Title

Comparison of Two Daily Disposable Lenses

Protocol Number:	CLD523-P001/NCT04013789
Development Stage of Project:	Product Support
Sponsor Name and Address:	Alcon Research, LLC, and its affiliates ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099
Test Product:	DAILIES® AquaComfort PLUS® (nelfilcon A) Soft Contact Lenses FreshTech (DACP FreshTech)

Investigator Agreement:

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

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

Principal Investigator:

Signature Date

Name and professional position:

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1 GLOSSARY OF TERMS

Names of test product(s)	Throughout this document, test product(s) will be referred to as DACP FreshTech (or DACP FreshTech contact lenses)
Name of Control Product(s)	Throughout this document, control product(s) will be referred to as DACP (or DACP contact lenses or DACP sphere)
Adverse Device Effect (ADE)	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 (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 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 (ASADE)	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.
Product Complaints	Any oral, electronic, or written communication that alleges deficiencies related to the identity (labeling), quality, durability, reliability, safety, effectiveness, or performance of a marketed product, including failure of the product, labeling or packaging to meet specifications, whether or not the product is related to or caused the alleged deficiency. A complaint may allege that an adverse event or medical device malfunction has occurred.

Randomized Subjects	Any subject who is assigned a randomized treatment.
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Serious Adverse Event (SAE)	Adverse event that led to any of the following: • Death. • A serious deterioration in the health of the subject that either resulted in: a. a life-threatening illness or injury. *Note: Life-threatening means that the individual was at immediate risk of death from the event as it occurred, ie, it does not include an event which hypothetically might have caused death had it occurred in a more severe form.* *b.* any potentially sight-threatening event or permanent impairment to a body structure or a body function.

	c. in-patient hospitalization or prolonged hospitalization. *Note: Planned hospitalization for a pre-existing condition, without serious deterioration in health, is not considered a serious adverse event. In general, hospitalization signifies that the individual remained at the hospital or emergency ward for observation and/or treatment (usually involving an overnight stay) that would not have been appropriate in the physician's office or an out-patient setting. Complications that occur during hospitalization are adverse events. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred, the event should be considered serious.* *d.* a medical or surgical intervention to prevent a) or b). *e.* any indirect harm as a consequence of incorrect diagnostic test results when used within manufacturer's instructions for use. • Fetal distress, fetal death, or a congenital abnormality or birth defect. *Refer to Section 11 for additional SAEs.*
Serious Public Health Threat	Any event type which results in imminent risk of death, serious deterioration in state of health, or serious illness that requires prompt remedial action. This would include: Events that are of significant and unexpected nature such that they become alarming as a potential public health hazard, eg, human immunodeficiency virus (HIV) or Bird Flu.

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
ASADE	Anticipated serious adverse device effect
BCVA	Best corrected visual acuity
BI	Prism base in
BO	Prism base out
CFR	Code of Federal Regulations
cm	Centimeter
CI	Confidence intervals
COL	Clinical Operations Lead
CRF	Case report form
CSM	Clinical Site Manager
[redacted]	[redacted]
CVS-Q	Computer Vision Syndrome Questionnaire
D	Diopter
DACP or DACP contact lenses or DACP sphere	DAILIES AquaComfort Plus (nelfilcon A) Soft Contact Lenses
DACP FreshTech or DACP FreshTech contact lenses	DAILIES AquaComfort Plus (nelfilcon A) FreshTech Soft Contact Lenses
DEF	Digital Eye Fatigue
DEP	Deviations and evaluability plan
eCRF	Electronic case report form
EDC	Electronic data capture
FAS	Full analysis set
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
GPCMS	Global Product Complaint Management System
HIV	Human immunodeficiency virus
ICF	Informed consent form
ICH	International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent ethics committee
IIT	Investigator initiated trial
IP	Investigational product
IRB	Institutional review board
IRT	Interactive response technology
ISO	International Organization for Standardization

Abbreviation	Definition
LID	Lens identification
logMAR	Logarithm of the minimum angle of resolution
m	Meter
mm	Millimeter
MOP	Manual of procedures
N	Number of subjects
NI	Non-inferiority
N/A	Not applicable
OD	Right eye
OS	Left eye
OU	Both eyes
PP	Per protocol
SADE	Serious adverse device effect
SAE	Serious adverse event
SD	Standard deviation
SOP	Standard operating procedure
UCL	Upper confidence limit
US	United States
USADE	Unanticipated serious adverse device effect
VA	Visual acuity

3 PROTOCOL SUMMARY

Investigational product type	Device
Study type	Interventional
Investigational products	Test Product: DACP FreshTech contact lenses Control Product: DACP contact lenses
Purpose and rationale	The purpose of this study is to demonstrate noninferiority in distance VA of DACP FreshTech when compared to DACP contact lenses. The rationale for this study to compare the clinical performance of the new DACP FreshTech contact lenses to an already marketed daily disposable contact lens (DACP).

