STUDY PROTOCOL 2020-02 / NCT03055897

iLUX™ SAFETY STUDY
Version 1.0 March 2, 2016

STUDY SPONSOR:
TEAR FILM INNOVATIONS, INC.
[redacted]
SAN DIEGO, CA 92130
[redacted]

STUDY SITE:
[redacted]

I have read this protocol and agree to conduct the study as outlined herein.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure they are fully informed regarding the device and the conduct of the study.

_____

Principal Investigator's Signature Date

_____

Name of Principal Investigator (Typed or Printed)

Principal Investigator:

[redacted]

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[redacted]

PROTOCOL SUMMARY

Protocol Number	2020-02, Version 1.0
Title	iLux Safety Study
Sponsor	Tear Film Innovations, Inc.
Regulatory Status	Non-Significant Risk Investigational Device Study
Objective	The objective of this study is to measure the [redacted] temperature of the cornea and surrounding eye tissue temperature immediately after heating the eyelids with the iLux device using the protocol treatment profile.
Study Design	Prospective, non-randomized, open label, trial
Number of Centers	1
Investigational Device	iLux 2020 System

Study Population	A total of up to 15 males and females ≥ 18 years old. Inclusion Criteria 1. Age 18 years and older of any gender or race 2. Provision of subject written informed consent prior to study participation Exclusion Criteria 1. History of ocular surgery [redacted] within 1 year 2. [redacted] 4. Active ocular infection [redacted] 6. Ocular surface abnormality [redacted] 7. Lid surface abnormalities [redacted] 9. Women who are pregnant, nursing, or not utilizing adequate birth control measures [redacted]

Study Procedures	Pre-Treatment Screening • Medical history • History of prior ophthalmic surgery • Contact lens usage, and systemic or ophthalmic medications, including artificial tears, lubricants, and rewetting drops • Systemic body temperature • Assessments required prior to informed consent [redacted] • Less than five minutes prior to the iLux procedure baseline corneal and surrounding eye tissue temperatures shall be measured. [redacted] iLux Procedure- (Both eyes shall be treated on the same day): 1 Eye makeup shall be removed. 2 Contact lens (if wearing) shall be removed 3 The iLux device shall be prepared for use in accordance with the iLux User Manual, a copy of which is provided in Appendix 2 4 Anesthetic eye drops shall be instilled in both eyes. 5 iLux inner eyelid pad on the iLux Disposable shall be positioned: a) behind the lower eyelid in the central-temporal zone in the first treatment, b) behind the lower eyelid in the central-nasal position in the second treatment, c) behind the upper eyelid in the central-temporal zone in the third treatment, d) behind the upper eyelid in the central-nasal position in the fourth treatment. In all cases, the support arms of the iLux Disposable shall be placed near the eye lid margin. 6 The iLux outer eyelid pad shall be advanced to cause this outer eyelid pad to apply pressure against the outer eyelid. The compression applied to the Compression Control button will be recorded using an external force sensor. 7 The iLux light/heat shall be activated by sliding the light/heat switch forward, [redacted] 8 Within ten seconds after the fourth warming cycle, the [redacted] nfrared camera will be used to measure the temperature of the cornea and surrounding eye tissue. [redacted]

	[redacted]
Primary Endpoint	[redacted] corneal and surrounding eye lid tissue temperature [redacted] [redacted] in each eye.
Safety Measures	Incidence of: • Adverse events (AE) of any type [redacted]
Statistical Methods	No formal hypotheses will be used in this study. [redacted] All subjects enrolled and treated in the study shall be included as part of the safety analysis.

1 BACKGROUND AND INTRODUCTION

Meibomian glands are located in the tarsal plate of the upper and lower eyelids, where they terminate along the interior rim (or margin) of the eyelids. These glands secrete meibum, which is a lipid-rich essential component of a healthy tear film. When sufficient meibum is not present in the tear film, the aqueous layer of the tear film is disrupted and readily evaporates causing irritation, redness, and inflammation of the lid margin and surrounding tissues. Meibomian Gland Dysfunction (MGD) is associated with a failure of these glands to produce adequate quantities of meibum due to atrophy, inflammation, or obstruction, and is thought to be the most common cause of evaporative dry eye disease (EDE)[1]. Recommended methods for diagnosis of MGD reported in the literature[2] includes evaluation of meibomian gland expressibility by applying digital pressure and observing gland response with a slit-lamp microscope.

1.1 INDICATION FOR USE

The iLux System is indicated for the application of localized heat and pressure therapy in adult patients with chronic cystic conditions of the eyelids, including meibomian gland dysfunction (MGD), also known as evaporative dry eye.

1.2 iLUX SYSTEM

The iLux system enables an eye care professional to apply a treatment to unclog blocked glands by heating the lids to melt the meibum while applying enough compression to the lid to unblock clogged glands. By unclogging the glands, the glands can resume providing lipids to the tear film, which is key to preventing the aqueous (tear) layer from evaporating.

Clogged and unproductive meibomian glands lead to increase evaporation of the aqueous layer of the tears leading to inflammation and eventually atrophy of the meibomian glands. It is not known if an atrophied gland can be “revived”, therefore it is important to maintain the health and viability of the existing meibomian glands. The iLux treatment is designed to unclogged meibomian glands thereby maintaining the health of the gland and the ocular surface.

The main components of the iLux system include a disposable tip section and a handheld battery-powered instrument. The disposable tip section is a sterile, single-use device that snaps onto the tip of the instrument. It has a thin back plate that slides underneath the eyelid, and a front plate that is pushed against the front surface of the eyelid. All materials that contact the patient are made from biocompatible silicone. The instrument portion has a high-quality magnifying lens that allows the clinician to view the eyelid margin throughout the procedure. There is also a compression control switch, when pressed, advances the front plate against the patient’s eyelid.

[1] Schaumberg, D.K. *et al*. The International Workshop on Meibomian Gland Dysfunction: Report of the Subcommittee on Epidemiology of, and Associated Risk Factors for MGD, Investigative Ophthalmology and Visual Science, Special Issue 2011, Vol. 52, No. 4, pp 1994-2005.

[2] Tomlinson, A *et al*. The International Workshop on Meibomian Gland Dysfunction: Report of the Diagnosis Subcommittee, Investigative Ophthalmology and Visual Science, Special Issue 2011, Vol. 52, No. 4, pp 2006-2049.

To treat clogged glands, the clinician presses the heating switch (located on the compression control switch) to turn on the energy source and warm the eyelid tissue. The inner eyelid temperature is displayed on the instrument, enabling the clinician to titrate the ideal amount of heating and compression to optimize unclogging of the blocked glands.

The handheld device includes circuitry with a heat safety limit of 44°C so the inside of the back plate that contacts the inner part of the eyelid and the front plate that contacts the outer part of the eyelid cannot go above this safe temperature.

The iLux system was used recently on 30 subjects in an IRB-approved non-significant risk study in the United States with no adverse events reported.

2 STUDY DESIGN

2.1 OBJECTIVE

The objective of this study is to measure the [redacted] temperature of the cornea and surrounding eye tissue temperature immediately after heating the eyelids with the iLux device using the protocol treatment profile.

2.2 DESCRIPTION OF THE STUDY

Up to 15 eligible subjects will be enrolled at 1 clinical site.

The primary effectiveness analysis shall be based on immediate post-heating assessments.

The clinical parameters outlined in Appendix 1 shall be evaluated for each eye treated with the iLux device per the schedule outlined.

1. Discomfort/pain during, and after treatment – A subjective pain scale shall be used. A subjective report of discomfort shall be recorded on a scale of from 0-10. Descriptive Anchors on the scale include: 0 = no discomfort or pain, 2 = slight or transient awareness of pressure without pain, 4 = moderate discomfort with minimal pain, 6 = moderate pain, 8 = severe pain, 10 = intolerable pain. In an effort to provide some level of consistency to the subjective discomfort report, a scale shall be provided for the subject to compare their level of discomfort to commonly experienced episodes of discomfort in every-day life (see Table 1 below).

