DE NOVO CLASSIFICATION REQUEST FOR
VIRULITE COLD SORE MACHINE

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Light based energy source device for topical application.** The device emits light energy at near infrared spectrum and is applied externally to the surface of herpes simplex labialis lesions on or around the lips.

NEW REGULATION NUMBER: 21 CFR 878.4860

CLASSIFICATION: II

PRODUCT CODE: OKJ

BACKGROUND

DEVICE NAME: ViruLite Cold Sore Machine (ViruLite)

SUBMISSION NUMBER: DEN090012 (K083767)

DATE OF DE NOVO: June 25, 2009

CONTACT: Virulite LLC
27631 Vista De Dons
Capistrano Beach, CA 92624

INDICATIONS FOR USE

The ViruLite Cold Sore Machine is indicated for shortening the time to healing of herpes simplex labialis lesions on or around the lips with time to healing defined as the time to patient described re-epithelialization.

LIMITATIONS

The ViruLite device is available as an over-the-counter (OTC) device and is intended for use by a single individual. As an additional measure to ensure that the end users of this device report all adverse events that may occur with its usage, the labeling states the following:

> "If you experience any of the following adverse events since using the device - lack of effectiveness, spread or worsening of herpes infection, blistering and skin pigmentation - then please contact MedWatch at 1-800-332-1088 or the internet at: https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm. "

Limitations on the ViruLite device are also achieved through the following statements included in the User Guide:

> *Do not use the ViruLite except for the treatment of cold sores on or around the lips. This device is not to be used for other skin conditions especially genital herpes. The effect of the device for cold sores in other areas has not been tested and the risk is unknown.*
>
> *Do not use the ViruLite to prevent cold sores on or around the lips area. The device is not intended to prevent cold sores. The safety of the device for the prevention of cold sores has not been tested and the risk is unknown.*
>
> *Virulite has not been studied in patients who have been diagnosed by their physician as having difficulty in fighting infections (immunocompromised) and should therefore not be used by these patients.*
>
> *ViruLite has not been evaluated on or around the lips of people with darker pigmented skin. If you have darker pigmented skin you may use the device, however stop using the device immediately if you encounter any problems or changes to your skin.*
>
> *Do not move the ViruLite from one lesion to another without cleaning and disinfecting the device between uses. The effect of moving the device between lesions without cleaning and disinfection has not been tested and there is a risk that you may spread the virus.*

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

DEVICE DESCRIPTION

The ViruLite is a solid state opto-electronic device that emits a controlled quantity of 1072nm +/- 12nm peak wavelength near infrared light for a period of approximately 3 minutes. The maximum peak light intensity across the treatment surface is 20mW/cm^2. The light output and

duration are monitored by a microprocessor. The power source is a standard alkaline 9V battery, which is replaceable. The tip of the device that contacts the patient is made out of Acrylonitrile Butadiene Styrene (ABS).

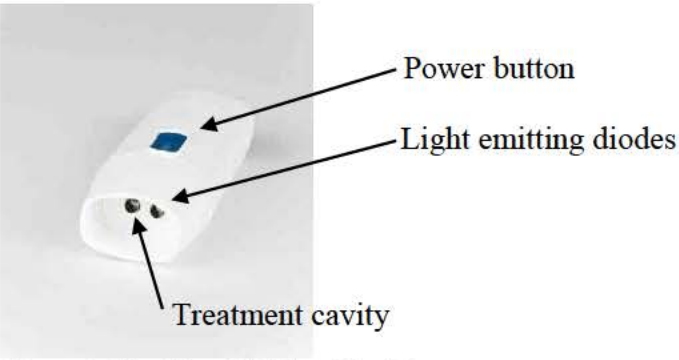

Figure 1: ViruLite Cold Sore Machine

Treatment with the ViruLite is commenced at the first symptoms of a cold sore 3 times a day with 4 hours in between each treatment for 2 consecutive days. The treatment area is approximately 7cm^2. There are 2 light emitting diodes (LEDs) in the treatment area. The light within the device is activated by the ON button and automatically powers down after the preprogrammed treatment time (3 minutes). The device is designed for external, limited duration skin contact in an environment free from fluids and is provided non-sterile. The LEDs do not come in direct contact with the patient based upon the design of the device.

