Study Implementation document:

CLINICAL EVALUATION OF MYDAY LENSES

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[redacted]

_____ Date:_____

[redacted]

PERSONNEL & FACILITTIES

STUDY SPONSOR: [redacted]

SPONSOR COORDINATOR: [redacted]

STUDY MONITOR: [redacted]

Protocol Synopsis

Protocol / Study Number	JP-MKTG-201709_02
Title	Clinical Evaluation of CooperVision MyDay® Lenses
Name of Device(s) and (by USAN material)	MyDay® (stenfilcon A), 1-DAY ACUVUE® TruEye® (narafilcon A)
Indications for Use	**Approved for use:** • stenfilcon A. (Single use daily wear) • narafilcon A. (Single use daily wear) **Indication for use in this study:** • 3 hours of single use daily wear
Study Design	3 hours, single masked, randomized, contralateral, single use daily wear, non-dispensing study.
Purpose	The aim of this non-dispensing study is to evaluate the fitting performance of MyDay® [redacted] compared it with 1-DAY ACUVUE® TruEye® [redacted] in a range of spherical powers.
Study Duration	The anticipated timeline for this study is as follows: • Patient enrolment: February 2018 • Visits: V1 (Baseline), V2 (After 3 hours of lens wear/Exit visit)
Patient Population	Adapted spherical soft contact lens wearers with myopia that provide written informed consent and meet protocol entry criteria.
Sample Size	Target enrollment and completion of 40 subjects total.
Clinical Site Destination	Japan
Number of Clinical Sites	4 Sites
Patient Follow-up	Patients enrolled in this study will be followed up: • Follow-up: 3 hours of lens wear/Exit visit
Primary Endpoints	*Objective:* Lens fitting characteristics, such as Lens movement, Horizontal lens centration, Vertical lens centration, Corneal coverage, Lens lag, Overall fitting performance, Investigator Fit Preference
Secondary Endpoints	Subjective: Subjective rating of wearing comfort, dryness, stinging/burning, edge awareness/lens awareness, and lens preference

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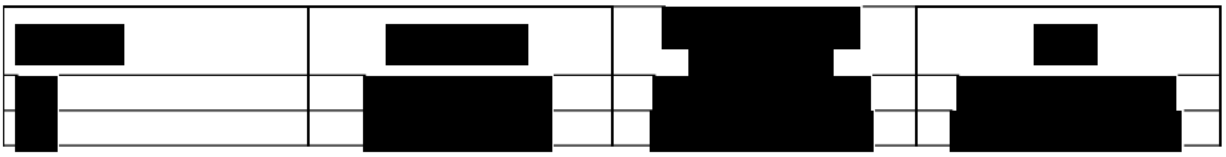
DOCUMENT CHANGE HISTORY



1 Introduction

Cooper Vision Inc. is interesting in evaluating the fitting characteristics of its MyDay lenses in an Japanese population.

2 Study Objective

This is a feasibility study to evaluate the fitting performance of MyDay [redacted] lens (Test) against TruEye [redacted] (Control) over 3 hour of lens wear in a Japanese population.

The key variables of interest is:

- Lens fit performance

Other variables of interest are:

- Subjective comfort, dryness, stinging/burning, edge awareness/lens awareness and preference
- [redacted]

2.1 Study Hypothesis

The study primary hypothesis is that there will be no differences between the Test and Control lenses in term of fitting characteristics.

3 Study Design

This will be a non-dispensing, randomized, contralateral study comparing a test lens against an appropriate control lens. Each subject will be randomized to wear the test lens in one eye and the control lens in the other eye. It is anticipated that this study will involve up to 2 visits.

4 Ethics Review / Statement of Compliance

4.1 Relevant Standards / Guidelines

This implementation document has been developed in accordance with the following:

- ISO 14155 Clinical Investigation of Medical Devices for Human Subjects, Parts 1 & 2
- ICH Harmonized Tripartite Guideline for Good Clinical Practice
- Declaration of Helsinki

4.2 Institutional Review Board

This study will be conducted in accordance with Institutional Review Board regulations (U.S. 21CFR Part 56.103) or applicable IEC regulations. Copies of all IRB/IEC correspondence with the investigator/sponsor will be kept on file.

