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DE NOVO CLASSIFICATION REQUEST FOR
CAPTION GUIDANCE

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REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Radiological acquisition and/or optimization guidance system.** A radiological acquisition and/or optimization guidance system is a device that is intended to aid in the acquisition and/or optimization of images and/or diagnostic signals. The device interfaces with the acquisition system, analyzes its output, and provides guidance and/or feedback to the operator for improving image and/or signal quality.
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> **NEW REGULATION NUMBER:** 21 CFR 892.2100
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> **CLASSIFICATION:** Class II
>
> **PRODUCT CODE:** QJU

BACKGROUND

> **DEVICE NAME:** Caption Guidance
>
> **SUBMISSION NUMBER:** DEN190040
>
> **DATE OF DE NOVO:** August 27, 2019
>
> **CONTACT:** Caption Health, Inc.
> 2000 Sierra Point Pkwy, 8th Floor
> Brisbane, CA 94005

INDICATIONS FOR USE

The Caption Guidance software is intended to assist medical professionals in the acquisition of cardiac ultrasound images. Caption Guidance software is an accessory to compatible general purpose diagnostic ultrasound systems.

Caption Guidance software is indicated for use in two-dimensional transthoracic echocardiography (2D-TTE) for adult patients, specifically in the acquisition of the following standard views: Parasternal Long-Axis (PLAX), Parasternal Short-Axis at the Aortic Valve (PSAX-AV), Parasternal Short-Axis at the Mitral Valve (PSAX-MV), Parasternal Short-Axis at the Papillary Muscle (PSAX-PM), Apical 4-Chamber (AP4), Apical 5-Chamber (AP5), Apical 2-Chamber (AP2), Apical 3-Chamber (AP3), Subcostal 4-Chamber (SubC4), and Subcostal Inferior Vena Cava (SC-IVC).

<u>LIMITATIONS:</u>
Prescription Use only: Federal (USA) law restricts this device for sale by or on the order of a physician.

<u>Warnings:</u>

- Product users are responsible for image quality and diagnosis. The images acquired using Caption Guidance are to be interpreted only by qualified medical professionals. A qualified medical professional must inspect the data being used for analysis and diagnosis, and ensure that the data is sufficient and appropriate in anatomical correctness and both spatial and temporal resolution for the measurement being employed.

- Caption Guidance is not intended for transesophageal echocardiography or any other type of ultrasound exam not listed under "Intended Use/Indications for use."

- Caption Guidance operates with the 3200t-compatible Terason 4V2A linear phased array probe (called a "transducer" in the Terason manual). Do not operate Caption Guidance with any other probe.

- The uSmart 3200t Plus ultrasound system, with which Caption Guidance functions as a software accessory, complies with the Standard for Real-Time Display of Thermal and Mechanical Acoustic Output Indices on Diagnostic Ultrasound Equipment (UD3-2004).

  It is important to observe the MI and TI values that are displayed during scanning. Follow the ALARA principle—exposure of the patient to ultrasound energy at a level that is As Low as Reasonably Achievable—when conducting ultrasound exams in order.

  PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION
The Caption Guidance software is a radiological acquisition and/or optimization guidance system that provides real-time guidance to the users during acquisition of echocardiography to assist them in obtaining anatomically correct images that represent standard 2D echocardiographic diagnostic views and orientations. Caption Guidance is a software-only device that uses artificial intelligence to emulate the expertise of sonographers.

Caption Guidance is comprised of several different features that, combined, provide expert guidance to the user. These include:

1. **Quality Meter:** The real-time feedback from the Quality Meter advises the user on the expected diagnostic quality of the resulting clip, such that the user can make decisions to

further optimize the quality, for example by following the prescriptive guidance feature below.

2. **Prescriptive Guidance:** The prescriptive guidance feature in Caption Guidance provides direction to the user to emulate how a sonographer would manipulate the transducer to acquire the optimal view.

3. **Auto-Capture:** The Caption Guidance Auto-Capture feature triggers an automatic capture of a clip when the quality is predicted to be diagnostic, emulating the way in which a sonographer knows when an image is of sufficient quality to be diagnostic and records it.

4. **Save Best Clip:** This feature continually assesses clip quality while the user is scanning and, in the event that the user is not able to obtain a clip sufficient for Auto-Capture, the software allows the user to retrospectively record the highest quality clip obtained so far, mimicking the choice a sonographer might make when recording an exam.

