DE NOVO CLASSIFICATION REQUEST FOR COMFORT MARKER 2.0.

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Radiation therapy marking device**. A radiation therapy marking device is a powered device that transdermally delivers a permanent or temporary colorant to the skin for the purpose of placing marks to guide radiation therapy. This classification does not include devices with reusable or reprocessed needles or devices intended for diagnostic, therapeutic, or aesthetic use or to deliver other products for these uses.

NEW REGULATION NUMBER: 21 CFR 892.5785

CLASSIFICATION: Class II

PRODUCT CODE: QRN

BACKGROUND

DEVICE NAME: Comfort Marker 2.0.

SUBMISSION NUMBER: DEN200041

DATE DE NOVO RECEIVED: June 22, 2020

SPONSOR INFORMATION:

Medical Precision B.V.
Telfordstraat 9 - 30
NL 8013 RL, Zwolle
Netherlands

INDICATIONS FOR USE

The Comfort Marker 2.0. is indicated as follows:

> The device is indicated for use for applying ink to the skin to identify the margins for radiation therapy. The device is intended to be used in clinical settings by Radiotherapy professionals.

LIMITATIONS

The sale, distribution, and use of the Comfort Marker 2.0 are restricted to prescription use in accordance with 21 CFR 801.109.

Colorant is not distributed with this device.

Do not use the device on damaged skin.

Do not use the device on skin with dermatitis.

The Safety Needle is sterile, single use and cannot be reprocessed.

Only use specified consumables.

Not intended for use in magnetic resonance imaging rooms.

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

DEVICE DESCRIPTION

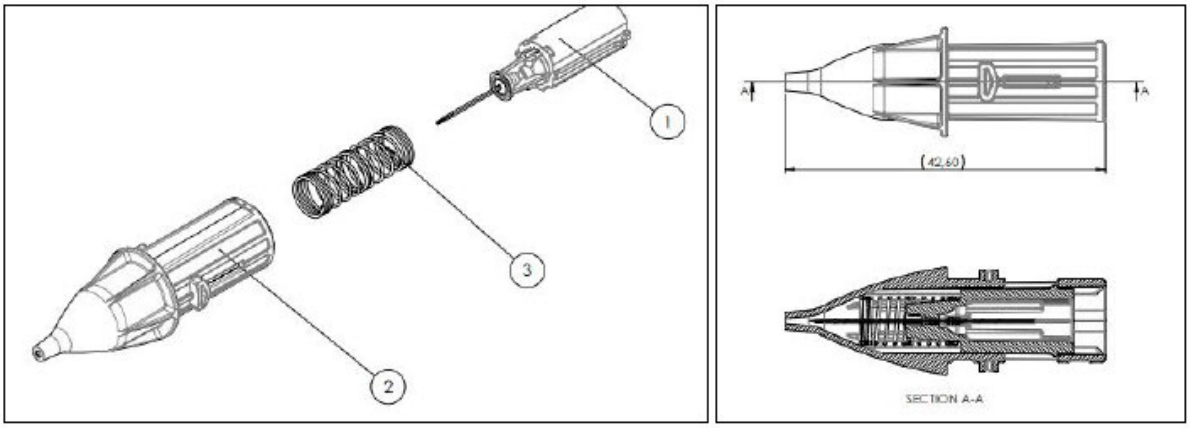
The Comfort Marker 2.0 is an application system for placing reference marks on or in patient's skin to facilitate set-up for radiation therapy treatment. The device includes the following components:

1. Battery powered control unit with pen
2. Main powered docking station with adapter and
3. Safety needle (single use, sterile)

Figure 1: Control unit, Pen (with safety needles) and docking station

Mode of operation: To achieve the intended use, the device uses a safety needle (shown in figure 2). This actuation is achieved by a longitudinal movement of the driving rod inside the pen. The driving mechanism comprises electromagnetic coils, switched on and off by the controller for generating magnetic fields. Hereby, the distance moved by the driving rod can be controlled precisely by controlling the amount of applied energy. The driving device comprises a guiding mechanism arranged for allowing only movement of the driving rod along the longitudinal direction. The actual distance travel is measured with a measuring coil and used to control the desired depth setting. The system contains a mechanical end stop in the safety needle to ensure that the needle will not protrude more than 1 mm. The docking station is used to re-charge the control unit.

