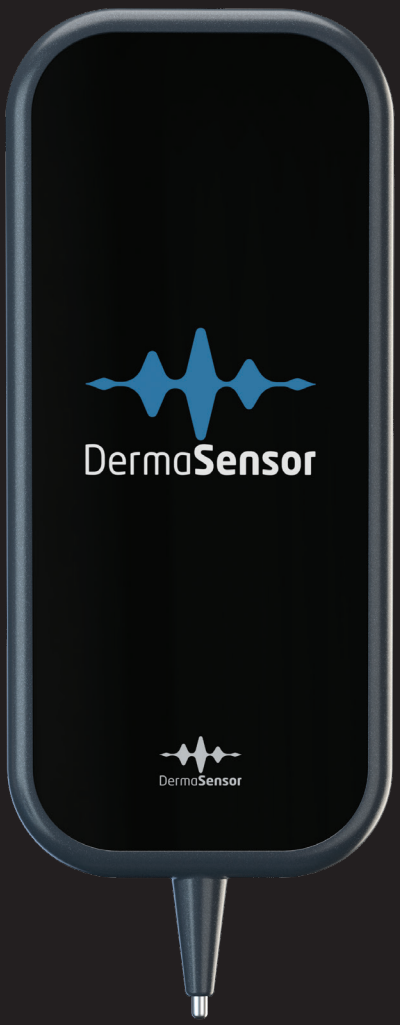


DermaSensor™
INSTRUCTIONS FOR USE

United States

IFU 40-0001 v8

Table of Contents

A. INCLUDED COMPONENTS

(1) Handheld Unit
(1) Base
(1) AC Wall Power Supply and
Regional Power Adapters Blades

B. INDICATIONS FOR USE

The DermaSensor™ device is indicated for use to evaluate skin lesions suggestive of melanoma, basal cell carcinoma, and/or squamous cell carcinoma in patients aged 40 and above to assist in the decision regarding referral of the patient to a dermatologist. The DermaSensor device should be used in conjunction with the totality of clinically relevant information from the clinical assessment, including visual analysis of the lesion, by physicians who are not dermatologists. The device should be used on lesions already assessed as suspicious for skin cancer and not as a screening tool. The device should not be used as the sole diagnostic criterion nor to confirm clinical diagnosis of skin cancer.

C. CONTRAINDICATIONS

There are no known contraindications.

D. WARNINGS

⚠ Do not use for the direct diagnosis of skin cancer.

⚠ Always wear gloves during use (or examination).

⚠ Do not use under direct focused light, such as a surgical or examination light or headlamp.

⚠ Do not point the tip of the Handheld Unit directly at the eye.

⚠ Do not attempt to disassemble, repair, or modify the DermaSensor device in any way.

⚠ Do not immerse the DermaSensor device in liquid.

⚠ Do not put the DermaSensor device in an autoclave or low temperature sterilizer.

⚠ Do not buff or use an abrasive cream cleanser that may scratch and damage the tip of the Handheld Unit.

⚠ Do not simultaneously make contact with the patient while touching or holding the Base or power adapter.

⚠ Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30cm (12 inches) to any part of the DermaSensor device, including cables specified by DermaSensor, Inc.; otherwise, degradation of the performance of this equipment could result.

⚠ DermaSensor performance has not been assessed for the following types of lesions; thus, safety and effectiveness have not been established when:

- Lesion is not accessible to the DermaSensor device Handheld Unit and tip (e.g., inside ears, under nails).
- Lesion is on areas of psoriasis, eczema, acne, or similar inflammatory skin conditions that may impede appropriate DermaSensor device tip placement on the lesion.
- Lesion is greater than 15mm in diameter at the widest point.
- Lesion has a targeted area less than 2.5mm in diameter where the DermaSensor device tip cannot be placed entirely within the border of the targeted area of the lesion.
- Lesion has no contiguous area of at least 2.5mm due to ulceration, erosion or liquid discharge (e.g., blood).
- Lesion is covered by a crust or scale, and lesion surface can not be cleared of crust or scale such that there is a contiguous area of at least 2.5mm of cleared intact skin that is free of any crust, ulceration, erosion or liquid discharge (e.g., blood).
- Lesion is obstructed by foreign matter that can not be non-invasively removed (e.g., tattoo, splinter).
- Lesion is not completely cleared of (i.e., free of any remaining residue) dermoscopy oils, makeup, sunscreen, other topical solutions or powders, markings, and staining treatments (e.g., iodine).
- Lesion is located on acral skin (e.g., sole or palms).
- Lesion is located within 10mm of the eye.
- Lesion is on or adjacent to scars, areas previously biopsied, or areas subjected to any past surgical intervention.
- Lesion is located on mucosal surfaces (e.g. genitals, lips).
- Lesion is located in an area with acute sunburn.

E. PRECAUTIONS

⚠ Caution: United States Federal law restricts this device to sale by or on the order of a physician.

⚠ A complete assessment, including
- the visual evaluation of the lesion,
- clinical considerations such as the patient's ultraviolet light exposure history, and
- the patient and patient's family's skin cancer history

should be considered, per standards of clinical care, in conjunction with DermaSensor results when making a formal clinical determination about a lesion.

⚠ The performance of the device has not been specifically evaluated in patients with increased risk for skin cancer, e.g., inherited or drug-induced photosensitivity; genetic predisposition to melanoma or BCC; immune compromise; or other medical conditions that increase the risk of skin cancer or its metastasis.

⚠ The device is intended to assist in clinical decisions related only to the skin malignancies melanoma (including severely atypical nevi), SCC, and BCC. It has been tested on each of these three common skin cancer types but has not been tested on rare skin cancer types; thus, it should not be used for lesions that are suggestive of malignancies other than melanoma, BCC and/or SCC.

⚠ The device is intended for use on primary lesions only and has not been tested on lesions that are previously biopsied, recurrent, or metastatic; on scars, tattoos, sunburned skin, or within a hairy area (i.e., dense hair on the scalp); or which are located on palms, soles, mucosal surfaces, genitals, ears, within 1 cm of the eye, or under nails.

⚠ Consistent with the lower prevalence of skin cancer in Fitzpatrick skin phototypes IV-VI, less data is available for sensitivity of the DermaSensor device for melanoma in these patients. The decision to refer patients with suspicious pigmented lesions in this group should be primarily based on clinical concern.

⚠ Protect the tip of the Handheld Unit by storing the Handheld Unit in the Base when not in use.

⚠ To maintain optimal device integrity, follow the cleaning and disinfection instructions before and after use.

⚠ Use of accessories, transducers, and cables other than those specified or provided by the manufacturer of this equipment could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.

⚠ Use of this equipment adjacent to or stacked with other equipment should be avoided as it may result in improper operation. If such use is necessary, this equipment, and the other equipment, should be observed to verify that they are operating normally.

⚠ Only use the included components and accessories provided as part of the DermaSensor medical equipment system.

⚠ Connection to IT networks including other equipment could result in previously unidentified risks to patients, operators, or third parties. The user should identify, analyze, evaluate, and control these risks.

⚠ Changes to the IT network (e.g., changes in network configuration, connection of additional items, disconnection of items, update of equipment, upgrade of equipment) could introduce new risks that require additional analysis.

⚠ To avoid EMC disturbances, floors should be wood, concrete, or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.

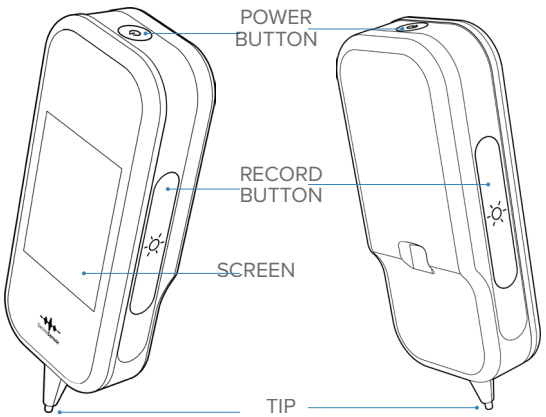
F. PRODUCT OVERVIEW

The DermaSensor™ device is indicated for use to evaluate skin lesions suggestive of melanoma, basal cell carcinoma, and/or squamous cell carcinoma in patients aged 40 and above to assist in the decision regarding referral of the patient to a dermatologist. The DermaSensor device should be used in conjunction with the totality of clinically relevant information from the clinical assessment, including visual analysis of the lesion, by physicians who are not dermatologists. The device should be used on lesions already assessed as suspicious for skin cancer and not as a screening tool. The device should not be used as the sole diagnostic criterion nor to confirm clinical diagnosis of skin cancer.

While the DermaSensor FDA pivotal validation study included 1,579 lesions biopsied by primary care physicians, and a supplemental melanoma validation study was conducted with biopsied lesions in the dermatology setting, note that the device indication for use is non-dermatologist physicians since the FDA's clearance was based on the benefit-risk evaluation for physicians who are not experts in the clinical diagnosis and management of skin cancer.

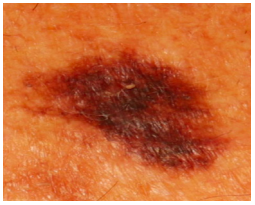
Figure 1
FRONT VIEW OF THE HANDHELD UNIT

Figure 2
BACK VIEW OF THE HANDHELD UNIT

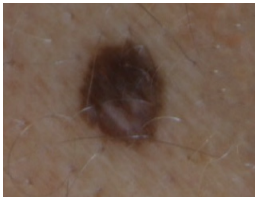


G. INDICATED LESION TYPES AND PERFORMANCE

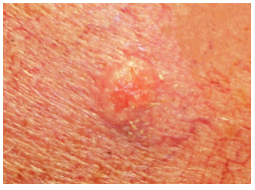
There are three common types of skin cancer and the DermaSensor device has been validated to detect these three cancer types. Melanomas, the most dangerous form of skin cancer, are commonly darkly pigmented lesions that are often evaluated based on their "ABCDE" characteristics: asymmetry, border, color, diameter, and evolution over time. Melanomas tend to have an asymmetric shape, irregular borders, non-homogenous coloration, larger diameters in size and show changes over time. Highly atypical nevi can be considered abnormal lesions and since they sometimes become melanoma, these lesions should also be referred to dermatology and are grouped with the cancerous lesions. Squamous cell carcinomas arise from squamous skin cells and are commonly found on sun exposed skin. These cancers can appear as scaly and often tender patches or plaques. In more serious cases they progress to raised nodules or tumors that will bleed or present with ulceration that does not heal. Basal cell carcinomas can look like many other lesions but often are shiny skin-colored bumps or red scaly areas. When neglected they can often look like large open sores that do not heal over time. These cancers also often occur on sun exposed skin.



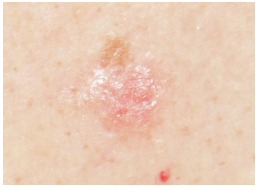
Melanoma: often evaluated using ABCDE (asymmetry, border, color, diameter, evolving), e.g., a changing, irregularly shaped and pigmented lesion often of a larger size than a typical nevus.



Highly Atypical Nevi: often have abnormal clinical features similar to melanoma and can become melanoma in future; these lesions should be referred to dermatology.



Squamous Cell Carcinoma: often scaly and tender patches or plaques and are often raised nodules or tumors that bleed or ulcerate; most commonly found on sun exposed areas.



Basal Cell Carcinoma: can look like many lesions, often a shiny skin colored bump or a red scaly rash-like area or when neglected a large open non-healing sore; occur most often on sun exposed areas.

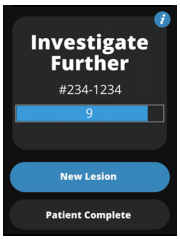
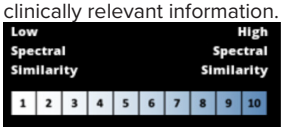
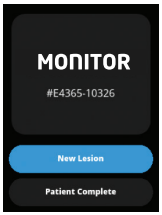
Skin Cancer Type	Sensitivity	Specificity
All Common Skin Cancers (Melanoma, BCC, SCC)	96.3% (209/217)	20.3% (234/1155)
BCC	97.8% (88/90)	15.3% (63/413)
SCC	97.7% (84/86)	15.3% (63/413)
Melanoma	90.2% (37/41)	23.0% (171/742)

Fitzpatrick Skin Types	Sensitivity	Specificity
BCC		
I	100% (7/7)	18.2% (8/44)
II	97.4% (37/38)	16.2% (22/136)
III	100% (35/35)	9.2% (12/131)
IV	100% (2/2)	17.6% (13/74)
V	85.7% (6/7)	32.0% (8/25)
VI	100% (1/1)	0% (0/3)
SCC		
I	90.0% (9/10)	18.2% (8/44)
II	100% (28/28)	16.2% (22/136)
III	100% (19/19)	9.2% (12/131)
IV	100% (18/18)	17.6% (13/74)
V	90.0% (9/10)	32.0% (8/25)
VI	100% (1/1)	0% (0/3)
Melanoma		
I	100% (9/9)	20.9% (14/67)
II	90.9% (10/11)	25.3% (45/178)
III	81.8% (9/11)	20.0% (48/240)
IV	80.0% (4/5)	22.5% (29/129)
V	100% (4/4)	26.7% (31/116)
VI	100% (1/1)	33.3% (4/12)

H. OUTPUT AND RESULTS

The DermaSensor device captures spectra that are generated from the reflectance of photons of light by different cellular and subcellular features (eg., nucleus size, condensed chromatin). The DermaSensor device records spectral signatures of skin lesions and uses a proprietary algorithm that has been developed and validated through clinical studies on thousands of diagnosed lesions to classify an investigated lesion's spectral properties against those of known malignant and benign lesions. The device provides an output of "Investigate Further" or "Monitor", for each assessed lesion and assigns a unique Device Record Number (DRN), which appears with the result of the assessment on the Handheld Unit display.

