DE NOVO CLASSIFICATION REQUEST FOR LUMENIS STELLAR M22

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Intense pulsed light (IPL) device for managing dry eye. An intense pulsed light device for managing dry eye is a prescription device intended for use in the application of intense pulsed light therapy to the skin. The device is used in patients with dry eye disease due to meibomian gland dysfunction, also known as evaporative dry eye or lipid deficiency dry eye.

NEW REGULATION NUMBER: 21 CFR 886.5201

CLASSIFICATION: Class II

PRODUCT CODE: QIU

BACKGROUND

DEVICE NAME: Lumenis Stellar M22

SUBMISSION NUMBER: DEN200028

DATE DE NOVO RECEIVED: April 4, 2020

CONTACT: Lumenis Ltd.
6 Hakidma Street PO Box 240,
Yokneam, ISR 2069204

INDICATIONS FOR USE

Universal IPL with a spectrum of 400-1200nm (with different filters) is indicated for: Improvement of signs of Dry Eye Disease (DED) due to Meibomian Gland Dysfunction (MGD), also known as evaporative dry eye or lipid deficiency dry eye, in patients 22 years of age and older with moderate to severe signs and symptoms of DED due to MGD and with Fitzpatrick skin types I-IV. IPL is to be applied only to skin on the malar region of the face, from tragus to tragus including the nose (eyes should be fully covered by protective eyewear). IPL is intended to be applied as an adjunct to other modalities, such as meibomian gland expression, artificial tear lubricants and warm compresses.

LIMITATIONS

The sale, distribution, and use of the Lumenis Stellar M22 is restricted to prescription use in accordance with 21 CFR 801.109.

IPL application combined with concurrent meibomian gland expression supports the proposed indication for use. Note that IPL treatment for this proposed indication is applied to the malar region of face from tragus to tragus (not to the eyes or eyelids).

During IPL treatment eyes are covered with adhesive eye patches and opaque goggles worn overlying them - these two types of eye protection completely occlude the eyes.

Serious safety consequences possible if eye protection is not worn per instructions for use and/or the IPL treatment is mis-used.

Known dermatologic adverse event risks largely consist of skin reactions including: flare-up, irritation, infection, blistering, pruritis, dryness, temporary skin color changes, burns, prolonged edema or erythema, Herpes simplex virus reactivation, post inflammatory hyperpigmentation (PIH), contact dermatitis, and scarring.

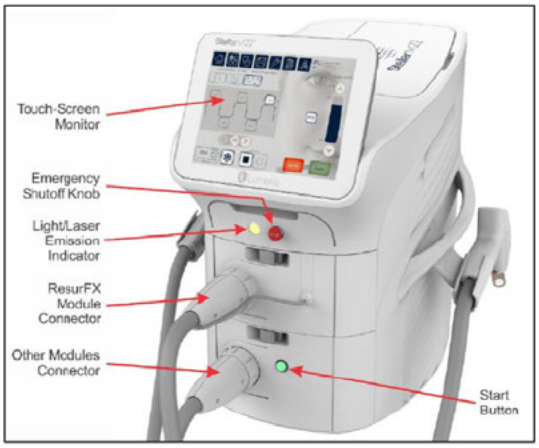
PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

