NCT03804502

PILOT STUDY OF THE TEARCARE™ SYSTEM – LONG-TERM EXTENSION

PROTOCOL ID #: 06215

CURRENT REVISION: Rev A

REVISION DATE: December 4, 2018

SPONSOR:

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Building 3, Suite 105
Menlo Park, CA 94025
877-266-1144

Agreement of Principal Investigator

I, _____ agree to conduct this trial in accordance with this clinical protocol and any amendments.

_____ _____

Signature Date

_____ _____

Center Name City, State, Country

1 REVISION HISTORY

Revision	Date Issued	ECO Number
A	December 4, 2018	2605

2 PROTOCOL SYNOPSIS

Protocol Title	Pilot Study of the TearCare™ System – Long-Term Extension
Protocol ID Number	06215
Study Device	TearCare™ System
Intended Use	The TearCare™ System is indicated for the application of localized heat when the current medical community recommends the application of a warm compress to the eyelids of adult patients. Such applications would include Meibomian Gland Dysfunction (MGD), Dry Eye, or Blepharitis.
Primary Objective	Evaluate the long-term clinical utility, safety, and effectiveness of re-treatment with the TearCare™ System in adult patients with dry eye syndrome.
Study Design	Single center, prospective, non-randomized case series
Primary Effectiveness Endpoint	Tear Breakup Time at 4 weeks

Secondary Effectiveness Endpoints	• Meibomian Gland (MG) Assessment:
	  ○ # Glands yielding clear liquid secretions
	  ○ # Glands secreting any liquid
	  ○ Total MG Score
	• Dry Eye Symptoms and Quality of Life as measured by:
	  ○ Standard Patient Evaluation of Eye Dryness (SPEED) Questionnaire
	  ○ Ocular Surface Disease Index (OSDI) Questionnaire
	  ○ Symptom Assessment in Dry Eye (SANDE) Questionnaire
	• Corneal & conjunctival staining scores

Safety Endpoints	• Device-related adverse events • Best spectacle-corrected Snellen visual acuity

Inclusion Criteria	1. Previously enrolled in the TearCare arm of the TearCare Pilot Study (protocol number 05429) 2. Reports dry eye symptoms within 3 months of the baseline examination with a Standard Patient Evaluation for Dryness (SPEED) score ≥ 6 3. TBUT of <10 seconds in at least one eye 4. Willing to comply with the study, procedures, and follow-up 5. Willing and able to provide consent

Exclusion Criteria	1. Any active ocular or peri-ocular infection or inflammation 2. Recurrent eye inflammation [redacted] 3. Ocular surgery, oculoplastic surgery, ocular injury, Ocular Herpes Simplex, or Herpes Zoster 4. Ocular surface abnormalities that may affect tear film distribution or treatment 5. Abnormal eyelid function in either eye 6. Diminished or abnormal facial, periocular, ocular or corneal sensation 7. Ocular surface abnormalities such as corneal epithelial defects, ulcers, corneal dystrophies 8. Systemic diseases resulting in dry eye (e.g. Sjogren's syndrome) 9. Allergies to silicone tissue adhesives 10. An absence or fibrosis of the Meibomian glands (e.g. ectodermal dysplasia) 11. Unwillingness to abstain for the duration of the study from systemic medication known to cause ocular dryness (e.g. Accutane, antihistamines, etc.) 12. Anyone who requires chronic use (i.e. for any portion of the study) of topical ophthalmic antibiotics, steroids, non-steroidal anti-inflammatory medications or who has been on any of these medications [redacted] 13. Participation in another ophthalmic clinical trial [redacted] 14. Co-existing conditions that could interfere with the assessment of safety or efficacy of treatment (e.g. macular disease, pregnancy, nursing, etc.)

Study Duration for Each Subject	6 months
Proposed Duration of Study	8 months
Schedule of Visits	Baseline/Treatment, 1 month, 3 month, 6 months
Number of Centers	1
Number of Subjects	12

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4 STUDY OBJECTIVE

The objective of the study is to evaluate the long-term clinical utility, safety, and effectiveness of re-treatment with the TearCare™ System in adult patients with dry eye syndrome who had previously been treated with the TearCare System.

5 BACKGROUND AND JUSTIFICATION FOR THE STUDY

Dry Eye Syndrome is a chronic eye condition that can cause an array of symptoms in patients, ranging from periodic ocular discomfort to severe corneal inflammation, scarring, and vision loss.[1,2] Approximately 1/3 of patients visiting their eye doctor suffer from dry eye. It is approximated that 23 million people over age 20 suffer from dry eye in the U.S.

Each year in the U.S., billions of dollars are spent on topical lubricants, medications, tear duct occlusions, and other treatments to control the chronic condition. For an individual patient, the annual direct cost ranges from $678 per year for mild cases to $1,200 annually for severe cases. Moreover, there is a great cost to society in terms of decreased productivity due to the symptoms of dry eye. Essentially, not only do dry eye patients directly suffer, but there is also a burden to healthcare, employers, and society.

Normal tears coat the ocular surface and perform many functions, including lubrication of the ocular surface, protection from infection, nourishing the ocular surface cells, and providing an optically clear surface to properly refract light. Tears consist of three layers:

1. An underlying mucin layer which acts as a wetting agent to spread tears uniformly on the ocular surface to prevent beading or irregularity;
2. An aqueous layer to maintain an optically clear medium and to keep the ocular surface moist and healthy; and
3. A superficial layer to retard evaporation of the aqueous layer.

When any of these layers is disturbed, tears may lose their protective and optical properties leading to a constellation of symptoms, including those associated with dry eye.

[redacted]

A great deal of evidence suggests that obstruction of the meibomian glands, which are the glands on the eyelid that produce the lipid layer of tears, is strongly associated with evaporative dry eye syndrome.[3,4,5,6] It is estimated that evaporative dry eye syndrome accounts for 65-85% of dry eye cases. As these glands become either inflamed or obstructed, their ability to supply the essential lipids to the ocular surface is diminished. This, in turn, leads to rapid evaporation of tears and thus to evaporative dry eye.[7] When this occurs, it can result in ocular discomfort and, in many cases, ocular surface disorders that can affect vision.

