A Prospective, Randomized, Controlled Trial of the TearCare MGX™ System with and without Warming Hold (Xtend)

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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

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Revision History

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1 PROTOCOL SYNOPSIS

Protocol Title	**A Prospective, Randomized, Controlled Trial of the TearCare MGX™ System with and without Warming Hold (Xtend)**
Protocol ID Number	CLN1 10280
Study Device	TearCare MGX System
Control Group	TearCare MGX System with Warming hold disabled
Study Objective	To demonstrate the utility of the Warming hold with the TearCare MGX System.
Study Design	Prospective, randomized, single site, assessor masked, controlled study.
Primary Endpoint	Inter-eye (OD – OS) difference in Meibomian Gland Secretion Score (MGSS)
Secondary Endpoints	• Mean change from Screening visit baseline in MGSS • Mean change from Screening visit baseline in Meibomian Glands Yeilding Any Liquid (MGYAL) • Mean change from Screening visit baseline in Meibomian Glands Yeilding Clear Liquid (MGYCL) • Subject Comfort during expression of second lid • Ease of expression (masked assessor rated)
Exploratory Endpoints	• Comparative comfort of SmartLids (MGX and TC 1.5) • Overall satisfaction of procedure (Investigator and subject) • Ease of Blinking (during SmartLids comfort assessment)
Safety Endpoints and Measures	• Rate of ocular adverse events • Slit lamp exam • BCVA • IOP
Inclusion Criteria	For inclusion in this study, subjects must meet all the following criteria. All ocular criteria apply to both eyes: 1. Male or female subjects, 22 years of age or older 2. Reports dry eye symptoms within the past 6 months 3. OSDI score of 23 to 79 4. Meibomian gland obstruction in both eyes based on a total **Meibomian Gland Secretion Score ≤12 in each eye.** 5. **At least 15 glands in each lower eyelid should be expressible, with a sterile cotton swab, at the slit lamp.** 6. **Best corrected visual acuity of 20/100 or better, OU.** 7. **Willing and able to comply with the study procedures and follow-up** 8. **Understands and signs the informed consent.**

Exclusion Criteria	1. **Use of:** a. **Cyclosporine, Xiidra, or serum tears within 60 days prior to Screening;** b. **Antihistamines (oral or topical) within 7 days prior to Screening;** c. **Oral tetracyclines or azithromycin within 30** days prior to Screening; d. **Topical ophthalmic** antibiotics, anti-glaucoma medications, steroids, non-steroidal anti-inflammatory medications within 30 days prior to Screening e. Isotretinoin (e.g. Accutane) at any time. 2. Any of the following dry eye treatments: a. Office-based dry eye treatment (e.g. IPL, TearCare, thermal pulsation [LipiFlow], iLux etc.) within 12 months prior to Screening either as part of routine care or clinical investigation; b. Planned or recent surgical procedures to the eye or eyelid (90 days prior to Screening); c. Meibomian gland expression within 6 months prior to Screening; d. Blephex or debridement within 3 months prior to Screening; e. Punctal occlusion (including collagen, e.g. Soft Plug, UltraPlug, or crosslinked hyaluronic acid, e.g. Lacrifill) or punctal plugs within 15 days of the Screening visit; f. Use of tear neurostimulators (i.e., True Tear, iTear100, Tyrvaya) within 2 weeks of the baseline visit. (Subjects must refrain from using tear neurostimulators for the duration of the study); g. Any history of meibomian gland probing. 3. History of eyelid, conjunctiva, or corneal surgery (including refractive surgery) within 12 months prior to Screening. 4. Any history of chalazion surgery, surgery on the tarsal conjunctiva, radial keratotomy (RK), complicated blepharoplasty, lid **reconstruction, or significant complications post-refractive surgery.** 5. **Contact lens use within 2 weeks of the Procedure visit. Subjects presenting at the Screening visit using contact lenses must agree to discontinue use for a full 2 weeks (14 days) prior to the Procedure visit.** 6. **Active hordeolum, stye, or chalazion at the time of the Screening visit.**

	7. History of Herpes Simplex or Herpes Zoster of the eye or eyelid. 8. Any active, clinically significant ocular or peri-ocular infection, inflammation, or irritation. 9. Recurrent clinically significant eye inflammation, other than dry eye, within 3 months prior to Screening. 10. Clinically significant anterior blepharitis. In addition, collarettes or flakes of more than one quarter of the eyelid are excluded. 11. Clinically significant eyelid abnormalities in either eye (e.g. entropion/ectropion, blepharospasm, aponeurotic ptosis, lagophthalmos, distichiasis, trichiasis). 12. Clinically significant dermatologic or cutaneous disease of the eyelid or periocular area. 13. In the clinical judgement of the Investigator, meibomian glands have significant capping, atrophy, or are unable to be expressed, digitally or with a cotton swab. 14. Corneal surface abnormalities such as corneal epithelial defects (other than punctate staining), ulcers, corneal epithelial dystrophies, keratoconus, and ectatic disease of the cornea 15. Any active, clinically significant allergic, vernal, or giant papillary conjunctivitis. 16. Ocular trauma within 3 months prior to Screening. 17. Known history of diminished or abnormal facial, periocular, ocular or corneal sensation 18. Systemic diseases, in the Investigator's medical judgement, resulting in dry eye (e.g. autoimmune diseases such as Sjogren's syndrome, rheumatoid arthritis, lupus, Graves' disease, sarcoidosis, etc.) 19. Subject is currently using Retin A /Retin A derivatives. 20. Subject has permanent eyeliner/lid tattoos, eyelash extensions or wears false eyelashes. 21. Subject is currently using Latisse, Lash Boost or any other type of eyelash growth serum. Prostaglandin analog products such as Latisse should not be used within 30 days of the Screening visit. 22. Temporary false eyelashes, lash extensions, or any other type of false eyelash within 15 days of the Screening Visit. 23. Allergies to silicone tissue adhesives, acrylates and/or copper. 24. Subject has a pacemaker or implantable cardiac defibrillators (ICD). 25. Co-existing condition, either ocular or non-ocular that, in the judgement of the Investigator could affect the safety or effectiveness of treatment or the compliance of the subject to the protocol.
Number of Subjects Enrolled	Up to 25 enrolled to ensure 20 evaluable subjects completing the study.