The software for the ViruLite device is designed to monitor ON button press by users, monitor ON button and near infrared LED control during treatment cycle and perform a 3-minute treatment cycle.

The device is for OTC use and single patient use as described in the patient and box labeling.

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The only patient-contacting component of the ViruLite is comprised of Acrylonitrile Butadiene Styrene (ABS).

The raw material contained in the patient-contacting component of the ViruLite was evaluated with respect to its intended use per ISO 10993-1:2003. The raw material was evaluated for cytotoxicity (ISO 10993-5), irritation and sensitization (ISO 10993-10). This was found acceptable because the ViruLite is used externally and ABS is a widely used material for products in medical use.

STERILIZATION/SHELF LIFE/REUSE

The ViruLite is not provided sterile, and sterilization for this use is not necessary because the device is not being used in a sterile environment. The ViruLite does not have a stated shelf life. Based on the nature of the components, the absence of a shelf life is acceptable.

Because the casing of the ViruLite does come in contact with the patient's lips and is intended for reuse by a single patient with herpes simplex labialis lesions, the Instructions for Use include sufficient cleaning and disinfection instructions to mitigate the risks of infection and transmissibility between uses.

Cleaning and disinfection validation data to verify the effectiveness of the cleaning and disinfection instructions are required prior to marketing the ViruLite, otherwise the device is considered to be misbranded and adulterated.

ELECTROMAGNETIC COMPATIBILITY AND ELECTRICAL SAFETY

The ViruLite was subjected to electromagnetic compatibility (EMC) and electrical safety testing performed in accordance to EN60601-1-2: 1993 and EN60601-1:1993.

SOFTWARE

The software for the ViruLite device is designed to monitor ON button press by users, monitor ON button and near infrared LED control during treatment cycle and perform a 3-minute treatment cycle.

The software for the ViruLite device presents a minor level of concern based on answers to the questions listed in FDA's *Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices* (May 11, 2005).

In the software requirements specification, the requester provides the general requirements and the functional requirements for traceability. The software design description provides the high level design of the ViruLite software application and firmware. The requester provided the traceability matrix and showed the traceability by testing the functional requirements through the software requirements specifications, verification/validation tests and risk analysis. The requester provided the verification and validation documentation. The documentation provides sufficient evidence that the specified requirements have been fulfilled.

All expected elements of software documentation per FDA's *Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices - Guidance for Industry and FDA Staff* are included in the request and in sufficient detail to provide reasonable assurance that the software performs as intended and all software-related risks have been adequately mitigated.

PERFORMANCE TESTING – BENCH TESTING FOR OCULAR SAFETY

The ViruLite was subjected to testing performed in accordance with IEC 64721:2008 Photobiological Safety of Lamps and Lamp Systems to establish ocular safety. ViruLite was tested while operating under the worst case failure mode, which is continuous operation of the LEDs for 8 hours.

The requester then took the measured exposure duration limit of the ViruLite and compared it to the exposure duration limit described in the IEC 64271:2008 standard to establish ocular safety. The exposure limit in IEC 64271:2008 is 2556097 $W/m^3/sr$. Although this is not an FDA recognized consensus standard, the exposure duration limit described in this standard is an acceptable limit because experiences with low level light devices within the near infrared spectrum with similar technical parameters and exposure limits have lead us to conclude that this exposure limit and test method is acceptable to determine ocular safety.

The requester stated that based on testing in accordance with IEC 64271:2008 at the worse case failure mode the exposure limit of the ViruLite is (b) (4) $W/m^3/sr$. This is below the exposure limit in IEC 64271:2008 and therefore deem acceptable in establishing ocular safety.

SUMMARY OF CLINICAL INFORMATION

To support the De Novo request, the requester provided usability testing as well as clinical data set information comparing the device to a placebo or the standard of care

SIMULATED USE (USABILITY) TESTING

The ViruLite device is intended for over-the-counter (OTC use. Consequently, to ensure that the ViruLite device could be used according to the proposed labeling and instructions for use, the requester conducted two usability studies.