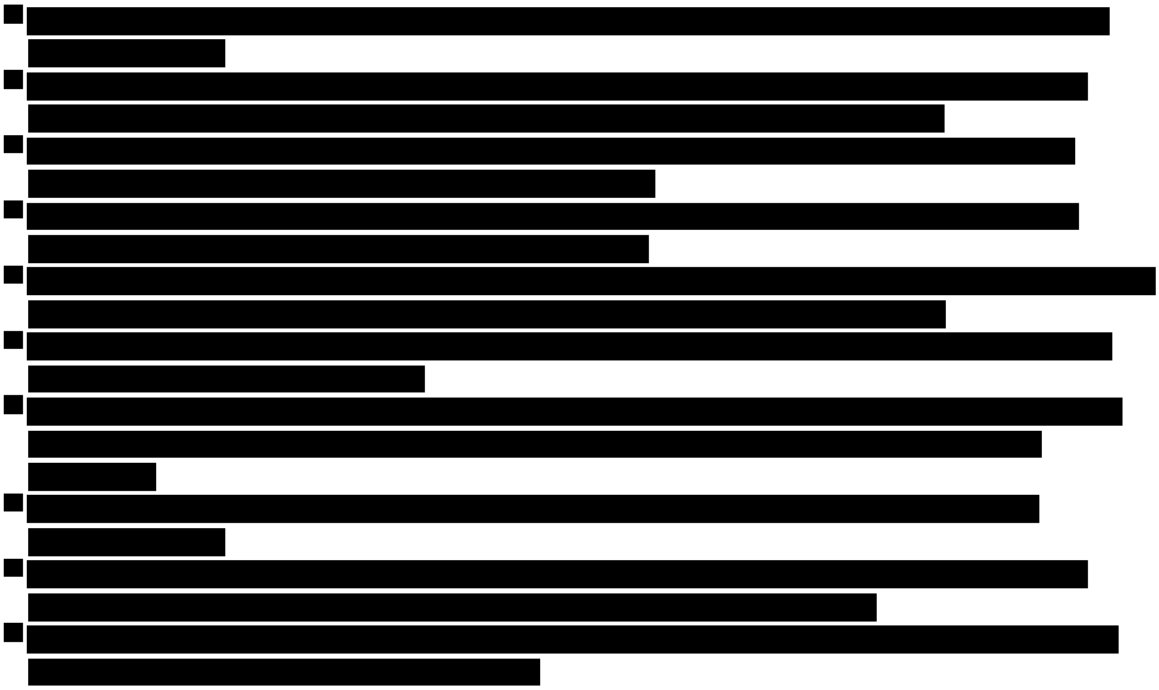
One of the most commonly prescribed treatments for evaporative dry eye and meibomian gland dysfunction is the use of warm compresses. It is believed that the heat from warm compresses helps melt the oily obstructions in the meibomian glands and helps reduce gland inflammation, thereby helping to restore the ability of the meibomian glands to effectively secrete oil onto the tear film and prevent rapid tear evaporation. It has been shown that warm compress therapy can lead to improved lipid production and flow on to the tear film.[8,9,10] This improved lipid delivery is associated not only with an improvement in the profile of the tear film but also an improvement in patient symptoms.[11,12,13] The tear film is demonstrably thicker and more stable with an increased contribution of lipid to its surface.[14,15,16] However, many

factors contribute to poor penetration of warm compress therapy in the dry eye population. More specifically, warm compress therapy has failed to achieve widespread acceptance among patients because:

- It is inconvenient and disruptive to a patient's schedule
- The temperature necessary to achieve an effective AND safe compress is difficult to achieve and maintain at home[17,18,19]
- Warm compresses, when used at home, tend to cool quickly thereby diminishing their efficacy
- Some patients may over heat the compress putting them at risk for injury[20,21]
- Patients are not able to enhance the effect by expressing molten secretions from their meibomian glands as a physician routinely does for his/her patients.

Various approaches to heating the eyelids have been proposed, but often they may be too cumbersome or costly for patients.[22,23,24,25,26]

Sight Sciences has developed a novel device, the TearCare™ System, to deliver controlled, precise heat to the meibomian glands for 12 minutes in the monitored setting of an ophthalmologist or optometrist office. (Refer to Section 6, Description of Device, below.) The TearCare session is then followed by routine manual expression of the meibomian glands by the physician. The goal of this is to more effectively and conveniently treat dry eye with an accepted proven treatment.



This study will enroll subjects who had been previously treated with the TearCare System over one year ago as part of their participation in the TearCare arm of the TearCare pilot study. This extension of the pilot study is being conducted in order to evaluate the long-term safety and effectiveness of re-treatment with the TearCare System.

6 DESCRIPTION OF DEVICE

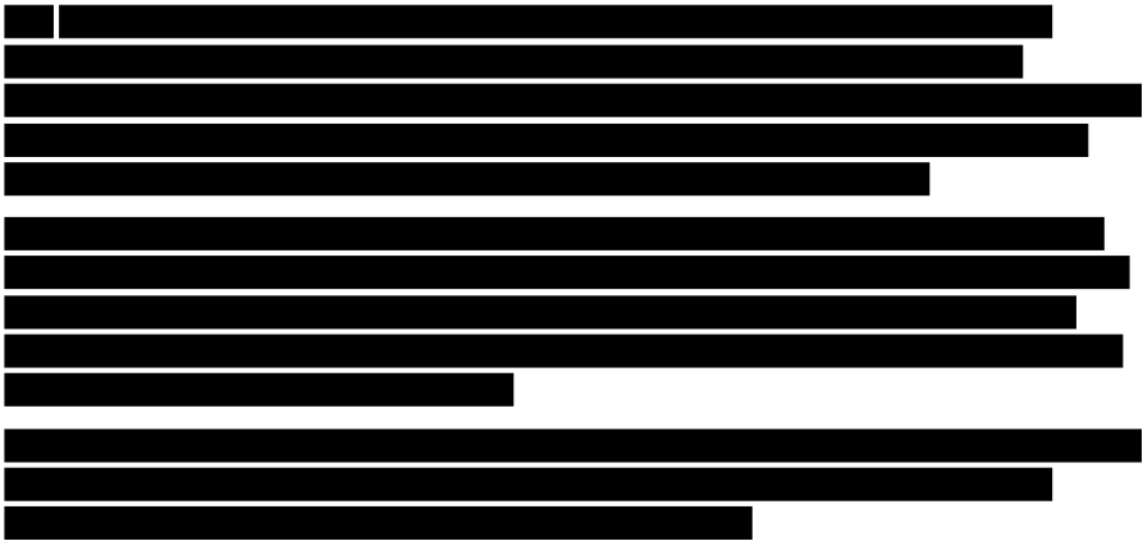
6.1 INTENDED USE

The TearCare™ System is indicated for the application of localized heat when the current medical community recommends the application of a warm compress to the eyelids of adult patients. Such applications would include Meibomian Gland Dysfunction (MGD), Dry Eye, or Blepharitis.

6.2 DEVICE DESCRIPTION

The TearCare™ System is comprised of the following components:

- iLid™ Device
- TearCare System, which includes the following:
  - Controller
  - Charging nest
  - Charging adapter
  - Clip



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6.3 INSTRUCTIONS FOR USE

Instructions for Use are provided with each TearCare System.

