January 9, 2021

CLEW Medical Ltd.
℅ Yarmela Pavlovic
Partner
Manatt, Phelps & Phillips, LLP
1 Embarcadero Center, 30th Floor
San Francisco, California 94111

Re: K200717
Trade/Device Name: CLEWICU System (ClewICUServer and ClewICUnitor)
Regulation Number: 21 CFR 870.2210
Regulation Name: Adjunctive Predictive Cardiovascular Indicator
Regulatory Class: Class II
Product Code: QNL
Dated: January 6, 2021
Received: January 8, 2021

Dear Yarmela Pavlovic:

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 LT Stephen Browning
Assistant Director
Division of Cardiac Electrophysiology,
Diagnostics and Monitoring Devices
Office of Cardiovascular Devices
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K200717

Device Name
CLEWICU System

Indications for Use *(Describe)*
CLEWICU provides the clinician with physiological insight into a patient's likelihood of future hemodynamic instability. CLEWICU is intended for use with intensive care unit (ICU) patients 18 years and over.
CLEWICU is considered to provide additional information regarding the patient's predicted future risk for clinical deterioration, as well as identifying patients at low risk for deterioration. The product predictions are for reference only and no therapeutic decisions should be made based solely on the CLEWICU predictions.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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

CLEW Medical's CLEWICU

Submitter

CLEW Medical, Ltd.
5 Hamelacha St.
Poleg, Netanya
Israel 4206002

Phone: +972-9-779-5995
Contact Person: Avigdor Faians

Date Prepared: January 7, 2021

Name of Device: CLEWICU System

Common or Usual Name: CLEWICU

Classification Name: Adjunctive Predictive Cardiovascular Indicator

Regulation Number: 21 CFR 870.2210

Regulatory Class: Class II

Product Code: QNL

Predicate Device

Acumen Hypotension Prediction Index feature by Edwards Lifesciences (DEN160044, K183646, K190205)

Device Description

The CLEWICU System is a stand-alone analytical software product that includes the ClewICUServer and the ClewICUnitor. It uses models derived from machine learning to calculate the likelihood of occurrence of certain clinically significant events for patients in the intensive care unit (ICU). ClewICUServer and ClewICUnitor are software-only devices that are installed on user-provided hardware.

The ClewICUServer is a backend software platform that imports patient data from various sources including Electronic Health Record (EHR) data and medical device data. The data are then used by models operating within the ClewICUServer to compute and store the CLEWHI index (likelihood of hemodynamic instability requiring vasopressor / inotrope support), and CLEWLR (indication that the patient is at "low risk" for deterioration).

The ClewICUnitor is the web-based user interface displaying CLEWHI, and CLEWLR associated notifications and related measures, as well as presenting the overall unit status.

Intended Use / Indications for Use

The CLEWICU's Indications for Use are as follows:

> CLEWICU provides the clinician with physiological insight into a patient's likelihood of future hemodynamic instability. CLEWICU is intended for use with intensive care unit (ICU) patients 18 years and over. CLEWICU is considered to provide additional information regarding the patient's predicted future risk for clinical deterioration, as well as identifying patients at low risk for deterioration. The product predictions are for reference only and no therapeutic decisions should be made based solely on the CLEWICU predictions.

While there are differences in the indications for use statements between CLEWICU and Acumen HPI, these differences are not critical to the intended use. Both devices are generally intended to calculate patient health status indices and predict the likelihood of future cardiovascular clinical events. The differences in the indications statements do not impact the safety or effectiveness, as neither device is intended to be the sole factor upon which a patient's clinical care is based. Instead, the analyses are intended to notify healthcare providers of potential patient deterioration and should be considered in conjunction with other physiological parameters before any treatment is provided.

Summary of Technological Characteristics

Both the subject and predicate devices are software decision support systems that receive patient data, process it, and display calculated insights. At a high level, the subject and predicate devices are based on the following same technological elements:

- Both devices receive near-real-time patient health data;
- Both devices analyze the available data to generate predictions of a patient's risk of experiencing a future clinically significant cardiac event;
- Both devices alert the healthcare provider when a patient's risk has reached a pre-defined threshold.

Although the two products produce slightly different outputs (e.g., risk of hypotensive event versus risk of hemodynamic instability), those differences do not raise different questions of safety or effectiveness, because in both instances, the key point is whether the predictions are accurate and in a timeframe that permits appropriate clinical review and action.

Additionally, though the subject device incorporates additional data inputs relative to the predicate device (i.e., vital signs, nursing assessments, flowsheet data, medications, lab data), this does not raise different questions of safety or effectiveness. The key question in both cases is whether the indices accurately predict the associated future cardiac events.

Performance Data

The CLEWICU was subjected to extensive software verification and validation testing, as well as risk analysis and cybersecurity review.

Human factors testing was conducted to confirm that the user manual provides adequate instructions and that the CLEWICU can be used by the intended users without use errors. Included in the study were 15 intended users, comprised of five nurses and ten physicians. Testing was successfully completed, demonstrating that the product has no expected user errors associated with potential for serious injury to users.

Further, CLEWICU was assessed in a retrospective clinical validation with a dataset from the WakeMed Health System. As an initial matter, a tagging system was developed and validated (against human physician readers as ground truth). Once validated, the tagging system was used to generate the clinical truth labels needed, both for training of the CLEWICU predictive models and for validation of the clinical performance of those models. The WakeMed dataset included patient stays in 7 intensive care units across 2 hospitals between 5 November 2019 and 30 June 2020. Patients were male or female and at least 18 years of age.

Following validation of the tagging system (comparing performance against human physician readers), the predictive models were evaluated by assessing each model's ability to predict the events of interest. The summary of the data from this study is presented below:

For the Hemodynamic Instability (HI) model

	Point Estimate	95% Lower CI	95% Upper CI
Sensitivity	60.6%	56.9%	63.9%
Positive Predictive Value	22.3%	20.7%	24.3%

	Median	25th Percentile	75th Percentile
Lead-time (true positive alerts)	3.0 hours	1.6 hours	4.8 hours

For the Low Risk (LR) model

	Point Estimate	95% Lower CI	95% Upper CI
Specificity	95.7%	94.8%	96.6%
Sensitivity	21.4%	21.2%	21.6%

The performance was determined acceptable considering the software is intended to provide visual-only indicators with a typical time horizon of several hours for an already closely monitored population.

Conclusions

The CLEWICU is as safe and effective as the Acumen HPI. The CLEWICU has the same intended uses and similar indications, technological characteristics, and principles of operation as its predicate device. The minor differences in indications do not alter the intended use of the device and do not raise different questions of safety and effectiveness when used as labeled. In addition, the minor technological differences between the CLEWICU and its predicate device raise no new issues of safety or effectiveness. Performance data demonstrate that the CLEWICU performs as expected and in a manner that is substantially equivalent to the Acumen HPI. Thus, the CLEWICU is substantially equivalent.