November 4, 2024

Novoxel Ltd.
Anne-Marie Ripley
Clinical & Regulatory Affairs Consultant
Regulatory Pathways Group, Inc.
440 N. Barranca Ave #2471
Covina, CA 91723

Re: K240512
Trade/Device Name: Tixel i (TXLI0001)
Regulation Number: 21 CFR 886.5200
Regulation Name: Eyelid Thermal Pulsation System
Regulatory Class: Class II
Product Code: ORZ
Dated: September 26, 2024
Received: September 26, 2024

Dear Anne-Marie Ripley:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

J Angelo Green -S

J. Angelo Green, Ph.D.
Assistant Director
DHT1A: Division of Ophthalmic Devices
OHT1: Office of Ophthalmic, Anesthesia,
Respiratory, ENT, and Dental Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

Submission Number *(if known)*

K240512

Device Name

Tixel i (TXLI0001)

Indications for Use *(Describe)*

The Tixel i is indicated for the application of localized heat and pressure therapy in adult patients with evaporative dry eye disease due to meibomian gland dysfunction (MGD).

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

510(k) SUMMARY
K240512

I. Submitter Information

510(k) Owner: Novoxel Ltd.
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Netanya, Israel 4250573
+972 9 7739074

Contact Person: Daniela Dov Elmaz
daniela@novoxel.com

Date Prepared: October 24, 2024

II. Device Name and Classification

Device Trade Name: Tixel i (TXLI0001)

Common Name: Eyelid thermal pulsation system

Regulation Number: 21 CFR 886.5200

Device Classification: Class 2

Product Code: ORZ

III. Predicate Device and Reference Devices

Predicate Devices

- LipiFlow Thermal Pulsation System by TearScience (K192623) – Primary Predicate
- iLux by Tear Film Innovation (K172645)
- TearCare MGX by Sight Sciences (K231084)

Reference Device

- Tixel C by Novoxel (K223033)

The Tixel C supports the methods (i.e., an ex vivo study) used to demonstrate the safety of the heat and pressure delivered by the Tixel i to the target tissue. In addition, many of the bench tests performed on the Tixel C are applicable to the Tixel i as only minor modifications have been made to the Tixel C to create the Tixel i.

IV. Device Description

The Tixel i is intended to deliver heat and pressure to the eyelids of patients with evaporative dry eye disease (DED) due to meibomian gland dysfunction (MGD). The Tixel i is comprised of a Console, which is connected via an umbilical tube to an applicator, referred to as “Handpiece.”

The Handpiece includes a therapeutic element, the "Tip," fixated on its distal end. A clear polycarbonate illuminated Distance Gauge, mounted on the distal end of the Handpiece, covers the Tip and allows proper and safe positioning of the Handpiece on the skin prior to performing a treatment pulse. The Distance Gauge is removed only when the Tip is being cleaned.

The Tip is comprised of a gold-plated copper base and a thin-walled titanium alloy cover. The active surface of the Tip consists of an array of 24 (6×4) square-based pyramids, evenly spaced. The pyramids have a blunt apex to allow effective heat transfer and prevent any risk of mechanical puncturing of the skin. The backplane of the Tip attaches to a ceramic heater that maintains a constant temperature during operation.

During a Tixel i procedure, an Aestek plastic ocular shield (Oculo-Plastik, Inc.) is to be inserted under the eyelids on the ocular surface to protect the eye during the procedure.

V. Indications for Use

The Tixel i is indicated for the application of localized heat and pressure therapy in adult patients with evaporative dry eye disease due to meibomian gland dysfunction (MGD).

VI. Comparison of Technological Characteristics with the Predicate Devices

Although the Tixel i device and the predicate devices do not share identical technological characteristics, these differences do not raise different types of questions of safety and effectiveness.

