March 20, 2026

IceCure Medical
% Margeaux Rogers
Senior Director, Regulatory Affairs
MCRA, LLC
803 7th Steet NW
Washington, District of Columbia 20001

Re: DEN220077
Trade/Device Name: ProSense Cryoablation System
Regulation Number: 21 CFR 878.4355
Regulation Name: Cryoablation device for local treatment of low-risk breast cancer
Regulatory Class: Class II
Product Code: QXW
Dated: October 18, 2022
Received: October 19, 2022

Dear Margeaux Rogers:

This letter corrects our previous classification order, dated October 3, 2025, to correct inconsistencies in the postmarket surveillance enrollment and reporting requirements.

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 ProSense Cryoablation System, a prescription device under 21 CFR Part 801.109 with the following indications for use:

> ProSense Cryoablation System is indicated for the local treatment of breast cancer in patients ≥70 years of age with biologically low-risk tumors ≤1.5 cm in size and treated with adjuvant endocrine therapy, including patients not suitable for surgery for breast cancer treatment.
>
> Biologically low-risk breast cancer is defined as unifocal tumor, size ≤1.5 cm, ER-positive, PR-positive, HER2-negative, Ki-67<15% and/or genomic testing indicative of low-risk breast cancer, infiltrating ductal carcinoma (excluding lobular carcinoma, extensive intraductal component, or evidence of lymphovascular invasion), and clinically negative lymph node (N0).

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the ProSense Cryoablation System, and substantially equivalent devices of this generic type, into Class II under the generic name cryoablation device for local treatment of low-risk breast cancer.

FDA identifies this generic type of device as:

Cryoablation device for local treatment of low-risk breast cancer. A cryoablation device for local treatment of low-risk breast cancer is a prescription device that uses cold temperatures to destroy a breast tumor and its surrounding tissue. The device is intended as a local treatment and may be used with adjuvant therapies (e.g., endocrine therapy, radiation therapy) to reduce the risk of local disease progression. The device is intended for use in patients with a well-defined solid tumor (e.g., invasive ductal carcinoma) and with low risk of recurrence and metastasis, as determined by clinical risk factors consistent with the indications for use. The device is not intended to treat breast cancers with high risk of local recurrence (e.g., lobular carcinoma), patients with aggressive forms of breast cancer (e.g., breast cancers with inflammatory features), or patients in whom targeted systemic therapy is indicated.

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 October 19, 2022, FDA received your De Novo requesting classification of the ProSense Cryoablation System. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the ProSense Cryoablation System 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, including a November 7, 2024 public advisory committee meeting of the General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee, FDA has determined that, for the previously stated indications for use, the ProSense Cryoablation System 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:

Table 1 – Identified Risks to Health and Mitigation Measures

Risks to Health	**Mitigation Measures**
Incomplete tumor ablation resulting in the need for additional treatment(s) and/or tumor recurrence	Clinical performance testing Postmarket surveillance Non-clinical performance testing Software verification, validation, and hazard analysis Labeling
Electrical, thermal, or mechanical injury	Clinical performance testing Non-clinical performance testing

	Software verification, validation, and hazard analysis Electrical, mechanical, and thermal safety testing Electromagnetic compatibility testing Labeling
Infection and cross-contamination	Sterilization validation Shelf life testing Labeling
Adverse tissue reaction	Biocompatibility evaluation

In combination with the general controls of the FD&C Act, the cryoablation device for local treatment of low-risk breast cancer is subject to the following special controls:

(1) Data obtained from premarket clinical performance testing and postmarket surveillance conducted per a protocol approved by FDA and acquired under anticipated conditions of use must demonstrate that the device performs as intended in the intended patient population, unless FDA determines based on the totality of the information provided for premarket review that data from postmarket surveillance is not required. Premarket and postmarket clinical performance testing must demonstrate the 5-year ipsilateral breast tumor recurrence rate or other clinically justified endpoint for defining local treatment of breast cancer (e.g., histological clearance rate compared to a clinical comparator with known ipsilateral breast tumor recurrence rate), based on prespecified cryoablation device design and treatment parameters (e.g., imaging protocol, number of freeze/thaw cycles, treatment margin around the tumor, and target ice ball size). A discussion of how the intended and studied patient populations constitute a low-risk breast cancer population must also be provided.

(2) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use, including the following:
   (i) Performance testing must demonstrate that the device meets cryogen pressure and flow rate specifications with the intended cryogen type;
   (ii) Performance testing must characterize the dimensions of the active part of the applicator and demonstrate that the cryoprobe meets temperature specifications for freezing and thawing; and
   (iii) Performance testing must demonstrate that the device meets freezing performance specifications under the anticipated load in a representative test medium.

(3) Software verification, validation, and hazard analysis must be performed.

(4) Performance testing must demonstrate the electrical safety, mechanical safety, thermal safety, and electromagnetic compatibility of any electrical components of the device.

(5) Performance data must demonstrate the sterility of all patient-contacting device components.

(6) Performance data must support the shelf life of the device components provided sterile by demonstrating continued sterility and package integrity over the labeled shelf life.

(7) Performance data must demonstrate that all patient-contacting components of the device are biocompatible.

