Lunit Inc.
% John Smith
Partner
Hogan Lovells US LLP
555 Thirteenth Street NW
Washington, District of Columbia 20004

February 7, 2022

Re: K211678
Trade/Device Name: Lunit INSIGHT MMG
Regulation Number: 21 CFR 892.2090
Regulation Name: Radiological computer assisted detection and diagnosis software
Regulatory Class: Class II
Product Code: QDQ

Dear John Smith:

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 October 7, 2021. Specifically, FDA is updating this SE Letter due to a typographical error in the 510(k) summary as an administrative correction. Specifically the substantial equivalence table contains an additional column, which could trigger a misinterpretation for members of the public.

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, 301-796-6167, Jessica.Lamb@fda.hhs.gov.

Sincerely,

Jessica Lamb
Assistant 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

Lunit Inc.
% John J. Smith, M.D., J.D.
Partner
Hogan Lovells US LLP
555 Thirteenth Street NW
WASHINGTON DC 20004

November 17, 2021

Re: K211678
Trade/Device Name: Lunit INSIGHT MMG
Regulation Number: 21 CFR 892.2090
Regulation Name: Radiological computer assisted detection and diagnosis software
Regulatory Class: Class II
Product Code: QDQ
Dated: October 7, 2021
Received: October 7, 2021

Dear Dr. Smith:

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,

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)*
K211678

Device Name

Lunit INSIGHT MMG

Indications for Use *(Describe)*

Lunit INSIGHT MMG is a radiological Computer-Assisted Detection and Diagnosis (CADe/x) software device based on an artificial intelligence algorithm intended to aid in the detection, localization, and characterization of suspicious areas for breast cancer on mammograms from compatible FFDM systems. As an adjunctive tool, the device is intended to be viewed by interpreting physicians after completing their initial read.

It is not intended as a replacement for a complete physician's review or their clinical judgement that takes into account other relevant information from the image or patient history. Lunit INSIGHT MMG uses screening mammograms of the female population.

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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510(k) Summary

Lunit INSIGHT MMG (K211678)

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

Date Prepared: November 15, 2021

I. SUBMITTER

Manufacturer:
Lunit Inc.
15 Floor, 27 Teheran-ro 2-gil, Gangnam-gu, Seoul, Republic of Korea 06241
Phone +82-2-2138-0827
Fax +82-2-2135-5413

Contact Person:
Joohee Lee
Regulatory Affairs Specialist

II. DEVICE

Name of Device: Lunit INSIGHT MMG
Common or Usual Name: Lunit INSIGHT MMG
Classification Name: Radiological Computer Assisted Detection/Diagnosis Software For Suspicious Lesions For Cancer
Classification Regulation: 21 CFR 892.2090
Regulatory Class: II
Product Code: QDQ

III. PREDICATE DEVICE

Predicate Device
Manufacturer Name: Screenpoint Medical B.V.
Device Trade Name: Transpara™
510(k) Number: K192287

IV. DEVICE DESCRIPTION

Lunit INSIGHT MMG is a radiological Computer-Assisted Detection and Diagnosis (CADe/x) software for aiding interpreting physicians with the detection, localization, and characterization of suspicious areas for breast cancer on mammograms from compatible FFDM (full-field digital mammography) systems. The software applies an artificial intelligence algorithm for recognition of suspicious lesions,

which are trained with large databases of biopsy proven examples of breast cancer, benign lesions and normal tissues.

Lunit INSIGHT MMG automatically analyzes the mammograms received from the client's image storage system (e.g., Picture Archiving and Communication System (PACS)) or other radiological imaging equipment. Following receipt of mammograms, the software device de-identifies the copies of images in DICOM format (.dcm) and then automatically analyzes each image and identifies and characterizes suspicious areas for breast cancer. The analysis result is converted into DICOM file and the result is saved within the designated storage location (e.g., PACS, x-ray system, etc.)

Lunit INSIGHT MMG processes mammograms and the output of the device can be viewed by interpreting physicians after completing their initial read. As an analysis result, the software device allows a visualization and quantitative estimation of the likelihood of the presence of a malignant lesion. The suspicious lesions are marked by a visualized map and an abnormality score, which reflects general likelihood of presence of malignancy, is presented for each lesion, as well as for each breast.