6.4 SUMMARY OF THE TRAINING AND EXPERIENCE NEEDED FOR USE OF DEVICE UNDER INVESTIGATION

This is a single-center study, conducted by Dr. David Badawi. Dr. Badawi is a co-inventor of the TearCare System and is familiar with its proper use. He will review the Instructions for Use in advance of initiating the investigation.

6.5 DESCRIPTION OF ASSOCIATED MEDICAL OR SURGICAL PROCEDURES

Within 10 minutes following the 15-minute TearCare session, the investigator will perform manual Meibomian gland expression of all 4 eyelids under topical anesthesia with ophthalmic tetracaine 0.5% drops.

7 PRIOR INVESTIGATIONS

7.1 PRECLINICAL TESTING

The TearCare System has been tested extensively on the bench to demonstrate that it meets all specified safety and performance requirements. The following testing and analyses was performed:

- Thermal Requirements: Testing was performed to demonstrate that the TearCare System meets the minimum, maximum and nominal therapeutic temperature requirements.
- Software Functionality: Testing was performed to demonstrate that the software in the TearCare Controller and iLid Devices meet all software requirements.
- Electrical Safety: Testing was performed to demonstrate that the System meets the electrical safety requirements specified in IEC 60601-1.
- Electromagnetic Compatibility: Testing was performed to demonstrate that the System meets the electromagnetic requirements specified in IEC 60601-1-2.
- Biocompatibility: All patient-contacting materials were reviewed to confirm that that they are biocompatible for short-term (<24 hours), skin contact.

- Mechanical Strength: Testing was performed to demonstrate that they system meets mechanical strength requirements.
- Shipping, Storage, and Shelf-Life Testing: Testing was performed to demonstrate that the TearCare System meets shipping, storage and shelf-life requirements.

The TearCare System passed all pre-clinical testing, demonstrating that they system meets its requirements.

7.2 PREVIOUS CLINICAL EXPERIENCE

The TearCare System has been studied in a single center pilot study conducted in 2017. The results were published in *Clinical Ophthalmology*[27] and are summarized below.

Objectives
The objective of this study was to evaluate the clinical utility, safety, and effectiveness of the TearCare™ System compared to standardized warm compress therapy.

Subjects
Twenty-four (24) subjects with symptoms of dry eye in the past 3 months were enrolled. The average age was 67.6 ± 13.5 years (range 29.7 – 89.8 years). All subjects were female, white and not Hispanic or Latino. All subjects had a SPEED score ≥6 at the Baseline visit. All subjects had a Tear Break-up Time (TBUT) of <10 seconds in at least one eye at baseline and 72% (17/24) had a Schirmer 1 score (non-anesthetized) of ≤10 mm in at least one eye at the Baseline visit.

Methods
This was a prospective, single-center, randomized, parallel-group, clinical trial. Subjects with DED were randomized to either a single TearCare treatment conducted at the clinic or 4 weeks of daily warm compress therapy. The TearCare procedure consisted of 12 minutes of thermal eyelid treatment immediately followed by manual expression of the meibomian glands. Warm compress therapy consisted of once daily application of the compresses to the eyelids for 5 minutes. Subjects were followed to 6 months post-treatment. The primary effectiveness endpoint was defined as change from baseline to 4 weeks for Tear Break-up Time (TBUT). Secondary effectiveness endpoints included meibomian gland assessment, corneal and conjunctival staining scores, and assessment of dry eye symptoms using validated questionnaires. Safety was evaluated by collecting device-related adverse events, intraocular pressure, and best spectacle-corrected Snellen Visual acuity.

Results

[redacted]

Twenty-four subjects were enrolled and completed 6 months follow-up. Data are summarized in Table 1 below.

At 1 month follow-up, TearCare subjects demonstrated an improvement from baseline in mean (± SD) TBUT of 11.7 ± 2.6 seconds compared with an average worsening of -0.3 ± 1.1 seconds for subjects in the warm compress group ($p<0.0001$). Significantly greater improvements in the change from baseline in meibomian gland scores, as well as corneal and conjunctival staining scores were observed in the TearCare group. Subjects in the TearCare group also showed significantly greater improvement in dry eye symptoms as measured by the three questionnaires.

No adverse events were reported in either group.

Conclusions

The TearCare Group consistently showed a significant improvement between the baseline and 4 weeks follow-up for all outcome measures, whereas the Warm Compress group did not. For all outcome measures, the TearCare Group's mean change between baseline and 4 weeks follow-up was better than the Warm Compress group. These results were maintained out to 6 months.

This pilot study provided preliminary evidence of the safety and effectiveness of the TearCare device in relieving the signs and symptoms of dry eye.

8 STUDY ENDPOINTS

8.1 EFFECTIVENESS ENDPOINTS

The **primary effectiveness endpoint** of the study is the change from baseline to 4 weeks in **Tear Break-Up Time (TBUT)**.

Secondary effectiveness endpoints include the change from baseline to follow-up in the following:

- **Meibomian Gland Assessment**[28] scores for the following:
  - The number of Meibomian glands yielding clear liquid secretions (grade 3)
  - The number of glands secreting any liquid (clear or cloudy with grade 2 or 3)
  - The total Meibomian Gland Score
- **Dry Eye Symptoms and Quality of Life**, as measured by:
  - The Standard Patient Evaluation of Dry Eye (SPEED) II questionnaire[29], which measures the severity and frequency of dry eye symptoms
  - Ocular Surface Disease Index (OSDI) Questionnaire[30]. The OSDI consists of 12 questions to assess ocular symptoms (the Ocular Symptoms subscale), their impact on patient vision-related functioning (Vision Related Function subscale), and environmental factors triggering the symptoms (Environmental Triggers subscale).
  - Symptom Assessment in Dry Eye (SANDE) Questionnaire.[31, 32] The SANDE is a 2-question survey which uses a visual analog scale to assess the frequency and severity of dry eye symptoms
- Corneal & conjunctival staining scores

8.2 SAFETY ENDPOINTS

Safety of the TearCare System will be evaluated by evaluating changes in the following measures:

[redacted]

- Device-related adverse events
- Best spectacle-corrected Snellen visual acuity

9 STUDY DESIGN

This is a prospective, non-randomized, single-center case series study. No specific attempts will be made for minimization of bias, such as blinding or masking.