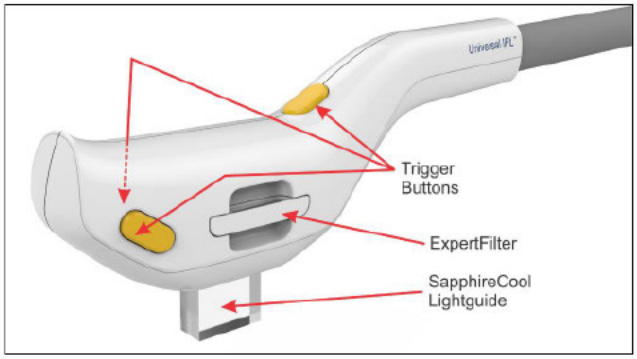
DEVICE DESCRIPTION

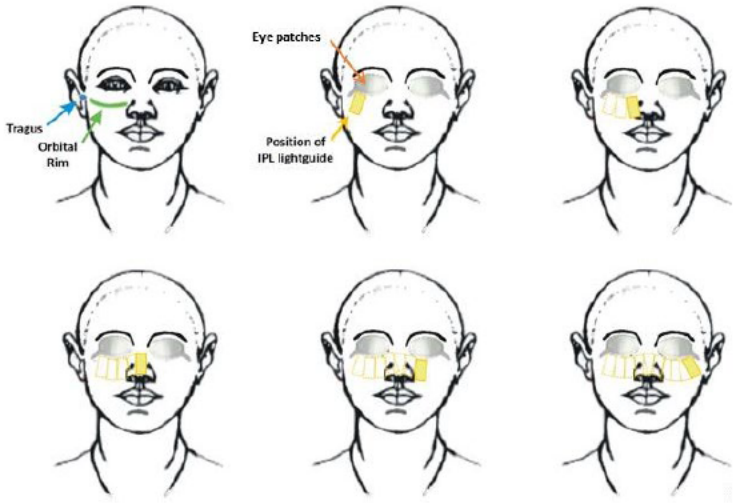
The purpose of this submission is to modify the Indication for Use cleared under K193500 for dermatological use to include ophthalmic use. The device and IPL handpiece are identical in materials and manufacturing processes to those described in K193500.

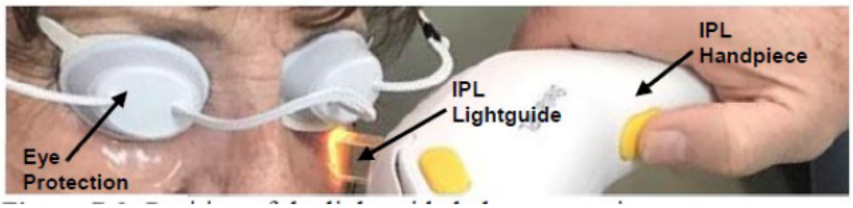
The Lumenis Stellar M22 System incorporates a touch-screen control panel, power supply modules, cooling unit, switching module and service panel, monitored and controlled by its control software. Selected parameter treatment options and corresponding relevant user information are displayed on the monitor screen. The subject device (ophthalmic use) uses the spectrum range of 400-1200 nm. The cut-off filters used in the Lumenis presets for Universal IPL pigmented lesions treatment with the Stellar M22 system are the 515, 560, 590, 615, 640 or 695nm filters. Each filter cuts off all light with a wavelength shorter than the number indicated on the filter. The filter is inserted inside the handpiece and is exchangeable.

Universal IPL skin treatments with the Stellar M22 may use one of the three lightguides, 8x15, 15x35 mm rectangles and 6 mm round, which are supplied as accessories. Lightguides are made of sapphire and couple the optical energy from the module to the treatment site.









Device Technology Description:	DEN200028
General Device Characteristics	
Universal Intense Pulsed Light (IPL) 400-1200 nm	IPL handpiece, comprised of: • Xenon IPL flash lamp assembly and cooling components • ExpertFilters • SapphireCool LightGuides and thermo-Electric cooler • 3 pulse buttons

The light pulse is activated by pressing one of the three pulse buttons (for right and left-handed users and different grips) located on the handpiece. Discharged light passes through an aperture containing a filter, into the LightGuide that is inserted in the bottom of the handpiece. The LightGuide delivers the emitted light energy to the treatment site.

Treatment time is brief, usually less than 10 minutes. The general treatment area includes the malar region, below the lower eyelids, from tragus (lower end of the ear) to tragus including the nose, and the peri-orbital area. At all times during IPL use, including during the test spot(s), the patient's eyes must be completely occluded.

Third-party Components and Accessories:

IPL third-party treatment accessories include:

For patients:

- coupling gel (transparent medical-grade, not contraindicated for use on facial skin)
- adhesive eye patches for patients ((b) (4))
- goggles for patients ((b) (4)

For healthcare providers:

- protective eyewear for healthcare providers (b) (4)

A 'one-time welcome pack' will be provided to the user that will include specific third-party accessories.