Figure 2: Safety needle assembly (includes carrier with needles, tip and spring)



Direction of use: Reference points / markers are placed transdermally to facilitate patient set-up for radiation therapy treatment. After disinfection of the skin area, placement of the Safety Needle on the pen, calibration of the system and applying the colorant, the user selects the shallow setting on the Control Unit and places the marker. If the user decides the marker point is not sufficiently visible, the medium setting on the control unit is selected.

SUMMARY OF NONCLINICAL/BENCH STUDIES

STERILITY

The safety needle is a sterile, single use component of the device system. The safety needle is sterilized using EO sterilization and sterilant residuals were quantified and under the acceptable limits for EO and ECH. The sterilization method was validated per ANSI/AAMI/ISO 11135:2014: *Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices*. The sterility assurance level (SAL) for the needle cartridge is at least 10^{-6}.

The requirements of the packaging system for the safety needle were evaluated in accordance with ISO 11607-1:2019 *Requirements for materials, sterile barrier systems and packaging systems.* The shelf-life of the needle cartridge was evaluated after accelerated aging equivalent to one year. The package integrity was evaluated using the seal strength test and the dye penetration test to demonstrate the performance of the sterile barrier system (SBS) over time. The test article met the acceptance criteria for each test.

ELECTRICAL SAFETY AND ELECTROMAGNETIC CAPABILITY (EMC)

The following Electrical Safety and EMC testing has been performed:

- ANSI/AAMI ES60601- 1:2005+A2 (R2012) +A1: *Medical Electrical Equipment - Part 1: General Requirements For Basic Safety And Essential Performance (IEC 60601-1:2005, MOD) (Consolidated Text) (Includes ANSI/AAMI ES60601-1:2005/(R)2012 And A1:2012, C1:2009/(R)2012 And A2:2010/(R)2012)*
- IEC 60601-1-2: 2014 (Edition 4): *Medical electrical equipment Part 1-2 – General requirements for basic safety and essential performance – Electromagnetic compatibility*
- IEC 60601-1-6: Collateral Standard: Usability

The Comfort Marker 2.0 passed all relevant portions of the testing.

SOFTWARE

The software is responsible for implementing and testing the required drivers, communication interface and the application software for both the Comfort Marker 2.0 control unit and pen. All of the elements of software information corresponding to moderate level of concern (LOC) devices as outlined in FDA's guidance document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" (issued May 11, 2005) were provided. Adequate documentation describing the software development program was provided. Verification and validation (V&V) activities were described at the unit, integration, and system level and the results of these activities met the pass/fail criteria. In addition, a hazard analysis from both the patient's and user's standpoint was performed, hazards were addressed; and an appropriate validation process has been carried out.

PERFORMANCE TESTING - BENCH

Bench testing was conducted to demonstrate that the Comfort Marker 2.0 performs as expected under the anticipated conditions of use. This testing included evaluation of key device parameters such as needle penetration depth, puncture rate, and the ability of the safety features of the device to mitigate the risk of cross-contamination. The following bench testing was conducted to demonstrate the device performance characteristics:

- Puncture Rate: The purpose of this test was to demonstrate that the device operates at the intended puncture rate at each depth setting when used on a skin substitute.

