EVALUATION OF AUTOMATIC CLASS III DESIGNATION (DE NOVO) FOR ZAP-IT!

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Limited output transcutaneous piezoelectric stimulator for skin reactions associated with insect bites. A limited output transcutaneous piezoelectric stimulator for skin reactions associated with insect bites is a device intended to alleviate skin reactions associated with insect bites via cutaneous, piezoelectric stimulation at the local site of the bite.

NEW REGULATION NUMBER: 21 CFR 882.5894

CLASSIFICATION: II (**Exempt** from premarket notification review, subject to the limitations in 21 CFR 882.9)

PRODUCT CODE: OSG

BACKGROUND

DEVICE NAME: Zap-It!

DE NOVO REQUEST: DEN100024

DATE OF DE NOVO REQUEST: September 8, 2010

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REQUESTOR'S RECOMMENDED CLASSIFICATION: II

INDICATIONS FOR USE

Zap-It! is indicated for temporarily reducing the itching caused by mosquito bites.

Limitations

The Zap-It! device is available as an over-the-counter (OTC) device.

Please refer to the package insert for a complete list of Warnings and Precautions

regarding the appropriate use of the Zap-It! device. The following statements are limitations of the device explicitly noted in the labeling:

Warnings

Do not use this device if you have a cardiac pacemaker, implanted defibrillator, or other implanted electrical device. Such use could cause electric shock, burns, or electrical interference.

Do not use Zap-It! in the presence of electronic monitoring equipment (e.g., cardiac monitors, ECG alarms), which may not operate properly when you are using the product.

Do not apply stimulation over open wounds or rashes, or over swollen, red, infected, or inflamed areas or skin eruptions (e.g., phlebitis, thrombophlebitis, varicose veins).

Do not use over viral lesions, as safety studies have not been performed to determine the effect of the Zap-It! on viral lesions; therefore, the effects are unknown.

Do not use on flammable materials. It may cause them to burn and burn your skin.

Zap-It! should not be used after applying insect repellent until it has fully dried to the touch, as repellant may be flammable and cause skin burns if ignited.

For external use only. Do not apply the Zap-It! inside the mouth or other body cavity as pain or injury may occur.

Do not apply the Zap-It directly to your eyes as this could cause damage to your eyesight.

Do not use the Zap-It! in situations where electrical stimulation could put you at risk of injury, such as while driving a car or operating machinery.

Cutaneous burns are a danger when applying repeated electrical stimulus to the skin in rapid succession, and the repeated excessive use of the device on bites has not been studied.

Precautions

Do not use Zap-It! to remove the toxins or infection associated with mosquito bites. Zap-It! was only found in clinical studies to temporarily remove the itching. If you believe your mosquito bite is infected, seek medical attention.

Do not use in the bath or shower as water may cause the device to not properly function.

The safety and effectiveness has not been established in neonates, infants and children.

Do not apply Zap-It! to your lips as this may cause pain.

Dispose of this device responsibly at the end of its useful life.

Discontinue use if irritation occurs.

Keep out of the reach of children.

Use caution if stimulation is applied over areas of skin that lack normal sensation.

The Zap-It! is a medical device. Do not let children play with Zap-It!.

CONDITIONS OF EXEMPTION

Limited output transcutaneous piezoelectric stimulator for skin reactions associated with insect bites are appropriate for exemption from premarket notification, subject to the limitations of exemptions identified in 21 CFR 882.9, because the applicable special controls and general controls provide reasonable assurance of safety and effectiveness, if device manufacturers follow the special controls requirements. Examples of exceeding the limitations of exemption are where the output (absolute charge delivered or current) exceeds the specifications for this device, the indications is for something other than itching or the indications specify bites other than insect bites.

Exemption from the requirement of premarket notification for limited output transcutaneous piezoelectric stimulator for skin reactions associated with insect bites does not mean that these devices would be exempt from any other statutory or regulatory requirements, unless such exemption is explicitly provided by order or regulation. FDA's proposal to exempt these devices from the requirement of premarket notification [510(k)] is based, in part, on the assurance of safety and effectiveness provided by other regulatory controls, such as current good manufacturing practice requirements (21 CFR part 820) and the identified special controls.

