DE NOVO CLASSIFICATION REQUEST FOR KLOX BIOPHOTONIC LUMIHEAL SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Phototherapy device for reducing the appearance of acute post-surgical incisions. This device consists of a light emitting device and a photoconverter gel and is intended to employ light energy for reducing the appearance of acute post-surgical incisions. This classification does not include products which contain drugs or biologics.

NEW REGULATION NUMBER: 21 CFR 878.4880

CLASSIFICATION: Class II

PRODUCT CODE: QPE

BACKGROUND

DEVICE NAME: Klox Biophotonic LumiHeal System

SUBMISSION NUMBER: DEN200005

DATE DE NOVO RECEIVED: February 4, 2020

SPONSOR INFORMATION:

Klox Technologies Inc.
275 boul. Armand Frappier
Laval, H7V 4A7 Canada

INDICATIONS FOR USE

The Klox Biophotonic LumiHeal System is indicated as follows:

The Klox Biophotonic LumiHeal™ System is indicated to provide blue light and fluorescent light energy for use on post-surgical incisions for scar management. The System is intended to be used in FST I-IV female patients 22 years and over.

LIMITATIONS

The sale, distribution, and use of the Klox Biophotonic LumiHeal System are restricted to prescription use in accordance with 21 CFR 801.109.

The device should not be used by people taking drugs or products or with conditions known to induce severe photosensitivity reactions.

The device should not be used by people with known skin hypersensitivity.

The device should not be used by women who are pregnant or breast-feeding.

Safety and effectiveness in pediatric population (<22 years old) have not been evaluated.

Safety and effectiveness in patients with Fitzpatrick Skin Type V-VI have not been evaluated.

Safety and effectiveness for patients with hypertrophic and keloid scars have not been evaluated.

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

DEVICE DESCRIPTION

The Klox Biophotonic LumiHeal System is a device which consists of a blue light emitting Multi-LED Light device (KT-L Lamp) with emitted wavelengths of 440-460nm and a topical photoconverter gel (LumiHeal Gel). When the gel is illuminated by the LED device, it will emit fluorescence with blue, green, yellow, and orange wavelengths between 400nm to 625nm. The fluorescence mixed with the excitation blue light is used for scar management (i.e., reducing the appearance of acute post-surgical incisions).

The KT-L Lamp (Figure 1) has a timer and a distance sensor with which the system set the illumination time at 5 min and distance between the lamp and the wound area at 5cm. For the KT-L Lamp interface, press the Distance Verification Button to measure the distance. Display Screen should read approximately 50mm. Press the Time Display Button to return display to Timer Mode. During the illumination, it is possible to toggle between the Timer Mode or Measure Mode by pressing either the Time Display Button or the Distance Verification Button. Time remaining during illumination will be displayed in minutes (min). The lamp comes equipped with a power cable, 2 pairs of protective eyeglasses, and a user manual. The device specification is shown in the Table 1.

Figure 1. KT-L Lamp and User Interface

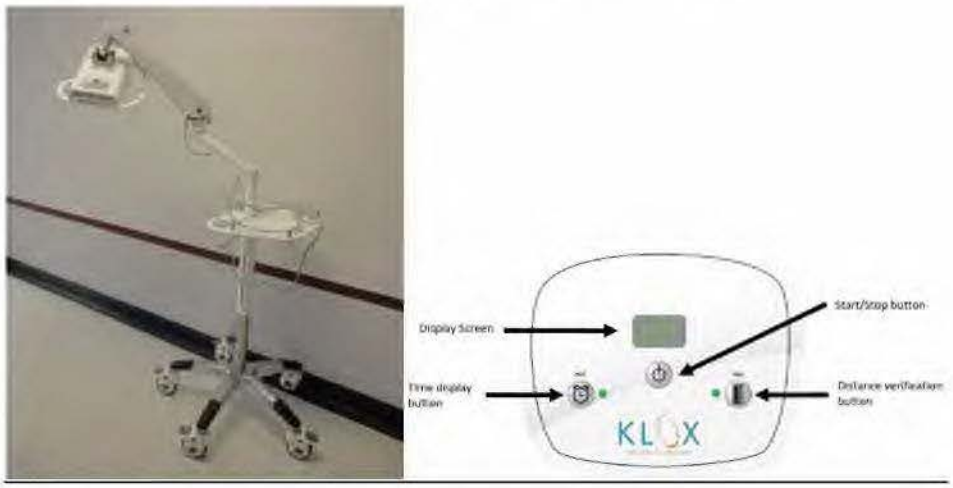


Table 1. KT-L Lamp Device Specification

Device Technology Description:	**Specifications**
Number of LEDs	446nm LEDs: 40; 415nm LEDs: 6
Power density	55-129 (mW/cm2)
Distance from light source to wound	5cm
Illuminated area	7.5 x 15cm
Duration of use	5min
Fluency	16.5-38.7 J/cm2