SUMMARY OF NONCLINICAL/BENCH STUDIES

The non-clinical testing (applicable to the subject device) includes performance testing, Electrical Safety and Electromagnetic compatibility (ES/EMC), and biocompatibility testing as explained below.

ELECTROMAGNETIC CAPABILITY (EMC) AND ELECTRICAL SAFETY

The sponsor provided a declaration of conformity that the device complies with the following FDA recognized consensus standards (similar to the previous K193500 device):

- IEC 60601-1
- IEC 60601-1-2

BIOCOMPATIBILITY/MATERIALS

The subject device IPL handpiece contacts intact facial skin for a limited duration. According to the FDA guidance document "Use of International Standard ISO 10993-1, Biological evaluation of medical devices Part 1: Evaluation and testing within a risk management process," the biocompatibility endpoints for this type of patient contact are cytotoxicity, sensitization, and irritation or intracutaneous reactivity. While testing for these endpoints was not performed for the subject device, these endpoints were adequately addressed because the handpiece is identical in materials and manufacturing processes to that described in K193500. The labeling includes several warnings, including to avoid eye contact with coupling gel. If coupling gel eye contact

accidentally occurs, the labeling includes warnings to halt treatment, rinse eyes out for 15 minutes, and consult a physician if eye irritation or redness is observed.

SHELF LIFE/STERILITY

The Lumenis Stellar M22 is provided non-sterile. Cleaning and maintenance instructions of the device and accessories are included in the labeling.

SOFTWARE

The provided software information for the subject device was consistent with the FDA guidance document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." The M22 system software version 6.0 allows the M22 system to recognize the filter for the IPL spectral range and block all other applications and modules while filter is connected. Since the new risks are addressed by labeling, the device has a moderate Software Level of Concern (LOC). The risks and hazards associated with Stellar M22 system, including risks related to cybersecurity were handled as part of Risk Management Process of the Stellar M22 system. Appropriate mitigations were put in place to address patient safety risks and ensure proper device performance. The risks related to the identified threats were identified, analyzed, mitigated and verified within the Risk Management Process of the Stellar M22 system.

PERFORMANCE TESTING - BENCH

The subject device, including the IPL handpiece are identical in performance, materials and method of manufacture to the previously cleared family of IPL devices (e.g., K193500, K170060, K142860, K060448, K020839, K994014, K950493). The thermal hazard risk mitigations for the subject device leveraged the non-clinical (and clinical) testing that were performed for these similar devices, which had very similar treatment parameters. Specifically, prior non-clinical testing conducted that is applicable to the subject device included verification of temperature specifications for the treatment head of the delivery handpiece to prevent tissue damage due to overheating (e.g., K020839); verification of the device recommended treatment parameters by assessing light guide output spectrum and filter transmission characteristics measured by a spectrometer, and pulse duration and light energy distribution using fluence measurements by a calorimeter (e.g., K950493). Engineering design was validated through bench testing including design verification (e.g. output stability) and/or validation tests with testing results. New risks due to the new indication for use are addressed by labeling.

SUMMARY OF CLINICAL INFORMATION

The Sponsor performed a multi-center, prospective, randomized, sham-controlled, superiority study. A summary of the trial is provided, in brief, below:

Population: Up to (b) (4) male or female subjects, 22-85 years of age, with signs and symptoms of DED caused by MGD.

Duration: (b) (4) weeks

Main Inclusion Criteria: moderate to severe signs and symptoms of DED due to MGD:

- Tear break-up time (TBUT) ≤ 7 seconds
- Meibomian Gland Score (MGS) ≤ 12, for (b) (4) glands in the lower eyelid
- At least 5 non-atrophied meibomian glands in the lower eyelid
- Symptoms self-assessed using the OSDI questionnaire ≥ 23
- Fitzpatrick skin type I-IV (b) (4)

Objectives:

Primary: To determine effectiveness of combined Intense Pulsed Light Therapy and Meibomian Gland Expression (IPL+MGX) treatment in improving TBUT in eyes with moderate to severe signs and symptoms of DED due to MGD assessed at single follow-up visit 4 weeks after final treatment session (b) (4) days, (b) (4) days), TBUT evaluated using FUL-GLO fluorescein ophthalmic strips, 3 successive readings averaged.

