    - OD & OS, distance only

    ***Note: Perform only as necessary**, ie, decrease of VA by 2 lines or more with IP. Record only in source document*
3. [redacted]

[redacted]

4. Conduct an ophthalmic examination of both eyes consisting of the following assessments:
    - Perform a slit-lamp biomicroscopic exam to evaluate the following:
        - Limbal hyperemia
        - Bulbar hyperemia
        - Other findings
5. Assess optimal prescription (*as necessary*). If subject needs a new prescription, then conduct Visit 2 Dispense 2 (Section 10.2.2.2) using your assigned fitting guide.
6. [redacted]
7. The PI will assess and record any AEs and device deficiencies reported or observed during the study visit.

If the subject is discontinuing at the unscheduled visit, the Exit form should also be completed and the Early Exit visit eCRFs should be used rather than the eCRFs from the Unscheduled Visit.

10.4 Discontinued Subjects

Discontinued subjects are those who withdraw or are withdrawn from the study after Visit 1. 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).

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 IPs, the Investigator must document those observations on an AE form.

Any subject who exits early from the study must undergo all procedures outlined at Visit 3. Additionally, the Exit form must be completed and the reason for discontinuation must be identified.

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 effectiveness
- 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

Continuous variables will be summarized using the number of observations, mean, standard deviation, 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 this 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.

11.1 Subject Evaluability

The final subject evaluability will be determined prior to breaking the code for the assignment of fitting guide and/or lens and locking the database, based upon the DEP.

11.2 Analysis Data Sets

11.2.1 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 study lenses evaluated in this study, except for the trial lenses used for parameterization and fitting at Visit 1. For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lenses exposed.

11.2.2 Full Analysis Set

The FAS will include:

1. all randomized subjects to AOA MF or DACP MF as well as subjects assigned to DT1 MF and
2. who are exposed to study lenses including those used for parametrization and fitting at Visit 1.

11.2.3 Per Protocol Analysis Set

The PP analysis set will include:

1. all randomized subjects to AOA MF or DACP MF as well as subjects assigned to DT1 MF and
2. all data/subjects which have not met any of the critical deviation or non-evaluable criteria identified in the DEP.

11.3 Demographic and Baseline Characteristics

Demographic information (age, sex, ethnicity, race) will be summarized on the safety, full, and PP analysis sets. Baseline characteristics on habitual lens [redacted] will be summarized on the full and PP analysis sets.

11.4 Effectiveness Analyses

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

For all planned inferential analyses, alternative models/methods may be considered if convergence cannot be achieved.

[redacted]

11.4.1 Primary Effectiveness

The primary objective of this study is to demonstrate noninferiority of the alternative fitting guide when compared to the current fitting guide in fitting.

The corresponding endpoint is the number of trial lenses needed to fit each eye at the Screening/Fitting visit (Visit 1), derived from the number of on-eye lens prescriptions.

11.4.1.1 Statistical Hypotheses

The null and alternative hypotheses are formulated as follows:

$$H_0: \mu_{(AFG)} - \mu_{(CFG)} \geq 0.5$$

$$H_a: \mu_{(AFG)} - \mu_{(CFG)} < 0.5$$

where $\mu_{(AFG)}$ and $\mu_{(CFG)}$ denote the mean number of trial lenses used to achieve fit in each eye using the alternative and current fitting guide, respectively, at the Screening/ Fitting visit. All Alcon MF lenses are to be included.

11.4.1.2 Analysis Methods

A mixed effect repeated measures model will be utilized to test these hypotheses, including terms for fitting guide, [redacted] Correlation between eyes will be accounted for in this analysis. Fitting guide difference (Alternative minus Current) and the corresponding one-sided 95% upper confidence limit (UCL) will be computed. Noninferiority in fitting will be declared if UCL < 0.5 at Visit 1.

[redacted]

11.4.2 Secondary Effectiveness

No secondary effectiveness objective is defined for this study.

