CLEWICU – Instructions for Use

CLEWICU solution

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This is a legal agreement between you, the end user, and CLEW Medical INC. (“Clew”).

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PLEASE READ THIS USER MANUAL BEFORE OPERATING THE SYSTEM.

ONLY TRAINED AND AUTHORIZED OPERATORS MAY ACCESS THE CLEWICU™ SYSTEM.

Note:

The CLEWICU System has been neither cleared nor approved;

The CLEWICU System has been authorized for the above emergency use by FDA under an EUA; and,

The CLEWICU System has been authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of medical devices under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

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1. Introduction

The CLEWICU System is a stand-alone analytical software product that uses models derived from machine learning to calculate the risk/likelihood of occurrence of certain clinically significant events for patients in the intensive care unit (ICU).

The CLEWICU System provides clinical benefits to all layers of ICU management and staff, that may result in operational and financial benefits as well. The System utilizes innovative prediction models derived from large volumes of data using advanced, high-dimensional analytic techniques.

The CLEWICU System harnesses the vast amount of available data to deliver accurate predictive clinical analytics that provide ICU/tele-ICU personnel with the preemptive information they need to provide high-quality care and better manage their resources.

1.1. About this user manual

This document includes instructions for using the CLEWICU System, a software service designed by CLEW Medical. **Please read this user guide carefully before using the system**.

If any part of this User Manual is not clear, contact CLEWMED customer support at: support@clewmed.com

1.2. Types of warnings, precautions and notes

Three types of special messages appear in this User Manual:

	Warning: A warning statement provides important information to avoid the possibility of personal injury or death.
	Precaution: A precaution statement indicates care that should be taken for safe and effective use of the device and to avoid conditions that may lead to damage to equipment, or a lower quality of treatment.
	Note: A note provides other important information.

1.3. Warnings and precautions

Below is a comprehensive list of the warnings and precautions. They also appear in the relevant sections throughout the User Manual.

Warnings

- DO NOT USE BEFORE READING THIS USER MANUAL.
- Use of controls or adjustments, or performance of procedures other than those described herein, may be hazardous. Personnel operating or maintaining the System should read this manual and be thoroughly familiar with all safety requirements and operating procedures before operating the system.
- Only CLEW Medical-authorized personnel are allowed to service the system.

- Precautions
- Use the system in a hospital environment only.
- The safety and effectiveness of the CLEWICU System has not been established in pediatric patients.
- Due to possible variability in CLEWICU 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, continuous monitoring data, diagnostic test results, and clinical judgment.

2. System Overview

2.1. ICU integration

CLEW aims to minimize the integration effort by building an ingestion solution that complements existing data channels in the hospital.

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. Each of the components of the CLEWICU System are described further below:

ClewICUServer

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 CLEWRF index (likelihood of respiratory failure requiring intubation), CLEWHI index (likelihood of hemodynamic instability requiring vasopressor / inotrope support).**ClewICUnitor**

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

The following diagram illustrates the integration of the CLEW System solution with the medical system in the hospital including identified and de-identified systems.

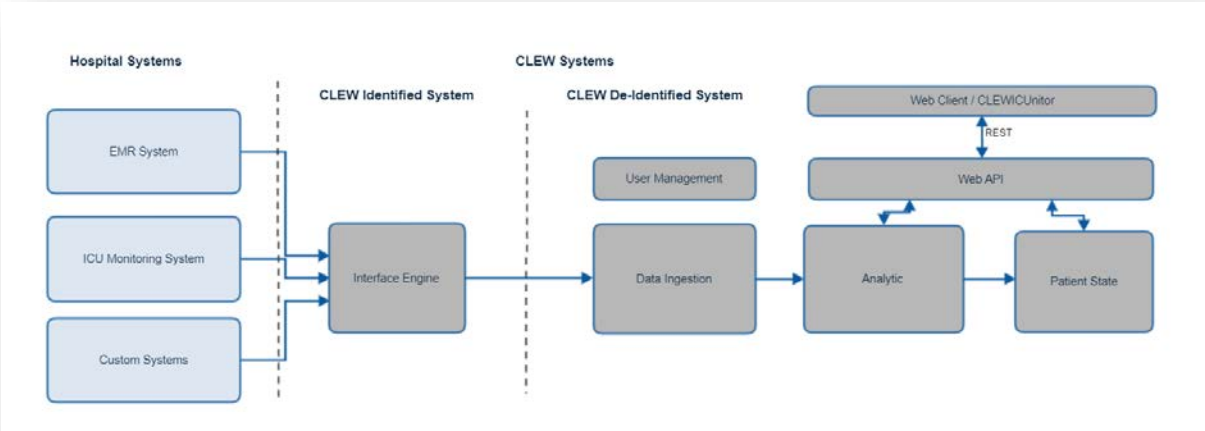


*Figure 1 - SEQ Figure * ARABIC \s 1*

3. Conditions for use

3.1. Indications for use

The CLEWICU System is to be used by healthcare providers (HCP) in the Intensive Care Unit (ICU) for adult patients 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 the 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.

3.2. Patient population

The CLEWICU System is validated for use with patients aged 18 and over being cared for in an intensive care unit setting.

3.3. Intended User

The intended user of the system is a tele-ICU or ICU clinician or any other authorized user within the hospital who has undergone training by CLEW in the use of the system

3.4. Statistical models

The statistical models that drive the CLEW System notifications were developed using machine learning methods that identify key variables and interrelations among them, which define the patient's clinical risk level. The algorithms were trained using supervised learning, a method where the system learns to predict outcomes (events) of interest using training data where these outcomes were clearly marked. The system is able to achieve high sensitivity with state-of-the-art precision for event prediction, with clinically meaningful lead times.

