July 30, 2021

ScreenPoint Medical B.V.
% Umar Waqas
Head of Regulatory and Quality Affairs
Mercator II, 7th floor, Toernooiveld 300
Nijmegen, Gelderland 6525EC
Netherlands

Re: K210404
Trade/Device Name: Transpara 1.7.0
Regulation Number: 21 CFR 892.2090
Regulation Name: Radiological computer assisted detection/diagnosis software for lesions suspicious for cancer
Regulatory Class: Class II
Product Code: QDQ

Dear Umar Waqas:

The Food and Drug Administration (FDA) is sending this letter to notify you of an administrative change related to your previous substantial equivalence (SE) determination letter dated June 2, 2021. Specifically, FDA is updating this SE Letter as an administrative correction in 510K Summary.

Please note that the 510(k) submission was not re-reviewed. For questions regarding this letter please contact Jessica Lamb, OHT7: Office of in vitro Diagnostics and Radiological Health, 307-796-6167, jessica.lamb@fda.hhs.gov.

Sincerely,

Thalia T. Mills, Ph.D.
Director
Division of Radiological Health
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

ScreenPoint Medical B.V.
% Umar Waqas, Ph.D.
Head of Regulatory and Quality Affairs
Mercator II, 7th floor, Toernooiveld 300
Nijmegen, Gelderland 6525EC
NETHERLANDS

June 2, 2021

Re: K210404
Trade/Device Name: Transpara 1.7.0
Regulation Number: 21 CFR 892.2090
Regulation Name: Radiological computer assisted detection/diagnosis software for lesions suspicious for cancer
Regulatory Class: Class II
Product Code: QDQ
Dated: May 3, 2021
Received: May 7, 2021

Dear Dr. Waqas:

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 and Part 809); 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,

Michael D. O'Hara For

Thalia T. Mills, Ph.D.
Director
Division of Radiological Health
OHT7: Office of In Vitro Diagnostics
and 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)*
K210404

Device Name
Transpara® 1.7.0

Indications for Use *(Describe)*
Transpara® software is intended for use as a concurrent reading aid for physicians interpreting screening full-field digital mammography exams and digital breast tomosynthesis exams from compatible FFDM and DBT systems, to identify regions suspicious for breast cancer and assess their likelihood of malignancy. Output of the device includes locations of calcifications groups and soft-tissue regions, with scores indicating the likelihood that cancer is present, and an exam score indicating the likelihood that cancer is present in the exam. Patient management decisions should not be made solely on the basis of analysis by Transpara®.

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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Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

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510(k) Summary Transpara® (K210404)

This 510(k) summary of safety and effectiveness information is prepared in accordance with the requirements of 21 CFR § 807.92.

1. Submitter

Manufacturer:

ScreenPoint Medical B.V.

Mercator II, 7th floor

Toernooiveld 300

6525 EC Nijmegen

Netherlands

www.screenpoint-medical.com

Contact person:

Umar Waqas

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Mercator II, 7th floor, Toernooiveld 300, 6525 EC Nijmegen, Netherlands

Date:

May 3, 2021

2. Device

Device trade name	Transpara® 1.7.0
Device	Radiological Computer Assisted Detection and Diagnosis Software
Classification regulation	21 CFR 892.2090
Panel	Radiology
Device class	II
Product code	QDQ
Submission type	Traditional 510(k)

3. Legally marketed predicate device

Device trade name	Transpara® 1.6.0
Legal Manufacturer	ScreenPoint Medical B.V.
Device	Radiological Computer Assisted Detection and Diagnosis Software
Classification regulation	21 CFR 892.2090
Panel	Radiology
Device class	II
Product code	QDQ
Clearance number	K193229

4. Device description

Transpara® is a software only application designed to be used by physicians to improve interpretation of digital mammography and digital breast tomosynthesis. The system is intended to be used as a concurrent reading aid to help readers with detection and characterization of potential abnormalities suspicious for breast cancer and to improve workflow. 'Deep learning' algorithms are applied to FFDM images and DBT slices for recognition of suspicious calcifications and soft tissue lesions (including densities, masses, architectural distortions, and asymmetries). Algorithms are trained with a large database of biopsy-proven examples of breast cancer, benign abnormalities, and examples of normal tissue.