At first, the requester completed their usability analysis on (b) (4) subjects, which was determined to not be a sufficient sample size to demonstrate generalizability to the intended patient population. The requester, therefore, conducted a second study on (b) (4) additional subjects to determine the usability and labeling comprehension of the ViruLite device. The subjects in both studies were given the contents of the proposed labeling. This was followed by a series of questions that were asked to determine the subjects' understanding of the appropriate action to take with the ViruLite device in several hypothetical scenarios. The responses to the questions were recorded and analyzed to determine whether the information presented on the box label and instructions for use were comprehensible to the target population. In the first study (b) (4) out of (b) (4) and in the second study (b) (4) out of (b) (4) subjects ((b) (4) subjects did not complete due to withdrawing from the study) correctly answered the questions presented. Therefore, the combined data (47 out of 49 subjects) in the two usability studies were acceptable to

address the labeling comprehension and usability of the ViruLite device for the OTC patient population.

The labeling allows for use of the ViruLite device for ages 16 years or older. In the clinical data sets, the ViruLite device was tested in patients 20 years or older to demonstrate a reasonable assurance of effectiveness and safety. Because the usability study was conducted on subjects 16 years of age or older and it was determined to include 16 year old patients for the following reasons: (i) patients 16 and older demonstrated an ability to comprehend and follow instructions written for OTC use within the usability study; and (ii) from a clinical perspective, it was determined that there is little difference in expected physiological response in response to patients between the ages of 16-19 and patients older than 20 years.

CLINICAL PERFORMANCE DATA

To support the De Novo request, the clinical performance data was provided from two main sources that included: 1) individual patient data (n = 95, 48 active arm) based on the requester conducting a double-blind, placebo-controlled, randomized clinical trial; and, 2) the requester's submission of four data sets. These data sets provided additional clinical evidence for using the ViruLite device and/or another related device using a similar wavelength and treatment parameters to the final device. Collectively these 5 data sets were used to support both device effectiveness (the four data sets) and safety (the four data sets and the requester's clinical data set).

Through utilization of data from these 5 studies it was determined that the clinical benefit outweighed any known risks. Therefore, FDA's granting of the De Novo request for the ViruLite for its intended use is based on an overall assessment of the clinical experience as demonstrated in the five studies.

The primary endpoint used in the evaluation of all studies provided was "time to healing" (subject described re-epithelialization) from the time of onset of the cold sore (as described by the subject).

The individual patient data from the requester's randomized data set in the De Novo request included a total of 95 subjects, ages 20 years and above, randomized either to control (placebo) or active (treatment with the ViruLite) arms. Of these 95 subjects, forty-eight (48) subjects were originally randomized to the active (treatment) arm and used to evaluate safety of the VireLite device. In the active (treatment) arm, 8 subjects were lost after the first follow-up visit and an additional 4 subjects were lost during the 3 month follow-up period. Of the 47 subjects randomized to control, 1 was lost after the first follow-up visit, and an additional 5 subjects were lost to follow-up during the 3 month follow up period.

It should be noted that in an evaluation of this data set, there were some concerns over data collection, missing data, data inconsistencies, and the interpretability of this dataset. Consequently, the results of the randomized data set did not by itself demonstrate a reasonable assurance of effectiveness

However, in a safety assessment of the requester's data set, there were no major long-lasting complications (there was some mild blistering, burning or redness in some patients) associated with the ViruLite device in this clinical data set. Further, similar low risk complications have been observed with other light-based technologies and in the four submitted data sets by the requester. Therefore, FDA has determined that these low risks can be appropriately mitigated through the final labeling and other measures identified as special controls.

Due to the limitations of the initial randomized dataset provided above to determine device efficacy, the requester as noted above, submitted a total of four data sets for Agency review describing the use of ViruLite and similar devices on subjects who presented with herpes simplex labilis.

These studies were therefore used to support the effectiveness of the ViruLite device as well as confirming a low risk profile as seen in the requester's clinical trial. The four data sets (Dougal/Kelly data set, Dougal/Haslam data set, Hargate, and Lee/Hargate/Dougal data set) each identified a clinical benefit (a difference in healing - subject described re-epithelialization) when comparing a reduction in healing time of the placebo and the active device.

