



Nano-Ditech Corporation
James Chang
QA/RA Director
259 Prospect Plains Rd, Bldg K
Cranbury, New Jersey 08512

January 23, 2024

Re: K231187

Trade/Device Name: Nano-Check COVID-19 Antigen Test
Regulation Number: 21 CFR 21 CFR 866.3982
Regulation Name: Simple Point-Of-Care Device To Directly Detect Sars-Cov-2 Viral Target From
Clinical Specimens In Near-Patient Setting
Regulatory Class: Class II
Product Code: QVF
Dated: January 10, 2024
Received: January 10, 2024

Dear James Chang:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm> identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (<https://www.fda.gov/media/99812/download>) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (<https://www.fda.gov/media/99785/download>).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems>.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, 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-comprehensive-regulatory-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).

Sincerely,

Silke

Schlottmann -S

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Schlottmann -S
Date: 2024.01.23 15:46:32 -05'00'

Silke Schlottmann, Ph.D.

Deputy Assistant Director

Bacteriology Respiratory and Medical Countermeasures Branch

Division of Microbiology Devices

OHT7: Office of In Vitro Diagnostics

Office of Product Evaluation and Quality

Center for Devices and Radiological Health

Indications for Use

510(k) Number (if known)

K231187

Device Name

Nano-Check COVID-19 Antigen Test

Indications for Use (Describe)

The Nano-Check COVID-19 Antigen Test is a lateral flow immunochromatographic assay for the rapid, qualitative detection of SARS-CoV-2 nucleoprotein 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 4 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 either: tested at least twice over three days with at least 48 hours between tests; or when tested once, and negative by the Nano-Check™ COVID-19 Antigen Test and followed up with a molecular test.

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

A negative test result is presumptive, and it is recommended these results be confirmed by a molecular SARS-CoV-2 assay. Positive results do not rule out co-infection with other bacteria or viruses and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

Performance characteristics for SARS-CoV-2 were established during the 2022-2023 SARSCoV-2 pandemic when SARS-CoV-2 Omicron was the predominant SARS-CoV-2 variant in circulation. When other SARS-CoV-2 virus variants are emerging, performance characteristics may vary.

Type of Use (Select one or both, as applicable)

☒ Prescription Use (Part 21 CFR 801 Subpart D)

☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary
Nano-Check™ COVID-19 Antigen Test
(K231187)

I. Submitter

Nano-Ditech Corporation
259 Prospect Plains Rd., Bldg. K
Cranbury, NJ 08512 USA

Contact Person: James B Chang (jchang@nanoditech.com)

Phone: 1-609-409-3300

Date Prepared: June 29, 2023

II. Device

A. Trade, Proprietary, and Established Name: Nano-Check™ COVID-19 Antigen Test
(Common name: Rapid COVID-19 Antigen Test)

B. Product Code: QVF

C. Classification: Class II

D. Regulation Number: 21 CFR 866.3982

E. Classification Name: Simple Point-Of-Care Device to directly detect SARS-CoV-2 viral target from clinical specimens in Near-Patient setting

F. Panel: MI-Microbiology

G. Purpose for Submission: New device 510(k) clearance for the Nano-Check™ COVID-19 Antigen Test

H. Measurand: Nucleocapsid protein antigen from SARS-Coronavirus 2 (SARS-CoV-2)

I. Type of Test: Qualitative lateral flow immunoassay

III. Predicate Device

A. Trade Name: Sofia 2 SARS Antigen+ FIA, Sofia 2 SARS Antigen+ FIA Control Swab Set

B. De Novo Number: DEN220039 (granted March 8, 2023)

C. Product Code: QVF

This predicate has not been subject to a design-related recall. No reference devices were used in this submission.

IV. Indications for Use**A. Intended Use(s):**

See Indications for Use below.

B. Indication(s) for Use:

The Nano-Check™ COVID-19 Antigen Test is a lateral flow immunochromatographic assay for the rapid, qualitative detection of SARS-CoV-2 nucleoprotein 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 4 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 either: tested at least twice over three days with at least 48 hours between tests; or when tested once, and negative by the Nano-Check™ COVID-19 Antigen Test and followed up with a molecular test.