Objective(s)	The primary objective is to demonstrate noninferiority in distance visual acuity (VA) of DACP FreshTech compared to DACP at the Week 1 follow-up visit. [redacted]
Endpoint(s)	Primary Effectiveness • Mean VA with study lenses (OU; logMAR; distance[4m]) [redacted]

	[redacted] Safety • AEs • Biomicroscopy findings • Device deficiencies
Assessment(s)	Effectiveness • VA with study lenses (OD, OS, OU; logMAR; distance [4m]) [redacted]

	[redacted] Safety • AEs • Biomicroscopy • Device deficiencies
Study Design	This is a prospective, randomized, double-masked, bilateral crossover, single site, of 3 weeks in duration, with 1-week exposure each to optimized habitual, test and control lenses. Follow-up visits are planned after 1 week wearing optimized habitual lenses as well as each study lens.
Subject population	Habitual soft contact lens wearers aged 18 to 35 years with normal eyes and a spherical distance contact lens prescription between -1.00 and -6.00D (inclusive). The subjects must be symptomatic, which means they have self-reported eye fatigue, use their digital devices for ≥ 4 hours/5 days a week, and score ≥ 6 on the Computer Vision Syndrome Questionnaire (CVS-Q). Planned to enroll: ~72 Target to complete: 66 Sample size reassessment is planned
Key inclusion criteria (See Section 8.1 for a	Volunteer subjects 18 to 35 years of age. Subjects must have at least 3 months of soft contact lens wearing experience and wear their habitual lenses at least 5 days per week and at least 8 hours per day. Subjects must be symptomatic (self-reported eye fatigue)

<table>
<tr><td>complete list of inclusion criteria)</td><td>who use digital devices ≥4 hours a day/5 days a week, and score ≥6 on the Computer Vision Syndrome Questionnaire (CVS-Q).</td></tr>
<tr><td>Key exclusion criteria
(See Section 8.2 for a complete list of exclusion criteria)</td><td>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.</td></tr>
<tr><td>Data analysis and sample size justification</td><td>Planned Analysis
To address the primary and key exploratory effectiveness objectives, planned analyses are summarized below:
<table>
<tr><th>Endpoint</th><th>Comparison</th><th>Statistical Method</th></tr>
<tr><td colspan="3">Primary</td></tr>
<tr><td>Distance VA</td><td>DACP digital vs DACP
Noninferiority</td><td>Mixed effects repeated measures
NI margin = 0.05 (logMAR)</td></tr>
<tr><td colspan="3">[redacted]</td></tr>
<tr><td>[redacted]</td><td>[redacted]</td><td>[redacted]</td></tr>
<tr><td>[redacted]</td><td>[redacted]</td><td>[redacted]</td></tr>
</table>
[redacted]

[redacted]

[redacted]

Sample Size Justification
Sample size calculations for distance VA [redacted] at 80% power, are summarized below:
<table>
<tr><th>Endpoint</th><th>Assumptions</th><th>Type I error</th><th>N</th></tr>
</table></td></tr>
</table>

	Primary Distance VA | SD (paired difference) = 0.075 NI margin = 0.05 | One-sided 0.05 | 16 [redacted]
Key words	Contact lens, vision correction, visual acuity, daily disposable contact lens, eye fatigue, digital devices, CVS-Q
Associated materials	Habitual lens care and rewetting/lubricating drops as applicable will be used during the wear of habitual lenses. No lens care will be needed during daily disposable study lens (test and control) exposure. Artificial tears and re-wetting drops will not be permitted to be used with study lenses (test and control).

Table 3–1 Schedule of Study Procedures and Assessments

Procedure/ Assessment	Pre-screening	VISIT 1	VISIT 2		VISIT 3		VISIT 4	Unscheduled Visit	Early Exit
		Day 1	1 Week (7±2 Days) from V1		1 Week (7±2 Days) from V2		1 Week (7±2 Days) from V3		
		Screening / Fitting / Dispense Optimized Habitual	Week 1 Follow-up and Baseline with Optimized Habitual	Dispense Study Product 1	Week 1 Follow-up Study Product 1	Dispense Study Product 2	Week 1 Follow-up Study Product 2 / Exit		
Digital Use Time	✓	-	✓	-	✓	-	✓	-	-
Symptomatology Question	✓	-	✓	-	-	-	-	-	-
CVS-Q	✓	-	✓	-	✓	-	✓	-	-
Informed Consent	-	✓	-	-	-	-	-	-	-
Demographics	-	✓	-	-	-	-	-	-	-
Habitual Lens (brand and wear schedule), Lens Care, Drops	-	✓	-	-	-	-	-	-	-
Medical History	-	✓	✓	-	✓	-	✓	✓	✓
Concomitant Medications	-	✓	✓	-	✓	-	✓	(✓)	✓
Inclusion/Exclusion	-	✓	✓	-	-	-	-	-	-
VA (OD, OS,OU logMAR distance with habitual contact lenses)	-	✓	-	-	-	-	✓	-	(✓)
Subjective (manifest) refraction*	-	✓	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)
BCVA (OD, OS, OU, logMAR distance with manifest refraction)*	-	✓	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)
Habitual contact lens power optimization (if needed)	-	✓	-	-	-	-	-	-	-
Biomicroscopy	-	✓	✓	-	✓	-	✓	(✓)	✓
Dispense new (optimized) habitual contact lenses	-	✓	-	-	-	-	-	-	-
VA (OD, OS, OU logMAR distance with new	-	✓	✓	-	-	-	-	-	-

(optimized) habitual contact lenses)									
Determine power and fit study lenses	-	✓	-	-	-	-	-	-	-
Randomization (after re-verifying qualifications)	-	-	✓	-	-	-	-	-	-
Dispense study lenses in a masked manner	-	-	-	✓	-	✓	-	-	-
VA (OD, OS, OU logMAR distance with study lenses)	-	-	-	✓	✓	✓	✓	-	-
Lens fitting assessment (lens movement and position)*	-	✓	✓	✓	✓	✓	✓	-	-
[redacted]									
[redacted]									
[redacted]									
[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 study product
*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

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

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

[redacted]

[redacted]

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[redacted]

[redacted]

[redacted]

[redacted]

	[redacted]

5 INTRODUCTION

5.1 Rationale and Background

Increasing numbers of contact lens wearers use digital devices for prolonged and demanding periods throughout the day and suffer from Digital Eye Fatigue (DEF). Near universal use of digital devices, and time spent on them, is becoming a growing short-term problem and a concern for long-term vision health. Currently, there are few products addressing DEF, and mostly in spectacle form.