The LumiHeal Gel is provided as a two-component gel (Figure 2), specifically Jar A (25g) and Jar B (2.5g). The two components of the LumiHeal Gel are intended to be mixed immediately prior to use. Jar A is the carrier gel and Jar B is the chromophore gel. The LumiHeal Gel is applied just before use and is intended to remain in contact with the surface of wound for 5 minutes during the light exposure and application. After the 5-minute application period, exposure to the KT-L Lamp is discontinued and the LumiHeal Gel is removed.

Figure 2. LumiHeal Gel

The purpose of the LumiHeal Gel is to facilitate conversion of the non-coherent blue light wavelength from the KT-L Lamp into blue, green, yellow and orange wavelength light between 400nm to 625nm at the skin surface. The composition, as well as the function of each of the ingredients in the LumiHeal Gel are provided in Table 2 below.

Table 2. LumiHeal Gel Ingredients

CHEMICAL NAME	CAS Number	Function	CONCENTRATION in individual Jar w/w
(b)(4)			

*Note: pH adjusted by adding sodium hydroxide until pH between 4.80 and 5.10 is obtained

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The KT-L lamp is a non-patient contacting component. The LumiHeal Gel is applied to the patient's post-surgical incisions area for an administration period of 5 minutes. The administration is repeated twice a week for a consecutive 8 weeks. The patient-contacting component is the photoconverter gel and the patient contact classification is a surface device, breached or compromised skin contact, prolonged duration (>24 hours to 30 days). Per the patient contact classification and Table A.1 of the FDA biocompatibility guidance entitled, "*Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process*"", the following biocompatibility endpoints assessments are recommended: cytotoxicity, irritation, sensitization, systemic toxicity (acute, and subacute/sub-chronic), material-mediated pyrogenicity, and implantation. The biocompatibility assessment was adequate for both the light-exposed and non-exposed photoconverter gel. The conclusion was reached that the risk of a clinically significant biocompatibility concern is low.

SHELF LIFE/STERILITY

The KT-L lamp is provided non-sterile. The LumiHeal Gel is provided as a two-component gel: Jar A as the carrier gel and Jar B as the chromophore gel. Jar A contains ingredients which are provided non-sterile. Urea peroxide is included as a preservative in Jar A. Jar B is terminally sterilized in an ISO 13485 certified sterilization facility via autoclaving.

To establish its shelf life, the following testing was performed: preservative effectiveness testing, per USP <51> for the real-time aged, final finished Jar A. Additionally, packaging integrity testing for the duration of the proposed shelf-life was provided, using edge dip dye application method per ASTM F1929-12. The test gels met the acceptance criteria for each test.

ELECTROMAGNETIC CAPABILITY & ELECTROMAGNETIC SAFETY

The following Electrical Safety and Electromagnetic Compatibility testing has been performed:

- IEC 60601-1:2005 + A1 2012 Medical Electrical Equipment – Part 1: General requirements for basic safety and essential performance with NRTL Deviations USA
- IEC 60601-1-2:2014 4th edition Medical Electrical Equipment – Part 1-2: General requirements for basic safety and essential performance – Collateral Standard: Electromagnetic disturbances – Requirements and tests

The KT-L lamp passed all relevant portions of the testing.

SOFTWARE

The KT-L Lamp comprises custom embedded software (firmware) to control the LEDs and Human-Machine Interface functions of the lamp. The Agency considers the software to be a minor level of concern (LOC) because inadvertent software errors are unlikely to cause any injury to the patient or operator.

All elements of software information corresponding to minor LOC devices as outlined in FDA's guidance document "*Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices*" (issued May 11, 2005) were provided and contain sufficient detail to provide reasonable assurance that the software will operate in a manner described in the specifications.