Randomization	1:1
Number of Centers	1
Study Duration for Each Subject	Up to 8 weeks
Schedule of Visits	Screening Visit (Day -30 to -7), Procedure Day (Day 0), Safety Follow-up (Day 7 to 30)
Study Treatment	Bilateral treatment with the TearCare MGX System with the Warming hold
Control Treatment	Bilateral treatment with the TearCare MGX System without the Warming hold

2 LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Expansion or Definition
AE	**Adverse event**
ADE	**Adverse device effect**
ALCOA	Attributable legible contemporaneous original accurate
AMD	Age-related macular degeneration
dB	Decibel
BCVA	Best corrected visual acuity
CCT	Central corneal thickness
C:D ratio	Cup disk ratio
CE	Cataract extraction
CE mark	Conformite Europeenne mark
CFR	Code of Federal Regulations
CI	Confidence Interval
CME	Cystoid macular edema
CRF	Case report form
CRO	Contract Research Organization
DED	Dry eye disease
DEWS	Dry Eye Workshop
EDS	Eye dryness score
EWH	Extended Warming hold
GCP	Good Clinical Practices
HIPAA	Health Insurance Portability and Accountability Act
ICD	Informed consent document
IOP	Intraocular pressure
IR	Infrared
IRB	Institutional Review Board
MGD	Meibomium gland disease
MGSS	Meibomium gland secretion score
MGYAL	**Meibomium glands yielding any liquid**
MGYCL	**Meibomium glands yielding clear liquid**
NSR	**Non-significant risk**
OD	**Oculus dexter (right eye)**

Abbreviation	Expansion or Definition
OS	Oculus sinister (left eye)
OU	Oculi uterque (both eyes)
OSDI	Ocular Surface Disease Index
SANDE	Symptoms Assessment questionnaire iN Dry Eye
SID	Subject identification number
TBUT	Tear break-up time
TC	TearCare

3 STUDY OBJECTIVE

To demonstrate the utility of the Warming hold with the TearCare MGX System.

4 BACKGROUND AND JUSTIFICATION FOR THE STUDY

Dry Eye Disease (DED) 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. The prevalence of dry eye disease increases with age, especially in postmenopausal women. It is estimated that dry eye disease affects more than 7 million Americans older 40 years of age[1], and approximately 1 million to 4 million Americans between 65 to 84 years of age.[3]

Historically, dry eye disease has been categorized into one of two forms, aqueous tear deficiency and evaporative tear deficiency. The current understanding is that evaporative dry eye is more common than aqueous deficient dry eye.[4] However, because the symptoms of aqueous-deficient dry eye are difficult to differentiate from those of evaporative dry eye, it is often impossible to truly separate patients into distinct groups.[5] In fact, American Academy of Ophthalmology guidelines state that

[1] The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye Work Shop. Ocul Surf. 2007;5:75–92.
[2] Lemp MA, Crews LA, et al. Distribution of Aqueous-Deficient and Evaporative Dry Eye in a Clinic-Based Patient Cohort: A Retrospective Study. Cornea. 2012: 31: 472-478.
[3] Fiscella RG. Understanding dry eye disease: a managed care perspective. Am J Manag Care 2011; 17 Suppl 16:S432-9.
[4] Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo CK, Liu Z, Nelson JD, Nichols JJ, Tusbota K, Stapleton F. TFOS DEWS II Definition and Classification Report. The Ocular Surface 2017;15:276-283.
[5] Geerling G, Tauber J, Baudouin C, et al. The international workshop on meibomian gland dysfunction: report of the subcommittee on management and treatment of meibomian gland dysfunction. Invest Ophthal-mol Vis Sci 2011;52:2050-64

these conditions coexist in the majority of the patients with the disease..[6]

In terms of the mechanism of action for dry eye disease, the International Dry Eye Workshop (DEWS)[1] explained that tear hyperosmolarity and the symptoms of dry eye result from water evaporation caused by low aqueous tear flow and/or excessive evaporation. This reduced, concentrated tear volume, in turn results in further inflammation and tear film instability creating a vicious cycle. The DEWS report concluded the following: "Since both aqueous tear deficiency and increased evaporative tear loss occur in most cases of dry eye disease and are linked by common pathogenetic mechanisms, expert clinicians are increasingly basing treatment decisions on an assessment of severity rather than discrete deficiencies."[7]

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 lipid layer to retard evaporation of the aqueous layer and contribute to a smooth ocular surface.

When any of these layers is disturbed, tears may lose their protective and optical properties leading to a constellation of symptoms, a cascade of inflammatory processes, and the vicious cycle of dry eye.

With the most recent etiologies of dry eye disease in mind, multiple standard-of-care, therapeutic approaches are employed:

1. Supplementation of the tear film with artificial tears to address evaporation and maintain tear volume
2. Use of warm compress and lid massage to improve lipid production and flow on the tear film
3. Use of immunosuppressives (cyclosporine, corticosteroids, lifitegrast) to reduce inflammation
4. Placement of punctal plugs to address evaporation and maintain tear volume

Recently, a great deal of evidence suggests that obstruction of the meibomian glands,

[6] American Academy of Ophthalmology's Dry Eye Syndrome Preferred Practice Pattern 2013.
[7] Lemp M, Foulks, G. The Definition & Classification of Dry Eye Disease: Guidelines from the 2007 International Dry Eye Workshop. April 2008.
http://www.tearfilm.org/pdfs/OM%20-%20Definition%20&%20Classification.pdf

which are the glands on the eyelid that produce the lipid layer of tears, is strongly associated with dry eye disease..[8,9,10,11] The DEWS II report states that meibomian gland disease is considered the leading cause of dry eye in clinic and population based studies..[12] As these glands become either inflamed or obstructed, their ability to supplythe essential lipids to the ocular surface is diminished. This, in turn, leads to rapid evaporation of tears and thus to the signs and symptoms of dry eye disease..[13] When this occurs, it can result in ocular discomfort and, in many cases, ocular surface disorders that can affect vision.

TearCare (TC) (Sight Sciences, Menlo Park, CA, USA) is an office-based thermal therapeutic eyelid technology cleared by the US Food and Drug Administration for the treatment of evaporative DED due to MGD.[14] The TC procedure involves the debridement of all four eyelid margins at the slit lamp, calibrated thermal liquification of gland obstructions, and the removal of melted meibum from the meibomian glands within all four eyelids. The TC system consists of 2 wearable devices (SmartLids) affixed to the upper and lower eyelids of both eyes using medical grade adhesive such that blinking is unimpeded. These devices are connected to a central controller (SmartHub) that gradually increases the temperature at the eyelid surface to 45°C (above the 41°C threshold necessary to soften and melt meibum).[15] The treatment temperature is safely maintained by constant (240x per second) SmartLid sensor/SmartHub communication on an eyelid-by-eyelid basis.[16] The thermal procedure is followed by manual gland expression using the provided purpose-designed device (Clearance Assistant Plus) supplied with the disposable SmartLids. In a pair of randomized clinical trials, the TC procedure provided statistically significant improvements in tear break-up time (TBUT), meibomian gland secretion score (MGSS), corneal and conjunctival staining, eye dryness score (EDS), symptoms assessment questionnaire in dry eye

[8] Korb DR, Blackie CA. Meibomian gland diagnostic expressibility: correlation with dry eye symptoms and gland location. Cornea. 2008;27: 1142–1147.
[9] Korb DR, Henriquez AS. Meibomian gland dysfunction and contact lens intolerance. J Am Optom Assoc. 1980;51:243–251.
[10] Blackie CA, Korb DR, Knop E, et al. Nonobvious obstructive meibomian gland dysfunction. Cornea. 2010;29:1333–1345.
[11] Maskin SL. Intraductal meibomian gland probing relieves symptoms of obstructive meibomian gland dysfunction. Cornea. 2010;29: 1145–1152.
[12] Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo CK, Liu Z, Nelson JD, Nichols JJ, Tsubota K, Stapleton F. TFOS DEWS II Definition and Classification Report. The Ocular Surface 2017;15:276-283.
[13] Bron AJ, Tiffany JM. The contribution of meibomian disease to dry eye. Ocul Surf. 2004;2:149–165.
[14] US Food and Drug Administration. TearCare System Indications for Use. https://www.accessdata.fda.gov/scripts/cdrh/devicesatfda/index.cfm?db=pmn&id=K213045; Accessed July 26, 2023.
[15] Blackie CA, Solomon JD, Greiner JV, Holmes M, Korb DR. Inner eyelid surface temperature as a function of warm compress methodology. Optom Vis Sci 2008;85:675-683.
[16] Dhamdhere K, Badawi D. A blink-assisted, cornea-sparing wearable eyelid device for the effective penetration of therapeutic thermal energy into the meibomian glands for the treatment of dry eye disease. J Clin Exp Ophthalmol 2021; S12:003.