3.5. Contraindications

There are no known contraindications for use of the CLEWICU system

3.6. Limitations

- There are no HI or RF notifications for the first 6 hours of an ICU stay.
- There are no RF notifications for 12 hours post extubation.
- There are no HI notifications for 6 hours after vasopressors / inotropes are completely stopped.
- The System identifies most but not all intubation (respiratory failure) events and need for vasopressors / inotropes (hemodynamic instability) events.
- The CLEWICU System uses prediction models: Not all deteriorations will be predicted, nor will all deterioration notifications accurately predict need for intervention.

3.7. Summary of CLEWICU Clinical Performance

CLEW Medical has performed a retrospective multi-center validation study to determine CLEWICU performance. The summary of the data from this study is presented below:

For the Respiratory Failure (RF), Intubation model:

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

Parameter	Value	Percentile 25%	Percentile 75%
The median lead-time for true positive alert	3.9 hours	2.7 hours	6.3 hours

For the Hemodynamic Instability (HI), Pressor model:

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

Parameter	Value	Percentile 25%	Percentile 75%
The median lead-time for true positive alert	3.7 hours	1.9 hours	5.6 hours

Average lead time represents the average time to a true positive index event following a notification. Average lead time was calculated independent of PPV and sensitivity and was not used as part of the analysis for those metrics

The analysis above reflects an assessment of performance where there was variability in the amount of data elements present at any given time (i.e., the system analyzed whatever data was available to it at a given time). However, it is acknowledged that there is a direct relationship between availability of data and ability of the system to predict events. Therefore, to provide an analysis of that relationship, the study data were re-analyzed where the total possible dataset was sequentially limited from all possible data elements (80 variables) down to 60, 50, 40 and finally 26 (i.e., reasonable worst case dataset). Performance on those decreased datasets is presented below. Given the

relationship between performance and data availability, it is critical, during implementation, to optimize the availability of data for the system.

For the Respiratory Failure (RF), Intubation model:

Data set	TPR Value	TPR 95% Lower CI	PPV Value	PPV 95% Lower CI
Decreased data (26 parameters)	25.9%	14.2%	8.2%	4.1%
40 parameters set	50.0%	36.7%	5.0%	3.1%
50 parameters set	53.7%	40.4%	5.3%	3.4%
60 parameters set	50.0%	36.7%	4.9%	3.1%
80 parameters set (full set)	53.7%	40.4%	4.7%	3.1%

For the Hemodynamic Instability (HI), Pressor model:

Data set	TPR Value	TPR 95% Lower CI	PPV Value	PPV 95% Lower CI
Decreased data (26 parameters)	27.4%	21.2%	35.8%	28.1%
40 parameters set	49.7%	42.8%	19.2%	15.8%
50 parameters set	57.4%	50.5%	18.8%	15.7%
60 parameters set	55.3%	48.4%	18.5%	15.4%
80 parameters set (full set)	56.9%	49.9%	18.5%	15.4%

3.8. Deteriorations

The current version of the CLEWICU System predicts two types of deteriorations: hemodynamic instability and respiratory failure.

- Hemodynamic instability (HI) – The system provides notifications for patients at high risk for hemodynamic instability, meaning that it tries to predict the need for initiation of vasopressor or inotrope support.
- Respiratory failure (RF) – The system provides notifications for patients at high risk for respiratory failure, meaning that it tries to predict the need for intubation.

3.9. Notifications

If an RF or HI event is predicted, a notification will be raised in the CLEWICU System to inform the practitioner of these impending deteriorations. The System notifications generally precede the deterioration events by an average of 3-4 hours. We expect that

patients will have better outcomes if the providers either take early action, thus making the interventions (intubation or starting vasopressors / inotropes) unnecessary, or use the advanced warning to better prepare for the predicted events.

4. Getting started

4.1. Starting your CLEWICU session

The CLEWICU System is a web-based application, it requires a URL to log in.

4.2. Logging in to the CLEWICU system

Enter your username and password, and then click Log In.

Each individual user of the CLEWICU System will have login credentials (user name and password). User credentials will be similar to the hospital's SSO (Single Sign On). If integration of the hospital Active Directory is not possible, then login credentials will be managed locally within the CLEWICU System (not part of the SSO).

4.3. Logging out of the CLEWICU system

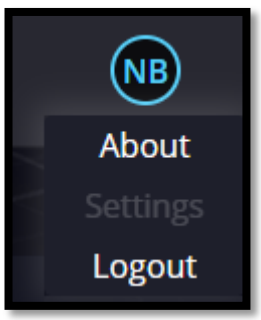


Figure 3 -CLEWICU Logout screen

When you are finished working with the CLEWICU System, click the Logout button.

5. The CLEWICU system

5.1. Screen layout

5.1.1. Common bar

Figure 4- Common bar

The common bar appears at the top of every screen; below is the common bar description, left to right:

- CLEW logo
- Dropdown list of the System view type ("View") - Use this to switch between the Unit View and Worklist View screens.
- Patient duplications - Lights up and displays the number of beds with more than one assigned patients. Click to bring up the Duplications list.
- Notification bell - Lights up and displays the number of new notifications. Click to bring up the notifications list for the last 24 hours.
- Refresh button - Click to refresh your system with the most updated available data. Otherwise, the system updates itself every minute.
- Timestamp of the last data refresh
- Username button with About, Settings, and Logout buttons