TABLE 1: DISCOMFORT/PAIN SCALE WITH COMPARATIVE EXPERIENCES

Score	Level of discomfort/pain	Description to anchor the subjective response
0	No discomfort or pain	Minimal recognition of pressure only. Equal to the touch of a finger on the skin. Awareness but no discomfort.
2	Slight or transient awareness of pressure without pain	Pressure tolerable and could be endured indefinitely without compromise to daily activities. Examples: bruise; medical injection; wearing dress shoes, which one would wear all day and might forget to remove when returning home; poorly adjusted glasses.
4	Moderate discomfort with minimal pain	Discomfort but tolerable. Examples: eye irritation from chlorine pool; pulled muscle; wearing tight dress shoes, which might be worn all day, but would definitely be removed when arriving home; smoke in eye; soap in eye; tight collar or clothes
6	Moderate pain	Constant awareness of moderate pain affecting daily activities. Examples: corneal abrasion; wearing tight dress shoes, which could not be worn for more than several hours due to excess pressure and pain; wasp or hornet sting.
8	Severe pain	Partially debilitating. Examples: broken bone; wearing tight dress shoes, which result in open blisters, making walking more than a few steps impossible; stepping on a nail.
10	Intolerable pain	Totally debilitating, preventing any activity. Examples: back pain preventing any movement; scalding water; severe migraine; slamming car door on finger; stick in eye.

A schedule of assessment procedures is provided in Appendix 1.

2.3 OUTCOME MEASURES

Safety Outcome Measures

Safety will be evaluated by assessing the following:

- Adverse events (AEs)
- Serious adverse events (SAEs)

2.4 STUDY POPULATION

Up to 15 subjects with health eyes as determined by the Exclusion criteria. After providing informed consent and documenting it in writing, subjects shall be screened for participation in the study. Subjects must fulfill the following criteria:

Inclusion Criteria

1. Age 18 years and older of any gender or race.
2. Provision of written informed consent prior to study participation.

Exclusion Criteria

1. History of ocular surgery [redacted] within 1 year
2. [redacted]

3. [redacted]
4. Active ocular infection [redacted]
5. [redacted]
6. Ocular surface abnormality [redacted]
7. Lid surface abnormalities [redacted]
9. Women who are pregnant, nursing, or not utilizing adequate birth control measures [redacted]

3 STUDY TREATMENTS

3.1 INVESTIGATIONAL TREATMENT

The iLux procedure shall be performed on both eyes on the same day.

1. Eye makeup shall be removed.
2. Contact lens (if wearing) shall be removed.
3. The iLux device shall be prepared for use in accordance with the iLux User Manual, [redacted]
4. [redacted]
5. [redacted]
6. iLux inner eyelid pad on the iLux Disposable shall be positioned: a) behind the lower eyelid in the central-temporal zone in the first treatment, b) behind the lower eyelid in the central-nasal position in the second treatment, c) behind the upper eyelid in the central-temporal zone in the third treatment, d) behind the upper eyelid in the central-nasal position in the fourth treatment. In all cases, the inner eyelid pad shall be positioned such that the support arms of the iLux Disposable are touching the eye lid margin.

7. The iLux outer eyelid pad on the iLux Disposable shall be advanced using the Compression Control button to cause this outer eyelid pad to apply pressure against the outer eyelid. The compression applied to the Compression Control button will be recorded using an external force sensor.
8. The iLux light/heat shall be activated by sliding the light/heat switch forward, [redacted].
9. Within ten seconds after the fourth warming cycle, [redacted] infrared camera will be used to measure the temperature of the cornea and surrounding eye tissue. Subjects shall be asked to close their eyes for five seconds, then hold them open while [redacted]

3.2 POST- TREATMENT DETAILS:

Post-procedure, the subject shall report any discomfort to the study site.

4 STUDY PROCEDURES

4.1 INFORMED CONSENT

Prior to recruitment of any subjects into the study, written approval of the protocol and informed consent form must be obtained from the Institutional Review Board (IRB).

Informed consent must be obtained and documented in writing prior to the initiation of any study procedures. The subject must be allowed sufficient time to thoroughly read the informed consent form, which will be written at a level that can be understood by someone educated to an 8th grade level. The Investigator or his/her designee should answer any questions that the patient might have. If the patient agrees to participate in the study, i.e., provides informed consent, the patient must sign both copies of the informed consent form. The witness and the Investigator or designee must also sign both copies of the informed consent form. One copy of the informed consent form shall be given to the subject/representative. If applicable, it shall be provided in a certified translation of the respective subject's language. The date of the subject's signature on the informed consent form shall be noted in the subject's medical chart.

Subjects who provide informed consent and with the consent documented in writing in their medical record may be screened for eligibility. Screened subjects' clinical identifiers shall be recorded on site-specific screening logs and once they are determined as being eligible, they may be enrolled into the study.

Individual patients may withdraw their consent to participate in the trial at any time. Also, an Investigator may discontinue a patient's participation in the trial at any time to protect the safety, rights, or welfare of the patient.

4.2 Assignment of Subject Identification

A subject identification number (ID) shall be assigned at screening. This ID shall be used on all study-related documents. To maintain confidentiality, the subject's name shall not be recorded on any study document other than the informed consent form.

4.3 Schedule of Study Assessments

All procedures shall be performed according to the schedule in Appendix 1 unless otherwise specified.

[redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- **Temperature of Cornea and Surrounding Eye Tissue Temperature** shall be measured using [redacted] infrared camera. [redacted]

[redacted]

5 SAFETY PARAMETERS

Safety assessments include adverse events/serious adverse events, [redacted]

5.1 Definition of Adverse Events

An adverse event is any untoward and unintended sign, symptom or disease temporally associated with the use of an investigational drug or device, or other protocol-imposed intervention, regardless of the suspected cause. Conditions or diseases that are chronic but stable should not be recorded on AE pages of the CRF. Changes in a chronic condition of disease that are consistent with natural disease progression are NOT adverse events and also should not be recorded on the AE pages of the CRF.

5.2 Definition of Serious Adverse Event

A serious adverse event (SAE) is defined as an adverse event that:

- Led to death
- Led to serious deterioration in the health of the patient that resulted in:
  - A life-threatening illness or injury
  - A permanent impairment of a body function
  - In-patient or prolonged hospitalization
  - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to body structure or a body function

.

5.3 Adverse Event Assessment and Documentation

All subjects who have been exposed to the study treatment shall be evaluated for adverse events. All adverse events, regardless of severity and whether or not they are ascribed to the study treatment, shall be recorded in the source documents and CRF using standard medical terminology.

All adverse events shall be evaluated beginning with onset, and evaluation shall continue until resolution is noted, or until the investigator determines that the subject's condition is stable. The investigator shall take appropriate and necessary therapeutic measures required for resolution of the adverse event. Any medication necessary for the treatment of an adverse event must be recorded on the adverse event case report form.

All AEs shall be characterized by the following criteria:

- Event diagnosis
- Intensity or severity
- Expectedness
- Relatedness to study treatment
- Treatment or action taken.
- Outcome

Whenever possible, recognized medical terms should be used when recording AEs. Colloquialisms and/or abbreviations should not be used. Only one medical concept, preferably a diagnosis instead of individual symptoms, shall be recorded as the event.

If more than one distinct adverse event occurs, each event shall be recorded separately.