- Needle Puncture Depth: The purpose of this test was to evaluate the depth of needle penetration into a skin substitute at each depth setting.
- Needle Sharpness: The purpose of this test is to test the sharpness of the needle based on required force for piercing standardized film.
- Needle Arrangement: The objective of this test is to demonstrate that the needles are properly arranged in a circular pattern after assembly.
- Needle Protrusion: The purpose of this test was to ensure that the needle does not protrude more than 1 mm from the tip housing.
- Needle Dimension: The purpose of this test was to ensure that the needle diameter and straightness are within specifications
- Tip-to-Tip Alignment: The purpose of this test was to evaluate the alignment of each needle tip within the needle assembly.
- Glue Strength: The purpose of this test was to evaluate the strength of the bond between the needles and the needle carrier.
- Squeeze Test: The purpose of this test was to demonstrate that the needle carrier stays within the protective housing when squeezed by hand during assembly.
- Drop Test: The purpose of this test was to demonstrate that the needle housing adequately shields the needle tips when dropped.
- Colorant Migration: The purpose of this test was to demonstrate adequate protection against fluid ingress into the handpiece.

SUMMARY OF CLINICAL INFORMATION

A limited study to validate the durability of reference points placed with the Comfort Marker 2.0 for a duration of twelve weeks was conducted on healthy volunteers. The study focused on the following elements: technique to place the mark, colorant to be used with the Comfort Marker 2.0, whether the mark is visible to the radiation therapy professional, whether the colorant migrates impacting the matter that would affect clinical management and duration that the mark remains visible.

(b) (4) healthy human volunteers participated in the study, between the age group of (b) (4) and (b) (4) men and (b) (4) women). They did not have any underlying skin conditions. All volunteers were informed about the test procedure and provided with details of the test center. Before participating, all the volunteers signed the consent form.

The procedure was performed in a radiotherapy preparation room by a radiotherapy technician. The procedure used Accu-tatt® - ink in the United States of America and the Comfort Marker 2.0 device. The colorant was applied to the arms of two volunteers and to the thoracic area of four volunteers. Endpoints defined were visibility, migration, and clearance.

The reference points were marked according to the Comfort Marker 2.0 instructions for use. Each volunteer received reference points using Accu-Tatt® at all the depth settings (0.25, 0.45 and 0.75 mm). Documentation of the reference points were taken immediately and followed for 12 weeks. Each reference point was made only once.

Results

a) The healthy volunteer study showed that Comfort Marker 2.0 can place well defined reference points using Accu-Tatt® at all three depth settings.
b) The reference points did not show any migration on the skin. All reference points from Accu-Tatt® were clearly visible during week (b) (4) until (b) (4) a period in which radiotherapy treatment is provided.
c) Generally, Accu-Tatt® when used at the lowest depth settings (0.25 mm) faded away at week 12 in most of the participants, however no impact on clinical treatment was observed.

Pediatric Extrapolation

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

LABELING

Labeling has been included which consists of a user manual, instructions for use, box labeling, and patient labeling. The user manual and instructions for use include a description of the device technical parameters, contraindications, warnings and precautions. These documents summarize the main steps for using the device as well as the necessary measures to properly dispose of any single use items and clean the reusable components of the device.

The instructions for use contain the following:

1. Only use specified consumables with the Comfort marker 2.0
    a. Safety Needle: Safety needle, Medical Precision B.V.
    b. Accu-tatt® ink
2. Warnings:
    a. Inadequate disinfection may lead to cross-contamination when used on multiple patients.
    b. During operation the needle is continuously exposed out of the Safety Needle. Be careful not to induce a needle stick incident.
3. Contraindications:
    a. Do not use on damaged skin.
    b. Do not use the Comfort Maker 2.0 on skin with dermatitis. Radiation therapy can cause radiation dermatitis. Due to superficial placement of the pigment, radiation dermatitis may alter the appearance or duration of the marker placed by the Medical Precision device. Radiation dermatitis may accelerate immune system dispersion or clearing of the tattoo pigment, resulting in loss of usable marker before the radiation mark is no longer needed.
4. Precautions
    a. The reference points made with a shallow depths 0.25 mm may not be visible immediately after placing the reference point in certain situations. In such cases, use medium depth setting 0.45 mm on the same location.

b. The shallow depth setting 0.25 mm may tend to fade after week 8. Assess the reference points at each patient visit. If signs of fading or clearing are noted, it is recommended to repeat the placement of reference points on intact skin as per established standard of care.