10 STUDY SELECTION CRITERIA

10.1 INCLUSION CRITERIA

For inclusion in this study, subjects must meet all of the following criteria:

1. Previously enrolled in the TearCare arm of the TearCare Pilot Study (protocol number 05429)
2. Reports dry eye symptoms within 3 months of the baseline examination with a Standard Patient Evaluation for Dryness (SPEED) score ≥ 6
3. TBUT of <10 seconds in at least one eye
4. Willing to comply with the study, procedures, and follow-up
5. Willing and able to provide consent

10.2 EXCLUSION CRITERIA

A subject who meets any of the criteria listed below will be excluded from the study:

1. Any active ocular or peri-ocular infection or inflammation
2. Recurrent eye inflammation within the past 3 months
3. Ocular surgery, oculoplastic surgery, ocular injury, Ocular Herpes Simplex, or Herpes Zoster
4. Ocular surface abnormalities that may affect tear film distribution or treatment
5. Abnormal eyelid function in either eye
6. Diminished or abnormal facial, periocular, ocular or corneal sensation
7. Ocular surface abnormalities such as corneal epithelial defects, ulcers, corneal dystrophies
8. Systemic diseases resulting in dry eye (e.g. Sjogren's syndrome)
9. Allergies to silicone tissue adhesives
10. An absence or fibrosis of the Meibomian glands (e.g. ectodermal dysplasia).
11. Unwillingness to abstain for the duration of the study from systemic medication known to cause ocular dryness (e.g. Accutane, antihistamines, etc.)

12. Anyone who requires chronic use (i.e. for any portion of the study) of topical ophthalmic antibiotics, steroids, non-steroidal anti-inflammatory medications or who has been on any of these medications within the past 30 days.
13. Participation in another ophthalmic clinical trial within the past 30 days
14. Co-existing conditions that could interfere with the assessment of safety or efficacy of treatment (e.g. macular disease, pregnancy, nursing, etc.)

11 STUDY PROCEDURES

11.2 NUMBER OF SUBJECTS AND STUDY DURATION

Up to 12 subjects will be enrolled in the study. Each subject will receive one in-office TearCare procedure and then will be followed for 6 months. It is anticipated that enrollment in the study will take 1-2 months. Including the 6-month follow-up period, the study is expected to last 7-8 months.

11.3 Material and Equipment

[redacted]

11.4 Informed Consent and Point of Enrollment

The IRB-approved informed consent will be presented and explained to each prospective subject by the investigator or a trained clinical professional. Once the subject has had ample time to read the consent form, has been informed of all aspects of the study, and has had an opportunity to ask questions, the subject will be given a choice to voluntarily confirm his or her participation in the study as documented by completion of the Informed Consent. After signing the Informed Consent and the HIPAA (Health Insurance Portability and Accountability Act) authorization, the subject can then proceed with the baseline visit. The subject has the right to withdraw from the study at any time without consequences, as indicated in the Informed Consent Document.

The subject's signed and dated informed consent must be obtained before conducting any procedure specifically for the study. Subjects are enrolled upon signing the ICD even if they subsequently fail to meet the eligibility criteria.

The principal investigator(s) must retain the original, signed written Informed Consent Document. A copy of the written Informed Consent Document must be given to the subject.

11.5 Baseline Visit

11.5.1 Scheduling the Baseline Visit

Since dry eye drops and lubricants can affect the endpoint assessments, instruct subjects not to use any of these products within 2 hours of the Baseline visit.

11.5.2 Baseline Exams and Questionnaires

After the subject has signed the informed consent form and agreed to participate in the study, the exams, tests and questionnaires listed in the Baseline column of Table 2 should be performed. Refer to Appendix A for instructions for performing the exams and administering the questionnaire.

[redacted]

If, at any point during the visit the subject fails to meet a subject selection criterion, then the visit can be terminated. Subjects who fail to meet all the selection criteria will be considered a screen failure and will be withdrawn from the study. Screen failures will not count toward the total enrolled and treated number of subjects.

After all required measurements have been obtained and it has been confirmed that the subject meets all the Subject Selection Criteria, then the subject will receive the TearCare procedure.

[redacted]

11.5.4 Management of Dry Eye Symptoms During Follow-Up

During follow-up, if subjects require relief of their dry eye symptoms, they should only use the same type of drops or lubricants they used prior to the start of the study. Subjects should record their daily use of lubricants on the Lubricant Drop log.

Subjects **should not use** any other method of relieving dry eye symptoms, including any of the following:

- Warm compress
- Restasis or Xiidra
- Other dry eye treatments (e.g. Lipiflow, TrueTear, iLux, punctal plugs, etc.)

NOTE: If a subject had a punctal plug at the baseline visit and it falls out during the study, it should be replaced.

Review these instructions with subjects at the end of the Baseline visit and provide them with the Lubricant Drop log. They should complete the log each day and bring it back to the clinic at each follow-up visit.

11.6 Follow-Up Visits

Prior to the Visit: Reminder Call

Since dry eye drops and lubricants can affect the endpoint assessments, it is important to call subjects a few days before their follow-up visits to remind them that on the day of the Follow-up visit, they should not to use any of these products before the Follow-up visit.

Order of Procedures During the Follow-Up Visit

Follow-up exams should not be performed by the clinician who performed the TearCare procedure.

[redacted]

11.7 Photography during Exams and TearCare Procedure

Photographs or videos may be made during the baseline or follow-up exams or during the TearCare procedure. These images may be used for educational, training or

marketing purposes. Subject consent must be obtained prior to taking any photographs or videos. Subjects do not have to agree to consent to being filmed in order to participate in the study.

11.8 Withdrawal and Discontinuation

All subjects have the right to withdraw at any point during the treatment without prejudice. The investigator can discontinue any subject at any time if continued participation in the study would result in harm to the subject. All efforts should be made by the investigator to retain the subject in the study. If a subject withdraws prematurely from the study, a genuine effort must be made to determine the reason(s) the subject discontinued the study. The reason must be recorded in the subject's file and on the End of Study Form.

If a subject withdraws from the study prior to receiving the TearCare, then that subject may be replaced in the study by a newly enrolled subject.

12 Adverse Events (AEs)

Adverse Events are defined below. Adverse events that occur in the eye during the trial, whether they are considered to be device related or not, must be documented in the subject's records. Date of the event, its severity, treatment (if any) and the assessed relationship of the event to the study device will be recorded on the Adverse Event Form. Conditions which exist at the time the subject is enrolled do not need to be recorded on the Adverse Event Form as adverse events unless they increase in severity during the study.