5.3.1 Classification of Adverse Events by Intensity/Severity

All adverse events shall be graded on a three-point scale (mild, moderate, severe) for intensity/severity, defined as a qualitative assessment of the level of discomfort of an adverse event as is determined by the Investigator or reported to him/her by the subject. The assessment of intensity is made irrespective of study procedure relationship or seriousness of the event and shall be evaluated according to the following scale:

Mild:	Awareness of sign or symptom, but easily tolerated.
Moderate:	Discomfort enough to cause interference with usual activity.
Severe:	Incapacitating with inability to work or do usual activity.

There is a distinction between the severity and the seriousness of an adverse event. Severity is a measurement of intensity; thus, a severe reaction is not necessarily a SAE.

5.3.2 Expectedness

All AEs shall be evaluated as to whether they are expected or unexpected.

Expected (anticipated):	An adverse event is expected when the nature, severity, or degree of incidence was previously described, including those events listed in section 5.4.2.
Unexpected (unanticipated):	An adverse event is unexpected when the nature, severity, or degree of incidence was not previously described.

5.3.3 Relatedness

The study investigator shall evaluate if the AE is related to the iLux heating. Relationship is defined in the following manner:

Not related:	The event is clearly related to other factors such as subject's clinical state, therapeutic interventions, concomitant disease or therapy administered to the subject, and does not follow a known response pattern to the procedure.

Related: The event **follows a reasonable, temporal sequence from the time of procedure and/or follows a known response pattern to the study procedure and cannot be reasonably explained by other factors** such as subject's clinical state, therapeutic interventions, or concomitant therapy administered to the subject.

5.3.4 Treatment or Action Taken

Action taken in response to an adverse event shall be recorded as:

- None
- OTC or Rx drug added
- Non-drug treatment/procedure
- Hospitalization or ER visit

Action taken with study procedure shall be recorded as:

- None
- Study procedure interrupted
- Study procedure discontinued

5.3.5 Outcome

The clinical outcome of an AE shall be characterized as follows:

- Resolved without sequelae
- Resolved with sequelae (specify)
- Ongoing (i.e. continuing at time of study discontinuation)
- Death
- Unknown

5.4 Risk Analysis & Anticipated Adverse Events

5.4.1 Risk Analysis

Risks associated with using the iLux 2020 were assessed in accordance with ISO 14971, which is an international standard for medical device risk management that is recognized by the FDA. Most of the potential hazards identified in the analysis are common to many medical devices and are addressed by compliance with international standards. Other potential hazards unique to the iLux were addressed by assessing risk using Failure Modes Effects and Criticality Analysis (FMECA) and identifying controls to reduce residual risks to acceptable levels.

The iLux is used in the eye and the sterile disposable may come in contact with the conjunctiva and or cornea during the treatment of each lid. The sterile disposable is covered with a biocompatible silicone similar to a contact lens. There is nothing implanted either temporarily or permanently in the eye related to the iLux and the risk is similar to other meibomian gland treatments. Testing demonstrated that the disposable meets the requirements for biocompatibility (ISO 10993) and sterilization and packaging (ISO 1135, ISO 11607).

Compliance to IEC 60601-1, which is an international standard for safety of electromedical devices, was evaluated by the nationally recognized test laboratory, Nemko. As part of the evaluation, the risk management files were reviewed to verify compliance with ISO 14971. Other IEC 60601-1 tests included electromagnetic compatibility (IEC 60101-1-2) and optical radiation safety (IEC 62471). The iLux system successfully met the requirements of all tests performed.

The instrument warms the eyelids using optical radiation (i.e., light) at two wavelengths, lime-green and infrared. Potential photobiological hazards were evaluated by David Sliney, PhD, who is an internationally-respected expert in the field of optical radiation hazards and consults frequently with both the FDA and industry. His testing was also witnessed by an expert from Nemko for certification to the standard IEC 62471. Their analysis concluded that the iLux system poses minimal risk for damage to the eye or skin and can be classified as exempt from warnings. To further reduce risk, the heating cannot be operated without a disposable attached, which blocks a significant portion of the emitted light.

A safety study was conducted at Absorption Systems in San Diego from November to December, 2014. The study involved exposing one shaved eyelid on each of four New Zealand white rabbits to the same energy wavelengths and levels that are emitted by the iLux device, using a back plate and front plate similar to the human device, and applying a controlled force to the eyelids. One cohort received two-minute treatments and the other received four-minute treatments, with each treatment applied once per week for five treatments. No adverse events occurred and there were no changes observed in the eyelids or eyes, and there were no adverse histological findings.

The iLux system measures temperatures on the inner and outer surfaces of the eyelid. Four redundant temperature sensors are included in the disposable. The instrument displays the highest inner eyelid temperature. If any of the four sensor readings exceeds 44 °C, the instrument automatically turns off the heat source. Bench top testing has shown that the back plate of the iLux disposable tip does not heat above 40°C.

Lastly, the iLux system was recently used on 30 subjects in an IRB approved, non-significant risk study in the United States with no adverse events.

The mitigations taken demonstrate that the risk of any adverse effects on study subjects participating in this study have been eliminated or minimized to the extent possible and therefore, the risk to study subjects is acceptable for this study.

5.4.2 Anticipated Adverse Events

- **Eyelid/eye Pain**
- **Eyelid Irritation or Inflammation**
- **Ocular Surface Irritation or Inflammation**
- **Ocular Symptoms** – Burning, stinging, tearing, itching, discharge, redness, foreign body sensation, visual disturbance, sensitivity to light.

5.5 Serious Adverse Event and Unanticipated Adverse Device Effect Reporting

SAEs and unanticipated adverse device effects (UADE) must be reported to the study sponsor (Tear Film Innovations, Inc.) and study Principal Investigator (PI) as soon as possible and no later than **24 hours** after the investigator first learns of the event.

For initial reports, Investigators shall record all case details that can be gathered within the reporting timeframe. The contact information for Tear Film Innovations, Inc. and the PI is below:

Study Sponsor:

TEAR FILM INNOVATIONS
[redacted]
SAN DIEGO, CA 92130
[redacted]

Relevant follow-up information shall be submitted to the sponsor as soon as it becomes available and/or upon request. For some events, the sponsor or his designee may follow up with the site by telephone, fax, electronic mail, and/or a monitoring visit to obtain additional case details deemed necessary to appropriately evaluate the event (e.g., hospital discharge summary, consultant report, or autopsy report). Reports relating to the subject's subsequent medical course must be submitted to the study sponsor until the event has subsided or, in case of permanent impairment, until the event stabilizes and the overall clinical outcome has been ascertained.

6 STUDY DISCONTINUATION

The study sponsor has the right to terminate this study at any time. Reasons for terminating the study may include, but are not limited to, the following:

- The incidence or severity of adverse events in this or other studies indicates a potential health hazard to subjects
- Subject enrollment is unsatisfactory
- Data recording is inaccurate or incomplete.

7 STATISTICAL PLAN

No formal hypotheses will be used in this study. Subject demographic characteristics and background variables shall be summarized.

Pre-treatment, post-treatment and maximum treatment temperatures will be summarized with N, mean, standard deviation, minima, maxima, median, and interquartile range. The maximum change recorded will be similarly summarized.

All subjects enrolled and treated in the study shall be included as part of the safety analysis.

7.1 EFFICACY ENDPOINTS

The primary efficacy endpoint of this trial is the [redacted] temperature of the cornea and the surrounding eye tissue [redacted] after heating with the iLux instrument.

7.2 SAMPLE SIZE JUSTIFICATION

A sample size of 15 subjects (30 eyes) has been chosen for an initial assessment of the safety of the iLux System in this patient population. This number was chosen to provide sufficient data to make an initial safety determination of the System while minimizing the number of patients subjected to a clinical trial.

7.3 SAFETY

AEs, SAEs, and other findings shall be summarized by presenting the number and percentages of subjects with each event. Continuous endpoints shall be summarized using summary statistics such as means, medians, standard deviations, minima, maxima, and relevant percentiles.