[redacted] The targeted population is pre-presbyopic (< 40 years of age) with heavier usage of digital devices.

5.2 Purpose of the Study

The purpose of this post-approval market support study is to demonstrate the benefit of the DACP FreshTech lens in non-presbyopic contact lens wearers with symptoms of eye fatigue as compared to the DACP (sphere) design. The primary objective is to demonstrate noninferiority in distance visual acuity of DACP FreshTech compared to DACP at the 1-week follow-up visit.

[redacted]

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

5.3 Risks and Benefits

There are no known risks to use of the test DACP FreshTech product. [redacted]

There may be unknown risks to use of the test DACP FreshTech product. Any risk to subjects in this clinical study will be minimized by compliance with the eligibility criteria and study procedures, clinical oversight and monitoring. The potential harms associated with on-eye exposure to the new lens design include blurred vision and ocular discomfort. In general, the risks with this new contact lens are anticipated to be similar to other marketed daily disposable soft contact lenses.

Refer to the product labeling for additional information.

6 STUDY OBJECTIVES

6.1 Primary Objective(s)

The primary objective of this study is to demonstrate noninferiority in distance visual acuity of DACP FreshTech contact lenses compared to DACP contact lenses.

Table 6–1 Primary Objective(s)

Objective(s)	**Endpoint(s)**
Demonstrate noninferiority of DACP FreshTech in distance visual acuity when compared to DACP	Mean VA with study lenses (OU; logMAR [4m])

6.2 Secondary Objective(s)

Not Applicable

[redacted]

6.4 Safety Objective(s)

Table 6–3 Safety Objective(s)

Objective(s)	Endpoint(s)
Describe the safety profile of investigational products based on evaluation of safety endpoints	• AEs • Biomicroscopy findings • Device deficiencies

7 INVESTIGATIONAL PLAN

7.1 Study Design

This is a prospective, randomized, double-masked, bilateral crossover, single site study, comparing 2 daily disposable contact lenses. The expected duration of subjects participation in the study is 16-28 days, with 4 scheduled visits. The study is expected to be completed in approximately 11 weeks.

7.2 Rationale for Study Design

This study design was selected to include symptomatic subjects as the appropriate population for this trial. Subjects will be fitted with their optimal habitual prescription and wear for approximately one week before wearing the test and control lenses. They will then be questioned again for symptoms of digital eye fatigue, with further assurance that any fatigue related symptoms are not related to a wrong prescription or old lenses that may have deposits or poor surface and thus inclusion in the study is appropriate. [redacted]

[redacted] The age of the study population is necessary to avoid confounding with the natural lessening of accommodation with an early presbyopic population. The remaining aspects of the study design are well established.

7.2.1 Purpose and Timing of Interim Analyses and Resulting Design Adaptations

Not applicable

7.3 Rationale for Duration of Treatment/Follow-Up

One week exposure of test and control for each subject [redacted]

7.4 Rationale for Choice of Control Product

The control product, DACP, was chosen to compare the effects of a spherical design versus the aspherical low plus design of the test product and to avoid any confounding factors related to lens material.

7.5 Data Monitoring Committee

Not applicable

8 STUDY POPULATION

The study population consists of male and female subjects 18 to 35 years of age with normal eyes (other than correction for refractive error). Subjects must be symptomatic (self-reported eye fatigue) who use digital devices ≥4 hours a day/5 days a week, and score ≥6 on the Computer Vision Syndrome Questionnaire (CVS-Q). It is aimed to enroll (consent) approximately 72 subjects in one site in the US. Estimated time needed to recruit subjects for the study is approximately 11 weeks.

8.1 Inclusion Criteria

1. Subject must be 18 to 35 years of age
2. Subjects must be able to understand and must sign an informed consent form (ICF) that has been approved by an Institutional Review Board (IRB/IEC).

3. Current wearers of commercial spherical soft daily wear lenses with at least 3 months wearing experience, with a minimum wearing time of 5 days per week and 8 hours per day
4. Requiring spherical contact lens distance correction in each eye within the range of -1.00 to -6.00 D in 0.25 D steps
5. Currently using digital devices (computer, tablet, and/or smart phone) for an average of 4 hours per day
6. Self-reported “eye fatigue” at least once per week attributable to digital device use with habitual lenses (at pre-screening) and with optimized habitual lenses
7. Subjects must score ≥ 6 on the Computer Vision Syndrome Questionnaire (CVS-Q) with habitual lenses (at pre-screening) and with optimized habitual lenses (at Visit 2)
8. Astigmatism less than or equal to 0.75 D (as determined by manifest refraction at screening)
9. Best corrected distance visual acuity greater than or equal to 0.10 or 20/25 in each eye (as determined by manifest refraction at screening)
10. Willing to NOT use rewetting/lubricating drops during the period of study product exposures
11. Willing to NOT use any near aid (eg, reading glasses) at any time during the study
12. Mobile digital device with active data and text plan, able to receive email and text messages

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.