12.1 Definitions of AE, SAE, SADE, USADE

Adverse Event	Any untoward medical occurrence in a subject who has been treated with the device that does not necessarily have causal relationship with the treatment.
Adverse Device Effect	Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease that is possibly related to the study device.
Serious Adverse Event (SAE)	Any untoward medical occurrence that: • Results in death • Is life-threatening • Requires in-patient hospitalization or prolongs existing hospitalization • Necessitates medical or

	surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure • Sight threatening
Unanticipated Adverse Device Effect	Any serious adverse effect on health or safety, any life-threatening problem or death caused by, or associated with a device if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the clinical investigational plan; or any other serious problem associated with a device that relates to the rights, safety, or welfare of subjects (21 CFR 812.3(s)). Any sight-threatening event, whether listed in the protocol or not, is considered to be reportable as a UADE

12.3 Reporting Adverse Events and Unanticipated Adverse Device Effects

Identification, collection and reporting of adverse event information is the responsibility of the principal investigator. The investigator records the date of the event, its severity, treatment (if any) and the assessed relationship of the event to the study device on the Adverse Event Case Report Form (AE CRF).

All unanticipated adverse device effects (UADE) will be reported as soon as possible, but no later than 10 working days after the investigator first learns of the event, to the following two entities:

1. The study sponsor - E-mail the AE CRF to safety@sightsciences.com; and
2. The reviewing IRB – per the IRB's instructions.

The sponsor will conduct an evaluation of unanticipated adverse device effects. If the sponsor determines that an unanticipated adverse device effect presents an unreasonable risk to subjects, parts of the investigation presenting risks will be terminated. Termination will occur not later than 5 working days after the sponsor makes such a determination and not later than 15 working days after the sponsor first received notice of the effect.

13 Risk-Benefit Analysis

13.1 Anticipated clinical benefits

The TearCare™ System will be performed with the aim of increasing tear break up time and improving meibomian gland function. The anticipated clinical benefit of these improvement is relief of the subjects' dry eye symptoms. The goal of the procedure is to provide a safe, reproducible, and practically feasible treatment for dry eye disease. Additionally, performing the procedure under the direct supervision of a trained corneal specialist further ensures the safety and proper delivery of therapy.

13.2 Anticipated adverse device effects

Anticipated adverse effects associated with the TearCare System have been described above in Section 12.2.

13.3 RESIDUAL RISKS ASSOCIATED WITH THE INVESTIGATIONAL DEVICE, AS IDENTIFIED IN THE RISK ANALYSIS REPORT

Sight Sciences believes that there are no Intolerable residual risks from this fully non-invasive, controlled heat treatment device that can be easily and quickly removed from the patient by the supervising ophthalmologist.

13.4 RISKS ASSOCIATED WITH PARTICIPATION IN THE CLINICAL INVESTIGATION

As with any type of eye procedure, there are potential risks that are associated participating in the investigation including:

- Post-procedure Discomfort
- Blurred Vision
- Inflammation of eyelids

In addition, subjects who are asked to discontinue pre-procedure dry eye medications may note that their eyes feel drier. All anticipated study risks are listed in Section 12.2.

13.5 POSSIBLE INTERACTIONS WITH CONCOMITANT MEDICAL TREATMENTS

It is anticipated that there will be no interactions with concomitant medical treatments.

13.6 STEPS THAT WILL BE TAKEN TO CONTROL OR MITIGATE THE RISKS

The major risks to the subjects and the steps taken to control or mitigate them are described below:

1. Overheating of the eyelids: All TearCare treatments will be done in the investigator's office under direct supervision of the investigator. The device delivers heat to the eyelids at a temperature ranging from 41-45°C. This temperature range was selected because it is both safe for eyelid heating and effective for melting obstructions in the meibomian glands.[33,34,35,36] The user can adjust the temperature up or down to a level that is comfortable and may also

[redacted]

shut off the System at any time if it is too uncomfortable or painful. In addition, the TearCare System continuously monitors and regulates the temperature at the tissue-contacting surface of the iLid devices and has been designed to not exceed the maximum allowable temperature.

2. Corneal abrasion: If the iLid devices are not positioned properly or come loose during the treatment, there is the potential for a corneal abrasion. To mitigate this, the supervising physician will apply the strips to the subject and will monitor their position during the treatment to ensure they remain in place and secure.

   In addition, there is the possibility of corneal abrasion or abrasion of the eyelid surface during expression of the meibomian glands. To reduce the chance of abrasion, the forceps have been designed with smooth surfaces (i.e. no rough edges) and only trained users will perform expression.

3. Worsening of dry eye symptoms: It is possible that subjects will experience a worsening of dry eye symptoms during the study. Subjects will undergo a complete eye exam at each visit and if any untoward or worsening signs of ocular surface disease are observed, they will be treated appropriately.

In addition to the above, the following mitigation steps have also been taken to reduce the risks in this study:

- The device has been tested to demonstrate that it meets performance and safety specifications, as described in Section 7.1.
- Instructions for Use are provided with each device.
- The ophthalmologist using the device is board-certified and has experience in how safely and correctly apply and remove the iLid devices, and operate the TearCare System.

13.7 RISK-TO-BENEFIT RATIONALE

The risks in this study are low, due to the non-invasive nature of the TearCare System. In addition, these risks are generally temporary and are readily treatable or reversible with no medical intervention or, in some cases, using standard medical treatment. Against these low risks are the potential for a reduction in subjects' eye discomfort and symptoms due to dry eye syndrome. Reduction in dry eye symptoms holds the possibility of several related benefits to the subjects, including:

- Improved vision
- Improved productivity
- Reduced dependence on medications and lubricants while simultaneously improving physiologic tear production ("your own tears")

- Reduced costs to subjects to treat their dry eye symptoms

On the basis of this analysis, the potential benefits to subjects related to treatment with the TearCare System outweighs the relatively low risk associated with the System.

14 Statistical Considerations

14.1 Hypothesis

This pilot study is not a hypothesis-driven study.

14.2 Sample Size Calculation

This is an extension of the original TearCare Pilot Study (Study # 05429). The sample size for this study is defined by the number of subjects who were enrolled in the TearCare arm of the pilot study (i.e. 12 subjects).

14.3 Pass/Fail Criteria

No pass/fail criteria are defined for the study.

14.4 Statistical Design, Method & Analytical procedures to be Used

Only basic descriptive statistics will be used to analyze data from the study.

14.5 Interim Analysis and Early Termination Criteria

No interim analysis or early termination criteria are planned for this study.

14.6 Deviation from the Statistical Plan

Any deviations from the statistical plan will be noted in the final report.

15 Monitoring Procedures

15.1 Monitoring to be Conducted during the Investigation

- Since Dr. Badawi has already conducted dry-eye related clinical trials with Sight Sciences, no site qualification visit will be required.

- Sight Sciences personnel will meet with the investigator(s) and clinical study staff at the time the site begins to enroll in order to ensure that subjects are being properly selected and that study data are being correctly recorded.
- Sight Sciences personnel or designee will visit the clinical site periodically during the study to review and/or collect the Case Report Forms.
- At the conclusion of the trial there will be a study closure visit during which, the following items will be reviewed and actions performed:
  - A final inspection of the study binder
  - Accountability and return of all devices and study materials to the sponsor
  - Close-out notification to the IRB

15.2 Extent of Source Data Verification

The study CRF will serve as both the source document and the CRF.