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

A negative test result is presumptive, and it is recommended these results be confirmed by a molecular SARS-CoV-2 assay. Positive results do not rule out co-infection with other bacteria or viruses and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

Performance characteristics for SARS-CoV-2 were established during the 2022-2023 SARS-CoV-2 pandemic when SARS-CoV-2 Omicron was the predominant SARS-CoV-2 variant in circulation. When other SARS-CoV-2 virus variants are emerging, performance characteristics may vary.

C. Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D. Special Instrument Requirements:

N/A

V. Device/System Characteristics:**A. Device Description :**

The Nano-Check™ COVID-19 Antigen Test is an immunochromatographic assay for detection of extracted SARS-CoV-2 nucleoprotein antigens in human anterior nasal swab specimens.

The assay kit consists of 20 test cassette devices, 20 reagent tubes containing extraction buffer for Set A or 20 empty reagent tubes and 20 ampules containing extraction buffer for Set B, 20 anterior nasal specimen collection swabs, one positive control swab, one negative control swab and an Instructions for Use/Quick Reference Instruction. An external positive control swab is used with recombinant SARS-CoV-2 nucleocapsid dried onto the swab and an external negative control swab contains blank universal viral transport media dried on the swab. The kit should be stored at 2°C - 30°C.

B. Principles of Operations :

The Nano-Check™ COVID-19 Antigen Test is based on antigen-antibody binding technology.

The viral antigens are released from the specimen during the extraction step. Two drops of the extracted sample are added to the cassette that contains a testing strip. During the migration through the strip, the viral antigens bind to anti-SARS-CoV-2 antibodies conjugated to indicator particles.

The antigen-antibody complexes migrate through the test strip and are captured by reagents on the membrane to form test lines. There are a test line detecting SARS-CoV-2 antigens and a control line serving as the internal control for the assay.

The test is visually read 15 minutes after the sample is added to the cassette.

Results Interpretation:

- The presence of two lines in the cassette, one for SARS-CoV-2 next to the letter “Ag” and one control line next to the letter “C”, indicates SARS-CoV-2 positive result.
- The presence of the control line in the cassette next to the letter “C” without the test line indicates a negative result.
- The absence of a “C” line, regardless of whether the test line is present or absent, represents an invalid result.

VI. Comparison of Technological Characteristics with the Predicate Device

The table below compares the Nano-Check™ COVID-19 Antigen Test to the predicate devices of Sofia 2 SARS Antigen+ FIA, Sofia 2 SARS Antigen+ FIA Control Swab Set.

Table 1. Comparison with Predicate(s)

	Similarities and Differences	
Items	Candidate	Predicate (DEN220039)
Device Trade Name	Nano-Check™ COVID-19 Antigen Test	Sofia 2 SARS Antigen+ FIA, Sofia 2 SARS Antigen+ FIA Control Swab Set

Intended Use/ Indication For Use	The Nano-Check™ COVID-19 Antigen Test is a lateral flow immunochromatographic assay 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 4 days of symptom onset.	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 either: tested at least twice over three days with at least 48 hours between tests; or when tested once, and negative by the Nano-Check™ COVID-19 Antigen Test and followed up with a molecular test.	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.	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. Positive results do not rule out co-infection with other bacteria or viruses and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Performance characteristics for SARS-CoV-2 were established during the 2022-2023 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.	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.
Sample Type	Anterior nasal swab	Same
Test Result	Qualitative	Same

Test Target	Nucleocapsid protein of SARS-CoV-2	Same
Test Design /Principle	Lateral flow immunochromatographic	Same
Test Time	15 minutes	Same
Reading Result	Visual determination of the presence or absence of colored line(s) for the test line(s) and a colored line on the test strip indicate the presence of SARS-CoV-2	Sofia 2 scans the test strip and measures the fluorescent signal by processing the results using method specific algorithms. Sofia 2 displays the test results (Positive, Negative, or Invalid) on the screen.