8.2 Exclusion Criteria

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

1. Any self-reported accommodative, binocular vision issues, or issues of eye alignment
2. Any anterior segment infection, inflammation, disease, or abnormality that contraindicates contact lens wears as determined by the Investigator
3. 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
4. History of refractive surgery or irregular cornea

5. Ocular or intraocular surgery within the previous 12 months (excluding placement of punctal plugs) or during the study
6. 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
7. Current or history of pathologically dry eye in either eye
8. Current or history of herpetic keratitis in either eye
9. Eye injury within 12 weeks immediately prior to enrollment for the study
10. 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
11. Monocular subjects (only one eye with functional vision
12. Known pregnancy at time of enrollment
13. Concurrent participation of the subject in a contact lens or contact lens care product clinical trial or within the previous 30 days
14. 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

Rescreening of subjects is not allowed in this study.

9 TREATMENTS ADMINISTERED

9.1 Investigational Product(s)

Test Product(s): DACP FreshTech

Control Product: DACP

Table 9–1 Test Product

Test Product	DACP FreshTech
	[redacted]
Manufacturer	Alcon Research, LLC 6201 South Freeway

	Fort Worth, Texas 76134-2099 USA
Indication for use and intended purpose in the current study	DACP FreshTech contact lenses are indicated for daily wear for the optical correction of refractive ametropia (myopia and hyperopia) in non-aphakic persons with non-diseased eyes with up to approximately 1.50 D of astigmatism that does not interfere with visual acuity.
Product description and parameters available for this study	• Material: nelfilcon A • Water content: 69% • Power range: -1.00 to -6.00 D in 0.25 D steps • Base curve (mm): 8.7 • Diameter (mm): 14.0
Formulation	Please see the package insert
Usage	• Wear: o Daily Wear o Bilateral • Replacement period: Daily Disposable • Exposure: At least 8 hours per day, over the study treatment duration (7±2 days) • Lens Care: N/A
Number/Amount of product to be provided to the subject	Lenses will be provided in packages of 10 lenses per power, identified with the following: • a color coded label stating the protocol number • LID Number • power • an investigational use only statement • tracking number
Packaging description	Blister foil pack
Labeling description	• Lens Foil label includes: - lens identifier

	- base curve - diameter - packing solution - power - lot number - expiration date - content statement - investigational device statement - Sponsor information
Storage conditions	Lenses should be stored at room temperature
Supply	Test product will be shipped to the site by Alcon

Table 9–2 Control Product

Control Product(s)	DACP
	[redacted]
Manufacturer	Alcon Research, LLC 6201 South Freeway Fort Worth, Texas 76134-2099 USA
Indication for Use	DACP contact lenses are indicated for daily wear for the optical correction of refractive ametropia (myopia and hyperopia) in non-aphakic persons with non-diseased eyes with up to approximately 1.50 D of astigmatism that does not interfere with visual acuity.
Product description and parameters available for this study	• Material: nelfilcon A • Water content: 69% • Power range: -1.00 to -6.00 D in 0.25 D steps • Base curve (mm): 8.7 • Diameter (mm): 14.0
Formulation	Please see the package insert

Usage	• Wear: o Daily Wear o Bilateral • Replacement period: Daily Disposable • Exposure: At least 8 hours per day, over the study treatment duration (7±2 days) Lens Care: N/A
Number/Amount of Product to be Provided to the subject	Lenses will be provided in packages of 10 lenses per power, identified with the following: • a color coded label stating the protocol number • LID Number • power • an investigational use only statement • tracking number
Packaging description	Blister foil pack
Labeling description	• Lens Foil label includes: - lens identifier - base curve - diameter - packing solution - power - lot number - expiration date - content statement - investigational device statement - Sponsor information
Storage conditions	Lenses should be stored at room temperature
Supply	Test product will be shipped to the site by Alcon.

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

During the clinical study, the following additional medical devices are required:

- Habitual optimized lenses will be optimized for power
    - Contact lenses will not be over labeled (subjects know they are wearing their habitual lenses)
    - Subjects will be instructed by site personnel to use their habitual lenses according to the instructions for use
    - Subjects will be provided with 1 to 10 habitual optimized lenses per eye, depending on replacement schedule
    - Subjects will be instructed to wear lenses each day for at least 8 hours per day over the study treatment duration (7±2 days)
    - Subjects will continue to use their habitual lens care products when wearing the optimized habitual lenses

9.3 Treatment Assignment / Randomization

Subjects will be randomized in a 1:1 ratio to receive treatment (lens) in crossover sequence DACP FreshTech then DACP or DACP then DACP FreshTech, 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 sequences to randomization numbers in the specified ratio. Subjects will be assigned treatment according to the randomization list uploaded in the IRT system. The randomization list will be generated and maintained by the Study Sponsor.

At Visit 2, all eligible subjects will be randomized via the EDC/IRT integration system to one of the treatment sequences. 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 FreshTech and DACP (in a crossover fashion) for approximately 7 days for each period. Subjects, the Investigator, and masked study personnel (site and Sponsor) will be masked to the assigned treatment sequence.