(SANDE) score, and ocular surface disease index (OSDI) score from baseline..[17,.][18]

The newest generation of the TearCare system, MGX has the same indications for use as the previous version of TearCare. MGX also shares many technological characteristics with the predecessor TearCare system including:

- the therapeutic temperature range (41 to 45C°),
- the maximum outer eyelid surface temperature (47°C – 2 seconds prior to downward temperature regulation), and
- the rate of heating (< 60 seconds to initial target level 1, 30 seconds each to reach each of the additional temperature levels).

Differences between MGX and the previous version include:

- a new SmarLids which has an added interconnect for the SmartCable (connector between SmartLids and the SmartHub controller) allowing for the cable to be reused
- a newly designed SmartHub including a touchscreen with a graphic user interface rather than a push-btton interface with graphic symbols and indicator lights
- earloops that wrap around the ear rather than adhesive foam for attachment of the SmartLids to the temple.

4. DESCRIPTION OF DEVICE

4.1. DEVICE DESCRIPTION

The Sight Sciences' TearCare MGX System being studied in this study is comprised of the following components:

- TearCare MGX SmartLids®
- TearCare MGX SmartHub, SmartCable, Charging Nest
- Clearance Assistant Plus™ devices with debridement edge

Also used in this study

- TearCare 1.5 SmartLids (for the purpose of comfort comparison only)

The SmartLid devices (Figure 1) are custom designed to conform to the tarsal plate of each respective eyelid allowing subjects to blink normally throughout the procedure

[17]Gupta PK, Holland EJ, Hovanesian J, et al. TearCare for the treatment of meibomian gland dysfunction in adult patients with dry eye disease: a masked randomized controlled trial. Cornea 2022;41:417-426.
[18] Ayres BD, Bloomenstein M, Loh J, Chester T, Saenz B, Echegoyen J, Kannarr SR, Perez V, Rodriguez T, Dickerson JE Jr. A randomized, controlled trial comparing TearCare and cyclosporine ophthalmic emulsion for the treatment of dry eye disease (SAHARA). Clin Ophthalmol 2023;17:3925-3940.

and naturally express melted meibum with every blink. Immediately following the thermal procedure, the physician uses the Clearance Assistant device to further express the meibomian glands manually to maximize the evacuation of melted meibum. The Clearance Assistant also provides a tool for debridement to thoroughly remove any blockages at the meibomian gland orifices to facilitate and enhance natural and manual meibum evacuation.

Each SmartLid is comprised of an earpiece with two flexible curved elements. The SmartLids contain a space where the SmartCable is connected to the SmartLid via a magnetic connector. SmartLids for OD and OS are provided in a single package so that all four eyelids may be heated in a single session. The SmartLids deliver heat in a preset temperature range, and ramps from approximately 41°C to 45°C when the procedure is initiated. A thin adhesive holds the SmartLid on the patient's eyelids and the fit is secured by a lightweight earpiece. The earpiece supports the flexible elements to be aligned with the lateral canthus and allows for the thermal elements to be placed right over the tarsal plates.

Figure 1: TearCare MGX SmartLid Devices applied to the Eyelids



The SmartLids are connected to the SmartHub. When attached to the SmartHub, the SmartLids deliver thermal energy (i.e., heat) to the eyelids. Embedded software and a closed loop sensor system ensures that the temperature delivered at the eyelids is maintained within a precise range. The user can adjust the temperature using control buttons on the SmartHub.

The SmartHub, shown in Figure 2 below, is a battery-powered unit that powers and controls the SmartLids. It features a circuit board, microprocessor, a port for receiving the SmartLid connector(s), and a port for connecting to the charging nest. The SmartHub features a built-in rechargeable Li-ion battery that, when fully charged, supplies power for at least 4 therapies. The SmartHub may be used with one or two SmartLids connected. The SmartLid connector is inserted into the SmartHub's device port.

A power button on the rear of the SmartHub is used to turn the system on and off TearCare MGX SmartHub. Therapy control is managed through a graphic user interface, and for therapy consists of 3 primary controls; Start, Pause, and Warmth Levels ("1"

through "5"). Warmth Level controls on the SmartHub allow the user to adjust the preferred temperature level. Therapy may be stopped by exiting the therapy menu after pausing an active therapy. The SmartHub also has a display of therapy remaining time during therapy mode use that indicates how much time is left in the Core Therapy session and the Extended Warming Hold period.

Figure 2: TearCare MGX SmartHub



The Clearance Assistant Plus device (shown in Figure 3 below) is single-use, sterile device that is designed to facilitate debriding the eyelid margin. It also allows for manual expression of the meibomian glands after the application of heat by the TearCare SmartLid devices.

Figure 3: Clearance Assistant Plus Device



In this study, the Investigator will use the Clearance Assistant device to debride all four eyelid margins by sweeping (very gently scraping) the debridement edge across the lid margin and line of Marx's back and forth going over meibomian gland orifices. Then the flexible SmartLid device will be applied to the external surface of the upper and lower eyelids of the subject (Figure 1). The SmartLids will then be connected to the TearCare

MGX SmartHub. When the SmartHub is turned on the Investigator will initiate the procedure and the TearCare System will begin delivering heat to the eyelids. The system should automatically and gradually increase the temperature over 2-3 minutes until it reaches the maximum set point temperature of 45°C. A complete TearCare procedure under this study is anticipated to last 15 minutes.

The SmartHub has 5 temperature set points (ranging from 41 to 45°C), which are intended to allow the Investigator to manually adjust the temperature up or down to a level that is comfortable for the subject. The set points can be adjusted at any time during the procedure. Subjects are able to blink naturally during the session.

The temperature range for the TearCare System was selected based on research that has shown that meibum will melt at temperatures between 32 to 45°C,but obstructed glands may require higher temperatures, around 45°C, to effectively melt meibomian obstructions.[19, 20, 21] The maximum temperature and 15 minute procedure duration for this study were also chosen because they are below the time- temperature threshold at which heat contacting the skin will first show signs of cutaneous damage and edema and are within the safety limits specified for medical electrical equipment.[22, 23, 24]

At the end of the 15-minute Core Therapy, the system will signal to the user that Core Therapy is complete with visible and audible cues. The system will then transition to the optional Extended Warming Hold (EWH) period which will last for 10 minutes. The transition is shown by a change in status to "Warming Hold" as well as an audible tone. The SmartLid on the eye not currently being expressed should be left in place; the Warming Hold will maintain a warmth level of "1" for the duration of the Warming Hold time.

