June 6, 2023

Cue Health Inc.
Roderick Castillo
Sr. Director Regulatory and Clinical Affairs
4980 Carroll Canyon Road Suite 100
San Diego, CA 92121 USA

Re: DEN220028
Trade/Device Name: Cue COVID-19 Molecular Test
Regulation Number: 21 CFR 866.3984
Regulation Name Over-the-counter test to detect SARS-CoV-2 from clinical specimens
Regulatory Class: Class II
Product Code: QWB
Dated: April 27, 2022
Received: May 2, 2022

Dear Roderick Castillo:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your De Novo request for classification of the Cue COVID-19 Molecular Test, an over-the-counter device with the following indications for use:

> The Cue COVID-19 Molecular Test is a nucleic acid amplification assay that is used with the Cue Monitoring System (Cue Cartridge Reader) for the rapid, qualitative detection of SARS-CoV-2 nucleic acid directly in anterior nasal swab specimens from individuals with signs and symptoms of COVID-19 (i.e., symptomatic).
>
> A negative test result is presumptive, and it is recommended these results be confirmed by a lab-based molecular SARS-CoV-2 assay if necessary for patient management. Negative results do not preclude SARS-CoV-2 infections and should not be used as the sole basis for treatment.
>
> Positive results do not rule out co-infection with other respiratory pathogens.
>
> This test is not a substitute for visits to a healthcare provider or appropriate follow-up and should not be used to determine any treatments without provider supervision.
>
> This test is intended to be sold over-the-counter (OTC) for testing of individuals 18 years of age and older.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the Cue COVID-19 Molecular Test, and substantially equivalent devices of this generic type, into Class II under the generic name over-the-counter test to detect SARS-CoV-2 from clinical specimens.

FDA identifies this generic type of device as:

> **Over-the-counter test to detect SARS-CoV-2 from clinical specimens**. An over-the-counter test to detect SARS-CoV-2 from clinical specimens is an in vitro diagnostic device for the detection of SARS-CoV-2 in clinical specimens to aid in the diagnosis of SARS-CoV-2 infection. The device is intended to be used by lay users and without required health care provider (HCP) intervention in home settings or similar environments in which lay users perform testing.

Section 513(f)(2) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This law provides two options for De Novo classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. On December 13, 2016, the 21st Century Cures Act removed a requirement that a De Novo request be submitted within 30 days of receiving an NSE determination. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register announcing the classification.

On May 2, 2022, FDA received your De Novo request for classification of the Cue COVID-19 Molecular Test. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Cue COVID-19 Molecular Test into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the De Novo request, FDA has determined that, for the previously stated indications for use, the Cue COVID-19 Molecular Test can be classified into class II with the establishment of special controls. FDA believes that class II special controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in the following table:

Risks to Health	Mitigation Measures
Risk of false results	Certain labeling information including limitations, device descriptions, performance information, and explanations of procedures as identified in special controls (1), (2), (3), (4), (5). Certain design verification and validation including documentation of device descriptions, certain analytical studies and clinical studies, risk analysis strategies identified in special control (6). Testing of characterized viral samples and labeling information identified in special control (7).
Failure to correctly interpret test results	Certain labeling information including limitations, device descriptions, performance information, and explanations of procedures as identified in special controls (1), (2), (3), (4), (5). Certain design verification and validation including documentation of device descriptions, certain analytical studies and clinical studies, risk analysis strategies identified in special control (6).
Failure to correctly operate the device	Certain labeling information including limitations, device descriptions, performance information, and explanations of procedures as identified in special controls (1), (2), (3), (4), and (5). Certain design verification and validation including documentation of device descriptions, certain analytical studies and clinical studies, risk analysis strategies identified in special control (6).

In combination with the general controls of the FD&C Act, the over-the-counter test to detect SARS-CoV-2 from clinical specimens is subject to the following special controls:

1. The intended use in the labeling required under 21 CFR 809.10 must include a description of the following: analytes the device detects and identifies, the specimen types tested, the results provided to the user, the clinical indications for which the test is to be used, the specific intended population(s), and other conditions of use as appropriate.

2. The intended use of the device must only include indications for testing of respiratory specimens that are appropriate for collection by lay users for which there are performance data that demonstrate lay users can collect specimens without health care provider (HCP) supervision in home settings or similar environments.