V. INDICATIONS FOR USE

Lunit INSIGHT MMG is a radiological Computer-Assisted Detection and Diagnosis (CADe/x) software device based on an artificial intelligence algorithm intended to aid in the detection, localization, and characterization of suspicious areas for breast cancer on mammograms from compatible FFDM systems. As an adjunctive tool, the device is intended to be viewed by interpreting physicians after completing their initial read.

It is not intended as a replacement for a complete physician's review or their clinical judgement that takes into account other relevant information from the image or patient history. Lunit INSIGHT MMG uses screening mammograms of the female population.

VI. COMPARISON OF TECHNOLOGICAL CHARACTERSTICS WITH THE PREDICATE DEVICE

The Lunit INSIGHT MMG and the predicate Transpara have the similar indications where both devices are intended to assist a clinical user in the detection, localization, and characterization suspicious areas for breast cancer on mammography images. Also, both devices have the same intended user, and patient populations, and use the same imaging modality. The differences in the indications are with respect to the clinical workflow where the predicate device is intended to be used for concurrent read of images while the Lunit INSIGHT MMG is intended to be viewed by interpreting physicians after completing their initial read. Neither device is intended as a replacement for the review of a clinician or their clinical judgement and the patient management decisions are not made solely on the basis of analysis of the device. The minor difference in the indications with respect to the clinical workflow does not raise different questions of safety or effectiveness.

Lunit INSIGHT MMG and predicate share similar technological characteristics. Both devices are radiological computer assisted detection and diagnostic software based on an artificial intelligence algorithm that detect, identify and characterize findings based on features or information extracted from images. Both devices provide information about the presence and location of the findings to the user. As both devices process radiological images using similar machine learning techniques to

highlight abnormalities, the same types of safety and effectiveness questions are raised between devices. Both devices are support tools that provide relevant clinical data as an additional resource to the physician and will not replace the clinical expertise and judgement of the clinical user.

Both devices provide users with a numeric score indicating the likelihood of a presence of a malignant lesion however, the scoring system is different. Both devices provide a lesion score indicating likelihood of presence of malignancy. Lunit INSIGHT MMG analyzes per-breast abnormality score that takes the maximum scores from two views (i.e. CC, MLO). However, the predicate device analyzes the overall likelihood that cancer is present in a mammogram and categorizes the exams on a scale of 1 to 10 with increasing likelihood of cancer. The minor differences do not raise any different questions for its performance or safety; both devices provide clinically useful information to physicians who are reviewing a mammogram.

A comparison of the technological characteristics with the predicate device is summarized in **Table 1**.

VII. PERFORMANCE DATA

Non-clinical performance Data

The Lunit INSIGHT MMG is considered as a “moderate” level of concern, since a failure or a latent design flaw of the software device could result in Minor injury, either to a patient or to a user of the device. Based on results of verification and validation tests, Lunit INSIGHT MMG is effective in the detection of suspicious lesion for breast cancer at an appropriate safety level in mammograms. Verification tests which consisted of software unit testing, integration testing and system testing were successfully completed to assure that the software application satisfied the software requirements. Validation testing determining standalone performance of the algorithms in Lunit INSIGHT MMG was also completed successfully. Validation and verification test results demonstrated that Lunit INSIGHT MMG is as safe and effective as the predicate device.

Standalone Performance Testing

Standalone Performance Study of the Lunit INSIGHT MMG assessed the performance of software algorithm for breast cancer detection in screening mammography.

Total of 2412 mammograms were collected using Hologic, GE Healthcare, and Siemens mammography equipment. The standalone performance of Lunit INSIGHT MMG for breast cancer detection in screening mammography is examined as comparing the reference standards and the analysis results of the device. The dataset used in the study is independent from the dataset used for development of the algorithm and the US pivotal reader study.