4.2. INSTRUCTIONS FOR USE

Instructions for Use for the TearCare MGX System and Clearance Assistant device for this study will be provided to the Investigator.

4.3. TRAINING

Prior to the start of the study, Investigators and study staff will be trained on the proper use of the TearCare System. Investigators will also be trained in the method of lid

[19] Bron AJ, Tiffany JM. The contribution of meibomian disease to dry eye. Ocul Surf. 2004;2:149-165.
[20] Bron AJ, Tiffany JM, Gouveia SM, Yokoi N, Voon LW. Functional aspects of the tear film lipid layer. Exp Eye Res 2004;78:347–60.
[21] Jones et al. TFOS DEWS II Management and Therapy Report. The Ocular Surface 2017;15:575-628.
[22] Moritz AR, Henriques FC. Studies of thermal injury: the relative importance of time and surface temperature in the causation of cutaneous burns. Am J Pathol 1947;23:695–720.
[23] Despa F, Orgill DP, Neuwalder J, Lee RC. The relative thermal stability of tissue macromolecules and cellular structure in burn injury. Burns 2005;31:568–77.
[24] Medical electrical equipment Part 1: General requirements for basic safety and essential performance (IEC 60601-1).

debridement and manual expression described in this protocol. All study staff will receive training on the protocol and execution of the study according to applicable regulations and Good Clinical Practices.

5. PRIOR INVESTIGATIONS

5.1. CLINICAL TESTING

The sponsor has studied the previous version of TearCare in multiple multicenter clinical trials including the single-arm Cheetah study[25], the Olympia randomized controlled trial[26], and the Sahara 24-month randomized, controlled, multicenter trial.[27]

Sight Sciences performed clinical validation testing of the current TearCare MGX System design to demonstrate in acute clinical study that the temperatures achieved met key performance and safety criteria. A total of 15 adult subjects (30 eyes) were enrolled in the study, 15 females. Testing demonstrated that the TearCare System met the minimum and maximum temperature specifications with 95% confidence and 90% reliability.

There were no adverse events, nor any clinically significant changes observed in slit lamp exams. A summary of the outer eyelid and corneal tissue temperatures measured at the lowest and highest SmartHub settings is presented in Table 1 below.

Table 1. Mean Tissue Temperatures at Lowest and Highest Temperature Settings (41°C, 45°C)

	Baseline (°C) Mean ± SD (Range)	**End of Procedure (°C)** Mean ± SD (Range)
Lowest Setting		
Outer Eyelid[a,c]	34.6 ± 0.42 (33.6 – 35.5)	41.2 ± 0.31 (40.1 – 41.8)
Cornea [b,c]	33.7 ± 0.63 (32.3 – 34.8)	35.0 ± 0.70 (33.4 – 36.7)
Highest Setting		
Outer Eyelid[a,c]	33.7 ± 0.56 (32.4 – 35.0)	44.2 ± 0.46 (42.9 – 45.1)
Cornea [b,c]	33.4 ± 0.72 (32.1 – 35.2)	35.6 ± 0.78 (34.0 – 36.9)

[25] Karpecki P, Wirta D, Osmanovic S, Dhamdhere K. A prospective, post-market, multicenter trial (CHEETAH) suggested TearCare system as a safe and effective blink-assisted eyelid device for the treatment of dry eye disease. Clin Ophthalmol. 2020;14: 4551–4559.

[26] Gupta PK, Holland EJ, Hovanesian J, et al. TearCare for the treatment of meibomian gland dysfunction in adult patients with dry eye disease: a masked randomized controlled trial. Cornea 2022;417-426.

[27] Ayres BD, Bloomenstein M, Loh J, Chester T, Saenz B, Echegoyen J, Kannarr SR, Perez V, Rodriguez T, Dickerson JE Jr. A randomized, controlled trial comparing TearCare and cyclosporine ophthalmic emulsion for the treatment of dry eye disease (SAHARA). Clin Ophthalmol 2023;17:3925-3940.

[a] Measured with thermocouples; includes upper and lower lids
[b] Measured with IR camera
[c] Mean (SD) values are mean of all measurements for upper and lower, OS, and OD for outer eyelids, and mean of all OD and OS measurements for inner eyelids and cornea

Based on the outer eyelid temperatures, the TearCare MGX System maintains the minimum steady state temperature of the device (41°C ± 2°C) and does not exceed the maximum temperature setting (45°C ± 2°C), as in the predicate TearCare System device. The effectiveness of the device is demonstrated in the final temperature of the outer eyelid targeted at 41-45°C to melt meibum blocking the meibomian glands, not the difference in temperatures from the baseline.

An additional clinical validation study was performed to validate the fit and retention of the of the TearCare MGX System Earloop using modified Instructions for Use. In this clinical validation study, the TearCare MGX System was applied to 21 subjects. The study evaluated updated instructions for use regarding additional steps to "check for earpiece fitment," in order to assess whether the earloops are properly installed and ensure that they can remain stable without the need for additional support. If a patient is identified through the earpiece fitment check to have "loose" fitment, then the eye care practitioner may proceed to use surgical tape to secure the earpiece. All earloop components remained affixed to the ears in all subjects for the duration of the 25-minute simulated therapy. The results of this clinical validation study demonstrate that the TearCare MGX device components remain securely affixed to the eyelid and head throughout a simulated 25-minute therapy when the SmartLids are applied according to updated instructions for use.

6 STUDY ENDPOINTS

6.1 ENDPOINTS

This study will collect data to assess the clinical utility of the Warming Hold period. The TearCare MGX Warming hold is a 10-minute period beyond completion of the Core Therapy time that serves to preserve elevated temperature by outputting only enough energy to maintain heat at the lowest setting of the system. At the minimum warmth setting the SmartLid device surfaces provide a steady state temperature of 39.0°C.

- **Primary endpoint**
  - Inter-eye (OD-OS) difference in Meibomian Gland Secretion Score (MGSS)
- **Secondary endpoints**
  - Mean change from Screening visit baseline in MGSS

- **Mean change from Screening visit baseline in the number of meibomian glands yielding clear liquid secretions (MGYCL)**
- **Mean change from Screening visit baseline in the number of meibomian glands secreting any liquid (MGYAL)**
- **Subject comfort during expression**
- **Ease of expression (masked assessor rating)**

- **Exploratory endpoints**
  - Comparative comfort of SmartLids (MGX and TC 1.5)
  - Subject satisfaction with procedure
  - Investigator satisfaction with procedure
  - Ease of blinking (during SmartLids comfort assessment)

- **Safety Endpoints**
  - Rate of ocular adverse events
  - Change in best corrected visual acuity
  - Change in intraocular pressure (IOP)

7 STUDY DESIGN

This is a prospective, randomized, assessor-masked, single-center, non-significant risk (NSR) study. To reduce potential bias in the study, study staff performing the endpoint assessments will be masked. Subjects will also be masked as to group assignment.

