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,

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

Enclosure
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)

- [x] Prescription Use (Part 21 CFR 801 Subpart D)
- [ ] Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

*DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.*

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

- Department of Health and Human Services
- Food and Drug Administration
- Office of Chief Information Officer
- Paperwork Reduction Act (PRA) Staff

PRASTAFF@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."
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 \( r=0.88, p<0.001 \).

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