Characteristic	Subject Device Tixel i Novoxel, Ltd. K240512	Primary Predicate LipiFlow® Thermal Pulsation System TearScience (now Johnson & Johnson) K192623	Predicate 2 iLux Tear Film Innovation (now Alcon) K172645	Predicate 3 TearCare MGX Sight Sciences, Inc. K231084	Comparison of Subject Device to Predicate Devices
Device Classification	2	2	2	2	
Product Code	ORZ	ORZ	ORZ	ORZ	Same
Regulation Number	886.5200	886.5200	886.5200	886.5200	Same
Intended Use	Application of localized heat and pressure therapy to the eyelids	Application of localized heat and pressure therapy to the eyelids	Application of localized heat and pressure therapy to the eyelids	Application of localized heat and pressure therapy to the eyelids	Same
Indication for Use	The Tixel i is indicated for the application of localized heat and pressure therapy in adult patients with evaporative dry eye disease due to meibomian gland dysfunction (MGD).	The LipiFlow® Thermal Pulsation System is intended 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 or lipid deficiency dry eye.	The iLux System is indicated for the application of localized heat and pressure therapy in adult patients with chronic diseases of the eyelids, including meibomian gland dysfunction (MGD), also known as evaporative dry eye.	The TearCare® MGX System is intended for the application of localized heat therapy in adult patients with evaporative dry eye disease due to meibomian gland dysfunction (MGD), when used in conjunction with manual expression of the meibomian glands.	Similar

Characteristic	Subject Device Tixel i Novoxel, Ltd. K240512	Primary Predicate LipiFlow® Thermal Pulsation System TearScience (now Johnson & Johnson) K192623	Predicate 2 iLux Tear Film Innovation (now Alcon) K172645	Predicate 3 TearCare MGX Sight Sciences, Inc. K231084	Comparison of Subject Device to Predicate Devices
Device Description	System is comprised of a Console which is connected via a cord to an applicator ("Handpiece"). The tip of the Handpiece delivers heat and pressure to the outer surface of the eyelid.	System is comprised of a control unit which is connected via a cord to an Activator. The Activator has a combined Eye Cup and Lid Warmer. The Eye Cup contacts the outer eyelid and applies pressure to the eyelids. The Lid Warmer contacts the inner eyelid and applies unidirectional heat to the inner surface of the eyelid.	Handheld instrument that is coupled to a Disposable component that is positioned between the eyelid and the globe. The iLux System delivers heat and pressure to the outer surface of the eyelid.	• SmartLids are attached to the outer surface of the eyelids and connect to the SmartHub controller which generates the heat that is delivered to the eyelids. • A separate Clearance Assistant is used in conjunction with TearCare to perform manual expression of the meibomian glands immediately following heat treatment with TearCare.	Similar
Single Use or Reusable	Both the Console and Handpiece are reusable	• Control Unit: reusable • Applicator: single use	• Handheld instrument: reusable • Disposable: single use	• SmartHub: reusable • SmartLid: single use	• Console/Control unit/handheld: Same. All are reusable. • Eyelid-contacting component: Different. The difference in reusability of the eyelid-contacting component does not raise different types of questions of safety and effectiveness. The Tixel i only contacts the outer eyelid surface. It includes the same handpiece and similar cleaning/disinfection instructions as the Reference Device. The