16 Data and Quality Management

All study-related data will be recorded on Case Report Forms. When subjects are enrolled in the study, they will receive a unique study identifier, which will be used to identify them on all Case Report Forms. The Enrollment log containing the subject identifying information and the subject study id will be maintained under the investigator's control at all times. No subject-identifying information will ever leave the site.

16.1 Database Management

Data Management will be performed by Sight Sciences who will create a database or spreadsheet in which the study data will be entered. Sight Sciences will be responsible for tracking the receipt of CRFs and data corrections, data entry, and preparing data reports for statistical analysis.

16.2 Retention Period

Clinical sites are to retain any and all clinical trial material (documentation, photographs, etc.) for a period of two years from the date the marketing application is approved or two years after the investigation has been discontinued and the FDA notified, or as directed by their institutional document retention requirements, whichever is the longest. After that time, the items must be returned to Sight Sciences for archiving. Unused medical devices are to be returned to the sponsor at the conclusion of the enrollment period.

17 Protocol Modifications and Deviations

Protocol modifications may occur during the study. Each will be approved by the sponsor before implementation. Each will undergo Institutional Review Board (IRB) review and approval, as necessary.

Any deviations from this protocol intended to protect the life or physical well-being of a subject in an emergency are to be reported to Sight Sciences, Inc. as well as the IRB as soon as possible, and no later than 5 working days after the emergency occurred.

All protocol deviations will be documented using Protocol Deviation form.

18 Device Failures and Malfunctions

All device failures or malfunctions should be recorded on the Case Report Forms and reported to Sight Sciences Customer Service (877-266-1144).

19 Statements of Compliance

This study shall be conducted in accordance with the Declaration of Helsinki (Appendix B). The study shall not begin until approval has been obtained from the reviewing IRB. The investigator shall conduct this investigation in accordance with the signed agreement with the sponsor, the investigational plan, the IDE regulation and other applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.

20 Study Administration

20.1 Device Accountability

With each shipment of study devices, Sight Sciences will include a Packing List that will provide the items shipped. This packing list must be reconciled by the site with the contents of the shipment and then the contents of the shipment should be entered on the Device Accountability Log (this log is contained within the regulatory binder at the site). All study devices at the site must be stored in a secured/locked area. Device reconciliation activities will also be conducted periodically in conjunction with site monitoring visits.

The investigator must maintain accurate records of the receipt of all devices shipped by Sight Sciences, including the date and lot numbers received with the use of the device inventory tracking log. The use of devices will also be recorded.

20.2 Early Termination or Suspension of an Investigation

If the study is terminated, subjects will be followed up in accordance with the normal standard of care and adverse events, if any, will be tracked. No other special procedures are necessary.

In the event that there are significant human use issues with the device, the investigator will be consulted to make a determination of whether the study should be terminated or not.

20.3 Investigator Responsibilities

20.3.1 General Responsibilities of Investigators

An Investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the Investigator's care, and for the control of devices under investigation. An Investigator also is responsible for ensuring that informed consent is obtained in accordance with 21 CFR part 50.

20.3.2 Specific Responsibilities of Investigators

1. Awaiting approval - An Investigator may determine whether potential subjects would be interested in participating in an investigation, but shall not request the written informed consent of any subject to participate, and shall not allow any subject to participate before obtaining IRB approval.
2. Subject Qualification -The Investigator is responsible for ensuring that all subjects entering the study conform to the patient selection criteria.
3. Compliance - An Investigator shall conduct an investigation in accordance with the signed agreement with the Sponsor, the investigational plan, all applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.

20.3.3 Investigator Records

A participating Investigator shall maintain the following accurate, complete, and current records relating to the Investigator's participation in an investigation for the period specified in Section 16.2:

1. All correspondence with another Investigator, an IRB, the Sponsor, a monitor, or FDA, including required reports.
2. Records of each subject's case history and exposure to the device. Case histories include the study CRF's/worksheets and supporting data including, for example, signed and dated consent forms and medical records. Such records shall include:
    a) Documents evidencing informed consent.
    b) All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
3. The protocol, with documents showing the dates and reasons for each deviation from the protocol.
4. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

20.3.4 Investigator Reports

An Investigator shall prepare and submit the following complete, accurate, and timely reports:

1. Unanticipated Adverse Device Effects - An Investigator shall submit to the Sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the Investigator first learns of the effect.
2. Withdrawal of IRB Approval - An Investigator shall report to the Sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the Investigator's part of an investigation.
3. Progress - An Investigator shall submit progress reports on the investigation to the Sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
4. Deviations from the Investigational Plan - An Investigator shall document and report to the Sponsor any deviation from the investigational plan.

5. Informed Consent - If an Investigator enrolls a subject without obtaining informed consent, the Investigator shall report such use to the Sponsor and the reviewing IRB within 5 working days after the use occurs.
6. Final Report - An Investigator shall, within 3 months after termination or completion of the investigation or the Investigator's part of the investigation, submit a final report to the Sponsor and the reviewing IRB.
7. Other - An Investigator shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

20.4 Investigator Agreement

The principal investigators in each center shall agree to the clinical protocol and any amendments and indicate their approval and agreement by signing and dating the Investigator Responsibility Agreement.