Table 9–3 Unmasked Individuals Associated with the Study

Unmasked Individual	**Extent of Unmasking**	**Rationale**
Unmasked Study Coordinator(s)	The Unmasked Study Coordinator(s) will manage IP inventory, as well as IP administration. This individual will have access to IP supply, accountability logs, and other documents or supplies pertaining to IP. The unmasked coordinator will also assist with device deficiency and AE reporting.	The Unmasked Study Coordinator(s) will be unmasked to allow for storage and dispensing, as well as accountability for all IP.
Clinical Operations Lead (COL)	The COL will have access to IP supply, accountability logs, and other documents or supplies pertaining to IP. This individual assist with masked and unmasked data reviews.	The COL will be unmasked to allow for oversight of the CSM, in conjunction with all IP accountability tasks.
Clinical Site Manager (CSM)	CSM will have access to IP supply, accountability logs, and other documents or supplies pertaining to IP accountability. This individual monitors unmasked and masked study data.	The CSM will be unmasked to allow for performance of IP accountability, management of device deficiencies and related AE lens returns, and other IP related tasks.

Clinical Supplies Coordinator	The Clinical Supplies Coordinator will have access to the IP inventory, accountability logs and other documents or supplies for management and reconciliation of the IP.	The Clinical Supplies Coordinator will be unmasked to allow for storage, management, and distribution of IP inventory and other IP related products/tasks.
Unmasked Data Manager(s)	The Unmasked Data Manager(s) will have access to restricted fields in EDC that would contain unmasking data.	The Unmasked Data Manager(s) will be unmasked to allow for review of all restricted data.
IRT Manager	The IRT Manager will be unmasked to allow for system programming, testing, and to allow for technical oversight of the system.	The IRT manager is unmasked to all aspects of the trial for system development purposes.
Randomization Specialist	The Randomization Specialist will be unmasked to allow for generation of the randomization list and uploading of that list into the IRT system.	Generates and therefore has full knowledge of treatment codes but otherwise is operationally not associated with the Clinical Trial Team or any decision-making aspects related to clinical trial design, execution, or reporting.
Unmasked Statistician	The Unmasked Statistician will be unmasked to treatment sequence assignment at time of sample size reassessment.	The Unmasked Statistician will be unmasked to allow for reassessment of sample size at the planned interim analysis.

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. Unmasking will also occur at the time of the interim analysis intended for sample size reassessment, with treatment-related information being revealed only to designated personnel as listed in the table above.

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

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

9.5 Accountability Procedures

Upon receipt of the 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 AE (ie, ADE or SADE) are returned to the Study Sponsor for investigation, unless otherwise directed by the Sponsor. Refer to Section 11 of this protocol for additional information on the reporting of device deficiencies and AEs and the return of study products associated with these events.

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

9.6 Changes to concomitant medications, treatments/ procedures

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

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

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

10 STUDY PROCEDURES AND ASSESSMENTS

10.1 Informed Consent and Screening

Pre-screening activities include questions of digital use time and symptomatology and also administering the CVS-Q. Subjects must also have use of a mobile digital device with active data and text plan, able to receive email and text messages.

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 Digital Use Questionnaire

Administer the digital use questionnaire at pre-screening and with details of digital use experiences at Visit 2-4 (follow-up visits). Subjects must answer at least 4 hours per day at pre-screening to qualify to participate in the study.

[redacted]

10.2.3 Computer Vision Syndrome Questionnaires (CVS-Q)

Administer the CVS-Q at pre-screening and Visit 2-4 (follow-up visits). Subjects total score must be ≥6 points at pre-screening and again at Visit 2 to qualify to participate in the study.

10.2.4 Demographics

Obtain demographic information including age, race, ethnicity, and sex. Collect at Visit 1.

10.2.5 Medical History and Concomitant Medications

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. Collect at each study visit.

10.2.6 Investigational Product compliance

Review subject compliance with the IP usage and adjunct product usage and collect all used and unused study IPs.

10.2.7 VA Assessment (logMAR)

Perform logMAR VA, distance only (4m), OD, OS and OU, with habitual contact lenses at Visit 1 and 4; with optimized habitual contact lenses at Visit 1 and 2; with study lenses at Visits 2-4, and with habitual lenses at Exit.

10.2.8 Subjective Refraction

Perform subjective (manifest) refraction. Required for Visit 1. Assessment should be performed at any other study visit if necessary (ie, decrease of VA by 2 lines or more). Capture data in source only.

10.2.9 BCVA (logMAR)

Perform BCVA (logMAR) at distance (4m) with manifest refraction, OD, OS, OU. Required for Visit 1. Assessment should be performed at any other study visit if necessary (ie, decrease of VA by 2 lines). Capture data in source only.

10.2.10 Slit-Lamp Biomicroscopy

Perform biomicroscopy examination of the cornea, adnexa and anterior segment of the eye must be performed, OD and OS, without contact lenses, and before instillation of any diagnostic eye drops, at each study visit.

10.2.11 Study Lens Fitting Assessment

Evaluate the study lenses at each scheduled study visit by performing the following assessments: Lens movement (overall fit) and Lens position (centration). Capture data in source only at dispensing.

10.2.12 Adverse Event Collection

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

10.2.13 Device Deficiencies

Assess and record any device deficiencies that are reported or observed at each study visit, including those associated with changes in concomitant medication dosing since the previous visit. Requirements for reporting device deficiencies in the study can be found in Section 11. Note: AEs and device deficiencies must be recorded for all enrolled subjects from the time of

signature of informed consent, regardless of subject enrollment status (screen failure or randomized).

