DiA Imaging Analysis Ltd
℅ Mr. George J. Hattub
Senior Staff Consultant
Medicsense USA
291 Hillside Avenue
SOMERSET MA 02726

June 23, 2020

Re: K200232
Trade/Device Name: LVivo Software Application
Regulation Number: 21 CFR 892.2050
Regulation Name: Picture archiving and communications system
Regulatory Class: Class II
Product Code: QIH
Dated: May 13, 2020
Received: May 18, 2020

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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) 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 Act); 21 CFR 1000-1050.

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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

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

Sincerely,

For

Thalia T. Mills, Ph.D.
Director
Division of Radiological Health
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K200232

Device Name
LVivo Software Application

Indications for Use *(Describe)*
LVivo platform is intended for non-invasive processing of ultrasound images to detect, measure, and calculate relevant medical parameters of structures and function of patients with suspected disease.

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.

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K200232 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:***	DiA Imaging Analysis Ltd HaEnergia Street 77 Beer-Sheva, Israel 8470912
	Mfg. Phone:	Tel.: +972 77 7648318
	Contact Person:	Mrs. Michal Yaacobi
	Date:	June 21, 2020
2.	***Device & Classification Name:***	Automated Radiological Image Processing Software- classified as Class 2 QIH, Regulation Number 21 CFR 892.2050 *LVivo* Software Application
3.	***Predicate Device:***	K132544 TomTec-Arena for RV Evaluation
	Reference Devices:	K161382 & K130779- DiaCardio's *LVivo* Software Application K180995 GE Viscan for Bladder and Android
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 and to evaluate the Right Ventricle and well as to measure the bladder.
5.	***Intended Use:***	DiA's LVivo platform is intended for non-invasive processing of ultrasound images to detect, measure, and calculate relevant medical parameters of structures and function of patients with suspected disease
6.	***Comparison of Technological Characteristics:***	With respect to technology and intended use, DiA's *LVivo* Software Application is substantially equivalent to its predicate devices. Based upon the outcomes from clinical trials, DiA 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:***	A summary of the clinical evaluation is provided on the proceeding pages.

	Submitted Device	Predicate Device
Features/Characteristics	**LVivo**	**TomTec-Arena 1.0 K132544**
Product Code	QIH	LLZ
Intended Use	Calculate and measurement of LV, RV and Bladder	Calculation and measurement LV, RV, fetal and abdomen
Indication for Use	DiA's LVivo platform is intended for non-invasive processing of ultrasound images to detect, measure, and calculate relevant medical parameters of structures and function of patients with suspected disease.	Indication for use of Tom-Tec- Arena software are diagnostic review, quantification and reporting of cardiovascular, fetal, and abdominal structures and functions of patients with suspected disease.
Automation	yes	yes
Manual Adjustment	yes	yes
RV Calculation from	2d	3d
RV ED Volume	no	yes
FAC	yes	yes
ED Area	yes	no
EDVi	no	yes
ES Vol	no	yes
Es area	yes	no
EF	no	yes
SV	no	yes
TAPSE	yes	yes
Strain values free wall	yes	yes
Strain values septum	no	yes
S prime	yes	no
View	4ch view	Multi 2d view
510(k) #	K200232	K132544

	Submitted Device	Reference Devices
Features/Characteristics	**LVivo**	**LVivo K130779 & K161382**
Product Code	QIH	LLZ
Indications For Use	DiA's LVivo platform is intended for non-invasive processing of ultrasound images to detect, measure, and calculate relevant medical parameters of structures and function of patients with suspected disease.	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.
Modules	LVivo EF, LVivo SG, LVivo SAX, LVivo RV & LVivo Bladder	LVivo EF, LVivo SG, LVivo SAX
Automation	Same	Fully Automated
Bi plane EF evaluation	Yes	Yes
Simultaneous 2CH and 4CH evaluation	Yes	Yes
Off line EF evaluation using DICOM clips of any vendor	Yes	Yes
Automated ED and ES frames selection	Yes	Yes
Dynamic left ventricular	Yes. Frame by frame tracking	Yes. Frame by frame tracking
Manual editing by user capability	Minimum of 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.
Visually confirm EF	Yes	Yes
Automated rejection of false results	Yes	Yes

