Title

Clinical Validation of DACP Digital Design

Protocol Number:	CLD523-C001 / NCT03567005
Development Stage of Project:	Development
Sponsor Name and Address:	Alcon Research, Ltd. and its affiliates ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099
Test Product:	DAILIES® AquaComfort Plus® (nelfilcon A) Digital Soft Contact Lenses
Investigator Agreement:	I have read the clinical study described herein, and recognize its confidentiality. I agree to conduct this study in accordance with the ethical principles contained within the Declaration of Helsinki, and the described study in compliance with the protocol, Good Clinical Practice (GCP), ISO 14155, 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 Study Sponsor.
Principal Investigator:	

Signature Date

Name and professional position:

Address:

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1 GLOSSARY OF TERMS

Names of test product(s)	DAILIES® AquaComfort Plus® Digital Soft Contact Lenses (DACP Digital)
Name of Control Product(s)	DAILIES® AquaComfort Plus® Sphere Soft Contact Lenses (DACP)
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 perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical investigation plan.
Non-serious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.
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.
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
ADE	Adverse device effect
AE	Adverse event
DACP or DACP lens(es)	DAILIES AquaComfort Plus Sphere Soft Contact Lenses
DACP Digital or DACP Digital lens(es)	DAILIES AquaComfort Plus Digital Soft Contact Lenses
BCVA	Best corrected visual acuity
CFR	Code of Federal Regulations
CI	Confidence interval
CRF	Case report form
CSM	Clinical site manager
CTT	Clinical trial team
D	Diopter
D/C	Discontinue
DEP	Deviations and evaluability plan
eCRF	Electronic case report form
EDC	Electronic data capture
FAS	Full Analysis Set
FDA	Food and Drug Administration
GCP	Good Clinical Practice
IB	Investigator's brochure
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
IRT	Interactive response technology
ISO	International Organization of Standardization
LCSM	Lead clinical site manager
LID	Lens identification
LogMAR	Logarithm of the minimum angle of resolution
MEDDEV	Designation indicating a guidance document from the European Commission
mm	Millimeter
MOP	Manual of procedures
N	Number
N/A	Not applicable
OD	Right eye

Abbreviation	Definition
OS	Left eye
OU	Both eyes
PP	Per protocol analysis set
pt	Point
PVA	Polyvinyl alcohol
RAVE	Medidata electronic data capture and management
SADE	Serious adverse device effect
SAE	Serious adverse event
SD	Standard deviation
SLE	Slit-lamp examination
SOP	Standard operating procedure
US	United States
USADE	Unanticipated serious adverse device effect
VA	Visual acuity

3 PROTOCOL SUMMARY

This is a prospective, randomized, bilateral crossover, double-masked, controlled study. The study population will include approximately 60 subjects across approximately 4 US sites enrolling approximately 15 subjects per site to meet the required target of 48 completed subjects. The study will consist of volunteer subjects with normal eyes (other than correction for refractive error) aged 18 to 35. Subjects should have at least 2 months of experience wearing DACP soft contact lenses on a daily wear, daily disposable basis, be using digital devices at least 4 hours per day at least 5 days per week, and experience symptoms of eye strain.

Subjects will be randomly assigned in a 1:1 manner to either receive DACP Digital or DACP lenses for use during Period 1 of the study. For Period 2, the contact lenses that were not allocated for use in Period 1 will then be assigned per the specified sequence group:

Sequence Group

1) DACP Digital → DACP
2) DACP → DACP Digital

Subjects will wear each study product in a daily wear, daily disposable modality for 7 ± 2 days per study product, with up to 4 scheduled visits.

- Visit 1 – Baseline/Fitting
- Visit 2 – Dispense Study Product 1 [0 - 7 days from Visit 1]
- Visit 3 – 1-Week Follow-up Study Product 1 [7 ± 2 days from Visit 2] / Dispense Study Product 2
- Visit 4 – 1-Week Follow-up Study Product 2 [7 ± 2 days from Visit 3] / Exit

The following assessments will be performed for each study product (see Section 10 for details):

- Distance VA with study lenses (logMAR, [redacted] OU)
- [redacted]
- [redacted]
- [redacted]
- [redacted]

[redacted]

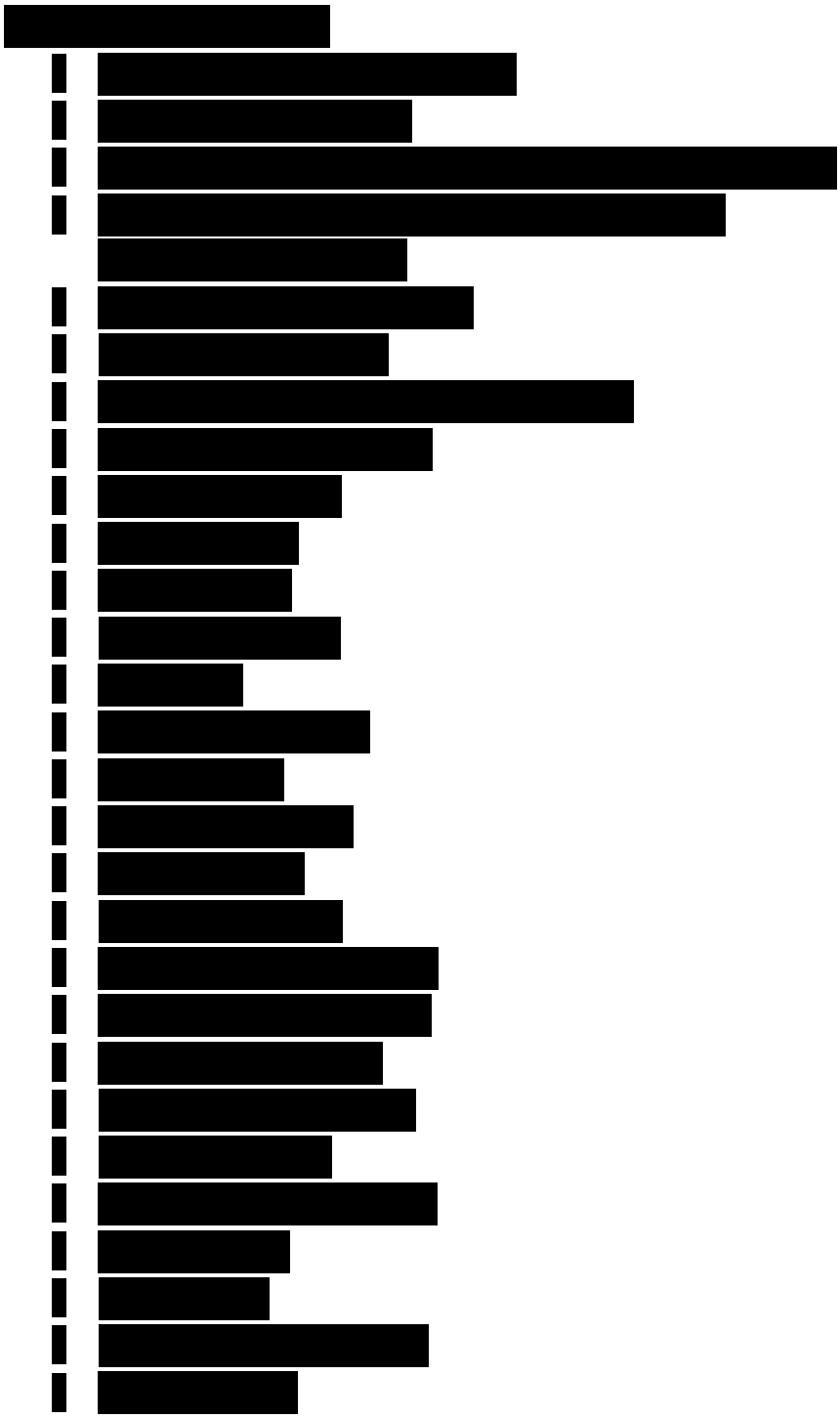
Subjects will also be asked to complete the following series of questionnaires related to their lens wearing experiences with each study product:

[redacted]

Investigational product type	Device
Study type	Interventional
Investigational products	Test Product: DACP Digital lenses Control Product: DACP lenses
Purpose and rationale	The overall purpose of this study is to evaluate the visual performance of the DACP Digital lens by assessing Distance VA as the primary variable compared to the commercially available DACP lens.
Objective(s)	• The primary objective is to demonstrate noninferiority in Distance VA with DACP Digital when compared to DACP at the 1-Week Follow-up Visit. • The secondary objective is to demonstrate noninferiority in subjective overall vision with DACP Digital when compared to DACP at the 1-Week Follow-up Visit.
Endpoint(s)	Primary Effectiveness • Distance VA (logMAR, OU)

Secondary Effectiveness

- Overall Vision



Safety

- AEs
- Biomicroscopy findings

	• Device deficiencies
Assessment(s)	Effectiveness • Distance VA with habitual correction (logMAR) [redacted] • Subjective ratings as related to [redacted] vision, [redacted] [redacted] Safety • AEs • Biomicroscopy • Device deficiencies
Study Design	This is a prospective, randomized, bilateral crossover, double-masked, controlled study. Subject participation in the study will be approximately 2 weeks with up to 4 visits where subjects will bilaterally wear the 1st study lens from the assigned lens sequence (Study Product 1) for approximately 7 ± 2 days before crossing over into the 2nd study lens of the assigned lens sequence (Study Product 2) bilaterally for approximately 7 ± 2 days.
Subject population	Volunteer subjects aged 18 to 35 with normal eyes (other than correction for refractive error), currently wearing DACP soft

	contact lenses on a daily wear, daily disposable basis. Subjects should have at least 2 months of DACP wearing experience, wear these lenses at least 5 days per week and at least 8 hours per day, use digital devices at least 4 hours per day at least 5 days per week, experience symptoms of eye strain, and require distance contact lenses in a power range from -1.50 D to -3.75 D.
Key inclusion criteria (See Section 8.1 for a complete list of inclusion criteria)	• Current wearers of commercial spherical DACP. Wearers with at least 2 months wearing experience in their current DACP lenses, with a minimum wearing time of 5 days per week and 8 hours per day. • Currently using digital devices (computer, tablet, and/or smart phone) for a minimum of 5 days per week and 4 hours per day. • Currently experiencing symptoms of eye strain from using technology. • Requiring spherical contact lens distance correction in each eye within the range of -1.50 D to -3.75 D in 0.25 D steps. • Manifest astigmatism less than or equal to 0.75 D (at screening). • Best corrected distance VA greater than or equal to 0.1 (20/25) in each eye.
Key exclusion criteria (See Section 8.2 for a complete list of exclusion criteria)	• Any anterior segment infection, inflammation, or abnormality or disease (including systemic) that contraindicates contact lens wear, as determined by the Investigator. • History of refractive surgery or irregular cornea. • Ocular or intraocular surgery within the previous 12 months (excluding placement of punctal plugs) or during the study. • Biomicroscopy findings at screening that are moderate (Grade 3) or higher and/or corneal vascularization that is mild (Grade 2) or higher in either eye at screening. • Current or history of herpetic keratitis in either eye. • Eye injury within 12 weeks immediately prior to enrollment for the study. • Wearing habitual contact lenses in an extended wear modality (routinely sleeping in lenses for at least 1 night per

<table>
<tr><td></td><td>week) over the last 3 months prior to enrollment.</td></tr>
<tr><td>Data analysis and sample size justification</td><td>To address the primary and secondary effectiveness endpoints, planned analyses are summarized below:

<table>
<tr><td>Endpoint</td><td>Comparison</td><td>Statistical Method</td></tr>
<tr><td colspan="3">Primary</td></tr>
<tr><td>Distance VA</td><td>DACP Digital vs. DACP Noninferiority (margin = 0.05 logMAR)</td><td>Mixed effect repeated measures model</td></tr>
<tr><td colspan="3">Secondary</td></tr>
<tr><td>Overall vision</td><td>DACP Digital vs. DACP Noninferiority (margin = 1.0)</td><td>Mixed effect repeated measures model</td></tr>
</table>

A sequential gatekeeping strategy will be implemented to control multiplicity, thereby controlling the overall type I error at one-sided 0.05.

No inferential testing will be carried out for safety endpoints.

Sample size calculation for primary and secondary effectiveness endpoints is summarized below:

<table>
<tr><td>Endpoint</td><td>Assumptions</td><td>Power</td><td>N per sequence</td></tr>
<tr><td colspan="4">Primary</td></tr>
<tr><td>Distance VA</td><td>Paired differences SD = 0.098</td><td>80% (one-sided α = 0.05)</td><td>18</td></tr>
<tr><td colspan="4">Secondary</td></tr>
<tr><td>Overall vision</td><td>Paired differences SD = 2.29</td><td>80% (one-sided α = 0.05)</td><td>24</td></tr>
</table>
</td></tr>
<tr><td>Key words</td><td>• DACP Digital
• DACP
• Visual acuity
• [redacted]</td></tr>
</table>

Associated materials	None. With the use of daily disposable lenses, lens care is not required. To prevent confounding the effectiveness endpoints, • Use of lubrication/re-wetting drops will not be permitted at any time during study. • Use of near aid (eg, reading glasses) will not be permitted at any time during study.