Output and Results

Output	Results
	**"Investigate Further"** The Handheld Unit will display "Investigate Further" for lesions found to contain certain properties associated with malignant skin lesions, the three most common being melanoma, squamous cell carcinoma, and basal cell carcinoma. **Spectral Score** For lesions with an "Investigate Further" result, the Handheld Unit will display a score from 1 through 10 to indicate the degree of similarity the lesion's spectral recordings are to malignant lesions in studies (the "spectral similarity", e.g., 1 indicating the least similar to malignant lesions and 10 indicating the most similar to malignant lesions). A pivotal clinical trial showed that higher scores had greater positive predictive value for malignancy. However, low scores are still classified as "Investigate further" and should be considered as positive output when the device is used in referral decisions in addition to clinically relevant information. 
	**"Monitor"** The Handheld Unit will display "Monitor" for lesions found to contain recorded properties associated with benign lesions. ***No Spectral Score is shown when the result is "Monitor".***

You can find the most current information and literature on the DermaSensor device performance at DermaSensor.com.

I. CHARGING AND STORAGE

The Handheld Unit is designed to remain charging while seated in the Base whenever not in use.

- Seating the Handheld Unit within the Base for charging and storage protects the Handheld Unit tip.
- The Base should always stay plugged into a standard wall outlet. The Handheld Unit should always be powered on while seated on the Base where it charges wirelessly and automatically calibrates in preparation for use.
- If the Handheld Unit is left powered on outside of the Base for more than 4 minutes, it will automatically power off.
- An LED light located on the Base and the display on the Handheld Unit provide information on the charging status as described in the tables on the next two pages.

Base LED Indicator

Base LED Indicator Light	Indication
LED Light is **OFF.**	The Handheld Unit is not charging because there is no power going to the Base and/ or the Handheld Unit is not seated properly on the Base
LED Light is **SOLID WHITE**.	The Handheld Unit is charging and properly seated on the base for continued storage.

Figure 3
FRONT VIEW OF THE BASE

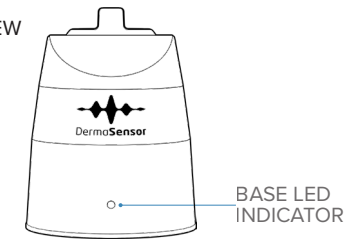
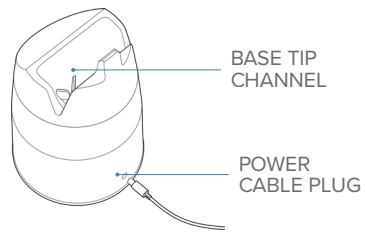


Figure 4
ISOMETRIC BACK VIEW OF THE BASE



Handheld Display

Handheld Display (shown at top right of screen)	**Indication**
Lightning Bolt Icon is ***present*** 	The Handheld Unit is charging.
Lightning Bolt Icon is ***absent*** 	The Handheld Unit is not charging.
Battery Icon is ***WHITE.*** 	The Handheld Unit battery is charged at 20% or more and at a sufficient level for use.
Battery Icon is ***SOLID RED.*** 	The Handheld Unit battery is charged less than 20% and not at a sufficient level for use.
WiFi Icon is ***WHITE*** 	The Handheld Unit is connected to the internet.
WiFi Icon is ***YELLOW WITH AN "X" THROUGH IT*** 	The Handheld Unit is using a WiFi network that is not connected to the internet.
WiFi Icon is ***BLANK*** 	The Handheld Unit is not connected to any WiFi network.
Settings Icon 	Use this icon to access the Settings Menu on the Handheld Unit.

i. To Charge and Store the Handheld Unit

1. Select the proper Regional Power Adapters Blades (*Fig. 6B–6E)* and slide them into the Power Supply (*Fig. 6A)* to lock them into place.
2. Plug the metal barrel end of the power cable into the back of the Base, as shown in *Figure 4,* and plug the Power Supply into a standard wall outlet (100-240 VAC, 50-60 Hz). The Base is now ready to seat and charge the Handheld Unit.
3. Turn on the Handheld Unit by pressing and releasing the Power button on top of the Handheld Unit, as shown in *Figure 1.*
4. Seat the Handheld Unit in the Base to charge and store:
   - Keep the Handheld Unit seated and charging in the plugged-in Base at all times when not in use, as shown in *Figure 5*.
   - Charge until the battery icon indicates the Handheld Unit is fully charged prior to the first use.
   - Charge for at least 15 minutes or until the battery icon indicates the Handheld Unit is fully charged between patients.
5. Monitor the Handheld Unit charging status according to the LED Indicator and the Handheld Display tables in I. CHARGING AND STORAGE on page 8.

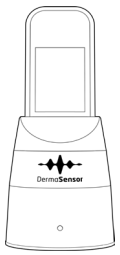


Figure 5

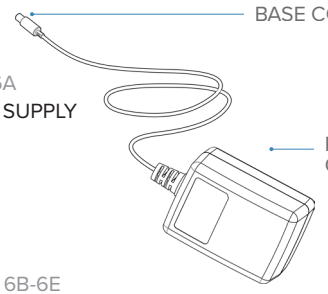
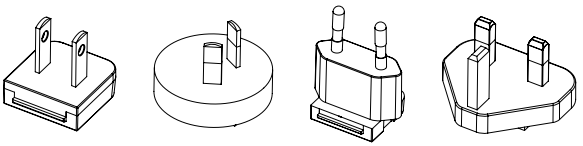


Figure 6A
POWER SUPPLY

Figures 6B-6E
REGIONAL POWER ADAPTERS BLADES

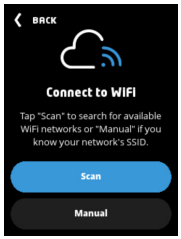


G. WI-FI SETUP AND ACTIVATION

Setup will be required the first time you power on the Handheld Unit. This includes establishing your WiFi connection, registering, and activating your DermaSensor device, selecting the desired language, and checking for updates.

NOTE: *The Base should be connected to power before setting up the DermaSensor device.*

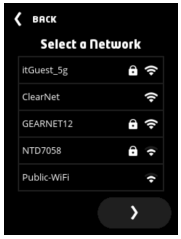
These steps are described below sequentially.



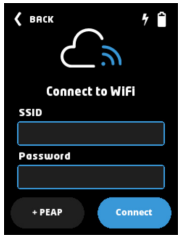
Scan for or enter a wireless network

i. WiFi Setup

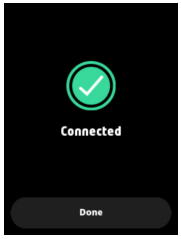
1. Press and release the power button on top of the Handheld Unit to turn it on.
2. Connect to the desired 2.4 GHz WiFi network name (the SSID) by doing one of the following:
   - Press Scan to search all available networks and select a network name (SSID) from the available wireless networks shown.
   - Press Manual to manually enter a private wireless network.
   - ***NOTE:*** *The WiFI network name/SSID for your network can often be located on the wireless router's label or settings. If the SSID cannot be located please contact your wireless network provider/IT personnel.*



Select a network



Confirm selection

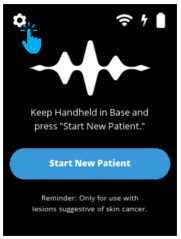


Confirmation screen

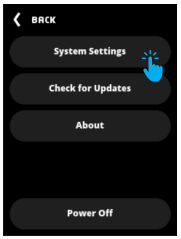
3. Enter the WiFi network's WPA2-Personal password using the on-screen keyboard.
   Select +PEAP for Protected Extensible Authentication Protocol (PEAP) networks.
4. Confirm the wireless network settings.
   - You will be notified of a successful connection after the correct details are entered.
   - You will be prompted to register and activate the DermaSensor device.
     For cybersecurity information and instructions for security, see Guidance and Manufacturer's Declaration — Cybersecurity on page 31.

PEAP Setup

NOTE: *You can always return to update wireless settings by selecting the settings icon in the top-left corner of the home screen and selecting* ***System Settings > WiFi Setup.***



Changing wireless network settings

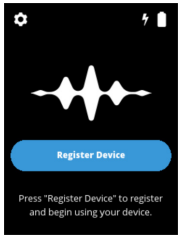


"System Settings"

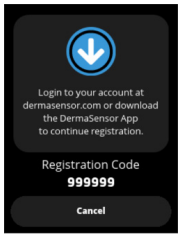
"WiFi Setup"

ii. Register and Activate Device

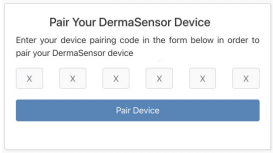
1. Visit www.DermaSensor.com on PC, smartphone or tablet.
2. Select **Login** and enter the account login and password information created during your DermaSensor sign up process.
3. Follow the prompts and enter the one-time use code displayed on the Handheld Unit. The DermaSensor device will activate automatically.
4. Press **Register Device** and the Handheld Unit will display a unique one-time code. This code is time-sensitive and will expire if not entered into your DermaSensor account's Device Activation Prompt shortly after displayed on the DermaSensor device. If your code expires, press Cancel on the Handheld Unit and repeat step 8 to create a new code.

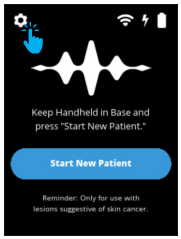


Registration prompt

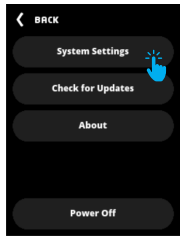


Registration code

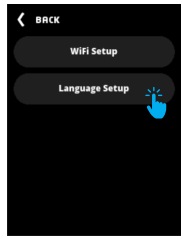




Selecting device language



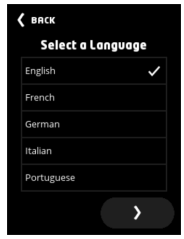
"System Settings"



"Language Setup"

iii. Set Device Language

1. Press the **Settings icon** in the top left corner of the home screen.
2. Select **System Settings > Language Setup.**
3. Select the desired language. DermaSensor device setup is complete.

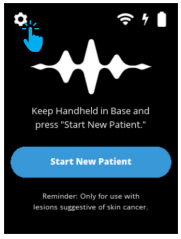


Select a language

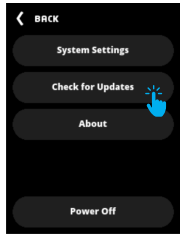
iv. Check for Updates

DermaSensor will provide a notification when an update is available. Check for and install these updates regularly.

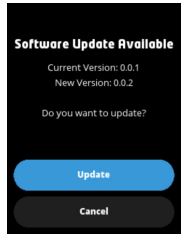
1. Make sure the Handheld Unit is actively connected to a WiFi network and that the white WiFi icon is displayed on the top right of the screen.
2. Select the **Settings icon** in the top-left corner of the Home screen.
3. Select **Check for Updates.**
4. If an update is available, select **Update** to begin the update process.
5. Make sure the Handheld Unit remains powered on, charging in the Base, and unused during the update process. A notification will appear on the Handheld Unit when the update is complete.



Checking for updates



"Check for Updates"



Available update notification

K. CLEANING AND DISINFECTING

i. Prior to First Use, Before and After Use on a Patient

Step 1. Gently wipe the **entire DermaSensor Handheld Unit** (including **touch-screen** and **tip**) using a soft, lint-free cloth dampened with purified water to remove any particles, dirt, or debris.

Step 2. Gently wipe the **entire DermaSensor Handheld Unit** with a lint-free wipe saturated with 70% isopropyl alcohol.

Step 3. Allow the Handheld Unit to air dry completely. ***NOTE:*** *Steps 1-3 may be used on the Base to remove any particles, dirt, or debris.*

Step 4. Use multiple CaviWipes or an equivalent (e.g., KavoWipe) to wipe the **entire Handheld Unit** and **Base** so that it is visibly wet for a minimum of 4 minutes.