Secondary: To determine effectiveness of combined IPL+MGX treatment in improving symptoms of DED due to MGD as evaluated by OSDI questionnaire self-evaluation at single follow-up visit and by self-evaluation of Eye Dryness Score (EDS) at single follow-up using a visual analog scale (VAS), to determine effect on appearance of eyelids, as well as to determine safety of IPL treatment for this indication.

Primary endpoint: The difference in change in TBUT from baseline (BL) to follow-up (FU), compared between the two study arms (TBUT change defined as FU minus BL).

Secondary endpoints:

- The difference in the change in OSDI score from BL to FU, compared between subjects in 2 arms.
- The difference in the change in EDS VAS from BL to FU, compared between subjects in 2 arms.

Sample Size: (b) (4) subjects/(b) (4) eyes total (b) (4) subjects/(b) (4) eyes per arm)

Study arm, the change of TBUT from BL to FU (b) (4)
Control arm, the change of TBUT from BL to FU (b) (4)
Type I error of 0.05 (two-tailed test)
Type II error of (b) (4) (power = (b) (4)
1:1 ratio of Treatment to Control

Number of sites: 3-4

Treatments: 4 sessions, each 2 weeks apart (b) (4) *days,* (b) (4) *days)*

1. Subjects report daily usage (frequency and dose) of eye drops, warm compresses and lid hygiene since the previous visit
2. Pre-treatment biomicroscopy with slit lamp (observation of lid margins, eyelashes, conjunctiva)
3. "Active IPL" treatment of malar region (tragus to tragus) or "Sham IPL" (control arm) on same facial area
4. Meibomian gland expression (MGX) of the upper and lower eyelids in both eyes in each study group (IPL treatment group and Sham control group)
5. Slit Lamp Biomicroscopy
6. Self-assessment of pain/discomfort during IPL administration, using a VAS

7. Self-assessment of pain/discomfort during MGX, using a VAS

Follow-up: 4 weeks after the final treatment *(b) (4) days, + (b) (4) days)*

Clinical Outcomes:

- **Primary effectiveness endpoint for improvement in TBUT was met**.

  The study demonstrates a statistically significant difference in improvement in TBUT between device treatment group and control group (change in TBUT baseline to follow-up was 1.99±0.36 sec for IPL+MGX arm and 0.75±0.34 sec for control sham+MGX arm, between-group mean difference in TBUT of 1.24±0.50 sec).

  Although a relatively small comparative benefit to TBUT improvement, support for "meaningful clinical benefit" is based on planned exploratory analyses and unplanned post-hoc analyses (see below).

- **Secondary endpoint for between-group difference in PRO symptoms score was not met**.

  The study did not demonstrate significantly greater benefit for the IPL device group with regard to self-reported dry eye symptoms (i.e., treatment group and control group showed similar overall mean improvement in dry eye symptom scores with no statistically significant difference in score improvement between groups, OSDI p=(b) (4) and EDS VAS p=(b) (4)).

- **Supportive analyses for Symptoms** of DED:
  - **Exploratory protocol-planned analysis of "OSDI responders" at follow-up** (defined as OSDI (b) (4) interpreted as improvement to "mild or better" PRO symptoms score), **shows clinical benefit** for active IPL treatment group (b) (4) vs. the control group (b) (4) This outcome supports clinically meaningful benefit for a proportion of study population.

- **Supportive analyses for Signs** of DED:
  - **Exploratory protocol-planned analysis of change in Meibomian Gland score (MGS) shows clinical benefit** for IPL treatment group, improvement (b) (4) units in active arm vs. (b) (4) units in control arm, a between-group difference of (b) (4) units. This outcome **supports clinically meaningful benefit for a subset of the study population**.
  - **Post-hoc categorical analyses of TBUT improvement** (i.e., change in TBUT clinical category defined by change of two or more severity categories**) shows clinical benefit** for IPL treatment group (b) (4) improved, (b) (4) worsened and (b) (4) no change) compared to the control group ((b) (4) improved, (b) (4) worsened, (b) (4) no change). A larger proportion of patients in the IPL/MGX group improved by two or more TBUT severity levels compared to sham/MGX group, a between-group difference of (b) (4) In a similar analysis, when change was defined by one or more TBUT severity categories, a larger proportion of patients in the IPL/MGX group improved by one or more TBUT severity levels compared to the MGX only arm, a between group difference of (b) (4) .