The primary endpoint of the standalone performance measured the Lunit INSIGHT MMG performance compared to radiologist performance alone. ROC AUC in the standalone performance analysis was 0.903 (95% CI: 0.889-0.917) with statistical significance ($p < 0.0001$), which demonstrates improvement compared to the interpretation performance of radiologists when reading mammograms unaided. The secondary exploratory endpoints are two types of LROC AUC, sensitivity and specificity and these results are as follow:

[Standalone Analysis Results]

ROC AUC [95% CI]	0.903 [0.889, 0.917]
	*p < 0.0001
Type I LROC AUC [95% CI]	0.781 [0.751, 0.812]
Type II LROC AUC [95% CI]	0.792 [0.763, 0.822]
Sensitivity (%) [95% CI]	85.74 [82.95, 88.53]
Specificity (%) [95% CI]	75.62 [73.64, 77.60]

Clinical Testing – Reader Study

Clinical Performance Assessment was conducted to evaluate effectiveness of Lunit INSIGHT MMG in the assistance of detection and diagnosis of breast cancer during screening mammography interpretation. A retrospective, multi-reader multi-case (MRMC) study was conducted comparing the reading panel's interpretation performance with and without the assistance of the Lunit INSIGHT MMG during the screening mammography interpretation.

Total of 240 mammograms were collected using Hologic and GE Healthcare mammography equipment in the US. During the study, 12 MQSA qualified reading panelists performed their interpretation independently using a setting similar to a screening procedure in the U.S. Reading panelists interpret cases without CAD assistance first then re-interpret of the same cases with Test 1 reading results in assistance of the Lunit INSIGHT MMG. To minimize any potential bias, the reading order for each reading panelists was randomized.

The primary objective of the reader study is to determine that the diagnostic ability of radiologist with CAD assistance is superior to without CAD assistance. Radiologist performance was assessed with an inter-test comparison of measuring FBR (Forced BI-RADS) ROC AUC between reader's interpretation and device-assisted interpretation for the detection of malignant lesions in the study. Success criteria of the study was defined as the p-value of the ROC AUC difference test is less than

the significance level of 5% and the lower bound of two-sided 95% CI (Confidence Interval) of the AUC difference (Test 2-Test 1) is above 0. Secondary exploratory endpoints of the reader study assessed inter-test difference in LCM (level of confidence of malignancy) LROC AUC, LCM ROC AUC, and recall rate in cancer and non-cancer group (sensitivity and 1-specificity).

For the primary endpoint, the average inter-test difference in ROC AUC between Test 2 and Test 1 was 0.051 (95% CI: 0.027-0.075) with statistical significance (P=0.0001), which indicates that physician's interpretation ability for breast cancer in mammograms is improved in Test 2 (with CAD) from Test 1 (without CAD).

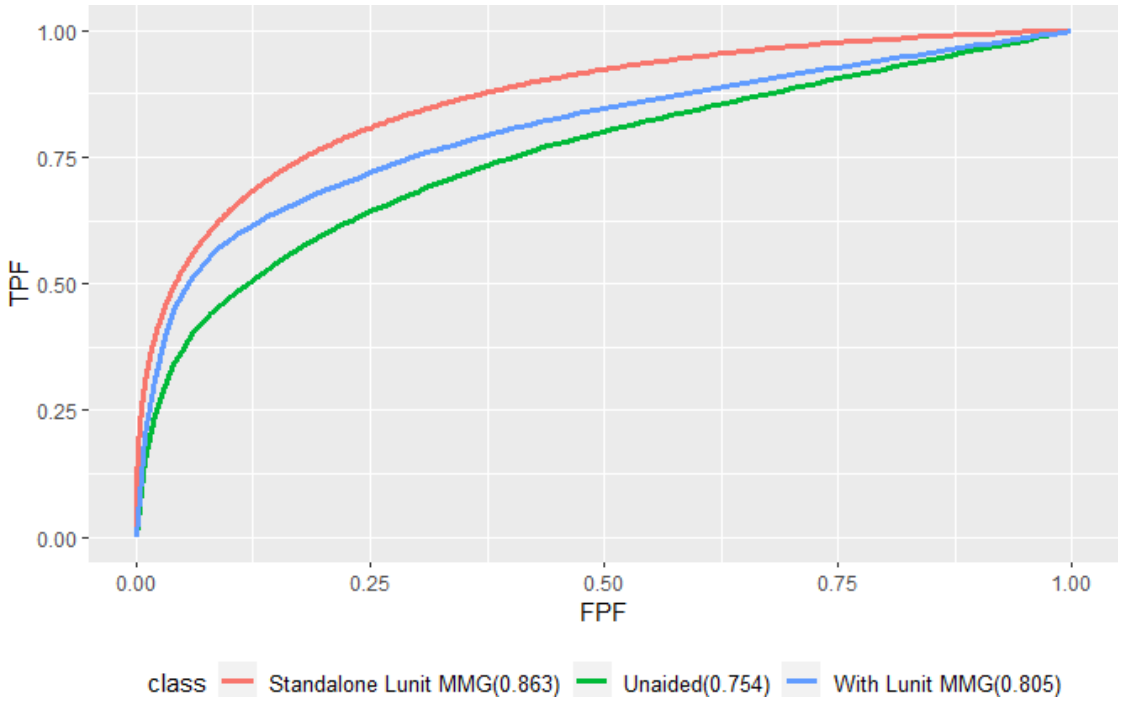
[Primary Endpoint Results of the Pivotal Reader Study]

