

September 24, 2020

Dascena, Inc.  
c/o Ms. Carol Gu  
Vice President, Operations  
PO Box 156572  
San Francisco, CA 94115

Dear Ms. Gu:

This letter is in response to your request on behalf of Dascena, Inc. that the U.S. Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of the COViage Hemodynamic Instability and Respiratory Decompensation Prediction System (COViage)<sup>1</sup> to be used by healthcare providers (HCP) in the hospital setting for adult patients<sup>2</sup> with confirmed COVID-19<sup>3</sup> for the computation of proprietary patient status indices referred to as Respiratory Decompensation Status<sup>4</sup> and Hemodynamic Instability Status<sup>5</sup> (collectively referred to as “risk level determinations”) as an adjunct to patient monitoring during the Coronavirus Disease 2019 (COVID-19) outbreak. The COViage indices provide HCP with predictive screening information as a diagnostic aid to assist with the early identification of COVID-19 patients who are likely to be diagnosed with hemodynamic instability or respiratory decompensation, which are common complications associated with COVID-19.

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<sup>1</sup> This EUA includes the emergency use of COViage, which is a single cloud-based software program intended for integration with existing electronic medical record (EMR) systems at healthcare facilities. COViage is standalone software as a medical device that receives patient data (age, gender, heart rate, diastolic and systolic blood pressure, temperature, and respiratory rate) from the hospital’s EMR system to compute patient status indices that have been defined as Respiratory Decompensation Status and Hemodynamic Instability Status. COViage is not FDA-cleared or approved for marketing in the United States. In addition, COViage does not have a marketing authorization in another country.

<sup>2</sup> For the purposes of this EUA, adult patients are defined as patients that are 18 years of age or older who are admitted to the hospital.

<sup>3</sup> Confirmed COVID-19 is defined as a positive PCR test result that is recorded in the EMR during the hospital encounter. The COViage software functionality includes checking for COVID-19 status in the EMR.

<sup>4</sup> Respiratory Decompensation Status is a measure of a patient’s predicted physiologic condition during their hospitalization based on the aggregate statistical risk of respiratory decompensation or failure. For purposes of this authorization, the condition of respiratory decompensation refers to the patient being mechanically ventilated (defined as invasive ventilation requiring endotracheal tube or mechanical ventilation not including BIPAP or CPAP) at any point in their hospital stay.

<sup>5</sup> Hemodynamic Instability Status is a measure of a patient’s predicted physiologic condition during their hospitalization based on the aggregate statistical risk of hemodynamic instability. For purposes of this authorization, the condition of hemodynamic instability refers to the patient needing vasopressor/inotrope therapy at any point during their hospital stay.

On February 4, 2020, pursuant to section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the Act), the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19.<sup>6</sup> Pursuant to section 564 of the Act, and on the basis of such determination, the Secretary of HHS then declared on March 24, 2020, that circumstances exist justifying the authorization of emergency use of medical devices pursuant to section 564 of the FD&C Act, subject to the terms of any authorization issued under that section.<sup>7</sup>

There are no FDA approved or cleared devices to provide predictive screening information as a diagnostic aid to assist with the early identification of adult COVID-19 patients who are likely to be diagnosed with respiratory decompensation or hemodynamic instability, which are common complications associated with COVID-19.

COViage provides HCP with advance warning if a patient diagnosed with COVID-19 is at high risk for developing hemodynamic instability that may require vasopressor or inotrope support, or respiratory decompensation that may require mechanical ventilation, during a hospital stay. The benefit of such an approach is the potential to identify COVID-19 patients at risk of hemodynamic instability or respiratory decompensation before they deteriorate, thus facilitating the effective allocation of limited resources and identifying those patients most likely to benefit from increased care. Without the benefit of timely warnings, rapid and unexpected deterioration in patient conditions come with high risk of emergency transfers to the intensive care unit (ICU) and emergency intubations. The predictive analytics provided by COViage can help caregivers synthesize the large amount of patient monitoring data. This is important during the COVID-19 outbreak, where ICUs may be at capacity and patients are requiring care for an extended period of time. By identifying high risk patients early in their hospitalization and prioritizing treatment based on patient acuity, this likely provides better care for patients and reduces the strain on hospital personnel. The COViage System was validated on a dataset of hospitalized, adult patients that were diagnosed with COVID-19 and were admitted between March 1, 2020, and June 3, 2020, from three hospitals. Based on FDA's review of retrospective clinical validation data, FDA has concluded that COViage may be effective for use by HCP as a diagnostic aid to assist with the early identification of adult COVID-19 patients who are likely to be diagnosed with hemodynamic instability or respiratory decompensation, which are common complications associated with COVID-19, as explained in Section II of this letter, and has therefore determined that the criteria for issuance under Section 564(c) of the Act are met.