Risks to Health

The table below identifies the risks to health that may be associated with use of a radiation therapy marking device and the measures necessary to mitigate these risks.

Table 1. Identified Risks to Health and Mitigation Measures

Identified Risks to Health	Mitigation Measures
Adverse tissue reaction	Biocompatibility evaluation
Cross contamination and infection	Reprocessing validation Sterilization validation Non-clinical performance testing Shelf-life testing Labeling
Needle stick injury to provider	Non-clinical performance testing Labeling
Device and/or software failure leading to ineffective marking	Clinical performance testing Non-clinical performance testing Software validation, verification, and hazard analysis Labeling
Electrical shock or electromagnetic interference with other devices	Electromagnetic compatibility testing Electrical safety testing Labeling

Special Controls

In combination with the general controls of the FD&C Act, the radiation therapy marking device is subject to the following special controls:

(1) Design verification and validation must include:
  (i) Documentation of performance data from studies that demonstrate:
    (A) The indicated colorant is compatible with the device and its method of delivery;
    (B) The device can reproducibly deliver the indicated colorant with the specifications described; and
    (C) The length of time that compatible colorants remain visible on the skin following device application.
  (ii) Documentation of performance data from studies that demonstrate:
    (A) Accuracy and reproducibility of needle penetration depth;

(B) Device protection from cross-contamination, including fluid ingress protection;
(C) Adequacy of the cleaning and disinfection instructions to ensure that the reusable components of the device can be cleaned and disinfected; and
(D) The sterility of all patient-contacting components (e.g., safety needle).

(iii) Documentation of performance data from studies that demonstrate electrical safety and electromagnetic compatibility (EMC) of all electrical components of the device.

(iv) Documentation of performance data from studies that demonstrate continued sterility, package integrity, and device functionality over the intended shelf life.

(v) Documentation of software verification, validation, and hazard analysis.

(2) The labeling required under 21 CFR 801.109(c) must include:

(i) An explanation of the device and the mechanism of operation;

(ii) Validated methods and instructions for reprocessing of any reusable components;

(iii) Disposal instructions; and

(iv) A shelf life for all sterile components.

BENEFIT-RISK DETERMINATION

The probable benefits of the Comfort Marker 2.0 outweigh the probable risks of the device in light of the special controls proposed for this device in addition to the applicable general controls. The device may be used to apply marks using Accu-tatt® to the skin to assist with patient set-up for radiation therapy. In the data provided, the marks were visible and durable for a minimum period of 8 weeks. Risks associated with adverse tissue reaction are addressed with biocompatibility evaluation. Risks related to infection and cross-contamination are mitigated by reprocessing validation, sterilization validation, and labeling. Labeling and other special controls related to needle performance and colorant delivery will also help address risks associated with ineffective marking. Risks associated with interference with other devices are mitigated by special controls concerning electromagnetic compatibility and software validation, verification, and hazard analysis. The performance data provided, including those data required by the special controls, when combined with the device labeling suggest that the device will be safe and effective for its proposed indications for use.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

BENEFIT/RISK CONCLUSION

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

> The device is indicated for use for applying ink to the skin to identify the margins for radiation therapy. The device is intended to be used in clinical settings by Radiotherapy professionals.

The probable benefits outweigh the probable risks for the Comfort Marker 2.0. The device provides benefits, and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the Comfort Marker 2.0 is granted and the device is classified as follows:

Product Code: QRN
Device Type: Radiation therapy marking device
Regulation Number: 21 CFR 892.5785
Class: II