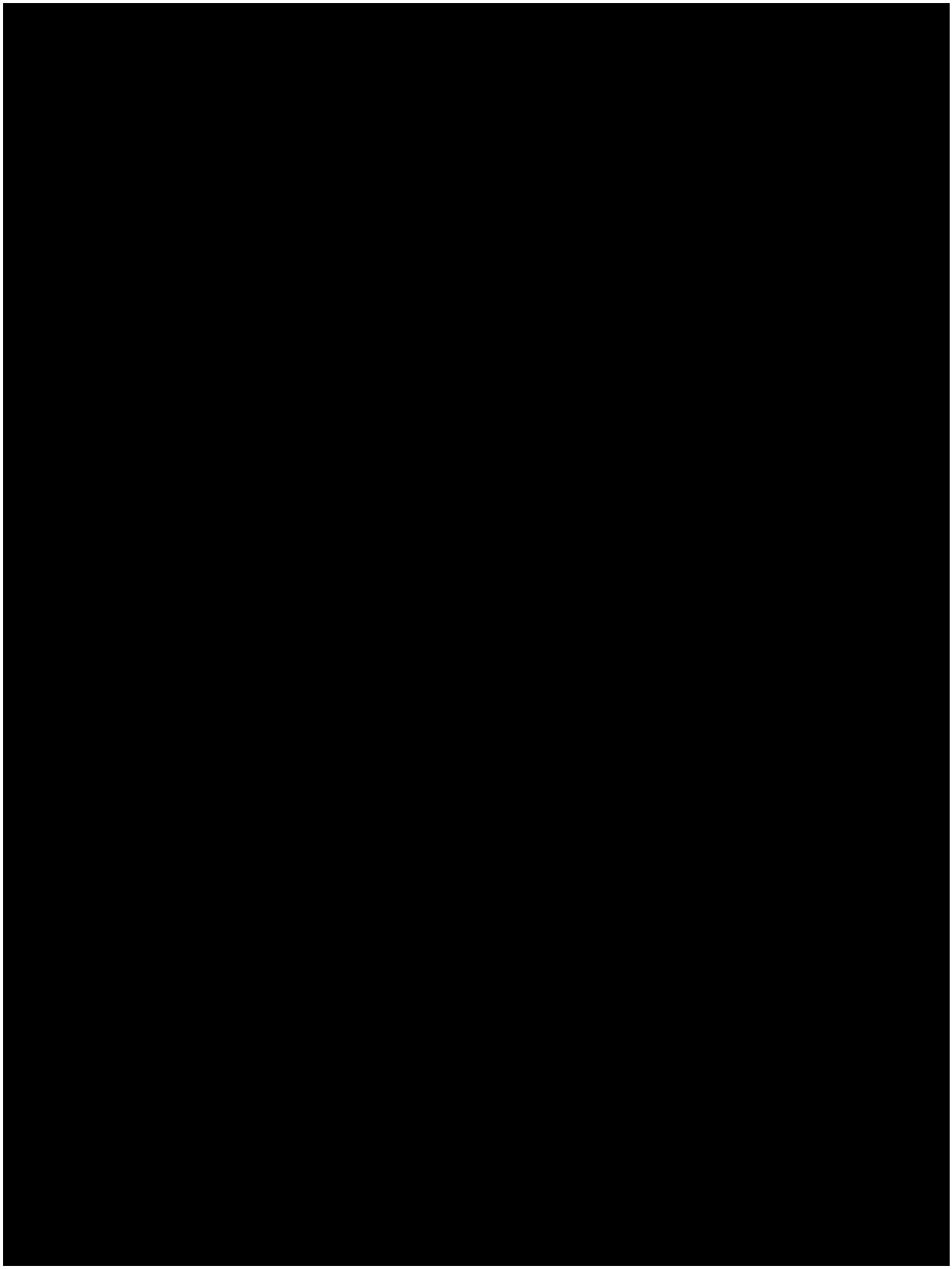
11.4.2.1 Statistical Hypotheses

Not applicable.

11.4.2.2 Analysis Methods

Not applicable.

[redacted]



[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 effectiveness analysis.

11.6 Multiplicity

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

- Noninferiority of primary endpoint
- [redacted]

11.7 Safety Analysis

The safety endpoints for this study are AEs, biomicroscopy findings, and device deficiencies.

Descriptive summaries (counts and percentages) for ocular and nonocular AEs will be presented by Medical Dictionary for Regulatory Activities Preferred Terms. In addition to an overall presentation of AEs, reports will be generated for serious AEs. AEs leading to study discontinuation 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 study lens not used for lens parametrization and fitting at Visit 1.

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 to any subsequent visit will be presented. Baseline is defined as Visit 2. A supportive listing will be generated which will include all biomicroscopy data from all visits for these eyes experiencing the increase.

Two listings (prior to exposure of study lenses not used for lens parametrization and fitting at Visit 1, and treatment-emergent) of device deficiencies will be provided. Additionally, each device deficiency category will be tabulated.

No inferential testing will be done for safety analysis.

11.8 Health Economics

Not applicable.

11.9 Interim Analyses

Not applicable.

11.10 Sample Size Justification

Sample size calculation for the primary effectiveness hypothesis on fit success is based upon results [redacted] With an assumed common standard deviation of 0.6 and expected difference of 0.25, a sample size of 80 (160 eyes) in each group will provide 83% power for a noninferiority margin of 0.5, at one-sided α=0.05, based upon a two group t-test.

