



May 30, 2025

Clairity, Inc.
Kris Zeschin
Acting Head of Operations and Regulatory
201 W 5th St., Ste 1500
Austin, Texas 78701

Re: DEN240047
Trade/Device Name: Allix5
Regulation Number: 21 CFR 892.8500
Regulation Name: Radiological software device to predict future breast cancer risk.
Regulatory Class: Class II
Product Code: SEZ
Dated: September 6, 2024
Received: September 6, 2024

Dear Kris Zeschin:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your De Novo request for classification of the Allix5, a prescription device under 21 CFR Part 801.109 with the following indications for use:

The Clairity Allix5 software device is intended to generate a 5-year risk prediction of breast cancer based on a bilateral screening mammogram. Allix5 provides a prediction of the percentage probability that the individual will receive a diagnosis of breast cancer or develop breast cancer within the 5-year timeframe following the screening mammogram, through analysis of mammography features and characteristics.

Eligible patients do not have a known breast cancer at presentation for their screening mammogram.

Allix5 is not intended to diagnose or detect breast cancer, or to provide care recommendations. Allix5 is not intended to replace or to be used as the sole determinant for clinical decision-making. Allix5 output is intended to be considered after the radiologist has completed the interpretation of the screening mammogram.

Allix5 analyzes full-field digital mammograms or directly acquired 2D images from Hologic Lorad Selenia and Selenia Dimensions Mammography Systems; it does not analyze synthetic-2D images.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the Allix5, and substantially equivalent devices of this generic type, into Class II under the generic name radiological software device to predict future breast cancer risk.

FDA identifies this generic type of device as:

Radiological software device to predict future breast cancer risk. A radiological software device to predict future breast cancer risk is a device that analyzes radiological images generated by breast imaging modalities and/or inputs derived from radiological images to provide qualified healthcare professionals with a prediction of the risk of future (incident) breast cancer. This device produces a numeric probability and/or risk category indicative of the patient’s future breast cancer risk from the time the analyzed images were acquired. This device is not intended to diagnose, detect, or inform the treatment of cancer. The output of this device is not intended to guide interpretation of imaging exams.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This law provides two options for De Novo classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. On December 13, 2016, the 21st Century Cures Act removed a requirement that a De Novo request be submitted within 30 days of receiving an NSE determination. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register announcing the classification.

On September 6, 2024, FDA received your De Novo requesting classification of the Allix5. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Allix5 into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the De Novo request, FDA has determined that, for the previously stated indications for use, the Allix5 can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in the following table:

Risks to Health	Mitigation Measures
Device provides inaccurate risk discrimination and/or calibration contributing to: <ul style="list-style-type: none"> • Falsely high risk output, leading to patients receiving unnecessary 	Clinical performance testing Software verification, validation, and hazard analysis Labeling Postmarket monitoring plan

Risks to Health	Mitigation Measures
additional imaging or preventive risk reduction measures <ul style="list-style-type: none"> • Falsely low risk output, leading to patients not receiving additional imaging or preventive risk reduction measures 	
Inconsistent device output due to differences in acquisition, equipment settings, or other factors affecting image selection or quality	Clinical performance testing Software verification, validation and hazard analysis Labeling Postmarket monitoring plan
User misinterpretation of device result(s) contributing to: <ul style="list-style-type: none"> • Inappropriate categorization of patient risk resulting in erroneous patient management decisions related to additional imaging or preventive risk reduction measures • Overreliance on device output Patient misinterpretation of device result(s) contributing to <ul style="list-style-type: none"> • Considering low risk to be negligible which may contribute to not receiving standard-of-care screening or preventive risk reduction measures 	Labeling Postmarket monitoring plan

In combination with the general controls of the FD&C Act, the radiological software device to predict future breast cancer risk is subject to the following special controls:

- (1) Data obtained from clinical performance validation testing acquired under anticipated conditions of use must demonstrate that the device performs as intended when used in the intended patient population. Documentation must include the following:
 - (i) A description of prespecified performance testing protocols (including the study objectives, study endpoints, statistical hypotheses, performance goals, sample size calculation, and statistical analyses, including adjustment for left- and/or right-censoring of the time of disease onset). Performance goals used to determine success of the clinical validation study must be clinically justified;
 - (ii) A description of the dataset(s) used. Validation must use a clinical test dataset acquired from a representative patient population. The test dataset must be representative of the range of data sources and data quality likely to be encountered in the intended use population and relevant use conditions in the intended use environment. The test dataset must be independent of the data used in the training/development of the device;

- (iii) Establishment of a reference standard, with clinical justification, to distinguish those who experience the disease by the designated future time from those who do not, or a time interval within which the disease onset is known to have occurred or not occurred. Study protocols must include a description of the methodology for determining the reference standard for training and test datasets;
 - (iv) Results to validate the device output pertaining to future disease risk prediction. The performance assessment must be based on clinically justified measures of discrimination and calibration of risk categorization or score estimates in the intended patient population. Agreement between device predicted risk outputs and observed risk must be calculated across the range of risks expected in the intended patient population;
 - (v) The clinical performance of discrimination and calibration of device outputs must demonstrate the generalizability of device performance across clinically important subgroups. Subgroup analysis of discrimination and calibration by study site, relevant demographic subgroups, image acquisition system, and any other applicable confounders of clinical interest must be provided; and
 - (vi) Data must demonstrate reproducibility of the device output across the range of input image acquisition settings including acquisition equipment and patient positioning.
- (2) Software verification, validation, and hazard analysis must be provided. Software documentation must include:
- (i) A technical description of the model/algorithm(s) and algorithm inputs and outputs; and
 - (ii) Verification and validation data that demonstrate software ensures input radiological images are adequate for processing.
- (3) Labeling must include:
- (i) Compatible imaging requirements for input;
 - (ii) A warning that the output of this device is not intended to guide interpretation of imaging exams;
 - (iii) A warning that the user of this device should consider other clinical information for patient management;
 - (iv) A warning that the device is not intended to diagnose, detect, or inform the treatment of disease;
 - (v) A summary of the clinical performance testing methods, including results of the performance testing for tested performance measures/metrics, selection criteria, truthing, patient dataset characteristics, and subgroup analyses by relevant confounders;
 - (vi) A description of output reproducibility and results of reproducibility testing;
 - (vii) Device limitations or a description of subpopulations for which the device may not perform as expected or for whom the device has not been validated; and
 - (viii) A summary of the device's current performance that incorporates clinical performance testing and data collected from post-market performance monitoring.
- (4) The device manufacturer must develop and implement a post-market performance management plan that ensures regular assessment of the generalizability and device performance in the intended patient population in real-world use. The plan must include:
- (i) Data collection, analysis methods, and procedures for:
 - (A) Monitoring relevant performance characteristics and detecting changes in performance;

- (B) Identifying sources of performance changes between validation and real-world environment over time; and
 - (C) Assessing the results from the performance testing on safety and effectiveness;
- (ii) Procedures for communicating the device's current performance to the users.

In addition, this is a prescription device and must comply with 21 CFR 801.109.

Although this letter refers to your product as a device, please be aware that some granted products may instead be combination products. If you have questions on whether your product is a combination product, contact CDRHProductJurisdiction@fda.hhs.gov.

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the radiological software device to predict future breast cancer risk they intend to market prior to marketing the device.

Please be advised that FDA's decision to grant this De Novo request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD&C 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 FD&C Act; 21 CFR 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>.

A notice announcing this classification order will be published in the Federal Register. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug

Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the De Novo request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

For comprehensive regulatory information about medical devices and radiation-emitting products, 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).

If you have any questions concerning the contents of the letter, please contact Yanna Kang at 301-796-6704.

Sincerely,

for Robert Ochs, Ph.D.
Director
OHT8: Office of Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health