The Caption Guidance software was trained using echocardiographic clips from studies performed by trained sonographers. The ideal probe pose for each cardiac view was used to determine the Prescriptive Guidance for maneuvering the probe to the ideal pose.

The Caption Guidance software is labeled for use with the Terason uSmart 3200t Plus, an FDA 510(k) cleared (K150533) ultrasound system. Caption Guidance is installed on the third-party ultrasound system. The user has access to both the Terason user interface (UI) and the Caption Guidance UI and will be able to switch between the two.

SUMMARY OF NON-CLINICAL/BENCH STUDIES

Software

Caption Guidance was identified as having a moderate level of concern as defined in the FDA guidance document "*Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices.*" The software documentation included:

1. Software/Firmware Description
2. Device Hazard Analysis
3. Software Requirement Specifications
4. Architecture Design Chart
5. Software Design Specifications
6. Traceability
7. Software Development Environment Description
8. Verification and Validation Documentation
9. Revision Level History
10. Unresolved Anomalies
11. Cybersecurity

Risk analysis was provided for the software with detailed description of the hazards, their causes and severity as well as acceptable methods for control of the identified risks. Caption Health provided a description, with test protocols including pass/fail criteria and report of results, of acceptable verification and validation activities at the unit, integration and system level.

Algorithm Performance Testing

Non-clinical performance testing of the deep learning algorithms used in the device was provided to further support their effectiveness.

The Caption Guidance algorithm was tested for the performance of the supported features: Quality Meter, Auto-Capture, and Save Best Clip. The following specific tasks of the algorithm were used as metrics of performance:

1. Frame-level prediction of the current pose of the probe, as compared to the ideal pose for a specific view of the heart.
2. Relative image quality predication of the current pose of the probe, as compared to the ideal pose for a specific view of the heart.
3. Auto-Capture of clinically-acceptable images and clips.

Furthermore, the subject device's algorithm was tested for the performance of providing Prescriptive Guidance (PG), using the following tasks:

1. Frame-level PG prediction of the probe maneuver needed to acquire an image/frame of heart, for a specific view.
2. Clip-level PG prediction of the probe maneuver needed to acquire a diagnostic-quality clip for a specific view.

Overall, the non-clinical performance testing results provide evidence in support of the functionality of Caption Guidance fundamental algorithms. Caption Health demonstrated a low-level verification of the algorithms, which was not powered with a p-value significance for all tested PG actions. Importantly, the effectiveness of the subject device was assessed by taking into consideration the evidence from both bench testing and clinical testing.

SUMMARY OF CLINICAL INFORMATION

Specialist (Sonographer) Study

Caption Guidance is designed for use both as an assistive tool for trained sonographers as well as medical professionals without specialized echocardiography training. Use by specialist users was evaluated in a prospective clinical study, in which 50 patients were scanned by sonographers with the Caption Guidance system (study exam), followed by a reference scan (control exam) on the same patient using the same ultrasound equipment, but unassisted by Caption Guidance. Study and control exams were assessed by three (3)

expert cardiologists who graded each clip using the American College of Emergency Physicians (ACEP) scale for echocardiography quality. The data from this study was used to provide descriptive supportive evidence of the use of Caption Guidance by users with specialized echocardiography training.

In this particular descriptive (non-pivotal) study, the results indicated that sonographers obtained diagnostic quality images in a high proportion of clips from both study and control exams, demonstrating comparable image quality in clips acquired using Caption Guidance compared to unassisted acquisition. Importantly, the high specificity of the auto-capture feature (97.85% of auto-captured clips were diagnostic) demonstrated that a registered sonographer can rely on the auto-capture feature when using Caption Guidance.

Pivotal (Nurse) Study
Caption Guidance is designed for as an assistive tool for trained sonographers as well as medical professionals without specialized echocardiography training. Use by sonographer users was evaluated in the specialist study described above. A prospective pivotal clinical study was subsequently conducted to evaluate use by medical professionals without specialized echocardiography training.

Study Design
A minimum of eight (8) RNs were trained and evaluated on their performance to acquire a 10-view 2D-TTE protocol. Participants were scanned by the RN (study exam) and 10 standard views were obtained using a Terason ultrasound system with Caption Guidance: PLAX, PSAX-AV, PSAX-MV, PSAX-PM, AP4, AP5, AP2, AP3, SubC4, and SC-IVC. In the event that an RN exited the study prior to completing their planned 30 scans, an additional nurse was trained to participate in the study. The study continued enrollment until eight RNs had completed scans of 30 patients each. For the sake of comparison, participants were also scanned by a trained sonographer without Caption Guidance and the same 10 views were obtained (control exam) using the same Terason ultrasound system.