Characteristic	Subject Device Tixel i Novoxel, Ltd. K240512	Primary Predicate LipiFlow® Thermal Pulsation System TearScience (now Johnson & Johnson) K192623	Predicate 2 iLux Tear Film Innovation (now Alcon) K172645	Predicate 3 TearCare MGX Sight Sciences, Inc. K231084	Comparison of Subject Device to Predicate Devices
					Reference Device supports the bench testing methods used to demonstrate the effectiveness of these procedures.
Provided Sterile?	No. Device only contacts the outer eyelid surface. The device is provided non-sterile and is cleaned and disinfected by the user before each use.	Yes. The Applicator contacts the cornea and inner eyelid and is thus provided sterile.	Yes. The Disposable contacts the cornea and inner eyelid and is thus provided sterile.	No. SmartLids only contact the outer eyelid surface and are thus provided non-sterile.	Similar to Predicate 3, which is provided non-sterile. The Tixel i has the same handpiece and similar cleaning/disinfection instructions as the Reference Device. The Reference Device supports the bench testing methods used to demonstrate the effectiveness of these procedures.
Device Operation	Eyecare professional operates handpiece to perform the procedure.	Eye care professional places Applicators in the eye, then starts the procedure. No handheld instrument is used to perform the procedure.	Eyecare professional operates handpiece to perform the procedure.	Eyecare professional applies SmartLids to the outer eyelid surface, connects the SmartLids to the SmartHub, then starts the procedure. After the warming procedure is complete, the ECP performs manual expression of the eyelids.	Similar to Predicate 2.
Tissue to which heat is directly applied	Outer eyelid surface	Inner eyelid surface (palpebral conjunctiva)	Outer eyelid surface	Outer eyelid surface	Same as Predicates 2 and 3

Characteristic	Subject Device Tixel i Novoxel, Ltd. K240512	Primary Predicate LipiFlow® Thermal Pulsation System TearScience (now Johnson & Johnson) K192623	Predicate 2 iLux Tear Film Innovation (now Alcon) K172645	Predicate 3 TearCare MGX Sight Sciences, Inc. K231084	Comparison of Subject Device to Predicate Devices
Heat Delivery Method	• High heat for extremely short duration • 385 - 405° C for 6 ms per pulse • 10 pulses per eyelid, 40 pulses per procedure • Total contact time between the tip and the outer eyelid is 60 ms per eyelid.	• Low heat for long duration • 40 - 43°C for 12 minutes	• Low heat for long duration • 38 - 44° C for approximately 8-12 minutes	• Low heat for long duration • 41 - 45° C for 15 minutes	Different, but difference does not raise different types of questions of safety or effectiveness. • Worst-case ex vivo testing, bench testing, and a computational analysis were used together to support the thermal safety of the Tixel i. • Like the predicate devices, the Tixel i underwent clinical validation in a randomized, controlled pivotal trial to demonstrate the safety and effectiveness for the intended use. • In addition, the Tixel i delivers the same temperature and pulse duration as the Reference device. • The Primary Predicate, Predicate 3 and Reference Device support the ex vivo testing methods used to demonstrate the safety and effectiveness of this technological feature.

Characteristic	Subject Device Tixel i Novoxel, Ltd. K240512	Primary Predicate LipiFlow® Thermal Pulsation System TearScience (now Johnson & Johnson) K192623	Predicate 2 iLux Tear Film Innovation (now Alcon) K172645	Predicate 3 TearCare MGX Sight Sciences, Inc. K231084	Comparison of Subject Device to Predicate Devices
Heat source	Ceramic heater within metallic housing conducts heat to an array of titanium-covered blunt-tipped pyramids	Resistive (plastic) electric heater	LEDs (lime-green and IR wavelengths)	Polymer encapsulated resistive heating element	Different, but difference does not raise different types of questions of safety or effectiveness. Heat source is the same as the Reference Device. The Primary Predicate, Predicate 3 and Reference Device support the ex vivo testing methods used to demonstrate the safety and effectiveness of this technological feature. Like the predicate devices, the Tixel i underwent clinical validation in a randomized, controlled pivotal trial to demonstrate the safety and effectiveness for the intended use.
Pressure Control	Automatic: Pre-programmed based on the protrusion depth.	Automatic: Pre-programmed with some adjustment allowed by the eye care professional	Manual: Eye care professional determines (based on patient feedback and direct viewing of glands)	Manual: Eye care professional performs manual expression.	Similar to Primary Predicate
Pressure Type	Compression	Massage	Compression	Compression	Similar to Predicates 2 and 3
Treatment of upper and lower eyelids	Sequential	Concurrent	Sequential	Heat delivery: Concurrent Manual expression: Sequential	Similar to Predicates 2 and 3
Software	Yes	Yes	Yes	Yes	Same
Power Source	AC-powered	AC-powered	Batteries, DC power	Batteries, DC power	Same as Primary Predicate
Safety per IEC 60601-1 & -2	Meets requirements	Meets requirements	Meets requirements	Meets requirements	Same