	Test1	**Test2**	**Test2-Test1**	**P-value**
ROC AUC (95%CI)	0.754 (0.702, 0.807)	0.805 (0.759, 0.852)	0.051 (0.027, 0.075)	0.0001

All secondary exploratory endpoints have shown higher performance in assistance of the device, the inter-test differences for each assessment are as follow: LCM LROC 0.094 (95% CI: 0.056 - 0.132), LCM ROC AUC 0.052 (95% CI: 0.026 - 0.079), recall rate in cancer group (sensitivity) 5.97(95% CI: 2.48 - 9.46), and recall rate in non-cancer group (1-specificity) -1.46 (95% CI: -3.41 - 0.05). Results of the primary and secondary analysis of the clinical testing demonstrate improvement for breast cancer detection and diagnosis using Lunit INSHGT MMG in mammograms.

Separated from the standalone performance test, an additional assessment of standalone algorithm performance was conducted with same cases from the reader study, using the Lunit INIGHT MMG without reader intervention as a sole means of reading mammograms compared to the software output. ROC AUC in the standalone performance analysis is 0.863 (95% CI: 0.818 - 0.909) which exceeds the results of every reading panelist in Test 1 (CAD unaided).

[Plot Comparison of the standalone performance, CAD unaided and aided reader interpretation]



VIII. CONCLUSIONS

The non-clinical performance data and clinical data showed that Lunit INSIGHT MMG is as safe and effective as the predicate device. In particular, the effectiveness of the Lunit INSIGHT MMG in assistance of detection and diagnosis of breast cancer during screening mammography interpretation has been verified in the US population by confirming that the improvement for breast cancer detection and diagnosis before and after use of the Lunit INSIGHT MMG. In addition, the study results lead a positive expectation in an aspect of the clinical benefit that false positives and false negatives are reduced in the screening mammograms with the use of the Lunit INSIGHT MMG. In a conclusion, with all the clinical evidence achieved from the clinical study, the Lunit INSIGHT MMG can be considered to perform effectively in assistance of detection and diagnosis of breast cancer.

The Lunit INSIGHT MMG has the similar intended uses, indications, technological characteristics, and principles of operation as its predicate device. Both devices 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. The minor differences in indications do not alter the intended of the device and do not affect its safety and effectiveness. In addition, the minor technological differences between the Lunit INSIGHT MMG and its predicate devices raise no new questions of safety or effectiveness. Performance data demonstrate that the Lunit INSIGHT MMG is as safe and effective as the predicate Transpara. Thus, the Lunit INSIGHT MMG is substantially equivalent.