DEVICE DESCRIPTION

The Zap-It! is a hand held device, consisting primarily of housing, a push button (which the user depresses to excite the piezoelectric crystal), a "Piezo unit" (containing piezoelectric crystal) and electrical output terminals (placed flush to the user's skin) intended to deliver electrical current to the skin. Please refer Figure 1 below for a graphical representation of the device:

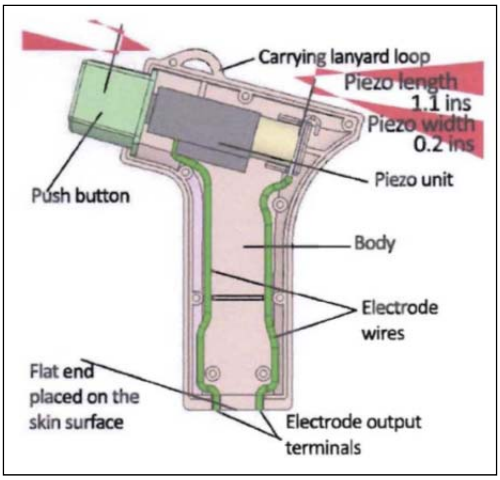

Figure 1 - Graphical Representation of the Device

The user of the device places the end of the device containing the electrode output terminals (the end of the device opposite the push button) flush against the skin, at the site of the mosquito bite. The push button is manually depressed, which mechanically deforms the piezoelectric crystal, and electrical charge (high voltage, low amperage) travels via the electrode wires to the skin. Electrical charge may reach the skin via electrical conductive channel between the electrode terminals and skin, or electrical conductive channel through a small air gap to the skin (electrical spark). The deposition of the charge in the skin is intended to reduce the itch associated with the underlying mosquito bite.

The user may repeat activation of the device (a maximum of five activations per bite) until the mosquito bite itch has been satisfactorily reduced; however, the user is also instructed that repeated use at the same site increases the risk of mild cutaneous burns.

The device is designed for external, limited duration intact skin contact in an environment free from fluids and is provided non-sterile.

The device contains no software.

The Zap-It! Device is for over-the-counter (OTC) use, as described in the package insert.

SUMMARY OF PERFORMANCE TESTING

Characterization of Electrical Output (Oscilloscope Tracings)

To characterize device electrical output, oscilloscope tracings of the output were provided, under loads of 500, 2000, and 10,000 ohms to simulate the load presented by dry skin, while using a controlled and repeatable pressure to activate the piezoelectric element. Oscilloscope tracings were also provided under a load of 50 ohms to simulate the load presented by wet skin. The device output, as characterized by oscilloscope

tracings measured in open circuit, was 13 kV, 0.7 mA, and 20 µS pulse duration.

Performance Testing, Mechanical Failure (or Degradation)

The sponsor provided testing which evaluated the ability of the device to confer charge after 5000 device actuations. This testing showed that the device still conferred charge, though after 5000 actuations, a 34% decrease in measured open circuit voltage was observed.

Biocompatibility Analysis

The patient-contacting material is a specific acrylonitrile butadiene styrene (ABS). Justification was provided supporting biocompatibility of this material for an externally-contacting device.

Human Performance Testing

The effect of the device on mosquito bite itch (device benefit) was evaluated in a clinical trial in which 53 healthy subjects 18-65 years of age with a history of mosquito bite reaction but with no active skin lesions were enrolled.

Study Design

Subjects were randomized 1:1 to active treatment (n = 27) versus placebo (n = 26). Each subject received a single mosquito bite under controlled conditions on the volar surface of the non-dominant forearm. Subjects were then instructed to test the device according to package instructions.

The sham (control) device was identical in appearance and function to the device, including the generation of an electrical discharge from piezoelectric crystals activated through mechanical stress. However, the sham device contained false electrical wires that did not transmit the electrical charge to the skin surface.

Itching was assessed using a visual analog scale (VAS) ranging from 0 (no itching) to 100 (severe itching). A mosquito bite was induced at t=0. A baseline assessment was made at t=5 minutes after the mosquito bite and prior to device use.

Assessments of itching were made following device/sham use at 15, 25, 40 minutes and 1, 2, 3, 4, 6, and 24 hours after the mosquito bite. These were compared to the baseline assessment made 5 minutes after the mosquito bite and prior to device use.

The primary effectiveness outcome was a responder analysis defined as the proportion of subjects whose itching at t=15 minutes decreased 40% relative to the baseline itching at t=5 minutes using the VAS in each study arm.

The key secondary outcome measure was an assessment of the length and width of edema (i.e., swelling of the erythematous area) associated with an individual mosquito bite.