8 RECORD RETENTION

The investigator shall maintain all subject records for a period of two years after the investigation is discontinued and FDA is notified.

The investigator must maintain accurate records of the receipt of all investigational material shipped by the sponsor, including the date and lot numbers received. In addition, accurate records must be kept on the amount and date that the investigational material, by lot number, was used and for each subject.

The investigator must assure that study supplies are used only in conjunction with subjects enrolled in the study and under the direct supervision of the investigator or co-investigators.

9 STUDY MONITORING REQUIREMENTS

It is the responsibility of the study sponsor, Tear Film Innovations, Inc., to ensure proper monitoring of the investigation and to see that all the clinical requirements are met. Either Tear Film personnel or a contracted third party will perform monitoring. In general, monitoring will consist of an initiation visit to train the site on the proper use of the device and execution of the protocol. Due to the small size of the study and the limited data being collected, monitoring will likely consist of 1-2 visits to the site to compare study CRF data with site source data. During these visits, the monitor may review the subject records to verify that all records and files are current and to assure compliance with all requirements of this protocol. The final monitoring visit may also serve as the study close-out visit.

10 PROTOCOL DEVIATIONS/AMENDMENTS

An investigator may deviate from the protocol to protect the life or physical well-being of a subject in an emergency, and must notify the sponsor and the reviewing IRB within 5 working days after the emergency occurred. Except in such an emergency, an investigator may not deviate from the protocol unless he/she obtains the prior approval of Tear Film

Innovations, Inc. Depending on the specifics of the deviation, IRB approval may also be required.

APPENDIX 1: SCHEDULE OF ASSESSMENTS

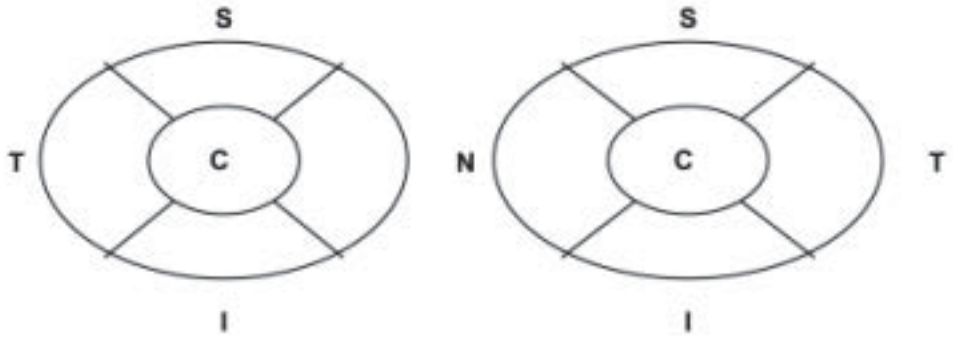
ASSESSMENT	PRE-TREATMENT	TREATMENT	POST-TREATMENT	FOLLOW UP
Treatment Window	**Day 0**	**Day 0**	**Day 0**	**Day 1 (-0/+3 days)**
Informed Consent	**X**			
Demographics/medical/ocular history	**X**			
Visual Acuity	**X**		**X**	
Slit Lamp for Anterior Segment health	**X**		**X**	
Lid Margin Abnormalities	**X**		**X**	
Corneal fluorescein staining slit lamp evaluation	**X**		**X**	
Intraocular pressure	**X**		**X**	
Cornea and surrounding eye tissue temperature	**X**		**X**	
iLux heating		**X**		
Discomfort/pain questionnaire	**X**		**X**	**X**
Adverse Events		**X**	**X**	**X**

APPENDIX 2: iLUX USER MANUAL

APPENDIX 3: CORNEAL FLUORESCEIN STAINING PROTOCOL

APPENDIX 4: GENERAL MEDICAL AND OPHTHALMIC HISTORY

OD		OS
Degree of Staining	Region	Degree of Staining
0 . . . . 1 . . . . 2 3	C - Central	0 . . . . 1 . . . . 2 3
0 . . . . 1 . . . . 2 3	S - Superior	0 . . . . 1 . . . . 2 3
0 . . . . 1 . . . . 2 3	T - Temporal	0 . . . . 1 . . . . 2 3
0 . . . . 1 . . . . 2 3	N - Nasal	0 . . . . 1 . . . . 2 3
0 . . . . 1 . . . . 2 3	I - Inferior	0 . . . . 1 . . . . 2 3



Grade 0 = Normal	No staining
Grade 1 = Mild	Superficial stippling micropunctate staining
Grade 2 = Moderate	Macropunctate staining with some coalescent areas
Grade 3 = Severe	Numerous coalescent macropunctate areas and/or patches

Appendix 2: Case Report Forms

FORM 1: INCLUSION/EXCLUSION - Page 1 of 1

Screening/Pre-Treatment Date (DD-MMM-YYYY) _____-_____-_____

Did subject meet all inclusion and no exclusion criteria? ❑ Yes ❑ No

If no, indicate which criteria the subject did not meet:

Inclusion criterion #/criteria #s not met: _____

Exclusion criterion #/criteria #s not met: _____

Was Sponsor notified of protocol deviation? ❑ Yes ❑ No ❑ N/A

Was IRB notified of protocol deviation? ❑ Yes ❑ No ❑ N/A

Did subject sign an informed consent form? ❑ Yes ❑ No

If "Yes", please provide date signed (DD-MMM-YYYY) _____-_____-_____

Subject Assessment Schedule:

ASSESSMENT	PRE-TREATMENT	TREATMENT	POST-TREATMENT	FOLLOW UP
Treatment Window	**Day 0**	**Day 0**	**Day 0**	**Day 1 (-0/+3 days)**
Informed Consent	X			
Demographics/medical/ocular history	X			
Visual Acuity	X		X	
Slit Lamp for Anterior Segment health	X		X	
Lid Margin Abnormalities	X		X	
Corneal fluorescein staining slit lamp evaluation	X		X	
Intraocular pressure	X		X	
Cornea and surrounding eye tissue temperature	X		X	
iLux heating		X		
Discomfort/pain questionnaire	X		X	X
Adverse Events		X	X	X

Required Case Report Forms by Assessment:

Pre-Treatment	Forms 1-5	
Treatment	Forms 6-7	*Form 8 with any Adverse Event* *Form 9 with Device Event*
Post-Treatment	Forms 4-5	*Form 8 with any Adverse Event*
Follow-Up	Form 5	*Form 8 with any Adverse Event*

FORM 2: DEMOGRAPHICS & MEDICAL HISTORY- Page 1 of 1

Demographics:

Date of birth (DD-MMM-YYYY) - -

Gender ❑ Male ❑ Female

Ethnicity ❑ Hispanic or Latino ❑ Not Hispanic or Latino

Race ❑ American Indian or Alaska Native ❑ Asian ❑ Black or African American ❑ Hawaiian or Other Pacific Islander ❑ White

Medical History

Does the subject have:		**# of Years**	**Treated w/ Medication?**
Diabetes?	❑ Yes ❑ No		❑ Yes ❑ No
Hypertension?	❑ Yes ❑ No		❑ Yes ❑ No
Hypercholesterolemia?	❑ Yes ❑ No		❑ Yes ❑ No
Allergies to medication?	❑ Yes ❑ No		❑ Yes ❑ No
Infection disease (HIV, TB)?	❑ Yes ❑ No		❑ Yes ❑ No

If yes, please specify: _____

List all medications subject is currently taking including OTC, homeopathic, birth control, or remedies

_____

_____

List all major injuries, surgeries, and/or hospitalizations subject has had:

_____

_____

Does the subject drive? ❑ Yes ❑ No

Does the subject have difficulty driving? ❑ Yes ❑ No

If Yes, please explain: _____

Does the subject use tobacco products? ❑ Yes ❑ No

Does the subject use alcohol products? ❑ Yes ❑ No

Does the subject use illicit drugs? ❑ Yes ❑ No

PCP Name: _____

PCP Phone #: _____

Last Medical Exam - - (DD-MMM-YYYY)

Is the subject currently under medical care for any condition? ❑ Yes ❑ No

If yes, please specify: _____

FORM 3: SYMPTOMS & OCULAR HISTORY- Page 1 of 1

Subject General Symptoms	
Constitutional: Fever, Weight Loss, Appetite	❑ Yes ❑ No
Integumentary: Skin conditions/ disorders	❑ Yes ❑ No
Neurological: Headaches, Migraine, Seizures	❑ Yes ❑ No
Ear, Nose, Throat: Allergies, Sinus, Cough, Dry Throat/Mouth	❑ Yes ❑ No
Respiratory: Asthma, Emphysema, Bronchitis	❑ Yes ❑ No
Vascular: Hypertension, Stroke, Heart Pain	❑ Yes ❑ No
Gastrointestinal: Diarrhea, Constipation	❑ Yes ❑ No
Genitourinary: Genitals, Kidneys, Bladder	❑ Yes ❑ No
Bones/ Joints: Rheumat Arthritis, Muscle Pain	❑ Yes ❑ No
Lymphatic/Hematologic: Anemia, Bleeding	❑ Yes ❑ No
Allergic Immunologic: Allergies, Immune	❑ Yes ❑ No
Psychiatric: Depression/Anxiety	❑ Yes ❑ No

Subject Ocular Symptoms		Which Eye?
Sudden Vision Loss	❑ Yes ❑ No	❑ OD ❑ OS
Blurred Vision	❑ Yes ❑ No	❑ OD ❑ OS
Loss of Side Vision	❑ Yes ❑ No	❑ OD ❑ OS
Double Vision	❑ Yes ❑ No	❑ OD ❑ OS
Floaters	❑ Yes ❑ No	❑ OD ❑ OS
Flashes	❑ Yes ❑ No	❑ OD ❑ OS
Mucus Discharge	❑ Yes ❑ No	❑ OD ❑ OS
Redness	❑ Yes ❑ No	❑ OD ❑ OS
Gritty Feeling	❑ Yes ❑ No	❑ OD ❑ OS
Itchy/Burning	❑ Yes ❑ No	❑ OD ❑ OS
Tearing/Watery	❑ Yes ❑ No	❑ OD ❑ OS
Glare	❑ Yes ❑ No	❑ OD ❑ OS
Eye Pain/Discomfort	❑ Yes ❑ No	❑ OD ❑ OS
Haloes at Night	❑ Yes ❑ No	❑ OD ❑ OS

Family Medical and Ocular History		Relative/Relationship:
Blindness	❑ Yes ❑ No	_____
Cataracts	❑ Yes ❑ No	_____
Glaucoma	❑ Yes ❑ No	_____
Macular Degeneration	❑ Yes ❑ No	_____
Retinal Disease	❑ Yes ❑ No	_____
Arthritis	❑ Yes ❑ No	_____
Cancer	❑ Yes ❑ No	_____
Diabetes	❑ Yes ❑ No	_____
Hypertension	❑ Yes ❑ No	_____
Heart Disease	❑ Yes ❑ No	_____
Kidney Disease	❑ Yes ❑ No	_____
Thyroid Disease	❑ Yes ❑ No	_____
Other:	❑ Yes ❑ No	_____

Please specify: _____

FORM 4: OCULAR ASSESSMENT - Page 1 of 2

Assessment Timeframe ❑ Pre-Treatment ❑ Post-Treatment ❑ Other, please specify _____

Visual Acuity

Total ETDRS Letters Read

	OD	OS	OD	OS
Uncorrected	_____	_____	❑ Finger Count OR ❑ Hand Movement ❑ Light Perception	❑ Finger Count OR ❑ Hand Movement ❑ Light Perception
Habitual correction	_____	_____	❑ Finger Count OR ❑ Hand Movement ❑ Light Perception	❑ Finger Count OR ❑ Hand Movement ❑ Light Perception
Best correction	_____	_____	❑ Finger Count OR ❑ Hand Movement ❑ Light Perception	❑ Finger Count OR ❑ Hand Movement ❑ Light Perception

Slit Lamp Examination

0 = No Clinical Finding; 1 = Non-Clinically Significant Finding; 2 = Abnormal Finding; ***if > 0, please specify below*** *:*

	OD	OS	OD	OS
Adnexa	❑ 0 ❑ 1 ❑ 2	❑ 0 ❑ 1 ❑ 2	_____	_____
Conjunctiva	❑ 0 ❑ 1 ❑ 2	❑ 0 ❑ 1 ❑ 2	_____	_____
Sclera	❑ 0 ❑ 1 ❑ 2	❑ 0 ❑ 1 ❑ 2	_____	_____
Corneal clarity	❑ 0 ❑ 1 ❑ 2	❑ 0 ❑ 1 ❑ 2	_____	_____
Tear film	❑ 0 ❑ 1 ❑ 2	❑ 0 ❑ 1 ❑ 2	_____	_____
Anterior chamber	❑ 0 ❑ 1 ❑ 2	❑ 0 ❑ 1 ❑ 2	_____	_____
Iris	❑ 0 ❑ 1 ❑ 2	❑ 0 ❑ 1 ❑ 2	_____	_____

Intraocular Pressure

	OD	OS
Goldmann (mmHg)	_____	_____

Lid Margin Assessment *check "Yes" for each condition that applies to each lid*

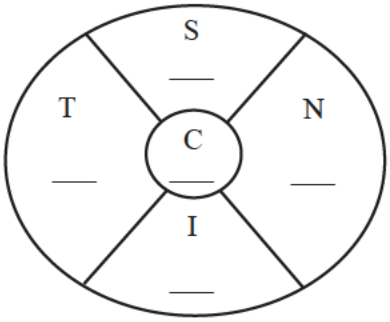
	Upper Lid		Lower Lid	
	OD	OS	OD	OS
0=None	❑ Yes ❑ No	❑ Yes ❑ No	❑ Yes ❑ No	❑ Yes ❑ No
1=Irregular Lid Margin	❑ Yes ❑ No	❑ Yes ❑ No	❑ Yes ❑ No	❑ Yes ❑ No
2=Vascular Engorgement	❑ Yes ❑ No	❑ Yes ❑ No	❑ Yes ❑ No	❑ Yes ❑ No
3=Ant/Post Replacement of Mucocutaneous Junction	❑ Yes ❑ No	❑ Yes ❑ No	❑ Yes ❑ No	❑ Yes ❑ No

FORM 4: OCULAR ASSESSMENT - Page 2 of 2

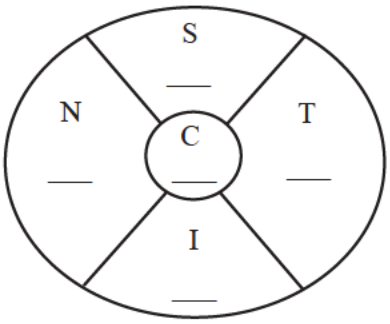
Corneal Fluorescein Staining Grading

Enter the staining grade for each segment of each eye

OD



OS



0 = Normal; No staining
1 = Mild; Superficial staining, micropunctate staining
2 = Moderate; Macropunctate staining with some coalescent areas
3 = Severe; Numerous macropunctate areas and/or patches

Manifest Refraction	**+/-**	**Sphere**		**Cylinder**	**Axis**
OD	____	_____	-	_____	X _____
OS	____	_____	-	_____	X _____

Keratotomy	**OD**		**OS**	
Steep	_____ D	_____ °	_____ D	_____ °
Flat	_____ D	_____ °	_____ D	_____ °