Transpara® offers the following functions which may be used at any time during reading (concurrent use):

a) Computer aided detection (CAD) marks to highlight locations where the device detected suspicious calcifications or soft tissue lesions.
b) Decision support is provided by region scores on a scale ranging from 0-100, with higher scores indicating a higher level of suspicion.
c) Links between corresponding regions in different views of the breast, which may be utilized to enhance user interfaces and workflow.
d) An exam score which categorizes exams on a scale of 1-10 with increasing likelihood of cancer. The score is calibrated in such a way that approximately 10 percent of mammograms in a population of mammograms without cancer falls in each category.

Results of *Transpara*® are computed in processing server which accepts mammograms or DBT exams in DICOM format as input, processes them, and sends the processing output to a destination using the DICOM protocol in a standardized mammography CAD DICOM format. Common destinations are medical workstations, PACS and RIS. *Transpara*® is offered as a virtual machine and runs on pre-selected standard PC hardware as well as a dedicated virtual machine cluster. The system can be configured using a service interface. Implementation of a user interface for end users in a medical workstation is to be provided by third parties.

5. Indications for use

Transpara® is a software medical device for use in a healthcare facility or hospital with the following indications for use:

Transpara® software is intended for use as a concurrent reading aid for physicians interpreting screening full-field digital mammography exams and digital breast tomosynthesis exams from compatible FFDM and DBT systems, to identify regions suspicious for breast cancer and assess their likelihood of malignancy. Output of the device includes locations of calcifications groups and soft-tissue regions, with scores indicating the likelihood that cancer is present, and an exam score indicating the likelihood that cancer is present in the exam. Patient management decisions should not be made solely on the basis of analysis by Transpara®.

Intended user population

Intended users of *Transpara*® are physicians qualified to read screening mammography exams and digital breast tomosynthesis exams.

Intended patient population

The device is intended to be used in the population of women undergoing screening mammography and digital breast tomosynthesis.

Warnings and precautions

Transpara® is an adjunct tool and not intended to replace a physicians' own review of a mammogram. Decisions should not be made solely based on analysis by Transpara®.

6. Predicate device comparison

The indication for use of Transpara® 1.7.0 is similar to that of the predicate device. Both devices are intended for concurrent use by physicians interpreting breast images to help them with localizing and characterizing abnormalities. The devices are not intended as a replacement for the review of a physician or their clinical judgement.

The overall design of Transpara® 1.7.0 is the same as that of the predicate device. Both versions detect and characterize findings in radiological breast images and provide information about the presence, location, and characteristics of the findings to the user in a similar way. There are differences in the algorithmic components, which have changed to improve detection accuracy for FFDM and of DBT. Support for Fujifilm DBT has been added.

Changes do not raise different questions of safety and effectiveness of the device when used as labeled.

7. Summary of non-clinical performance data

In the design and development of Transpara® 1.7.0, ScreenPoint applied the following voluntary FDA recognized standards and guidelines:

Standard ID	Standard Title	FDA Recognition #
IEC 62366-1 Edition 1.1 2020-06	Medical devices - Part 1: Application of usability engineering to medical devices	5-129
IEC 62366-1 Edition 1.0 2015-02	Medical devices - Part 1: Application of usability engineering to medical devices [Including CORRIGENDUM 1 (2016)]	5-114

ISO, 14155 Third edition 2020-07	Clinical investigation of medical devices for human subjects - Good clinical practice	2-282
ISO, 14155 Second edition 2011-02-01,	Clinical investigation of medical devices for human subjects - Good clinical practice	2-205
ISO 14971:2019	Medical Devices - Application Of Risk Management To Medical Devices	5-125
IEC 62304:2015	Medical Device Software - Software Life Cycle Processes	13-79
ISO, 15223-1 Third Edition 2016-11-01,	Medical devices - Symbols to be used with medical device labels labelling and information to be supplied - Part 1: General requirements	5-117
DEN180005	Decision summary with special controls for class II radiology device	

The following guidance documents were used to support this submission:

- Guidance for Industry and FDA Staff - Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices (Issued on May 11, 2005)
- Computer-Assisted Detection Devices Applied to Radiology Images and Radiology Device Data – Premarket Notification [510(k)] Submissions (Issued on July 3, 2012)
- Guidance for Industry and FDA Staff - Clinical Performance Assessment: Considerations for Computer-Assisted Detection Devices Applied to Radiology Images and Radiology Device Data in Premarket notification [510(k)] Submissions (Issued on January 2020)
- The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)] (Issued on July 28 2014)

Transpara®1.7.0 is a software-only device. The level of concern for the device is determined as Moderate Level of Concern.

