



Quidel Corporation
Xiaoxi Wang
Senior Regulatory Affairs Specialist
10165 McKellar Court
San Diego, California 92121

March 8, 2023

Re: DEN220039

Trade/Device Name: Sofia 2 SARS Antigen+ FIA, Sofia 2 SARS Antigen+ FIA Control Swab Set

Regulation Number: 21 CFR 866.3982

Regulation Name: Simple point-of-care device to directly detect SARS-CoV-2 viral targets from clinical specimens in near-patient settings

Regulatory Class: Class II

Product Code: QVF

Dated: June 14, 2022

Received: June 16, 2022

Dear Xiaoxi Wang:

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 Sofia 2 SARS Antigen+ FIA, Sofia 2 SARS Antigen+ FIA Control Swab Set, a prescription device with the following indications for use:

The Sofia 2 SARS Antigen+ FIA is a lateral flow immunofluorescent sandwich assay that is used with the Sofia 2 instrument for the rapid, qualitative detection of SARS-CoV-2 nucleocapsid protein antigens directly in anterior nasal swab specimens from individuals with signs and symptoms of upper respiratory infection (i.e., symptomatic) when testing is started within 6 days of symptom onset. The test is intended for use as an aid in the diagnosis of SARS-CoV-2 infections (COVID-19) in symptomatic individuals when tested at least twice over three days with at least 48 hours between tests.

The test does not differentiate between SARS-CoV and SARS-CoV-2.

A negative test result is presumptive, and it is recommended these results be confirmed by a molecular SARS-CoV-2 assay. Negative results do not preclude SARS-CoV-2 infections and should not be used as the sole basis for treatment or other patient management decisions.

Positive results do not rule out co-infection with other respiratory pathogens.

Performance characteristics for SARS-CoV-2 were established during the 2021-2022 SARS-CoV-2 pandemic when SARS-CoV-2 Omicron was the predominant SARS-CoV-2 variant in circulation. When other SARS-CoV-2 virus variant are emerging, performance characteristics may vary.

This test is intended for prescription use only and can be used in Point-of-Care settings.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the Sofia 2 SARS Antigen+ FIA, Sofia 2 SARS Antigen+ FIA Control Swab Set, and substantially equivalent devices of this generic type, into Class II under the generic name simple point-of-care device to directly detect SARS-CoV-2 viral targets from clinical specimens in near-patient settings.

FDA identifies this generic type of device as:

Simple point-of-care device to directly detect SARS-CoV-2 viral targets from clinical specimens in near-patient settings. A simple point-of-care device to detect SARS-CoV-2 viral targets directly from clinical specimens in near-patient settings is an in vitro diagnostic device for the direct detection of SARS-CoV-2 in clinical specimens and is intended as an aid in the diagnosis of SARS-CoV-2 infections (COVID-19). The device is simple to use and does not involve sample manipulation, transportation of the sample to another functional area (e.g., a central laboratory or other specialized area), or measurement of reagents or analytes that could be affected by conditions such as sample turbidity or cell lysis. The design and procedures of the device are appropriate for use by healthcare professionals in near-patient settings outside a centralized laboratory.

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 June 16, 2021, FDA received your De Novo requesting classification of the Sofia 2 SARS Antigen+ FIA, Sofia 2 SARS Antigen+ FIA Control Swab Set. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Sofia 2 SARS Antigen+ FIA, Sofia 2 SARS Antigen+ FIA Control Swab Set 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 Sofia 2 SARS Antigen+ FIA, Sofia 2 SARS Antigen+ FIA Control Swab Set can be classified in class II with the establishment of special controls for class II. 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
False results	Certain labeling information including limitations, device descriptions, explanations of procedures and performance information identified in special controls (1) and (4). Use of certain specimen collection devices identified in special control (3). Certain design verification and validation including documentation of device descriptions, certain analytical studies and clinical studies, risk analysis strategies identified in special control (5). Testing of characterized viral samples and labeling information identified in special control (6).
Failure to correctly interpret test results	Certain labeling information including limitations, device descriptions, explanations of procedures and performance information identified in special controls (1) and (4). Use of certain specimen collection devices identified in special control (3). Certain design verification and validation including documentation of device descriptions, certain analytical studies and clinical studies, risk analysis strategies identified in special control (5).
Failure to correctly operate the device	Certain labeling information including limitations, device descriptions, explanations of procedures and performance information identified in special controls (1), (2), and (4). Use of certain specimen collection devices identified in special control (3).

In combination with the general controls of the FD&C Act, the simple point-of-care device to directly detect SARS-CoV-2 viral targets from clinical specimens in near-patient settings 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), the intended use locations including testing location(s) where the device is to be used (if applicable), and other conditions of use as appropriate.
2. The intended use of the device must only include indications for testing of respiratory specimens.
3. If sample collection devices are used, any sample collection device used must be FDA-cleared, -approved, or -classified as 510(k) exempt (standalone or as part of a test system) for the collection of specimen types claimed by this device; alternatively, the sample collection device must be cleared in a premarket submission as a part of this device.