[redacted]

[redacted]

10.3 Unscheduled Visits

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

- Collect AE information
- Record changes in medical condition or concomitant medication
- Assess and record VAs
- Collect device deficiency information
- Perform 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 Exit procedures according to Table 3-1 Schedule of Study Procedures and Assessments, as possible.

10.4 Discontinued Subjects

10.4.1 Screen Failures

Subjects who were excluded from the study after signing the informed consent and prior to randomization and product/dispense of study product.

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 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

Not applicable.

10.5 Clinical Study Termination

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

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

- The Study Sponsor must:
    - Immediately notify the Investigator(s) and subsequently provide instructions for study termination.
    - Inform the Investigator and the regulatory authorities of the termination/suspension and the reason(s) for the termination/suspension.
- The Investigator must:
    - Promptly notify the IRB/IEC of the termination or suspension and of the reasons.
    - Provide subjects with recommendations for post-study treatment options as needed.

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

10.5.1 Follow-up of subjects after study participation has ended

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

11 ADVERSE EVENTS AND DEVICE DEFICIENCIES

11.1 General Information

An AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device (test product). Refer to the Glossary of Terms for categories of AEs and SAEs.

Figure 11–1 Categorization of All Adverse Events

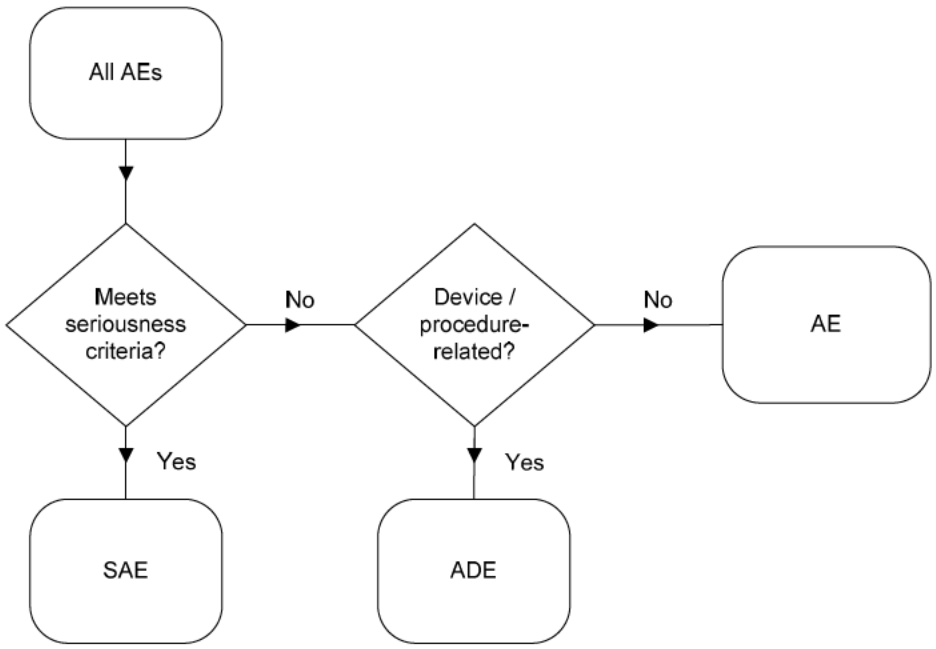
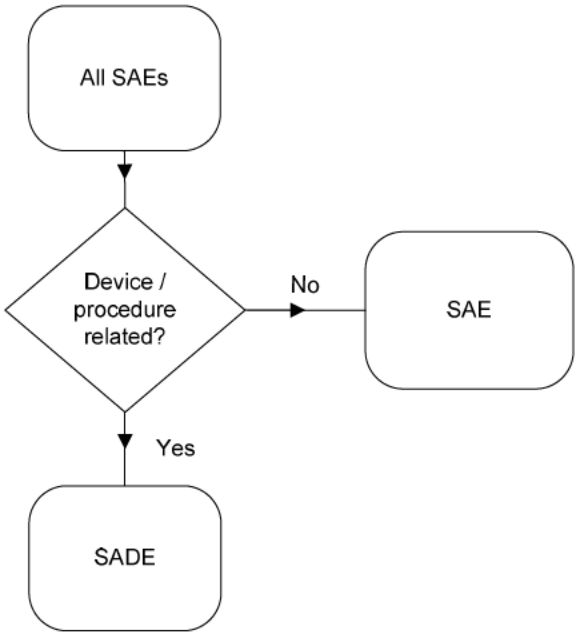


Figure 11–2 Categorization of All Serious Adverse Events



11.2 Monitoring for Adverse Events

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

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

Changes in *biomicroscopy parameters and/or questionnaires* evaluated during the study are to be reviewed by the Investigator. Any untoward (unfavorable and unintended) change in *a biomicroscopy 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 (i.e., 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 products on the Device Deficiency eCRF. The site must submit all available information on ADEs, SAEs, and device deficiencies to the Study Sponsor immediately as follows:

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

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

Any AEs and device deficiencies for non-study marketed devices/products (i.e., habitual contact lenses and contact lens care products) will be considered and processed as spontaneous following the post-market vigilance procedures and should be communicated to the device's/product's manufacturer as per local requirements.