The data from each of these trials were summarized in Table 1 below

Table 1: Additional Data Sets to Support Effectiveness

Trial	Design	Protocol	Data set Size	Healing Time in Days (Device)	Healing Time in Days (Placebo)	Endpoint
Dougal and Kelly 2001[1]	Double Blind, Placebo: 3 Arms with Acyclovir	Single Application vs Acyclovir or Placebo cream or Placebo light. 36 hour initiation(within 36 hours of the onset of symptoms)	56	4.3 +/- 1.8	8.5 +/- 1.8	Healing Time was determined by self assessment
Dougal and Haslam 2004[2]	Double Blind vs. Placebo Device	Up to 2 days, up to 3 TX. 36 hour initiation (within 36 hours of the onset of symptoms)	54	5.1 +/- 3.1	6.8 +/- 2.8	Same
Hargate 2006[3]	Double Blinded Placebo	Same (as Dougal Haslam 2004)	32	6.3 +/- 3.0	9.4 +/- 4.6	Same
Lee, Hargate and Dougal 2004[4]	Double Blinded Placebo	Same (as Dougal Haslam 2004)	87	5.9 +/- 2.6	7.9 +/- 0.3	Same

1. G Dougal and P Kelly. "A pilot study of treatment of herpes labialis with 1072 nm narrow waveband light". *Clinical and Experimental Dermatology*. 2006.
2. G Dougal and J Haslam. 2004 data set.

3. G Hargate. “A randomized double-blind study comparing the effect of 1072-nm light against placebo for the treatment of herpes labialis” *Clinical and Experimental Dermatology*. 2006.
4. G Dougal, G Hargate, SY Lee. 2004 data set.

LABELING

The ViruLite device complies with the labeling requirements under 21 CFR 801 and the recommendations within FDA’s *Guidance on Medical Device Patient Labeling* (2001).

The ViruLite device is available as an OTC device and is intended for use by a single individual.

As an additional measure to ensure that the end users of this device report all adverse events that may occur with its usage, the labeling states the following:

> “If you experience any of the following adverse events since using the device- lack of effectiveness, spread or worsening of herpes infection, blistering and skin pigmentation - then please contact MedWatch at 1-800-332-1088 or the internet at: https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm. “

RISKS TO HEALTH

Table 2 below identifies the risks to health that may be associated with the use of a light based energy source device for topical application and the measures necessary to mitigate these risks.

Table 2: Identified Risks to Health and Mitigation Measures

Identified Risk	Mitigation Measures
Redness and discomfort	Clinical performance testing Usability testing Labeling
Burns and blisters	Clinical performance testing Usability testing Labeling
Adverse tissue reaction	Biocompatibility evaluation
Infection/transmissibility	Labeling Cleaning and disinfection validation Usability testing
Electrical shock	Electrical safety testing Labeling
Electromagnetic incompatibility	Electromagnetic compatibility testing Labeling
User error	Usability testing Labeling
Ocular injury	Labeling Non-clinical performance testing for ocular safety

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the light based energy source device for topical application is subject to the following special controls:

1. The technical parameters of the device, including wavelength, treatment time, treatment area, energy density, spot size, and power, must be characterized.

2. The cleaning and disinfection instructions for the device must be validated.

3. The device must be demonstrated to be biocompatible.

4. Performance testing must validate electromagnetic compatibility (EMC), ocular safety, and electrical safety of the device.

5. Labeling must direct end-users to contact the device manufacturer and MedWatch if they experience any adverse events when using this device.

6. Labeling must include specific information pertinent to use of the device by the intended patient population and the treatment regimen.

7. Simulated use testing must include information from a usability, label comprehension and self-selection study to demonstrate that the device can be used by the intended patient population without any assistance.

8. Clinical data must show adequate reduction in time to healing and assess risks of redness, discomfort, burns, and blisters.

BENEFIT/RISK DETERMINATION

To determine the benefit FDA used the non clinical information submitted by the requester as well as the four data sets in Table 1 that are in the clinical section above. To determine the risk, FDA used the data from the five clinical data sets (the requester's clinical data set and the four data sets in Table 1). The primary risks (adverse events) in the data included: 1) potential redness; and, 2) some discomfort with application. Incorrect use or user error also led to a small number of minor (transient) burns and blistering. No serious or long lasting complications were reported. Therefore, FDA has evaluated the risk as low.

In summary, based on the submitted data (pre-clinical and clinical) the device provides a reasonable assurance of a clinical benefit, and the low device risks can be mitigated by the use of general and special controls, including the submitted final labeling for the indicated population.

CONCLUSION

The De Novo request for the ViruLite is granted and the device is classified under the following:

Product Code: OKJ
Device Type: Light based energy source device for topical application
Class: II
Regulation: 21 CFR 878.4860