Step 5. Gently wipe the **Handheld Unit** and **Base** with a sterile lint-free cloth that has been dampened with purified water to remove disinfectant.

Step 6. Allow the Handheld Unit and Base to air dry completely.

ii. Between Lesions on the Same Patient

Step 1. Gently wipe the Handheld Unit **tip** with a lint-free wipe saturated with 70% isopropyl alcohol *to remove visible and non-visible debris that could obstruct the tip.*

Step 2. Allow the Handheld Unit tip to air dry completely.

iii. After Use on a Patient

Fully clean and disinfect the **DermaSensor Handheld Unit** and **Base** prior to placing the Handheld Unit back into the Base according to Steps 1-6 in the instructions above, *i. Prior to First Use, Before and After Use on a Patient on page 14.*

⚠ Do not use any liquids in the inner recessed areas of the Base or Base tip-channel. *(see Fig. 4 on p. 6)*

⚠ Do not insert anything other than the Handheld Unit into the Base tip-channel. *(see Fig. 4 on p. 6)*

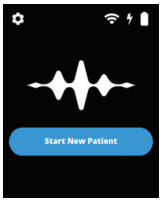
⚠ Failure to clean the DermaSensor device before disinfection can lead to contamination risk.

L. OPERATING THE DERMASENSOR

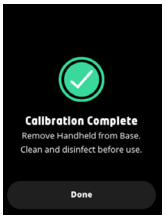
i. Preparing for Use

Follow these steps to properly use the DermaSensor to assess a lesion.

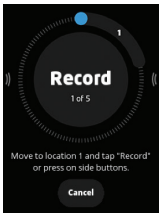
1. Review how to read and interpret the device output and results in H. OUTPUT AND RESULTS on page 6.
2. Verify the DermaSensor is ready for use:
   - The Handheld Unit should be powered on and seated in a charging state on the Base.
   - The Base should display a solid white LED light and the Handheld Unit battery icon should display as solid white. *(K. CLEANING AND DISINFECTING on page 14)*
   - The Handheld unit has been setup with WiFi, and is activated and registered online. *(J. WI-FI SETUP AND ACTIVATION on page 11)*
   - All DermaSensor device updates are installed. *(v. Check for Updates on page 13)*
   - The entire DermaSensor device is fully cleaned and disinfected. *(K. CLEANING AND DISINFECTING on page 14)*
   - The DermaSensor device is located and operated in a patient treatment room with floors made of wood, concrete, or ceramic tile. Floors in this room can be made of other synthetic material if the present relative humidity of the room is 30% or higher. The DermaSensor device is not operated under direct focused light, such as a surgical or examination light or headlamp. (Review D. WARNINGS on page 1 and E. PRECAUTIONS on page 3.)
3. Position the patient in the treatment room and put on disposable gloves. (Review C. CONTRAINDICATIONS on page 1 to ensure lesion is appropriate for assessment.)
4. Completely clean all lesion areas for examination even if no debris is visible.
   - Remove all makeup, sunscreen and other topical solutions, powders, and any residue.
   - If any area of the lesion is crusted or scaled, place the tip to areas of the lesion not covered by the crusts or scale. Removal of crust or scale is advised when such removal does not cause bleeding or any other liquid discharge. If such discharge occurs, device is not indicated for use.
   - Wait for the surface of the lesion to fully dry before use on a lesion.
5. The Handheld Unit must complete a calibration procedure prior to each first use on a patient. The Handheld Unit must be placed in the Base to begin calibration. While the Handheld Unit is in the Base, press the **START NEW PATIENT** button on the Handheld Unit display. The calibration process will start automatically.
   - If the Handheld Unit is removed from the Base before calibration is complete, it will display, “Place device in Base to calibrate”. Return Handheld Unit to the Base and repeat the process until the display indicates calibration is complete.
   - When calibration is complete, the Handheld Unit will display, “Move to location 1 and press record.”



Start New Patient



Calibration Complete



Record

ii. Tip Placements on Lesion

Keep these guidelines in mind when taking lesion recordings:

- Hold the Handheld Unit so the tip touches the lesion at a 90-degree angle to the surface of the lesion (see Figure 7).
- **Touch the Handheld Unit tip to the lesion completely and gently** so that the tip does not significantly depress the tissue (e.g. similar pressure to marking the skin with a marking pen, see Figure 8).

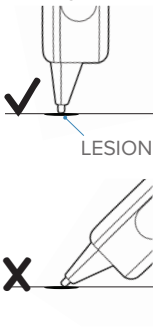


Figure 7

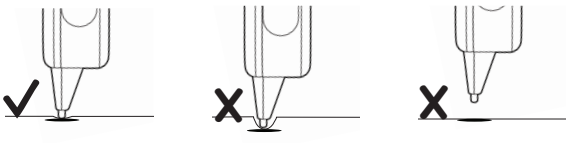


Figure 8

- The Handheld Unit requires five recordings to be made for each lesion on five distinct points within the lesion border including the center of the lesion, as shown in *Figure 9*.

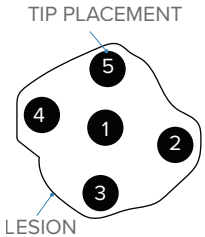


Figure 9

- The placement of the Handheld Unit tip for each recording should be made after careful clinical assessment of the lesion to decide if there are any lesion areas that exhibit especially concerning clinical properties, as the tip placement should be adjusted to include lesion areas that have especially concerning clinical properties as shown in *Figure 10*.

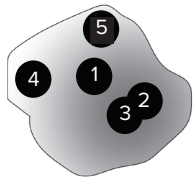


Figure 10

- Avoid recording on or outside the border of the lesion, or on any crusted or scaled area of the lesion, as shown in *Figure 11*.

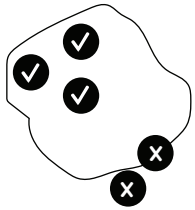


Figure 11

- When using the DermaSensor device on a small lesion of around 2.5-4mm in diameter, for each location recording lift the Handheld Unit tip and place the Handheld Unit tip back on the lesion, even if the recordings overlap or appear to overlap partially or fully with previous recordings. See *Figure 12*.


Figure 12

iii. Recording a Lesion

⚠ *Wipe the tip with an alcohol wipe prior to use on every lesion to ensure accurate recordings.*

1. Remove the calibrated and charged Handheld Unit from the Base in preparation of taking a series of recordings for a specific lesion.
2. Take one recording at a time of the lesion tissue.
   - Press either of the **Side** buttons on the Handheld Unit (see *Figure 13*) or the **RECORD** button on the Handheld Unit display to record while the Handheld Unit tip is touching the lesion.
   - There will be multiple flashes, tones, and clicks during the recording process, which may be audible and visible.
     DO NOT LIFT THE TIP OFF OF THE LESION OR MOVE THE TIP WHILE A RECORDING IS IN PROGRESS.
   - When the recording of a location is complete, you will be prompted to continue recording in a new location on the same lesion until five recordings are made.
   - If the DermaSensor does not capture a usable recording (e.g., if the DermaSensor detects that the tip is not in contact with a lesion), you will be prompted to repeat the last individual recording.

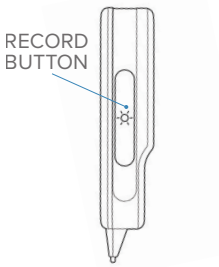
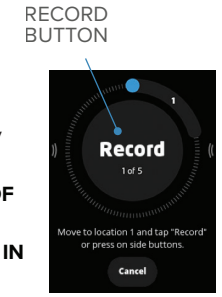
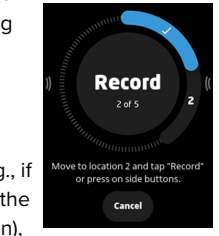


Figure 13



Record Screen

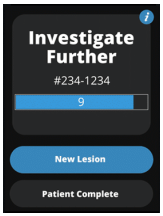
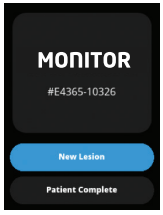


Record Second Location

3. Lift the tip of the Handheld Unit off sampled tissue when the Handheld Unit displays “Move to location 2 and press record.” (*Figure 9*)
4. If any of the five individual recordings is taken in error (e.g. tip placement error) or with suboptimal positioning, press **CANCEL** to be prompted to restart the lesion recordings.
5. Repeat the steps above when prompted to move to **locations 3, 4 and 5 on the same lesion**.

iv. Understanding Results

1. After all five recordings for a specific lesion have been acquired, the Handheld Unit will assign and display a unique **Device Record Number (DRN)** for the lesion. The Handheld Unit will also analyze the spectral data from the five recordings and provide a result as follows:

Output and Results	
Output	**Results**
	**"Investigate Further"** The Handheld Unit will display "Investigate Further" for lesions found to contain certain properties associated with malignant skin lesions, the three most common being melanoma, squamous cell carcinoma, and basal cell carcinoma. **Spectral Score** For lesions with an "Investigate Further" result, the Handheld Unit will display a score from 1 through 10 to indicate the degree of similarity the lesion's spectral recordings to malignant lesions in studies (the "spectral similarity", e.g., 1 indicating the least similar to malignant lesions and 10 indicating the most similar to malignant lesions). A pivotal clinical trial showed that higher scores had greater positive predictive value for malignancy. However, low scores are still classified as "Investigate further" and should be considered as positive output when the device is used in referral decisions in addition to clinically relevant information. 
	**"Monitor"** The Handheld Unit will display "Monitor" for lesions found to contain recorded properties associated with benign lesions. ***No Spectral Score is shown when the result is "Monitor".***

See G. INDICATED LESION TYPES AND PERFORMANCE

Device melanoma sensitivity has been observed to be slightly lower than overall skin cancer sensitivity, which is thought to be due to the heterogeneity of melanoma pathology as documented in literature. Given the high mortality rate of melanoma and that the device sensitivity was observed to be slightly lower for melanoma, for darkly pigmented lesions of concern for melanoma, it is important to consider referring these lesions for any "Investigate Further" device result, regardless of the 1-10 spectral score.

v. Additional Lesion Recordings

1. *Wipe the tip with an alcohol wipe prior to use on every subsequent lesion to ensure accurate recordings.*
2. Press the **NEW LESION** option on the Handheld Unit and repeat steps **i** through **iii** in **L. OPERATING THE DERMASENSOR on page 15** for each lesion to be recorded on the same patient.

vi. Recordings Complete

1. Press the **PATIENT COMPLETE** option on the Handheld Unit when all lesions for this patient have been assessed.
2. Thoroughly clean and disinfect the DermaSensor. *(K. CLEANING AND DISINFECTING on page 14)*
3. Reseat the Handheld Unit in the Base to store and charge until next use.
4. Wipe areas contacted on the patient with a lint-free wipe saturated with water.

For operating and storage information, see N. TECHNICAL DATA, GUIDANCE, AND MANUFACTURER'S DECLARATIONS on page 23.

M. TROUBLESHOOTING

If any problem persists after following the provided instructions and troubleshooting, contact customer support at https://support.dermasensor.com or *support@dermasensor.com*.

Problem Cause Solution

The Handheld Unit does not charge when placed in the Base.	The Handheld Unit is not placed correctly in the Base. The power cord is not plugged into the Base and/or wall correctly.
The white LED light on the front of the Base illuminates when the Base is properly plugged into a power outlet and the Handheld Unit is properly inserted on the Base. Remove and reinsert the Handheld Unit onto the Base so it is seated securely. Check that all connections between the Base, the power cable, and wall outlet are all firmly connected together according to *I. CHARGING AND STORAGE on page 8*.	
Handheld Unit cannot calibrate. *"Calibration Error - An error occurred during calibration (118)."*	Debris and/or residue may be blocking the end of the tip. The Handheld Unit is not placed correctly in the Base. The power cord is not plugged into the Base and/or wall correctly.
Follow the cleaning and disinfection process *(K. CLEANING AND DISINFECTING on page 14)* to ensure the bottom of the Handheld Unit tip is completely clear of debris or residue, even though debris may not be visible. Additional force may be needed. Check for any debris within the inner channel of the Base. Remove and reinsert the Handheld Unit onto the Base so it is seated securely. Check that all connections between the Base, the power cable, and the wall outlet are all firmly connected together according to *I. CHARGING AND STORAGE on page 8* If all connections are secure, the white LED light on the front of the Base should illuminate indicating the Handheld Unit is able to calibrate.	
The display is blank.	Battery is discharged or the unit is damaged.
Revisit *I. CHARGING AND STORAGE on page 8*. If the problem persists, contact customer support. *(See MANUFACTURER AND CONTACT INFORMATION on p. 35).*	
The Handheld Unit does not power on.	Battery is discharged or the unit is damaged.
Follow instructions for *I. CHARGING AND STORAGE on page 8*. Place the Handheld Unit in the Base for 2-3 hours while the white LED indicator light is illuminated. If the problem persists, contact customer support.	
The display is unresponsive.	The display is defective, damaged and/or dirty.
Review the cleaning and disinfection process *(K. CLEANING AND DISINFECTING on page 14)* to remove any material from the screen and/or restart the Handheld Unit by holding the power button for 10 seconds and then releasing. Follow instructions for *I. CHARGING AND STORAGE on page 8*. Place the Handheld Unit in the Base for 1-2 hours while the white LED indicator light is illuminated. If the problem persists, contact customer support.	
The Handheld Unit cannot connect to WiFi or the internet.	A compatible 2.4GHz WiFi router is not connected to an active internet connection or the WiFi password is invalid.
Follow instructions J. WI-FI SETUP AND ACTIVATION on page 11 to reset the WiFi connection and verify that the WiFi router has an active connection.	
The Handheld Unit says insufficient credits or says not registered or activated.	The Handheld Unit has not been activated or assigned a valid usage plan.
Visit www.DermaSensor.com to log into your account and manage your DermaSensor device details. Make sure the device is connected to an active WiFi network with internet access.	
The Handheld Unit does not pulse or tone and says battery low when trying to record a lesion or begin a calibration.	The Handheld Unit battery is too low to begin assessing a new lesion.
The Handheld Unit must be charged in the Base until the battery level is above 20% to begin a new lesion. Revisit *I. CHARGING AND STORAGE on page 8*.	