VII. Performance Data

A. Analytical Performance

1. Precision/Reproducibility:

a) Precision and Repeatability

The repeatability study was undertaken by two operators with each operator conducting 24 test runs over a 12-days period, resulting in total 96 replicates per level. The study employed blind sample panels comprising true negative (TN), high negative (HN, $0.1 \times \text{LoD}$), low positive (LP, $1 \times \text{LoD}$), and moderate positive (MP, $4 \times \text{LoD}$) samples. The precision testing was conducted according to the Package Insert and the qualitative results are summarized in Table 2 below.

Table 2. Precision and Repeatability Study-Summary Result

Run	True negative		High Negative		Low Positive		Moderate Positive	
	1	2	1	2	1	2	1	2
Run 1	24/24	24/24	24/24	23/24	24/24	23/24	24/24	24/24
Run 2	24/24	24/24	23/24	23/24	22/24	23/24	24/24	24/24
Total	48/48	48/48	47/48	46/48	46/48	46/48	48/48	48/48
% Agreement	100%	100%	97.9%	95.8%	95.8%	95.8%	100%	100%
95% CI	[92.6 - 100%]	[92.6 - 100%]	[89.1 - 99.6%]	[86.0 - 98.9%]	[86.0 - 98.9%]	[86.0 - 98.9%]	[92.6 - 100%]	[92.6 - 100%]
% Agreement	100%		96.9%		95.8%		100%	
95% CI	96.2 - 100%		91.2 - 98.9%		89.8 - 98.4%		96.2 - 100%	

The study results demonstrated a 100% agreement between the test results and sample properties for MP samples and TN samples. Additionally, there was over 95% agreement for LP samples and HN samples.

b) Reproducibility

The reproducibility study was designed to evaluate site-to-site, operator-to-operator, and level-to-level variability and demonstrate that the Nano-Check™ COVID-19 Antigen Test can be performed consistently and correctly. This study was conducted at 4 distinct sites, each with two (2) or three (3) different operators, testing three (3) test lots, using a coded panel of contrived samples consisting of a true negative (TN), a high negative sample (HN, 0.1x LoD), a low positive (LP, 1.0 x LoD) and a medium positive (MP, 3.0 x LoD). A total of 7 assigned operators at 3 POC sites and 3 operators in the internal site each tested using 60 coded samples (TN: 15, HN: 15, LP: 15 and MP:15 samples, respectively) over five nonconsecutive days. The summary of results is presented in Table 3 below.

Table 3. Reproducibility Study- Summary Result

Sample	Site 1 Agreement (Count)	Site 2 Agreement (Count)	Site 3 Agreement (Count)	Site 4 Agreement (Count)	All Sites	
					Agreement (Count)	95% CI
True Negative	100% (45/45)	100% (30/30)	100% (30/30)	100% (45/45)	100% (150/150)	97.5-100.0
High Negative	100% (45/45)	100% (30/30)	100% (30/30)	100% (45/45)	100% (150/150)	97.5-100.0
Low Positive	93.3% (42/45)	100% (30/30)	100% (30/30)	100% (45/45)	95% (147/150)	94.3-99.3
Medium Positive	100% (45/45)	100% (30/30)	100% (30/30)	100% (45/45)	100% (150/150)	97.5-100.0

All samples tested in the reproducibility study generated no significant difference in performance between sites.

2. Linearity:

This section is not applicable as this test device is a qualitative assay.

3. Cross-reactivity (Analytical Specificity):

a) Cross-reactivity and Microbial Interference Study

Cross-Reactivity and Interference study of the Nano-Check™ COVID-19 Antigen Test was conducted with 43 potential cross-reactive or interfering pathogens of bacteria (10), fungi (1), virus (31), and negative matrix (1). Each microorganism was tested in three (3) replicates in the absence or presence of 2xLoD of SARS-CoV-2 Omicron Variant (hCoV-19/USA/MD-HP20874/2021). The concentrations of potentially interfering microorganisms tested and the results from the cross-reactivity study are presented in Table 4 below.