7.1 Study Device and Control Group

In this randomized study, TearCare procedures using the TearCare MGX System (study device) with the extended Warming hold feature will becompared with TearCare procedures using the TearCare MGX System without the Warming hold (control group).

TearCare procedures in this study will include an in-office eyelid debridement, 15-minute bilateral thermal session with the TearCare System, immediately followed by manual expression of the meibomian glands using the Clearance Assistant Plus device. Subjects will receive one in-office TearCare procedure at the Procedure Visit (Day 0).

7.2 Study Centers

This study will be conducted at a single center in the United States.

8 STUDY SELECTION CRITERIA

8.1 Inclusion Criteria

For inclusion in this study, subjects must meet all the following criteria. All ocular criteria apply to both eyes:

1. **Male or female subjects, 22 years of age or older**
2. Reports dry eye symptoms within the past 6 months
3. OSDI score of 23 to 79
4. Meibomian gland obstruction in both eyes based on a total; Meibomian Gland Secretion Score ≤12 in each eye.
5. At least 15 glands in each lower eyelid should be expressible, with a sterile cotton swab, at the slit lamp.
6. Best corrected visual acuity of 20/100 or better.
7. Willing and able to comply with the study procedures and follow-up
8. Understands and signs the informed consent.

8.2 Exclusion Criteria

A subject who meets any of the criteria listed below (in either eye) will be excluded from the study:

1. Use of:
    a. cyclosporine, Xiidra, or serum tears within 60 days prior to Screening;
    b. Antihistamines (oral or topical) within 7 days prior to Screening;
    c. Oral tetracyclines or azithromycin within 30 days prior to Screening;
    d. Topical ophthalmic antibiotics, anti-glaucoma medications, steroids, non-steroidal anti-inflammatory medications within 30 days prior to medication
    e. Isotretinoin (e.g. Accutane) at any time.
2. Any of the following dry eye treatments:
    a. Office-based dry eye treatment (e.g. IPL, TearCare, thermal pulsation [LipiFlow], iLux etc.) within 12 months prior to Screening either as part of routine care or clinical investigation;
    b. Planned or recent surgical procedures to the eye or eyelid (90 days prior to Screening)
    c. Meibomian gland expression within 6 months prior to Screening
    d. Blephex or debridement within 3 months prior to Screening;
    e. Punctal occlusion (including collagen, e.g. Soft Plug, UltraPlug, or crosslinked

hyaluronic acid, e.g. Lacrifill) or punctal plugs within 15 days of the Screening visit;

f. **Use of tear neurostimulators (i.e., True Tear, iTear100, Tyrvaya) within 2 weeks of the baseline visit. (Subjects must refrain from using tear neurostimulators for the duration of the study);**

g. Any history of meibomian gland probing

3. History of eyelid, conjunctiva, or corneal surgery (including refractive surgery) within 12 months prior to the Screening visit.
4. Any history of chalazion surgery, surgery on the tarsal conjunctiva, radial keratotomy (RK), complicated blepharoplasty, lid reconstruction, or significant complications post-refractive surgery.
5. Contact lens use within 2 weeks of the Procedure visit. Subjects presenting at the Screening visit using contact lenses must agree to discontinue use for a full 2 weeks (14 days) prior to the Procedure visit.
6. Active hordeolum, stye, or chalazion at the time of the Screening visit.
7. History of Herpes Simplex or Herpes Zoster of the eye or eyelid.
8. Any active, clinically significant ocular or peri-ocular infection, inflammation, or irritation.
9. Recurrent clinically significant eye inflammation, other than dry eye, within 3 months prior to Screening.
10. Clinically significant anterior blepharitis. In addition, collarettes or flakes of more than one quarter of the eyelid are excluded.
11. Clinically significant eyelid abnormalities in either eye (e.g.entropion/ectropion, blepharospasm, aponeurotic ptosis, lagophthalmos, distichiasis, trichiasis).
12. Clinically significant dermatologic or cutaneous disease of the eyelid or periocular area.
13. In the clinical judgement of the Investigator, meibomian glands have significant capping, atrophy, or are unable to be expressed, digitally or with a cotton swab.
14. Corneal surface abnormalities such as corneal epithelial defects(other than punctate staining), ulcers, corneal epithelial dystrophies, keratoconus, and ectatic disease of the cornea
15. **Any active, clinically significant allergic, vernal, or giant papillaryconjunctivitis.**
16. **Ocular trauma within 3 months prior to Screening.**
17. **Known history of diminished or abnormal facial, periocular, ocular or corneal sensation**
18. **Systemic diseases, in the Investigator's medical judgement, resulting in dry eye**

(e.g. autoimmune diseases such as Sjogren's syndrome, rheumatoid arthritis, lupus, Graves' disease, sarcoidosis, etc.)

19. **Subject is currently using Retin A /Retin A derivatives.**
20. **Subject has permanent eyeliner/lid tattoos, eyelash extensions orwears false eyelashes.**
21. Subject is currently using Latisse, Lash Boost, or any other type of eyelash growth [illegible] serum. Prostaglandin analog products such as Latisse should not be used within 30 days of the Screening visit.
22. Temporary false eyelashes, lash extensions, or any other type of false eyelash within 15 days of the Screening Visit.
23. Allergies to silicone tissue adhesives, acrylates and/or copper.
24. Subject has a pacemaker or implantable cardiac defibrillators (ICD).
25. Co-existing condition, either ocular or non-ocular that, in the judgement of the Investigator could affect the safety or effectiveness of treatment or the compliance of the subject to the protocol.

9 STUDY VISITS AND PROCEDURES

9.1 PROCEDURES PER STUDY VISIT

Procedures required by the protocol to be conducted at each study visit are listed in Table 1, Study Visit Schedule and detailed in Section 20, Methods for Exams, Tests, and Questionnaires.

A brief summary of the procedures performed by visit is provided here.

- At the Screening Visit, the subject will complete the informed consent process and sign an informed consent document. Standard procedures will be performed to determine subject eligibility (medical history, OSDI, BCVA, slit-lamp exam, IOP, MGSS). Eligible subjects will assess SmartLid/ear loop comfort, have blink rate measured, and be scheduled to return for the TearCare procedure visit.
- At the Procedure Visit (Day 0), subjects will be randomized to treatment group and then undergo treatment with the TearCare MGX system.

Subjects will be seen for a post-treatment safety follow-up visit, a minimum of 1 week and no more than 30 days later.

9.2 STUDY VISIT SCHEDULE

Table 2: Study Visit Schedule

Procedure	Screening (Day -30 to -7)	Procedure (Day 0)	Safety Follow-up (Day 7-30)
Informed Consent	X		
Demographics, Ocular & Medical History	X		
Ocular Surface Disease Index	X		
BCVA[a]	X		X
Slit Lamp Exam	X		X
Screening/baseline MGSS	X		
IOP [b]	X		X
Ear Loop/SmartLids Comfort and Ease of Blinking	X		
Randomization		X	
TearCare Procedure		X	
MGSS		**X**	
Subject comfort questionnaire		**X**	
Investigator questionnaire		**X**	
Subject Eligibility	**X**		
Assign Subject ID number	**X**		
AE Assessment	**X**	**X**	**X**

[a] BCVA should be measured with subject wearing their current eyeglasses
[b] IOP measured via Goldmann applanation tonometry

9.3 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 Document (ICD). After signing the ICD and the HIPAA (Health Insurance Portability and Accountability Act) authorization the subject can then proceed with the Screening visit. The subject has the right to withdraw from the study at any time without consequences, as indicated in the ICD.