Table 3–1 Schedule of Study Procedures and Assessments

Procedure/ Assessment	Pre-screening	Visit 1	Visit 2	Visit 3	Visit 3	Visit 4	Unscheduled Visit	Early Exit
			0-7 days from V1	7 (±2) days from V2		7 (±2) days from V3		
		Baseline/ Fitting	Dispense Study Product 1	Follow-up Study Product 1	Dispense Study Product 2	Follow-up Study Product 2 / Exit		
Digital Use Time	✓*			✓		✓	✓	✓
Symptomatology Questionnaire	✓*							
Informed consent		✓						
Demographics		✓						
Medical history		✓	✓	✓		✓	✓	✓
Concomitant Medications		✓	(✓)	(✓)		(✓)	(✓)	(✓)
Inclusion/Exclusion		✓						
Distance VA w/habitual lenses (logMAR, OD, OS)*		✓						
Over-refraction w/ habitual lenses (OD, OS)*		✓						
Manifest refraction*		✓	(✓)	(✓)		(✓)	(✓)	(✓)
[redacted]		✓	(✓)	(✓)		(✓)	(✓)	(✓)
Biomicroscopy		✓	✓	✓		✓	✓	✓
Dispense study lenses / Rx			✓		✓			
VA w/ study lenses ([redacted] OU, logMAR distance) [redacted]			✓	✓	✓	✓	(✓)	✓
[redacted]			✓		✓			
[redacted]			✓		✓			
[redacted]				✓		✓	(✓)	(✓)
[redacted] sites)				✓		✓	(✓)	(✓)
[redacted]		✓		✓		✓	(✓)	✓

Procedure/ Assessment	**Pre-screening**	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 3**	**Visit 4**	**Unscheduled Visit**	**Early Exit**
			0-7 days from V1	**7 (±2) days from V2**		**7 (±2) days from V3**		
		Baseline/ Fitting	**Dispense Study Product 1**	**Follow-up Study Product 1**	**Dispense Study Product 2**	**Follow-up Study Product 2 / Exit**		
Subjective ratings with study lenses				✓		✓	(✓)	✓
[redacted]						✓	(✓)	(✓)
[redacted]		✓		✓		✓	(✓)	(✓)
[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

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

Amendment 1

Purpose of Amendment: To clarify Inclusion Criteria for subject eligibility

Rationale: Revision of certain Inclusion Criteria to improve enrollment rate across all sites without compromising quality of data

Current Study Status: Active, enrolling subjects.

Case Report Form Revision Required: ☐ Yes ☒ No

Informed Consent Modifications Required: ☐ Yes ☒ No

Applicable Investigators: ☒ All ☐ Selected (list below)

Itemized Changes:

1	**Changed From Section 3:** Subjects should have at least 3 months of experience wearing DACP soft contact lenses on a daily wear, daily disposable basis, be using digital devices at least 4 hours per day at least 5 days per week, and experience symptoms of eye strain.	**Changed To Section 3:** Subjects should have at least 2 months of experience wearing DACP soft contact lenses on a daily wear, daily disposable basis, be using digital devices at least 4 hours per day at least 5 days per week, and experience symptoms of eye strain.
2	**Changed From Section 3 (Subject Population):** Subjects should have at least 3 months of DACP wearing experience, wear these lenses at least 5 days per week and at least 8 hours per day, use digital devices at least 4 hours per day at least 5 days per week, experience symptoms of eye strain, and require distance contact lenses in a power range from -1.50 D to -3.75 D.	**Changed To Section 3 (Subject Population):** Subjects should have at least 2 months of DACP wearing experience, wear these lenses at least 5 days per week and at least 8 hours per day, use digital devices at least 4 hours per day at least 5 days per week, experience symptoms of eye strain, and require distance contact lenses in a power range from -1.50 D to -3.75 D.

3	**Changed From Section 3 (Key Inclusion Criteria):** Current wearers of commercial spherical DACP. Wearers with at least 3 months wearing experience in their current DACP lenses, with a minimum wearing time of 5 days per week and 8 hours per day.	**Changed To Section 3 (Key Inclusion Criteria):** Current wearers of commercial spherical DACP. Wearers with at least 2 months wearing experience in their current DACP lenses, with a minimum wearing time of 5 days per week and 8 hours per day.
4	**Changed From Section 8.1 (Inclusion Criteria):** Current wearers of commercial spherical DAILIES AquaComfort Plus. Wearers with at least 3 months wearing experience in their current DAILIES AquaComfort Plus correction, with a minimum wearing time of 5 days per week and 8 hours per day.	**Changed To Section 8.1 (Inclusion Criteria):** Current wearers of commercial spherical DAILIES AquaComfort Plus. Wearers with at least 2 months wearing experience in their current DAILIES AquaComfort Plus correction, with a minimum wearing time of 5 days per week and 8 hours per day.

5 INTRODUCTION

5.1 Rationale and Background

The objective of the DACP Digital project is to introduce a modification to the DAILIES AquaComfort Plus Contact Lens (DACP) family, [redacted]

This clinical evaluation is a performance verification trial [redacted] The primary and secondary endpoints were selected to fulfil the primary and secondary objectives of the study. Procedures for measurement of these endpoints were selected based on common practice for these assessments.

5.2 Purpose of the Study

The overall purpose of this study is to evaluate the visual performance of the DACP Digital lens by assessing Distance VA as the primary variable compared to the commercially available DACP lens.

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

There are no immediate plans to submit the results of this development study for publication; however, the results may be offered for publication if they are of scientific interest, or if the results relate to a product that is subsequently approved or cleared for marketing.

5.3 Risks and Benefits

Contact lenses are intended to 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 (over spectacles). Material properties and design characteristics of DACP Digital lenses are features consistent with successful contact lens wear.

Clinical studies involving DACP Digital have not yet been conducted. However, the core lens material used for DACP Digital is identical to the currently marketed DACP, for which there are multiple clinical studies, postmarket data, and literature reports that established a positive benefit/risk ratio for the lens.

In general, the risks with DACP Digital are anticipated to be similar to other marketed daily wear daily disposable contact lenses. Specifically, the safety profile is expected to be similar to other lenses in the nelfilcon A family since the core lens material used for DACP Digital is identical to DACP.

