December 11, 2023

Screenpoint Medical B.V.
% Robin Barwegen
Head of Regulatory and Quality Affairs
Mercator II, 7th floor, Toernooiveld 300
Nijmegen, Gelderland 6525EC
NETHERLANDS

Re: K232096
Trade/Device Name: Transpara Density 1.0.0
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical Image Management and Processing System
Regulatory Class: Class II
Product Code: QIH
Dated: July 6, 2023
Received: July 13, 2023

Dear Robin Barwegen:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

Yanna S. Kang -S

Yanna Kang, Ph.D.
Assistant Director
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OHT8: Office of Radiological Health
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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)*
K232096

Device Name
Transpara Density 1.0.0

Indications for Use *(Describe)*
Transpara Density is a software application intended for use with data from compatible digital mammography and digital breast tomosynthesis systems. Transpara Density utilises deep learning artificial intelligence algorithms to automatically determine volumetric breast density (VBD), breast volume, and an ACR BI-RADS 5th Edition breast density category to aid health care professionals in the assessment of breast tissue composition. It is not a diagnostic aid.

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.

510(k) Summary Transpara Density

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

1. Submitter

Manufacturer:

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Date:

11 December 2023

2. Device

Device trade name	Transpara Density
Device	System, Image Processing, Radiological
Classification regulation	21 CFR 892.2050
Panel	Radiology
Device class	II
Product code	QIH
Submission type	Traditional 510(k)

3. Legally marketed predicate device

Device trade name	Volpara Imaging Software
Legal Manufacturer	Volpara Health Technologies Limited
Device	System, Image Processing, Radiological
Classification regulation	21 CFR 892.2050
Panel	Radiology
Device class	II
Product code	LLZ
Clearance number	K182310

4. Device description

Transpara Density is a software module that uses artificial intelligence techniques to assess breast density in mammography (DM) and breast tomosynthesis (DBT) images and provide support to radiologists in this task. The novel methods of Transpara Density, extend the capabilities of computer aided detection systems for mammography by providing radiologists with decision support via the output of density assessment.

The Transpara Density outputs are:

- Density Grade, in accordance with categories defined in the ACR BI-RADS Atlas 5th Edition (A = almost entirely fat; B = scattered fibroglandular densities; C = heterogeneously dense; and D = extremely dense)
- Volumetric Breast Density in %
- Breast volume in cm^3

Transpara Density is designed as an optional feature of Transpara. To operate in a clinical environment the software must be embedded in a software application that generates output in standardized formats (e.g. DICOM) and handles communication with external devices (such as PACS systems).

5. Indications for use

Transpara Density is a software application intended for use with data from compatible digital mammography and digital breast tomosynthesis systems. Transpara Density utilizes deep learning artificial intelligence algorithms to automatically determine volumetric breast density (VBD), breast volume, and an ACR BI-RADS 5th Edition breast density category to aid health care professionals in the assessment of breast tissue composition. It is not a diagnostic aid.

Intended user population

Intended users of Transpara Density are healthcare professionals involved in breast imaging.

Intended patient population

The device is intended to be used in the population of women having a digital mammogram or digital breast tomosynthesis exam.

Safety and Effectiveness Concerns

The device labeling contains instructions for use and any necessary cautions and warnings to provide for safe and effective use of the device. Risk management is ensured via a risk analysis, which is used to identify potential hazards and mitigations. These potential hazards are controlled by software means, user instructions, verification and validation testing to ensure that the product meets its intended uses.

6. Predicate device comparison

It can be concluded that the subject device Transpara Density is substantially equivalent to the commercially available predicate device Volpara Imaging Software (K182310). It has the same intended use, intended users, and numeric output as the predicate device. The substantial equivalence comparison table below provides details.

	Transpara Density	**Predicate Device Volpara Imaging Software K182310**	**Comments**
Intended Use	Transpara Density is a software application intended for use with data from compatible	VolparaDensity is a software application intended for use with the raw data from digital	Similar from the user perspective. Main outputs for the user are volumetric density and

	digital mammography and digital breast tomosynthesis systems. Transpara Density utilizes deep learning artificial intelligence algorithms to automatically determine volumetric breast density (VBD), breast volume, and an ACR BI-RADS 5th Edition breast density category to aid health care professionals in the assessment of breast tissue composition. It is not a diagnostic aid.	breast x-ray systems, including tomosynthesis. VolparaDensity calculates and quantifies a density map and from that determines volumetric breast density as a ratio of fibroglandular tissue and total breast volume estimates. Volpara provides these numerical values along with a BI-RADS breast density 4th or 5th Edition category to aid health care professionals in the assessment of breast tissue composition. VolparaDensity is not an interpretive or diagnostic aid and should be used only as adjunctive information when the final assessment of breast density category is made by an MQSA-qualified interpreting physician.	the BI-RADS 5th Edition density category. These outputs are the same.
Intended Users	Health Care Professionals	Health Care Professionals	Same
Image Source	Digital mammograms from mammography or tomosynthesis systems (any paddle type)	Digital mammograms from mammography or tomosynthesis systems, including those obtained using with curved paddles.	Same. The subject device is insensitive for paddle shapes because it uses images processed by the manufacturer which are not affected by paddle shape.
Input image type	FOR PRESENTATION (processed) images for mammography and Synthetic 2D images for DBT	FOR PROCESSING (raw) images for mammography and the central raw projection image for DBT	The core algorithm for density computation of the subject device has a different design which does not require raw data.
Anatomical area	Breast	Breast	Same
Assessment Scope		Volumetric	
Image Storage and Report Generation		Yes Output to the console.	
Numeric Output	Volume of Breast Volumetric Breast Density	Volume of Breast Volumetric Breast Density	Similar, the clinically relevant outputs in practice are the same.

	BIRADS 5th Edition Breast Density Category	BIRADS 4th or 5th Edition Breast Density Category Volume of Fibroglandular tissue Average thickness of dense tissue Maximum thickness of dense tissue (and location) Maximum volume of dense tissue above any 1cm2 square region	
Image Output	None	Density map in DICOM SCI format, for visualization as user specifies.	Density maps are not required in clinical practice
Classification	21 CFR 892.2050	21 CFR 892.2050	Same
Software Level of Concern	Moderate	Moderate	Same

7. Summary of non-clinical performance data

In the design and development of Transpara Density, 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
ISO 14155 Third edition 2020-07	Clinical investigation of medical devices for human subjects - Good clinical practice	2-282
ISO 14971 Third Edition 2019-12	Medical devices - Application of risk management to medical devices	5-125
IEC 62304 Edition 1.1 2015-06 CONSOLIDATED VERSION	Medical Device Software - Software Life Cycle Processes	13-79
IEC 82304-1: 2016	Health software - Part 1: General requirements for product safety	13-97

ISO 15223-1 Fourth Edition 2021-07	Medical devices - Symbols to be used with medical device labels labelling and information to be supplied - Part 1: General requirements	5-134
ISO 20417 First edition 2021-04 Corrected version 2021-12	Medical devices – Information to be supplied by the manufacturer	5-135

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)

- Guidance for Industry and Food and Drug Administration Staff - 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 July 3, 2012)

- Guidance for Industry and Food and Drug Administration Staff - The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)] (Issued on July 28, 2014)

- Guidance for Industry and Food and Drug Administration Staff - Unique Device Identification: Direct Marking of Devices (Issued on November 17, 2017)

- Guidance for Industry and Food and Drug Administration Staff - Technical Performance Assessment of Quantitative Imaging in Radiological Device Premarket Submissions (Issued on June 16, 2022)

Transpara Density 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.

Transpara Density was evaluated by tests covering accuracy, reproducibility, consistency, and agreement with visual assessment by healthcare professionals involved in breast imaging.

Test data

The test data used for the evaluation of the automated density algorithm included exams from 10,804 women with ages ranging from 40-92. The dataset includes FFDM (10,804 exams) and DBT (833 exams) from multiple vendors including GE (26%), Siemens (16%), Hologic (37%) and Fujifilm (21%). All exams contained at least the four standard views (left and right MLO/CC). The test data was not used for algorithm training and was not accessible to members of the research and development team.