Eye Temperature Assessment	**OD**	**OS**
1st Reading - Pre-Treatment and Post-Treatment		
Corneal Temp (close eye for 5 sec, then open)	_____	_____
Surrounding Tissue Temp (close eye for 5 sec)	_____	_____
*2nd Reading - **Post-Treatment Only***		
Corneal Temp (close eye for 5 sec, then open)	_____	_____
Surrounding Tissue Temp (close eye for 5 sec)	_____	_____
*3rd Reading- **Post-Treatment Only***		
Corneal Temp (close eye for 5 sec, then open)	_____	_____
Surrounding Tissue Temp (close eye for 5 sec)	_____	_____

FORM 5: PAIN/DISCOMFORT ASSESSMENT- Page 1 of 1

Assessment Date (DD-MMM-YYYY) ____-____-_____

Assessment Timeframe

❑ Pre-Treatment ❑ Post-Treatment ❑ Follow-Up

❑ Other, please specify: _____

	OD	OS
Subject's pain level (scale 0-10)	_____	_____

Score	Level of Discomfort/Pain	Description to Anchor Subjective Response
0	No discomfort or pain	Minimal recognition of pressure only. Equal to the touch of a finger on the skin. Awareness but no discomfort.
2	Slight or transient awareness of pressure without pain	Pressure tolerable and could be endured indefinitely without compromise to daily activities. Examples: bruise; medical injection; wearing dress shoes, which one would wear all day and might forget to remove when returning home; poorly adjusted glasses.
4	Moderate discomfort with minimal pain	Discomfort but tolerable. Examples: eye irritation from chlorine pool; pulled muscle; wearing tight dress shoes, which might be worn all day, but would definitely be removed when arriving home; smoke in eye; soap in eye; tight collar or clothes
6	Moderate pain	Constant awareness of moderate pain affecting daily activities. Examples: corneal abrasion; wearing tight dress shoes, which could not be worn for more than several hours due to excess pressure and pain; wasp or hornet sting.
8	Severe pain	Partially debilitating. Examples: broken bone; wearing tight dress shoes, which result in open blisters, making walking more than a few steps impossible; stepping on a nail.
10	Intolerable pain	Totally debilitating, preventing any activity. Examples: back pain preventing any movement; scalding water; severe migraine; slamming car door on finger; stick in eye.

FORM 6: iLux PROCEDURE- Page 1 of 1

Procedure Date (DD-MMM-YYYY) ___-___-___

Preparation for iLux Use *If no to any question below, please explain:*

Eye makeup removed?	❑ Yes ❑ No	_____
Contact lenses removed?	❑ Yes ❑ No	_____
iLux prepared per Directions for Use?	❑ Yes ❑ No	_____
Anesthetic eyedrops applied to each eye?	❑ Yes ❑ No	_____
Baseline temperature measured?	❑ Yes ❑ No	_____
iLux serial number	_____	
iLux disposable lot number	_____	

iLux Treatment	**OD**	**OS**		*Explain any ND below*
#1: Central-temporal lower eyelid				
Heating Time (sec)	_____	_____	❑ ND	_____
Holding Force (lbs.)	_____	_____	❑ ND	_____
Maxiumum Temperature (°C)	_____	_____	❑ ND	_____
#2: Central-nasal lower eyelid				
Heating Time (sec)	_____	_____	❑ ND	_____
Holding Force (lbs.)	_____	_____	❑ ND	_____
Maxiumum Temperature (°C)	_____	_____	❑ ND	_____
#3: Central-temporal upper eyelid				
Heating Time (sec)	_____	_____	❑ ND	_____
Holding Force (lbs.)	_____	_____	❑ ND	_____
Maxiumum Temperature (°C)	_____	_____	❑ ND	_____
#4: Central-nasal upper eyelid				
Heating Time (sec)	_____	_____	❑ ND	_____
Holding Force (lbs.)	_____	_____	❑ ND	_____
Maxiumum Temperature (°C)	_____	_____	❑ ND	_____

Were there any adverse events during treatment?	❑ Yes ❑ No	***If Yes, please fill out AE Form***
Were there any device events during treatment?	❑ Yes ❑ No	***If Yes, please fill out DER Form***

Investigator Signature: _____ Date: _____

FORM 7: iLux USABILITY ASSESSMENT - Page 1 of 1

Were you able to turn the iLux Device On and Off?	❑ Yes ❑ No
Were you able to read the screen on the iLux clearly without difficulty?	❑ Yes ❑ No
Were you able to remove the disposable from the packaging and load the disposable into the device as instructed by the User's manual?	❑ Yes ❑ No
Were you able to apply pressure to the eyelid without difficulty?	❑ Yes ❑ No
Were you able to apply heat to the eyelid without difficulty?	❑ Yes ❑ No
Were you able to view the eyelid margin with the magnifier without difficulty?	❑ Yes ❑ No
Were you able to recharge the battery as described in the User's manual?	❑ Yes ❑ No

For an answer of "No" above, please provide additional details below:

FORM 8: ADVERSE EVENT- Page 1 of 1

Timepoint of adverse event:	❑ Treatment ❑ Post-Treatment ❑ Follow-Up ❑ No Adverse Events for this Subject
Date adverse event began (DD-MMM-YYYY)	- -
Time adverse event began (24-hour format, HH:MM)	:
Was the event a serious adverse event (SAE)?	❑ Yes ❑ No
If Yes, indicate which criteria meets the protocol definition of SAE	
Led to death	❑
Led to serious deterioration in the health of the patient that resulted in: - A life-threatening illness or injury - A permanent impairment of a body function - In-patient or prolonged hospitalization - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to body structure or a body function	❑
Was the event device-related?	❑ Related ❑ Not Related
Was the event procedure-related?	❑ Related ❑ Not Related
Was the event an unanticipated adverse event?	❑ Yes ❑ No
Event severity	❑ Mild ❑ Moderate ❑ Severe
Diagnosis of adverse event:	_____

Treatment or action taken to treat adverse event:	❑ None ❑ OTC/Rx Drug ❑ Non-Drug Treatment/Procedure ❑ Hospitalization/ER Visit
Action taken during procedure:	❑ None ❑ Study Procedure Interrupted ❑ Study Procedure Discontinued
Outcome of event:	❑ Resolved without sequelae ❑ Resolved with sequelae (specify below) ❑ Ongoing ❑ Death ❑ Unknown

Date of resolution: _____-_____-_____ Time of resolution: _____:_____ ❑ N/A

Briefly describe the event, including any sequelae:

_____

_____

_____

_____

Investigator Signature: _____ Date: _____

FORM 9: DEVICE EXPERIENCE REPORT FORM- Page 1 of 1

Date of event (DD-MMM-YYYY)	- -
Time of event (24-hour format, HH:MM)	:
Did the event result in an adverse event?	❑ Yes ❑ No ***If Yes,please fill out an AE Form***
Device(s) involved in the event (check all that apply):	❑ iLux Instrument ❑ iLux Disposable ❑ Batteries ❑ Charging Stand ❑ QC Checkor ❑ Magnifier ❑ Other, please specify: _____
Type of event (check all that apply):	❑ Package Damaged ❑ Unit Won't Turn On ❑ Software Malfunction ❑ Product Damaged ❑ No Temperature Increase ❑ Temperature Cutoff ❑ Compression Malfunction ❑ LED Malfunction ❑ Display Malfunction ❑ Switch Malfunction ❑ Disposable Won't Engage with Unit ❑ Other, please specify: _____
Action taken during procedure:	❑ None ❑ Study Procedure Interrupted ❑ Study Procedure Discontinued
Device disposition:	❑ Continued with Original Device ❑ New Device Used

Briefly describe the event:

_____

_____

_____

_____

_____

_____

Investigator Signature: _____ Date: _____

Appendix 3: Informed Consent Form

INFORMED CONSENT TO PARTICIPATE IN CLINICAL RESEARCH STUDY

iLux™ Safety Study

Sponsor:	**Tear Film Innovations, Inc.**
Protocol Number:	**2020-02**
Principal Investigator:	James Owen, O.D. Encinitas Optometry 681 Encinitas Blvd., #302 Encinitas, CA 92924
24-Hour Telephone Number:	**(760) 436-1877**

This is a research study. This study includes only individuals who voluntarily choose to participate. Please take your time to make your decision. Discuss it in confidence with your regular doctor, friends and family if you want. Be sure to ask questions about anything you do not understand in this document. Taking part in a research study is entirely voluntary and you can stop being in the study at any time you want to, without any penalty or impact on your medical care or benefits.