DACP Digital is intended for single use, daily disposable wear. Since DACP Digital is disposed of after a single use, lens care cleaning or disinfecting products are not needed and were not tested.

A summary of the known potential risks and benefits associated with DACP Digital lenses can be found in the IB. Any risks to subjects in this trial are minimized by compliance with the eligibility criteria and study procedures, and through close supervision by a licensed clinician during exposure to the study lenses.

There may also be unknown risks with the use of DACP Digital lens. During clinical exposure, study conditions, controls and oversight by qualified eye care professionals are factors designed to further minimize risk to study subjects. Under the conditions of these studies, adequate informed consent and subject instructions, scheduled wear, replacement and follow-up visit schedules, risks to study subjects are controlled and minimized.

Refer to the IB for additional information.

6 STUDY OBJECTIVES

6.1 Primary Objective(s)

Table 6–1 Primary Objective(s)

Objective(s)	Endpoint(s)
Demonstrate noninferiority in Distance VA with DACP Digital when compared to DACP at the 1-Week Follow-up Visit.	Distance VA (logMAR, OU)

6.2 Secondary Objective(s)

Table 6–2 Secondary Objective(s)

Objective(s)	Endpoint(s)
Demonstrate noninferiority in subjective overall vision with DACP Digital when compared to DACP at the 1-Week Follow-up Visit.	Overall Vision

[redacted]

6.4 Safety Objective(s)

Table 6–3 Safety Objective(s)

Objective(s)	Endpoint(s)
Describe the safety profile of the investigational products	• AEs • Biomicroscopy findings • Device Deficiencies

7 INVESTIGATIONAL PLAN

7.1 Study Design

This is a prospective, randomized, bilateral crossover, double-masked, controlled study.

The study population will include volunteer subjects with normal eyes (other than correction for refractive error) aged 18 to 35, and have at least 2 months of experience wearing DACP soft contact lenses on a daily wear, daily disposable basis. Subjects must be using digital devices at least 4 hours per day at least 5 days per week, and experience symptoms of eye strain.

Subjects will be randomly assigned in a 1:1 manner to either receive DACP Digital or DACP lenses for use during Period 1 of the study. For Period 2, the contact lenses that were not allocated for use in Period 1 will then be assigned per the specified sequence group:

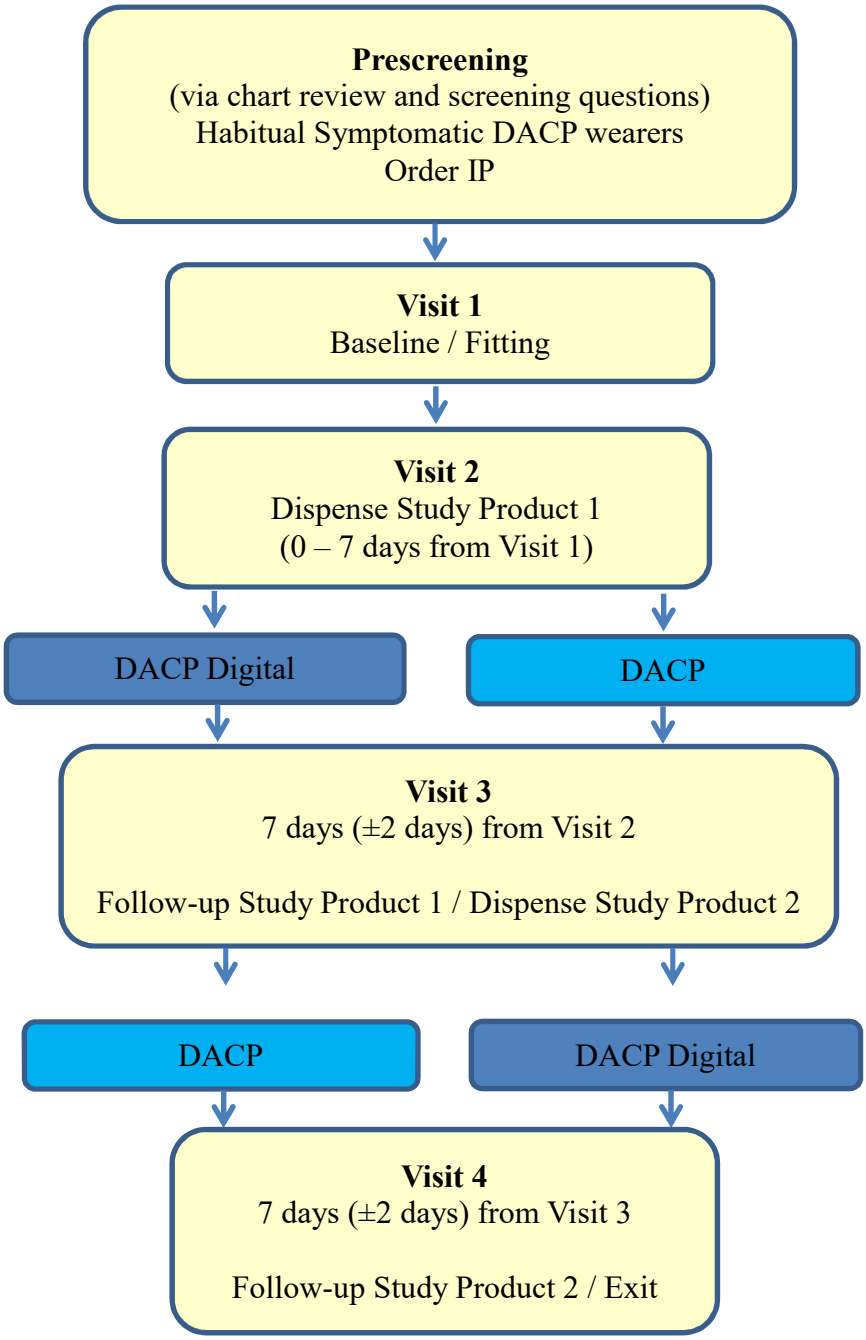
Sequence Group

1) DACP Digital → DACP
2) DACP → DACP Digital

Subjects will wear each study product bilaterally in a daily wear, daily disposable modality for 7 ± 2 days per IP, with up to 4 scheduled visits.

