CooperVision™

Study Implementation document: Protocol

A 6-HOUR CLINICAL EVALUATION OF [redacted] DAILY-WEAR SOFT CONTACT LENSES

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[redacted]

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[redacted]

CooperVision, Inc.

Site Principal Investigator: [redacted] Date: 26-July-2017

[redacted]

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DOCUMENT CHANGE HISTORY

Version	Originator	Description of Change(s)	Date
1.0	[redacted]	Original Protocol	18 July 2017

1 Introduction

CooperVision is evaluating the clinical performance of the [redacted] lens (test) compared to Alcon Focus Dailies All Day Comfort lens (control) when worn on over a period of 6 hours of wear.

2 Study Objective

The purpose of this study is to validate the clinical performance of [redacted] lenses when worn over a period of 6 hours of wear.

The primary variable of interest is:

- Lens fit and lens fit preference

Additional variable of interest are:

- [redacted]

2.1 Study Hypothesis

The study hypothesis is that the [redacted] contact lenses will be clinically equivalent to the Focus Dailies All Day Comfort contact lenses.

3 Study Design

This will be a non-dispensing, randomized, double-masked, contralateral study comparing [redacted] test lens against a FDADC control lens. Subjects will be randomized to wear the test lens in one eye and the control lens in the other. It is anticipated that this study will involve up to 2 scheduled visits, at Baseline (BL) and 6 hours.

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
- 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.

This implementation document adheres to a protocol approved by the Institutional Review Board at CORL, Indiana University.

The following specific documents from the IRB approval of the Master Protocol will be implemented in this work:

Informed Consent Letter

Master Protocol

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

This Study will be registered with ClinicalTrials.gov in accordance with Section 801 of the Food and Drug Administration Act (FDAA) which mandates the registration of certain clinical trials of drugs and medical devices.

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 6 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. The risks to the subjects are also reduced based on the results of cytoxicity testing.

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.

Routine clinical procedures including auto-refraction, auto-keratometry, visual acuity, anterior ocular health assessment, and contact lens fitting will be used. In addition, high magnification imaging of the lens fit may be made using 35 mm or digital cameras, in vivo confocal microscopy, and/or specular microscopy.

7 Materials and Methods

7.1 Participants

Approx. 30 subjects [redacted] will be recruited for this study. Each subject will be given a unique ID number. ID numbers will not be reused in event of screen failure or discontinuation. All subjects must meet the study inclusion and exclusion criteria listed below.

Inclusion criteria

- Is at least 18 years of age and has full legal capacity to volunteer
- Has read, fully understood and signed the information consent letter
- Currently wears or has previously worn soft contact lenses
- Has spectacle cylinder ≤1.00D in both eyes.
- Has spherical contact lens power requirement between -1.00D and -6.00D in both eyes.
- Has manifest refraction visual acuities (VA) equal to or better than logMAR equivalent of 20/25 in each eye.
- Has clear corneas and no active ocular disease
- Is willing and able to follow product usage instructions and maintain the visit schedule.

Exclusion criteria:

- Has never worn contact lenses before
- Has a systemic condition that in the opinion of the investigator may affect a study outcome variable
- Is using any systemic or topical medications that in the opinion of the investigator may affect a study outcome variable
- Has any known active ocular disease and/or infection
- Has a monovision correction
- Has any ocular pathology or severe insufficiency of lacrimal secretion (moderate to severe dry eyes) that would affect the wearing of contact lenses
- Is aphakic
- Has undergone corneal refractive surgery
- Is pregnant or lactating, determined by self-report

7.2 Study Materials

7.2.1 Contact lens

Subjects will be randomized to wear the Test lens in one eye and the Control lens in the other as an unmatched pair, per a predetermined randomization schedule. Subjects will be fitted with the

lens power closest to their refractive requirement. Details of the contact lenses are shown in Table 1.

Table 1: Study lenses

	Test [redacted]	Control Focus Dailies All Day Comfort
Manufacturer	CooperVision	Alcon Ciba
Material	riofilcon A	nelfilcon A
Base curve (mm)	8.60	8.60
Diameter (mm)	14.00	13.80
Lot numbers	See lens traceability forms	See lens traceability forms
Power (D)	-1.00 to -6.00 (0.25 steps)	-1.00 to -6.00 (0.25 steps)

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 solutions used and/or study lenses worn by participants will be collected and retained on completion of the study.

7.2.6 Masking and Control of Study Materials

Both subject and investigator will be masked to lens type. A different investigator will select the study lenses for insertion by the subject, from those performing the assessments in order to maintain masking.