Volume calculation by Simson's method of discs	Yes	Yes
Volume curve Presentation	Yes	Yes
EF results presentation	Displaying full clip with border tracking. And table with results for each cycle for selected ED & ES frames for each beat.	Displaying full clip with border tracking. And table with results for each cycle for selected ED & ES frames for each beat.
Enables presentation EF results for different cycle	Yes	Yes
Algorithm	Image segmentation for border detection For the RV- Deep Learning Technology	Image segmentation for border detection From image processing
Calculation speed	Less than 1s per cycle for biplane evaluation	Less than 1s per cycle for biplane evaluation
Capability or a part of a bigger package (device) for LV function evaluation	Yes	Yes
Segmental Longitudinal Strain Measure	Yes	Yes
Global Longitudinal Strain Measure	Yes	Yes
Segmental wall motion evaluation	Yes	Yes
RV Evaluation	Yes	No

Bladder Measurement	Yes	No
Operating System	Windows/Linux (with Android Mobile Option for LVivo EF)	Windows
510(k) #	K200232	K130779 & K161382

	Submitted Device	**Reference Device**
Features/Characteristics	**LVivo**	**Viscan K180995**
Indication for Use	DiA's LVivo platform is intended for non-invasive processing of ultrasound images to detect, measure, and calculate relevant medical parameters of structures and function of patients with suspected disease.	Vscan Extend is a general-purpose diagnostic ultrasound imaging system for use by qualified and trained healthcare professionals enabling visualization and measurement of anatomical structures and fluid. The specific clinical applications and exam times include Cardiac, Abdominal and Urology]
Automation	yes	yes
Calculate From Border	yes	yes
Display Calipers	yes	yes
Allow User to Adjust Calibration	yes	yes
Present Volume	yes	yes
Present Diameter	yes	yes
Image processing algorithm	yes	yes
Frame	Trans and Long View	Trans and Long View
Operating System	Windows, Android Option (With LVivo EF)	Android
510(k) #	K200232	K180995

Clinical Summary -

LVivoRV

Technology

The LVivo RV, a part of the LVivo platform, is a decision support system that uses 2D echocardiographic examinations to automatically evaluate the Right Ventricular (RV) function from 4 chamber apical views (focused or modified). The LVivoRV utilizes clips in DICOM format from the apical 4CH view, focused or modified, as an input without any additional user input (such as selection of a starting frame or manual starting points as required by Epsilon). The Algorithm combines image processing and Deep Learning Neural Network (NN) for the RV analysis. The endocardial boundaries and the location of the anulus of the tricuspid valve are identified by the NN model. These boundaries are further enhanced and tracked using image processing methods that are already established in other approved modules of the LVivo Platform. The algorithm provides measurements of RV size and function: ESA, EDA, FAC, TAPSE S' and Free Wall Strain. There are 3D technologies available for RV evaluation, the most known is Image-Arena Platform by TomTec

Protocol:
In this presented clinical validation, the LVivoRV output for RV function was compared with conventional methods that are used in echocardiography for RV function evaluation (2D manual measurements by technicians and when relevant to M-Mode, doppler and VVI).

Study: Retrospective, single center study.