The reason we are doing this research study is to gather information. In this document, you will see the term “treatment.” This term is used in research studies and is not meant to indicate that you will be receiving medical treatment for your condition as the device being used in this investigational study is experimental.

WHAT IS THIS STUDY ABOUT?

The purpose of this study is to measure corneal temperature as well as the surrounding eye tissue temperature including the eye lids after heating the eyelids with the iLux device after treatment with the iLux™ device. Bench top safety testing has shown that the back plate of the iLux disposable tip does not heat above the safe temperature of 40°C (104°F). The study device is investigational, which means that it is not approved by the Food and Drug Administration (FDA).

If you participate in this study, you will be receiving one treatment with the iLux device.

HOW LONG IS THIS STUDY? HOW MANY OTHER PEOPLE WILL BE IN THIS STUDY?

About 15 adults with healthy eyes will take part in this study. You will be in the study for about one week, including a screening evaluation, a single treatment and a follow up evaluation one day after the treatment visit.

WHAT IF NEW INFORMATION BECOMES AVAILABLE?

If new information in relation to the study DEVICE becomes available, that may be relevant to the purpose and safety of the study and your willingness to continue participation in this study, you will be informed by the study doctor.

WHAT WILL HAPPEN DURING THE STUDY?

If you agree to take part in this research study, you will be required to sign this informed consent form before any procedures take place.

STUDY PROCEDURES:
During the screening and if you qualify and continue, during the study the following procedures will occur:

- Demographics/medical/ocular history
- Visual acuity (a test to evaluate your vision)
- Slit lamp evaluation for anterior segment health (an exam allowing the doctor to see the front of the eye)
- Evaluation of any eyelid margin abnormalities
- Corneal fluorescein staining slit lamp evaluation (a variation of the slit lamp exam that allows for the doctor to see abrasions and scarring on the eye)
- Intraocular pressure (an exam to assess the fluid pressure inside the eye)
- iLux™ treatment

The study doctor will talk to you and give you a list of the things you must do to participate, such as:

- Your history of contact lens wear in the last 30 days and intention on wearing contact lenses during this study.

You may have additional tests, for example, to follow up on tests previously done.

Please tell your regular health care providers and any emergency care providers that you are participating in this research study.

At the screening visit, your eyes will be examined and you will be asked questions about your health to make sure that you meet the requirements to participate in the study without unacceptable risk to your safety and health. If it is found that you do meet those requirements, you will have a detailed eye exam including the assessments included in the above list. The iLux device will then be used on your eyelids for a single treatment. The device is a small instrument that the study doctor will hold in their hand. You will have eye drops with numbing medicine dripped into your eye to keep the eye surfaces numb during the treatment (the effects of these eye drops will wear off in 10-20 minutes after the procedure). The study doctor will gently pull your eyelid away from the eyeball and place the eyelid between two pads on the device then gently squeeze the eyelid between the pads.

The study doctor will then push a button on the device that activates a green light and some infrared (warming lights) on the eyelids for 90 seconds. The light will warm the eyelids to between 104 and 107.5 degrees Fahrenheit. The study doctor will also look through a magnifying lens on the device to get it into the proper place on your eyelids.

The device is designed to shut off automatically if you eyelids get too hot. It is also designed NOT to touch your eyeball. However, if it accidentally did touch your eyeball, the device will be cool enough that you eyeball is not warmed higher than your normal body temperature. This helps prevent any risk of damage to you eye.

You will be asked to answer questions about whether you are having any eye discomfort on the day of the procedure or the next day.

After the one day follow up phone call, your participation in the study will end.

WHAT ARE THE RISKS AND DISCOMFORTS OF PARTICIPATING IN THIS STUDY?

The iLux™ is used in the eye and the sterile disposable may come in contact with the conjunctiva and or cornea during the treatment of each lid. The sterile disposable silicone pads are covered with a biocompatible silicone similar to a contact lens. There is nothing implanted either temporarily or permanently in the eye related to the iLux™.

David Sliney, PhD, a nationally-respected expert in the field of ocular radiation hazard who consults frequently with both the FDA and industry, performed an on-site evaluation of Tear Film's benchtop system. He concluded that the iLux™ system conforms to applicable safety standards.

The iLux has also undergone safety testing by NEMKO and has passed all test which were based on international standards.

An animal safety study was conducted at Absorption Systems in San Diego from November to December, 2014. No adverse events occurred and there were no changes observed in the eyelids or eyes, and there were no adverse histological findings.

Anticipated risks include: Eyelid/eye pain (during and after procedure), eyelid irritation or inflammation, ocular surface irritation or inflammation and ocular symptoms (stinging, tearing, itching, discharge, redness, foreign body sensation, visual disturbance, sensitivity to light).

There may be risks to being in this study that we cannot predict.

You should discuss these risks with the study doctor and/or your regular doctor.

Side effects occurring during the trial can be treated by the study doctor, if this is deemed necessary. It is important that you inform the study doctor any unusual or unpleasant effects which you should feel.

Are there pregnancy risks?

While it is not expected that the study device will pose risk to an unborn baby, no information about possible risk is available. You cannot participate in this study if you are pregnant or nursing a baby. If you think you are pregnant during the study, you must tell the study doctor immediately.

If you are a male, you should not father a baby or be a sperm donor while in this study.

For more information about risks and side effects, ask the study doctor**.**

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

Subjects participating in this study may or may not benefit from the study device. If you agree to take part in this study, there may or may not be direct medical benefit to you. Information learned from this study may benefit others in the future.

WHAT, IF ANY, ARE THE ALTERNATIVES TO PARTICIPATING IN THIS STUDY?

This study is not designed to diagnose, treat or prevent any disease. Your alternative is to not participate.

CONFIDENTIALITY

Your personal information will be kept confidential to the extent permitted by law. We cannot guarantee absolute confidentiality. By signing this document, you give permission to access your medical records, including after withdrawal, for data verification purposes.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as:

- The study staff and other researchers involved in the study
- Tear Film Innovations, Inc., (Sponsor of this study) or those who work for or represent the Sponsor
- The U.S. Food and Drug Administration (FDA)
- Aspire Independent Review Board (IRB)

The results from the study may be published for scientific purposes, but your identity will be kept confidential.

In the rare event that your information is required to be disclosed by law to another entity, privacy laws may not apply, and neither the Sponsor nor Aspire IRB can protect your information.

WHAT ARE THE COSTS?

There are no additional costs associated with being in this study. You are responsible for your regular health care while in this study. You will not have to pay for the device during study visits, or tests/procedures that are part of the study.

INVESTIGATOR PAYMENT

The Sponsor is paying the study doctor and the study site for conducting this study.

WILL YOU BE COMPENSATED DURING THE STUDY?

You will be compensated for participating in and completing this research study. If you complete the study, you will receive $100. This amount is prorated as follows:

- $100 for the screening/treatment visit

This money is meant to compensate your travel expenses, lost wages from work, child care, etc. that you may have as a result of participating in this study.