5.2. Unit view

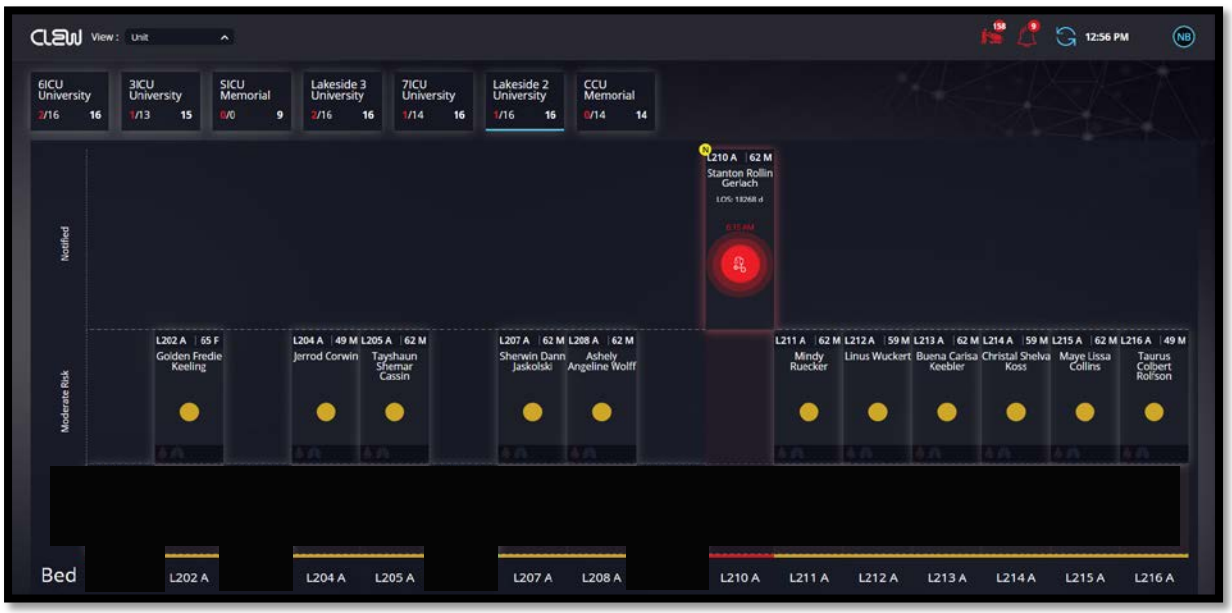


Figure 5- Unit view diagram

5.2.1. Unit View Overview

The Unit View screen displays all units that are part of the System, the patients in the selected unit, and the patient status based on the CLEWICU System's prediction.

The Unit View screen gives you a full view of the units covered by the CLEWICU System (one or more units).

At the top of the screen, each available unit is displayed in a box. The selected unit's data are displayed below the unit boxes.

For each selected unit the following is displayed: which patients are predicted to be at high risk for deterioration (including which notifications are new), which patients are predicted to be at moderate risk for deterioration, and which patients are predicted to be at low risk for deterioration.

In addition, the Unit View will display which patients are intubated, which patients are on vasopressors / inotropes, and which beds are empty. The screen will give you a high-level estimation of the overall unit acuity.

5.2.2. Display

Selecting a unit will display the full unit. The unit is laid out in vertical lanes, with each lane having an associated bed and, if occupied, patient. The lane is divided into risk level

categories (Moderate Risk, and High Risk [Notified]), and the patient is placed in the section of the lane corresponding to the patient's predicted risk for deterioration.

5.2.3. Patient Risk Level

Patients will be in one of 2 predicted risk levels:

Risk Level	Display	
Moderate		Moderate Risk for Hemodynamic Instability and/or Respiratory Failure
High Risk		High Risk for Hemodynamic Instability and/or Respiratory Failure

5.2.4. Patient Information

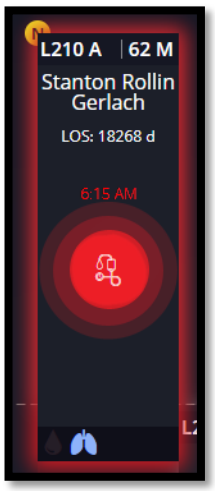


Figure 6 Patient information

For an authorized and authenticated user, the system displays each patient with the following data:

- Bed number
- Age
- Gender
- Patient Name
- LOS (Length of stay)
- Notification status (Snoozed/Removed)
- Notification icon and timestamp (in case of a notified patient)

Hemodynamic instability

Respiratory failure

If there is a notification icon, the time of the notification is displayed above it.

- Patient status (intubated, on vasopressors / inotropes)

Lung icon: The patient is intubated

Blood Drop icon: The patient is on vasopressors / inotropes

For an authorized and authenticated user, hovering over the patient's name will provide additional patient detail:

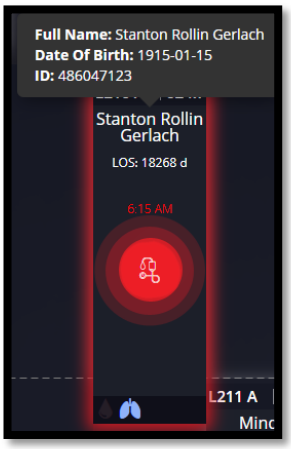


Figure 7 Patient identifier

- Patient Full Name
- Date of Birth
- Medical Record Number (MRN)

5.2.5. Missing Vitals Data

If the system fails to receive patient vital sign data (please refer to 046DGD rev.01 - Inbound Data Integration Specifications, section 3.1) for more than one hour, the system will not be able to calculate patient risk level. The patient will be displayed as follows:

Figure 8 Patient without vitals

Hovering over this patient will display the following message: "No recorded vitals"