PERFORMANCE TESTING - BENCH

Bench testing was conducted on the KT-L Lamp (the "lamp") and the LumiHeal Gel (the "gel") to demonstrate that the Klox Biophotonic LumiHeal System (the "system") performs as expected under the anticipated conditions of use. The following bench testing was conducted to demonstrate the device performance characteristics:

- Evaluation of heat dissipation following the system application: The temperatures of skin was measured after a 2mm layer of gel was spread on the skin of the hand and illuminated for 5 min. The skin temperatures can remain within a safe temperature range (<43°C) throughout the illumination for the indicated skin types (up to Type IV on the Fitzpatrick skin scale).
- Evaluation of the biophotonic properties of the gel: The absorbance, fluorescence spectra and photobleaching of the gel were measured before and after illumination with the blue light lamp. The distance with efficient photobleaching, the best time for illumination, and the gel thickness with least % residual fluorescence were determined.
- Verification of photonic parameters for the lamp: the peak wavelength and the power density of the blue light were measured and met the specification.
- Validation of method for power intensity measurement on the lamp: the method to measure power density values from the lamp was validated to ensure the accuracy of the measurement.
- Determination of radiant fluence delivered by the system: the average radiant fluence of fluorescence and transmitted blue light through the gel by the lamp were determined and the photoconverting function of the gel was verified.
- Determination of the lowest and highest viscosity of the gel: the minimum and the maximum viscosity were determined to ensure that the gel is able to be easily spread, to stay in place and to be easily removed after light exposure.
- Verification of the removal of gel in a wound model after application: the complete removal of photoconverter gel after clinical procedures was verified.
- Verification of the mechanical functions of the lamp: the mechanical performance of the lamp was tested and met the specifications.

- Verification of the performance of the lamp after the simulated service life: the performance including illumination power output, interface functions, mechanical functions met specifications after the simulated 5 years of service life.
- Verification of packaging and transport on the lamp: the packaging of the KT-L lamp resisted the testing and preserved the integrity.

HUMAN FACTORS/USABILITY TESTING

Usability testing was performed to demonstrate that the lamp design and associated labeling are sufficient to enable intended operation of the device by each intended user populations (i.e., nurses and medical practitioners). Intended users were asked to perform the critical tasks under simulated use conditions and address the questions. Modifications of the labeling and the lamp design were followed based on usability testing result.

SUMMARY OF CLINICAL INFORMATION

Overview

A clinical study (the "Study") was conducted to evaluate the safety and effectiveness of the Klox Biophotonic LumiHeal System when applied to acute post-surgical incisions.

The study was conducted at a single center in two locations. Patients were randomized into one of the following six administration schedules. The product was administered during the proliferative phase of the wound.

1. Initiated at Day [redacted] post-surgery, [redacted] weekly
2. Initiated Day [redacted] post surgery, [redacted] weekly
3. Initiated Day [redacted] post surgery with double (two consecutive) application [redacted] a week
4. Initiated at Day [redacted] post surgery, [redacted] weekly
5. Initiated at Day [redacted] post surgery, [redacted] weekly
6. Initiated at Day [redacted] post surgery with double (two consecutive) application [redacted] a week

The product was administered for [redacted] or [redacted] weeks on one breast and the other with Silicone sheets (Cica-Care Silicone Sheeting) for [redacted] to [redacted] weeks. The administration site was randomly allocated.

Subsequently, all patients were followed for an additional [redacted]-week post administration.

Study Methodology

Administration of the product were conducted by one of four plastic surgeons that were trained on the study protocol and procedures.

The patients underwent bilateral breast reduction surgery and immediately after surgery were provided post- operative instructions. The surgical incision was cleaned and dried prior to application. A thin layer of LumiHeal Gel was applied on the wound and illuminated with the KT-L Lamp for 5 minutes, at

~2 inches (~5 cm). For patients receiving two consecutive applications during the visit, once the first illumination of the whole breast incision had been performed, the used gel was gently removed and a second application was performed right away, followed by illumination. A priori to administration to protect from the blue light from the lamp, eye protectors (goggles) had to be worn by the patient and the physician. If needed, the breast incision could be divided into two to three areas depending on the size of the incisions. Following application, the site was then wiped with a moist towel or gauze, and then rinsed with saline solution. During the administration period, approximately (b)(weeks post-surgery, all patients were invited to perform breast massage with (b)(4), every day, twice per day for four weeks.