- Visit 1 – Baseline/ Fitting
- Visit 2 – Dispense Study Product 1 [0 - 7 days from Visit 1]
- Visit 3 – 1-Week Follow-up Study Product 1 [7 ± 2 days from Visit 2] / Dispense Study Product 2
- Visit 4 – 1-Week Follow-up Study Product 2 [7 ± 2 days from Visit 3] / Exit

Figure 7-1 Study Flow Chart



7.2 Rationale for Study Design

In this study, the on-eye performance of the investigational DACP Digital lens and the commercially available DACP lens will be assessed in a prospective, double-masked, bilateral crossover design with 7 ± 2 days of exposure to each study lens. The study design as well as the exposure duration of study lenses is supported by the nonclinical and clinical data presented in the IB. The study design is well-established.

7.3 Rationale for Duration of Treatment/Follow-Up

The duration of exposure to the investigational product was chosen to address the objective of this study, and is aligned with the duration of use of the product in accordance with product labeling.

7.4 Rationale for Choice of Control Product

DACP lenses were chosen as the control product to address the study objectives.

DACP contact lenses were chosen as the control product because these lenses have the same wear modality, material, and parameters to the test product DACP Digital, and are the spherical design as compared to the test product's aspherical design.

7.5 Data Monitoring Committee

Not Applicable.

8 STUDY POPULATION

The intended study population consists of volunteer subjects aged 18 to 35 with normal eyes (other than correction for refractive error), currently wearing DACP soft contact lenses on a daily wear, daily disposable basis. Subjects should have at least 2 months of DACP wearing experience, wear these lenses at least 5 days per week and at least 8 hours per day, use digital devices at least 4 hours per day at least 5 days per week, experience symptoms of eye strain, and require distance contact lenses in a power range from -1.50 D to -3.75 D.

It is aimed to enroll approximately 60 subjects in approximately 4 sites in the US, with an approximate target of 15 subjects per site. Site-specific targets may vary based upon individual site capabilities. Estimated time needed to recruit subjects for the study is approximately 4 weeks.

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.	Subjects must be 18 to 35 years of age and be able to understand and sign an IRB/IEC approved Informed Consent form.
2.	Current wearers of commercial spherical DAILIES AquaComfort Plus. Wearers with at least 2 months wearing experience in their current DAILIES AquaComfort Plus correction, with a minimum wearing time of 5 days per week and 8 hours per day.
3.	Requiring spherical contact lens distance correction in each eye within the range of -1.50 D to -3.75 D in 0.25 D steps.
4.	Currently experiencing symptoms of eye strain from using technology.
5.	Subjects are willing to wear the study lenses each day as possible (including the day of the follow-up visits) and at least 8 hours per day unless contact lens wear is contraindicated.
6.	Subject must possess spectacles that provide a corrected visual acuity of 0.40 (20/40) or better OU and be willing to wear them (as needed).
7.	Manifest astigmatism less than or equal to 0.75 D (at screening)
8.	Best corrected distance visual acuity greater than or equal to 0.10 (20/25) in each eye (as determined by manifest refraction at screening).
9.	Willing to NOT use rewetting/lubricating drops at any time during the study.
10.	Currently using digital devices (computer, tablet, and/or smart phone) for a minimum of 5 days per week and 4 hours per day.
11.	Willing to NOT use any near aid (eg, reading glasses) at any time during the study.

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, disease, or abnormality that contraindicates contact lens wears as determined by the Investigator.
2.	Any use of systemic medications or ocular medications for which contact lens wear could be contraindicated, as determined by the Investigator, including use of any topical ocular medications and lubrication drops that would require instillation during contact lens wear.
3.	History of refractive surgery or irregular cornea.
4.	Ocular or intraocular surgery within the previous 12 months (excluding placement of punctal plugs) or 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 in either eye at screening.
6.	Current or history of pathologically dry eye in either eye.
7.	Current or history of herpetic keratitis in either eye.
8.	Eye injury within 12 weeks immediately prior to enrollment for the study
9.	Wearing habitual contact lenses in an extended wear modality (routinely sleeping in lenses for at least 1 night per week) over the last 3 months prior to enrollment.
10.	Monocular subjects (only one eye with functional vision).
11.	Known pregnancy at time of enrollment.
12.	Concurrent participation of the subject in a contact lens or contact lens care product clinical trial or within the previous 30 days.
13.	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.

8.3 Rescreening of Subjects

Subjects must be screened according to the full list of inclusion/exclusion criteria in Section 8.1 and 8.2 of this protocol.

After informed consent is signed, a separate screening visit is allowed for the following criteria:

- INC01 – Subject must be 18 to 35 years of age
- EXC12 – Participation of the subject in a clinical trial within the previous 30 days or currently enrolled in any clinical trial

This separate screening visit can take place regardless of whether any other criterion has been verified.

Rescreening of subjects is not allowed in this study.

9 TREATMENTS ADMINISTERED

9.1 Investigational Product(s)

Test Product(s): DACP Digital soft contact lenses (LID014466)
Control Product(s) (If applicable): DACP Sphere soft contact lenses (LID007861)

Table 9–1 Test Product

Test Product	DAILIES AquaComfort Plus Digital Soft Contact Lenses (DACP Digital) (LID014466)
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 purpose of this contact lens is for the vision correction. A limited range of powers is available for use in this study in accordance with the study objective.

Product description and parameters available for this study	• Material: Nelfilcon A • Water content: 69% • Power range: -1.50 D to -3.75 D in 0.25 D steps • Base curve (mm): 8.7 (target) • Diameter (mm): 14.0 (target) • Other: Additional details can be found in the IB
Formulation	NA
Usage	• Wear: o Daily Wear o Bilateral • Replacement period: Daily Disposable • Exposure: 7 ± 2 days and at least 8 hours per day • Lens Care: N/A • Additional details can be found in the MOP
Number/Amount of product to be provided to the subject	A box containing 10 lenses (per eye) will be provided to the subject at either Visit 1 or Visit 2, *based on the subject's randomized sequence assignment*.
Packaging description	Blister containing phosphate buffered saline solution with wetting agents
Labeling description	• Lens Foil label includes: - material name and/or identifier - base curve - diameter - manufacturing protocol number - packing solution - power - lot number - expiration date - content statement - investigational device statement - Sponsor information • Provided in boxes of 10 lenses per power per box, identified with the following:

	- a color coded label stating the protocol number - identifier - power - an investigational use only statement - tracking number
Storage conditions	Stored at room temperature.
Additional identifying information	N/A
Supply	Refer to the MOP for a detailed description