7.2.7 Ordering and Accountability of Study Materials

The study lenses will be provided by the sponsor and the control lenses by the site. 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 and used 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 Baseline Visit (Visit 0)

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:

- The patient is expected to attend the baseline visit not wearing their habitual contact lens products.
- The subject will be required to read and sign an Informed Consent Form prior to enrolment. When the subject has signed the consent form, the subject will be considered to be enrolled on to the study.
- Sphero-cylindrical refraction will be conducted and monocular High Illumination High Contrast (**HIHC**) and High Illumination Low Contrast (**HILC**) distance logMAR baseline distance visual acuities recorded.
- Slit lamp biomicroscopy will be assessed according to the guidelines set out in the CVI Grading scales.
- The investigator will confirm that the patient meets the criteria set out in the inclusion criteria.

Dispensing (Visit 1)

- Baseline auto-keratometry if not done within the previous 6 months.
- HVID (mm) and palpebral aperture size (mm) measurements using slit lamp oculars.
- The study pair of contact lenses will be selected according to the randomization table (Appendix 1).
- The contact lenses will be provided by a study coordinator/technician to maintain masking of the investigator. The lenses will be inserted by the subject from the blister pack after the label is removed by the study coordinator/technician.
- [redacted]
  - [redacted]
  - [redacted]

- The lenses will be allowed to settle for 5 minutes.
- An initial fit assessment will be made to ensure lens fit is acceptable. The subject should be discontinued and exited if either lens fit is found unacceptable, and the primary reason for poor fit recorded.
- Monocular spherical over-refraction (SOR) will be conducted to determine if a different lens power is required.
- Final lenses will be inserted and allowed to settle for another 5 minutes, if applicable.
- The subject will be asked to give subjective ratings after settling on:
  - [redacted]
  - [redacted]
  - [redacted]
    - [redacted]
- Lens fit will be assessed and graded according to the CVI grading scales (Appendix 2). [redacted]
  - Lens centration (mm)
  - Post-blink movement (mm)
  - Primary gaze lag (mm)
  - Upgaze lens lag (mm)
  - Horizontal lens lag/mobility rating (0-4)
  - Lens tightness (%)
  - Lens movement characteristics (slow, medium, fast)
  - Overall lens fit acceptance (0-4 scale) and investigator reason, if unacceptable.
- The subject will be discharged and asked to return for a follow-up visit after 6 hours.

7.3.2 6-Hour Visit (Visit 2)

- The subject will be asked to score their subjective response as detailed in CVI Grading scales.

[redacted]

- [redacted]
- [redacted]
- [redacted]
  - [redacted]
- Lens fit (OD/OS) will then be assessed and graded according to the CVI grading scales (Appendix 2). [redacted]
  - Lens centration (mm)
  - Post-blink movement (mm)
  - Upgaze lens lag (mm)
  - Horizontal lens lag/mobility rating (0-4)
  - Lens tightness (%)
  - Lens movement characteristics (slow, medium, fast)
  - Overall lens fit acceptance (0-4 scale) and investigator reason, if unacceptable.
- The lenses will be removed by the subject and their subjective responses for ease of lens removal (0-100 scale) (OD/OS) will be recorded. The lenses will be retained for return to the Sponsor.
- Slit lamp biomicroscopy will be assessed according to the guidelines set out in CVI Grading scales.
- 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 0 *Screening / Baseline*	**Visit 1** *Dispense*	**Visit 2** *6-hour follow-up & Exit*
Informed consent	✓	-	-
Meet inclusion/exclusion criteria	✓	-	-
History at baseline	✓	-	-
Demographics	✓	-	-
HVID / palpebral aperture size	✓	-	-
Auto-refraction & keratomtery	✓	-	-
Sphero-cylindrical refraction	✓	-	-
HIHC & HILC VAs with spectacle refraction	✓	-	-
Slit-lamp biomicroscopy	✓	-	✓
[redacted]	-	✓	-
[redacted]	-	✓	✓
[redacted]	-	✓	✓
Lens fit assessments	-	✓	✓
[redacted]	-	✓	-
[redacted]	-	✓	✓
Exit VAs	-	-	✓
Study Exit	-	-	✓

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)	Notify sponsor as

22	Papillary conjunctivitis if ≥ mild scattered papillae/follicles approximately 1mm in diameter (e.g. ISO 11890 Grade 2), if 2 grade change from baseline	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.