Results

Both the active (test) and placebo groups had similar baseline VAS scores for itching, with each group demonstrating a decreasing score over time. The primary endpoint was based on an individual success criterion of a 40% or greater relative decrease in Degree of Itching on the VAS from t=5 minutes to t=15 minutes. Out of 27 test subjects, 19 met the success criterion. Out of 26 placebo subjects, 3 met the success criteria. The difference in responder rates between the two study arms was statistically significant ($p<0.05$). There was an improvement in the reported mean VAS score for the active group compared to the placebo group following application of the device as illustrated in Figure 2 below. The mean VAS at baseline for each study group was very similar. The differences of the mean VAS between study groups were found to be statistically significant using t tests for two independent samples ($p<0.05$) at all time points after the baseline measurement at t=5 minutes.

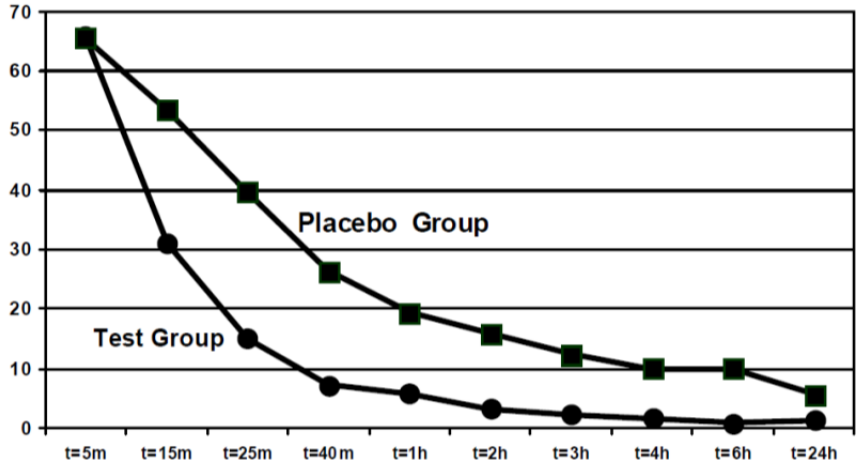

Figure 2 – Mean VAS Scores from t=0 to t=24h

Both the active and placebo groups had similar baseline erythematous area sizes; slightly more edema was observed in the active group but scores were similar at the final 24-hour assessment point. This observed difference was not statistically significant.

Subjects were monitored for 24 hours and no adverse events were noted.

Based on the similarities of skin between adults and adolescents, the data collected on adult population was extrapolated to justify the safe and effective use of the device on the adolescent population.

LABELING (PACKAGE INSERT)

To mitigate concerns regarding cutaneous burns, the following instruction is included in the labeling:

Press the button a maximum of 5 times per mosquito bite.

To mitigate concerns regarding mechanical failure (or degradation), the following statement is included in the labeling:

The device's effectiveness will, however, degrade over time. If after several (e.g., 1,000) uses, you no longer feel the slight pinching or prickling sensation when you activate the device or you no longer get relief from the mosquito bite when using the device, it is time to dispose of the device and purchase a new one.

To mitigate concerns regarding interference with implanted and patient care devices, the following warnings are included in the labeling:

Do not use this device if you have a cardiac pacemaker, implanted defibrillator, or other implanted electrical device. Such use could cause electric shock, burns, or electrical interference.

Do not use Zap-It! in the presence of electronic monitoring equipment (e.g., cardiac monitors, ECG alarms), which may not operate properly when you are using the product.

To mitigate concerns regarding damage to sensitive tissues of the body, the following warnings are included in the labeling:

For external use only. Do not apply the Zap-It! inside the mouth or other body cavity as pain or injury may occur.

Do not use over viral lesions, as safety studies have not been performed to determine the effect of the Zap-It! on viral lesions; therefore, the effects are unknown.

Do not apply the Zap-It directly to your eyes as this could cause damage to your eyesight.

Do not apply Zap-It! to your lips as this may cause pain.

To mitigate concerns regarding infection and damage to sensitive tissues, the following contraindication is included in the labeling:

Do not apply stimulation over open wounds or rashes, or over swollen, red, infected, or inflamed areas or skin eruptions (e.g., phlebitis, thrombophlebitis, varicose veins).

To mitigate concerns regarding ignition of flammable substances, the following warnings are included in the labeling:

Do not use on flammable materials. It may cause them to burn and burn your skin.

Zap-It! should not be used after applying insect repellent until it has fully dried to the touch, as repellant may be flammable and cause skin burns if ignited.

To mitigate concerns regarding the lack of treatment of other medical conditions that are not intended to be treated with this device, the following precautions are included in the labeling:

Do not use Zap-It! to remove the toxins or infection associated with mosquito bites. Zap-It! was only found in clinical studies to temporarily remove the itching. If you believe your mosquito bite is infected, seek medical attention.

Furthermore, regarding the above concern, instructions are included in the labeling for the user to correctly identify mosquito bites.