VII. Summary of Non-Clinical Testing

Based on the risk assessment, design control requirements, and an assessment of the changes between the reference Tixel C device and the Tixel i, the following verification and validation testing was performed on the Tixel i:

- Electromagnetic compatibility (EMC) was conducted per:
  - IEC 60601-1-2:2020 Medical electrical equipment – Part 1-2: General requirements for safety and essential performance – Collateral Standard: Electromagnetic compatibility – Requirements and tests
  - IEC 60601-4-2: 2016 Medical electrical equipment - Part 4-2: Guidance and interpretation - Electromagnetic immunity: performance of medical electrical equipment and medical electrical systems
- Electrical safety testing was conducted per IEC 60601-1:2020 Medical electrical equipment – Part 1: General requirements for safety 1: collateral standard: Safety Requirements for Medical Electrical Systems.
- Human factors testing was conducted per
  - FDA guidance, "Applying Human Factors and Usability Engineering to Medical Devices"
  - IEC 62366-1:2020 Medical devices – Part 1: Application of usability engineering to medical devices, and
  - IEC 60601-1-6:2020 Medical electrical equipment – Part 1-6: General requirements for basic safety and essential performance – Collateral standard: Usability
- Ex Vivo Testing: Novoxel performed an ex vivo study, applying worst-case assumptions, to assess the thermal and mechanical effects of the Tixel i device. This study was conducted in ex vivo Yucatan pig eyelid specimens. The ex vivo study demonstrated that the Tixel i met the acceptance criteria with respect to inner eyelid temperature, pressure on the globe, and acute histopathological observations in the eyelids tissue.
- Bench Testing: Novoxel performed bench testing, applying worst-case assumptions, to assess the effect of Tixel i pulses accidentally being delivered directly to the ocular shield. This testing demonstrated that the ocular shield remains intact and maintains its structural integrity after exposure to several Tixel i pulses.
  NOTE: Ocular shields were not placed during the pivotal clinical study and no injury to the ocular surface was reported in the study. However, as a conservative measure it was determined that ocular shields should be used as part of the Tixel i procedure to mitigate risk to the ocular surface. Only the Aestek plastic ocular shield (Oculo-Plastik, Inc.) was evaluated in the bench testing and the computational analysis described in the next bullet.
- Computational Analysis: Novoxel performed a computational analysis which demonstrated that the plastic ocular shield protects the ocular surface from thermal exposure in the unlikely event that Tixel i pulses are accidentally delivered directly to

the ocular shield. This analysis was conducted per specifications in IEC 60601-1:2020 using worst-case assumptions.

- Software verification and validation testing were conducted, and documentation was provided as recommended by FDA Guidance for the Content of Premarket Submissions for Software Device Software Functions, June 2023. The software was found to fit in the category of products that would require Basic Documentation Level because the failure or latent flaw of the device software function would not present a hazardous situation with a probable risk of death or serious injury to either a patient, user of the device or others in the environment of use prior to the implementation of the risk controls.

Results of the non-clinical testing support a substantial equivalence determination. The Tixel i device is substantially equivalent to its predicate devices for the indications for use.

VIII. Clinical Performance Testing

A prospective, multi-center, randomized, controlled, pivotal trial was conducted to evaluate the safety and effectiveness of the Tixel device compared to the LipiFlow device (one of the predicate devices). The study was conducted at 5 centers in the United States between September 2022 and June 2023.