Patient Population

A total of (b)(subjects were enrolled and (b)(patients completed the study. Every patient had the LumiHeal System administered to one breast and the second one received Silicone sheets.

Accordingly, all patients who had completed the trial were included in the safety and effectiveness analyses.

Subjects enrolled in the study included women (100%) over the age of 23. The study included no subject with Fitzpatrick Skin Type (FST) V and VI.

Table 3. Summary of Demographic Information

	All Subjects	
Number	(b)(	
Age (years)		
Mean (standard deviation)	47.5 (11.7)	
Minimum, Median, Maximum	31, 46, 65	
	N	(%)
Sex		
Male	0	0
Female	(b)(	100
Race		
American Indian or Alaska Native	(b)	2.4
Asian	0	0
Black or African American	0	0
White	(b)(	93.0
Others	(b)(	4.6
Fitzpatrick Skin Type		
I	(b)(	16.7
II	(b)(4)	42.9
III	(b)(4)	33.3
IV	(b)(4)	7.1
>V	0	0

Endpoints

Safety

Safety information was collected throughout the trial during study visits.

Effectiveness

Table 4 presents the Study Endpoints. The results of the study are provided in Tables 10-15.

Table 4. Study Endpoints

Primary objectives	Evaluation of the safety and tolerability of the subject device compared with the ones of Silicone Sheets (Cica-Care® Silicone Sheeting) for surgical wounds via assessment of adverse events, serious adverse events, device incidents, and rates of incision healing complications at every visit.
Secondary objectives	Evaluation of the effectiveness of the LumiHeal System compared with one of Silicone Sheets as assessed via:
	• Physician Observer Scar Assessment Scale (POSAS) at Weeks (b)(4) (b)(4) and (b)(4) post-surgery
	• Patient Observer Scar Assessment Scale (POSAS) at Weeks (b)(4) (b)(4) and (b)(4), post-surgery
	• Vancouver Scar Assessment Scale (Observer) at Weeks (b)(4) and (b)(4) post-surgery
	• Patient's self-assessment of ease of wound management at Weeks (b)(4) (b)(4) and (b)(4) post-surgery

The effectiveness assessments scales used in this study included:

- POSAS (Observer Scar Assessment Scale)- Blinded Evaluators using Photographs at Week (b)(4) compared to Last Study Visit. The POSAS (observer) is validated for surgical incisions using photography.
- POSAS –Patient, completed by the patients
- Patients' Overall ease of use and satisfaction questionnaire

Results

Safety

Compliance to the Study was considered high as only four visits were missed, out of the 420 required according to the Study protocol. Overall, 99.0% of Study visits planned by the protocol were received during the period. T (b)(4) patients (92.9%) received all applications as planned in the protocol. The mean number of study applications was 12.5, and the median was 14.0 (minimum of (b)(4) and maximum of (b)(4) applications).

A total of fourteen adverse events were reported. They concerned eleven patients, representing 26.2% of the total number of patients in the ITT population. There were no specific adverse event trends to report. More specifically, the incidence of the events were as follows: infections (7.1%, breast cellulitis, mastitis, viral upper respiratory infection), injury/procedural complications (4.8% wound dehiscence), reproductive system/breast disorders (9.5%), and skin/subcutaneous disorders (7.1%).

The number of adverse events (number of patients and number of events) was comparable between the different groups, except for the group which underwent administration (b)(days post-surgery, (b)(4) a week, in which no adverse event was observed.

Eight adverse events were assessed as mild: one case of viral upper respiratory tract infection, three cases of breast discharge or discomfort, and four cases of skin irritations (eczema, erythema, pruritus or rash). Six other adverse events were reported as moderate in terms of intensity. They were primarily expected after a breast reduction surgery: infection (mastitis and cellulitis- Silicone and Klox groups), wound/breast dehiscence (Klox and Silicone groups), and breast hematoma (Silicone group).

No events were reported as severe.

None of these adverse events was considered as related to the study application (LumiHeal™) according to the investigators.

Four adverse events (breast discomfort, erythema and pruritus) were considered as related to Silicone sheets.