N. TECHNICAL DATA, GUIDANCE, AND MANUFACTURER'S DECLARATIONS

Product Description	For use to evaluate skin lesions suggestive of melanoma, basal cell carcinoma, and/or squamous cell carcinoma.
Model	10101 (System)
Display	Glass LCD with touchscreen feature
Power Source	AC-DC adapter: Input 100-240 V, 50-60 Hz, 0.6 A Base: Input 12VDC Output 6W Handheld Unit: 700 mAh 3.7 volt Li-ion battery
Battery Life	6 years
Applied Part	Handheld Unit - Type B Handheld Unit Tip (Plastic and Metal) when discharging; no defibrillation-proof applied parts
Protection Against Electric Shock	Class II ME equipment, externally powered when charging, internally powered ME equipment when discharging
Operating Temperature, Air Pressure and Humidity	10-30 degrees centigrade (59-104 degrees Fahrenheit) 70kPa-106 kPa atmospheric pressure 30-75% relative humidity Not intended for use in an oxygen rich environment
Storage/ Transportation Temperature, Air Pressure and Humidity	-40 to 70 degrees centigrade (-40 to 158 degrees Fahrenheit) 50kPa-106kPa atmospheric pressure 10%-100% relative humidity
Handheld Unit Weight	0.55 lbs.
Package Content	Base, Handheld Unit, wall charger with regional adapters, Instructions for Use
IP Rating	IP20
Sterilization	Nonsterile (not intended to be sterilized)
Mode of operation	Continuous
Essential Performance	The DermaSensor device does not have any Essential Performance characteristics as defined per IEC 60601-1:2012 Ed. 3.1

Guidance and Manufacturer's Declaration - Electromagnetic Compatibility (EMC)

Medical devices in use are susceptible to electromagnetic interference from other electronic devices such as PCs and cellular phones, which are ubiquitous. Electromagnetic interference may result in incorrect operation of the medical device and create a potentially unsafe situation. Medical devices should also not interfere with other devices.

In order to regulate the requirements for Electromagnetic Compatibility (EMC) with the aim to prevent unsafe product situations, the IEC 60601-1-2 standard has been implemented. This standard defines the levels of immunity to electromagnetic interferences as well as maximum levels of electromagnetic emissions for medical devices. This medical device, manufactured by DermaSensor Inc., conforms to this IEC60601-1-2:2014 standard for both immunity and emissions.

Nevertheless, special precautions need to be observed:

- The use of accessories and cables other than those specified by DermaSensor, with the exception of cables sold by DermaSensor as replacement parts, may result in increased emission or decreased immunity of the device.
- The medical devices should not be used adjacent to or stacked with other equipment. In case adjacent or stacked use is necessary, the medical device should be observed to verify normal operation in the configuration in which it will be used.

Guidance and Manufacturer's Declaration — Disposal of This Product (Waste Electrical and Electronic Equipment)	
	This marking, shown on the product or its literature, indicates this device should not be disposed of with other business or household wastes at the end of its working life. Prevent possible harm to the environment or human health from by separating this device from other types of wastes and recycling it responsibly to promote the sustainable reuse of material resources. Business users should contact their supplier and check the terms and conditions of the purchase contract. This product should not be mixed with other commercial wastes for disposal. This product does not contain any hazardous substances.

Guidance and Manufacturer's Declaration — MRI (Magnetic Resonance Imaging) Unsafe
This equipment includes materials known to be incompatible with the MRI environment and is considered MRI Unsafe.

Guidance and Manufacturer's Declaration — Use Environment
The emissions characteristics of this equipment make it suitable for use in industrial areas and hospitals (CISPR 11 class A).

Guidance and Manufacturer's Declaration — Electromagnetic Emissions		
The DermaSensor device is battery-operated and intended for use in the electromagnetic environment specified below. The customer or the user of this device should ensure that it is used in such an environment. The emissions characteristics of this equipment make it suitable for use in industrial areas and hospitals (CISPR 11 class A). If it is used in a residential environment (for which CISPR 11 class B is normally required), this equipment might not offer adequate protection to radio-frequency communication services. The user may need to take mitigation measures, including as relocating or reorienting the equipment.		
Emission test	**Compliance Level**	**Electromagnetic environment**
RF emissions (CISPR 11)	Class A	DermaSensor device is suitable for use in professional establishments.
Conducted RF emissions (CISPR 11)	Class A	
Harmonic distortion (IEC 61000-3-2)	Class A	
Voltage fluctuations and flicker	Complies	

Guidance and Manufacturer's Declaration — Electromagnetic Immunity			
DermaSensor device is intended for use in the electromagnetic environment specified below.		The customer or the user of this device should assure that it is used in such an environment.	
Immunity Test	**IEC 60601 test level**	**Compliance Level**	**Electromagnetic environment**
Electrostatic discharge (ESD) IEC 61000-4-2	± 8 kV contact ± 2 kV, ±4 kV, ±8 kV, ±15 kV air	± 8 kV contact ± 2 kV, ±4 kV, ±8 kV air	The DermaSensor device is not intended to be used in environments which exceed a potential ±8kV of air ESD. Floors should be wood, concrete, or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.
Electrical fast transient/ burst IEC 61000-4-4	± 2 kV 100 kHz repetition frequency	± 2 kV 100 kHz repetition frequency	Mains power quality should be that of a typical commercial or hospital environment.
Surges IEC 61000-4-5	±0.5 kV, ±1 kV Line-to-Line ±0.5 kV, ±1 kV, ±2 kV Line-to-Ground	±0.5 kV, ±1 kV Line-to-Line ±0.5 kV, ±1 kV, ±2 kV Line-to-Ground	Mains power quality should be that of a typical commercial or hospital environment.
Radiated RF EM IEC 61000-4-3 **Conducted disturbances induced by RF fields IEC 61000-4-6**	3 V/m 80 MHz – 2,7 GHz 80% AM at 1 kHz 3 V 0,15 MHz – 80 MHz 6 V in ISM and amateur radio bands between 0,15 MHz and 80 MHz 80% AM at 1 kHz	3 V/m 80 MHz – 2,7 GHz 80% AM at 1 kHz 3 V 0,15 MHz – 80 MHz 6 V in ISM and amateur radio bands between 0,15 MHz and 80 MHz 80% AM at 1 kHz	Portable and mobile RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30cm (12 inches) to any part of the DermaSensor device or cables provided by DermaSensor, Inc. Otherwise, degradation of the performance of this equipment could result.
Voltage dips, short interruptions, and voltage variations on power supply IEC 61000-4-11	0% UT; 0,5 cycle At 0°, 45°, 90°, 135°, 180°, 225°, 270° and 315°	0% UT; 0,5 cycle At 0°, 45°, 90°, 135°, 180°, 225°, 270° and 315°	Mains power quality should be that of a typical commercial or hospital environment if the user of DermaSensor device requires continued operation during power mains interruptions, it is recommended that DermaSensor device be powered from an uninterruptible power supply or a battery that is certified for use in a hospital environment.
	0% UT; 1 cycle and 70 % UT; 25/30 cycles Single phase: at 0°	0% UT; 1 cycle and 70 % UT; 25/30 cycles Single phase: at 0°	
	0% UT; 250/300 cycle	0% UT; 250/300 cycle	
Rated power frequency magnetic fields IEC 61000-4-8	30 A/m 50 Hz or 60 Hz	30 A/m 50 Hz and 60 Hz	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.

Guidance and Manufacturer's Declaration — FCC Compliance Statement
Contains FCC ID: Z64-WL18SBMOD **NOTE:** This equipment has been tested and found to comply with the limits for a Class A digital device, pursuant to part 15 of the FCC Rules. These limits are designed to provide reasonable protection against harmful interference when the equipment is operated in a commercial environment. This equipment generates, uses, and can radiate radio frequency energy and, if not installed and used in accordance with the instruction manual, may cause harmful interference to radio communications. Operation of this equipment in a residential area is likely to cause harmful interference in which case the user will be required to correct the interference at their own expense.
⚠ Any changes or modifications not expressly approved by DermaSensor Inc. could void the user's authority to operate this equipment. This device is limited to operation on permissible Part 15 frequencies and does not have the ability to be configured by end users or professional installers to operate outside the authorized bands.

Guidance and Manufacturer's Declaration — RF Systems	
Frequency or frequency band of reception	2.412 GHz - 2.484 GHz
Preferred frequency or frequency band	2.426 GHz - 2.448 GHz
Bandwidth of the receiving section of the ME Equipment	20MHz / 40MHz
Frequency or frequency band of transmission	2.412 GHz – 2.484 GHz
Type	Wi-Fi / Bluetooth, IEEE Std 802.11b, 802.11g, and 802.11n
Frequency characteristics of the modulation	QPSK
Effective Radiated Power (ERP)	17.3 dBm = 53.7 mW

Guidance and Manufacturer's Declaration — Expected Service Life
To ensure EMC compatibility during the expected service life, only use the included components and accessories provided as part of the ME (Medical Equipment) system by DermaSensor™.

Guidance and Manufacturer's Declaration — Non-Laser Light Source Equipment	
The DermaSensor device should be protected against unauthorized use.	
Spectral irradiance or spectral radiant exposure for all intended configurations of LS (Light Source) equipment	Actinic UV is less than 0.001 $W.m^2$ Near UV is less than 10 $W.m^2$ Blue light small source is less than 2.7E-04 $W.m^2$
Maximum output of optical radiation for all intended configurations of LS equipment	Retinal thermal, weak visual stimulus is less than 6000/ alpha=2E06
Pulse duration of individual pulses	<10 µseconds
Duration of a pulse train	<1 second
Pulse interval	<500 µseconds
Repetition rate	2
Number of pulses in a pulse train	3

Guidance and Manufacturer's Declaration — Cybersecurity

The device communicates with an application backed service ("Backend") hosted on Amazon Web Services and operated by DermaSensor through WiFi access points connected to teh internet. The backend exposes a REST API accessible only to authorized DermaSensor devices over a secure HTTPS communication channel.

DermaSensor operates the backend and assumes full responsibility for maintaining its security, including patching and securing the infrastructure and application code. Restricting access to the DermaSensor device is the responsibility of the user. The company recommends installing appropriate physical and digital protection to prevent compromises to networks and computers on your network and ensuring to the extent possible that the DermaSensor device remains physically secured and that data on the network is not manipulated, intercepted or otherwise stolen.

In the event of a security incident detected and reported on your network, it is advisable to stop using the DermaSensor device until the compromise is remediated. The DermaSensor device is not able to detect or report on your network's security events. Security events related to the backend service are reported to DermaSensor, who is responsible for addressing them.

In the event that the DermaSensor device loses its connection to the backend, then it will not be possible to activate the device or renew expired activations. To troubleshoot the connectivity issues, please contact your local network administrator, and if needed, DermaSensor support.

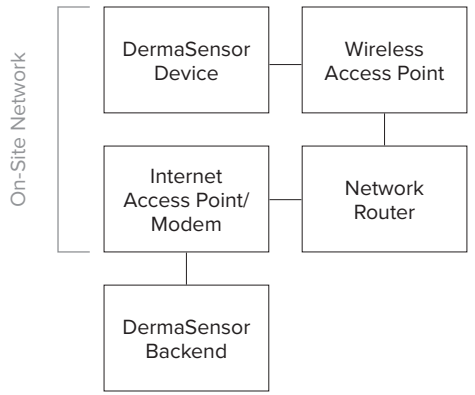
Guidance and Manufacturer's Declaration — Device Instructions for Network Security

The following cybersecurity controls are recommended:
• The network used for WiFi connectivity should require authenticated access.
• The network should be set up with a firewall which whitelists the dermasensor.com domain and ports required for operation of the DermaSensor device. The URLs mentioned in must be whitelisted and HTTPS (port 443) must allow traffic.
• The network firewall should not allow external connection requests to be routed to the DermaSensor device.
• Only authorized personnel may have physical access to the DermaSensor device.