- **Post-hoc TBUT analyses of proportion of subjects with a TBUT consistent with MGD** (defined as TBUT (b) (4) seconds at baseline) **who improved to non-MGD TBUT at follow-up** (defined as TBUT (b) (4) seconds at follow-up) **shows clinical benefit** for IPL treatment group ((b) (4) improved to non-MGD TBUT) compared to the control group ((b) (4) improved to non-MGD TBUT).

NOTE: Regarding post-hoc analyses to support magnitude of TBUT primary endpoint as clinically meaningful benefit, categories were chosen as pre-defined in Tomlinson, et al., 2011 (i.e., Normal: ≥10 sec; Subclinical: < 10 to ≥7 sec; Minimal: < 7 to ≥5 sec; Mild: < 5 to ≥3 sec; Moderate: < 3 to ≥1 sec; Severe: < 1 or instant breakup). According to Wolffsohn et al. (Ocul Surf 2017;15:539-574, p. 546, referencing Abelson et al., 2002, "Alternative reference values for tear film breakup time in normal and dry eye populations"), a TBUT cut-off of 5 seconds reasonably distinguishes between patients with normal amount of lipid in the tear film and those diagnosed with DED."

NOTE: Regarding exploratory (protocol-planned) OSDI-responder analysis, responder was defined as OSDI < 23, this score represents "mild or better" as described in Miller Et Al and TFOS DEWS II Diagnostic Methodology report.

- **Safety Outcomes**:
  - **No Serious Adverse Events (SAEs), no UADEs**

  - **AE incidence** 8.9% in IPL active treatment arm (2 ocular AEs, 2 skin AEs) compared to 20% incidence in the control arm:
    - IPL+MGX study group: 1 subject experienced 2 AEs ocular (allergic conjunctivitis and bacterial conjunctivitis), 2 subjects experienced 1 skin-related AE each (blepharitis and pain). Subject 01-005 experienced bacterial conjunctivitis and was withdrawn from study. The remaining 3 AEs were ongoing at the time of study exit.
    - Control group (sham+MGX): 2 subjects experienced 1 systemic AE each (bronchitis and sinus infection), 1 subject experienced 2 different systemic AEs (sinus infection and hyperlipidemia), 1 subject experienced 2 episodes of the same systemic AE (worsening of seasonal allergy), 1 subject experienced 1 ocular-related AEs (conjunctival telangiectasia), 2 subjects experienced 1 skin-related AE each (chalazion and stye).

LABELING

The professional and patient labeling are adequate and meet the requirements of 21 CFR 801.109. The labels summarize the clinical trial results that characterized the probable benefit and the identified risks of the device, including tissue damage, pain, headache, and discomfort. The labeling (Operator's Manual) contains requirements for use by prescription only, Indications for Use, contraindications, device description, technical parameters, warnings, precautions, potential complications, instructions for use (including an explanation of all user-interface components for ocular protection and information regarding proper device placement),

recommended schedule, instructions for device maintenance/cleaning, summary of clinical trials, information related to electromagnetic compatibility.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of an intense pulsed light (IPL) device for managing dry eye and the measures necessary to mitigate these risks.