Table 9–2 Control Product

Control Product(s)	DAILIES AquaComfort Plus Sphere Soft Contact Lenses (DACP) (LID007861)
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
Indication for Use	The intended of this contact lens is for the vision correction. A limited range of powers is available for use in this study in accordance with the study objective.
Product description and parameters available for this study	• Material: Nelfilcon A • Water content: 69% • Power range: -1.50 D to -3.75 D in 0.25 D steps • Base curve (mm): 8.7 (target) • Diameter (mm): 14.0 (target) Other: Additional details can be found in the IB
Formulation	Nelfilcon A. Additional details can be found in the IB for DACP.
Usage	• Wear: o Daily Wear o Bilateral

	• Replacement period: Daily Disposable • Exposure: 7 ± 2 days and at least 8 hours per day • Lens Care: N/A • Additional details can be found in the MOP
Number/Amount of Product to be Provided to the subject	A box containing 10 lenses (per eye) will be provided to the subject at either Visit 1 or Visit 2, *based on the subject's randomized sequence assignment*.
Packaging description	Blister containing phosphate buffered saline solution with wetting agents
Labeling description	• Lens Foil label includes: - material name and/or identifier - base curve - diameter - packing solution - power - lot number - expiration date - content statement - investigational device statement - Sponsor information • Provided in boxes of 10 lenses per power per box, identified with the following: - a color coded label stating the protocol number - identifier - power - an investigational use only statement - tracking number
Storage conditions	Stored at room temperature.
Additional identifying information	N/A
Supply	Refer to the MOP for a detailed description

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

Subjects will be randomized in a 1:1 ratio to receive treatment in crossover sequence DACP Digital then DACP or DACP then DACP Digital respectively.

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

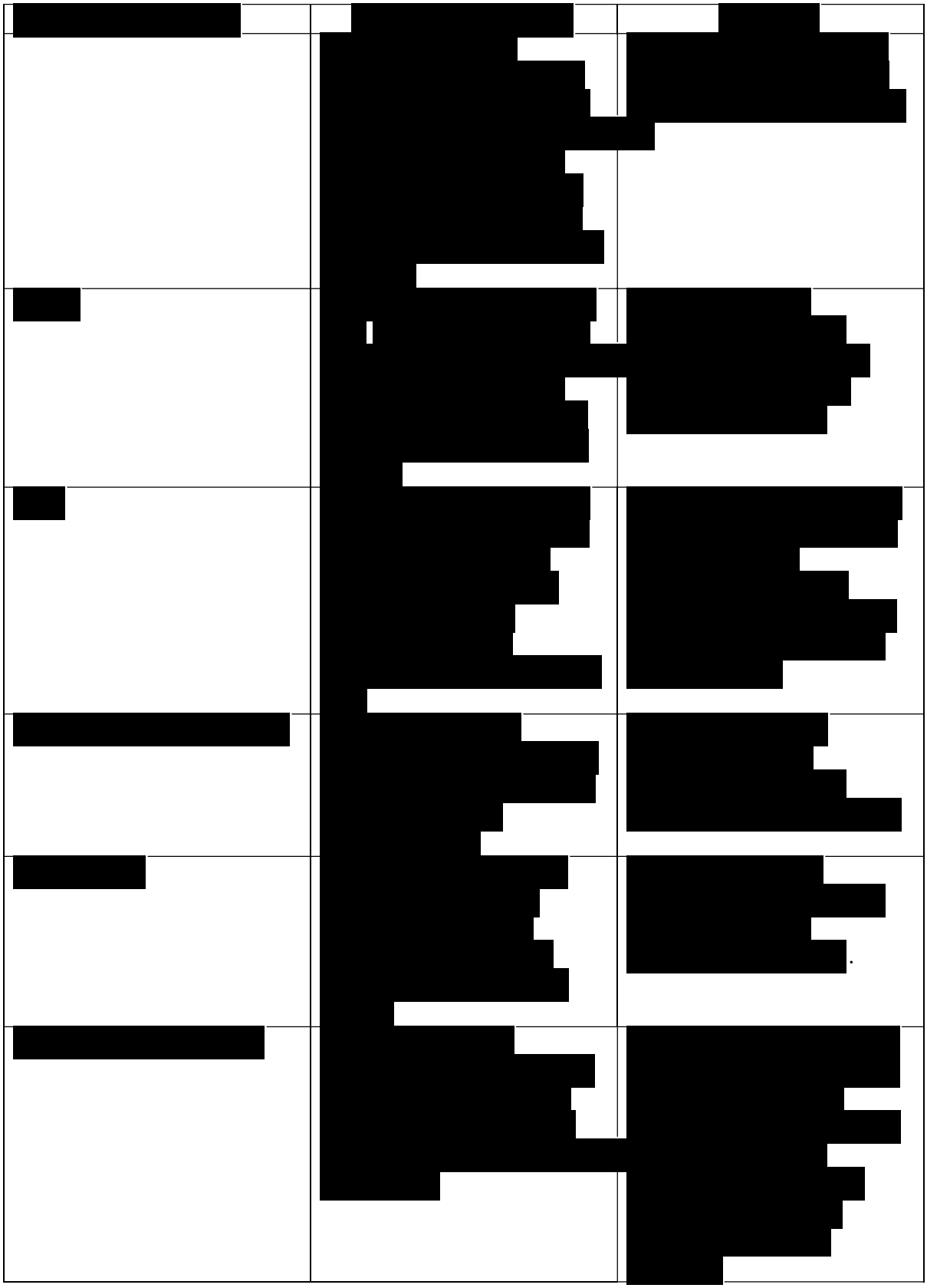
A randomization list will be generated using a validated system that automates the random assignment of treatment arms to randomization numbers in the specified ratio. Subjects will be assigned treatment according to the randomization list uploaded in the iMedidata BALANCE system. The randomization list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

IRT

At Visit 1, all eligible subjects will be randomized via the EDC/IRT integration system to one of the treatment arms. The Investigator or delegate 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 sequence assignment to be dispensed to the subject.

9.4 Treatment masking

This study is double-masked, with subjects randomized to use DACP Digital and DACP lenses (in a crossover fashion) for the duration of the 7 ± 2 day treatment period for each lens product.



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.

9.5 Accountability Procedures

Upon receipt of the IPs, the Investigator or delegate must conduct an inventory. During the study, unmasked designated study staff must provide the IPs 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 IPs sent to the Investigator 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.

9.6 Changes to concomitant medications, treatments/ procedures

Changes in concomitant treatments after Visit 1 are not allowed unless needed for the proper medical care and treatment of the subject for a specific medical condition.

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.

