Medical Precision BV
% Cherita Jones
Regulatory Consultant
M Squared Associates, Inc
127 West 30th St. Floor 9
NEW YORK NY 10001

March 30, 2023

Re: K222112
Trade/Device Name: Comfort Marker 2.0
Regulation Number: 21 CFR 892.5785
Regulation Name: Radiation therapy marking device
Regulatory Class: Class II
Product Code: QRN
Dated: February 27, 2023
Received: February 27, 2023

Dear Cherita Jones:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Lora D. Weidner -S

Digitally signed by Lora D. Weidner -S
Date: 2023.03.30 20:36:13 -04'00'

Lora D. Weidner, Ph.D.
Assistant Director
Radiation Therapy Team
DHT8C: Division of Radiological Imaging and Radiation Therapy Devices
OHT8: Office of Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K222112

Device Name

Comfort Marker 2.0

Indications for Use *(Describe)*

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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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K222112

510(K) Summary

The following information is provided as required by 21 CFR § 807.87 for Traditional 510(k) premarket notification. In response to the Safe Medical Devices Act of 1990, the following is a summary of the information upon which the substantial equivalence determination is based.

Contact Details	
Applicant Name	Medical Precision b.v.
Applicant Address	Telfordstraat 9 - 30 NL 8013 RL, ZWOLLE The Netherlands
Applicant Contact	Blerta Kukaj
Applicant Contact E-mail	kukaj@medicalprecision.nl
Correspondent Name	M Squared Associates, Inc
Correspondent Address	901 King Street, Suite 200 Alexandria, VA 22314
Correspondent Telephone Number	347-954-0624
Correspondent Contact	Cherita James
Correspondent E-mail	cjames@msquaredassociated.com
Submission Date	27 February 2023
Device Name	
Device Trade Name	Comfort Marker 2.0
Common Name	Radiation Therapy Marking Device
Classification	II
Regulation	21 CRF 892.5785
Product Code	QRN
Legally Marketed Predicate Device	
Predicate Trade Name	Comfort Marker 2.0 (DEN200041)
Product Code	QRN
Device Description Summary	
Comfort Marker 2.0 is an application system for placing reference marks on patients eligible for Radiotherapy treatments. The Comfort Marker 2.0 allows the user to place accurate tattoo markers (reference points) on patients enabling radio therapy. The device consists of a Control and Pen module which drives a Safety Needle. Different depth settings can be chosen to accommodate for different skin types. When the tattoo marking has been placed the Control Unit can be stored and charged in the Docking station.	
Intended Use/Indications for Use	
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.	
Indications for Use Comparison	
No change in intended use	
Technological Comparison	
Both the subject (Comfort Marker 2.0 in this 510k) and the predicate device (Comfort Marker 2.0, De Novo DEN200041) are the same in this case. No technological differences exist. Comfort Marker 2.0 received De novo clearance on 10th of December 2021. This 510(K) is prepared to include clinical	

data on pain experience by patients undergoing radiotherapy treatment. Therefore, the predicate and the legally marketed device are substantially equivalent.