Sponsor contact details are:

Contact:
Email:
Phone:
Address:

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). Paired t test will be used to compare slit lamp biomicroscopy, lens fit and subjective scores between study lens types. Repeated Measures Analysis of Variance (ANOVA) or paired analysis will be used to compare the variables between study visits. 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

No monitoring will be required for this short feasibility 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.

11.4 Data Entry / Data Management

[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.

All records will also be handled in accordance with HIPAA (1996) standards.

11.6 Publication

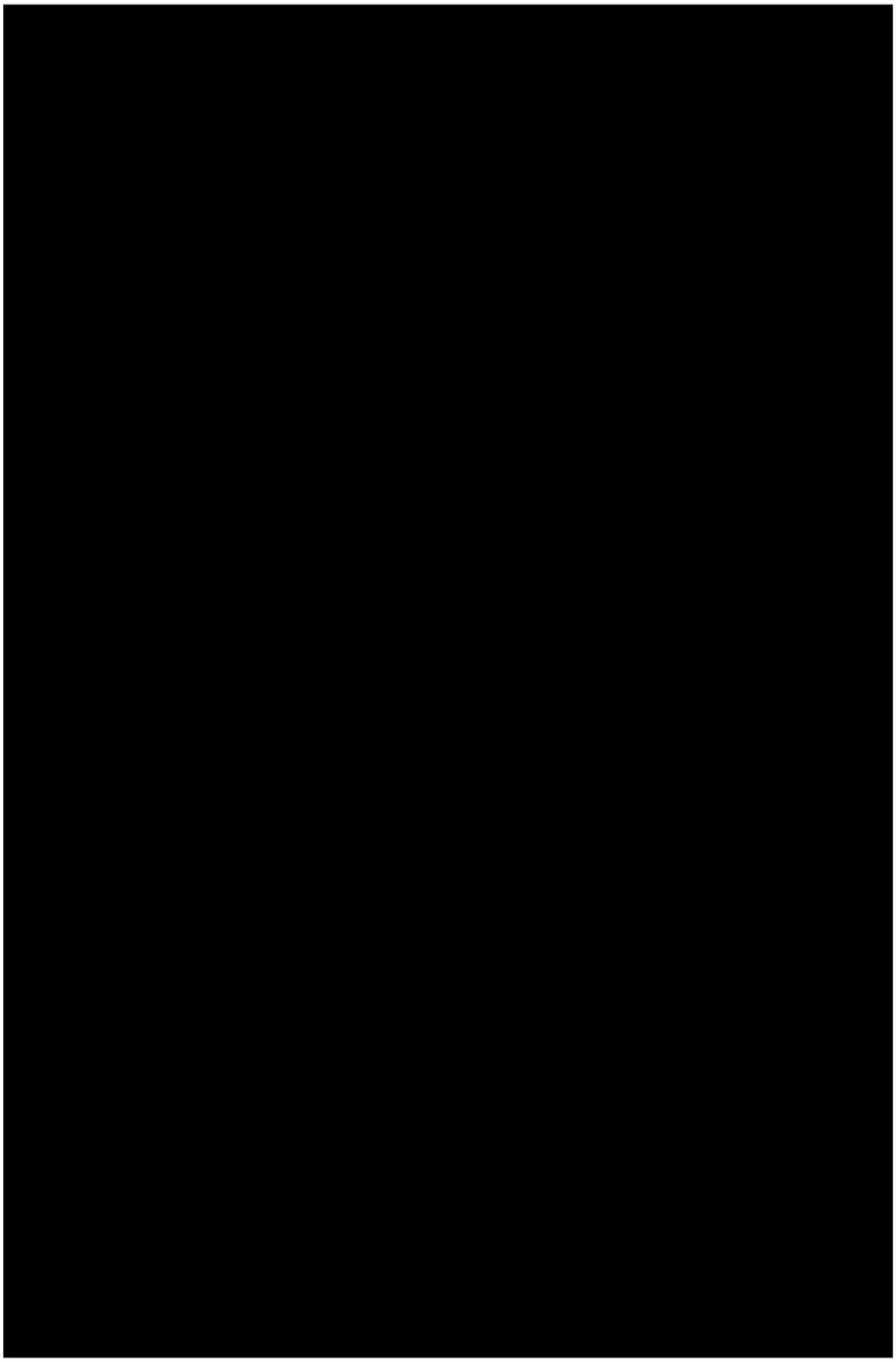
Due to the confidential and proprietary nature of the clinical study, any presentation and/or publication including but not limited to those made at scientific meetings, in-house, in peer-review journals, professional publications, etc. need to be approved by the sponsor.

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.

APPENDIX 1



APPENDIX 2

Grading Scales: