FACT SHEET FOR HEALTHCARE PROVIDERS

Emergency Use of the CLEWICU System During the COVID-19 Pandemic

June 15, 2020

Coronavirus Disease 2019 (COVID-19)

This Fact Sheet informs you of the significant known and potential risks and benefits of the emergency use of the CLEWICU System for use by healthcare providers (HCP) in the Intensive Care Unit (ICU) in patients who are 18 years of age or older for the computation of proprietary patient status indices referred to as CLEWRF and CLEWHI as an adjunct to patient monitoring during the Coronavirus Disease 2019 (COVID-19) outbreak. The CLEWRF and the CLEWHI indices provide HCP with predictive screening information to assist with the early identification of patients who are likely to be diagnosed with respiratory failure or hemodynamic instability which are common complications associated with COVID-19.

During ICU hospitalization, continuous monitoring results in the accumulation of vast amounts of data. Without predictive analytics, identification of clinically meaningful trends can be more easily overlooked. Thus, while decisions can be made based on the patient's current state of health, consideration of trends and future potential events may help. The CLEWICU System uses commonly recorded data sets (e.g., vital signs, nursing assessments, flowsheet data, medications and lab data) to analyze trends over time and compute proprietary patient status indexes for use by healthcare providers (HCP).

All patients who are monitored with this device during the COVID-19 pandemic will receive the Fact Sheet for Patients: Emergency Use of the CLEWICU System During the COVID-19 Pandemic

What do I need to know about COVID-19 treatment?
Current information on COVID-19 infection for HCP, including case definitions and information about clinical signs and symptoms and/or epidemiological criteria, is available on CDC website listed at the end of this Fact Sheet.

What is the CLEWICU System?
The CLEWICU System is a stand-alone analytical software product. It uses models derived from machine learning on recorded ICU patient data to calculate the likelihood of occurrence of certain clinically significant events. Notifications regarding individual patients are displayed on the user-interface based on these models. The CLEWICU System includes the ClewICUServer and the ClewICUnitor, which are both software-only devices that are installed on user-provided hardware. The CLEWICU System integrates with existing electronic health record (EHR) systems and medical devices and is designed to be deployed on hospital servers.

The CLEWICU System uses models derived by applying machine learning to recorded multiparameter patient data to calculate the likelihood of occurrence of certain clinically-significant events. It then notifies HCP of patients who, according to the model, are expected to experience respiratory deterioration/failure (need intubation in the next 8 hours) via the CLEWRF index output, and hemodynamic instability (need for initiation of vasopressor or inotrope support in the next 8 hours) via the CLEWHI index output.

The models used by the CLEWICU System to identify at-risk patients were developed using patient data from 7 adult ICUs at two hospitals in the University of Massachusetts during the period of July 2006 – September 2017. The performance of these models was subsequently externally validated on data from 7 ICU's at two hospitals in the WakeMed Health System during the period of December 2019 - March 2020. The resulting performance is shown in the tables below. The training and testing data for the models did not include any COVID-19 patients and may not specifically represent COVID-19 patients.

Respiratory Failure (RF), Intubation Model

Parameter	Value	95% Lower CI
Sensitivity (TPR)	53.7%	40.4
Positive Predictive Value (PPV)	4.7%	3.1%

Hemodynamic Instability (HI), Pressor Model

Parameter	Value	95% Lower CI
Sensitivity (TPR)	56.9%	49.9%
Positive Predictive Value (PPV)	18.5%	15.4%

The analysis of model performance presented above, reflects an assessment of performance where there was variability in the amount of data elements present at any given time (i.e., the CLEWICU System analyzed whatever data were available to it at a given time).

Please note that there is a direct relationship between availability of data and ability of the CLEWICU System to predict events; performance decreases notably when data are not available. For more information, please see the product labeling which includes a re-analysis of model performance where the total possible dataset was sequentially limited from the full data elements to decreased datasets, including a reasonable worst case dataset. Given the relationship between performance and data availability, it is critical, to optimize the availability of data for the CLEWICU System to analyze.

Personnel operating or maintaining the CLEWICU System should read the user manual and be thoroughly familiar with all safety requirements and operating procedures before operating the system.

All personnel using the CLEWICU System must also be trained in and be familiar with the interpretation of results of the CLEWICU System.

