October 6, 2022

Hologic, Inc.
℅ Deborah Thomas
Senior Principal Regulatory Affairs
250 Campus Drive
MARLBOROUGH MA 01730

Re: K221449
Trade/Device Name: Genius AI Detection 2.0
Regulation Number: 21 CFR 892.2090
Regulation Name: Radiological computer assisted detection and diagnosis software
Regulatory Class: Class II
Product Code: QDQ
Dated: August 24, 2022
Received: August 25, 2022

Dear Deborah Thomas:

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,

Yanna Kang, Ph.D.
Assistant Director
Mammography and Ultrasound 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)*
K221449

Device Name
Genius AI Detection 2.0

Indications for Use *(Describe)*
Genius AI Detection is a computer-aided detection and diagnosis (CADe/CADx) software device intended to be used with compatible digital breast tomosynthesis (DBT) systems to identify and mark regions of interest including soft tissue densities (masses, architectural distortions and asymmetries) and calcifications in DBT exams from compatible DBT systems and provide confidence scores that offer assessment for Certainty of Findings and a Case Score. The device intends to aid in the interpretation of digital breast tomosynthesis exams in a concurrent fashion, where the interpreting physician confirms or dismisses the findings during the reading of the exam.

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.

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K221449

Traditional 510(k) Summary

This 510(k) Summary is submitted in accordance with the requirements of 21 CFR Part 807.92

Date Prepared: October 06, 2022

Manufacturer: Hologic, Inc.
36 Apple Ridge Road
Danbury, CT 06810 USA

Establishment Registration #: 1220984

Contact Person: Deborah Thomas
Senior Principal Regulatory Affairs
P: 508.210.6107

Identification of the Device:

Proprietary/Trade Name:	Genius AI Detection 2.0
Classification Name:	Radiological Computer Assisted Detection/Diagnosis Software for Lesions Suspicious For Cancer
Regulatory Number:	21 CFR 892.2090
Product Code:	QDQ
Device Class:	Class II
Review Panel:	Radiology

Identification of the Legally Marketed Predicate Device:

Trade Name:	Genius AI Detection
Classification Name:	Radiological Computer Assisted Detection/Diagnosis Software for Lesions Suspicious For Cancer
Regulatory Number:	21 CFR 892.2090
Product Code:	QDQ
Device Class:	Class II
Review Panel:	Radiology
Submitter/510(k) Holder:	Hologic, Inc.
Clearance:	K201019 (cleared November 18, 2020)

Device Description:

Genius AI Detection is a software device intended to identify potential abnormalities in breast tomosynthesis images. Genius AI Detection analyzes each standard mammographic view in a digital breast tomosynthesis examination using deep learning networks. For each detected lesion, Genius AI

Detection produces CAD results that include the location of the lesion, an outline of the lesion and a confidence score for that lesion. Genius AI Detection also produces a case score for the entire tomosynthesis exam.

Genius AI Detection packages all CAD findings derived from the corresponding analysis of a tomosynthesis exam into a DICOM Mammography CAD SR object and distributes it for display on DICOM compliant review workstations. The interpreting physician will have access to the CAD findings concurrently to the reading of the tomosynthesis exam. In addition, a combination of peripheral information such as number of marks and case scores may be used on the review workstation to enhance the interpreting physician's workflow by offering a better organization of the patient worklist.

Indications for Use:
Genius AI Detection is a computer-aided detection and diagnosis (CADe/CADx) software device intended to be used with compatible digital breast tomosynthesis (DBT) systems to identify and mark regions of interest including soft tissue densities (masses, architectural distortions and asymmetries) and calcifications in DBT exams from compatible DBT systems and provide confidence scores that offer assessment for Certainty of Findings and a Case Score. The device intends to aid in the interpretation of digital breast tomosynthesis exams in a concurrent fashion, where the interpreting physician confirms or dismisses the findings during the reading of the exam.

Standards:

- IEC 62304: 2015 – Medical device software – Software Life Cycle Processes (#13-79)
- ISO 14971: 2012 – Medical devices – Application of Risk Management to Medical Devices
- DEN180005 Evaluation of automatic class III designation for OsteoDetect – Decision summary with special controls.