Guidance and Manufacturer's Declaration — Cybersecurity Event Notification

In the event of a security incident detected by DermaSensor on the DermaSensor backend, users effected will be directly notified of the issue, the extent and contents of any exposure, and steps needed by the users to resolve any outstanding issues.

Guidance and Manufacturer's Declaration — Cybersecurity Diagram



O. LIMITED WARRANTY

For warranty information please visit
https://support.dermasensor.com

P. SUMMARY OF CLINICAL INFORMATION

Ten clinical studies have been conducted that provide clinical evidence supporting the safety and effectiveness of the DermaSensor device and algorithm. These do not include studies used solely for algorithm training. The first four studies below included portions of their datasets in algorithm training (i.e., DERM-ASSESS II, Skin Center IIS, only test set data is included below), were conducted using a different device result structure (i.e., DERM-ASSESS II Reader Study), or included lesions other than those solely suggestive of skin cancer to physicians (i.e., PATIENT-SELECT included patient-selected lesions of concern). There were no safety issues or adverse events in any of these four studies.

Summary of Early Clinical Effectiveness Studies			
Clinical Study Name	**Design, Setting and Sample Size**	**Objective**	**Effectiveness Results**
DermaSensor Use in the Assessment of Skin Lesions Suggestive of Cancer (DERM-ASSESS II)	US-based, multicenter, prospective, blinded clinical study at four dermatology sites in the US 333 lesions (169 malignant, 164 benign)	To train the device algorithm and validate clinical performance for melanoma, BCC, and SCC	Device sensitivity of 97.0% (95% CI: 92.4-98.9%) and specificity of 26.2% (95% CI: 20.3-33.2%)
Use of an ESS-based Adjunctive Tool in the Assessment of Lesions Suggestive of Skin Cancer (Skin Center Investigator-Initiated Study (IIS))	Single-site, prospective, blinded clinical study at one dermatology site in New Zealand 410 lesions (50 malignant, 360 benign)	To evaluate DermaSensor device performance as an adjunctive tool for evaluating patients with skin lesions suggestive of melanoma, BCC, and SCC.	Device sensitivity of 96.0% (95% CI: 86.3-99.5%) and specificity of 31.4% (95% CI: 26.6-36.5%)
Use of DermaSensor on Patient-Selected Lesions that are Concerning for Skin Cancer (PATIENT-SELECT)	US-based prospective. blinded clinical study at one primary care site in the US 155 lesions (10 malignant, 145 benign)	To assess device performance on skin lesions identified by patients as concerning for skin cancer	Device sensitivity of 90.0% (95% CI: 71.4-100.0%) and specificity of 60.7% (95% CI: 52.5-68.4%)
A Multi-Reader Multi-Case Companion Study to the DERM-ASSESS II Clinical Study (DA-II Reader Study)	US-based prospective multi-reader, multi-case study; 57 primary care physicians (PCPs) completed 5,700 lesion assessments	To assess and compare the management sensitivity and specificity of primary care physicians for the most common types of skin cancer (Melanoma, BCC, SCC), with and without use of the device result	PCP sensitivity with device result of 94.2% (95% CI: 91-96%) was superior to PCP sensitivity without device result of 81.4% (95% CI: 77-85%) (p=0.0009). Management specificity with (31%) and without (36%) device use was not significantly different (P = 0.3558)

The remaining six studies, summarized in the table below, used the current device and algorithm. In total, the three clinical studies in the table below included over 1,300 subjects and over 2,000 pathology-verified lesions enrolled by more than 30 study sites. The three reader studies included over 250 lesions and patients with over 300 physician readers. There were no safety issues or adverse events in any of these six studies.

Summary of Principal Clinical Effectiveness Studies			
Clinical Study Name	**Design, Setting and Sample Size**	**Objective**	**Effectiveness Results**
Pivotal Clinical Study: DermaSensor Study of Primary Care Physician use of Elastic-Scattering Spectroscopy (ESS) on skin lesions suggestive of skin cancer (DERM-SUCCESS)	International, multicenter, prospective, blinded clinical study at 22 primary care sites (18 in the US, 4 in Australia) 1,005 subjects, 1,579 lesions (224 malignant)	To assess device performance in classifying biopsied lesions suggestive of skin cancers when used by PCPs	**Co-Primary Endpoint 1:** Device sensitivity of 95.5% (95% CI: 91.7-97.6%) was superior to PCP sensitivity of 83.0% (95% CI: 77.7-87.3%) (p-value<0.0001). **Co-Primary Endpoint 2:** Device Odds Ratio of 4.93 (95% CI: 2.84-8.56) (p-value<0.0001) **Secondary Endpoint:** Device was non-inferior to the 90% performance goal (p-value<0.0001)
Pivotal Reader Study: A Multi-Reader, Multi-Case (MRMC) Companion Study to the DERM-SUCCESS Clinical Study	US-based prospective multi-reader, multi-case study 108 board-certified PCP readers completed 10,800 assessments	To assess whether the availability of the device result can improve PCPs referrals and detection of skin cancers	**Co-Primary Endpoint 1:** PCP sensitivity with device result of 91.4% (95% CI: 85.7%-97.1%) was superior to PCP sensitivity without device result of 82.0% (95% CI: 76.4-87.6%) (p=0.0027) **Co-Primary Endpoint 2:** PCP with device result with Odds Ratio of 6.8 (95% CI: 4.7-9.8) (p-value<0.0001) **Accuracy Analysis:** AUROC increased 5.4%, from 0.708 to 0.762
DermaSensor Use in the ASSESSment of Skin Lesions Suggestive of Melanoma III (DERM-ASSESS III)	International, multicenter, prospective, blinded, clinical study; 10 sites (8 in the US, 2 in Australia) 311 subjects, 440 lesions (88 high risk melanocytic lesions)	To evaluate device performance in classifying biopsied lesions suggestive of melanoma	**Co-Primary Endpoint 1:** Device sensitivity for high risk lesions of 90.9% (95% CI: 83.1-95.3% **Co-Primary Endpoint 2:** Device sensitivity for melanoma of 95.5% (95% CI: 84.5-98.8%) **Co-Primary Endpoint 3**: Device specificity of 32.5% (95% CI: 27.2-38.3%)
DermaSensor Repeatability and Reproducibility Study (DERM R and R)	International, multicenter, prospective, blinded, clinical study; 2 sites (1 in the US, 1 in Australia) 52 subjects, 64 lesions (23 malignant lesions)	To evaluate device repeatability and reproducibility for all lesions and for malignant lesions	**Co-Primary Endpoint 1:** Overall repeatability of 84.2% (95% CI: 78.2-89.1%) agreement, 94.8% (95% CI: 92.1-97.1%) Positive Percent Agreement, 46.0% (95% CI: 32.1-60.0%) Negative Percent Agreement **Co-Primary Endpoint 2:** Overall reproducibility of 87.8% (95% CI: 82.2-92.1%) agreement, 92.7% (95% CI: 88.1-96.4%) Average Positive Agreement, 64.4% (95% CI: 38.7-80.4%) Average Negative Agreement **Secondary Endpoint:** For malignant lesions only, repeatability of 97.1% (95% CI: 89.9-99.6%) agreement, with an associated PPA of 97.8% (95% CI: 93.8%- 99.3%) and NPA of 75.0% (95% CI: 30.1-95.4%), and reproducibility of 97.1% (95% CI: 89.9-99.6%) agreement, with an associated APA of 86.4% (95% CI: 62.0-97.4%) and ANA of 2.1% (95% CI: 0.5-6.2%)

Summary of Principal Clinical Effectiveness Studies			
Clinical Study Name	**Design, Setting and Sample Size**	**Objective**	**Effectiveness Results**
A Multi-Reader, Multi-Case (MRMC) Study for Evaluating the Impact of the DermaSensor Device on Primary Care Physicians' Assessment of Pigmented Lesions (DS Pigmented Reader Study)	US-based prospective multi-reader, multi-case study 77 board-certified PCP readers completed 10,472 assessments	To demonstrate performance of PCPs for pigmented skin cancers when aided by the device	**Primary Endpoint:** Aided PCP AUROC increased 1.5% for all skin cancers, achieving non-inferiority ($p<0.001$) **Secondary Endpoint 1:** Aided PCP sensitivity increased 5.8%, achieving non-inferiority ($p<0.001$) and superiority ($p<0.001$) **Secondary Endpoint 2:** Aided PCP sensitivity increased 6.6% for melanoma, achieving non-inferiority ($p<0.001$) and superiority ($p=0.029$) **Secondary Endpoint 3:** Aided PCP specificity decreased 10.6%, achieving its non-inferiority margin ($p=0.003$)
A Multi-Reader, Multi-Case (MRMC) Study for Evaluating the Impact of the DermaSensor Device on Primary Care Physicians' Assessment of Lesions Suggestive of Melanoma (DERM-ASSESS III Reader Study)	US-based prospective multi-reader, multi-case study 118 board-certified PCP readers completed 11,800 assessments	To demonstrate performance of PCPs for melanoma when aided by the device	**Primary Endpoint:** Aided PCP AUROC increased 4.1% for all skin cancers, achieving non-inferiority ($p<0.001$) and superiority ($p=0.036$) **Secondary Endpoint 1:** Aided PCP sensitivity for all skin cancers increased 8.1%, achieving non-inferiority ($p<0.001$) and superiority ($p<0.001$) **Secondary Endpoint 2:** Aided PCP sensitivity for melanoma increased 8.8%, achieving non-inferiority ($p<0.001$) and superiority ($p<0.001$) **Secondary Endpoint 3:** Aided PCP specificity decreased by 5.6%, achieving its non-inferiority margin ($p<0.001$)

i. Pivotal Study Design (DERM-SUCCESS)

The DERM-SUCCESS Pivotal Study was an international, multicenter, prospective, blinded clinical study conducted at 22 study sites with 30 primary care physicians, with a total of 1,005 subjects with 1,579 lesions included in the effectiveness population. DermaSensor device results were compared to pathology findings that were validated by two to five dermatopathologists depending on the clinical severity and discordance for the diagnoses. Subjects with skin lesions suggestive of melanoma, BCC, and/or SCC that merited biopsy to assess risk of malignancy were enrolled, and each lesion was scanned with the device. Investigators and subjects were blinded to the device results, with all clinical management provided per standard of care. The device provided a negative result of "Monitor" and a positive result of "Investigate Further". All positive "Investigate Further" results include a score of 1-10 to indicate the degree of spectral similarity to malignant lesions. Biopsy pathology results were the study reference standard.

1. Clinical inclusion and exclusion criteria:

Subjects aged 22 years and older were enrolled in the study if they had a lesion that the physician believed was suggestive of skin cancer. Lesions that were excluded were those where:

1. Lesion < 2.5mm in diameter or > 15mm in diameter
2. Lesion surface not accessible (e.g. inside ears, under nails, completely covered by a crust or scale)
3. Lesion on area of crust, psoriasis, eczema or similar skin condition
4. Lesion has erosion and/or ulceration with no area >2.5mm intact
5. Lesion has foreign matter (e.g. tattoo, splinter, dermoscopy oils, or other medicated or non-medicated topical solutions)
6. Lesion in which the device tip cannot be placed entirely within the border of the targeted area
7. Lesion located on acral skin (e.g. sole or palms)
8. Lesion located within 1 cm of the eye
9. Lesion on or adjacent to scars, areas previously biopsied, or areas subjected to any past surgical intervention
10. Lesion located on mucosal surfaces (e.g. genitals, lips)
11. Lesion located on acute sunburn
12. Six (6) or more lesions suggestive of melanoma,

basal cell carcinoma, and/or squamous cell carcinoma requiring biopsy to assess risk of malignancy
13. Dementia or other neurologic, physical or psychological limitation that would prevent the patient from signing informed consent

2. Clinical endpoints:

The co-primary endpoints of the DERM-SUCCESS study were DermaSensor sensitivity compared to that of the study physicians (primary care physicians) and a sensitivity + specificity > 1 regression model using biopsy as the reference standard. The endpoint of sensitivity compared to the primary care physicians was selected to determine if the device provides superior sensitivity for skin cancer than the primary care physicians. The second co-primary endpoint was selected to assess if performance of the device in the primary care setting was statistically meaningful. The secondary endpoint of the DERM-SUCCESS study was DermaSensor sensitivity as compared to a performance goal of 90% based on dermatologist sensitivity in literature. This endpoint was selected to compare the skin cancer detection rate (i.e., sensitivity) of the DermaSensor device to that of the current gold standard for skin lesion evaluation, i.e., dermatologist evaluation and management of skin cancers.