3. The labeling required under 21 CFR 809.10(b) must include the following:
   (i) A statement in the intended use that positive results do not rule out co-infection with other respiratory pathogens;
   (ii) Summary instructions and information written in appropriate language for the intended user that includes easy to follow step-by-step instructions for sample testing,

explanation of test results, any warnings and precautions relevant to testing, and FAQs, as required by paragraph (b)(5)(iii);

(iii) Limiting statements including the following, as applicable:

(A) For those devices intended for testing in symptomatic subjects, a specification of the number of days post symptom onset validated for use of the device and/or a range in which the performance of the test is known, where applicable;

(B) Statements that a negative test result does not preclude the possibility of infection with other pathogens, and that a positive test result does not preclude the possibility of co-infection with additional pathogens;

(C) A statement that persons with risk factors for severe disease from respiratory pathogens (e.g., chronic lung or heart disease, compromised immune system, diabetes, and other conditions listed by the CDC) should consult and follow-up with a healthcare provider, who will advise if additional testing or treatment are necessary;

(D) A statement that the test is not a substitute for consultation with a healthcare provider and should not be used to determine any treatments without provider supervision. A statement that the healthcare provider will consider additional information such as the patient's personal medical history and symptoms, current disease prevalence in the community, and additional test results if applicable, to help determine what steps are best for diagnosis and treatment if needed;

(E) A statement that it is especially important to discuss any test results with a healthcare provider if any of the following occur:

- The symptoms persist or worsen;
- The patient has high risk for severe illness based on age or medical condition;
- The patient has a condition that makes it difficult to use the test (e.g., problems with vision, handling the test components, or understanding test instructions or results); or
- The patient is performing this test on behalf of a person who has any of the above conditions;

(F) A statement that accurate results are dependent on adequate product storage, and adherence to the specimen collection and testing procedures. A statement that failure to follow test procedures can lead to incorrect results;

(G) A statement that the test must not be used beyond the expiration date listed on the packaging. A statement that use of expired tests can lead to incorrect results;

(H) A statement that false positive test results are more likely when prevalence of SARS-CoV-2 is low in the community; and

(I) A statement that includes all of the following: The performance characteristics for SARS-CoV-2 were established when [insert predominant strain, subtype, or variant and timeframe] was dominant. Test accuracy may change as new SARS-CoV-2 viruses emerge. Additional testing with a lab-

based molecular test (e.g., PCR) should be considered in situations where a new virus or variant is suspected.

4. The outer box label required under 21 CFR 809.10(a) must include the following:
   (i) A description of who may use the test, including the presence of symptoms, the days post symptom onset and age restrictions (as applicable);
   (ii) A list of the components included with the test;
   (iii) A list of the components required to run the test, but not provided;
   (iv) A statement that persons with risk factors for severe disease from respiratory pathogens should consult and follow-up with a healthcare provider.

5. The device's labeling must include a prominent hyperlink to the manufacturer's public website where the manufacturer must make the information, identified in this section, publicly and prominently available. The information must include, written in language appropriate for the intended user:
   (i) A brief summary of the purpose of the test;
   (ii) Instructions that describe how to appropriately perform the test, interpret the results, and, if applicable, perform follow up testing. The instructions must include the name and intended use of the test, detailed step-by-step instructions of the sample testing procedures, the result(s) interpretation guidance, warnings and limitation statements, information for troubleshooting, and technical assistance with the device (e.g., Help-line contact information).
   (iii) Frequently Asked Questions (FAQ): this document must provide technical and educational information (e.g., What does this test do and not do, Who should and should not use this test, and directions to resources for further information on the disease and epidemiology).
   (iv) Information that demonstrates the performance characteristics established in the studies required under paragraph (b)(6).

6. Design verification and validation must include:
   (i) A detailed device description, including, but not limited to, device components, and a detailed explanation of the methodology, including viral target(s), identification of target detection reagents (e.g., primers, antibodies), internal controls, and computational path from collected raw data to reported result (e.g., how collected raw signals are converted into a reported signal and result), as applicable to the detection method and device design;
   (ii) Detailed documentation of data from a prospective multisite clinical study with a design and performance that is appropriate for the intended use of the device, including performance estimates derived from a sufficient number of samples from the intended use population for each claimed specimen type. Results must be obtained from geographically diverse locations, such that the performance of the test device is appropriately representative of all present, circulating strains of the claimed viral analyte(s) at the time of the study and submission. Additionally, the clinical study must include diversity across the intended use population and across the clinical range

of the claimed viral analyte. The clinical study must be performed in the intended use setting (e.g., at home or a home-like environment). The results obtained with the candidate device must be compared to results obtained using a molecular comparator method that FDA has determined to be appropriate. Detailed documentation must include the clinical study protocol (including a predefined statistical analysis plan), study report, testing results, and results of all statistical analyses;

(iii) The clinical study designs, including number of samples tested, must be sufficient such that the lower bound of the two-sided 95% confidence interval of the positive percent agreement with the comparator must be greater than 70% and additional and appropriate risk mitigation measures are established (e.g., presumptive negative results, serial testing).