Having concluded that the criteria for issuance of this authorization under section 564(c) of the Act are met, I am authorizing the emergency use of the COViage, as described in the Scope of

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<sup>6</sup> U.S. Department of Health and Human Services, Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3, 85 FR 7316 (February 7, 2020).

<sup>7</sup> U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act*, 21 U.S.C. § 360bbb-3, 85 FR 17335 (March 27, 2020).

Authorization of this letter (Section II) and pursuant to the Conditions of Authorization (Section IV) of this letter.

### **I. Criteria for Issuance of Authorization**

I have concluded that the emergency use of COViage, as described in the Scope of Authorization (Section II) of this letter meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. SARS-CoV-2, the virus that causes COVID-19, can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;
2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that COViage may be effective when used by HCP as a diagnostic aid to assist with the early identification of adult COVID-19 patients (18 years of age or older who are admitted to the hospital) who are likely to be diagnosed with hemodynamic instability or respiratory decompensation, which are common complications associated with COVID-19, and that the known and potential benefits of COViage, for such use, outweigh the known and potential risks; and,
3. There is no adequate, approved, and available alternative to the emergency use of COViage when used by HCP as a diagnostic aid to assist with the early identification of adult COVID-19 patients who are likely to be diagnosed with hemodynamic instability or respiratory decompensation, which are common complications associated with COVID-19.<sup>8</sup>

### **II. Scope of Authorization**

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of COViage to be used by HCP in the hospital setting for adult patients (18 years of age or older who are admitted to the hospital) with confirmed COVID-19 for the computation of proprietary patient status indices referred to as Respiratory Decompensation Status and Hemodynamic Instability Status as an adjunct to patient monitoring during the COVID-19 outbreak. The COViage indices provide HCP with predictive screening information as a diagnostic aid to assist with the early identification of COVID-19 patients who are likely to be diagnosed with hemodynamic instability or respiratory decompensation, which are common complications associated with COVID-19.

COViage should not be used as the sole basis to determine risk of hemodynamic instability or respiratory decompensation in a patient. COViage is not intended to be used on a standalone basis for clinical decision-making. Results should be combined with monitoring data, diagnostic

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<sup>8</sup> No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

test results, best clinical judgment, other clinical observations, patient history, and epidemiological information. COViage is only functional when age, gender, temperature, heart rate, respiration rate, systolic blood pressure, and diastolic blood pressure are included in the patient’s EMR. Negative results do not preclude risk of hemodynamic instability or respiratory decompensation in a patient and should not be used as the sole basis for patient management decisions. COViage results are only calculated one time for the patient during their hospitalization. Older results may become less relevant as the patient’s condition changes.

### The Authorized COViage

The COViage Hemodynamic Instability and Respiratory Decompensation Prediction System (“COViage” or “COViage System”) is a HIPAA-compliant cloud-based software that uses a set of two algorithms, one to calculate the risk level determination for hemodynamic instability (Hemodynamic Instability Status) and the other to calculate the risk level determination for respiratory decompensation (Respiratory Decompensation Status) (collectively “risk level determinations”), that together:

- Receive patient data (age, gender, heart rate, diastolic and systolic blood pressure, temperature, and respiratory rate) from the hospital’s EMR system,
- Analyze each patient’s data using each algorithm to compute the patient’s risk level as a one-time assessment, and
- Provide a real-time updated report of risk status for all hospitalized patients aged 18 or over that are diagnosed with COVID-19.

### *Algorithm Inputs*

Each of the two machine learning algorithms use the following inputs, which constitute the minimum required data elements. “Minimum” is defined to mean at least one value is required for each of the data elements listed. There are no additional data elements accepted as inputs to the algorithms. There may be more than one value available per data element, which occurs when a patient has multiple sets of vitals recorded in the EMR at the time the data are made available to COViage. In this case, each algorithm uses the most recently available measurement for each of the data elements at the time of risk prediction calculation.

- Age
- Gender
- Heart Rate (HR)
- Diastolic Blood Pressure (DiasBP)
- Systolic Blood Pressure (SysBP)
- Temperature
- Respiratory Rate

### *Notification Configuration*

COViage will provide a real-time report in the following form for all hospitalized patients with an age of 18 or older who have been determined to be COVID-19 positive according to a positive PCR test result that is recorded in the EMR during the current hospital stay. “Real-time”

is defined to mean that the report is updated virtually instantaneously as a patient’s status changes. COViage generates this risk level determination report only once during the patient’s hospitalization. The risk level determination calculated applies to the duration of the patient’s hospital stay. In other words, COViage assesses risk for the patient at any point in their hospital stay after the software receives the minimum required data inputs. There is one risk level determination per visit, and it is made automatically upon the system's collection of the minimum required data inputs from the EMR. The determination is not recalculated at the provider’s request.