Item	**Subject Device**	**Predicate Device DEN200041**	**Similarities/Differences**
Product Code	QRN	QRN	No difference in FDA product code
Trade Name	Comfort Marker 2.0	Comfort Marker 2.0	No difference
510 (K) number	Not assigned	De Novo: DEN200041	N/A
Intended use	The device is intended to be used in clinical setting by Radiotherapy professionals	The device is intended to be used in clinical setting by Radiotherapy professionals	No difference
Indications for use	The device is indicated for use for applying ink to the skin to identify the margins of radiation therapy.	The device is indicated for use for applying ink to the skin to identify the margins of radiation therapy.	No difference
Target population	Patients with undamaged skin undergoing repeated radiotherapy.	Patients with undamaged skin undergoing repeated radiotherapy.	No difference:
Contra indications	Do not use the device on damaged or dermatitis skin.	Do not use the device on damaged or dermatitis skin.	No difference
Where used	In a Radiotherapy department of a hospital	In a Radiotherapy department of a hospital	No difference
Energy used / delivered	Battery: Rechargeable battery, 3.7 V, 2.4 Ah, Lithium Ion AC/DC power supply: 18W, 12V, 1.5A	Battery: Rechargeable battery, 3.7 V, 2.4 Ah, Lithium Ion AC/DC power supply: 18W, 12V, 1.5A	No difference
Design / operating principle	Longitudinal movement of the driving rod in the pen actuates the safety needle. The movement of the safety needle is measured by a measuring coil and to control desired depth setting.	Longitudinal movement of the driving rod in the pen actuates the safety needle. The movement of the safety needle is measured by a measuring coil and to control desired depth setting.	No difference
Clinical Performance	Clinical trial was performed on 100 patients. Pain and user experience was recorded.	N/A	Clinical data on pain experience, user experience and clinical effectiveness was recorded in this study.
Bench Performance	• Needle depth • Needle sharpness test • Drop test • Ink migration test • Needle pattern test • Glue strength test • Needle protrusion test	• Needle depth • Needle sharpness test • Drop test • Ink migration test • Needle pattern test • Glue strength test • Needle protrusion test	No difference

	• Durability of reference points on human volunteers	• Durability of reference points on human volunteers	
Standards met	Biological evaluation: • ISO 10993-1, 2018 • ISO 10993-10, 2009, • ISO 10993-5, 2009 Sterilization: • ISO 11135,2014/Amd 1:2018 Packaging: • ISO 11607-1, 2019 • ISO 11607-2, 2019 Risk Management: • ISO 14971:2012 Electrical safety: • IEC 60601-1, 2005/A1:2012 • IEC 60601-1-2, 2014 • IEC 60601-1-6, 2010 Clean rooms: • ISO 14644-1, 2015 • ISO 14644-2, 2015	Biological evaluation: • ISO 10993-1, 2018 • ISO 10993-10, 2009, • ISO 10993-5, 2009 Sterilization: • ISO 11135,2014/Amd 1:2018 Packaging: • ISO 11607-1, 2019 • ISO 11607-2, 2019 Risk Management: • ISO 14971:2012 Electrical safety: • IEC 60601-1, 2005/A1:2012 • IEC 60601-1-2, 2014 • IEC 60601-1-6, 2010 Clean rooms: • ISO 14644-1, 2015 • ISO 14644-2, 2015	No difference
Device materials	Safety Needle: • Needle housing: Zylar 960 (Methyl Methacrylate Butadiene Styrene) • Needles: Stainless Steel AISI 304H • Spring: Stainless steel UGI S4310-6 • Glue: Dymax 1405-M-UR-SC Pen : • Pen shield : Ferro Magnetic steel 1018 • Pen ring: Ferro Magnetic iron-ETG100 • Pen actuator: ABS PA 757_CHIMET_PolylacR • Pen coilformer: ABS PA 757_CHIMET_PolylacR	Safety Needle: • Needle housing: Zylar 960 (Methyl Methacrylate Butadiene Styrene) • Needles: Stainless Steel AISI 304H • Spring: Stainless steel UGI S4310-6 • Glue: Dymax 1405-M-UR-SC Pen : • Pen shield : Ferro Magnetic steel 1018 • Pen ring: Ferro Magnetic iron-ETG100 • Pen actuator: ABS PA 757_CHIMET_PolylacR • Pen coilformer: ABS PA 757_CHIMET_PolylacR	No difference