Non-clinical performance tests

Verification testing was conducted, which consisted of software unit testing, software integration testing and software system testing. The verification tests showed that the software application satisfied the software requirements.

Standalone performance tests were conducted to demonstrate substantial equivalence with the predicate device. For these tests an independent dataset was used, which

was acquired from multiple centers and had not been used for development of the algorithms. This testset contained 2D and 3D mammograms acquired with devices from different manufacturers (2D: Hologic, GE, Philips, Siemens and Fujifilm, 3D: Hologic, Siemens and Fujifilm), representative for regular breast cancer screening and asymptomatic patients collected from multiple clinical centers in seven EU countries and the US.

The testset consisted of 7882 non-cancer exams, and 1240 exams with cancer. Of the non-cancer exams 4797 were 2D and 3085 were DBT. Of the exams with cancer 819 and 421 were 2D and DBT, respectively. In total, 61% of the lesions in the exams with cancer in the testset were characterized as a mass, 33% as suspicious calcifications, and 6% as architectural distortions or asymmetries. The three main histological cancer types were invasive ductal carcinoma (60.5%), ductal carcinoma in situ (25.9%), and invasive lobular carcinoma (9.0%). The median lesion extent (defined as maximum diameter in two dimensions) was 16 mm in both 2D data (IQR: 11-24) and 3D data (IQR: 11-25).

Exam based sensitivity was computed by taking the fraction of cancers that were correctly localized in it least one view (MLO or CC). For 2D sensitivity is measured separately for calcifications and soft tissue lesions while for DBT the sensitivity is reported without distinguishing lesion types. False positive rates were computed in exams without cancer, by dividing the number of regions detected per image by the number of images. For 2D, the sensitivity for calcifications is 94.7% (95% CI: 91.7-96.7) at a false positive rate of 0.11 FP/image. The sensitivity for soft tissue lesions is 80.2% (95% CI: 76.8-83.2) at a false positive rate of 0.02 FP/image and 92.6% (95% CI: 90.2-94.6) at a false positive rate of 0.17 FP/image. For DBT, sensitivity is 91.3% (95% CI: 88.1-93.6) at a false positive rate of 0.3 FP/volume.

Exam-based ROC analysis was performed to compare AUC of the device with the predicate device on the testset, excluding Fujifilm DBT exams because this input was not validated in the predicate device. For 2D, AUC of the device is 0.949, which is higher is non-inferior in comparison to the AUC of 0.929 of the predicate device. The difference is +0.021 (0.013,0.038). For DBT, AUC of the device is 0.931, which is higher is non-inferior in comparison to the AUC of 0.917 of the predicate device. The difference is +0.014 (0.003-0.042).

AUC performance for Fujifilm was 0.952, which is higher is non-inferior in comparison to the AUC of 0.917 of the predicate device.

Based on results of verification and validation tests it is concluded that Transpara® 1.7.0 is effective in the detection of soft lesions and calcifications at an appropriate safety level.

8. Conclusions

The data presented in this 510(k) includes all required information to support the review by FDA. Standalone performance tests with FFDM and DBT demonstrate that Transpara® 1.7.0 achieves non-inferior detection performance compared to the predicate device.

ScreenPoint has applied a risk management process in accordance with FDA recognized standards to identify, evaluate, and mitigate all known hazards related to Transpara® 1.7.0. These hazards may occur when accuracy of diagnosis is potentially affected, causing either false-positives or false-negatives. All identified risks are effectively mitigated and it can be concluded that the residual risk is outweighed by the benefits.

Considering all data in this submission, the data provided in this 510(k) application supports the safe and effective use of Transpara® 1.7.0 for its indications for use and substantial equivalence to the predicate device.