Table 1 – Identified Risks to Health and Mitigation Measures

Identified Risks to Health	Mitigation Measures
Tissue damage due to overheating	Thermal safety assessment Software verification, validation, and hazard analysis Labeling
Tissue damage or loss of vision due to light radiation	Clinical performance testing Labeling
Adverse tissue reaction	Biocompatibility evaluation
Electrical shock or burn	Thermal safety assessment Electrical safety testing Software verification, validation, and hazard analysis Labeling
Interference with other devices	Electromagnetic compatibility (EMC) testing Software verification, validation, and hazard analysis Labeling
Pain or discomfort	Clinical performance testing Labeling
Failure to mitigate dry eye signs and/or symptoms	Clinical performance testing Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the intense pulsed light (IPL) device for managing dry eye is subject to the following special controls:

(1) Clinical performance testing must evaluate adverse events and improvement of dry eye signs and symptoms under anticipated conditions of use.
(2) Thermal safety assessment in a worst-case scenario must be performed to validate temperature safeguards.
(3) Performance testing must demonstrate electrical safety and electromagnetic compatibility (EMC) of the device in the intended use environment.
(4) Software verification, validation, and hazard analysis must be performed.
(5) The patient-contacting components of the device must be demonstrated to be biocompatible.
(6) Physician and patient labeling must include:
    (i) Device technical parameters;
    (ii) A summary of the clinical performance testing conducted with the device;
    (iii) A description of the intended treatment area location;

(iv) Warnings and instructions regarding the use of safety-protective eyewear for patient and device operator;
(v) A description of intense pulse light (IPL) radiation hazards and protection for patient and operator;
(vi) Instructions for use, including an explanation of all user interface components; and
(vii) Instructions on how to clean and maintain the device and its components.

BENEFIT-RISK DETERMINATION

Benefits:

- Primary effectiveness endpoint shows statistically significant difference in improvement in TBUT between device treatment and control arm (~1.25 second mean difference).

Risks:

- Adverse events (AEs) or outcomes related to the device itself
- Discomfort related to IPL treatment (as compared to MGX alone)
- Lack of data on repeated exposure to the device/use

Summary

Benefits are demonstrated for IPL application combined with concurrent meibomian gland expression (i.e., the clinical study compared this combined treatment with sham treatment combined with MGX as the control group). Clinical study outcomes support the conclusion that treatment with Lumenis Stellar IPL combined with Meibomian Gland Expression (IPL+MGX) provides meaningful clinical benefit compared to the control group (Sham+MGX), and the benefit is considered to outweigh risks when IPL is used as indicated with eye protection as evaluated in the clinical study. Overall, the totality of clinical outcomes and benefit-risk profile support meaningful clinical benefit for the proposed indication for use.

Known dermatologic adverse event (AE) risks largely consist of skin reactions including: flare-up, irritation, infection, blistering, pruritis, dryness, temporary skin color changes, burns, prolonged edema or erythema, Herpes simplex virus reactivation, post inflammatory hyperpigmentation (PIH), contact dermatitis, and scarring. Note that IPL treatment for this proposed indication is applied to the malar region of face from tragus to tragus (not to the eyes or eyelids, which must be fully covered by protective eyewear).

In addition, serious safety consequences are possible if eye protection is not worn per instructions for use and/or the IPL treatment is misused. During IPL treatment in the pivotal clinical study, eyes were covered with adhesive eye patches and opaque goggles were worn overlying them -- these two types of eye protection completely occluded the eyes. With this protection in place, there were no ocular AEs attributed to the IPL system. User error by application of IPL treatment to eyelid skin is mitigated with language incorporated in the User Manual labeling.

Overall, the totality of clinical outcomes and benefit-risk profile demonstrate meaningful benefit and support the proposed indication for use. Given patient willingness to undergo treatment with known dermatologic risks, for the benefit of improvement in TBUT and meibomian gland score (MGS), and possible improvement in dry eye symptoms as reported in the exploratory planned analysis of Ocular Surface Disease Index (OSDI) responders, benefits are considered to outweigh risks.

Patient Perspectives

Patient perspectives, which included assessment of change in OSDI severity score and Eye Dryness Score (EDS) by visual analog scale, were taken into account for this device.

Benefit/Risk Conclusion

In conclusion, given the available information above, the probable benefits outweigh the probable risks for the Lumenis Stellar M22 device. The device provides benefits, and the risks can be mitigated by use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the Lumenis Stellar M22 is granted and the device is classified as follows:

Product Code: QIU
Device Type: Intense pulsed light device for managing dry eye
Class: II
Regulation Number: 21 CFR 886.5201