Following the study and control exams, a panel of five (5) expert cardiologist readers independently provided assessments of whether the patient study, in its totality, provided sufficient information to assess ten clinical parameters. In addition, a panel of five (5) expert cardiologists also independently provided assessments of diagnostic image quality per clip using the ACEP scale. In addition, each of the cardiologist readers were asked to provide a repeat assessment on a certain percentage of the exams or clips they reviewed in order to assess intra-grader variability. To reduce possible sources of bias in the design, the RNs, sonographers, and cardiologists were all blinded to results determined by others.

Four (4) prospectively defined primary endpoints were evaluated for the study, all of which assessed whether the patient study exam conducted by the RN, taken as a whole, was of sufficient image quality to make these clinical assessments. Specifically, the endpoints assessed whether, in the judgment of expert cardiologists, the studies permitted

qualitative visual assessment of left ventricular (LV) size, LV function, right ventricular (RV) size, and non-trivial pericardial effusion.

Results

The four primary endpoints were satisfied and demonstrated the clinical utility of Caption Guidance for users without specialized echocardiography training. Specifically, the eight (8) RNs acquired echocardiographic exams of sufficient image quality to make clinical assessments in the following proportion of study exams conducted:

#	Clinical Parameter	% of Scans of Sufficient Quality (MRMC CI)
1	Qualitative Visual Assessment of Left Ventricular Size	98.8% (96.7%, 100%)
2	Qualitative Visual Assessment of Global Left Ventricular Function	98.8% (96.7%, 100%)
3	Qualitative Visual Assessment of Right Ventricular Size	92.5% (88.1%, 96.9%)
4	Qualitative Visual Assessment of Non-Trivial Pericardial Effusion	98.8% (96.7%, 100%)

The results of the primary analyses met the predetermined criteria for study success.

Additional secondary endpoints were evaluated. The secondary endpoints provide descriptive clinical assessments, as no hypothesis testing was performed for the assessment of these endpoints.

Specifically, the eight (8) RNs acquired echocardiographic exams of sufficient image quality to make clinical assessments in the following proportion of study exams conducted:

#	Clinical Parameter	% of Scans of Sufficient Quality (MRMC 95% CI)
1	Qualitative visual assessment of inferior vena cava size	57.5% (41.5%, 73.5%)
2	Qualitative visual assessment of right ventricular function	91.3% (85.7%, 96.8%)
3	Qualitative visual assessment of left atrial size	94.6% (90.7%, 98.5%)
4	Qualitative visual assessment of aortic valve	91.7% (88.0%, 95.3%)
5	Qualitative visual assessment of mitral valve	96.3% (93.9%, 98.6%)
6	Qualitative visual assessment of tricuspid valve	83.3% (77.0%, 89.7%)

In addition to assessing if image quality was sufficient to make assessments, cardiologists also made specific qualitative visual assessments based on the study and control exams (e.g., presence or absence of non-trivial pericardial effusion). The proportion of scans in which the diagnostic decision was the same between study and control exams was very high, further demonstrating the usability of Caption Guidance. For primary clinical parameters, the range of agreement in qualitative visual assessment was 92.5% to 99.6%. Similarly, for secondary clinical parameters, the range was 83.2% to 95.2%.

Furthermore, it was evaluated whether the RN users were able to obtain a high proportion of clips that were considered of diagnostic quality. Specifically, the eight (8) RNs acquired echocardiographic clips of diagnostic image quality for each of the standard views in the following proportion of study exams conducted:

#	View	% of Clips of Diagnostic Quality [MRMC CI]
1	PLAX	92.1% (87.9%, 96.3%)
2	PSAX-AV	66.3% (59.0%, 73.5%)
3	PSAX-MV	75.8% (70.7%, 80.9%)
4	PSAX-PM	92.9% (89.1%, 96.7%)
5	AP4	88.8% (81.5%, 96.0%)
6	AP5	78.8% (66.9%, 90.6%)
7	AP3	80.0% (70.4%, 89.7%)
8	AP2	71.3% (61.6%, 80.9%)
9	SubC4	76.3% (70.2%, 82.3%)
10	SC-IVC	59.2% (43.1%, 75.2%)

The Auto-Capture feature was utilized in 46.2% of the clips acquired by the RNs. In addition, 93.8% of clips acquired via the Auto-Capture feature were rated diagnostic by the panel of cardiologists, indicating high effectiveness of the feature.