Subjects were recruited for the study in primary care offices where physicians performed their own clinical assessments, used the DermaSensor device, and performed biopsies of the lesions. All results were validated using the dermatopathology results of the biopsy.

3. Patient Disposition

The following table summarizes the subjects and lesions that were excluded from the ITT safety and mITT effectiveness populations. Subjects were enrolled prior to lesion enrollment, hence there were instances in which a subject was enrolled but no lesion was enrolled (e.g., device malfuction prior to lesion enrollment). Only five lesions (0.3%) were excluded due to device data capture issues and five lesions (0.3%) excluded due to lack of dermatopathology consensus.

Subject Accountability and Disposition

	Subjects n (%)	Lesions n (%)
Enrolled	1,021	1,598
ITT Safety Population	1,013 (99.2%)	1,591 (99.6%)
Excluded from ITT Population	8 (0.8%)	7 (0.4%)
mITT Effectiveness Population	1,005 (98.4%)	1,579 (98.8%)
Excluded from mITT Population	8 (0.8%)	12 (0.8%)

4. Study population demographics

The following table provides the subject characteristics of the study effectiveness population (1,005 subjects, 1,579 lesions). The demographics and characteristics of the study population are typical for the population that is at risk for skin cancer in the US. Among subjects enrolled, 51.5% were female with a mean age of 59 years, and 72.5% of subjects were Fitzpatrick Skin Types I-III (27.5% were IV-VI). The majority of lesions were located on the trunk (52.3%). The average size of enrolled lesions was 7mm x 5mm, and the majority of lesions were elevated (60.6%), smooth (54.7%) and dark (63.2%). 67.8% of lesions were identified by the subject, 27.2% were identified by the PCP and 5.0% by a family member/partner. 657 (65.4%) of subjects had one lesion enrolled, 207 (20.6%) had two lesions enrolled, and 141 (14.0%) had three to five lesions enrolled.

Description of Subject Characteristics (n=1,005)

Characteristics	n (%)[1]
Sex	
Male	487 (48.5%)
Female	518 (51.5%)
Age	
Mean (STD) Median (Q1-Q3) Min-Max	58.5 (15.1) 60.0 (49.0-69.0) 22-95
Fitzpatrick Skin Type	
I - Always burns, never tans	99 (9.9%)
II - Always burns, tans minimally	278 (27.7%)
III - Sometimes mild burn, tans uniformly	352 (35.0%)
IV - Burns minimally, always tans well	148 (14.7%)
V - Very rarely burns, tans very easily	110 (10.9%)
VI - Never burns	18 (1.8%)

[1]Unless otherwise noted

5. Safety and Effectiveness Results

a. Safety Results

Of the 1,021 subjects that completed enrollment in the study, there were no adverse events, serious adverse events or discontinuations due to adverse events reported for the study.

b. Effectiveness Results – Co-Primary Endpoints

Co-Primary Endpoint 1: Sensitivity of DermaSensor for Detecting Malignant Skin Lesions is Greater than PCP Clinical Assessment Sensitivity

The DermaSensor device sensitivity of 95.5% (95% CI: 91.7-97.6%) was statistically significantly higher than the PCP clinical assessment sensitivity of 83.0% (95% CI:

77.6-87.3%) with a p-value <0.0001 that was smaller than the a priori one-sided α=0.025 (shown in the following table). The null hypothesis was rejected. The observed specificity was 20.7% (95% CI: 18.5-23.1%).

Co-Primary Endpoint 1 - Sensitivity of DermaSensor Device and Primary Care Physician Assessment for Malignant Lesion Detection				
Sensitivity (%) and 95% Confidence Interval[1]				
	#Malignant Lesions	**Device**	**PCP**	**P-value[2]**
All Malignant Lesions	224	95.5% (91.7% - 97.6%)	83.0% (77.7% - 87.3%)	<.0001

[1]95% CI calculated accounting for within-subject correlations using Wilson method (Gallas et al Commun Stat A Theory 2009; 38(15):2586-2603)

[2]P-value obtained using the method of moments for clustered paired data

Co-Primary Endpoint 2: Sensitivity + Specificity > 1 for Malignant Lesion Detection by DermaSensor

This endpoint assessed whether the DermaSensor device is better at detecting malignant skin lesions than random chance. In order to statistically assess this, the odds ratio from statistical logistic regression modelling was used. An odds ratio statistically greater than 1 from this model means that the sum of sensitivity and specificity is also statistically greater than 1. Some of the subjects in the pivotal study contributed multiple lesions. All lesions were included for this analysis. The results are given in the following table. The odds ratio is 4.93 (95% CI: 2.84-8.56, p-value <0.0001), meaning that the sum of sensitivity and specificity and the odds ratio are both significantly greater than 1. The null hypothesis was rejected.

Co-Primary Endpoint 2 - Sensitivity + Specificity > 1 for Malignant Lesion Detection by the DermaSensor Device	
Odds ratio (95% CI)[1]	**P-value[2]**
4.93 (2.84 - 8.56)	<.0001

[1]95% CI calculated accounting for within-subject correlations

[2]P-value obtained using generalized estimation equation accounting for within-subject correlations

The study achieved its two planned co-primary endpoints, the first yielded device sensitivity of 95.5% superior to the PCP sensitivity of 83.0% (p-value <0.0001) and the second demonstrated that the sum of the sensitivity and specificity of the device has 4.93 times the odds as compared to random chance to detect malignant skin lesions (p-value <0.0001). Therefore, these primary endpoint results validate the device performance and support the utility of the device as a helpful aid to PCPs' clinical assessment of suspicious lesions in determining which lesions warrant referral to a dermatologist.

c. Effectiveness Results – Other Analyses

There was one planned secondary analysis, comparing the device sensitivity to a performance goal (PG) based on dermatologist sensitivity of 90% as reported in the literature; specifically, dermatologist sensitivity for skin cancer detection of 81-96% was estimated from the literature based on past studies that assessed dermatologist management (i.e., biopsy) sensitivity. The DermaSensor device sensitivity of 95.5% (95% CI: 91.7-97.6%) was non-inferior to the performance goal (p-value<0.0001) as shown in the following table.

Comparison of Device and Dermatologists: Sensitivity Performance Goal			
Performance	**Number of lesion cases**	**Device Sensitivity (95% CI)**	**P-value[1]**
Sensitivity	224	95.5% (91.7% to 97.6%)	<.0001

[1]Non-inferiority testing: Reject if 95% CI lower bound > 80%, one-sided exact binomial test at a=0.025, superiority P-value for sensitivity >90% is 0.0019

An analysis was performed to estimate the device's overall accuracy, i.e. AUROC, of the device. The device AUROC was calculated to be 0.7796, which is classified as very good in the context of diagnostic devices (Simundic et al EJIFCC 2009; 19(4): 203-211). This was greater than the AUROC for PCPs, which was 0.7404 for all lesions and 0.5555 for lesions for which they reported low confidence in their clinical assessment. Analyses were also performed to determine the Negative Predictive Value (NPV) and Positive Predictive Value (PPV) of the DermaSensor device. For the study effectiveness population, there were 224 malignant lesions and 1,579 total lesions. The device yielded a NPV of 96.6% (95% CI: 93.5-98.2%), i.e., a negative "Monitor" device result was negative for disease 96.6% of the time, and a PPV of 16.6% (95% CI: 14.2%-19.3%), i.e., a positive "Investigate Further" result was positive 16.6% of the time (i.e., one out of every six positive results was malignant). For positive "Investigate Further" device results, the device provides a spectral score between 1 and 10 based on the degree of similar spectral features to malignant lesions. Accordingly, the study found that the PPV increases as the spectral score increases. For low scores of 1-3 the PPV was 5.9% (95% CI: 4.1-8.5%), for medium scores of 4-7 the PPV was 18.4% (95% CI: 14.8-22.7%), and for high scores of 8-10 the PPV was 39.6% (95% CI: 33.4-46.2%).

Positive Predictive Value Across Spectral Scores			
Spectral Score	**PPV (Malignant/Total)**	**Spectral Score**	**PPV (Malignant/Total)**
1	6.4% (13/202)	**6**	24.0% (25/104)
2	3.3% (7/213)	**7**	28.2% (33/117)
3	8.5% (15/177)	**8**	25.7% (26/101)
4	10.6% (14/132)	**9**	40.3% (31/77)
5	11.7% (12/103)	**10**	61.3% (38/62)

ii. Reader Studies

Reader Eligibility Criteria

Readers participating in each of the three studies were considered eligible if he/she reported: 1) a board-certification and active practice in family medicine or internal medicine physician, 2) performing skin checks on more than 0% of his/her patients 3) not always nor never referring patients presenting with skin lesions to a dermatologist, 4) not previously participating in the DERM-SUCCESS clinical study, and 5) did not have any financial conflicts of interest with DermaSensor, Inc. or any competitors.

Study Design

Each Reader Study was designed as a Multi-Reader, Multi-Case (MRMC) study to supplement the DERM-SUCCESS pivotal study with the purpose of assessing the referral performance of primary care physicians (PCPs) when evaluating lesions with and without the DermaSensor result. For each lesion case, readers were provided with a high-resolution clinical photograph of the lesion and with all pertinent clinical data collected on the patient and lesion. Readers were not aware of whether the patient whose lesion case was presented was referred or biopsied and were not provided with the lesion diagnosis. None of the PCPs that participated in a reader study participated in the pivotal clinical study.

1. **DERM-SUCCESS Pivotal Reader Study, titled "A Multi-Reader, Multi-Case (MRMC) Companion Study to the DERM-SUCCESS Clinical Study"**
   Study Design: Cross-over
   Cases: 50 lesion cases (25 malignant, 25 benign)
   Study Objective: To assess and compare the sensitivity of primary care physicians in their clinical assessment of lesions suggestive of skin cancer with and without knowledge of the DermaSensor device result.
2. **DERM-SUCCESS Pigmented Reader Study, titled "A Multi-Reader, Multi-Case (MRMC) Study for Evaluating the Impact of the DermaSensor Device on Primary Care Physicians' Assessment of Pigmented Lesions"**
   Study Design: Sequential
   Cases: 136 lesion cases (69 malignant, 67 benign)
   Study Objective: The study objective was to assess and compare the referral performance of PCPs in their clinical assessment of pigmented lesions with and without knowledge of the DermaSensor device output.
3. **DERM-ASSESS III Reader Study, titled "DERM-ASSESS III Reader Study, titled "A Multi-Reader, Multi-Case (MRMC) Study for Evaluating the Impact of the Derma-Sensor Device on Primary Care Physicians' Assessment of Lesions Suggestive of Melanoma"**
   Study Design: Sequential
   Cases: 100 lesion cases (50 malignant, 50 benign)
   Study Objective: The study objective was to assess and compare the referral performance of PCPs in their clinical assessment of lesions suggestive of melanoma with and without knowledge of the DermaSensor device output.

C. Study Results

Three reader studies demonstrated that use of the DermaSensor resulted in superiority of the aided PCP sensitivity over the unaided sensitivity of the same PCP and that the device led to a greater increase in true positive aided referral decisions than false negative aided referral decisions.

1. **DERM-SUCCESS Pivotal Reader Study, titled "A Multi-Reader, Multi-Case (MRMC) Companion Study to the DERM-SUCCESS Clinical Study"**

   Lesion Characteristics

   A total of 108 US PCPs completed 100 lesion case assessments. A randomized lesion selection process was used to select lesions from the DERM-SUCCESS study lesion population, 25 of the 50 lesion cases were malignant and 25 were benign. A total of 25 malignant lesions were included with 10 BCCs, 9 SCCs, and 6 melanomas to best represent the proportions among the malignant pathologies in the DERM-SUCCESS clinical study. Benign lesions included 9 benign melanocytic nevi, 9 seborrheic keratoses and 7 other benign lesions to best represent the proportions among the benign pathologies in the clinical study. The overall device performance on the 50 lesions in the reader study was 96.0% sensitivity and 20.0% specificity; the device performance in the clinical study was 95.5% and 20.7%.

   Study Safety and Effectiveness Results

   For the first co-primary endpoint, PCP management sensitivity significantly increased from 82.0% (95% CI: 76.4-87.6%) to 91.4% (95% CI: 85.7-97.1%) with use of DermaSensor (p=0.0027) thereby decreasing false negative PCP referrals by half from 18.0% to 8.6% as shown in the following table. The study succeeded in demonstrating an increase in readers' referral sensitivity with the aid of the DermaSensor result.

   Similarly, PCP diagnostic sensitivity also significantly increased (p-value=0.0085, from 71.1% (95% CI: 63.4% to 78.8%) to 81.7% (95% CI: 72.4-90.9%) with device use as shown in the following table. These PCP diagnostic and management sensitivity increases with device use were accompanied by clinically acceptable decreases

in specificity of 60.9% (95% CI: 52.5-69.3%) to 54.7% (95%: 42.3-67.1%) for diagnostic specificity and 44.2% (95% CI: 36.0-52.4%) to 32.4% (95% CI: 20.7-44.1%) for management specificity.