Data originated from multiple clinical centers located in the US, the UK, Turkey, and five countries in the EU (the Netherlands, Sweden, Germany, Spain, Belgium, Italy). Data collection sites are representative for regular breast cancer screening and diagnostic assessment in hospitals.

Characteristics of the test set, i.e. Density Grade distribution, were evaluated and compared to those reported in literature, confirming that the test set is representative of the target population in the intended use.

Accuracy

Volumetric breast density (VBD) and breast volume (BV) should be in agreement with measurements obtained using a validated physics based model described in the literature (van Engeland *et a*l., IEEE Trans Medical Imaging, 2006). https://doi.org/10.1109/TMI.2005.862741). Performance was tested with a dataset of 5,468 exams. The Pearson correlation between VBD computed with Transpara Density and the physics model was 0.935 [95% CI: 0.931 - 0.938]. For breast volume the Pearson correlation coefficient was 0.997.

VBD obtained with Transpara Density was also compared to volumetric measurements based on breast MRI studies in the same patients, for exams acquired within a short time frame. Using a dataset of 190 exams, the Pearson correlation coefficient was 0.908 [95% CI: 0.878 - 0.931].

Results show that Transpara Density provides accurate estimates of VBD compared to breast MRI and a physics based model.

Reproducibility

VBD computed in MLO and CC views of the same breast should be similar. In a comparison performed using 10,804 exams, Transpara Density has a Pearson correlation coefficient of 0.947 [95% CI: 0.945 - 0.948] and a mean absolute deviation of 1.22% [95%

CI: 1.19% - 1.24%] between CC and MLO views. Minor deviations may be explained by differences in breast positioning.

Using the same dataset, a comparison was also made of VBD computed in the right and left breast of the same patient. The Pearson correlation coefficient was 0.953 [95% CI: 0.951 - 0.955] with a mean absolute deviation of 1.14% [95% CI: 1.10% - 1.17%] between the left and right breast.

To compare VBD and DG for DM and DBT acquisitions a dataset of 433 exams was used in which images of both modalities were available. The Pearson correlation coefficient in this comparison was 0.912 [95% CI: 0.904 - 0.920], with a mean absolute deviation of 1.68% [95% CI: 1.57% - 1.78%] between VBD values on FFDM and DBT acquisitions. There was a high agreement in the four category DG values for DM and DBT with a quadratically weighted kappa of 0.810 [95% CI: 0.787 - 0.835].

Agreement with human readers

A study was performed with 400 digital mammography and 400 digital breast tomosynthesis examinations from 800 women with a median age of 56, originating from multiple clinical centers and representative for screening and diagnostic assessment procedures. Breast tissue composition in these examinations was independently assessed by eight MQSA-qualified radiologists according to the ACR BI-RADS Atlas 5th Edition. A panel majority vote was computed for each exam to serve as a reference standard in a comparison with the automated breast density grades determined by Transpara Density. Ties in the panel majority-vote were resolved by taking the majority vote of the three most experienced radiologists in the panel. Five exams were excluded from analysis because of non-compliant DICOM headers which caused a failure of the density measurement.

Agreement was assessed by computing accuracy using 4x4 and 2x2 (for non-dense (a+b) and dense (c+d) confusion matrices (figure 1 and figure 2). Also, Cohen's quadratically weighted kappa was calculated to measure the inter-rater agreement for categorical items. Overall the accuracy was 70.8% [95% CI: 67.6% - 73.9%] [Cohen's weighted kappa = 0.74 [95% CI: 0.70 - 0.79] for the four breast density categories (a-b-c-d), and 88.9% [95% CI: 86.6% - 90.9%] [Cohen's weighted kappa = 0.78 [95% CI: 0.72 - 0.84]] for the dense vs non-dense assessment.

For dense vs. non-dense classification, Transpara Density has a sensitivity of 87.3% [95% CI: 83.6% - 90.3%], and a specificity of 90.4% [95% CI: 87.2% - 92.9%].

