July 3, 2025

Therapixel
% Alex Cadotte
VP, Digital Health, AI and Radiology
MCRA, an IQVIA Business
803 7th St NW
Washington, District of Columbia 20001

Re: K243679
Trade/Device Name: MammoScreen® (4)
Regulation Number: 21 CFR 892.2090
Regulation Name: Radiological Computer Assisted Detection And Diagnosis Software
Regulatory Class: Class II
Product Code: QDQ, QIH
Dated: June 3, 2025
Received: June 3, 2025

Dear Alex Cadotte:

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.

FDA's substantial equivalence determination also included the review and clearance of your Predetermined Change Control Plan (PCCP). Under section 515C(b)(1) of the Act, a new premarket notification is not

required for a change to a device cleared under section 510(k) of the Act, if such change is consistent with an established PCCP granted pursuant to section 515C(b)(2) of the Act. Under 21 CFR 807.81(a)(3), a new premarket notification is required if there is a major change or modification in the intended use of a device, or if there is a change or modification in a device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process. Accordingly, if deviations from the established PCCP result in a major change or modification in the intended use of the device, or result in a change or modification in the device that could significantly affect the safety or effectiveness of the device, then a new premarket notification would be required consistent with section 515C(b)(1) of the Act and 21 CFR 807.81(a)(3). Failure to submit such a premarket submission would constitute adulteration and misbranding under sections 501(f)(1)(B) and 502(o) of the Act, respectively.

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.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

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.
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Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

Submission Number *(if known)*

K243679

Device Name

MammoScreen® (4)

Indications for Use *(Describe)*

MammoScreen 4 is a concurrent reading and reporting aid for physicians interpreting screening mammograms. It is intended for use with compatible full-field digital mammography and digital breast tomosynthesis systems. The device can also use compatible prior examinations in the analysis.

Output of the device includes graphical marks of findings as soft-tissue lesions or calcifications on mammograms along with their level of suspicion scores. The lesion type is characterized as mass/asymmetry, distortion, or calcifications for each detected finding. The level of suspicion score is expressed at the finding level, for each breast, and overall for the mammogram.

The location of findings, including quadrant, depth, and distance from the nipple, is also provided. This adjunctive information is intended to assist interpreting physicians during reporting.

Patient management decisions should not be made solely based on the analysis by MammoScreen 4.

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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510(k) Summary
K243679

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

Applicant Information:

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Date Summary Prepared: November 21, 2024

Device Information:

Trade Name:	MammoScreen®
Model;	4
Common Name:	Computer-Assisted Detection Device
Device Classification Name:	Radiological Computer Assisted Detection/Diagnosis Software For Lesions Suspicious For Cancer
Regulation Number:	892.2090
Regulation Class:	Class II
Product Code:	QDQ
Associated Product Code:	QIH
Submission type	Traditional 510(k)
510(k) number:	K243679

Predicate Device:

The predicate device is MammoScreen 3, cleared under K240301 (Product code QDQ).

Device Description:

MammoScreen 4 is a concurrent reading medical software device using artificial intelligence to assist radiologists in the interpretation of mammograms.

MammoScreen 4 processes the mammogram(s) and detects findings suspicious for breast cancer. Each detected finding gets a score called the **MammoScreen Score™**. The score was designed such that findings with a low score have a very low level of suspicion. As the score increases, so does the level of suspicion. For each mammogram, **MammoScreen 4** outputs the detected findings with their associated score, a score per breast, driven by the highest finding score for each breast, and a score per case, driven by the highest finding score overall. The **MammoScreen Score** goes from one to ten.

MammoScreen 4 is available for 2D (FFDM images) and 3D processing (FFDM & DBT or 2DSM & DBT). Optionally, **MammoScreen 4** can use prior examinations in the analysis.

The results indicating potential breast cancer, identified by **MammoScreen 4**, are accessible via a dedicated user interface and can seamlessly integrate into DICOM viewers (using DICOM-SC and DICOM-SR). Reporting aid outputs can be incorporated into the practice's reporting system to generate a preliminary report.

Note that the **MammoScreen 4 outputs** should be used as complementary information by radiologists while interpreting mammograms. For all cases, the medical professional interpreting the mammogram remains the sole decision-maker.

Indication for Use:

MammoScreen® 4 is a concurrent reading and reporting aid for physicians interpreting mammograms. It is intended for use with compatible full-field digital mammography and digital breast tomosynthesis systems. The device can also use compatible prior examinations in the analysis.