(iv) Detailed documentation of analytical studies, including those demonstrating the limit of detection (LoD), inclusivity (including relevant variants), cross-reactivity, microbial interference, interfering substances, competitive inhibition, specimen stability, within-lab precision, hook effect, carryover, cross contamination, as applicable;

(v) Detailed documentation and characterization (e.g., determination of the identity, supplier, purity, and stability) of all critical reagents and protocols for maintaining product integrity throughout its labeled shelf-life, i.e., reagent stability studies. Data and protocols, including acceptance criteria, from a multi-lot reagent stability study must include testing of samples with challenging analyte concentration, be provided as part of the regulatory submission and must include in-use/open-kit stability, shipping stability, and freeze-thaw stability (as applicable);

(vi) Risk analysis and documentation demonstrating how risk control measures are implemented to address device system hazards, such as Failure Modes Effects Analysis and/or Hazard Analysis.

(A) This documentation must include a detailed description of a protocol (including all procedures and methods) for the continuous monitoring, identification, and handling of genetic mutations and/or novel isolates or strains (*e.g.,* regular review of published literature and periodic in silico analysis of target sequences to detect possible mismatches). Protocols must include plans to update labeling with additional performance data. All results of this protocol, including any findings, must be documented and must include any additional data analysis that is requested by FDA in response to any performance concerns identified under this section or identified by FDA during routine evaluation. Additionally, if requested by FDA, these evaluations must be submitted to FDA for FDA review within 48 hours of the request and any results that are reasonably interpreted to support the conclusion that novel SARS-CoV-2 strains or isolates impact the stated expected performance of the device must be sent to FDA immediately to the email provided in FDA's request;

(B) This must include detailed documentation that demonstrates the effectiveness of risk control measures and device robustness, including the entire testing procedure from sampling to result interpretation, based

on results from the following studies, as applicable per the intended use of the test device: usability studies, user label comprehension, and flex studies;

(vii) For devices with associated software or instrumentation, documentation must include a detailed description of device software, including software applications and hardware-based devices that incorporate software. The detailed description must include documentation of verification, validation, and hazard analysis and risk assessment activities, including an assessment of the impact of threats and vulnerabilities on device functionality and end users/patients as part of cybersecurity review; and

(viii) For devices intended for the detection of SARS-CoV-2 for which an FDA recommended reference material and/or test panel is available, the performance results of an analytical study testing the FDA recommended reference material. Detailed documentation must be kept of that study and its results, including the study protocol, study report for the proposed intended use, testing results, and results of all statistical analyses.

7. If one of the actions listed in section 564(b)(1)(A)–(D) of the Federal Food, Drug, and Cosmetic Act occurs with respect to one or more of the analytes claimed in the intended use, or if the Secretary of Health and Human Services (HHS) determines, under section 319(a) of the Public Health Service Act, that a disease or disorder presents a public health emergency, or that a public health emergency otherwise exists, with respect to SARS-CoV-2:

   (i) Within 30 days from the date that FDA notifies manufacturers that characterized samples are available for test evaluation, the manufacturer must have testing performed on the device with those samples in accordance with a standardized protocol considered and determined by FDA to be acceptable and appropriate; and

   (ii) Within 60 days from the date that FDA notifies manufacturers that characterized samples are available for test evaluation and continuing until 3 years from that date, the results of the emergency analytical reactivity testing, including the detailed information for the samples tested as described in the certificate of authentication, must be included in a tabular format on the hyperlink the manufacturer's public website as described in paragraph (b)(5).

Although this letter refers to your product as a device, please be aware that some granted products may instead be combination products. If you have questions on whether your product is a combination product, contact CDRHProductJurisdiction@fda.hhs.gov.

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus,

persons who intend to market this device type must submit a premarket notification containing information on the over-the-counter test to detect SARS-CoV-2 from clinical specimens.

Please be advised that FDA's decision to grant this De Novo request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD&C Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); 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-reportingcombination-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 FD&C Act; 21 CFR 1000-1050).

A notice announcing this classification order will be published in the Federal Register. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the De Novo request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

For comprehensive regulatory information about medical devices and radiation-emitting products, 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-comprehensiveregulatory-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).

If you have any questions concerning the contents of the letter, please contact John McManus at john.mcmanus@fda.hhs.gov.

Sincerely,

Uwe Scherf -S

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