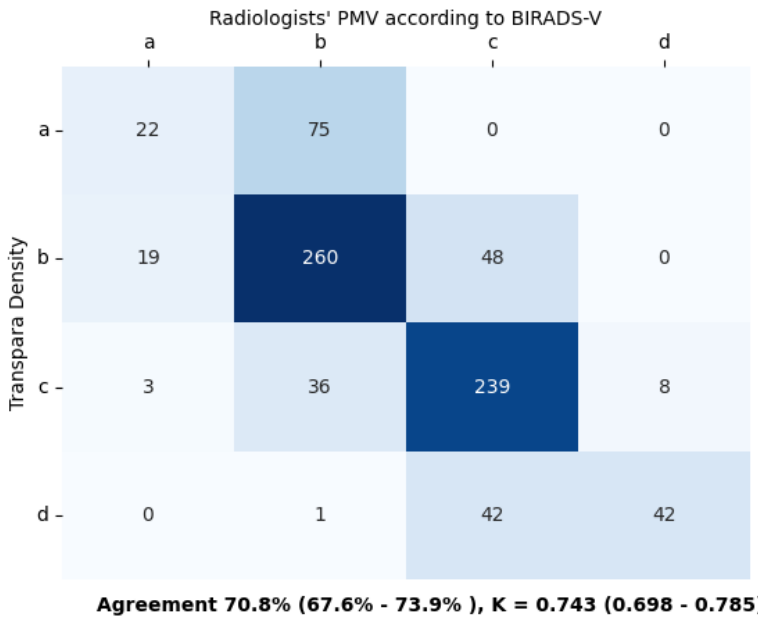

Fig. 1 Confusion matrix between Transpara Density and PMV for the four breast density categories (a-b-c-d).

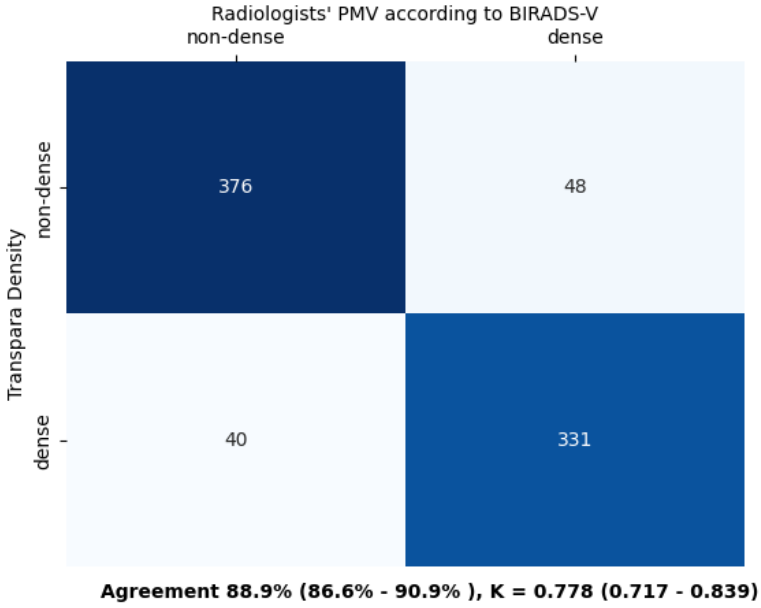

Fig. 2 Confusion matrix between Transpara Density and PMV for the two breast density categories (non-dense (a+b) vs dense (c+d)).

Compatibility

Compatibility with multiple vendors was demonstrated for the Breast Density score: GE, Siemens, Hologic and Fujifilm. For VBD and BV compatibility with GE, Siemens and Hologic was demonstrated.

8. Conclusions

The data presented in this 510(k) includes all required information to support the review by FDA. Performance tests have shown that Transpara Density delivers results that are in high agreement with the visual assessment done by radiologists and that standalone performance requirements were met. Agreement was found between the majority vote of a panel of eight MQSA-qualified radiologists and Transpara Density in classifying dense from non-dense breasts. Standalone performance tests demonstrated that requirements were met.

ScreenPoint has applied a risk management process in accordance with FDA recognized standards to identify, evaluate, and mitigate all known hazards related to Transpara Density. 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 Density for its indications for use and substantial equivalence to the predicate device.