5.3. **Worklist view**

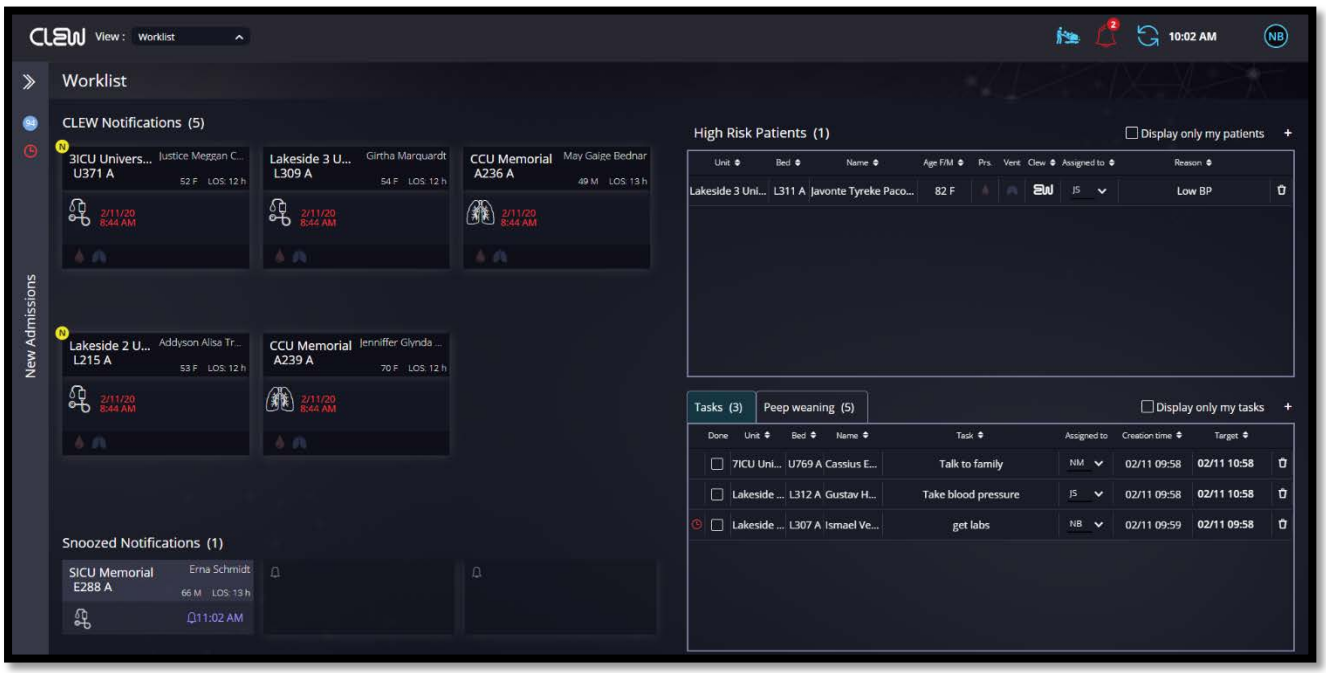


Figure 9 worklist diagram

The Worklist View contains four main sections:

- Notifications
- High Risk Patients
- Tasks
- New Admissions (pulled from the left sidebar)

5.3.1. Notifications

The Notifications section displays patients predicted to be at high risk for HI and/or RF deteriorations, with the display ordered by their notification creation time.

For each notification, the following details are available: New or Snoozed notification icon (top left corner), Unit, Bed number, Patient name, Gender, Age, Length of stay (LOS), Notification type, Notification time, Is the patient intubated, and Is the patient on vasopressors / inotropes.

Notification type:

Hemodynamic instability

Respiratory failure

For an authorized and authenticated user, by hovering over the patient name, additional patient details:

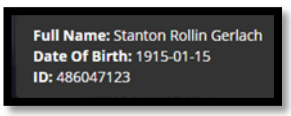


Figure 10 Patient identifier

- Patient full name
- Date of Birth
- Medical Record Number (MRN)

5.3.1.1. New Notification

A notification will display a yellow New icon until one of the following actions has been performed: Remove, Acknowledge, Add task, or Snooze.

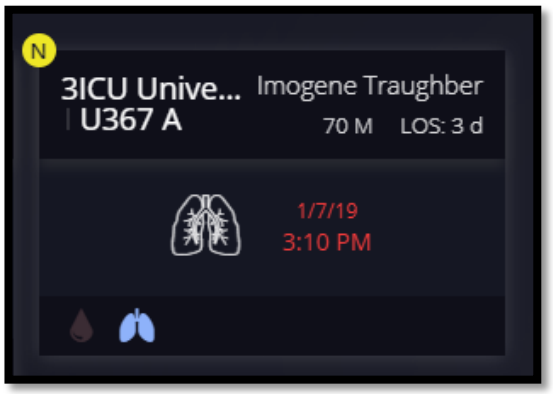


Figure 11 New Notification

5.3.1.2. User Feedback

The user can add feedback to a notification to manage the notifications list.
To add a feedback:

i. Hover over a notification.

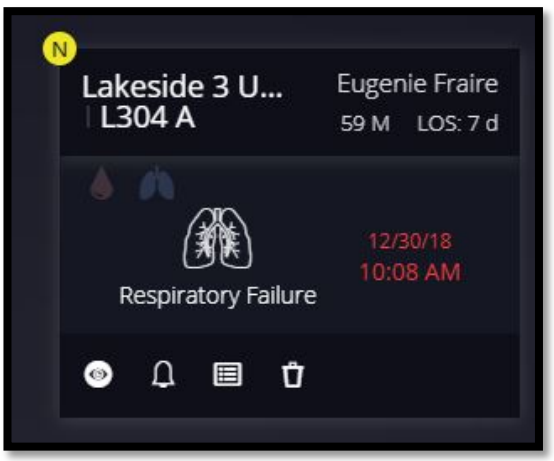


Figure 12 Notification feedback menu

ii. The following feedback icons will be displayed:

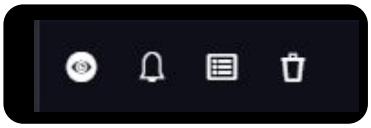


Figure 13 Notification feedback icons

iii. Click to choose desired action:

Acknowledge

The user can mark a notification as acknowledged, meaning that this notification was reviewed. When acknowledging a notification, the "New notification" mark is removed. This may be used to let the user's coworkers know the notification was viewed and is being managed.

Remind me later (snooze)

The user can "snooze" a notification for a set amount of time. This will move the notification to a snoozed section. After the set snooze period, the notification will return to the main notification area.

A "Remind Me Later" window pops up:

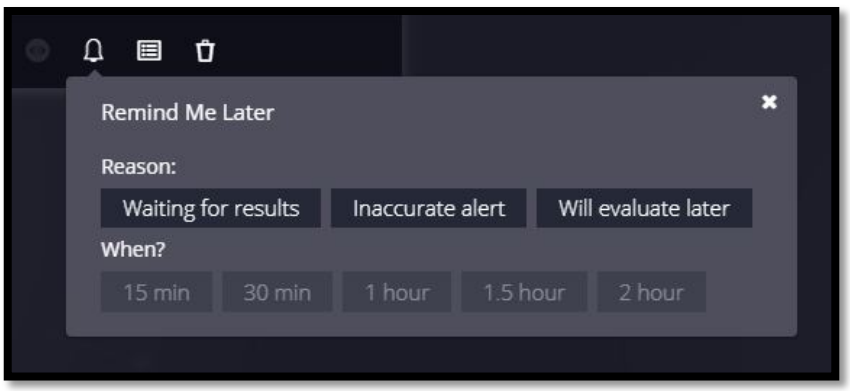


Figure 14 Notification feedback snooze menu

- Select one of the reasons and a snooze period.
- The notification will be placed in the "Snoozed Notifications" area of the Worklist View screen.

Add a task

The user can add a task directly from the notification. See the Add Task section for instructions on adding a task. In this instance, the patient unit and name will be pre-filled.

Remove notification

The user can remove a notification from the notifications list. The notification will be removed for four (4) hours. After this time frame, a new notification (if it exists) may be displayed.

To remove a notification:

- Click the "Remove" icon. A remove notification window pops up:

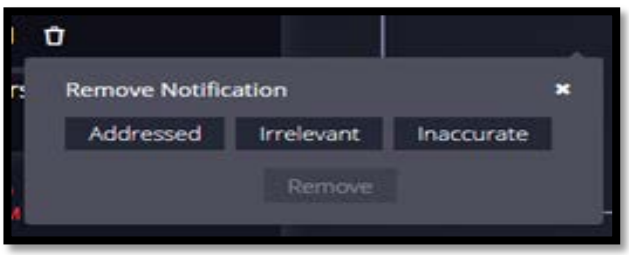


Figure 15 Notification feedback remove menu

- Choose one of the "remove" reasons, then click "remove."

5.3.1.3. Snoozed Notifications

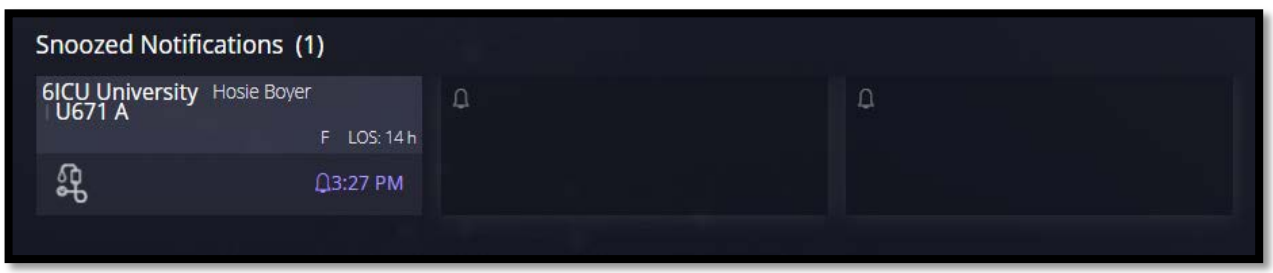


Figure 16 Worklist - Snoozed Notifications section

This section of the Worklist View page lists all of the snoozed notifications in the CLEWICU System. When the user hovers over a snoozed notification, a menu pops up with the options to un-snooze or remove the notification:

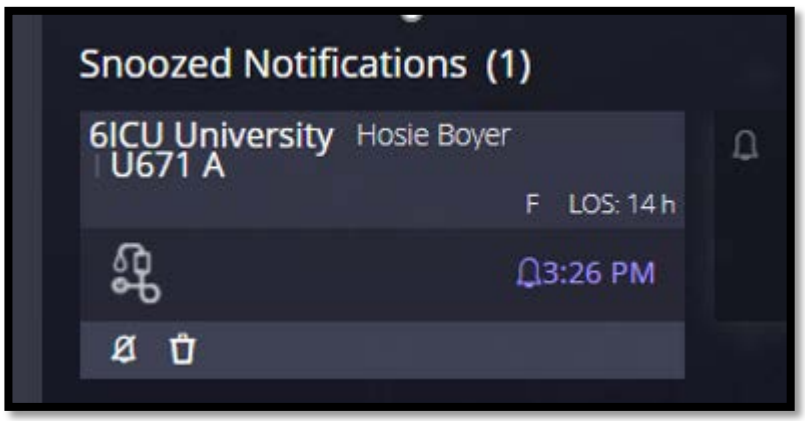


Figure 17 Snoozed Notification

Un-snooze notification

Activates the notification; the notification will now be displayed in the Notifications section and will be removed from the Snoozed Notifications section.

Remove notification

The Remove Notification menu pops up as above in the Remove Notification section.

5.3.2. High-risk Patients

The high-risk patients section displays patients identified by the user as high risk. It may be used for patients that require higher monitoring/attention than other patients. The high-risk classification is not related to CLEWICU System notifications; it is created by and managed by the user.

In this list, you can see all user-designated high-risk patients or only those high-risk patients that are assigned to you.

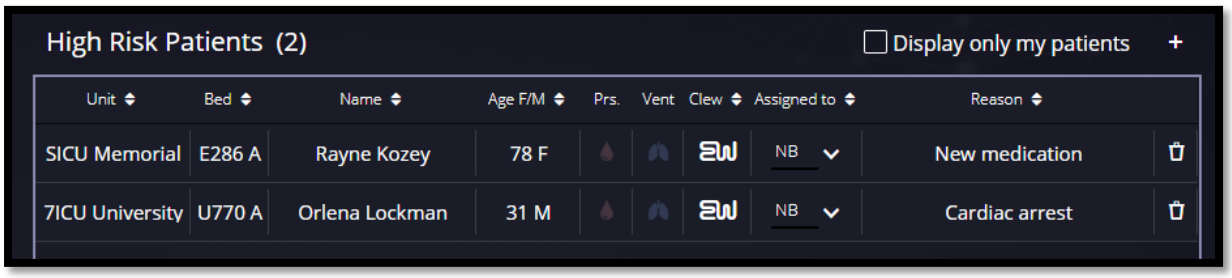


Figure 18 High Risk Patients

Unit - patient's unit.

- Bed - Patient's bed
- Name - Patient's name
- Age F/M -Patient's age and gender
- Prs – Is the patient on vasopressors / inotropes
- Vent – Is the patient invasively ventilated
- CLEW – Does the patient have a CLEWICU HI or RF notification
- Assigned to – Clinician to whom this patient is assigned
- Reason – Free text – why this patient was added to the high-risk patient list

Add a High-risk Patient:

Click on the '+' sign at the top right corner of the High-Risk Patients section on the Worklist screen.

Figure 19 Worklist - Add a high-risk patient

Insert the following:

- Unit – From the Unit dropdown list, select the patient's unit.
- Bed – From the Bed dropdown list, select the patient's bed (including patient name).
- Assign to – From the User dropdown list, select a team member that the patient is assigned to. Defaults to the logged in user.
- Reason – Free text, a reason for the patient to be on the high-risk list.

Then click "Save".

By default, all high-risk patients will be displayed.

Click "Display only my patients" to display only high-risk patients that are assigned to you.

5.3.3. Tasks

The Tasks section helps the ICU staff manage their tasks. A task is assigned to one patient and one provider, with a target date and time for the task to be completed. A task can be assigned to any patient being tracked by the CLEWICU System.

Tasks will be sorted by creation time (oldest on top) by default but can also be sorted by unit, bed, patient name, task, or target time.

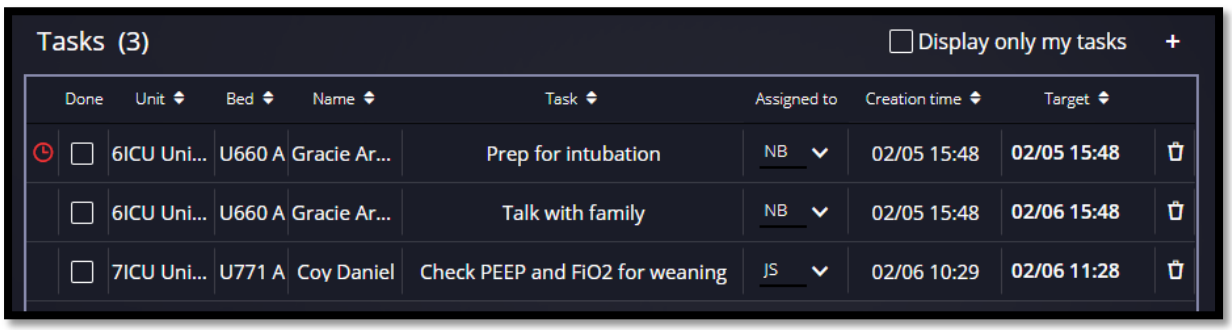


Figure 20 Task list

You may add a task in one of two ways:

1. Feedback on a notification

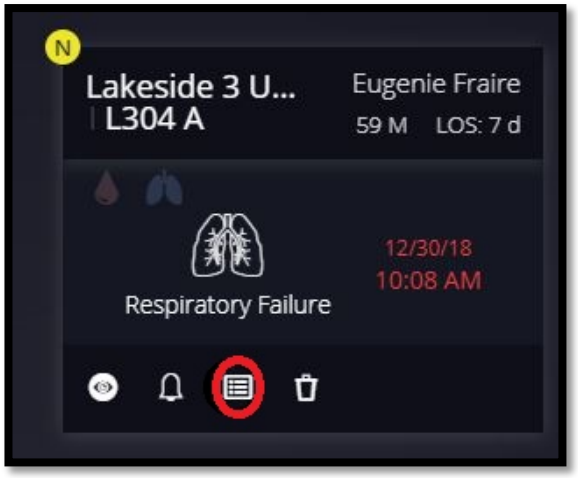


Figure 21 Notification feedback - Add task

i. Click the "add task" icon in the notification feedback (of a specific notification) area.
ii. Follow the instructions in the "Add a task" section below.

2. Add a new task from the Tasks section

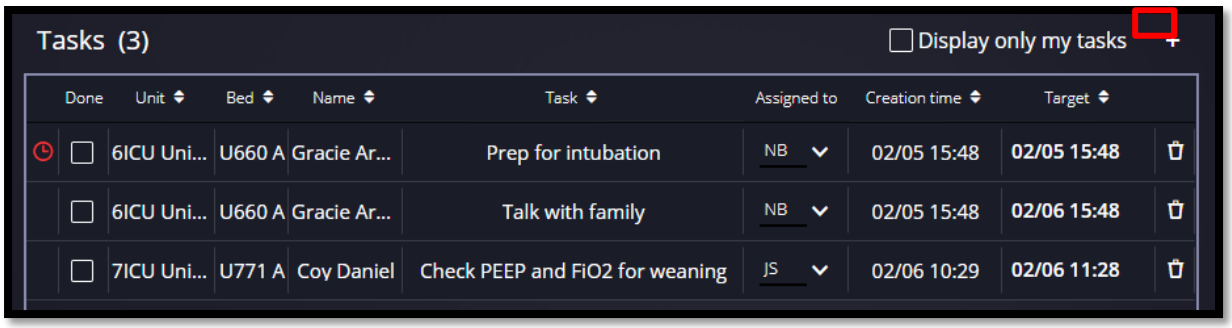


Figure 22 Task list - Add task

i. Click the + icon on the top right corner of the Tasks section.
ii. Follow the instructions below to add a task.

5.3.3.1. Add a Task

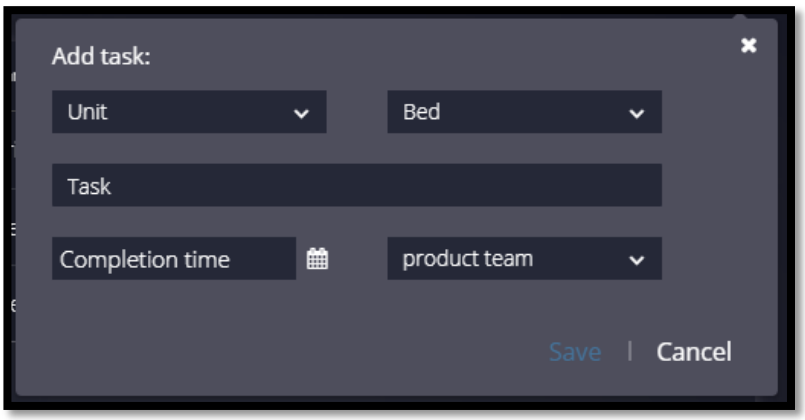


Figure 23 Add a task

Insert the following details:

Unit – From the Unit dropdown list, select the patient's unit.

Bed –From the Bed dropdown list, select the patient's bed (including patient name).

Task – Free text, description of the task.

Completion time – The time when the task is expected to be completed.

Assign to – From the User dropdown list select a team member to whom the task is assigned. Defaults to the logged in user.

By default, all tasks will be displayed.

Click "Display only my tasks" to display only tasks that are assigned to you.

5.3.3.2. Mark Task as "Done"

Clicking the checkbox to the left of each task, opens the following window:

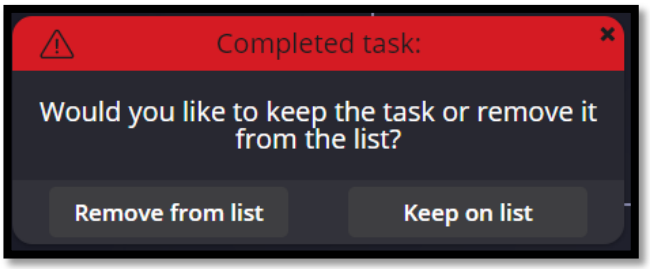


Figure 24 Completed task window

Click "Remove from list" to update the task status to "done" and remove it from the list.

Click "Keep on list" to to update the task status to "done" and keep the task in the list (for example, if the user would like to inform a colleague that this task is done).

Click on the x to cancel the operation.

5.3.3.3. Remove Task

The user can remove a task from the display by clicking the remove icon.

When removing a task, the following message is displayed:

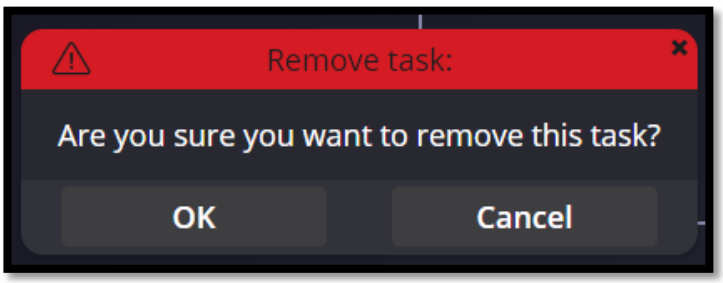


Figure 25 Remove task assigned to another user

Click OK to remove the task or Cancel to cancel this action.

In case you remove a task, that is assigned to another user, the following message is displayed:

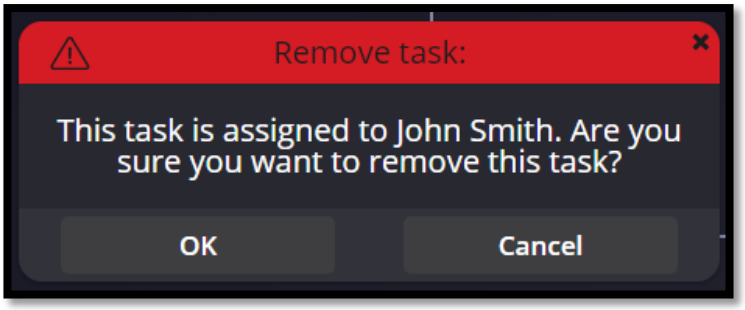


Figure 26 Remove task assigned to another user

Click OK to remove the task or Cancel to cancel this action.

5.4. **Worklist – New Admissions**

The New Admission section presents all new admissions to remind you of their admission time and to keep you focused on actions required during the critical period following an ICU admission. After a period of time (based on hospital protocol), the patient will be displayed with the red clock icon to remind you to complete required actions based on your unit's admission protocol.

New Admissions has a double arrow, count, and clock icons.

Figure 27 New admission panel

Double arrow

Displays and hides the New Patients evaluation sidebar.

- **Count**

Shows a count of how many new admissions are in the system.

- **Clock icon**

When lit, there are new admissions with incomplete protocol tasks in the system that are past their deadlines. Click on the clock icon to display a list of these new admissions.

5.4.1. New Admissions – Functionality

When a new patient is added to the CLEWICU System, the patient is added to the New Admissions section.

Open the section to get a full view of the new admissions:

Each unit will display its new admissions count and the new admissions beds.