Effectiveness

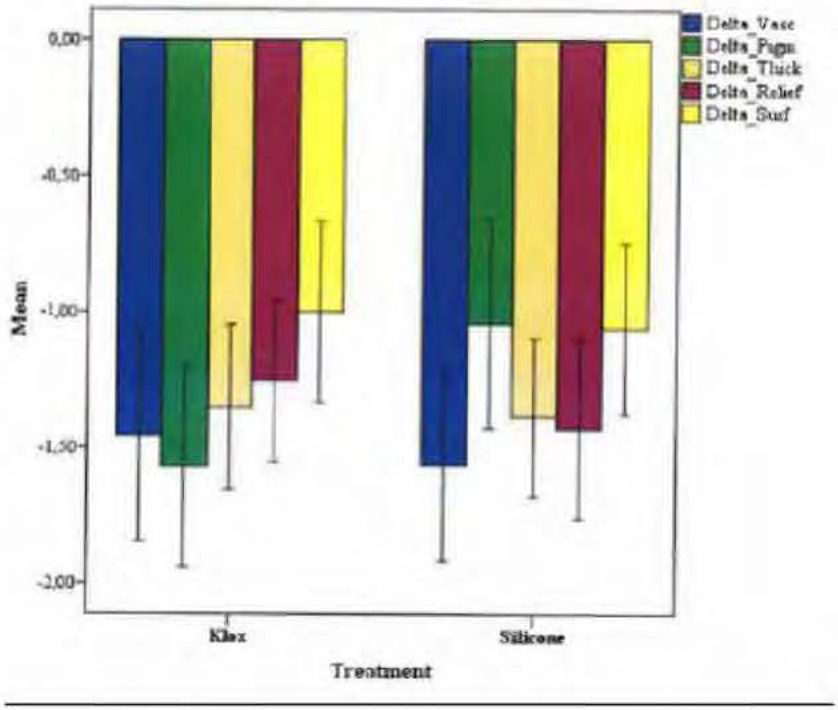
POSAS- Blinded Evaluators Using Photographs

As planned in the clinical protocol, a blinded review by experts was performed. (b)(4) subjects were enrolled and evaluated in the study, with (b)(lost to follow-up by the study completion.

For each image, the blinded experts had to score each criterion of the POSAS Observer scale: Vascularity, Pigmentation, Thickness, Surface area, Relief, Overall opinion. The total score was also calculated. This evaluation had to be made for Week (b)(Visit (b)(and at last study visit.

The mean results demonstrate there was at least a 1point improvement in each sub-category for the subject device and control, Silicone. Amongst the different results, the evolution of each POSAS Observer sub-category (Vascularity, Pigmentation, Thickness, Relief and Surface area) was considered as similar in all sub-groups combined analysis, except for the pigmentation which showed a trend to be lower in the Silicone group, as shown on Figure 3.

Figure 3. Blinded Review – Evaluation of POSAS Observer scoring changes between visit (b)(and last study visit – Mean scores for each sub-category – All sub-groups combined



POSAS- Patient – Total Score and Overall Opinion

Similar to the POSAS Observer Non-blinded Investigators, the total score of the POSAS Patient is obtained by the addition of each of the sub-scores (Thickness, Irregularity, Color, Stiffness, Pain and Itching), except Overall opinion.
The baseline mean scores were comparable between LumiHeal (b) (4) (SD (b) (4) and Silicone (b) (4) (SD (b) (4). There was a trend toward improvement throughout the study with lower scores at Week (b)(The LumiHeal score was (b) (4) a decrease of (b) (4) and the Silicone score was (b) (4) a decrease of (b) (4)

The Patient Overall Opinion score was comparable between LumiHeal, (b) (4) (SD (b) (4)) and Silicone, (b) (4) (SD (b) (4)) at baseline and there was a trend toward improvement over the course of the study. At week (b)(the LumiHeal score was (b) (4) a decrease of (b) (4) and the Silicone score was (b) (4) a decrease of (b) (4)

Pediatric Extrapolation

In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

LABELING

Device labeling includes an instruction for use for the KT-L lamp, an instruction for use for the LumiHeal Gel, LumiHeal Gel box labeling. The instruction for use for the KT-L lamp includes

description of the optical specification and warnings for eye safety. The instruction for use for the LumiHeal Gel includes information of gel shelf-life and instructions on the gel preparation, conjunction use with the lamp and its removal.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a phototherapy device for reducing the appearance of acute post-surgical incisions and the measures necessary to mitigate these risks.