The subject's signed and dated informed consent must be obtained before conducting any study specific procedures that are not part of the standard of care. Subjects are enrolled upon signing the ICD even if they subsequently fail to meet the eligibility criteria.

The Investigator must retain the original, signed written ICD. A copy of the written ICD must be given to the subject.

9.3.1.1 Subject Identification

Subjects providing written informed consent will be assigned a 2-digit enrollment number (e.g., 01 to 25). Subjects meeting eligibility criteria and proceeding to the Procedure visit will be assigned a 7-digit subject identification number (SID) consisting of a two-digit study identification number, a two-digit center identification number followed by a three-digit sequential subject number. The SID will be assigned to eligible subjects at the successful completion of the Screening visit. In this way, information contained in the study records will be kept as confidential as possible.

Example: 29-01-001 (Sight Sciences study 29, Site number 01, subject 001)

9.4 STUDY VISITS

9.4.1 SCREENING VISIT; 7 TO 30 DAYS PRIOR TO PROCEDURE VISIT

After obtaining an understanding of the purpose of this study, then reviewing and signing the ICD, all potential subjects will undergo a screening examination in order to determine their eligibility for the study. The Screening exam must take place at least 7 days and no more than 30 days prior to the Procedure visit.

The exams and tests listed in Table 2 should be performed in the order listed to

determine final eligibility for the study. Conduct ocular assessments in both eyes. Both eyes must meet the eligibility criteria.

Subjects who meet all screening eligibility criteria will be scheduled for the TearCare procedure visit. If a subject does not meet the inclusion/exclusion criteria, he/she should be exited from the study.

Subjects meeting eligibility criteria will undergo the earloop/SmartLids comfort assessment.

1. Collect subject's demographics, ocular, and medical history
2. Have subject complete the OSDI questionnaire (Section 20.1)
3. Assess monocular best corrected visual acuity using a Snellen chart at 6 meters (20 ft) for both eyes. (Section 20.2)
4. Conduct slit lamp examination (Section 20.3).
5. Assess meibomian glands (MGSS, MGYAL, MGYCL) (Section 20.4)
6. Measure IOP (Section 20.5)
    - ***Subjects who fail screening may be re-screened for the study after 30 days. If they are re-enrolled, they should be assigned a new 2-digit enrollment number***
    - ***Subjects meeting all inclusion criteria and no exclusion criteria continue the Screening visit below:***
7. Conduct subject comfort assessment of SmartLids/earloop including ease of blinking (Section 20.6)
8. Assign sequential Subject Identification Number
9. Record any adverse events
10. Schedule subject to return for the Procedure visit in a minimum of 7 days and no more than 30 days

9.4.2 TEARCARE PROCEDURE VISIT; DAY 0

1. **Update subject ocular and medical history with any changes since the Screening visit as needed.**
2. **Determine the randomized treatment group assignment by opening the sealed envelope corresponding to the assigned SID number; the subject will be assigned to either Group A or Group B (Section 20.7). *The masked assessor must not be informed of group assignment.***

3. **Perform the TearCare procedure with the Warming hold (Group A) or without the Warming hold (Group B) according to the subject's group assignment. (refer to Section 20.8)**

4. **Assess meibomian glands (MGSS, MGYAL, MGYCL) (Section 20.4). The second eye** gland assessment/expression will not be started until 10 minutes after the end of the 15-minute TearCare treatment period.

5. Have subject complete the Subject Comfort Questionnaire (Section 20.9)

6. Complete the Investigator Questionnaire (**must be completed immediately following MGSS by the masked individual performing the MGSS**) (Section 20.9)

7. Record any adverse events

8. Schedule subject to return for the Safety follow-up visit in a minimum of 7 days and no more than 30 days

9.4.3 SAFETY FOLLOW-UP VISIT; DAY 7-30

1. Assess monocular best corrected visual acuity using a Snellen chart at 6 meters (20 ft) for both eyes. (Section 20.2)

2. Conduct slit lamp examination (Section 20.3)

3. Measure IOP (Section 20.5)

4. Record any adverse events

5. Dismiss the subject from the study

9.5 MASKED ASSESSOR

To reduce potential bias in the study, study staff performing meibomian gland expression/assessment will be masked as to the subject's study group. In addition, to ensure consistency in performing the endpoint assessments the study staff member who performs the baseline assessments should also perform the follow-up (post-procedure) assessment. The masked assessor may not perform the randomization or be informed of treatment group assignment.

Meibomian Gland Secretion Scoring (MGSS) must be performed by a Masked Assessor.

9.6 WITHDRAWAL AND DISCONTINUATION

All subjects have the right to withdraw at any point during the study 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 file and on the Study Exit Form.

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

9.7 SUBJECTS LOST TO FOLLOW-UP

Subjects who do not show up for a follow-up must be contacted to attempt to have them come for the follow-up. For those subjects who cannot be reached, at least 3 phone call attempts should be made and documented. If a subject misses two consecutive follow-up visits without any contact with the study staff, the subject will be considered lost-to-follow-up unless there is further communication by the subject.

10 ADVERSE EVENTS (AEs)

Adverse Events are defined below. Adverse events that occur in the eye during the trial, whether considered to be device related or not, must be documented in the subject's records. Non-ocular adverse events do not need to be recorded as adverse events unless they meet the definition of serious adverse event or are believed to be related to the study device or a study procedure. 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 will be considered pre-existing conditions and do not need to be recorded as adverse events unless they increase in severity during the study.

10.1 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

10.2 LIST OF ANTICIPATED POTENTIAL OCULAR ADVERSE EVENTS

Anticipated potential adverse events include those that might reasonably be expected to occur in this study because they are associated with dry eye disease, the risk analysis for TearCare System or study testing methods.

- Eyelid/eye pain requiring discontinuation of the study procedure
- Eyelid/eye pain requiring treatment ≥1 day after the study procedure
- **Eyelid irritation, or inflammation**
- **Discomfort or pain of eyelids or orbit**
- **Ocular symptoms (such as burning, redness, tearing, visual disturbance, redness)**
- **Burn, erythema, or swelling of the eyelids**
- **Thermal injury to the eye, including conjunctiva, cornea or lens**
- **Allergic or inflammatory reaction to medical adhesive on the SmartLid device**
- **Physical pressure-induced injury to the eyelid**

- **Corneal deformation**
- **Foreign body sensation**
- **Formation of a chalazion or stye**
- **Infection of the eyelid or ocular surface**
- **Ocular surface irritation or inflammation (e.g., Conjunctival injection,conjunctival or corneal abrasion, chemosis)**
- Allergic or inflammatory reaction to the SmartLid
- Worsening of dry eye symptoms
- Loss in BCVA (ETDRS) of ≥10 letters

10.3 Reporting Adverse Events and Unanticipated Adverse Device Effects

Identification, collection, and reporting of adverse event information is the responsibility of the Principal Investigator or designated 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).