[redacted]

4.3 Informed Consent

Informed consent shall be obtained in writing from the subject and the process shall be documented before any procedure specific to the clinical investigation is carried out.

5 Clinical Trial Registration

1. This study will be registered in www.ClinicalTrials.gov.
2. Prior to the implementation of the study, the contents of the study protocol will be registered with masking the key words and numbers to protect the company confidentiality in the publication database set up by the Japan Pharmaceutical Information Center and will be updated suitably according to the change and progress.

Results of this study will be released with masking the key words and numbers to protect the company confidentiality only in the publication database set up by Japan Pharmaceutical Information Center after taking necessary measures for the protection of the human rights of study subjects and related parties or the rights and profits of researchers, etc. and related parties, without delay after the completion of the study.

6 Potential Risks and Benefits to Human Subjects

There might not be direct benefits to the subjects in this study. However, participation in a study may contribute to scientific research information that may be used in the development of new contact lens products. In addition, subjects will receive an examination of the front part of their

eyes and may have the opportunity to try a different type of soft contact lenses and/or different lens care products at no cost to them.

The investigational contact lenses used in this study are intended for daily wear (NOT extended wear) with usage of up to 12 hours only, in contrast to the average wearing time of 10-16 hours for daily wear lenses. In addition, this study is a non-dispensing study, meaning the lenses are not dispensed to subjects to take home and lens wear will be monitored closely by the investigators. This study is considered to be a non-significant risk study based on United State Food and Drug administration (FDA) and International Standards Organization (ISO) guidelines due to the daily wear nature of the study.

Complications that may occur during the wearing of contact lenses include discomfort, dryness, aching or itching eyes, excessive tearing, discharge, hyperemia and variable or blurred vision. More serious risks may include photophobia, iritis, corneal edema or eye infection. Although contact lens-related infections are very infrequent, the possibility does exist. The incidence of infection due to day-wear soft lenses is 0.035%. Almost always an infection will occur only in one eye. This risk is assumed by 35-million Americans who currently wear contact lenses.

The lenses being used may not have the exact prescription power needed by the subject. The prescription closed to the available SKUs without the over minus correction will be made for each eye. This may require that subjects wear their spectacle correction over the study lenses in order to see well at distance. In this case, it is possible that subjects may experience “eye strain” when focusing through this extra power which may cause headaches. Routine clinical procedures including auto-refraction, auto-keratometry, visual acuity, anterior ocular health assessment, and contact lens fitting will be used.

7 Materials and Methods

7.1 Participants

Approximately 40 subjects will be enrolled for this study. All subjects will be Japanese. Each subject will be given a unique ID number. Additionally, all subjects must meet the study inclusion and exclusion criteria listed below.

Inclusion criteria

A person is eligible for inclusion in the study if he/she:

- Is Japanese
- Has had a self-reported oculo-visual examination in the last two years.
- Is at least 18 years of age and has full legal capacity to volunteer.
- Has read and understood the informed consent letter.
- Is willing and able to follow instructions and maintain the appointment schedule.
- Is correctable to a visual acuity of 20/40 or better (in each eye) with their habitual vision correction or 20/20 best-corrected.
- Currently wears soft contact lenses.
- Has clear corneas and no active ocular disease.

Exclusion Criteria

A person will be excluded from the study if he/she:

- Has never worn contact lenses before.
- Has any systemic disease affecting ocular health.
- Is using any systemic or topical medications that will affect ocular health.
- Has any ocular pathology or severe insufficiency of lacrimal secretion (moderate to severe dry eyes) that would affect the wearing of contact lenses.
- Has persistent, clinically significant corneal or conjunctival staining using sodium fluorescein dye.
- Has any clinically significant lid or conjunctival abnormalities, active neovascularization or any central corneal scars.
- Is aphakic.
- Has undergone corneal refractive surgery.
- Is participating in any other type of eye related clinical or research study.