FDA Guidance Documents:

- 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 - Premarket Approval (PMA) and Premarket Notification [510(k)] Submissions (Issued on January 22, 2020)
- "Off-the-Shelf Software Use in Medical Devices," issued on September 9, 1999
- "Content of Premarket Submissions for Management of Cybersecurity in Medical Devices" issued on October 2, 2014.

Summary of Substantial Equivalence:

Features and Characteristics	Subject Device Hologic, Inc. Genius AI Detection 2.0	Predicate Device Hologic, Inc. Genius AI Detection	Difference and comments
510(k) Number	Pending	K201019	
Regulation Number/Name	21 CFR 892.2090 / Radiological Computer Assisted Detection and Diagnosis Software	Same	N/A
Product Code	QDQ	Same	N/A
Regulation Description	A radiological computer assisted detection and diagnostic software is an image processing device intended to aid in the detection, localization, and characterization of fracture, lesions, or other disease specific findings on acquired medical images (e.g. radiography, MR, CT). The device detects, identifies and characterizes findings based on features or information extracted from images, and provides information about the presence, location, and characteristics of the findings to the user. The analysis is intended to inform the primary diagnostic and patient management decisions that are made by the clinical user. The device is not intended as a replacement for a complete clinician's review or their clinical judgment that takes into account other relevant information from the image or patient history.	Same	N/A

Indications for Use	Genius AI Detection is a computer-aided detection and diagnosis (CADe/CADx) software device intended to be used with compatible digital breast tomosynthesis (DBT) systems to identify and mark regions of interest including soft tissue densities (masses, architectural distortions and asymmetries) and calcifications in DBT exams from compatible DBT systems and provide confidence scores that offer assessment for Certainty of Findings and a Case Score. The device intends to aid in the interpretation of digital breast tomosynthesis exams in a concurrent fashion, where the interpreting physician confirms or dismisses the findings during the reading of the exam.	Same	N/A
Compatible DBT Systems	Hologic Selenia Dimensions Hologic 3Dimensions Supports both models in the following	Same	N/A
Type of CAD Software	Radiological computer assisted detection and diagnostic software.	Same	N/A
Mode of Action	Image processing device utilizing machine learning to aid in the detection, localization, and characterization of soft tissue densities (masses, architectural distortions and asymmetries) and calcifications in the 1-mm 3D DBT slices. Findings are co-registered to 6-mm SmartSlices.	Same	N/A
Clinical Output	To inform the primary diagnostic and patient management decisions that are made by the clinical user.	Same	N/A
Patient Population	Symptomatic and asymptomatic women undergoing mammography	Same	N/A
End Users	MQSA-Qualified Interpreting Physicians and Radiologists	Same	N/A
Image Source Modalities	Digital breast tomosynthesis slices	Same	N/A

Output Device	Softcopy Workstation	Same	N/A
Deployment	Stand-alone computer	Same	N/A
Method Of Use	Concurrent read	Same	N/A
Visualization Features	Places mark within suspicious lesion by default (Emphasize™; RightOn™) and reports confidence of finding next to each identified lesion in the image. CAD display may be toggled on/off. Option to automatically zoom into or contour the suspicious region of interest (PeerView™).	Same	N/A

Comparison with Predicate Device:

The Summary of Substantial Equivalence Table above details the similarities and differences between the Genius AI Detection 2.0 device and its predicate device, Genius AI Detection, K201019. Both the proposed and predicate devices use the same technology per 21 CFR 892.2090. Both devices aid in the detection, localization, and characterization of disease specific findings on acquired medical images. The outputs of both devices serve to augment the interpretation of digital breast tomosynthesis exams as a concurrent reading tool. The output is used to inform and assist the interpreting physician, supplementing their clinical expertise and judgment.

Genius AI Detection 2.0 is the follow-up release to the initial launch of the product and provides better performance both in terms of improved specificity and fewer false positives. Algorithm enhancements as well as the expanded training data set were used during development of the 2.0 version. These changes do not raise any issues of safety and effectiveness.

Genius AI Detection 2.0 is compatible with the same imaging systems as the predicate device.