Only CLEW Medical-authorized personnel are allowed to service the CLEWICU System.

Due to possible variability in CLEWICU System results, system output should be viewed as one clinical data point that should be integrated by an appropriately trained clinician with the patient's clinical history, physical exam, continuous monitoring data, diagnostic test results, and clinical judgment.

What are the known and potential benefits and risks of using the CLEWICU System?

Known and potential benefits of the CLEWICU System include:

- Uses available patient data to provide predictive clinical analytics for likelihood of patient respiratory deterioration/failure (CLEWRF Index) and hemodynamic instability (CLEWHI Index) that can be used to optimize patient workflows and clinical resource allocation, as well as for centralized oversight and management.
- The CLEWRF and the CLEWHI indices provide HCP with predictive screening information to assist with the early identification of patients who are likely to be diagnosed with respiratory failure or hemodynamic instability which are common complications associated with COVID-19.

The CLEWICU System has been designed to minimize the risk of misuse with guidelines provided in the CLEWICU – Instructions for Use, Inbound Data Integration Specification, and System Specification and Infrastructure Guide. However, should misuse occur, they may present the following risks to patients:

- Alerts provided by CLEWICU may be falsely positive or falsely negative; that is, alerts may be mistakenly issued for a patient or patients who should not be flagged, or alerts may mistakenly fail to issue and a patient or patients may be overlooked. It is important to consider the known performance of the CLEWICU System when interpreting the clinical information provided by the CLEWICU System.

Overall, it is reasonable to conclude that the known and potential benefits of the CLEWICU System outweigh the known and potential risks.

What are the Alternatives to the CLEWICU System?
There are several other available solutions for helping hospitals manage their workload and/or providing predictions for patient status, such as products that make use of Early Warning Scores (EWS). While these systems assist in identifying patient deterioration, they do not identify specific predicted future clinical events in the ICU setting, particularly regarding respiratory failure and hemodynamic instability. This specific supporting functionality may provide benefit when monitoring large numbers of COVID-19 ICU patients.

Limitations of the CLEW ICU System
The CLEWICU System is intended to be used as a decision support tool and is to be used together with the patient's clinical history, continuous monitoring data, diagnostic test results, and clinical judgment.

The CLEWICU System does not provide a solution for acute situations (such as pulmonary embolism) as the tool analyzes developing trends in data and may not be able to identify suddenly occurring events.

The CLEWICU System performance is dependent on the hospital network. If communication is not provided the system will be unable to provide results for the patients and the user is notified.

The CLEWICU System has been authorized only for the measurement of risk of respiratory failure using the CLEWRF Index or hemodynamic instability using the CLEWHI Index.

The CLEWICU System has neither been cleared or approved to provide predictive screening information to assist with the early identification of patients who are likely to be diagnosed with respiratory failure or hemodynamic instability which are common complications associated with COVID-19 during the COVID-19 pandemic.

What is an EUA?
The United States Food and Drug Administration (FDA) has made the CLEWICU System available under an Emergency Use Authorization (EUA). The EUA is supported by the Secretary of Health and Human Service's declaration that circumstances exist to justify the emergency use of medical devices during the COVID-19 outbreak.

The CLEWICU System made available under this EUA has not undergone the same type of review as an FDA-approved or cleared device. However, in the absence of an FDA-approved or cleared alternative and based on the totality of scientific evidence, it is reasonable to believe that the CLEWICU may be effective to provide HCP with predictive screening information to assist with the early identification of patients who are likely to be diagnosed with respiratory failure or hemodynamic instability which are common complications associated with COVID-19.

The EUA for the CLEWICU System is in effect for the duration of the COVID-19 declaration justifying emergency use of these devices, unless terminated or revoked (after which the products may no longer be used).

How can I learn more?

CDC websites:
General: https://www.cdc.gov/COVID19
Healthcare Professionals:
https://www.cdc.gov/coronavirus/2019-nCoV/guidance-hcp.html

FDA websites:
General: www.fda.gov/novelcoronavirus
EUAs: https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations

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Report Adverse events, including problems with test performance or results, to MedWatch by submitting the online FDA Form 3500 (https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home) or by calling **1-800-FDA-1088**