10STUDY PROCEDURES AND ASSESSMENTS

Subjects will wear each study product in a daily wear, daily disposable modality for 7 ± 2 days per study product, with up to 4 scheduled visits. Per Inclusion Criteria #5, subjects are willing to wear the study lenses each day as possible (including the day of the follow-up visits) and at least 8 hours per day unless contact lens wear is contraindicated.

- Visit 1 – Baseline/ Fitting
- Visit 2 – Dispense Study Product 1 [0 - 7 days from Visit 1]
- Visit 3 – 1-Week Follow-up Study Product 1 [7 ± 2 days from Visit 2] / Dispense Study Product 2
- Visit 4 – 1-Week Follow-up Study Product 2 [7 ± 2 days from Visit 3] / Exit

The following assessments will be performed for each study product:

- Distance VA with study lenses (logMAR, [redacted], OU)
- [redacted]
- [redacted]
- [redacted]

[redacted]

Subjects will also be asked to complete the following series of questionnaires related to their lens wearing experiences with each study product:

[redacted]

- Subjective ratings as related to [redacted] vision,

[redacted]

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.

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 study IPs and other products that were dispensed.

10.2.4 Adverse Event Collection: Safety Assessment

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

10.2.5 Biomicroscopy: Safety Assessment

SLE of the cornea, iris/anterior chamber and lens must be performed in both eyes before instillation of any diagnostic eye drops.

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 Adverse Event information
- Record changes in medical condition or concomitant medication
- Biomicroscopy

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 Early Exit procedures according to Table 3-1 Schedule of Study Procedures and Assessments and Section 10.4.3, as possible.

10.4 Discontinued Subjects

10.4.1 Screen Failures

Subjects who were excluded from the study after signing the informed consent, not meeting inclusion/exclusion criteria, and prior to randomization to product/dispense (exposure) of study product will be considered a screen failure.

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 the 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 Early 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

Other than screen failures, if a subject discontinues from the study the subject should undergo an Early Exit Visit. Refer to Table 3-1, Schedule of Study Procedures and assessments.

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.

11ADVERSE 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 and figures below for categories of AEs and SAEs.

Figure 11–1 Categorization of All Adverse Events

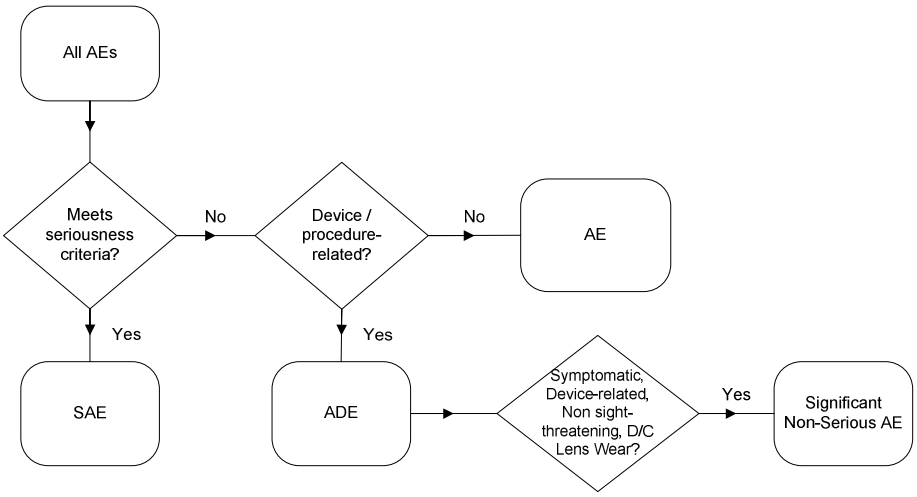
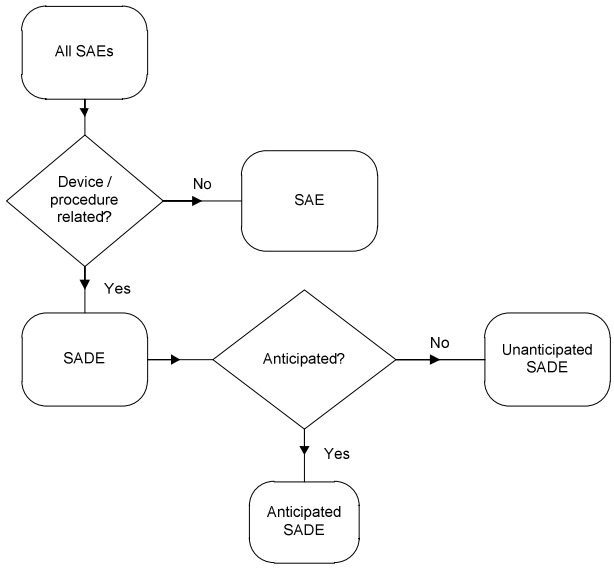


Figure 11-2 Categorization of All Serious Adverse



Specific Events Relevant to this Protocol

Serious Adverse Events

In addition to reporting all AEs (serious and non-serious) meeting the definitions, the Investigator must report any occurrence of the following as an SAE:

- An ocular infection including a presumed infectious ulcer with any of the following characteristics:
    - Central or paracentral location
    - Penetration of Bowman's membrane
    - Infiltrates > 2 mm diameter
    - Iritis
    - Increase in intraocular pressure
    - Culture positive for microorganisms
    - Increasing size or severity at subsequent timepoints
- Any central or paracentral corneal event (such as neovascularization) that results in permanent opacification
- Hypopyon
- Hyphema
- Neovascularization within the central 6 mm of the cornea
- Permanent vision loss as defined by loss of 2 or more lines of BCVA from enrollment that fails to resolve
- Uveitis (anterior, intermediate, or posterior)
- Corneal abrasion affecting ≥ 50% of corneal surface area

Significant Non-Serious Adverse Events

A significant non-serious AE is a device-related, non-sight threatening adverse event that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks. In addition, the Investigator must report any occurrence of the following as a Significant Non-Serious Adverse Event:

- Peripheral non-progressive non-infectious ulcers
- All symptomatic corneal infiltrative events
- Corneal staining score greater than or equal to Grade 3 (Refer to MOP for grading scales)
- Temporary vision loss as defined by loss of 2 or more lines of BCVA from enrollment that persists for 2 or more weeks

- Neovascularization score greater than or equal to Grade 2 (Refer to MOP for grading scales)

The above events are based upon the categories provided in the ISO 11980 and the US FDA Premarket Notification (510(k)) Guidance Document for Daily Wear Contact Lenses.