1. All examinations were retrospectively retrieved from the PACS systems available on site. Examinations of patients referred to the echo unit who have had a standard echo examination were collected over a period of 22 months retrospectively according to the inclusion / exclusion criteria
2. All examinations were performed as part of the routine and according to the ASE guidelines, using available ultrasound systems (EPIQ, Affinity, IE33, & Philips)

3. Only RV Clips from 4CH and 4CH modified views that have 2-3 stable recorded beats were included. Also, the dataset included only examinations in which measurements of TAPSE and S' were reported

4. The selected RV clips, were anonymized and saved separately without the patient's details according to the patient number

5. conventional methods were used to evaluate RV function:
    - EDA and ESA were measured by 2 sonographers by selection and manually tracing the ED and ES frames, and FAC results were calculated from the EDA and the ESA.
    - TAPSE was measured by a sonographer using M-Mode and by an echo cardiologist using VVI.
    - S' was measured by a sonographer using M-Mode and by an echo cardiologist using VVI.
    - RV Strain was measured by echo cardiologist using VVI

6. LVivoRV evaluation was done by an automated batch processing after all data was ready and considered locked

7. Manual measurements were compared to automated measurements according to statistical plan

Study Objectives

- Primary endpoint was to compare LVivoRV measurement of FAC to manual FAC measurement
- Secondary endpoints were:
  - to compare LVivoRV measurements to the manual measurements of EDA, ESA, TAPSE, S' and FREE WALL STRAIN
  - To compare RV function by visual assessment to the categorized result from FAC, TAPSE, S' and STRAIN and
  - To evaluate inter and intra observer variability.

Acceptance of the statistical data was 75% correlation between FAC by LVivoRV and the same measurements performed manually by sonographers. This value is based on statistical data reported by FDA cleared system for semi-automated RV function evaluation (EchoInsight by Epsilon)

Results and Conclusions

The results showed that the primary end point was successfully met with a very good correlation of FAC between LVivoRV and manual measurements ($r=0.79$, $p<0.0001$). RV Global function is evaluated by measuring EDA and ESA and calculating FAC accordingly. The values obtained automatically by the LVivoRV were compared to the average of the values obtained manually by the 2 sonographers.

The correlations between the sonographer's average for EDA and ESA and the LVivoRV EDA and ESA were excellent with $r=0.92$ and $r=0.93$ respectively ($p<0.0001$).
For the TAPSE, we saw that the correlation of the LVivoRV to the manual measurement using M-Mode was 0.62, similarly to the correlation found between VVI and M-Mode that was $r=0.66$. With these correlations, the LVivoRV performance is close to "real life" performance of VVI in compare to M-mode. When looking at the TAPSE correlation without 5 outlier cases, we got $r=0.72$.
The Free Wall Strain correlation between 2D VVI and LVivoRV was evaluated and found to be a positive correlation of $R=0.6$. When omitting 6 outlier cases from the correlation analysis, we obtained $r= 0.78$.
The inter-observer reliability between readers within the same group was also tested. Inter-observer reliability between sonographers for EDA, ESA and FAC was 0.85, 0.9 and 0.77 respectively ($p<0.0001$).

10 subjects were randomly chosen for the evaluation of the intra-observer reliability. The intra-observer reliability was evaluated for the 2 sonographers that reported measurable values using 2D and one physician that reported measurable values with VVI. The intra-observer correlation for FAC for sonographer1 was 0.95 [95%CI: 0.80-0.98] and for sonographer 2 it was 0.94 [95%CI: 0.72-0.98]. The intra-observer correlation for TAPSE for the physician used the VVI was 0.85 [95%CI: 0.40-0.96]

It is known that the conventional RV assessment is not perfect and has its own inter-measurement variabilityF, thus we don't expect a perfect agreement between the LVivoRV and currently used techniques. However, the differences between RV parameters obtained using the LVivoRV software and the conventional measurements were similar to the variability of the current conventional methods.

Overall, the correlation of the LVivoRV to acceptable used methods for RV evaluation was very good. The LVivoRV can use as a decision support system.