	Control Unit: • PC +ABS PC510 CHIMEI WONDERLOY • Silicone rubber Docking station: • PC +ABS PC510 CHIMEI WONDERLOY	Control Unit: • PC +ABS PC510 CHIMEI WONDERLOY • Silicone rubber Docking station: • PC +ABS PC510 CHIMEI WONDERLOY	
Biocompatibility	Complies with ISO 10993 series of standards for • Cytotoxicity • Skin Irritation • Skin Sensitization • Material Mediated pyrogenicity • Acute Systemic Toxicity	Complies with ISO 10993 series of standards for • Cytotoxicity • Skin Irritation • Skin Sensitization • Material Mediated • Pyrogenicity • Acute Systemic Toxicity	No difference
Electrical safety and EMC	Complies with IEC 60601 series of standards: • IEC 60601-1 ,2005/A1:2012 • IEC 60601-1-2, 2014 • IEC 60601-1-6, 2010	Complies with IEC 60601 series of standards: • IEC 60601-1 ,2005/A1:2012 • IEC 60601-1-2, 2014 • IEC 60601-1-6, 2010	No difference
Sterility of safety needle	SAL: 10^{-6} Ethylene oxide sterilization Single use component of the device system	SAL: 10^{-6} Ethylene oxide sterilization Single use component of the device system	No difference
Mechanical safety	• The safety Needle extends max up to 1 mm during operation (mechanical stop) • The safety needle is covered by housing to prevent needle stick injuries while not in operation	• The safety Needle extends max up to 1 mm during operation (mechanical stop) • The safety needle is covered by housing to prevent needle stick injuries while not in operation	No difference
Software and Cybersecurity	• The software does not impact any risk related solutions and no injury or damage to health is possible due to software. The software is therefore classified as class A • Complies with IEC 62304:2006-05 and IEC62304:2015-06	• The software does not impact any risk related solutions and no injury or damage to health is possible due to software. The software is therefore classified as class A • Complies with IEC 62304:2006-05 and IEC62304:2015-06	No difference
MRI safety	MRI unsafe	MRI unsafe	No difference

Non-Clinical and/or Clinical test Summary and Conclusions

Non-Clinical and Clinical Summary

Product functionality: The Control unit, the pen and the safety needle all meet the requirements presented in bench testing.

Biocompatibility: The Safety Needle meets cytotoxicity requirements of ISO 10093-5 Biological evaluation of medical devices -Part 5: Tests for in vitro cytotoxicity.

Biocompatibility: The Safety Needle meets sensitization requirements of ISO 10993-10 Biological evaluation of medical devices -Part 10:Tests for irritation and skin sensitization.

Biocompatibility: The safety Needle meets the Material Mediated pyrogenicity requirements of ISO 10993-11:2017 Biological Evaluation of Medical Devices Part 11: Tests for systemic toxicity.

Biocompatibility: The safety Needle meets the Acute Systemic Toxicity requirements of ISO 10993-11:2017 Biological Evaluation of Medical Devices Part 11: Tests for systemic toxicity.

Sterilization: A Sterility Assurance Level (SAL) of 10-6 has been validated in accordance with the requirements of ISO 11135:2014 for Ethylene Oxide.

Electrical Safety and EMC: The device meets safety and EMC standards requirements of IEC 60601-1 ,2005/A1:2012, IEC 60601-1-2, 2014 and IEC 60601-1-6, 2010

Software and Cybersecurity: The software is compliant with Complies with IEC 62304:2006-05 and IEC62304:2015-06 Medical device software life cycle processes.

Clinical simulated use testing: The performance of Comfort Marker 2.0 and durability of reference points (at 3 different depth settings) were tested on 6 healthy volunteers. The reference points were tracked for 12 weeks for visibility, migration and clearance. The healthy volunteer study showed that Comfort Marker 2.0 can place well defined reference points at all three depth settings using three inks. The reference points did not show any migration on the skin. All reference points from three inks were clearly visible during week 2 until 8, a period in which radiotherapy treatment is provided.

Clinical testing: The aim of the randomized, multi-arm, double-blind study with concurrent ("active") control was to establish whether the use of Comfort Marker 2.0 translates into a benefit in terms of comfort, satisfaction, effectiveness, and cosmesis compared to the use of lancets (standard, control). The clinical study was performed in Portugal between October 2021 and January 2022. Target one hundred patients (18 years or older) were enrolled (50 assigned to lancet arm and 50 assigned to Comfort Marker 2.0 arm.