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

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

Intensity and Causality Assessments

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

Intensity (Severity)

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

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

Causality

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

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

11.4 Return product analysis

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

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

11.5 Unmasking of the Study Treatment

Masked information on the identity of the assigned medical device should not be disclosed during the study (see Section 9.4). 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 (i.e., medical emergency), the code may be broken prior to contact with the Study Sponsor. The Study Sponsor must be informed of all cases in which the code was broken and of the circumstances involved. Additionally, the Study Sponsor may be required to unmask the information in order to fulfill expedited regulatory reporting requirements.

11.6 Follow-Up of Subjects with Adverse Events

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

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

All complaints received after this time period will be considered and processed as spontaneous (following the 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

Pregnancy should be included in the Medical History section of the eCRF 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. An Alcon form will be utilized to capture all pregnancy-related information until birth of the child.

12 ANALYSIS PLAN

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

12.1 Subject Evaluability

Final subject evaluability must be determined prior to breaking the code for masked treatment assignment and locking the database, based upon the Deviations and Evaluability Plan (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 (DACP FreshTech or DACP) evaluated in this study. The optimized habitual lenses and trial-fit lenses are not considered study lenses for the purpose of safety evaluation. 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) will include all randomized subjects who are exposed to any study lenses evaluated in this study, not including the optimized habitual and trial-fit lenses.

12.2.3 Per Protocol Analysis Set

The Per Protocol (PP) analysis set is a subset of FAS and excludes all data/subjects that 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, [redacted] endpoints.

[redacted]

12.4.1 Analysis of Primary Effectiveness Endpoint(s)

The primary objective of this study is to demonstrate noninferiority in mean distance visual acuity of DACP FreshTech compared to DACP sphere at the Week 1 Follow-up visit.

The primary endpoint is the mean distance VA with study lenses. The corresponding assessment is collected bilaterally (OU) in logMAR, at the Dispense and Week 1 Follow-up visits.

12.4.1.1 Statistical Hypotheses

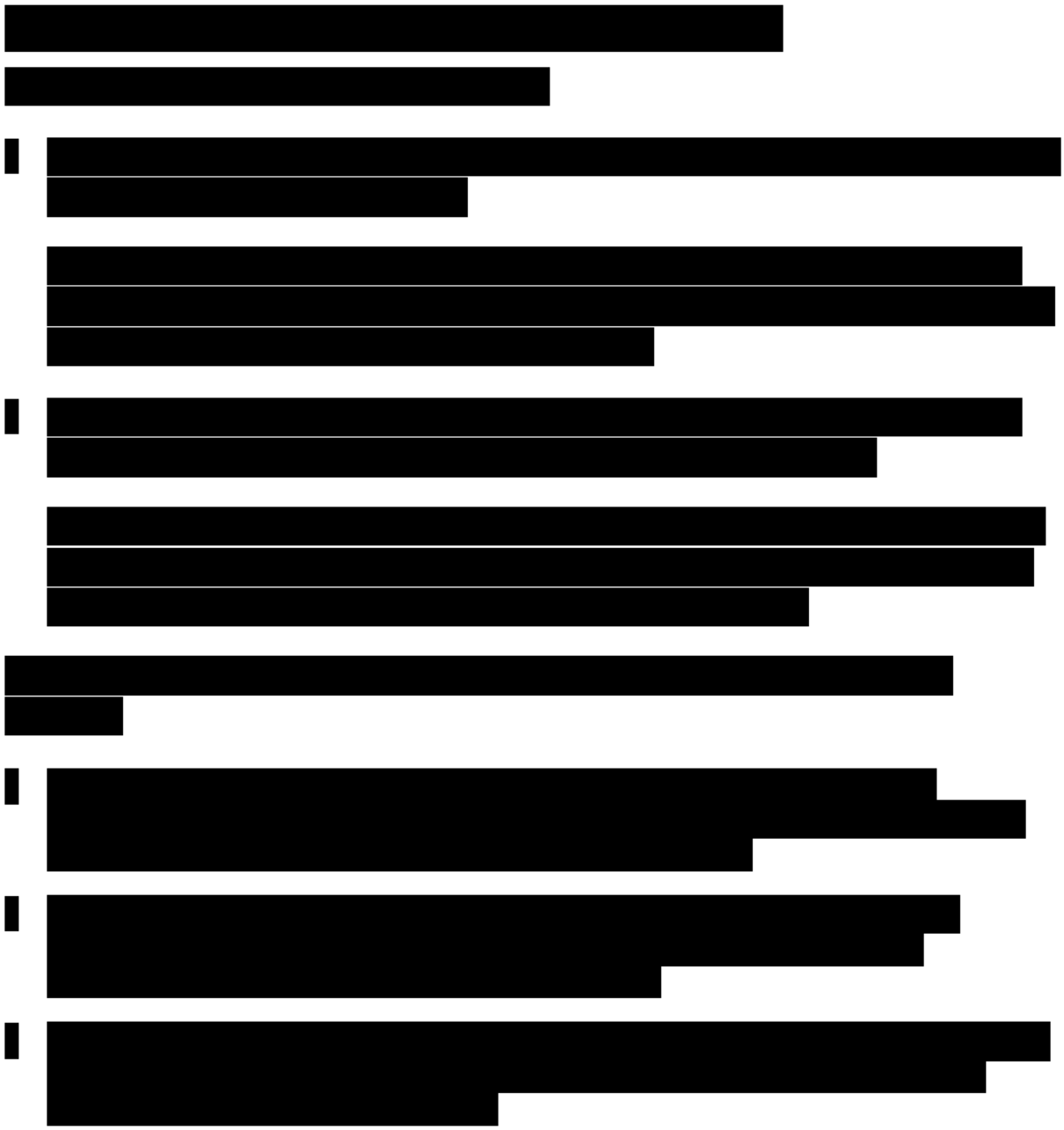
The null and alternative hypotheses are formulated in terms of the predefined margin of 0.05 for noninferiority:

H_0: $\mu_{(T)} - \mu_{(C)} \geq 0.05$
H_a: $\mu_{(T)} - \mu_{(C)} < 0.05$

where $\mu_{(T)}$ and $\mu_{(C)}$ denote the mean distance logMAR VA for DACP FreshTech and DACP, respectively, at Week 1 Follow-up.

12.4.1.2 Analysis Methods

A mixed effects 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 crossover will also be accounted for in the model. Lens difference (DACP FreshTech minus DACP) and the corresponding one-sided 95% upper confidence limit (UCL) will be computed. Noninferiority in VA will be declared if the UCL is less than 0.05.



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12.4.2.1 Statistical Hypotheses and Model

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[redacted]

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[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 any of the 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 non-serious 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.

12.7 Safety Analyses

[redacted]

[redacted]

Actions to be taken following the communication of the new sample size will depend on the new sample size, as detailed below:

New Sample Size	***Action***
Smaller than or equal to 66	No changes and complete the study with the originally planned sample size of 66 completers
Larger than 66 but smaller or equal than 90	Update and complete the study as per new sample size requirement
Larger than 90	No changes and complete the study with the originally planned sample size of 66 completers

12.8 Sample Size Justification

Sample size calculations are based on prior clinical study (CLD523-C001) which evaluated performance of DACP Digital and DACP sphere, preliminary results from IIT #42145213, as well as other publications.

Primary Effectiveness

To demonstrate noninferiority (margin = 0.05 in logMAR; ½ line in Snellen) in mean distance VA as a one-tailed hypothesis with α=0.05, and using a standard deviation of 0.075 for paired differences based on CLD523-C001, 80% power can be attained with a sample size of 16 (8 per sequence).

[redacted]

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13 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

13.1 Subject Confidentiality

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

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

13.2 Completion of Source Documents and Case Report Forms

The nature and location of all source documents will be identified to ensure that original data required to complete the CRFs exist and are accessible for verification by the site monitor, and all discrepancies shall be appropriately documented via the query resolution process. Site monitors are appointed by the Study Sponsor and are independent of study site staff.

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

At a minimum, source documents include the following information for each subject:

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

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

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

13.3 Data Review and Clarifications

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

13.4 Sponsor and Monitoring Responsibilities

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

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

13.5 Regulatory Documentation and Records Retention

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

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

13.6 Quality Assurance and Quality Control

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

14 ETHICS

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

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

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

Before clinical study initiation, this protocol, the informed consent form, any other written information given to subjects, and any advertisements planned for subject recruitment must

be approved by an IRB/IEC. The Investigator must provide documentation of the IRB/IEC approval to the Study Sponsor. The approval must be dated and must identify the applicable protocol, amendments (if any), informed consent form, assent form (if any), all applicable recruiting materials, written information for subject, and subject compensation programs. The IRB/IEC must be provided with a copy of the Package Insert, any periodic safety updates, and all other information as required by local regulation and/or the IRB/IEC. At the end of the study, the Investigator must notify the IRB/IEC about the study's completion. The IRB/IEC also must be notified if the study is terminated prematurely. Finally, the Investigator must report to the IRB/IEC on the progress of the study at intervals stipulated by the IRB/IEC.

Voluntary informed consent must be obtained in writing from every subject and the process shall be documented before any procedure specific to the clinical investigation is applied to the subject. The Investigator must have a defined process for obtaining consent. Specifically, the Investigator, or their delegate, must explain the clinical study to each potential subject and the subject must indicate voluntary consent by signing and dating the approved informed consent form. The subject must be provided an opportunity to ask questions of the Investigator, and if required by local regulation, other qualified personnel. The Investigator must provide the subject with a copy of the consent form written in a language the subject understands. The consent document must meet all applicable local laws and provide subjects with information regarding the purpose, procedures, requirements, and restrictions of the study, along with any known risks and potential benefits associated with the IP and the study, the available compensation, and the established provisions for maintaining confidentiality of personal, protected health information. Subjects will be told about the voluntary nature of participation in the study and must be provided with contact information for the appropriate individuals should questions or concerns arise during the study. The subject also must be told that their records may be accessed by appropriate authorities and Sponsor-designated personnel. The Investigator must keep the original, signed copy of the consent (file in subject's medical records) and must provide a duplicate copy to each subject according to local regulations.

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

15 REFERENCES

15.1 References applicable for all clinical studies

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

15.1.1 US references applicable for clinical studies

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

15.2 References for this clinical study

Orsborn G, Vega JA, Chamberlain P. Assessment of a new lens design to improve symptoms of eye fatigue in users of digital devices. Presented at: Annual Global Specialty Lens Symposium; 2016 Jan 21-24; Las Vegas, Nevada.

Tilia D, Sha J, Yeotikar N, et al. Visual performance, accommodative function and digital eye strain with digital zone optics contact lenses. Optom Vis Sci. 2018;95:E-abstract 180017.

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