LVivoBladder

Technology

The LVivo Bladder, a part of the LVivo platform, is a decision support system for automated Bladder Volume evaluation from ultrasound examinations.
The LVivo Bladder utilizes images in DICOM format. It automatically Identifies the bladder borders on the ultrasound scan and locates the calipers for measuring the bladder's 3 dimensions on the longitudinal and sagittal views, with a corresponding value for the 3 dimensions and for the bladder volume. The calipers can be changed by the sonographer to make adjustments if required.
This application automatically measures bladder volume by segmenting bladder contours from sagittal and transverse ultrasound views using a combination of machine learning and active contour

Protocol:

In this clinical validation study the automated bladder volume measurements obtained by DiA's automated tool were compared to manual measurements obtained by an expert.

Study: Retrospective, single center study.

1. 226 bladder images (113 pairs) were included
2. All examinations were retrospectively retrieved from the PACS systems available in Terem's clinic. Since the data is retrospectively collected, all examinations are acquired as part of routine abdominal examinations, by qualified sonographers using available ultrasound systems (Siemens, Mindray). Collected data will be in DICOM format.
3. Since Abdominal tests do not necessarily include bladder volume measurements, the first step of data collection was filtering of the abdominal tests to include only cases where bladder volume is reported.
4. Assuming ~30% of tests with bladder volume examinations will not include full sets of images (as described in item 2 under 'exclusion criteria), 80 consecutive bladder ultrasound examinations with bladder volume higher than 200ml and 80 consecutive bladder ultrasound examinations with bladder volume less than 200ml were extracted from the database
5. An expert sonographer reviewed extracted cases to include only cases with full sets of images (as described in the inclusion criteria)
6. All images were anonymized by the study coordinator and were sent to the sponsor via Dropbox. Patient details including demographic details were collected anonymously and reported as well in the excel sheet.
7. Since some of the tests included more than one long view image and more than one trans view image and since these images do not represent the images that were used to measure the volume in practice, the pairs of images that were selected for the validation were the ones that were most similar to the ones that appear in the biplane view from which the original reported measurements were obtained. The rest of the pairs were used for verification
8. In tests that included post voiding good quality interpretable images in addition to pre-voiding images, both were used for the validation
9. After obtaining the required data set for the validation test, all pairs (trans and long views) were sent to an expert sonographer for manual measurements of the bladder volume, to acquire the 3 dimensions of the bladder in long and trans views (i.e. D1, D2 and D3). For standardization purposes the dimension measured by the expert in the long view was always marked from top right to bottom left of the image.
10. The LVivo Bladder algorithm was applied by an automated batch processing on all pairs of trans and long views. Here as well the algorithm was configured to draw the dimension in the long view from top right to bottom left of the image, for standardization purposes

11. The calculated volume by the manual measurements was compared to the automated calculated volume by LVivo Bladder.

Study Objectives

The clinical validation objective was to compare LVivo Bladder measurement of bladder volume to bladder volume by manual tracing.
Post Voiding Residual volume of 200mL indicates inadequate emptying and may be associated with catheter insertion. In Point of care settings, it is specifically important to evaluate whether the residual volume is lower or higher than this 200ml threshold, thus the method that was used to compare the automated and the manual methods were based on categorial evaluation of more/less than 200mL.

We expected to have a good agreement between the automated and the manual method (which is an accepted method for BV measurement) based on 200ml threshold, with kappa of at least 0.61 which is considered substantial agreement according to accepted Kappa interoperations.

Results and Conclusions

The results showed that the primary end point was successfully met- excellent agreement between methods was obtained by differentiating between post voiding volume, which is considered to be large (200ml) and is indicative for catheter placement, with excellent Kappa of 0.84, as well as very high agreement (0.93) and high sensitivity and specificity (100 and 80 respectively). Excellent results were also obtained comparing automated bladder volume calculation by LVivo Bladder to volume calculated by manual tracing which is the routinely used method with very high correlation (r=0.94).
The LVivo Bladder can easily, accurately and automatically measure the bladder volume from 2D ultrasound. Such a tool addresses the need in rapid and accurate evaluation in the POC environment. The LVivo Bladder's algorithm was found to be very robust and accurate in automatically measure bladder volume.