7.2 Study Materials

7.2.1 Contact lens

Subjects will be randomized to receive either the Test or Control lens as a matched pair at each visit per a predetermined randomization schedule. The Test lenses used in this study will be

provided by the Sponsor. The Control lenses will be sourced by the site. Details of the contact lenses are shown in Table 1.

	MyDay (Test)	TruEye (Control)
Material	stenfilcon A	narafilcon A
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	

Table 1: Study lenses

7.2.2 Contact Lens care

No contact lens care is required for this study as lenses are to be worn for a single day only.

7.2.3 Storage of Lenses and Lens Care Solutions

The study materials must be stored in a secured area. All lenses and lens care solutions should be stored at controlled room temperature (59-86°F).

7.2.4 Clinical Supply Inventory

The investigator must keep an accurate accounting of the study product during the study. A detailed inventory must be completed for study supplies. The study supplies are to be used in accordance with the implementation document by subjects who are under the direct supervision of an investigator.

7.2.5 Disposal of Consumables

This study dispenses consumables (lenses) to participants for use during the study. Study lenses worn by participants will be discarded at the each site.

7.2.6 Masking and Control of Study Materials

The contact lenses coding will be masked to subject.

7.2.7 Ordering and Accountability of Study Materials

The test lenses and the control lenses will be provided by the sponsor.

The investigator must complete an accurate accounting of the study product at the completion of the study. A detailed inventory must be completed for study supplies. All unused materials will be

returned to the Sponsor at the end of the study unless the investigator is otherwise directed by the study Sponsor.

7.3 Visit Schedule and Procedures

7.3.1 Visit 1: Baseline Visit

Procedures to be Performed

The following evaluations will be performed to assess eligibility according to the Inclusion and Exclusion Criteria at the baseline visit only:

- [redacted]
- The study lenses will be fitted according to the randomization table.
- Subjective ratings on insertion will be recorded according to the CVJ defined 0-10 scales. Lens preference will be recorded.
- The study pair of contact lenses will be allowed to settle for 5 minutes.
- The subject will be asked to score their subjective response according to the CVJ defined 0-10 scales. Lens preference will be recorded.
- Lens fit will then be assessed and graded according to the CVJ defined Grading scales.
- The subject will be discharged and asked to return for a follow-up visit after 3 hours.

7.3.2 Visit 2: 3 Hour Visit/Exit

- The subject will be asked to score their subjective response according to the CVJ defined 0-10 Grading scales. Lens preference will be recorded.
- [redacted]
- The lenses will be removed and retained.
- [redacted]
- The subject will be discharged and will sign the exit statement.

7.3.3 Summary of Visits and Procedures

Table 2 summarizes the visits and procedures for the study.

Table 2: Summary of Visits and Procedures

	Visit 1	Visit 3
Informed Consent	✓	
Meet inclusion/exclusion criteria	✓	
History at baseline	✓	
Demographics	✓	
[redacted]	[redacted]	
[redacted]	[redacted]	
Instillation of lens at office	✓	
Subjective assessments	✓	✓
Lens fit assessments	✓	✓
[redacted]	✓	✓
Exit study		✓

8 Adverse Event Reporting

8.1 Adverse Event Definitions

An 'adverse event' refers to any undesirable clinical occurrence in a participant, whether it is considered to be device-related or not. Adverse events (AE) may be classified as 'unanticipated adverse device effects,' 'serious adverse events,' 'significant adverse events,' or 'non-significant adverse events,' as defined below.