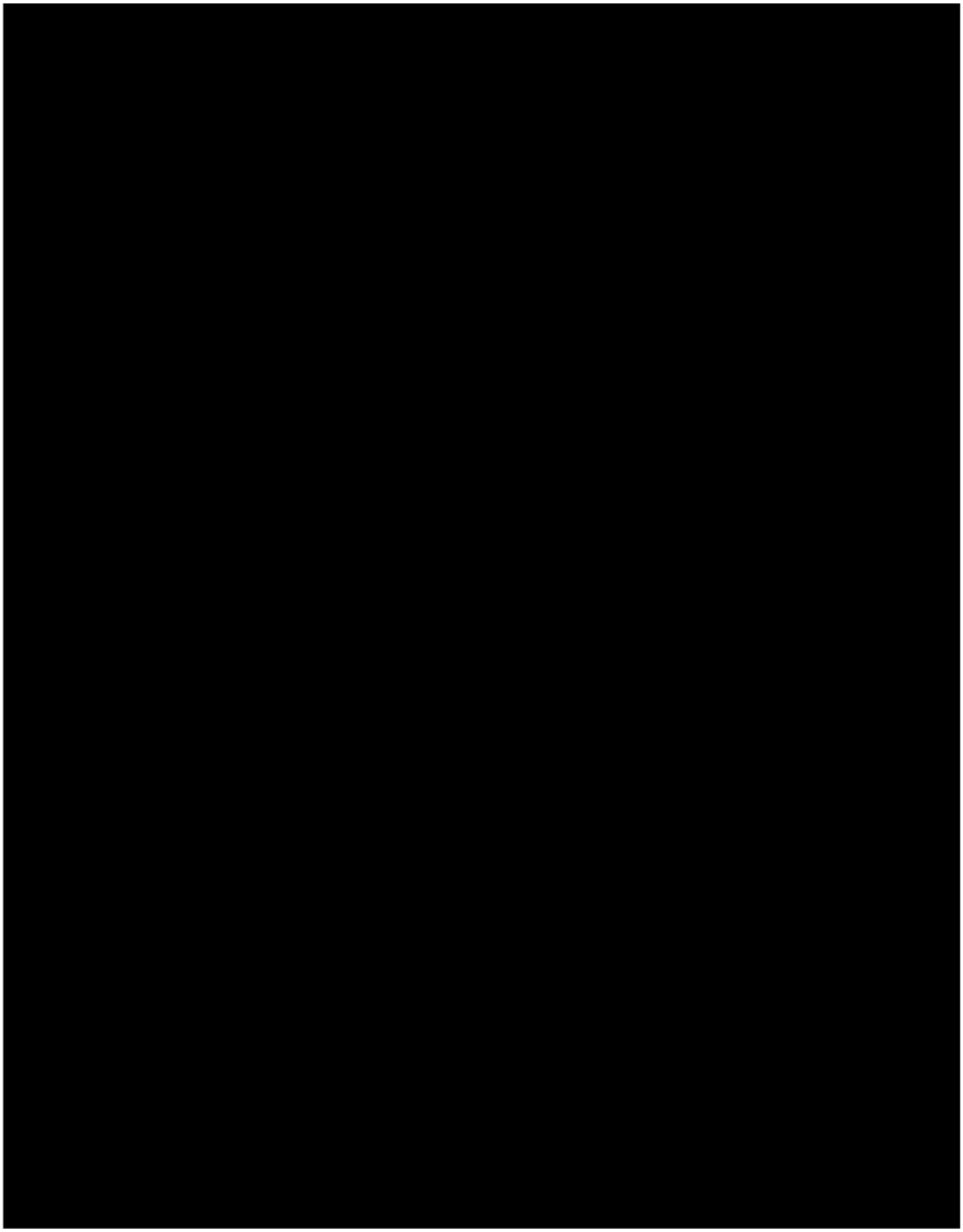
21 Associated Documents

The investigator should refer to the TearCare Instructions for Use for instructions in how to operate the study device.

22 Publication Policy

Dr. David Badawi, the Principal Investigator, may publish the data in a medical newsletter or ophthalmic journal.

[redacted]



24 APPENDIX A – METHODS FOR OCULAR EXAMS AND TESTS AND ADMINISTRATION OF QUESTIONNAIRES

24.1 EYE EXAM

A standard eye exam shall be performed, including slit lamp examination to look for the presence of erythema, conjunctival discharge, tear meniscus, thickening of the lid margins, and telangiectasia.

24.2 MEIBOMIAN GLAND ASSESSMENT

Meibomian gland assessment should be performed and the following should be scored:

- Total number of glands from which a fluid secretion can be expressed, regardless of qualitative appearance
- Quality of secretions scored per the scale:[37]
  - 0 = nothing
  - 1 = toothpaste
  - 2 = cloudy
  - 3 = clear

From this scoring the following endpoints will be assessed:

- The number of Meibomian glands yielding clear liquid secretions
- The number of glands secreting any liquid (clear or cloudy)
- The total Meibomian Gland Score

24.3 TEAR BREAKUP TIME (TBUT)

TBUT is an indicator of tear film instability and detects dry eye syndrome due to evaporative causes such as meibomian gland disease.

To measure TBUT, instill fluorescein into the eye using 2% fluorescein solution prepared according to the method defined by Gyau et al.[38] Ask the subject to blink several times. Record the break-up time using a stopwatch. Repeat the test 3 times and take the average of the 3 measurements.

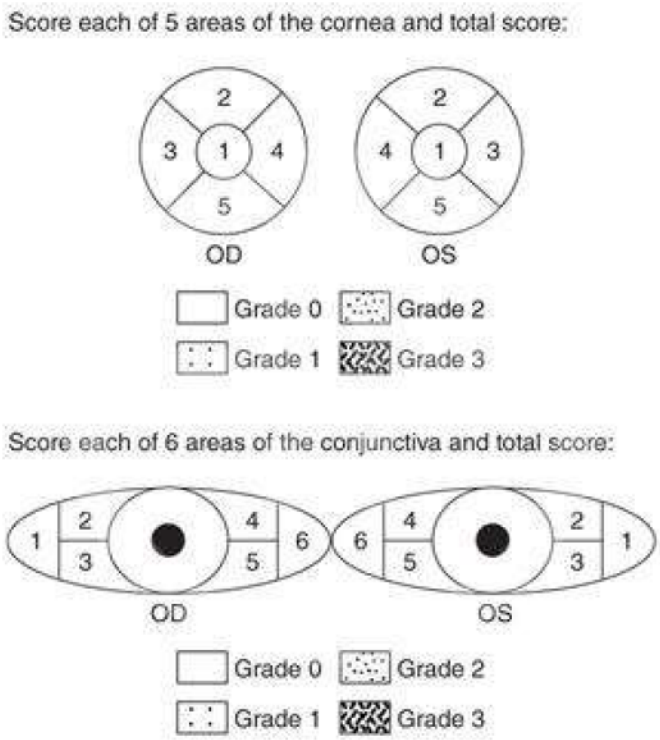
[redacted]

24.4 CORNEAL AND CONJUNCTIVAL STAINING

Corneal staining should be assessed immediately following TBUT measurements (i.e. within 1-4 minutes after instillation of fluorescein dye) to assure the dye does not diffuse into stroma, blurring the discrete margin of any staining defects. A yellow Wratten filter should be used to improve any visualization of corneal staining. Grade the corneal staining using the NEI/Industry Grading System provided below in Figure 1

Conjunctival staining: Prepare 1% lissamine green solution according to the method defined by Gyau et al.[39] Instill the dye into the lower conjunctival fornix. Wait at least one minute before grading the conjunctival staining. The conjunctival staining grading should be performed 1 minute after instillation of stain and within 4 minutes of staining. Perform a slit lamp exam to score the conjunctival staining per the NEI grading system shown above below in Figure 1. Start with a low illumination and increase the level until the lissamine green staining is most visible.