Output of the device includes graphical marks of findings as soft-tissue lesions or calcifications on mammograms along with their level of suspicion scores. The lesion type is characterized as mass/asymmetry, distortion, or calcifications for each detected finding. The level of suspicion score is expressed at the finding level, for each breast, and overall for the mammogram.

The location of findings, including quadrant, depth, and distance from the nipple, is also provided. This adjunctive information is intended to assist interpreting physicians during reporting.

Patient management decisions should not be made solely based on the analysis by MammoScreen 4.

Predicate device comparison:

	Predicate device (MammoScreen 3)	**Subject device (MammoScreen 4)**
Manufacturer	Therapixel	Therapixel
Regulation number	892.2090	892.2090
Product Code	QDQ	QDQ
Intended Use	MammoScreen 3 is a concurrent reading and reporting aid for physicians interpreting screening mammograms. It is intended for use with compatible full-field digital mammography and digital breast tomosynthesis systems. The device can also use compatible prior examinations in the analysis. Output of the device includes graphical marks of findings as soft-tissue lesions or calcifications on mammograms along with their level of suspicion scores. The lesion type is characterized as mass/asymmetry, distortion, or calcifications for each detected finding. The level of suspicion score is expressed at the finding level, for each breast, and overall for the mammogram. The location of findings, including quadrant, depth, and distance from the nipple, is also provided. This adjunctive information is intended to assist interpreting physicians during reporting. Patient management decisions should not be made solely based on the analysis by MammoScreen 3.	MammoScreen® 4 is a concurrent reading and reporting aid for physicians interpreting mammograms. It is intended for use with compatible full-field digital mammography and digital breast tomosynthesis. The device can also use compatible prior examinations in the analysis. Output of the device includes graphical marks of findings as soft-tissue lesions or calcifications on mammograms along with their level of suspicion scores. The lesion type is characterized as mass/asymmetry, distortion, or calcifications for each detected finding. The level of suspicion score is expressed at the finding level, for each breast, and overall for the mammogram. The location of findings, including quadrant, depth, and distance from the nipple, is also provided. This adjunctive information is intended to assist interpreting physicians during reporting. Patient management decisions should not be made solely based on the analysis by MammoScreen 4.
Intended user population	Physicians qualified to read mammograms.	Physicians qualified to read mammograms.
Intended patient population	Women undergoing mammography.	Women undergoing mammography.
Anatomical Location	Breast	Breast
Design	Software-only device	Software-only device
Type of artificial intelligence	MammoScreen 3 is powered by artificial intelligence/machine learning-based software algorithm	Same.
Level of suspicion	MammoScreen 3 outputs a level of suspicion at the finding, breast and case level.	Same.

	Predicate device (MammoScreen 3)	Subject device (MammoScreen 4)
Lesion type	For each detected finding MammoScreen 3 classifies them as mass/asymmetry, distortion or calcifications.	Same.
Localization	For each finding MammoScreen 3 provides a quadrant, a depth and a distance to the nipple.	Same.
Inputs	FFDM or 2DSM & DBT or FFDM & DBT, with an optional prior (FFDM or 2DSM & DBT) expect for the former.	Same.
Support of Hologic Envision system	Not included.	Included.
Inclusion of PCCP	Not Included.	Included. The PCCP in the subject device includes proposed modifications related to extending supported image acquisition systems.

The indication for the use of MammoScreen 4 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 findings. The devices are not intended as a replacement for the review of a physician or their clinical judgment.

The predicate device and the subject device are two software versions of MammoScreen. They both rely on the same fundamental scientific technology.

The design changes of this new version of MammoScreen have been assessed at the software design level and do not raise different questions of safety and effectiveness than the previous version. For both devices, a choice of medical image processing and machine learning techniques are implemented. The system includes 'deep learning' modules for the detection of suspicious calcifications and soft tissue lesions. These modules are trained with very large databases of biopsy-proven examples of breast cancer and normal tissue.

The overall design of MammoScreen 4 is the same than the design 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 manner. While MammoScreen 4 has been evaluated on mammograms produced by a wider range of systems to accept those, these modifications do not raise different questions about the safety and effectiveness of the device as compared to the predicate device. The devices have the same intended use. The modifications do not raise different questions about the safety and effectiveness of the device as compared to the predicate device. The safety and effectiveness of the device have been evaluated with a similar methodology as for the predicate device.

