Diacardio, Ltd.   July 28, 2016
℅ Mr. George Hattub
Senior Staff Consultant
MedicSense, USA
291 Hillside Avenue
SOMERSET MA 02726

Re: K161382
    Trade/Device Name: LVivo Software Application
    Regulation Number: 21 CFR 892.2050
    Regulation Name: Picture archiving and communications system
    Regulatory Class: II
    Product Code: LLZ
    Dated: May 14, 2016
    Received: May 18, 2016

Dear Mr. Hattub:

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. 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); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

For

Robert Ochs, Ph.D.
Director
Division of Radiological Health
Office of In Vitro Diagnostics
  and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number *(if known)*

K161382

Device Name

LVivo Software Application

Indications for Use *(Describe)*

DiaCardio's *LVivo* Software Application is intended for non-invasive processing of already acquired echocardiographic images in order to detect, measure, and calculate the left ventricular wall for left ventricular function evaluation. This measurement can be used to assist the clinician in a cardiac evaluation.

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.

510(k) Summary

Pursuant to CFR 807.92, the following 510(k) Summary is provided:

1. (a) **Submitter Address:**
George J. Hattub
MedicSense, USA
291 Hillside Avenue
Somerset, MA 02726
www.medicsense.com

1. (b) *Manufacturer Address:*
DiACardio, Ltd.
HaEnergia Street 77
Be'er Street, Israel

Mfg. Phone:
Tel.: +972 77 7648318

Contact Person:
Mrs. Michal Yaacobi

Date:
July 21, 2016

2. *Device & Classification Name:*
Picture Archiving Device- classified as Class 2 LLZ, Regulation Number 21 CFR 892.2050
LVivo Software Application

3. *Predicate Devices:*
K072090- Siemens Medical Solution SYNGO Auto Left Heart and VVL Clinical Feature
K091286- Siemens Medical Solution SYNGO US Workplace
K130779- DiaCardio's *LVivoEF* Software Application

4. *Description:*
The LVivo System analyzes echocardiographic patient examination DICOM movies for Global ejection fraction (EF) evaluation. EF is evaluated using two orthogonal planes, four-chamber (4CH) and two-chamber (2CH) views, to provide fully automated analyses of LV function from the echo examination movies. It also has the ability to measure strain

5. *Intended Use:*
DiaCardio's *LVivo* Software Application is intended for non-invasive processing of already acquired echocardiographic images in order to detect, measure, and calculate the left ventricular wall for left ventricular function evaluation. This measurement can be used to assist the clinician in a cardiac evaluation.

6. *Comparison of Technological Characteristics:*
With respect to technology and intended use, DiaCardio's *LVivo* Software Application is substantially equivalent to its predicate devices. Based upon the outcomes from clinical trials, DiaCardio believes that their device does not raise additional safety of efficacy concerns. At the end of this summary, a comparison table is provided.

7.   *Clinical Tests:*   In this study, the performance of LVivoSG was compared with conventional methods used for SG function evaluation in echocardiography, including manual evaluation by sonographers and visual estimation by physicians. In the blinded clinical trial, ultrasound clips of 100 subjects were evaluated with the LVivo System. Average values were calculated for each variable measured by Manual Biplane Method (MBP) and Pearson correlation coefficients were calculated between MBP and LVivoEF results. The primary end point defined for this study was met with a correlation coefficient calculated for biplane EF (r=0.88, p<0001).

	Devices		
	Submitted Device	**Predicate Device**	**Predicate Device**
Features/Characteristics	**LVivo (Diacardio)**	**LVivoEF (Diacardio)**	**Syngo (Siemens)**
Product Code	LLZ	LLZ	LLZ (K091286) IYN(K072090)
Intended Use	Calculate of Ejection Fraction and measure strain	Calculate of Ejection Fraction	Calculate Ejection Fraction and measure strain
Automation	Fully Automated	Fully Automated	Fully Automated
Bi plane EF evaluation	YES	YES	YES
Simultaneous 2CH and 4CH evaluation	YES	YES	NO
Off line EF evaluation using DICOM clips of any vendor	YES	YES	YES
Automated ED and ES frames selection	YES	YES	YES
Dynamic left ventricular assessment	YES. Frame by frame tracking	YES. Frame by frame tracking	YES. Frame by frame tracking