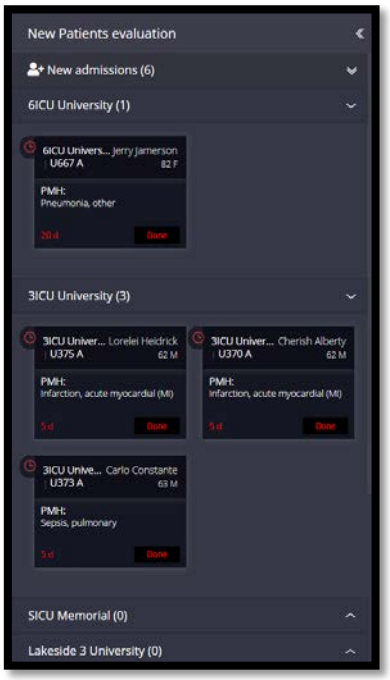


Figure 28 worklist- new admissions

Each bed will contain the following information:

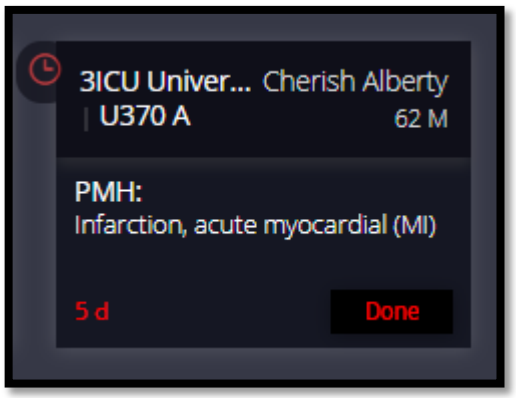


Figure 29 -Worklist – New admissions – specific patient

Unit – The Patient unit.

Name – Patient name.

Bed –The Patient bed.

PMH – Past Medical History.

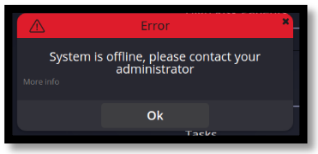
Timer – Time since the patient was admitted. The Timer is green for the first 60 minutes (or for the time period defined by the hospital protocol), after which it turns red.

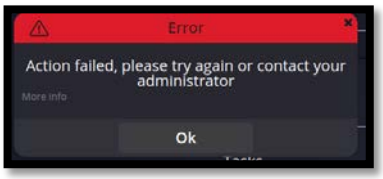
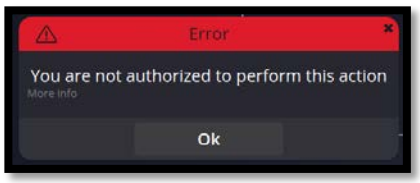
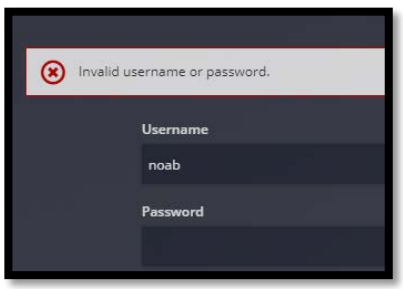
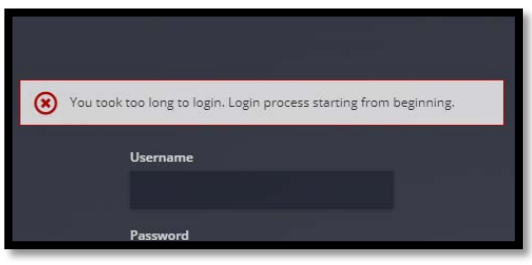
Done button – For clinician use, when completing the new patient review protocol. Removes the patient from the "New admissions" list.

For an authorized and authenticated user, hovering over the patient name will display the following additional patient information:

- Full name
- Date of Birth
- Medical Record Number (MRN)

6. Troubleshooting

#	Section	Issue	Possible reason	Solution
1	Patient data	Detailed Patient identity data are missing	Unauthorized user	Update user authorizations Change user to an authorized user
2		Patient is grayed out	No vital sign data received for at least an hour	Check if patient is in bed. If yes – contact your administrator
3	System	System offline  "System is offline, please contact your administrator"	Technical issue in the system or in the environment	Contact your administrator
4		Can't load the system	Technical issue in the system or in the environment	Contact your administrator
5	Notifications	CLEW notification disappears	Notification is outdated	Check bell icon to see notification status (should be "Outdated").
6			Notification snoozed by you or by another user	Check in Snoozed notification area. If notification appears.you can unsnooze it
7			Notification manually removed by you or by another user	Find patient in Unit View. If the notification was removed, patient will be red with "Removed" mark over the notification.
8	User Action	Cannot add a task	System technical issue	Try again in a few minutes. If it still fails, contact your administrator
9		Cannot add a high risk patient		

10		Cannot add feedback to a notification	 "Action failed, please try again or contact your administrator"		
11		Cannot perform an action with the following message:  "You are not authorized to perform this action"		The user is a "View only" user who does not have permission to perform actions in the system	Contact you administrator. In order to perform any actions, the user must be authorized by the system administrator.
12	Logging in	When trying to login, the following message appears: "Invalid username or password" 		Username or password is incorrect	Try again with correct credentials. If you still can't log in, contact your administrator
13		When trying to login, the following message appears: "You took too long to login. Login process starting from beginning" 		Login screen was opened without any action for a longer than 15 minutes	Enter your credentials and try again

7. Regulatory

Manufacturer

Manufactured by: CLEW Medical Ltd.

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Note:

The CLEWICU System has neither been cleared or approved for the indication to assist in measurement of risk of respiratory failure using the CLEWRF Index or hemodynamic instability using the CLEWHI Index within the next 8 hours during the COVID-19 pandemic;

The CLEWICU System has been authorized for the above emergency use by FDA under an EUA; and,

The CLEWICU System has been authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of medical devices under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

7.1. Description of symbols

The following table shows a list of standard symbols which may appear on the device and shipping labels and a brief description of each symbol.

Symbol	Description
	General warning sign
	Manufacturer
Rx Only	Federal (U.S.) law restricts this device to sale by or on the order of a licensed physician.