Non clinical Testing

MammoScreen is a software-only device.

Tests have been performed in compliance with the following recognized consensus standards:

- IEC 62304:2006/A1:2016- Medical device software - Software life-cycle processes
- IEC 62366-1:2015+AMD1:2020- Medical devices - Application of usability engineering to medical devices.

MammoScreen 4 has successfully completed integration and verification testing and beta validation. In addition, potential hazards have been evaluated and mitigated, and have acceptable levels.

The standalone performance testing carried out to validate the device is summarized in what follows:

Statistics tests for primary objective	Non-inferiority in standalone cancer detection performance compared to the previous version of MammoScreen
Primary endpoint	• AUC at the mammogram level MS4: 0.894 (0.870, 0.919), MS2: 0.867 (0.839, 0.896), Δ: 0.027 (0.002, 0.052), $p<0.0001$ • AUC at the breast level: MS4: 0.919 (0.897, 0.941), MS2: 0.895 (0.871, 0.920), Δ: 0.023 (0.002, 0.045), $p<0.0001$ • AUC LROC at the finding level: MS4: 0.891 (0.862, 0.921), MS2: 0.837 (0.797, 0.877), Δ: 0.055 (0.032, 0.077), $p<0.0001$
Acceptance criteria	Positive lower bound of the 95% CI of the difference in endpoints between the version under evaluation (MammoScreen 4 on Envision) and the reference version (MammoScreen 2 on Dimension)
Number of included patients	1,475
Number of included studies	2,950 (each patient underwent a DBT acquisition with two Hologic mammography systems)
Age distribution	*Age <= 50*: 446 *50 < Age <= 65*: 642 *65 > Age*: 372
Race and Ethnicity distribution	*Asian*: 16 *White*: 1180 *Black*: 94 *Other (including American Indian, Alaska Native, Native Hawaiian or Other Pacific Islander):* 14 *Hispanic*: 88 *Not Hispanic*: 1136
Considered subgroups	Density, Lesion type (mass/asymmetries, calcifications, distortion), Age, Lesion size, Lesion severity, Race, Ethnicity, Data provenance, Reference standard for negative cases.
Truthing process	Positive cases: biopsy-proven presence of cancer. Benign cases: cases confirmed by biopsy result and cases confirmed by imaging follow-up. Negative cases: verified by imaging follow-up.
Independence of test data from training data	Data sources are separated into the training/tuning group and the test group. Sources in the training/tuning group may only be used for model training and tuning. Sources in the test group may only be used for external validation of the model's performances on

	unseen data (i.e., from sources entirely left out during training and tuning). Data used for the standalone performance testing only belongs to the test group.

Clinical Testing

The clinical validation of MammoScreen 4 includes three multi-reader multi-case (MRMC) studies:

- One for FFDM
- One for DBT
- One for combined DBT and 2D mammograms (FFDM or 2DSM), and using prior examinations.

The objective of these MRMC studies was to determine whether the radiologist's performance when using MammoScreen is superior to unaided radiologist performance for interpretation of mammograms.

The three studies used a multi-reader multi-case cross-over design with an enriched sample set with MQSA-qualified and ACR-certified readers to compare the performance of unaided radiologists to that of radiologists using MammoScreen.

The studies demonstrated the superiority of the Area Under the Receiver Operating Characteristic Curve of the radiologist using the MammoScreen algorithm compared to the unaided radiologist.

Predetermined Change Control Plan (PCCP)

MammoScreen is powered by machine-learning neural architecture. Therapixel will make future algorithm improvements under a PCCP. The plan describes future modifications and assesses their impact, and a modification protocol details how data management, re-training, performance evaluation and update procedures will be handled.

The table below lists and describes the anticipated modifications:

Modification #1 summary	Support of GE mammograms (no re-training required)
Modification #2 summary	Support of a new mammography manufacturer other than Hologic and GE (re-training required) – this modification may also include the support of GE mammograms in case Modification #1 does not conclude to the non-inferiority on GE mammograms compared to Hologic
Statistics tests for primary objective	Non-inferiority of device standalone performance on mammograms of the manufacturer under evaluation compared to Hologic mammograms
Primary endpoints	AUC at the mammogram, breast and finding level (AUC LROC)

Acceptance criteria	• Modification #1: See Table 1. • Modification #2: See Table 1 (unpaired comparisons) and Table 2 (paired comparisons).
Validation activities	Upon demonstration of the non-inferiority through the standalone performance testing, changes will be documented in a minor release amending: - The Algorithm test protocol and results documents - The User Guide - The device label
Communication plan	Upcoming updates are communicated to users through advisory notices sent by email at least 2 weeks before deployment. Users may choose to opt-out the update during the 2-week notice period.