The study also demonstrated the safety profile of Caption Guidance. One adverse event was reported (pain at skin site due to elevated temperature of the transducer), but determined to be unrelated to the guidance software.

Objective Quantitative Metrics

Two analyses were performed on the Pivotal Study data in order to assess the performance of Caption Guidance using objective quantitative metrics:

- **AutoEF:** The exams acquired in the pivotal study were processed by the 510(k) cleared Bay Labs AutoEF software (K173780). AutoEF provides an automated estimation of left ventricular ejection fraction, and requires an AP4 and AP2 clip of sufficient quality (automatically selected by AutoEF) in order to return an estimate. AutoEF returned an EF estimate in 65.5% of study exams and 85.1% of control exams. The panel of cardiologists rated 70.4% of study exams as having a diagnostic quality AP2 and AP4 clips, indicating close agreement between the panel and the AutoEF in assessing echocardiographic image quality. Mean absolute deviation between AutoEF estimates from nurse- and sonographer-acquired exams was 3.96 EF%, which is well within the inter-physician variability for calculation of EF observed in the literature. The results indicate that when EF is computed, AutoEF performs similarly on nurse- and sonographer-acquired exams.

- **PLAX Sonographer Measurements**: Three (3) registered cardiac diagnostic sonographers independently provided measurements for each of the PLAX clips acquired in the pivotal study: septal wall thickness (diastole), posterior wall thickness (diastole), left ventricular internal diameter (diastole), left ventricular internal diameter (systole), and aortic root. The sonographers were blinded from the measurements of the other registered cardiac diagnostic sonographers. The purpose of the test was to assess the measurability of the study exam clips and to compare the similarity of linear measurements of the study and control exam clips. Measurability of study exam clips (defined as a majority of the three (3) sonographers assessing a clip to be suitable for measurement) ranged from 89.17% (aortic root) to 92.08% (the remaining four measurements). In analyzing the correspondence of actual measurements, the results demonstrated that variability (RMSD) between study and control clip measurements was comparable to the observed inter-sonographer measurement variability. The results demonstrate that PLAX clips acquired by nurses were highly suitable for linear measurements in clinical use.

In sum, the pivotal (nurse) clinical study validated clinical use of the Caption Guidance software by users with no prior scanning experience to acquire limited (10-view) two-dimensional, point-of-care echocardiograms. The study demonstrated that Caption Guidance confers a clinically meaningful benefit and is safe for use as intended.

Human Factors Validation Testing Study
A Human Factors Validation Study was performed to demonstrate the usability of the device. The Caption Guidance user interface and training materials were developed through a series of preliminary human factors analyses. The device and training were then implemented and tested during the Human Factors Validation Study, which was conducted in a clinical setting at Northwestern Memorial Hospital.

The study enrolled five (5) user groups:
- Physicians (Hospitalists)
- Nurse Practitioners and Physician Assistants
- Registered Nurses (RNs)
- Medical Residents
- Certified Medical Assistants

Non-RN users had a one-day training session consisting of 1.5 hours of didactic/hands-on practice prior to the human factors evaluation. In contrast, the RNs had two days of training consisting of 5-6 hours of didactic/hands-on practice prior to the human factors evaluation, which took place on Day 3 for the RN users. There were differences in training and evaluation between the RNs and the other user types, because the RNs were participating in the Pivotal Study, and were required to follow the corresponding training as described in the study protocol. Following training, the users were asked to begin a new study and complete all 10 views independently on a model. Auto-capture rates were documented, and critical tasks understanding were assessed on Pass/Fail ("pass" was defined as being able to auto-capture at least one view). The users had access to all training materials and product labeling, including the Operator's Manual, during the training and independent scanning.

The human factors usability validation testing demonstrated 100% of critical tasks passed across all user types. No use errors were found that could cause harm for the scanner or patient. In addition, non-critical tasks that are essential for skills assessment and scanning ability were tested and evaluated, including the Auto-Capture rate across 10 views. An average of 76% of views were auto-captured per user across all 5 user groups. The results did not indicate significant differences in performance amongst user types. Given the same level of training, medical professionals across the backgrounds that were tested from certified medical assistants to hospitalists performed consistently during independent scans with Caption Guidance on a patient model.