Table 1: Example Report Format (not from actual data)

<b>Patient Last Name</b>	<b>Patient First Name</b>	<b>Medical Record Number</b>	<b>Hemodynamic Instability Status (timestamp)</b>	<b>Respiratory Decompensation Status (timestamp)</b>
Smith	John	1210001	High Risk (June 01, 2020; 16:20)	Not High Risk (June 01, 2020; 16:20)

Each Status field will have three possible results<sup>9</sup>:

i) *Insufficient Data*: Patient does not yet have at least one entry for each of the following inputs: age, gender, temperature, heart rate, respiration rate, systolic blood pressure, and diastolic blood pressure. At the first timepoint that all required inputs include an entry, the most recent entries for all inputs (some of which may have been collected earlier) will be used for the algorithm calculations. There will NOT be a prediction from the algorithm displayed if the patient has insufficient data.

ii) *Not High Risk*: Risk level generated by the respective machine learning algorithm is below the pre-set threshold. This means that the patient is predicted to NOT be at high risk for hemodynamic instability or for respiratory decompensation, as applicable.

iii) *High Risk*: Risk level generated by the respective machine learning algorithm is above the pre-set threshold. This means that the patient is predicted to be at high risk for hemodynamic instability or for respiratory decompensation, as applicable.

Status fields may be updated from “Insufficient Data” (when the minimum required data inputs are not yet received by COViage) to either “Not High Risk” or “High Risk,” but do not toggle between “Not High Risk” to “High Risk.” There is one analysis made per visit, and no analyses are made when there are not sufficient data collected.

### *Software and Algorithm Overview*

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<sup>9</sup> Note: The thresholds for the risk level status fields have been set and were derived from prior algorithm development testing. The clinician cannot change the thresholds for the risk levels.

Each COViage algorithm is a gradient boosted tree algorithm (built with XGBoost) for risk level determination for either hemodynamic instability or respiratory decompensation. Model predictions are generated after all required data are received into the EMR system. At the time age, gender, and all five required vital signs are available, the data are inputted into the software automatically without intervention from the HCP. For each vital sign, the most recent measurement of each vital sign is used. The data are analyzed and risk level determinations for hemodynamic instability and respiratory decompensation are generated based on individual patient data. If the risk level exceeds a predefined threshold, the patient is reported as high risk.

COViage will be implemented as a single software program that contains two algorithms, one for hemodynamic instability risk prediction and one for respiratory decompensation risk prediction. The software is installed by Dascena, Inc. to analyze data from a hospital's EMR system within the context of that system's existing configuration.

The software is non-interventional and does not require any additional inputs from HCP beyond what the software collects from the EMR.

Reports will be provided in file(s) stored on a HIPAA-compliant secure drive to the hospital on an hourly basis for all patients who are being monitored.

COViage requires the following components, which are not provided with the stand-alone software, but must be used in conjunction with COViage:

- User-provided hardware for installation of the software according to the *COViage* Instructions for Use; and
- COViage also requires the use of EMR data and medical device data commonly used in hospital facilities.

The above described COViage is authorized to be accompanied with labeling, entitled “*COViage* Instructions for Use,” (available at <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations>), together with the following product-specific information pertaining to emergency use, which is required to be made available to HCP and patients, respectively:

- Fact Sheet for Healthcare Providers: Emergency Use of the COViage System During the COVID-19 Pandemic
- Fact Sheet for Patients: Emergency Use of the COViage System During the COVID-19 Pandemic

The above described product, when accompanied with the “*COViage* Instructions For Use” (identified above) and the two Fact Sheets (referred to as “authorized labeling”) is authorized to be distributed under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

I have concluded, pursuant to section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of COViage when used as described in the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of this product.

I have concluded, pursuant to section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that the authorized COViage may be effective when used consistent with the Scope of Authorization of this letter (Section II), pursuant to section 564(c)(2)(A) of the Act.