12 ADVERSE EVENTS AND DEVICE DEFICIENCIES

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

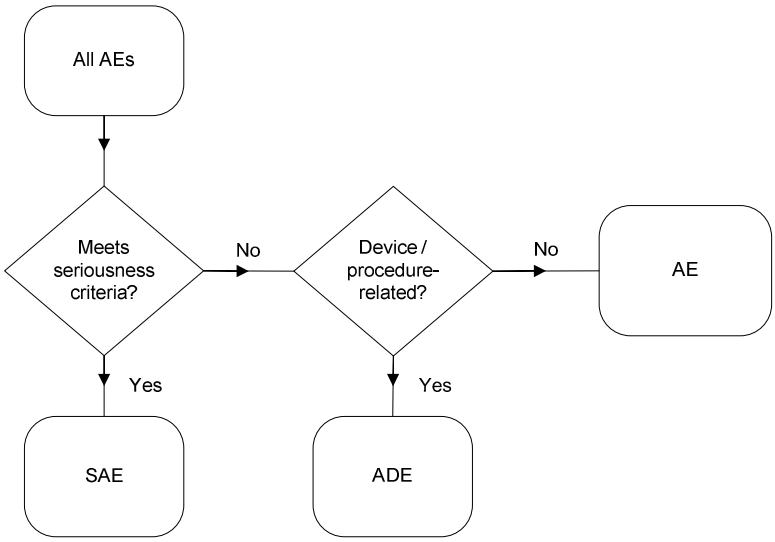
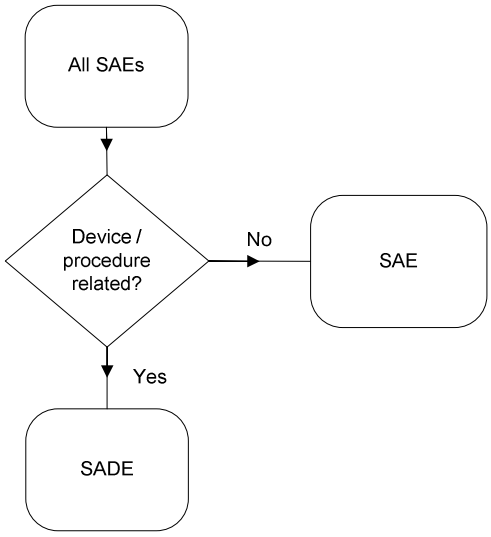


Figure 12-2 Categorization of All Serious Adverse Events



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 *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.

12.3 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. [Refer to CLK027-P001 MOP for instructions on 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 [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 products (ie, habitual contact lens care products) used concomitantly during the study will be considered and processed as spontaneous (following the postmarket vigilance procedures) and should be communicated to the 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 IEC/IRB.

Intensity and Causality Assessments

Where appropriate, the Investigator must assess the intensity (severity) of the AE based upon 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.

12.4 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. To maintain study team masking, device deficiency and ADE returns may be collected by the end of the study along with all other supplies returns.

12.5 Unmasking of the Study Treatment

Masked information on the identity of the assigned fitting guide should not be disclosed to the subject during the study [See Section 9.4 for additional detail on study masking]. 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.

12.6 Follow-Up of Subjects with Adverse Events

The PI 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 PI 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).

Any additional data received up to 1 month after subject discontinuation or exit must be documented and available upon the Study Sponsor's request. All complaints received after this time period will be considered and processed as spontaneous (following the postmarket vigilance procedures) and should be communicated to Alcon as the medical device's manufacturer per local requirements.

12.7 Pregnancy in the Clinical Trial

Pregnancy should be included in the Medical History section of the eCRF when a pregnant woman enters the study or if a woman becomes pregnant during the study. 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 eCRFs 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 eCRF are consistent with the original source data.

Electronic CRFs 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 PI 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.

13.2 Data Review and Clarifications

The eCRF 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 eCRFs 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 eCRFs.

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

Any information other than that which is disclosed upon registration should not be discussed with persons outside the study. The protocol, study data, and information related to the study or to Alcon's products or research programs that is provided by Alcon (Confidential Information) is to be kept confidential, and not disclosed directly or indirectly to any third party other than those involved in the study who have a need to know.

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.

The existence of this clinical study is confidential and should not be discussed with persons outside of the study. You shall hold confidential, and not disclose directly or indirectly to any third party other than those persons involved in the study who have a need to know, the protocol, the data arising out of the study, and any other information related to the study or to Alcon's products or a research program that is provided by Alcon to you (the "Confidential

Information"). All such persons must be instructed not to further disseminate this information to others. You shall not use the Confidential Information for any purpose other than the study.

The foregoing obligations of confidence and non-use assumed by you shall not apply to: (a) information which at the time of disclosure is in the public domain; (b) information which thereafter lawfully becomes part of the public domain other than through disclosure by or through you; (c) information which, as evidenced by your written records, was known by you prior to Alcon's disclosure; (d) information which is lawfully disclosed to you by a third party not under any obligation of confidence to Alcon; or (e) information which is required to be disclosed by law or government regulatory agency, provided reasonable advance notice of such disclosure is given to Alcon.

In signing this protocol, you agree to the release of the data from this study and acknowledge the above confidentiality and publication policy. The provisions of this Statement shall survive the completion of the study.

14 REFERENCES

Not applicable.

15 APPENDIX

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

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