4. The labeling required under 21 CFR 809.10(b) must include:
- (i) A detailed and comprehensive device description, including reagents, instruments, ancillary materials, all control elements, and a detailed explanation of the methodology, including all pre-analytical methods for processing of specimens;
 - (ii) Detailed descriptions of the performance characteristics of the device for each specimen type claimed in the intended use based on analytical studies including the following, as applicable: Limit of Detection, inclusivity, cross-reactivity, interfering substances, competitive inhibition, hook-effect, carryover/cross contamination, specimen stability, precision, reproducibility, human factors analysis, flex studies, and clinical studies;
 - (iii) Detailed descriptions of the test procedure(s), the interpretation of test results for clinical specimens, and acceptance criteria for any quality control testing;
 - (iv) A statement in the intended use that positive results do not preclude co-infection with bacteria or other viruses and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions;
 - (v) Detailed instructions for minimizing the risk of user's exposure to infectious microbial agents that may be present in test specimens and those used as control materials;
 - (vi) Detailed instructions for minimizing the risk of generating false positive test results due to carry-over contamination from positive test specimens and/or positive control materials, as applicable to the design of the test device;
 - (vii) A brief reference sheet (Quick Reference Instructions) for the intended user(s) that includes, at a minimum, the name and intended use of the test, easy to follow step-by-step instructions of all control and sample testing procedures for the claimed sample types, including graphic illustrations targeted towards lay users (as applicable), the result(s) interpretation guidance, warnings and limitation statements, toxicology information and safety considerations for any hazardous materials, information for troubleshooting (e.g., Frequently Asked Questions), and technical assistance with the device (e.g., Help-line contact information);
 - (viii) Limiting statements indicating that:
 - (A) For those devices intended for testing in symptomatic subjects, a statement that specifies 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;
 - (B) A negative test result does not preclude the possibility of infection with other bacteria or viruses;
 - (C) The test results should be interpreted in conjunction with other clinical and laboratory data available to the healthcare provider (as applicable);
 - (D) There is a risk of erroneous results (i.e., false negatives) due to the presence of novel, emerging respiratory viral variants (e.g., specific strains or isolates);
 - (E) False positive test results are more likely when prevalence of upper respiratory infection is low in the community;
 - (F) Accurate results are dependent on adequate specimen collection, transport, storage, and processing (as applicable). Failure to observe proper procedures in any one of these steps can lead to incorrect results;
 - (G) This test should not be used beyond the expiration date listed on the packaging. Use of expired tests can lead to incorrect results;
 - (H) The performance characteristics for that analyte were established when [insert predominant strain, subtype, or variant] was prevalent and that due to the propensity

of the virus to mutate, new strains emerge over time which may affect the performance of this device and have serious public health implications. Additional testing with a molecular test and/or sequencing should be considered in situations where a new virus strain or variant is suspected.

5. Design verification and validation must include:

- (i)** A detailed device description, including device components, ancillary reagents required but not provided, and a detailed explanation of the methodology, including viral target(s), identification of target detection reagents (e.g., primers, antibodies), internal and external 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 a geographically diverse population, such that the performance of the test device is appropriately representative of all present, circulating strains of the target respiratory virus, at the time of the study and submission. The clinical study must be consistent with and support the intended use population and intended operators (as applicable) and must be conducted in a representative intended use setting. The clinical study must compare the results of the candidate device to results obtained using an FDA accepted molecular comparator method. 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 to meet either of the following criteria:
 - (A)** The lower bound of the two-sided 95% confidence interval of the positive percent agreement must be greater than or equal to 80% and appropriate risk mitigation measures are established (e.g., presumptive negative results); or
 - (B)** The lower bound of the two-sided 95% confidence interval of the positive percent agreement must be greater than or equal to 70% and additional and appropriate risk mitigations measures are established (e.g., presumptive negative results and 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, and site-to-site reproducibility, 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 a samples with adequately 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). The shelf-life stability assessment must include the most challenging sample type identified in the device's intended use and are formulated using whole virus;

- (vi) Final release criteria to be used for manufactured test lots with appropriate evidence that lots released at the extremes of the specifications will meet the claimed analytical and clinical performance characteristics as well as the stability claims;
 - (vii) 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. Results that are reasonably interpreted to support the conclusion that novel respiratory pathogen strains or isolates impact the stated expected performance of the device must be sent to FDA immediately;
 - (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: human factors engineering (*e.g.*, usability studies and user label comprehension), flex studies, and performance with weakly-reactive samples in the hands of the intended user(s);
 - (viii) 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
 - (ix) For devices intended for the detection and identification of an analyte for which an FDA recommended reference material is available, design verification and validation must include 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.
6. 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 one or more of the analytes claimed in the intended use:
- (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;
- (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 as part of the device's labeling in a tabular format.

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 simple point-of-care device to directly detect SARS-CoV-2 viral targets from clinical specimens in near-patient settings.

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/combo-products/guidance-regulatory-information/postmarketing-safety-reporting-combo-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 Eric Kong at (301) 837-7362.

Sincerely,

Uwe Scherf, M.Sc., Ph. D.
Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health