Classification	Definition
Serious Adverse Event	Those events that are life-threatening, or result in permanent impairment of a body function, or permanent damage to a body structure or necessitate medical (therapeutic) or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.
Significant Adverse Event	Those non-serious adverse events that occur with contact lens usage that are not sight-threatening but are usually symptomatic and may warrant therapeutic management and /or temporary or permanent discontinuation of contact lens wear.
Non-Significant Adverse Events	Those less severe non-serious adverse events that occur with contact lens usage that are not sight-threatening, may or may not be symptomatic and may warrant palliative management, such as ocular lubricants or temporary interruption of contact lens wear.
Unanticipated Adverse Device Effect	Adverse events in a clinical trial that were not previously identified in the protocol in terms of nature, severity, or degree of incidence. An Unanticipated Serious Adverse Device Effect is an unanticipated adverse event that is serious in nature and caused by or associated with the device and is considered reportable.

AE classification, coding (for reporting to the sponsor) and examples are provided in the following table of Contact Lens Adverse Event Classification and Reporting table:

Code	Condition	Reporting
Serious Adverse Events		
01	Presumed infectious keratitis or infectious corneal ulcer	Notify sponsor as soon as possible, **within 24 hours;** IRB reporting as per requirements
02	Permanent loss of ≥ 2 lines of best spectacle corrected visual acuity (BSCVA)	
03	Corneal injury that results in permanent opacification within central cornea (6mm)	
04	Uveitis or Iritis (e.g. presence of anterior segment inflammation as described in ISO 11980, Annex B)	
05	Endophthalmitis	
06	Hyphema	
07	Hypopyon	
08	Neovascularization within the central 6mm of cornea	
00	Other serious event	
Significant Adverse Events		
11	Peripheral (outside central 6mm), non-progressive, non-infectious ulcer	Notify sponsor as soon as possible, **within 5 working days**; IRB reporting as per requirements
12	Symptomatic corneal infiltrative event	
13	Superior epithelial arcuate lesions (SEALs) involving epithelial split	
14	Corneal staining ≥ dense coalescent staining up to 2mm in diameter (e.g. moderate, ISO 11980 grade 3)	
15	Corneal neovascularization ≥ 1.0mm vessel penetration (e.g. ≥ ISO 111980 Grade 2), if 2 grade change from baseline	
16	Any temporary loss of ≥ 2 lines BSCVA for ≥ 2wks	
17	Any sign and/or symptom for which subject is administered therapeutic treatment or which necessitates discontinuation of lens wear for ≥ 2 weeks	
10	Other significant event	
Non-significant Adverse Events		
21	Conjunctivitis (bacterial, viral or allergic)	

22	Papillary conjunctivitis if ≥ mild scattered papillae/follicles approximately 1mm in diameter (e.g. ISO 11890 Grade 2), if 2 grade change from baseline	Notify sponsor as soon as possible, **within 5 working days**; IRB reporting as per requirements
23	Asymptomatic corneal infiltrative events	
24	Any sign and/or symptom for which temporary lens discontinuation for > 1 day is recommended (if not already classified)	
20	Other sign and/or symptom warranting classification as a non-significant adverse event	

Normal or adaptive symptoms

Transient symptoms such as end-of-day dryness, lens awareness, itching or burning or other discomfort may occur with contact lens wear and may occasionally reduce wearing time. ***These are not reported as adverse events unless in the investigator's opinion they are unexpected in nature, severe or have a high rate of occurrence.***

This clinical study will also ascertain satisfaction or preference with subjective attributes such as comfort, vision, or lens handling. Responses to these subjective questionnaires will not be considered as Adverse Events.

8.2 Procedures for Adverse Events

Treatment of an adverse event will depend on its nature and severity. Based on the clinical judgment of the investigator the subject may be referred to an ophthalmologist for treatment. The investigator will attempt to determine whether the reaction is related to the test device or a result of other factors. An Adverse Event Form will be completed for each adverse event. If both eyes are involved, a separate Adverse Event Form will be completed *for each eye*. Whenever possible, the adverse event will be photo-documented.

Expenses incurred for medical treatment as part of study participation will be paid by the sponsor (bills and prescription receipts kept). The subject must be followed until resolution and a written report completed indicating the subsequent treatment and resolution of the condition.