Table 11. Identified Risks to Health and Mitigation Measures

Identified Risks to Health	Mitigation Measures
Adverse tissue reaction	Biocompatibility evaluation
Infection	Sterility testing Shelf life testing Labeling
Thermal damage and ocular injury	Non-clinical performance testing Thermal safety testing Labeling
Shock or burns from electrical malfunction or electromagnetic interference with other devices	Electrical safety testing Electromagnetic compatibility (EMC) testing Software verification, validation, and hazard analysis
Use error that may result in injury	Labeling Software verification, validation, and hazard analysis

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the phototherapy device for reducing the appearance of acute post-surgical incisions is subject to the following special controls:

(1) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. Testing must include the following:
   (i) Verification and validation testing of the spectrum and power intensity of the light source;
   (ii) Heat dissipation from the area following device application; and
   (iii) Biophotonic properties of the photoconverter gel, including radiant fluence (transmitted light and fluorescence) delivered through the photoconverter gel by the device.

(2) The patient-contacting components of the device must be demonstrated to be biocompatible.

(3) Performance data must evaluate the sterility of the patient-contacting components of the device.

(4) Performance data must support the shelf life of the photoconverter gel by demonstrating continued sterility and functional performance over the identified shelf life.
(5) Performance testing must demonstrate the electromagnetic compatibility, electrical safety, and thermal safety of the device in the intended use environment.
(6) Software verification, validation, and hazard analysis must be performed for any software components.
(7) Labeling must include the following:
    (i) A summary of the device technical specifications, including light wavelength, irradiance and application area;
    (ii) Warnings for ensuring eye safety, including use of protective eyeglasses used for both the operator and the patient; and
    (iii) A shelf life for the photoconverter gel.

BENEFIT-RISK DETERMINATION

The risks of the device are based on nonclinical laboratory studies as well as data collected in a clinical study described above.

A total of fourteen adverse events were reported. They concerned eleven patients, representing 26.2% of the total number of patients in the ITT population. There were no specific adverse event trends to report. None of these adverse events was considered as related to the study application (LumiHeal™) according to the investigators. Four events (breast discomfort, erythema and pruritus) were considered as related to Silicone sheets.

The probable benefits of the device are also based on nonclinical laboratory studies as well as data collected in a clinical study as described above.

The mean results of effectiveness assessments from the blinded evaluators using POSAS scale demonstrate there was at least a 1 point improvement in each sub-category (Vascularity, Pigmentation, Thickness, Relief and Surface area) for the subject device. And the mean 1 point improvement was also seen in the control, Silicone group. The validation data was provided for using the POSAS scale on photographs of closed surgical incisions. Therefore, a benefit has been demonstrated with the use of the device on scars from closed surgical incisions.

PATIENT PERSPECTIVES

Patient perspectives considered for the Klox Biophotonic LumiHeal System during the review included:

- Patients were asked at several timepoints during the administration and follow-up periods if they were satisfied with the application with LumiHeal and Silicone, and on the appearance of the wound/scar. The questions were as follows:
    - How satisfied are you with the care received (LumiHeal™ or Silicone)?
    - How satisfied are you with the steps required (LumiHeal™ or Silicone)?
    - How easy was the treatment to receive / manage (LumiHeal™ or Silicone)?

- How satisfied are you with the appearance of your wound (LumiHeal™ or Silicone)?

The results showed patients were satisfied with the LumiHeal application option.

BENEFIT/RISK CONCLUSION

In conclusion, given the available information above, for the following indication statement:

> The Klox Biophotonic LumiHeal™ System is indicated to provide blue light and fluorescent light energy for use on post-surgical incisions for scar management. The System is intended to be used in FST I-IV female patients 22 years and over.

The probable benefits outweigh the probable risks for the Klox Biophotonic LumiHeal System. The device provides benefits and the risks can be mitigated by the use of general controls and special controls.

CONCLUSION

The De Novo request for the Klox Biophotonic LumiHeal System is granted and the device is classified as follows:

> Product Code: QPE
> Device Type: Phototherapy device for reducing the appearance of acute post-surgical incisions
> Regulation Number: 21 CFR 878.4880
> Class: II