PCP Management and Diagnostic Sensitivity Without and With Device				
	Lesion Assessments[1]	Estimate (%) and 95% Confidence Interval[2]		P-value[2]
		Without Device	With Device	
Management Sensitivity (co-primary endpoint 1)	n=5,400	82.0% (76.4% to 87.6%)	91.4% (85.7% to 97.1%)	0.0027
Diagnostic Sensitivity	n=5,400	71.1% (63.4% to 78.8%)	81.7% (72.4% to 90.9%)	0.0085

[1]For sensitivity analyses, only positive (malignant) lesion cases are included

[2]MRMC analysis of variance (ANOVA) method desribed in Obuchowski et al Comm in Stats 1995; 24(2):285-308

The regression model demonstrated that the sensitivity + specificity of the PCPs with the device result was greater than 1 as the odds ratio of the PCPs with device use was 6.8 (95% CI: 4.7 to 9.8) (p value<0.0001). Thus, the performance of PCPs with use of the device was not random, since their odds of detecting malignant lesions were 6.8 times higher than the odds by chance. AUROC analyses were also performed to compare overall accuracy of the unaided PCPs to the aided PCPs. PCPs' device-aided AUROC of 0.693 was also greater than their unaided AUROC of 0.582 for lesions in which they reported low confidence in their unaided assessment.

Sensitivity + Specificity > 1 (i.e., Odds Ratio >1) for PCP Management	
Odds Ratio (95% CI)	P-value
6.8 (4.7 to 9.8)	<.0001

Note: Mixed logistic regression with physician and subject lesion nested within physician random effects.

The participants were asked a series of seven questions using a Likert scale relating to the applicability of the device to their clinical practice. 99% of the 108 physicians reported that the device would provide at least one benefit, and the most commonly reported benefits were: “providing an immediate, objective result to inform your management of suspicious lesions” (82%), “detecting more skin cancer” (82%) and “providing you with greater confidence in your clinical assessments and management decisions” (81%). Also, 98% of the physicians agreed (81% strongly agreed, 17% agreed) that skin cancer is a disease that deserves better surveillance in the primary care setting, and the physicians’ most commonly reported estimate of their own sensitivity for correctly managing malignant lesions was 71-80%. There were no safety issues since this was a reader study.

2. **DERM-SUCCESS Pigmented Lesion Reader Study, titled “A Multi-Reader, Multi-Case (MRMC) Study for Evaluating the Impact of the DermaSensor Device on Primary Care Physicians’ Assessment of Pigmented Lesions”**

   Lesion Characteristics

   A total of 77 US PCPs completed assessments of 136 lesion cases. A randomized lesion selection process was used to select pigmented lesions from the DERM-SUCCESS study lesion population, 69 of the 136 lesion cases were malignant and 67 were benign. The reader study pathology distribution was similar to the clinical study pigmented pathology distribution, with 25 melanomas, 26 BCCs, and 18 SCCs. Benign lesions included 28 benign melanocytic nevi, 24 seborrheic keratoses and 15 other benign lesions to best represent the proportions among the benign pathologies in the clinical study. The overall device performance on the 136 lesions in the reader study was 92.7% sensitivity and 23.9% specificity; the device performance for pigmented lesions in the clinical study was 90.6% and 23.7%.

   Safety and Effectiveness Results

   For the primary endpoint, the AUROC (primary endpoint) was 0.702 (95% CI: 0.635-0.751) unaided compared to 0.717 (95% CI: 0.661-0.773) when aided with the device, a non-inferior difference (p<0.001). The change in AUROC and sensitivity is shown below in the following table. The 5.8% increase in aided sensitivity of the PCPs for all skin cancers was superior (p<0.001) to the unaided sensitivity of the PCPs. The 6.6% increase in aided melanoma sensitivity of the PCPs was superior (p=0.029) to the unaided melanoma sensitivity of the PCPs. The PCPs’ aided specificity was also found to be non-inferior to unaided specificity (p=0.003). For melanoma, false negative unaided reads had a 43% conversion rate to true positive reads with device true positive output. True positive unaided reads only had a 3.7% conversion rate after false negative device results.

PCP Management AUROC and Sensitivity Without and With Device				
	Lesion Assess-ments[1]	Estimate (%) and 95% Confidence Interval[2]		P-value[2]
		Without Device	With Device	
AUROC	n=20,944	0.702 (0.653 - 0.751)	0.717 (0.661 - 0.773)	<0.001
Sensitivity	n=10,626	80.5% (75.1 - 85.9%)	86.3% (81.1% - 91.5%)	<0.001*
Sensitivity for Melanoma	n=3,850	68.8% (59.6 - 78.1%)	75.4% (65.3 - 85.6%)	0.029*
Specificity	n=10,318	45.7% (39.2 - 52.2%)	35.1% (27.4 - 42.9%)	0.003

[1]For sensitivity analyses, only true positive (malignant lesion cases) are included

[2]MRMC Average reader AUROC estimates and standard errors obtained from iMRMC package with Gallas et al (Commun Stat A Theory 2009; 38(15):2586-2603) approach, p value for non-inferiority

*p-value for superiority, otherwise p-value is for non-inferiority

PCP AUROC performance difference was consistent across a wide range of reader, patient, and lesion subgroups. PCPs' sensitivity and specificity was fairly consistent across a wide range of subgroups. This study had a large number of melanoma lesion cases (n=25) to provide meaningful evidence with regard to the device's impact on PCPs' detection of melanoma. This study also demonstrated that device use significantly improves PCPs' melanoma sensitivity in addition to AUROC for all cancers and melanoma. There were no safety issues since this was a reader study.

3. **DERM-ASSESS III Reader Study, titled "A Multi-Reader, Multi-Case (MRMC) Study for Evaluating the Impact of the DermaSensor Device on Primary Care Physicians' Assessment of Lesions Suggestive of Melanoma"**

Lesion Characteristics

A total of 118 US PCPs completed assessments of 100 lesion cases. A randomized lesion selection process was used to select lesions from the DERM-ASSESS III study lesion population, 50 of the 100 lesion cases were malignant and 50 were benign. The reader study pathology distribution was similar to the clinical study pathology distribution, with 34 melanomas, 8 BCCs, and 8 SCCs. Benign lesions included 31 benign melanocytic nevi, 10 seborrheic keratoses and 9 other benign lesions to best represent the proportions among the benign pathologies in the clinical study. The overall device performance on the 100 lesions in the reader study was 90.0% sensitivity and 32.0% specificity; the device performance for pigmented lesions in the clinical study was 90.3% and 32.5%.

Safety and Effectiveness Results

PCP unaided AUROC was 0.630 (95% CI: 0.582-0.678) compared to 0.671 (95% CI: 0.611-0.732) when aided with the device, which was demonstrated to be non-inferior (p<0.001) and superior (p=0.036) to PCP unaided AUROC. The change in AUROC and sensitivity is shown in the following table. The unaided sensitivity of the physicians was 73.7% (95% CI: 67.7-79.6%), and the aided sensitivity of physicians was 81.8% (95% CI: 76.0-87.6%). This 8.1% increase in aided sensitivity of the PCPs' management decisions was non-inferior (p<0.001) and superior (p<0.001) to the unaided sensitivity of the PCPs' management decisions. PCP unaided melanoma sensitivity increased from 70.2% (95% CI: 62.9-77.6%) to 79.1% (95% CI: 72.4%-85.7%) when aided. This 8.8% increase in aided melanoma sensitivity of the PCPs' management decisions was non-inferior (p<0.001) and superior (p<0.001) to the unaided melanoma sensitivity of the PCPs' management decisions.

PCP Management AUROC and Sensitivity Without and With Device				
	Lesion Assesments[1]	Estimate (%) and 95% Confidence Interval[2]		P-value[2]
		Without Device	With Device	
AUROC	n=11,800	0.630 (0.582-0.678)	0.671 (0.611-0.732)	0.036*
Sensitivity	n=5,900	73.7% (67.7-79.6%)	81.8% (76.0-87.6%)	<0.001*
Sensitivity for Melanoma	n=3,850	70.2% (62.9-77.6%)	79.1% (72.4-85.7%)	<0.001*
Specificity	n=5,900	44.2% (38.1-50.2%)	38.6% (30.9-46.2%)	<0.001

[1]For sensitivity analyses, only true positive (malignant lesion cases) are included

[2]MRMC Average reader AUROC estimates and standard errors obtained from iMRMC package with Gallas et al (Commun Stat A Theory 2009; 38(15):2586-2603)approach

*p-value for superiority, otherwise p-value is for non-inferiority

PCP AUROC performance was consistent across a wide range of reader, patient, and lesion subgroups. Since this study had a large number of melanoma lesion cases (n=34), this study provided meaningful evidence demonstrating superior melanoma sensitivity and overall sensitivity with device use, as well as a significant increase in overall AUROC. There were no safety issues since this was a reader study.

Q. SUMMARY OF ADDITIONAL STUDIES

Clinical Studies

Due to the low prevalence of melanoma in the US primary care setting, additional evidence was generated to assess device performance for melanoma with the clinical study "DERMaSensor Use in the ASSESSment of Skin Lesions Suggestive of Melanoma III (DERM-ASSESS III)." The DERM-ASSESS III study was conducted in high-volume melanoma dermatology practices where the dermatologists were blinded but provided their lesion diagnosis using their standard of care, including dermoscopic assessment prior to biopsy. As participants were seen at high-volume melanoma dermatology practicies, they may have been referred or had a history of skin cancer, as such the data from this study may not reflect how the device would perform when used in the PCP practice setting. The objective was to investigate the sensitivity and specificity of the DermaSensor device in evaluating skin lesions suggestive of melanoma. The co-primary endpoints were DermaSensor 1) sensitivity for high risk melanocytic lesions, 2) sensitivity for melanoma, and 3) specificity for benign lesions.

The effectiveness population included 311 subjects with 440 biopsied lesions from 10 dermatology practices (sites) in the United States (8) and Australia (2). Approximately half of the subjects (53.7%) enrolled in the DERM-ASSESS III study were male with a median age of 65. The most common Fitzpatrick Skin Type was Type II (52.9%), followed by Type III (20.2%) and Type I (11.6%). Benign diagnoses were benign melanocytic nevus (24.5%, 108/440), mildly atypical melanocytic nevus (20.0%, 88/440), and seborrheic keratosis (13.0%, 57/440). Melanoma was reported in 10% (44/440) and highly atypical melanocytic nevus was reported in 10% (44/440) of biopsied lesions.

Device sensitivity was 90.9% (95% CI: 83.1-95.3%) for all high risk melanocytic lesions. For melanoma only, device sensitivity was 95.5% (95% CI: 84.5-98.8%). Specificity for all biopsied but ultimately benign lesions (via histopathology) was 32.5% (95% CI: 27.2-38.3%). The study dermatologists' sensitivity for all high risk melanocytic lesions was 71.6% (95% CI: 61.3-80.0%) and for melanoma only was 90.9% (95% CI: 80.6-96.0%), as such the secondary endpoint comparing device sensitivity with a performance goal of 90% was achieved, Device NPV for melanoma was 98.1% (95% CI: 91.8-99.6%), associated PPV was 16.0% (95% CI: 11.6-21.7%). PPV increased with increasing spectral scores, for scores of 1-3 PPV was 10.3% (95% CI: 6.3-16.5%), which increased to 20.5% (95% CI: 12.7-31.5%) for 4-7 and 47.4% (95% CI: 24.9-69.8%) for scores of 8-10. With regard to device safety, there were no adverse events reported in this study.

A separate study was also conducted with the objective of characterizing the repeatability and reproducibility of the DermaSensor device (i.e., the primary endpoints) in evaluating skin lesions suggestive of melanoma, basal cell carcinoma, and/or squamous cell carcinoma. The secondary endpoints included a repeat of the primary analysis, separately for all malignant lesions. The study involved at least two investigators completing the full lesion recording process four times for each enrolled lesion, twice with one device and twice with a second device. The study enrolled 52 subjects and 64 lesions (23 lesions were malignant). The device agreement between device scans (i.e., repeatability) for all 64 lesions was 84.2% (95% CI 78.2-89.1%), with an associated PPA of 94.8%(95% CI: 92.1-97.1%) and NPA of 46.0% (95% CI: 32.1-60.0%). The agreement between physicians (i.e., reproducibility) was 87.8% (95% CI: 82.2-92.1%) with an associated APA of 92.7% (95% CI: 88.1-96.4%) and ANA of 64.4% (95% CI: 38.7-80.4%). For lesions that were malignant, the agreement was 97.1% (95% CI: 89.9-99.6%) for repeatability and 97.1% (95% CI: 89.9-99.6%) for reproducibility. For repeatability, the majority of lesions scanned fell within 2 spectral scores of each other, as shown in the table below.