Manual editing by user capability	YES. 7 border points manipulation (dragging) and online contour presentation. Possible to apply to any frame in the clip. Border detection is recalculation is applied to the entire clip.	YES. 7 border points manipulation (dragging) and online contour presentation. Possible to apply to any frame in the clip. Border detection is recalculation is applied to the entire clip.	YES. Click and drag of the contour. Applied to present ED/ES frame. Enable also Manual user input.
Visually confirm EF	YES	YES	YES
Automated rejection of	YES	YES	NO
Volume calculation by	YES	YES	YES
Volume curve	YES	YES	YES
EF results presentation	Displaying full clip	Displaying full clip	Displaying image
Enables presentation EF	YES	YES	YES
Algorithm	Image segmentation	Image segmentation	Adjustment of learned
Calculation speed	Less than 1s per	Less than 1s per cycle	~ 15s for each view
Capability or a part of a	YES	NO	YES
Global Longitudinal	YES	NO	YES
Segmental Longitudinal	YES	NO	YES
Segmental wall motion	YES	NO	Calculation motion
Operating System	Windows	Windows	Unknown
510(k) #	Pending	K130779	K072090 & K091286

Clinical Summary - LVivoSG

Technology and predicate device
The segmental evaluation by LVivoSG is based on the LVivo decision support platform for fully automated edge detection and tracking of the LV borders. The LVivoSG calculates segmental wall motion scores using a classification system based on wall motion parameters. The wall motion scores by LVivoSG were compared to wall motion scores by visual estimation. The segmental endocardial longitudinal strain is calculated in a way that resembles the VVI technology (Siemens) in which the LV borders are traced in a semi-automated way by initial user input. The strain calculated by LVivoSG was compared to the strain calculated by VVI.

Protocol:
In this study, segmental wall motion evaluation and segmental strain evaluation by LVivoSG system calculated from 3 apical views (4CH, 2CH and 3CH), were compared with Visual Estimation (done by physicians) and with the semi-automated Velocity Vector Imaging (VVI, Siemens) technology (Applied by a physician).

1. Study: Retrospective, single center study.

2. Ultrasound examinations that were collected prospectively according to protocol 100 rev 03 (clinical-protocol-1.4.doc) were used in the LVivoSG clinical trial. These examinations were

routinely evaluated for segmental wall motion evaluation qualitatively by visual estimation by the physicians of the echo department in Soroka university medical center.

3. The WM evaluation by the physician was collected retrospectively using patient number and name initials assigned according to protocol 100 rev 03.

4. Examinations with impaired global LV function that did not have segmental WM scores from routine evaluation will be evaluated by the PI.

5. Additional investigator (expert echocardiologist) performed segmental strain evaluation by longitudinal strain using Syngo® Velocity Vector Imaging (VVI) SW
(Siemens) blindly.

6. Segmental WM evaluation by LVivoSG was compared to the Segmental WM evaluation by the visual estimation

7. Segmental longitudinal strain evaluation by LVivoSG was compared to segmental longitudinal strain evaluation by VVI.

Study Objectives
a. Compare the strain results by LVivoSG to strain evaluated with VVI.
b. Compare the automated wall motion results by LVivoSG to wall motion evaluation
by visual estimation.
c. Compare the global strain calculated by LVivoEF to the global strain calculated by
LVivoSG.

Since the global longitudinal strain (GLS) is an important parameters of LV function adopted by the Guidelines* **the primary end point** was to show that there is a good agreement between GLS calculated by both methods with correlation coefficient of r=0.8. Additional goals were to compare wall motion scores by LVivoSG to the wall motion scores by visual estimation and.
Results and Conclusions

Global
The results showed that the primary end point was successfully met with a very good correlation between LVivoSG and VVI for GLS (**r=0.85**, p<0.0001). Excellent inter-observer reliability between methods for GLS, was also demonstrated by intraclass correlation (**ICC=0.92**). The agreement between LVivoSG and VVI demonstrated by kappa coefficient was calculated from categorical data where the
GLS was divided into two categories Normal/Abnormal. The cutoff value for LVivoSG was -12% and for VVI -15%. The agreement by kappa coefficient was also very good (**kappa=0.77**) and specificity and sensitivity were high (0.86 and 0.95 respectively) emphasizing the similarity between methods.
Average difference of -3% between VVI and LVivoSG was found. This average difference affects the Normal/Abnormal cutoff value. It is known that different vendors use slightly different methods to evaluate strain, and therefore have different cutoff values for LV function. Even in different labs using the same methods, different cutoff values can be determined.