Device Deficiencies

A device deficiency is inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. A device deficiency may or may not be associated with patient harm (ie, ADE or SADE); however, not all ADEs or SADEs are due to a device deficiency. The Investigator should determine the applicable category listed in the Device Deficiency eCRF for the identified or suspect device deficiency and report any patient harm separately. Examples of device deficiencies include the following:

- Failure to meet product specifications (eg, incorrect lens power/diameter/base curve/color)
- Lens/solution cloudy
- Lens surface/edge defect
- Torn lens during handling/in pack
- Packaging deficit (eg, mislabeled product, tampered seal, leaking bottle/container)
- Suspect product contamination
- Lack of performance

11.2 Monitoring for Adverse Events

At the study 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 enrolling in the study?”
- “Have there been any changes in the medicines you take since enrolling in the study?”

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:

- ADEs or SAEs are documented on the *Serious Adverse Event and Adverse Device Effect* eCRF within 24 hours of the Investigator's or site's awareness.
- Device deficiencies are documented on the *Device Deficiency* eCRF within 24 hours 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 *Serious Adverse Event and Adverse Device Effect* eCRF.

Note: Should the EDC system become non-operational, the site must complete the appropriate paper *Serious Adverse Event and Adverse Device Effect* and/or *Device Deficiency* Form. The completed form is emailed to the Study Sponsor to 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.

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 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.

11.4 Return product analysis

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

When study products include Alcon marketed products (ie, DACP) such products associated with device deficiencies and/or product related AEs [ie, ADE or SADE] 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, as applicable. These products should be returned to the Sponsor at the end of the study, unless instructed otherwise by the Sponsor. Investigational product (ie, DACP Digital) associated with device deficiencies and/or product related AEs [ie, ADE or SADE] will also be returned for investigation as detailed in the MOP.

11.5 Unmasking of the Study Treatment

Masked information on the identity of the assigned study product should not be disclosed during the study (See 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).

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 post-market 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

Women who are pregnant at the time of study entry are excluded from participation. If any pregnancy is reported during the study, it should be included in the Medical History section of the eCRF. Pregnancy is not reportable as an AE; however, complications may be reportable and will be decided on a case–by-case basis.

12ANALYSIS PLAN

Continuous variables will be summarized using the number of observations, mean, standard deviation (SD), median, minimum and maximum, as well as confidence intervals (CIs) 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 lens sequence assignment and locking the database, based upon the Deviations and Evaluability Plan (DEP).

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 lenses evaluated in this study. For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lenses exposed in the corresponding lens sequence.

12.2.2 Full Analysis Set

The full analysis set (FAS) is the set of all randomized subjects who are exposed to any study lenses evaluated in this study.

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 DEP.

12.3 Demographic and Baseline Characteristics

Demographic and baseline characteristics will be summarized by lens sequence 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, 1 secondary, [redacted] effectiveness endpoints. All effectiveness evaluations will use the FAS as the primary analysis set. [redacted]

12.4.1 Analysis of Primary Effectiveness Endpoint(s)

The primary objective of this study is to demonstrate noninferiority in Distance VA with DACP Digital when compared to DACP at the 1-Week Follow-up Visit. The primary endpoint is distance VA with study lenses, collected bilaterally (OU) in logMAR.

12.4.1.1 Statistical Hypotheses

The null and alternative hypotheses are formulated in terms of the predefined margin of 0.05 for noninferiority:

$$H_0: \mu_{(DACP\ D)} - \mu_{(DACP)} \geq 0.05$$
$$H_a: \mu_{(DACP\ D)} - \mu_{(DACP)} < 0.05$$

where $\mu_{(DACP\ D)}$ and $\mu_{(DACP)}$ denote the mean distance VA (in logMAR) for DACP Digital and DACP, respectively.

12.4.1.2 Analysis Methods

A mixed effect repeated measures model will be utilized to test these hypotheses. The model will include terms for lens, visit, lens by visit interaction, period, and sequence.
Within-subject correlation due to the crossover will also be accounted for in the model. Lens

difference (DACP Digital minus DACP) and the corresponding one-sided 95% upper confidence limit will be computed at 1-Week. Noninferiority in VA will be declared if upper confidence limit is less than 0.05.

12.4.2 Analysis of Secondary Effectiveness Endpoints

The secondary objective of this study is to demonstrate noninferiority in subjective overall vision with DACP Digital when compared to DACP at the 1-Week Follow-up Visit. The secondary endpoint is the subjective rating of overall vision on a scale of 1 (Poor) to 10 (Excellent).

12.4.2.1 Statistical Hypotheses

The null and alternative hypotheses are formulated in terms of the predefined margin of 1.0 for noninferiority:

$$H_0: \mu_{(DACP\ D)} - \mu_{(DACP)} \leq -1.0$$
$$H_a: \mu_{(DACP\ D)} - \mu_{(DACP)} > -1.0$$

where $\mu_{(DACP\ D)}$ and $\mu_{(DACP)}$ denote the mean overall vision rating for DACP Digital and DACP, respectively.

12.4.2.2 Analysis Methods

A mixed effect repeated measures model will be utilized to test these hypotheses. The model will include terms for lens, period, and sequence. Within-subject correlation due to crossover will also be accounted for in the model. Lens difference (DACP Digital minus DACP) and the corresponding one-sided 95% lower confidence limit will be computed. Noninferiority in overall vision will be declared if lower confidence limit is greater than -1.0.

[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 adverse events 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 lenses and treatment-emergent, will be provided. Additionally, each device deficiency category will be tabulated.

No inferential testing will be done for safety analysis.

[redacted]

12.8 Sample Size Justification

Sample size calculation is based on a prior clinical study (M-14-010) which partly evaluated performance of DACP Multifocal and DACP lenses.

To demonstrate noninferiority (margin = 0.05 logMAR) as a one-tailed hypothesis with α=0.05, and using a standard deviation of 0.098 for paired differences, 80% power can be attained with a sample size of 36 (18 per sequence group).

To demonstrate noninferiority (margin = 1.0) as a one-tailed hypothesis with α=0.05, and using a standard deviation of 2.29 for paired differences, 80% power can be attained with a sample size of 48 (24 per sequence group).

13DATA 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.

14ETHICS

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 Clinical IB, package insert of DACP, 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.

15REFERENCES

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:
07/14/2018 03:58:10	[redacted]	Global Device Medical Safety
07/16/2018 19:00:03	[redacted]	biostatistics
07/16/2018 20:49:20	[redacted]	Clinical Project Lead & SME