Table 1 – Comparison Between Subject and Predicate Devices

Technical Characteristics	Subject Device Lunit INSIGHT MMG	Predicate Device Transpara™ (K192287)
Classification Regulation	21 CFR 892.2090 Radiological Computer Assisted Detection and Diagnosis software	21 CFR 892.2090 Radiological Computer Assisted Detection and Diagnosis software
Medical Device Classification	Class II	Class II
Product Code	QDQ	QDQ
Level of Concern	Moderate	Moderate
Intended Use	A reading aid for physicians interpreting screening FFDM acquired with compatible mammography systems, to identify findings and assess their level of suspicion.	A reading aid for physicians interpreting screening FFDM acquired with compatible mammography systems, to identify findings and assess their level of suspicion.
Target patient population	Women undergoing FFDM screening mammography	Women undergoing FFDM screening mammography
Target user population	Physicians interpreting FFDM screening mammograms	Physicians interpreting FFDM screening mammograms
Design	Software-only device	Software-only device
Indication for Use	Lunit INSIGHT MMG is a radiological Computer-Assisted Detection and Diagnosis (CADe/x) software device based on an artificial intelligence algorithm intended to aid in the detection, localization, and	The ScreenPoint Transpara™ system is intended for use as a concurrent reading aid for physicians interpreting screening mammograms from compatible FFDM system, to identify regions suspicious for breast

Technical Characteristics	Subject Device Lunit INSIGHT MMG	Predicate Device Transpara™ (K192287)
	characterization of suspicious areas for breast cancer on mammograms from compatible FFDM systems. As an adjunctive tool, the device is intended to be viewed by interpreting physicians after completing their initial read. It is not intended as a replacement for a complete physician's review or their clinical judgement that takes into account other relevant information from the image or patient history. The Lunit INSIGHT MMG uses screening mammograms of the female population.	cancer and assess their likelihood of malignancy. Output of the device includes marks placed on suspicious soft tissue lesions and suspicious calcifications; region-based scores, displayed upon the physician's query, indicating the likelihood that cancer is present in specific regions; and an overall score indicating the likelihood that cancer is present on the mammogram. Patient management decisions should not be made solely on the basis of analysis by Transpara™.
Device output in case of positive detection	Output of the device includes marks with visualized map such as heatmap placed on suspicious lesions for breast cancer; lesion score, indicating the likelihood of presence of the malignancy in specific regions; and an abnormality score indicating the likelihood of the presence of malignancy per-breast in the mammogram. The per-breast abnormality score takes maximum score from two views (i.e., CC, MLO) of a breast which is the maximum lesion score in the breast.	Output of the device includes marks in outlines placed on suspicious soft tissue lesions and suspicious calcifications; region-based scores, displayed upon the physician's query, indicating the likelihood that cancer is present in specific regions; and an overall score indicating the likelihood that cancer is present on the mammogram.
Score	Finding level:	Finding level:

Technical Characteristics	Subject Device Lunit INSIGHT MMG	Predicate Device Transpara™ (K192287)
	Score 1-100 indicating likelihood of presence of malignancy (from low suspicion to high suspicion). Breast level: Score 1-100 indicating the level of suspicious of malignancy. The maximum scores from two view (i.e., CC, MLO) of a breast which is the maximum lesion score in the breast Exam level: None	Continuous score 1-100 indicating the level of suspicion of malignancy (from low suspicion to high suspicion). Breast level: None Exam level: 10-point scale score indicative of higher frequency of cancer positive
Performance	<u>Reader study:</u> · 240 cases · 12 radiologists cf. Reading time was not measured in this study. ROC AUC: radiologists AUC (unaided) = 0.754 radiologists AUC (aided) = 0.805 <u>Standalone Performance Test:</u> · 2412 cases	<u>Reader study:</u> · 240 cases · 14 radiologists Reading time: · 146 seconds (unaided session) · 149 seconds (with Transpara™) AUC: · radiologists AUC (unaided) = 0.866 · radiologists AUC (aided) = 0.886

Technical Characteristics	Subject Device Lunit INSIGHT MMG	Predicate Device Transpara™ (K192287)
	ROC AUC = 0.903	· standalone AUC = 0.887
Image Source Modality	FFDM	FFDM
Fundamental scientific technology	In Lunit INSIGHT MMG, a range of medical image processing and machine learning techniques are implemented. The system includes 'deep learning' algorithm applied to images for recognition of suspicious lesions for breast cancer. The machine learning components are trained to detect suspicious lesions for breast cancer with large databases of biopsy-proven cases of breast cancer, benign lesions and normal tissues.	In Transpara, a range of medical image processing and machine learning techniques are implemented. The system includes 'deep learning' algorithm applied to images for recognition of suspicious lesions for breast cancer. The machine learning components are trained to detect suspicious lesions for breast cancer with large databases of biopsy-proven cases of breast cancer, benign lesions and normal tissues.