WM score index was calculated as average of segmental wall motion scores and compared between LVivoSG and Visual estimation. The agreement calculated by ICC was very good (**ICC=0.86**). Specificity and Sensitivity were calculated by divided the results into two categories Normal/Abnormal. The cutoff value =0.51 for LVivoSG was determined by ROC analysis where the threshold for the visual estimation was zero. The accuracy indicated by **AUC=0.86** was very good and the specificity and sensitivity were 0.8 and 0.78 respectively. These results show very good agreement comparing WM score index calculated by LVivoSG to WM score index calculated by visual estimation where WM score index<=0.51 by LVivoSG indicates Normal LV function.

Territories

Good agreement was demonstrated comparing territories of coronary arteries between strain by LVivoSG and strain by VVI with ICC =0.86, 0.84 and 0.9 for LAD, RCA and CX respectively. The best agreement was for CX with kappa=0.71 and specificity and sensitivity 0.8 and 0.94 respectively.

Good results were also demonstrated comparing average of wall motion scores by LVivoSG to wall motion scores by Visual Estimation over territories of coronary arteries. The **ICC** comparing LAD, RCA and CX was **0.8, 0.82 and 0.83** respectively. Normal/Abnormal cutoff values for the results of the LVivoSG were calculated by ROC analysis for each territory. The accuracy by **AUC** for LAD, RCA and CX was **0.86, 0.82 and 0.81** respectively. The highest agreement was obtained for LAD territory using cutoff value=0.34 (kappa=0.65). The level of agreement was 0.83 and specificity and sensitivity were 0.86 and 0.81 respectively. The lowest agreement was obtained for the CX territory using cutoff value=0.51 (kappa=0.51). The level of agreement was 0.76 and specificity and sensitivity were 0.75 and 0.76 respectively. The cutoff value for WM scores by visual estimation was zero.

It is interesting to note that findings from studies in the literature showed that the inter-observer reliability for visual estimation (physicians) was highest for segments in the left anterior descending artery territory (ICC, 0.73) and lowest in the circumflex territory (ICC, 0.61). In our study the WM scores by LVivoSG were compared to WM scores by visual estimation of different physicians from the echo department and the highest agreement was for the LAD territory and lowest for the CX as well, indicating that, the results of the current study reflect the "real life" agreement between physicians.

Individual segments

In the current study, good inter-observer reliability between LVivoSG and VVI was for apical and mid segments where the best was for Mid-lateral (**ICC=0.83**) and Midanterior (**ICC=0.79**) and the lowest for the basal segments. It was reported in the literature that the highest intra-observer correlation (R > 0.8) was for mid segments of all walls, while low correlation (R<=0.65) was basal lateral, basal anterior and apical anterior segments, implying that mid segment are easier to evaluate than basal segments. The results of the current study show that the agreement between LVivoSG and VVI is higher in segments for which the diagnosis is more conclusive for physicians in "real life".

Wall motion scores were compared between individual segments and the separation error between normal and akinetic segments was calculated. For most segments, the separation error was <=15%. For the segments Apical Septal, Mid Lateral, Basal Lateral, Mid Anterior, Basal Anterior and Mid Inferolateral the Normal/Akinetic **separation error was <=5%**.

GLS vs WM score index

To show the connection between strain evaluation by LVivoSG and segmental wall motion evaluation, comparison between WM score index by LVivoSG and GLS by LVivoSG was made. Very high correlation (**r=0.87**) was obtain between methods, showing that both GLS and WM score index calculated by LVivoSG are comparable.

GLS from LVivoSG vs GLS from LVivoEF

Finally, due to the addition of GLS to the LVivoEF module, GLS by LVivoEF, calculated as average of the strain of the walls from two views was compared to GLS by LVivoSG calculated as average of segmental strain. The results showed very high correlation between methods (r=0.92). This result indicates that users of the LVivoEF module can benefit from the addition of the GLS calculation and obtain important information about the global state of the left ventricle.

The present study has demonstrated that the LVivoSG system provides accurate measurements of segmental LV function. The performance of LVivoSG demonstrated high agreement between

strain results in compare to the strain calculated by VVI and segmental wall motion evaluation in compare to segmental scores by visual estimation. Therefore, the LVivoSG system can be used as a decision support tool for segmental wall motion evaluation and segmental strain.

* Lang RM, Badano LP et al. Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults:An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. JASE 2015;28:1–39.