Any ocular-related **serious adverse event** (SAE) should be reported to the study sponsor within one working day of learning of the event. Non-ocular-related SAEs should be reported to the study sponsor within two working days of learning of the event. Record all applicable information in the source document, enter on the AE CRF and email the AE CRF to [redacted]

Any **unanticipated adverse device effects (UADE)** must be reported to the following two entities:

1. The study sponsor – Within one working day of the Investigator first learning of the event, record all applicable information in the source document, enter into AE form and e-mail the AE CRF to [redacted] and
2. The reviewing IRB – As soon as possible, but no later than 10 working days after the investigator first learns of the event, report 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 no later than 5 working days after the sponsor **makes such a determination and no later than 15 working days after the sponsor first received notice of the effect.**

11 STATISTICAL CONSIDERATIONS

11.1 ANALYSIS POPULATIONS

- **Safety Population – The safety population will include all enrolled (providing informed consent) subjects.**

- Intent-to-Treat Population - The intent-to-treat (ITT) population includes all randomized subjects. Subjects will be analyzed as randomized.

- Per Protocol Population – The per protocol (PP) population includes all subjects completing the study with no major protocol deviations.

11.2 SUBJECT ACCOUNTABILITY

A complete accounting of subjects by visit will be provided, including reasons for dropout, if known.

11.3 DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Demographic variables of gender, race, ethnicity, and age will be summarized for all enrolled subjects, along with medical history. Descriptive statistical summaries of pre-treatment parameters (min, max, median, mean, standard deviation) will also be provided for each group. This includes baseline measurements for the study endpoints: Total Meibomian Gland Secretion Score, Number of Meibomian glands with any/clear liquid.

11.4 EFFECTIVENESS ENDPOINTS AND ANALYSIS METHODS

All primary and secondary endpoints will be evaluated based on data collected post-procedure at the TearCare procedure visit.

12.5.1 DESCRIPTIVE ANALYSES

The quantitative variables will be summarized using number of subjects (n), mean, median, standard deviation, minimum and maximum. The qualitative variables will be summarized using counts and percentages.

Summaries of all endpoints will be presented by treatment group and visit. Summaries will also be provided for demographics, baseline medical history, concurrent therapies, and subject disposition.

12.5.2 PRIMARY EFFECTIVENESS ENDPOINTS

The primary effectiveness endpoint is:

- Inter-eye (OD-OS) difference in Meibomian Gland Secretion Score (MGSS)

The primary endpoint of the inter-eye (OD-OS) difference in MGSS will be analyzed using a 2-sample one-sided t-test with statistical significance set at p<0.05. If the data are determined to violate the assumption of normality, a Wilcoxon Rank-Sum test will be used.

12.5.3 PRIMARY EFFECTIVENESS HYPOTHESES

The primary study hypothesis is that the TearCare procedure with the Warming hold allows for better 2nd eye lid expression than without the Warming hold. The statistical hypotheses are stated in terms of one-sided hypotheses, and statistical testing will be one-sided.

To demonstrate superiority of the TearCare procedure with the Warming hold to the same procedure without the Warming hold (control) we will test the following hypotheses:

H_{01}: There is no difference between TearCare with Warming hold and TearCare without Warming hold in the difference between MGSS scores for OD and OS.

H_{11}: The difference between MGSS scores for OD and OS is greater when the Warming hold is not used.

12.5.5 MISSING DATA

No missing data imputation will be carried out.

No secondary effectiveness endpoints or safety endpoints will be imputed.

12.5.6 SECONDARY EFFECTIVENESS ENDPOINTS

The secondary effectiveness endpoints include change from baseline at the post-procedure measurement for the following outcomes:

1. Meibomian Gland Secretion Score (MGSS), OD and OS
2. Number of Meibomian Glands Yielding any liquid, OD and OS
3. Number of Meibomian Glands Yielding clear liquid, OD and OS

These end points will be compared between treatment groups for OD and OS separately using a 2-sample two-sided t-test with statistical significance set at p<0.05. If the data are determined to violate the assumption of normality, a Wilcoxon Rank-Sum test will be used.

Other secondary effectiveness endpoints are:

4. Subject comfort during expression
5. Ease of expression (masked assessor rating)

These subject-level outcomes will be analyzed comparing the two treatment groups using a 2-sample two-sided t-test with statistical significance set at p<0.05. If the data are determined to violate the assumption of normality a Wilcoxon Rank-Sum test will be used.

A Bonferroni adjustment to the significance level alpha will be used to control the family-wise type 1 error rate for the secondary endpoints.

For the eye level variables (MGSS, MGYAL, MGYCL) two-sample t-tests and Wilcoxon rank sum tests will be conducted on the average of the two eyes as supportive analyses. No imputation will be performed for secondary efficacy variables.

All secondary effectiveness variables collected will be summarized descriptively (n,mean, standard deviation, median, min and max) by treatment group.

12.5.7 Additional Exploratory Analyses

The following will be summarized by treatment group

- Comfort of SmartLids and earloop
- Subject satisfaction with procedure
- Investigator satisfaction with procedure
- Ease of blinking

11.5 Safety Endpoints and Analysis

12.6.1 Descriptive Analyses

All adverse events, changes in IOP, and changes in BCVA will be tabulated byvisit and study group.

12.6.2 Primary Safety Endpoint

The primary safety endpoint is the incidence of procedure (TearCare)/treatment.

12.6.3 Secondary Safety Endpoints

The secondary safety endpoints include:

- **Change in best corrected visual acuity**
- **Change in intraocular pressure (IOP)**

These endpoints will be summarized by treatment group and visit.

12.6.4 Safety Analysis

All adverse events will be reported by study group and AE category. Any serious adverse events will be completely described in the study report. The primary safety endpoint will be summarized for each study group.

We will compute the incidence of ocular events in two ways: first as a simple proportion, counting the number of subjects with any event (that is, counting the first event per person in either eye), then as an incidence rate, counting all events includingrepeated events per subject.

11.6 Sample Size Calculation

A convenience sample of 20 subjects has been selected for this study.

11.7 Deviation from the Statistical Plan

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

12 Monitoring Procedures

Sight Sciences or its contract personnel will monitor the study in a manner consistent with FDA regulations, GCP and Sight Sciences procedures. Study monitoring will consist of on-site and remote monitoring visits. Study monitoring will involve the following elements:

- Site Qualification: Sight Sciences will meet with the Investigator and clinical study staff prior to the initiation of the study in order to review the adequacy of the subject population, facilities, and equipment with respect to the needs of the study, and to familiarize the investigator with the study protocol.
- Site Initiation: Sight Sciences will meet with the Investigator and clinical study staff when the site is ready to begin enrolling subjects in order to train them in how to properly select subjects, perform the study procedure, and record study data. This visit will include, but not be limited to a review of the following:
  - Detailed review of the protocol
  - Informed consent procedures
  - Randomization procedures
  - Instruction in how to use the TearCare System
  - Instruction in how to perform study procedures
  - Guidance in how to administer questionnaires to subjects
  - Procedures for maintaining masking of study personnel
  - Records and reports
- Interim Monitoring: Sight Sciences its contract personnel will visit the clinical site during the study to review charts and to perform source document verification, to ensure proper adherence to the study protocol, and to review regulatory documents. Interim monitoring visits and telephone consultation will occur as

necessary during the course of the study to ensure the proper progress and documentation of the study findings.