To mitigate concerns regarding failure to identify the correct population (specifically children), the following precaution is included in the labeling:

The safety and effectiveness has not been established in neonates, infants and children.

To mitigate concerns regarding failure to report malfunctions or adverse events for this OTC device, the following instructions are included in the labeling:

Please inform the manufacturer about eventual problems or malfunctions to reinforce post-market surveillance. If you experience adverse events when using the device, please contact MedWatch at 1-800-332-1088 or the internet at: https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm.

Finally, the output parameters [maximum output voltage (instantaneous), maximum output current (instantaneous), and pulse duration] are included in the labeling:

Maximum output voltage (instantaneous): 13kV
Maximum output current (amperage): 0.7mA
Duration of single discharge: 10 microseconds

The Zap-It! device complies with the labeling requirements under 21 CFR 801 and the recommendations within FDA's *Guidance on Medical Device Patient Labeling* (2001).

The Zap-It! device is available as an OTC device.

Labeling Comprehension Study

The Zap-It! device is intended for over-the-counter (OTC) use. Consequently, to ensure that the device could be used according to the proposed labeling and instructions for use, the sponsor conducted a labeling comprehension study. The study included 15 subjects who were instructed to read the device labeling and subsequently complete a questionnaire. The questionnaire included 24 questions, each of which was intended to test the ability of each subject to understand the use of the device. The results indicated that patients understood the cautionary language and instructions for how to use the device.

RISKS TO HEALTH

Risks to health based on the technological characteristics of the Zap-It! were identified. Table 1 identifies the risks to health that may be associated with the use of limited output transcutaneous piezoelectric electrical stimulators for skin reactions associated with insect bites as well as the methods used to mitigate each risk.

Table 1: Identified Risks to Health and Mitigation Measures

Identified Risk	Mitigation Measure
Cutaneous burns	Characterization of Electrical Output Labeling
Adverse skin reactions	Biocompatibility Assessment
Damage to sensitive tissue (e.g., eyes, lips, inside mouth, open wounds)	Labeling
Infection	Labeling
Burns and other injuries due to ignition of flammable substances which may be used in the same intended use environment (e.g., insect repellant)	Labeling
Interference with implanted devices and other patient care devices	Labeling
Failure to identify correct population and condition	Labeling
Device failure	Non-clinical (Bench) Testing Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the Limited output transcutaneous piezoelectric stimulator for skin reactions associated with insect bites is subject to the following special controls:

1. Appropriate testing to characterize the electrical output specifications of the device (i.e., total charge delivered, maximum instantaneous output current, maximum instantaneous output

voltage, pulse duration, charge density) must be conducted.
2. Mechanical bench testing must demonstrate that the device will withstand the labeled number duration of uses.
3. All elements of the device that may contact the patient must be assessed to be biocompatible.
4. Labeling must include:
    a. Validated instructions which addresses the following:
        i. Identification of areas of the body which are appropriate and not appropriate for contact with the device;
        ii. Whether use of the device in conjunction with flammable materials (e.g., insect repellent) is appropriate;
        iii. Use of the device on or near implanted devices;
        iv. How to identify the correct type of skin condition
    b. Technical parameters of the device [maximum output voltage (instantaneous), maximum output current (instantaneous), and pulse duration].
    c. Language to direct end-users to contact the device manufacturer and MedWatch if they experience any adverse events with this device.
    d. The anticipated number of device uses prior to failure.

BENEFIT/RISK DETERMINATION

The human performance study demonstrated a reduction of itching following mosquito bites when this device was used. No adverse events were reported during the human performance study. Given the limited duration of the output and the small amount of charge delivered to the patient for one actuation, risks associated with the device are low.

Additionally, this device and devices similar to this device are on the market outside of the United States (OUS). A minimal number of adverse events have been reported and no regulatory actions have been taken in OUS jurisdictions in which this device is legally marketed, nor do any reports appear in the literature regarding adverse events for this type of device.

In conclusion, the data support that for the reduction of itch associated with mosquito bites, the probable benefits outweigh the probable risks. These data also suggest that the individual patient's benefit from the device can be variable. In addition, the risks of the device can be mitigated by the use of general and special controls, including the labeling mitigations for the intended population.

CONCLUSION

The *de novo* request for the Zap-It! is granted and the device is classified under the following:

Product Code: OSG
Device Type: Limited output transcutaneous piezoelectric stimulator for skin reactions associated with insect bites
Class: II (exempt from premarket notification, subject to the limitations in 21 CFR 882.9)
Regulation: 21 CFR 882.5894