Methods

The primary effectiveness endpoint of the study was the change from baseline to 4 weeks in TBUT.

Secondary effectiveness endpoints were:

- The change from baseline to 4 weeks and 12 weeks in the OSDI score,
- The change from baseline to 4-weeks and 12-weeks in the MGS, and
- The change from baseline to 12-weeks in TBUT.

The key safety endpoint was the rate of ocular adverse events. Secondary safety endpoints included evaluation of pain and discomfort during treatment, ocular surface staining, intraocular pressure, and best corrected distance visual acuity.

The study was designed to include adult subjects with symptoms of dry eye disease and MGD. Subjects were required to be 22 years or older who reported dry eye symptoms for 3 months prior to the study. They were required to have an Ocular Surface Disease Index (OSDI) score between 23-79, a tear break-up time (TBUT) <10 seconds in both eyes, and a meibomian gland score (MGS) ≤12 in both eyes. In addition, they had to have at least 15 glands in each lower eyelid that could be expressed with a cotton swab. They were required to use artificial tears or lubricants regularly the month prior to enrollment and had to agree to abstain from use of dry eye medications, other than lubricants, for the duration of the study.

The sample size target was approximately 110 subjects to account for drop-out and show that Tixel is non-inferior to LipiFlow with respect to the primary effectiveness endpoint.

After providing written informed consent, participants were screened for eligibility and underwent baseline exams and assessments, including completion of the OSDI questionnaire, refraction and best-corrected distance visual acuity, keratometry, slit lamp examination including evaluation of the lid margin, TBUT, corneal and conjunctival staining assessments, meibomian gland assessments, and measurement of intraocular pressure. Subjects who met all study eligibility criteria were randomized on a 1:1 basis to receive treatment either with the Tixel device or the LipiFlow device.

Subjects randomized to Tixel underwent 3 treatment sessions with the Tixel device on Day 0, Day 14, and Day 28. Subjects randomized to LipiFlow underwent 1 treatment on Day 0. Immediately following each treatment (either Tixel or LipiFlow), subjects underwent a slit lamp exam, corneal and conjunctival staining, IOP measurement, completed a pain and discomfort questionnaire and were assessed for adverse events. A post-treatment instructions sheet was given to Tixel subjects following the initial Tixel treatment. On Day 1, subjects had a post-treatment checkup call or video call, if necessary, with the physician assistant. Follow-up visits were conducted at 4- and 12-weeks following the last treatment visit, with the last treatment visit being on Day 28 for Tixel subjects and Day 0 for LipiFlow subjects. Subjects were asked to report their usage of dry eye lubricants throughout the study.

To reduce bias in the study, all safety and effectiveness endpoint assessments were performed by a masked assessment (i.e., not the person who conducted the Tixel or LipiFlow procedure).

Results

A total of 109 subjects were enrolled and randomized, 54 to Tixel and 55 to LipiFlow. Of these, 106 underwent the assigned procedure. Mean age of subjects was 62.3 years ± 12.0 for Tixel and 61.6 years ± 13.0 for LipiFlow (overall range of 29 – 88 years old). Women represented 68.5% of the Tixel group and 63.6% of the LipiFlow group.

The primary effectiveness endpoint was defined as the change from baseline to 1 month in tear break-up time (TBUT), analyzed using a mixed model analysis with baseline TBUT as a covariate. Tixel subjects had a mean baseline TBUT of 4.3 ± 1.5 seconds compared with 4.6 ± 1.8 seconds for the LipiFlow group. Per the mixed model analysis, Tixel subjects had a mean (±SE) improvement in TBUT of 3.0 ± 0.4 seconds compared with 2.8 ± 0.4 seconds for LipiFlow. The difference in mean (± SE) improvement in TBUT at 1 month between LipiFlow and Tixel was -0.17 ± 0.55 seconds). The difference in mean improvement in TBUT at 1 months was tested for non-inferiority, where a $p<0.05$ indicates non-inferiority. Tixel was non-inferior to LipiFlow for the improvement in TBUT at 1 month (upper bound of one-sided 95% CI of 0.73; $p<0.0001$).