FDA has reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, and concludes that the authorized COViage, as described in the Scope of Authorization of this letter (Section II), meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the COViage must be consistent with, and may not exceed, the terms of this letter, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section IV). Subject to the terms and conditions of this EUA and under the circumstances set forth in the Secretary of HHS's determination under section 564(b)(1)(C) of the Act described above and the Secretary of HHS's corresponding declaration under section 564(b)(1) of the Act, COViage described above is authorized to be used by HCP as a diagnostic aid to assist with the early identification of adult COVID-19 patients (18 years of age or older who are admitted to the hospital) who are likely to be diagnosed with hemodynamic instability or respiratory decompensation, which are common complications associated with COVID-19.

### **III. Waiver of Certain FDA Requirements**

I am waiving the applicable good manufacturing practice requirements otherwise applicable to the manufacture, processing, packing, or holding of products subject to regulations under the Act, including the quality system requirements under 21 CFR Part 820, for COViage during the duration of this EUA.<sup>10</sup>

### **IV. Conditions of Authorization**

Pursuant to section 564(e) of the Act, I am establishing the following conditions on this authorization:

#### Dascena, Inc., as Sponsor of Authorized Product

- A. Dascena, Inc. must comply with the labeling requirements under 21 CFR 801 Subpart A (general labeling provisions) and 21 CFR 801.109 (labeling for prescription devices), as well as those described in Section II of this letter, Scope of Authorization. As such, compliance with unique device identification regulations (see Subpart B of 21 CFR Part 801) is not required under this EUA.

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<sup>10</sup> For purposes of this EUA, compliance with 21 CFR Part 806 (Reports of Corrections and Removals) and 21 CFR Part 807 (Registration and Listing) is not required.

- B. Dascena, Inc. may request changes to this EUA for COViage. Such requests should be submitted to the Office of Health Technology 2 (OHT2)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH) and require appropriate authorization from FDA prior to implementation.
- C. Dascena, Inc. will have a process in place for reporting adverse events of which they become aware to FDA pursuant to 21 CFR Part 803. Dascena, Inc. will establish a process to collect adverse event information from healthcare facility customers.
- D. Dascena, Inc. will notify FDA of any authorized distributor(s)<sup>11</sup> of COViage, including the name, address, and phone number of any authorized distributor(s), and provide authorized distributor(s) with a copy of this EUA and any updates.

Dascena, Inc., and any Authorized Distributor(s)

- E. Dascena, Inc. and authorized distributors will distribute the authorized product with the authorized labeling only to healthcare facilities with HCP who are adequately equipped, trained, and capable of using the COViage according to the authorized labeling.
- F. Dascena, Inc. and authorized distributors will make authorized labeling available on their websites.
- G. Authorized distributors will make Dascena, Inc. aware of any adverse events of which they become aware.
- H. Through a process of software license control, Dascena, Inc. and authorized distributors will maintain records of the healthcare facilities to which they distribute COViage and the number of each product they distribute.
- I. Dascena, Inc. and authorized distributor(s) are authorized to make available additional information relating to the emergency use of the product that is consistent with, and does not exceed, the terms of this letter of authorization.
- J. Dascena, Inc. and authorized distributor(s) will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

Healthcare Facilities

- K. Healthcare facilities using the authorized product must make available to patients the

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<sup>11</sup> “Authorized Distributor(s)” are identified by Dascena, Inc. in an EUA submission as an entity allowed to distribute the device.



accompanying Patient Fact Sheet and make available to HCP the accompanying Healthcare Provider Fact Sheet.

- L. Healthcare facilities using the authorized product must make Dascena, Inc. and FDA aware of any adverse events pursuant to 21 CFR Part 803.
- M. Healthcare facilities will ensure HCP using the authorized product are adequately equipped, trained, capable, and will maintain records of device usage. All HCP using the authorized product must also be trained in and be familiar with the interpretation of results of COViage.

#### Conditions Related to Advertising and Promotion

- N. All descriptive printed matter, including advertising and promotional materials, relating to the use of the authorized COViage shall be consistent with the authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.
- O. No descriptive printed matter, including advertising or promotional materials, relating to the use of the authorized product may represent or suggest that this product is safe or effective for use by HCP as a diagnostic aid to assist with the early identification of adult COVID-19 patients who are likely to be diagnosed with hemodynamic instability or respiratory decompensation, which are common complications associated with COVID-19.
- P. All descriptive printed matter, including advertising and promotional materials, relating to the use of the authorized COViage shall clearly and conspicuously state that:
  - COViage has neither been cleared or approved for the authorized indications for use (Section II of this letter);
  - COViage has been authorized for emergency use by FDA under an EUA; and,
  - COViage 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 Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

#### **V. Duration of Authorization**

This EUA will be effective until the declaration that circumstances exist justifying the authorization of COViage is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Sincerely,

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RADM Denise M. Hinton  
Chief Scientist  
Food and Drug Administration

Enclosures