8.3 Reporting Adverse Events

All potential Serious and Unanticipated Adverse Device Effects that are related or possibly related to subject participation will be reported to the Principal Investigator and the sponsor within 24

hours of the investigator becoming aware of the event. The Principal Investigator will report the event to the IRB as soon as possible (by fax, mail/delivery, phone, or email). All fatal or life threatening events will be reported immediately to the IRB.

Significant and Non-Significant Adverse Events will be reported to the sponsor as soon as possible, but no later than 5 working days after the occurrence.

8.4 Discontinuation from the Study

A subject's study participation may be discontinued at any time if, in the opinion of the sponsor or the investigator it is in the best interest of the subject. All discontinuations will be fully documented on the appropriate study forms and the Discontinuation Form will be completed.

9 Device Malfunctions

A device malfunction means the failure of the device to meet its performance specification or otherwise perform as intended. *Any defective lens that is likely to cause or contribute to a Serious Adverse Event should be reported to the Principal Investigator and the sponsor* ***within 24 hours*** *of the investigator becoming aware of the malfunction.*

Other defective lenses should be reported to the Sponsor as soon as possible.

This clinical study will also ascertain satisfaction or preference with subjective attributes such as comfort, vision, or lens handling. Responses to these subjective questionnaires will not be considered as complaints or Device Malfunctions.

10 Statistical Analysis

10.1 Statistical analysis

Summary statistics will be produced (e.g. mean, standard deviation). [redacted] and subjective scores between study lens types. $\chi 2$ test will be used to compare the fitting performance between study lens types. The critical alpha level for statistical significance will be set at $p \leq 0.05$, with adjustment for multiple comparisons.

All participants who were evaluated will be used in the analysis. In the event of missing data, individual data points will be excluded in the analysis and not extrapolated from the collected data.

11 Data Quality Assurance

11.1 Study monitoring

Site qualification of the each investigative site has been completed to ensure that the site facility is adequate, personnel are qualified and resources are satisfactory to conduct clinical studies for the Sponsor. The protocol will be reviewed by the investigators prior to enrollment of the first subject. This will involve an overview of the protocol, which includes information on study objectives, inclusion and exclusion criteria, study visits and adverse event reporting. Data collection forms will also be reviewed and this will provide an opportunity to discuss any questions.

Prior to final data freeze, a close-out visit/discussion may be warranted to check for accuracy and completeness of records. The sponsor or sponsor's representatives will be authorized to gain access to the source documentation for the purposes of monitoring and auditing the study.

11.2 Record keeping

Detailed records of all study visits will be made using the Case Report Forms (CRFs). All data recorded on forms will be in ink. Any corrections to the forms will be initialed and dated at the time they are modified.

11.3 Record retention

Following study completion, data will be available in electronic and/or paper format for audit, sponsor use, or subsequent analysis. The original clinical raw data (including completed CRFs and Informed Consent forms) will be retained according to guidelines set forth in the general work agreement with the site. The Sponsor will be notified and consulted if ever the files are to be destroyed. In the event that this implementation document is indicated for design verification and validation purposes, as indicated on the title page, all original raw data forms and completed CRF's will be forwarded to the sponsor at completion of the final report.

[redacted]

[redacted]

11.5 Confidentiality

This study is confidential in nature. All information gathered during this study is proprietary and should be made available only to those directly involved in the study. Information and reports arising from this project are the property of the sponsor.

11.6 Publication

Due to the confidential and proprietary nature of the clinical study, any presentation and/or publication including but not limited to those made at scientific meetings, in-house, in peer-review journals, professional publications, etc. need to be approved by the sponsor.

12 Study Costs

The sponsor will compensate the clinical site and the subjects for their time and participation in this voluntary study.

Expenses incurred for medical treatment as part of study participation will be paid by the sponsor (bills and prescription receipts kept). The participant must be followed until resolution and a written report completed indicating the subsequent treatment and resolution of the condition.