Figure 1: NEI/Industry Grading System for Corneal and Conjunctival Staining[40]



[redacted]

24.5 VISUAL ACUITY

Best spectacle-corrected visual acuity will be measured using the Snellen method.

24.6 SPEED QUESTIONNAIRE

The SPEED Questionnaire will be administered to the subjects in the doctor's office by either the study coordinator or the Investigator. A total SPEED score is calculated by adding the Frequency and Severity scores.

24.7 OSDI QUESTIONNAIRE

The OSDI Questionnaire will be administered to the subjects in the doctor's office by either the study coordinator or the Investigator. The overall OSDI Total score (from 0-100) and scores for the three subscales will be totaled according to the OSDI instructions. Based on the recommended cutoffs for OSDI Total score, subject results are grouped as follows:

- Mild – 13-22
- Moderate – 23-32
- Severe – 33 or higher

24.8 SANDE QUESTIONNAIRE

The SANDE is a simple dry eye instrument containing two items measuring the frequency and severity of symptoms, each was assessed on a 100 mm visual analog scale (VAS) ranging from 'Never/Very comfortable' to 'All the time/Very severe' and scored from 0 to 100. Refer to Figure 2.

A SANDE Total score (also ranging from 0 to 100) is calculated as the square-root of the product of the two item scores.

Based on the SANDE total score, subject results are grouped into three categories:

- Mild: <40
- Moderate: 40-50
- Severe: >50

[redacted]

[redacted]

25 DECLARATION OF HELSINKI

I. PREAMBLE

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.

   The Declaration is intended to be read as a whole and each of its constituent paragraphs should be applied with consideration of all other relevant paragraphs.

2. Consistent with the mandate of the WMA, the Declaration is addressed primarily to physicians. The WMA encourages others who are involved in medical research involving human subjects to adopt these principles.

II. GENERAL PRINCIPLES

1. The Declaration of Geneva of the WMA binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act in the patient's best interest when providing medical care."

2. It is the duty of the physician to promote and safeguard the health, well-being and rights of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.

3. Medical progress is based on research that ultimately must include studies involving human subjects.

4. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best proven interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.

5. Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights.

6. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.

7. It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, even though they have given consent.

8. Physicians must consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.

9. Medical research should be conducted in a manner that minimizes possible harm to the environment.

10. Medical research involving human subjects must be conducted only by individuals with the appropriate ethics and scientific education, training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional.

11. Groups that are underrepresented in medical research should be provided appropriate access to participation in research.

12. Physicians who combine medical research with medical care should involve their patients in research only to the extent that this is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects.

13. Appropriate compensation and treatment for subjects who are harmed as a result of participating in research must be ensured.

III. RISKS, BURDENS AND BENEFITS

- In medical practice and in medical research, most interventions involve risks and burdens.

  Medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subjects.

- All medical research involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and groups involved in the research in comparison with foreseeable benefits to them and to other individuals or groups affected by the condition under investigation.

  Measures to minimize the risks must be implemented. The risks must be continuously monitored, assessed and documented by the researcher.

- Physicians may not be involved in a research study involving human subjects unless they are confident that the risks have been adequately assessed and can be satisfactorily managed.

  When the risks are found to outweigh the potential benefits or when there is conclusive proof of definitive outcomes, physicians must assess whether to continue, modify or immediately stop the study.

IV. VULNERABLE GROUPS AND INDIVIDUALS

- Some groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm.

  All vulnerable groups and individuals should receive specifically considered protection.

- Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.

V. SCIENTIFIC REQUIREMENTS AND RESEARCH PROTOCOLS

- Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and,

as appropriate, animal experimentation. The welfare of animals used for research must be respected.

- The design and performance of each research study involving human subjects must be clearly described and justified in a research protocol.

  The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, potential conflicts of interest, incentives for subjects and information regarding provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study.

  In clinical trials, the protocol must also describe appropriate arrangements for post-trial provisions.

VI. RESEARCH ETHICS COMMITTEES

- The research protocol must be submitted for consideration, comment, guidance and approval to the concerned research ethics committee before the study begins. This committee must be transparent in its functioning, must be independent of the researcher, the sponsor and any other undue influence and must be duly qualified. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration.

  The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No amendment to the protocol may be made without consideration and approval by the committee. After the end of the study, the researchers must submit a final report to the committee containing a summary of the study's findings and conclusions.

VII. PRIVACY AND CONFIDENTIALITY

- Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information.

VIII. INFORMED CONSENT

- Participation by individuals capable of giving informed consent as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees.

- In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information.

  After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.

  All medical research subjects should be given the option of being informed about the general outcome and results of the study.

- When seeking informed consent for participation in a research study the physician must be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent must be sought by an appropriately qualified individual who is completely independent of this relationship.

- For a potential research subject who is incapable of giving informed consent, the physician must seek informed consent from the legally authorized representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the group represented by the potential subject, the research cannot instead be performed with persons capable of providing informed consent, and the research entails only minimal risk and minimal burden.

- When a potential research subject who is deemed incapable of giving informed consent is able to give assent to decisions about participation in research, the

physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject's dissent should be respected.

- Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research group. In such circumstances the physician must seek informed consent from the legally authorized representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research must be obtained as soon as possible from the subject or a legally authorized representative.

- The physician must fully inform the patient which aspects of their care are related to the research. The refusal of a patient to participate in a study or the patient's decision to withdraw from the study must never adversely affect the patient-physician relationship.

- For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must seek informed consent for its collection, storage and/or reuse. There may be exceptional situations where consent would be impossible or impracticable to obtain for such research. In such situations the research may be done only after consideration and approval of a research ethics committee.

IX. USE OF PLACEBO

- The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best proven intervention(s), except in the following circumstances:

  Where no proven intervention exists, the use of placebo, or no intervention, is acceptable; or

  Where for compelling and scientifically sound methodological reasons the use of any intervention less effective than the best proven one, the use of placebo, or no intervention is necessary to determine the efficacy or safety of an intervention

and the patients who receive any intervention less effective than the best proven one, placebo, or no intervention will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention.

Extreme care must be taken to avoid abuse of this option.

X. POST-TRIAL PROVISIONS

- In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process.

XI. RESEARCH REGISTRATION AND PUBLICATION AND DISSEMINATION OF RESULTS

- Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.

- Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication and dissemination of the results of research. Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. All parties should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results must be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest must be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.

XII. UNPROVEN INTERVENTIONS IN CLINICAL PRACTICE

In the treatment of an individual patient, where proven interventions do not exist or other known interventions have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgment it offers hope of saving life, re-establishing health or alleviating suffering. This intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information must be recorded and, where appropriate, made publicly available.