Per the mixed model analysis, Tixel subjects had a mean (±SE) TBUT improvement of 3.0 ± 0.6 seconds at 3 months compared with 3.4 ± 0.5 seconds for LipiFlow. Per the mixed model

analysis, the difference in mean (± SE) improvement in TBUT at 3 months between LipiFlow and Tixel was 0.39 ± 0.79 seconds.

Both Tixel and LipiFlow subjects had, on average, severe symptoms at baseline (OSDI score of 50.2 vs. 49.4, respectively). Tixel subjects' mean (± SD) improvement in OSDI was 26.4 ± 21.1 at 1 month and 28.6± 22.4 at 3 months. Similarly, LipiFlow subjects had an 18.8 ± 21.0 improvement in OSDI at 1 month and 21.9 ± 18.5 at 3 months.

Tixel and LipiFlow subjects had similar baseline Meibomian Gland Scores (MGS) (7.2 ± 2.5 vs. 7.4 ± 2.6; range 0.0 – 12.0), which were consistent with the study entry criteria which required an MGS score ≤12 per eye. Per the mixed model analysis, Tixel subjects' MGS score increased a mean (± SE) of 8.9 ± 1.3 from baseline to 1 month and 11.2 ± 1.7 from baseline to 3 months. Likewise, LipiFlow subjects' MGS scores increased a mean (± SE) of 7.4 ± 1.3 at 1 months and 10.6 ± 1.6 at 3 months.

Only 7 ocular adverse events were reported during the study, all of which were mild and none of which were related to the study device or procedure. There were 4 events in 3 subjects in the Tixel group, all of which resolved within 8 days of onset. There was one case of viral conjunctivitis and one corneal abrasion due to a tree branch.

In addition, one Tixel subject had a non-macular, operculated retinal tear/hole with a retinal detachment in the left eye and a retinal tear in the right eye reported 27 days after the 3rd Tixel procedure, both of which were classified as serious adverse events. The 72- year old subject had a history of diabetes and was pseudophakic in both eyes, a known risk factor for this event. In addition, the subject had a history of an operculated hole in the left eye diagnosed 6 years prior to the Tixel procedure. These 2 SAEs were attributed to the peripheral retinal pathology diagnosed prior to enrollment and additional associated risk factor of pseudophakia, and were thus determined to be unrelated to the Tixel treatment. The left eye was treated with laser for the retinal hole and pneumatic retinopexy for the retinal detachment. The right eye was treated with laser retinopexy for the retinal tear. Both SAEs were successfully treated and the events were considered resolved within 1 day (OS) and 5 days (OD), respectively.

There were 3 events in 2 subjects in the LipiFlow group: one conjunctival cyst and one subject who had allergic conjunctivitis reported in both eyes. All events in the LipiFlow group resolved within 27-71 days.

A visual analog scale was used to assess subjects' pain and discomfort experienced in or around the eyelids or face during the Tixel or LipiFlow procedure. Immediately after the procedure, subjects rated discomfort on a scale from 0 (no discomfort) to 10 (worst possible discomfort) and pain on a scale from 0 (no pain) to 10 (worst possible pain). Tixel subjects reported an average discomfort of 2.8 (OD) and 2.6 (OD) versus 1.5 (OD) and 1.7 (OS) for LipiFlow subjects. Tixel subjects reported an average pain of 2.5 (OD) and 2.5 (OD) versus 0.8 (OD) and 0.9 (OS) for LipiFlow subjects. The number and proportion of subjects experiencing each discomfort and pain score are presented in the tables below.