Table 1: Primary endpoints and acceptance criteria for unpaired comparisons.

	Primary endpoints			**Acceptance criteria proposed for PCCP**		
	AUC ROC (exam level)	AUC ROC (breast level)	AUC LROC (finding level)	Exam level	Breast level	Finding level
MammoScreen (K192854) on Hologic FFDM only	0.89 (0.87, 0.91)	0.91 (0.89, 0.92)	0.88 (0.86, 0.90)	LB 95% CI diff ≥ -0.02	LB 95% CI diff ≥ -0.02	LB 95% CI diff ≥ -0.02
MammoScreen 2 (K211541) on Hologic DBT + FFDM	0.89 (0.87, 0.91)	0.92 (0.90, 0.93)	0.88 (0.86, 0.90)	LB 95% CI diff ≥ -0.02	LB 95% CI diff ≥ -0.02	LB 95% CI diff ≥ -0.02
MammoScreen 2 (K211541) on Hologic DBT + 2DSM	0.89 (0.87, 0.91)	0.92 (0.90, 0.93)	0.88 (0.86, 0.90)	LB 95% CI diff ≥ -0.02	LB 95% CI diff ≥ -0.02	LB 95% CI diff ≥ -0.02
MammoScreen 3 (K240301) on Hologic DBT + FFDM with FFDM priors	0.93 (0.91, 0.94)	0.95 (0.93, 0.97)	0.93 (0.91, 0.95)	LB 95% CI diff ≥ -0.02	LB 95% CI diff ≥ -0.02	LB 95% CI diff ≥ -0.02
MammoScreen 3 (K240301) on Hologic DBT + 2DSM with DBT + 2DSM priors	0.89 (0.84, 0.93)	0.92 (0.88, 0.96)	0.87 (0.83, 0.94)	LB 95% CI diff ≥ -0.05	LB 95% CI diff ≥ -0.04	LB 95% CI diff ≥ -0.04

Table 2: Primary endpoints and acceptance criteria for paired comparisons.

	Primary endpoints			**Acceptance criteria proposed for PCCP**		
	AUC ROC (exam level)	AUC ROC (breast level)	AUC LROC (finding level)	Exam level	Breast level	Finding level

MammoScreen (K192854) on Hologic FFDM only	0.89 (0.87, 0.91)	0.91 (0.89, 0.92)	0.88 (0.86, 0.90)	LB 95%CI ≥0.84	LB 95%CI ≥0.86	LB 95%CI ≥0.83
MammoScreen 2 (K211541) on Hologic DBT + FFDM	0.89 (0.87, 0.91)	0.92 (0.90, 0.93)	0.88 (0.86, 0.90)	LB 95%CI ≥0.84	LB 95%CI ≥0.87	LB 95%CI ≥0.83
MammoScreen 2 (K211541) on Hologic DBT + 2DSM	0.89 (0.87, 0.91)	0.92 (0.90, 0.93)	0.88 (0.86, 0.90)	LB 95%CI ≥0.84	LB 95%CI ≥0.87	LB 95%CI ≥0.83
MammoScreen 3 (K240301) on Hologic DBT + FFDM with FFDM priors	0.93 (0.91, 0.94)	0.95 (0.93, 0.97)	0.93 (0.91, 0.95)	LB 95%CI ≥0.88	LB 95%CI ≥0.9	LB 95%CI ≥0.88
MammoScreen 3 (K240301) on Hologic DBT + 2DSM with DBT + 2DSM priors	0.89 (0.84, 0.93)	0.92 (0.88, 0.96)	0.87 (0.83, 0.94)	LB 95%CI ≥0.84	LB 95%CI ≥0.87	LB 95%CI ≥0.83

Conclusions

Standalone performance tests on FFDM and DBT demonstrate that MammoScreen 4 achieves non-inferior performance compared to the predicate device.

MRMC studies and standalone tests demonstrated that the device is safe and effective.

Therapixel has applied a risk management process following FDA-recognized standards to identify, evaluate, and mitigate all known hazards related to MammoScreen 4. These hazards may occur when the 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 these 510(k) supports the safe and effective use of MammoScreen 4 for its indications for use and substantial equivalence to the predicate device.