Distribution of First vs Second Spectral Score

First Device Output \ Second Device Output	0	1	2	3	4	5	6	7	8	9	10	All
0	8	2	4	7	1	1	1	1	0	0	0	**25**
1	3	2	5	0	3	0	0	0	0	0	0	**13**
2	0	2	5	0	3	2	0	0	0	0	0	**12**
3	0	1	4	5	8	1	1	0	0	0	0	**20**
4	0	1	0	0	2	3	0	0	0	0	0	**6**
5	0	0	0	1	1	0	2	2	1	0	0	**7**
6	0	0	0	0	0	1	5	2	2	0	0	**10**
7	0	0	0	0	0	1	2	0	2	1	0	**6**
8	0	0	0	0	0	0	0	3	4	5	1	**13**
9	0	0	0	0	1	0	0	1	3	9	4	**18**
10	0	0	0	0	0	0	0	0	1	3	9	**13**
All	**11**	**8**	**18**	**13**	**19**	**9**	**11**	**9**	**13**	**18**	**14**	**143**

Human Factors Validation Study

After formative testing, summative human factors validation testing assessed use-related safety of the device and evaluated user tasks through simulated-use. Key attributes of the intended users, uses, and use environments were considered and sufficiently simulated to test safe and effective operation of the device under actual conditions of use.

Two (2) user groups participated in the testing: 15 primary care physicians (PCPs) representing a range of clinical experiences working in primary care, and 15 mid-level practitioners that included Physician Assistants (PAs), Nurse Practitioners (NPs), and Registered Nurses (RNs). All 30 participants were able to identify the indications for use and all contraindications for use, and that this device should not be used for the sole diagnosis of skin cancer. Use difficulties, close calls, and use errors were analyzed to determine their likely root cause(s) and were adequately mitigated. The results demonstrated that participating PCPs were able to independently and appropriately take recordings from mock lesions with acceptable levels of residual risk.

R. SUBGROUP ANALYSES

Additional analysis of the DERM-SUCCESS pivotal and two reader study results was performed based on key demographic variables such as age and Fitzpatrick skin type, as shown in the following tables.

DermaSensor was evaluated in a limited number of patients aged below 40. In the pivotal study, there were 207 total lesions in patients 20-39 years old with 7 skin cancers (3.1% of the total of 224). For these 207 lesions, the device melanoma sensitivity was 71.4% (n=7), there were no nonmelanoma skin cancer (NMSC, i.e. SCC or BCC) enrolled, and specificity was 23.5% (n=200); for patients 40 years and older, the device overall sensitivity was 96.3% (n=217), melanoma sensitivity was 90.2% (n=41), NMSC sensitivity was 97.7% (n=176), and specificity was 20.3% (n=1155).

When evaluating device standalone performance and the device impact on PCPs' sensitivity by age groups, the results are consistent across all age groups for 40 and above.

Age Group	Device Sensitivity	Device Specificity	PCP Unaided Sensitivity	PCP Aided Sensitivity	% Increase
40-49*	100% (9/9)	22.9% (39/170)	83.1%*	91.8%*	8.7%*
50-59	95.6% (43/45)	24.1% (72/299)	77.7 - 83.6%	90.3 - 94.4%	6.8 - 16.8%
60-69	93.9% (62/66)	22.0% (89/405)	72.9 - 84.9%	82.0 - 91.0%	6.2 - 9.2%
70-79	98.3% (59/60)	12.6% (27/214)	84.6 - 90.7%	87.4 - 98.6%	2.8 - 7.9%
80-89	97.3% (36/37)	10.8% (7/67)	79.6 - 93.9%	98.9 - 99.1%	5.0 - 19.4%

* Only DERM-SUCCESS Pigmented Reader Study results are reported.

When evaluating device standalone performance and the device impact on PCPs' sensitivity by Fitzpatrick skin type, the results are consistent across all skin types for 40 and above.

All Skin Cancer - For All Patients 40 and Above					
Skin Type and Age Subgroups	Device Sensitivity	Device Specificity	PCP Unaided Sensitivity	PCP Aided Sensitivity	% Increase
I	96.2% (25/26)	19.8% (22/111)	78.1 - 86.4%	79.7 - 98.5%	1.5 - 12%
II	97.4% (75/77)	21.3% (67/314)	85.0 - 87.6%	93.0 - 94.4%	5.4 - 9.5%
III	96.9% (63/65)	16.2% (60/371)	75.8 - 84.3%	87.2 - 98.6%	11.4 - 14.4%
IV	96.0% (24/25)	20.7% (42/203)	81.0 - 81.3%	83.9 - 90.3%	2.6 - 9.3%
V	90.5% (19/21)	27.7% (39/141)	74.1 - 78.6%	83.7 - 95.4%	5.1 - 21.3%
VI	100% (3/3)	26.7% (4/15)	73.1 - 93.5%	96.8 - 97.2%	3.2 - 24.1%

In addition to analyzing the impact of skin type on all cancers, the impact on individual cancer subtypes was also assessed. The table below shows results for melanoma, where some variability was observed. NMSC performance was found to be consistent across the various subgroups in these tables; all standalone device results ranged between 88.2% and 100%. The PCP-aided NMSC sensitivity increases all ranged between 2.5% and 9.6% for the DERM-SUCCESS Pigmented Reader Study; all sensitivity increases ranged between 11.1% and 16.4% for the DERM-SUCCESS Pivotal Reader Study. Note that for melanoma, only results from the pigmented lesion reader study are presented because only this DERM-SUCCESS reader study had a sufficient number of melanomas to permit meaningful sub-stratified analyses by skin type.

Melanoma - For All Patients 40 and Above					
Skin Type and Age Sub-groups	**Device Sensitivity**	**Device Specificity**	**PCP Un-aided Sensi-tivity**	**PCP Aided Sensi-tivity**	**% In-crease**
I	100% (9/9)	20.9% (14/67)	72.7%	82.7%	10.0%
II	90.9% (10/11)	25.3% (45/178)	79.4%	86.4%	7.0%
III	81.8% (9/11)	20.0% (48/240)	59.1%	76.4%	17.3%
IV*	80.0% (4/5)	22.5% (29/129)	72.7%	57.8%*	-14.9%*
V	100% (4/4)	26.7% (31/116)	57.1%	66.2%	9.1%
VI	100% (1/1)	33.3% (4/12)	N/A	N/A	N/A

Note: Unaided and Aided Sensitivity are reported from the DERM-SUCCESS Pigmented Reader Study

*Device melanoma sensitivity in this reader study was under-represented by 30% for Fitzpatrick Skin Type IV

S. EFFECTIVENESS CONCLUSIONS

Overall, the data presented demonstrate that the DermaSensor device is safe and effective for its intended purpose of assisting physicians in their assessment and management of lesions suggestive of skin cancer. There is a well-recognized public health need for additional tools to aid PCPs' in assessing skin cancers (Brown et al J Gen Intern Med 2022:37(9):2267-2279). The DermaSensor device addresses this need by providing a highly sensitive, objective test result to better inform PCPs' clinical management decisions. Both pivotal studies demonstrated the device improves the existing standard of care through an improvement in skin cancer detection at the primary care level.

Overall, the safety and performance data of the DermaSensor device support its benefits in the primary care setting for aiding providers in assessment of lesions suggestive of skin cancer. There are no mechanical safety concerns with device use on patients. The device's high sensitivity in the PCP setting, along with its significant improvement of PCP referral sensitivity, also support its utility in this setting. While there are risks associated with device false negatives, the device performance was found to decrease PCPs' false negatives by half, from 18.0% without device use to 8.6% with device use. Two supplemental reader studies also demonstrated that device use significantly decreases PCPs' false negatives for all skin cancers and for melanoma.

T. SAFETY CONCLUSIONS

There were no adverse events documented in the pivotal clinical study. 4.5% of malignant lesions were false negatives in that the device provided a negative Monitor result (i.e., sensitivity of 95.5%). However, the three reader studies found that use of the DermaSensor result decreased PCPs' false negatives by 5.8% to 9.4%. 79.3% of benign biopsied lesions were false positives by the device (i.e., specificity of 20.7%). However, the reader study found that the PCPs' false positive referral rate with device use was 61.4% to 67.6%. Potential indirect adverse effects of any skin examination for skin cancer include: false negative results may lead to delays in the timely referral, diagnosis and treatment of skin cancer, allowing an undetected condition to worsen and potentially increasing morbidity, and mortality; false positive results could lead to more patient concern and patients unnecessarily undergoing more frequent dermatology evaluations.

U. PEDIATRIC EXTRAPOLATION

Existing clinical data were not leveraged to support the use of the device in a pediatric population.

V. LABEL REFERENCE

Symbol	Standard Title and Designation	Symbol Title (Reference Number)	Explanatory Text
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Manufacturer (5.1.1)	Indicates the medical device manufacturer
	IEC 60601-1 Edition 3.1 2012-08 Medical electrical equipment – Part 1: General requirements for basic safety and essential performance	Type B Applied Part (IEC 60417-5840)	Indicates part/accessory of the medical device that comes into direct physical contact with the patient, and which neither has a patient connection (point through which current can flow), nor is suitable for direct cardiac application
	IEC 60601-1 Edition 3.1 2012-08 Medical electrical equipment – Part 1: General requirements for basic safety and essential performance	Class II equipment (IEC 60417-5172)	Medical device/accessory in which protection against electric shock includes Double Reinforced insulation and in which there is no scope for protective earthing
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Catalog number (5.1.6)	Indicates the manufacturer's catalog number so that the medical device can be identified
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Serial Number (5.1.7)	Indicates the manufacturer's serial number so that a specific medical device can be identified
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Authorized representative of the EU Community (5.1.2)	Indicates the authorized representative
	47 CFR § 2.1074(b)	FCC Logo	Serves as a visual indication that the product, authorized under the SDoC procedure complies with the applicable FCC requirements
	IEC 60601-1 Edition 3.1 2012-08 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Follow instructions for use (ISO 7000-1641)	Indicates the need for the user to consult the instructions for use
	§801.109 Prescription devices	Prescription Use	United States Federal law restricts this device to sale by or on the order of a physician
	DIRECTIVE 2012/19/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 4 July 2012 on waste electrical and electronic equipment (WEEE)	WEEE Symbol	Indicating separate collection for EEE- Waste
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Keep dry (5.3.4.)	Indicates a medical device that needs to be protected from moisture

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Symbol	Standard Title and Designation	Symbol Title (Reference Number)	Explanatory Text
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Do not use if package is damaged (5.2.8)	Indicates a medical device that should not be used if the package has been damaged or opened
	IEC 60601-1 Edition 3.1 2012-08 Medical electrical equipment – Part 1: General requirements for basic safety and essential performance	Caution (5.4.4)	Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself.
	IEC 60601-1 Edition 3.1 2012-08 Medical electrical equipment – Part 1: General requirements for basic safety and essential performance	General warning sign (ISO 7010-W001)	Indicates to signify a general warning
	REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 April 2017 on medical devices	CE marking (Article 20)	Indicates that a device is in conformity with the applicable requirements set out in the Medical Devices Regulation (2017/745) and other applicable Union harmonisation legislation providing for its affixing
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Fragile, handle with care (5.3.1)	Indicates a medical device that can be broken or damaged if not handled carefully.
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Temperature limit (5.3.7)	Indicates the temperature limits to which the medical device can be safely exposed.
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Humidity limitation (5.3.8)	Indicates the humidity limits to which the medical device can be safely exposed.
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Atmospheric pressure limitation (5.3.9)	Indicates the range of atmospheric pressure to which the medical device can be safely exposed
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Importer (5.1.8.)	Indicates the entity importing the medical devices into the locale
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Distributor (5.1.9)	Indicates the entity distributing the medical devices into the locale
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Model Number (5.1.10)	Indicates the model number or type of the product
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Country of Origin (5.1.11)	To identify the country of manufacture of products

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Symbol	Standard Title and Designation	Symbol Title (Reference Number)	Explanatory Text
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Unique Device Identifier (5.7.10)	Indicates a carrier that contains Unique Device Identifier Information
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Medical Device (5.7.7)	Indicates the item is a medical device
	ISO 15223-1 Fourth edition 2021-07 Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements	Translation (5.7.8)	Indicates the original medical device information has undergone a translation which supplements or replaces the original information
	Nemko certification mark	Certification Mark	Indicates that the product has been certified by an accepted certification body after successful testing for product-specific standards products applicable in the USA and Canada
	DermaSensor created	Reissued	Indicates the device has been previously issued to customers for commercial purposes, repaired, or serviced.

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W. MANUFACTURER AND CONTACT INFORMATION

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MD Rx Only

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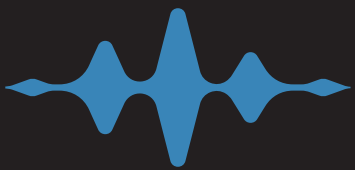

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