Proportion of Subjects Reporting Discomfort During the Procedure

Discomfort Score	Tixel (N=53 subjects)						LipiFlow (N=53 subjects)	
	Treatment 1 visit (Day 0)		Treatment 2 visit		Treatment 3 visit		Treatment 1 visit (Day 0)	
	N eyes	%	N eyes*	%	N eyes*	%	N eyes	%
0	16	15.1%	10	10.0%	18	18.0%	40	37.7%
1	15	14.2%	20	20.0%	26	26.0%	19	17.9%
2	20	18.9%	18	18.0%	15	15.0%	16	15.1%
3	18	17.0%	18	18.0%	12	12.0%	15	14.2%
4	17	16.0%	17	17.0%	3	3.0%	9	8.5%
5	13	12.3%	12	12.0%	19	19.0%	4	3.8%
6	7	6.6%	2	2.0%	3	3.0%	0	0.0%
7	0	0.0%	3	3.0%	4	4.0%	1	0.9%
8	0	0.0%	0	0.0%	0	0.0%	1	0.9%
9	0	0.0%	0	0.0%	0	0.0%	1	0.9%
10	0	0.0%	0	0.0%	0	0.0%	0	0.0%

* 50 subjects received Tixel Treatments 2 and 3. 2 Tixel subjects withdrew from the study between Treatments 1 and 2 and 1 Tixel subject was withdrawn between Treatments 2 and 3 due to a non-ocular SAE.

Proportion of Subjects Reporting Pain During the Procedure

Pain Score	Tixel (N=53 subjects)						LipiFlow (N=53 subjects)	
	Treatment 1 visit (Day 0)		Treatment 2 visit		Treatment 3 visit		Treatment 1 visit (Day 0)	
	N eyes	%	N eyes*	%	N eyes*	%	N eyes	%
0	20	18.9%	21	21.0%	22	22.0%	63	59.4%
1	22	20.8%	12	12.0%	18	18.0%	16	15.1%
2	8	7.5%	19	19.0%	26	26.0%	13	12.3%
3	16	15.1%	17	17.0%	5	5.0%	9	8.5%
4	21	19.8%	16	16.0%	14	14.0%	2	1.9%
5	13	12.3%	11	11.0%	9	9.0%	1	0.9%
6	5	4.7%	1	1.0%	3	3.0%	1	0.9%
7	1	0.9%	3	3.0%	2	2.0%	1	0.9%
8	0	0.0%	0	0.0%	1	1.0%	0	0.0%
9	0	0.0%	0	0.0%	0	0.0%	0	0.0%
10	0	0.0%	0	0.0%	0	0.0%	0	0.0%

* 50 subjects received Tixel Treatments 2 and 3. 2 Tixel subjects withdrew from the study between Treatments 1 and 2 and 1 Tixel subject was withdrawn between Treatments 2 and 3 due to a non-ocular SAE.

Conclusions of the Pivotal Study

The results of this study demonstrate that the Tixel device provides an improvement in tear break-up time, dry eye symptoms as measured by the OSDI, and meibomian gland scores through 3 months, and that the Tixel device is non-inferior to the LipiFlow device in terms of tear break-up time at 1 month. No device- or procedure-related adverse events were reported with the Tixel device. In addition, the Tixel device had a similar safety profile as compared to the LipiFlow device. The results of this study support that the Tixel device is safe and effective for the treatment of evaporative dry eye disease in adult patients with meibomian gland dysfunction.

IX. Conclusions

The Tixel i device has the same intended use as the legally marketed predicate devices identified in this premarket notification. Some of the technological characteristics of the Tixel i device differ from those of the predicate devices, but the differences do not raise new or different types of questions of safety or effectiveness. The results of the non-clinical performance testing demonstrate that the Tixel i device functions as intended. The results of the clinical performance testing support an acceptable safety and effectiveness profile that supports a determination of substantial equivalence. The non-clinical and clinical performance testing demonstrate that the Tixel i device is substantially equivalent to the predicate devices.