Patient demographic and clinical characteristics: The median age of all patients included in the trial was 61 (25-85 years). The majority of patients within the clinical trial were women (73%) with men making up 27% of the patient population. The number of set-up markings was also well balanced: 64.0% of the patients in the lancets group and 68.0% of those in the CM group had received >4 set-up markings, with a median of 9 in both groups. Most of the patients included were referred to irradiate breast or chest wall (61.0%), followed by pelvis (22.0%) and thorax (11.0%).

Patient accountability for the four endpoints defined for the trial is presented in the table below:

Stage	Investigational device arm (Comfort Marker 2.0)	Control arm (lancets)	Total
Enrollment	50	50	100
Treatment (reference points tattooing)	50	50	100
Primary outcome endpoint analysis: Patient's comfort (experienced pain during tattooing process)	50	50	100
Primary outcome endpoint analysis: effectiveness (reference points visibility for radiotherapy professionals)	50	48	98
Secondary outcome endpoint analysis: Radiotherapy professional satisfaction	50	50	100
Secondary outcome endpoint analysis: Cosmesis (aesthetic appearance of reference points)	50	48	98

The Comforttatto trial met all endpoints (outcome measures) set at the start of the trial. No adverse events were reported during the trial.

1. Patients comfort endpoint: The percentage of patients that graded the tattooing process as painless was significantly higher for patients receiving Comfort Marker 2.0 compared to lancets (44.0% vs. 16.0%, respectively; p = 0.008). (Table 2 and Figure S1)
2. Effectiveness endpoint: No fading of the reference points for both lancet and Comfort Marker 2.0 arms was recorded. During tattoo quality assessment by radiotherapy professionals on 4-point scale (bad, reasonable, good and excellent), patient's receiving Comfort Marker 2.0 had a significantly higher proportion of radiotherapy professionals reported good and excellent quality markings compared to those receiving lancets. The median score of set-up markings graded as good/excellent on the last evaluation compared to the first evaluation was significantly worse in patients receiving lancets (67% v 89% respectively; p =0.003). The same effect wasn't found on patients receiving CM (100.0% for both evaluations; p=0.173).
3. Satisfaction endpoint: Compared to those receiving lancets, patients receiving Comfort Marker 2.0 had significantly higher radiotherapy professionals reported tattooing processes evaluated as easy (78.0% vs. 98.0%, respectively; p=0.008).
4. Cosmesis endpoint: The photographic assessment (reference points photos were taken on one of the last three days of treatment and grading radiotherapy professionals were blind to patient identify and trial arm) of the reference points in both trial arms was performed by 20 observers (both physicians and radiotherapy professionals) on 4-point scale (bad, reasonable, good and excellent). Patients receiving Comfort Marker 2.0 had a significantly higher score on the photographic assessment (Table 5), with a median score of 3.5 and 4.5 for the lancets and the Comfort Marker 2.0 group, respectively ($p < 0.001$).While 84.0% of the patients in the Comfort Marker 2.0 group had a mean score of at least 4, in the lancets group that number is five times lower (16.7%; $p < 0.001$).

Additionally, data on sharps injuries was collected. Sharp injuries were considered any incident which causes the needle of the lancet or the CM to inadvertently penetrate the skin of the radiotherapy professionals performing the tattooing during any of the tattooing process (material assembly, tattooing, or sharps disposal). Outcome: no sharp injuries were registered during the Comforttattoo trial.

Conclusion: Based on the two device comparison characteristics presented in this 510K, the subject device is substantially equivalent to the legally marketed predicate device DEN200041. Clinical data

provided supports the Comfort Marker 2.0 claims as: a) Patients marked with Comfort Marker 2.0 reported less procedural pain than patients marked with lancets, b) Physicians and radiation therapist doing photographic assessment of cosmesis rated Comfort Marker 2.0 better than lancets. - Limitation/ additional claim information: study performed in Europe where majority of the population is Caucasian race, specific to Portugal where the study was performed the majority is from a Mediterranean ethnicity,
c) Radiation therapists rated placing tattoos with Comfort Marker 2.0 easier compared to the use of lancets.