(8) Labeling must include:
  (i) Recommended training for safe use of the device;
  (ii) Instructions for determining and achieving the appropriate ice ball size relative to the intended ablation volume;
  (iii) A summary of clinical performance testing, including device treatment parameters and procedures, characteristics of the patient population, and treatment outcomes (e.g., recurrence rate, disease-free or event-free survival, overall survival, histological clearance rate, adverse events, patient-reported outcomes);
  (iv) Warnings regarding uncertainty or limitations in the clinical data, including:
    (A) The duration of oncological outcomes that have been evaluated; and
    (B) A statement that oncological outcomes have not been studied in direct comparison to surgical tumor resection, unless such data are available, in which case comparison data must be included; and
  (v) When postmarket surveillance is required per paragraph (1) of this section, a description of the postmarket surveillance purpose, and a summary of all postmarket surveillance data collected, including updated labeling to accurately reflect outcomes observed in postmarket surveillance.

(9) Patient labeling must include:
  (i) A description of the intended patient population characteristics;
  (ii) Treatment outcomes observed in clinical performance testing;
  (iii) Warnings regarding uncertainty or limitations in the clinical data, including the duration of oncological outcomes that have been evaluated;
  (iv) Warning regarding the limitations of using imaging to confirm the completeness of tumor destruction after cryoablation; and
  (v) When postmarket surveillance is required per paragraph (1) of this section, a description of the postmarket surveillance purpose, and a summary of all postmarket surveillance data collected, including updated labeling to accurately reflect outcomes observed in postmarket surveillance.

In order to satisfy special control (1) above, FDA has determined that you must collect and report post-market surveillance data acquired under anticipated conditions of use to demonstrate that the device performs as intended when used to treat the intended patient population. Specifically, you must conduct post-market clinical validation performance testing of the ProSense Cryoablation System in patients to assess long-term tumor recurrence and other serious adverse events.

FDA expects that the postmarket study will enroll 400 patients at 30 sites to further characterize the ipsilateral breast tumor recurrence (IBTR) rate following cryoablation without resection for the treatment of low-risk, early-stage breast cancer in the indicated population. The co-primary endpoints will be the percentage of patients who develop confirmed IBTR and confirmed and suspected IBTR up to 5 years after cryoablation. IBTR will be defined as recurrent invasive or in situ cancer confirmed histologically in the ipsilateral breast or based on imaging suspicion in the absence of histological information, and measured from the time of treatment to the time of documented ipsilateral recurrence. Histology showing a different molecular signature than the primary tumor treated with cryoablation will be defined as a second primary tumor (not IBTR). Time to recurrence and any subsequent ipsilateral breast surgeries (e.g., lumpectomy, mastectomy) performed for the treatment of residual or recurrent disease will be documented. The study is also expected to observe disease-free survival and overall survival rates.

Within 30 days of receipt of this order, you must submit a complete study protocol for your study(ies) as described above. FDA expects to work with you to approve your study protocol within 60 days of this order. Your submission should be clearly labeled "Postmarket Study Protocol" and submitted to the Agency as specified below. Please reference the De Novo number above to facilitate processing. If there are multiple protocols being finalized after granting of this De Novo request, please submit each protocol as a separate submission, identified by their unique study name(s).

From the date of study protocol approval, you must meet the following timelines:

- First subject enrolled within 6 months
- 20% of subjects enrolled within 12 months
- 50% of subjects enrolled within 18 months
- 100% of subjects enrolled within 36 months

In addition, you must submit separate periodic reports on the progress of the study(ies) as follows:

- Postmarket surveillance progress reports every six (6) months until subject enrollment has been completed, and annually thereafter, from the date of the protocol approval letter, unless otherwise specified by FDA.
- If any enrollment milestones are not met, you must begin submitting enrollment status reports every three (3) months, in addition to your periodic postmarket study progress reports, until enrollment has been completed, or FDA notifies you otherwise.
- Submit the final postmarket study report three (3) months from study completion (i.e., last subject's last follow-up date).

Each postmarket surveillance report should be submitted to the Agency as specified below, identified "Postmarket Surveillance Report" in accordance with how the study is identified above, and bearing the applicable De Novo reference number.

Be advised that failure to comply with any special control requirement, including the initiation, enrollment, completion, and reporting per the postmarket surveillance data requirements outlined above, may result in the adulteration and misbranding of your device.

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 cryoablation device for local treatment of low-risk breast cancer 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).

All required documents should be submitted, unless otherwise specified, to the address below and should reference the above De Novo number to facilitate processing.

Postmarket Mandated Studies Program
U.S. Food and Drug Administration
Center for Devices and Radiological Health

Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Alternatively, documents can be submitted electronically through the CDRH Portal. For more information on the CDRH Portal, please visit https://www.fda.gov/medical-devices/industry-medical-devices/send-and-track-medical-device-premarket-submissions-online-cdrh-portal.

If you have any questions concerning the contents of the letter, please contact Jessica Carr at 301-796-5997.

Sincerely,

ANGELA C. KRUEGER -S

Digitally signed by ANGELA C. KRUEGER -S
Date: 2026.03.20 16:29:22 -04'00'

Angela Krueger
Deputy Director for Regulatory Policy
Office of Product Evaluation and Quality
Center for Devices and Radiological Health