Compatible DBT Systems

The following image types have been tested and are compatible with Genius AI Detection 2.0:

- Hologic standard resolution tomosynthesis slices (1 mm)
- Hologic high resolution tomosynthesis slices (1 mm, Clarity HD)
- Hologic high resolution SmartSlices (6 mm, 3DQuorum)

The CAD marks generated by Genius AI Detection 2.0 for the above image types can also be projected on their corresponding synthesized 2D images, providing that the diagnostic review workstation supports such a feature similar to the predicate device.

Summary of Updates of Genius AI Detection 2.0

Genius AI Detection 2.0 has two changes compared to the previously released product aiming to improve performance, mainly in term of improved specificity, particularly for micro-calcification cancer detection.

The first change is an enlarged cancer data set used to train the deep learning AI models. The cancer database for training and evaluation is enlarged by two-fold. Subsequently, all deep learning AI models have been retrained on the enlarged dataset.

The second change in Genius AI Detection 2.0 is the adoption of a more sophisticated Convolutional Neural Network (CNN) model for the key processing step of calcification cluster classification, replacing the previously used, simpler conventional Artificial Neural Network (ANN) model. The significantly expanded dataset made it possible to train this newly introduced more complex neural network model, and to deliver significantly better performance especially for micro-calcification cancer detection.

In addition, Genius AI Detection 2.0 can now operate directly on processed tomosynthesis reconstructed slices, instead of first having to process the raw projections to a for presentation 3D reconstructed volume as it was the case for the previously approved product. This simplifies processing flow and eliminates the dependency on tomosynthesis raw projection data.

Standalone Performance Testing:

Genius AI Detection 2.0 is a software-only device. The level of concern for the device is determined as Moderate Level of Concern.

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

Validation testing consisted of determining stand-alone performance of Genius AI Detection 2.0 using a sequestered dataset of digital breast tomosynthesis exams acquired from multiple centers. This dataset was not used for training of Genius AI Detection 2.0 and included tomosynthesis exams of asymptomatic women acquired with Hologic Dimensions 3D Mammography systems.

The sequestered dataset consisted of 764 tomosynthesis exams including 106 biopsy proven cancers, 97 biopsy proven benign cases, 81 recalls and 480 screening negative cases all collected using Hologic's Dimensions 3D Mammography systems. The average patient age was 58 years and collected from multiple sites across the United States. The location for ground truth was determined by a radiology expert using radiology reports, pathology reports, and diagnostic and post-biopsy images when available. The truth was verified by another MQSA-qualified, board-certified radiologist to ensure accuracy and consistency.

To evaluate the performance of Genius AI Detection 2.0 in comparison to its predicate device, a standalone study was conducted on the sequestered dataset described above. Comparison of performance between Genius AI Detection 2.0 and its predicate device was conducted using fROC analysis and by comparing key performance metrics including detection sensitivity, specificity, and rate of false positive marks per view. The fROC curves demonstrated significant improvement for Genius AI Detection 2.0 over its predicate device, Genius AI Detection (K201019). The specificity measured at the operating point of Genius AI Detection 2.0 demonstrated significant increase of 12% as compared to

the original Genius AI Detection predicate device (McNemar's $p < 0.001$), while maintaining the sensitivity.

Based on results of the verification and validation tests, it is concluded that the Genius AI Detection 2.0 device is safe and effective in detecting soft tissue lesions and calcification lesions at an appropriate safety level in tomosynthesis exams acquired with Hologic's 3D Mammography systems.

Assessment of Benefit-Risk, Safety and Effectiveness, and Substantial Equivalence:

Risk management is ensured through risk analysis which is used to identify and mitigate potential hazards. Any potential hazards are controlled via software development, verification, and validation testing. In addition, device labeling contains instructions for use and any necessary cautions and warnings to provide for safe and effective use of this device. Hologic finds that the proposed device has a positive balance in terms of probable benefits vs probable risks and thus may be considered safe and effective based verification and validation testing.

Conclusion:

Based on the required information submitted in this premarket notification, the proposed Genius AI Detection 2.0 device has been found to be substantially equivalent to the predicate Genius AI Detection, K201019. Both devices have the same indications for use and aid in the detection, localization, and characterization of disease specific findings on acquired medical images. Standalone performance tests with the updated algorithm demonstrate that Genius AI Detection 2.0 achieves better detection performance compared to the predicate device. The are no issues of safety and effectiveness of the proposed Genius AI Detection 2.0 device.