WHAT HAPPENS IF YOU HAVE COMPLICATIONS OR ARE INJURED?

If you have serious side effects, complications or are injured because of participating in this study, please contact the study doctor promptly. The study doctor will provide any necessary medical treatment to help you promptly recover from the injury. Your insurance will be billed for the medical treatment and the study Sponsor will pay for the costs not covered by your insurance or by third party governmental programs. Such reimbursement will be offered only for reasonable costs and only if the Study Device has been used in accordance with the Protocol and any other instructions provided by the Sponsor.

YOUR RIGHTS AS A RESEARCH SUBJECT

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to the study doctor and your regular doctor first.

YOUR RESPONSIBILITIES AS A RESEARCH SUBJECT

You will be asked to adhere to all instructions issued by the study doctor and other study staff. This also includes arriving on time for examinations. Furthermore, you should answer all asked questions truthfully.

Should you not comply with instructions, the study doctor may stop your study participation. Your study doctor may also exclude you from this trial if he/she deems it beneficial for your health, or if you do not meet the study requirements. Your participation in this study may be ended if the Sponsor stops the study for any reason.

WHOM TO CALL IF YOU HAVE QUESTIONS

For questions, concerns or complaints about the study or a research-related injury, contact the study doctor at the number on page 1.

This study was reviewed by Aspire Independent Review Board (IRB). An IRB reviews research to protect the rights and welfare of study participants. If you have problems, concerns, suggestions, complaints, questions or information about the study, and for information regarding research subject's rights, please call Aspire's Study Participant Advocate at 1-877-366-5414 (toll free).

Although Aspire IRB has approved the information provided in this informed consent form and has granted approval for the investigator to conduct the study this does not mean Aspire has approved your participation in the study. You must evaluate the information in this informed consent form for yourself and decide whether or not you wish to participate.

SIGNATURE AND CONSENT TO BE IN THE STUDY

Your signature below means that you have read the above information about this study and have had a chance to ask questions to help you understand what you will be expected to do and that you agree to participate in this study. Your signature also means that you have had all your questions answered to your satisfaction and that you have been told that you can change your mind later if you want to. You will be given a signed and dated copy of this agreement. By signing this consent form, you are not giving up any of your legal rights**.**

_____ _____/_____
SIGNATURE OF SUBJECT DATE

_____
PRINTED NAME OF SUBJECT

I confirm that a copy of this consent form has been given to this person to read and that this person has been told about the study. The contents of the consent form describing the study has been discussed with this person and I have made every effort to answer all questions to his or her satisfaction. I have watched this person sign the consent form.

_____ _____/_____
SIGNATURE OF PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

Appendix 4: IRB Approval

STUDY APPROVAL NOTIFICATION

iLux™ Safety Study

Sponsor:	**Tear Film Innovations, Inc.**
Protocol Number:	**2020-02** **March 2, 2016**

The new study listed above was reviewed at the **March 08, 2016** meeting of *Aspire IRB*. In addition, the **iLux User Manual dated August 22, 2015 & iLux Device Description dated July 15, 2015** was given full review.

This study was approved at that time with the following conditions:

- **Informed Consent revised for readability and clarity purposes and to ensure all applicable required elements of consent are satisfied.**

The above-referenced conditions have been met and this study received unconditional approval on March 16, 2016.

Jim Owen, OD was approved to conduct this study at the following locations:

Encinitas Optometry
681 Encinitas Blvd., #302
Encinitas, CA 92924

In addition, Aspire IRB is in receipt of requested changes to the Informed Consent document for the above referenced study. This document has been revised to:

- Clarification and explanation of the slit lamp procedure

Changes to this document do not negatively impact subject safety or study integrity. These changes have been approved through expedited review by Susan Abramson, MD, Aspire IRB Board Member, on March 16, 2016.

You must use the enclosed approved consent documentation stamped with “Aspire IRB Approved” located at the bottom of each page.

- **Informed Consent Document dated March 16, 2016**

Additional Materials:

- **Print Advertisement - Approved March 8, 2016**
- **Corneal Fluorecein Staining Guide - Acknowledged March 8, 2016**
- **Medical Ocular History - Approved March 8, 2016**

The IRB has determined that your study is **More Than Minimal** risk. This study involves an investigational medical device; the Board agrees with the Sponsor's submitted **Non-Significant** determination for the proposed use in this study. It has been assigned an approval period of **Annual** review. Your approval period ends **March 7, 2017**; as a reminder, you will receive a Research Status Report Form approximately sixty days prior to this date.

The Principal Investigator is responsible for providing the IRB with the necessary materials for re-approval by the due date provided on the form. **This form must be received by the due date to allow ample time for adequate review prior to the study's expiration date.** Missed submissions are the responsibility of the Principal Investigator regardless of whether or not the IRB notifies you.

The continuation of research after expiration of IRB approval is a violation of the regulations governing research.

Please be aware that while your study has now received IRB approval, FDA approval to proceed is still required (if applicable). It is your responsibility to ensure that you have a valid FDA approval/clearance, before you move forward with study procedures or subject recruitment. It is your responsibility to notify Aspire, if the FDA or any other regulatory agency delays or puts a hold on your research.

It is required that *Aspire IRB* be notified of:

- All amendments or changes to the protocol
- Changes to the protocol that are implemented without prior IRB approval to eliminate an apparent immediate hazard to subjects (must be reported within 24 hours of implementation)
- Unanticipated problems involving risks to subjects or others (within 10 calendar days of discovery) this includes protocol deviations that fit the criteria for an unanticipated problem.
- All material used to recruit study subjects (prior IRB approval is required before use)
- Any other changes in the research activity

The Principal Investigator may not make any changes in the research, without prior approval of *Aspire IRB,* except when necessary to eliminate immediate risk to study subjects. In addition, it is the responsibility of the Principal Investigator to uphold the following three ethical principles outlined in the Belmont Report during the conduct of this study:

- Respect for persons: individuals should be treated as autonomous agents, and persons with diminished autonomy are entitled to protection.
- Beneficence: maximize possible benefits and minimize possible harms.
- Justice: benefits and burdens of research should be distributed equally.

Aspire IRB is duly constituted and has written procedures in compliance with requirements defined in 21 CFR Parts 50 and 56, 312, 812, 45 CFR 46 and ICH Guidelines relating to Good Clinical Practice. Aspire IRB's mission is to ensure that research is conducted ethically according to the principles of the Belmont Report and in compliance with federal regulations, international regulations, ICH Guidelines for Good Clinical Practice, applicable state and local laws, Aspire IRB Standard Operating Procedures, and that the rights and welfare of human subjects are protected.

Sincerely,

Aspire IRB
AFD

April 27, 2016

Jim Owen, OD
Encinitas Optometry
681 Encinitas Blvd., #302
Encinitas, CA 92924

Re: Protocol Amendment No. 1 dated April 25, 2016
Sponsor: Tear Film Innovations, Inc.
Protocol Number: 2020-02

Dear Dr. Owen,

Aspire IRB is in receipt of **Protocol Amendment No. 1 dated April 25, 2016** for the above referenced study. This amendment was issued to:

- **Clarify the i-Lux procedure**
- **Update the statistical methods**
- **Update the name of the scores of the discomfort/pain scale from " specific scores" to "descriptive anchors"**
- **Make typographical, formatting and grammatical changes**

This amendment required no changes to the previously approved Informed Consent document and this document will not be reissued.

This amendment does not negatively impact subject safety or study integrity. These changes have been approved through expedited review by Susan M. Abramson, MD, Aspire IRB Board Member, on April 27, 2016.

A copy of this documentation should be forwarded to the sponsor/CRO for their records and maintained in your files for future reference.

If we can be of further assistance, please do not hesitate to contact our office.

Sincerely,

Aspire IRB
AFD