Pediatric Extrapolation
In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

PREDETERMINED CHANGE CONTROL PLAN

The Caption Guidance device is powered by deep learning image analysis algorithms that assist medical professionals in the acquisition of echocardiograms. Caption Health will make future algorithm improvements under a Predetermined Change Control Plan (PCCP). In the plan, a protocol was provided to mitigate the risk of algorithm changes leading to changes in the device's technical specifications or negatively affecting clinical functionality or performance specifications directly associated with the intended use of the device.

The test methods for the proposed changes consist of non-clinical, and limited, feasibility-level clinical testing of the algorithm for its basic functionalities of predicting the PG for maneuvering the probe to an ideal pose. Assessment metrics, acceptance criteria, and statistical methods have been described for the performance testing of the proposed changes.

TRAINING

Caption Guidance provided the following training to the users in the pivotal study.

The training program includes:

1. A didactic and hands-on guided training, provided by a Caption Health representative. This component included both classroom instruction, and guided hands-on scanning while the representative provided verbal instructions.

2. An independent hands-on practice, where the Caption Health representative did not provide verbal instructions. Feedback on areas of improvement was provided by the company representative between the exams of the volunteers.

The training materials, developed for the users of the device, include a slide presentation, and a training handbook to provide an introduction to technical foundations of basic ultrasound principles, a discussion on ergonomics of scanning, basic techniques of probe positioning, cardiac anatomy, scanning protocols, and the actual ultrasound scanning of the heart.

At the end of the training, the trainees undergo a user readiness evaluation to determine if they had the appropriate skills for scanning, and if the acquired images were of sufficient diagnostic quality.

LABELING

The labeling supports the decision, including information on all required and/or compatible parts, to grant the De Novo request for this device. The labeling includes a detailed description of the device, description of the patient population for which the device is indicated for use, a description of the intended user population and the recommended user training, and instructions for use.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a Radiological acquisition and/or optimization guidance system and the measures necessary to mitigate these risks.

Identified Risks to Health	Mitigation Measures

Device Error – Failure to provide guidance on acquiring diagnostic-quality images or signals, leading to delay, prolonged examination, or additional unnecessary procedures, due to: • Algorithm failure • Hardware or software failure	• Design verification and validation • Labeling
User Error – Operator failure to follow the guidance provided by the device to acquire diagnostic-quality images or signals, leading to delay, prolonged examination, or additional unnecessary procedures, due to human error	• Design verification and validation • Labeling

BENEFIT/RISK DETERMINATION

Benefit/Risk Summary	
Summary of Benefits	• Echocardiography is a highly valuable method for assessment of various structural and functional characteristics of the heart. Additionally, with the development of point-of-care ultrasound imaging, echocardiography at the bedside could provide a valuable first line of cardiac assessment in settings outside of a traditional cardiology department, or hospitals. Caption Guidance is a tool to fulfill this important clinical need. • Echocardiography is highly operator-dependent, and the training for echocardiography takes a significant amount of time, leading to a shortage of skilled cardiac sonographers. Caption Guidance provides a tool to enable non-cardiac sonographers to acquire standard echocardiography images that can be later reviewed by an expert cardiac healthcare professional. The pivotal study for non-users of cardiac ultrasound was significant and clinically meaningful. • Echocardiography is a highly operator-dependent imaging modality, and there is variation of echocardiograms' quality. Caption Guidance is a tool to address the variability of echocardiograms' quality by providing a quantitative image quality metric.
Summary of Risks	Low-quality images from software/algorithm error, hardware error, or user error, leading to additional unnecessary examinations, and/or delay of diagnosis.

Summary of Other Factors	As a Breakthrough-designated device, no other devices address the medical need being met by Caption Guidance.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

Benefit/Risk Conclusion

In conclusion, given the available information above, the data support that for the intended use and indications for use statements above, the probable benefits outweigh the probable risks for the Caption Guidance device. The benefits outweigh the risks given the mitigations employed, including the special controls in combination with the general controls, as the subject device provides a tool to acquire echocardiography images and video clips, with a quantified image quality metric, to allow for acquisition of such images in settings not possible currently. The patients would have faster access, along with less inconvenience, to echocardiography, with a relatively-standardized image quality.

CONCLUSION

The De Novo request for the Caption Guidance device is granted and the device is classified under the following and subject to the special controls identified in the letter granting the De Novo request:

    Product Code: QJU
    Device Type: Radiological acquisition and/or optimization guidance system
    Class: II
    Regulation: 21 CFR 892.2100