- Study Closure: At the conclusion of the trial there will be a study closure visit during which several actions, including but not limited to the following, will be performed:
  - A final inspection of the study binder
  - Accountability and return of all devices and study materials to the sponsor
  - Discussion of record retention requirements with the Investigator
  - Close-out notification to the IRB

13 DATA AND QUALITY MANAGEMENT

13.1 DATABASE MANAGEMENT

The study database will be created using Microsoft Excel. Data will be entered directly from copies of the case report form (CRF). The database will be maintained by Sponsor personnel and entered data will be validated subsequent to database lock.

13.2 SUBJECT IDENTIFICATION

The subjects will be identified by a seven-digit subject number composed of a two-digit study identification number, a two-digit center identification number followed by a three-digit sequential subject number. The subject identification will be assigned when eligibility is established.

13.3 SUBJECT ACCOUNTABILITY

All subjects who are randomized and treated in this clinical investigation shall bemonitored for the duration of the investigation. The clinical investigation shall be considered completed when all subjects that have been enrolled in the investigation have reached the final study visit, excluding subjects who were withdrawn.

13.4 CONFIDENTIALITY

All medical records associated with the clinical investigation will be made available for review by Sight Sciences personnel, or its agents (e.g., CRO or contract CRA) and governmental/regulatory agencies involved. The results of the study may be publishedin the future for scientific and marketing purposes, but the identity (name) of each subject will not be revealed. All records will be stored in a secure area at the investigator's facility.

13.5 SOURCE DATA AND CASE REPORT FORMS

Source data will be entered into a case report form (CRF) at each site by trained personnel in accordance Good Documentation Practices (GDP) and following the ALCOA principle (Attributable, Legible, Contemporaneous, Original, Accurate). CRF entries will be 100% verified against corresponding source data at the sites and queried/corrected if needed to the extent possible. Medical site records serve as source data.

All entries must be made in black or blue ink and changes must be made by strike-through only (no "white out", original entry must remain legible) with date and initials or signature.

13.6 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 a marketing application is approved or two years after the investigation has been discontinued, 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.

14 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 the Protocol Deviation form.

15 DEVICE FAILURES AND MALFUNCTIONS

All device failures or malfunctions should be recorded on the Device Deficiency Formand reported to [redacted]

16 ETHICAL CONSIDERATIONS

16.1 DECLARATION OF HELSINKI

This study shall be conducted in accordance with the Declaration of Helsinki which may be accessed at https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/.

16.2 INSTITUTIONAL REVIEW BOARDS (IRB)

The study shall not begin at a site until approval has been obtained from the reviewing IRB. It is the Investigators' responsibility to obtain and maintain written approval of the study protocol and Informed Consent documents from the appropriate IRB. It is also the Investigators' responsibility to notify that body about any amendments to these documents and to follow the IRBs rules regarding the reporting of Adverse Events and Protocol Deviations related to the device and/or this study. Copies of all written approvals (identifying the study, the submitted and approved documents and the date reviewed) and the approved versions of the documents must be provided to SightSciences.

The Investigators must file all correspondence with the IRB and forward copies of such correspondence to Sight Sciences.

16.3 INFORMED CONSENT Document (ICD)

An Informed Consent template that covers all protocol procedures and follows GCP Guidelines will be prepared by Sight Sciences and made available to each Investigator. The Investigator may adapt these templates to the requirements of the local IRB and ofthe institution where the study is conducted, but any revisions made to the ICD must be submitted to the sponsor for review prior to submission to the IRB. A copy of each IRB-approved ICD version is to be made available to Sight Sciences. The IRB-approved ICD is to be kept in its full length in the study Regulatory Binder. Original, signed ICDs are to be maintained in the subject's study records and must be made available for monitoring review.

16.4 PUBLIC LISTING OF STUDY

The study will be listed on the NIH website www.clinicaltrials.gov.

17 STUDY ADMINISTRATION

17.1 DEVICE ACCOUNTABILITY

With each shipment of study devices, Sight Sciences will include a Packing List that will give the amount shipped and the lot numbers. This packing list must be reconciled by the investigational site with the contents of the shipment and then recorded on the Device Accountability Log. All study products at the site must be stored in a secured/locked area. When study devices are used, returned or disposed of, their disposition (including the disposition and date of disposition) must be recorded on the Device Accountability log.

Device reconciliation activities will also be conducted periodically in conjunction with site monitoring visits. The Investigator must maintain accurate recordsof the receipt and disposition of all devices shipped by Sight Sciences.

17.2 EARLY TERMINATION OR SUSPENSION OF AN INVESTIGATION

Sight Sciences may terminate the study, in which case the investigators and associatedIRBs will be notified in writing. Possible reasons for study termination include but are not limited to:

- The discovery of an unexpected, significant, or unacceptable risk to the study subjects treated with the device
- Insufficient enrollment in the study

Sight Sciences reserves the right to stop the study at a center any time after theinitiation visit if there have been no subject enrollments or if significant protocol/deviations are observed at the site.

Likewise, a principal investigator may terminate the study at his/her institution. This decision must be followed by written notification to Sight Sciences within five working days, stating the reasons for termination.

If the study is terminated, every effort should be made to obtain final follow-up from all subjects.

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

17.3 INVESTIGATOR RESPONSIBILITIES

An Investigator is responsible for ensuring that an investigation is conducted accordingto the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the Investigator's care, andfor 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.

17.4 INVESTIGATOR AGREEMENT

The Principal Investigators shall agree to the clinical protocol and any amendments and indicate approval and agreement by signing and dating the cover page of the study protocol.

18 PUBLICATION POLICY

Publications Review Policy

Investigators must submit all presentations, posters, abstracts and manuscripts pertaining to this study to Sight Sciences for review in advance of their submission. Sight Sciences conducts this review to protect its proprietary rights to information, inventions, or products developed under the Study. Please use the following guidelineto determine the absolute minimum advance time for submitting an item to Sight Sciences for review:

- Presentations/Posters: S business days in advance of presentation
- Abstracts: 5 business days in advance of submission
- Manuscripts: 30 calendar days in advance of submission for publication

In accordance with the Clinical Trial Agreement, these items must receive written approval from Sight Sciences in order for them to be submitted or presented. If an itemis not received in the timeframe listed above, approval may not be granted due to insufficient time for considered review. In addition, since most of our Clinical Trial Agreements require that Sight Sciences has 60 days to review publications, Sight Sciences reserves the rights granted in those Agreements if circumstances require a longer review.

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