Table 4. Results of Cross-Reactivity/Microbial Interference

Microorganism (Strain)	Concentration Tested	Positive Sample (# Positive/ # Tested)	Negative Sample (# Positive/ # Tested)	Cross-Reactivity/ Microbial Interference
Human Coronavirus, 229E	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Human Coronavirus, OC43	4.45×10^4 TCID ₅₀ /mL	3/3	0/3	No
Coronavirus, NL63	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
MERS-CoV, EMC/2012,	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
SARS-CoV, Urbani	1.0×10^5 PFU/mL	3/3	0/3	No
Adenovirus Type 2, C	1.0×10^5 TCID/mL	3/3	0/3	No
Human Adenovirus 1	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Human Mastadenovirus B, Type 7	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Human Metapneumovirus, TN/83-1211	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Human Parainfluenza Virus 1, HPIV1/FRA/29221106/2009	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Human Parainfluenza Virus 2, Greer	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Human Parainfluenza Virus 3, NIH 47885	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Human Parainfluenza Virus 4B, 19503	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Influenza A Virus/New Caledonia/20/1999 (H1N1)	1.0×10^5 CEID ₅₀ /mL	3/3	0/3	No
Influenza A Virus/A/San Diego/1/2009 (H1N1) pdm09	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Influenza A Virus/A/Victoria/361/2011 (H3N2)	1.0×10^5 CEID ₅₀ /mL	3/3	0/3	No
Influenza A Virus/A/Wisconsin/67/2005 (H3N2)	1.0×10^5 CEID ₅₀ /mL	3/3	0/3	No
Influenza B Virus/B/Brisbane/60/2008 (Victoria Lineage)	1.0×10^5 CEID ₅₀ /mL	3/3	0/3	No
Influenza B Virus/B/Texas/06/2011 (Yamagata Lineage)	1.0×10^5 CEID ₅₀ /mL	3/3	0/3	No
Influenza B Virus/B/GL/1739/54	1.0×10^5 CEID ₅₀ /mL	3/3	0/3	No
Enterovirus 71 (EV-71), MP4	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No

Enterovirus Species D Type 68, USA/2018-23087	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Human Respiratory Syncytial Virus, A/Long	1.0×10^5 PFU/mL	3/3	0/3	No
Human Respiratory Syncytial Virus A/2001/2-20	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Human Respiratory Syncytial Virus B/PR-348-00 MISC082	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Human Respiratory Syncytial Virus A/1998/12-21	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Rhinovirus 20, 15-CV19	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Measles Virus, Edmonston	1.7×10^4 TCID ₅₀ /mL	3/3	0/3	No
Mumps Virus, MuV/Iowa.US/2006	1.0×10^5 TCID ₅₀ /mL	3/3	0/3	No
Coxsackie Virus B4	1×10^5 U/mL TCID ₅₀	3/3	0/3	No
Epstein-Barr (Strain: B95-8)	1.0×10^5 cp/mL	3/3	0/3	No
<i>Haemophilus influenzae</i> , (Type b; Eagan)	1.0×10^6 CFU/mL	3/3	0/3	No
<i>Streptococcus pneumoniae</i> , (Strain Z022, 19F)	1.0×10^6 CFU/mL	3/3	0/3	No
<i>Streptococcus pyogenes</i> Strain Bruno	1.0×10^6 CFU/mL	3/3	0/3	No
<i>Streptococcus salivarius</i>	1.0×10^6 CFU/mL	3/3	0/3	No
<i>Candida albicans</i> , Z006	1.0×10^6 CFU /mL	3/3	0/3	No
<i>Bordetella pertussis</i>	1.0×10^6 CFU /mL	3/3	0/3	No
<i>Mycoplasma pneumoniae</i>	1.0×10^6 CFU /mL	3/3	0/3	No
<i>Chlamydomphila pneumoniae</i>	1.0×10^6 IFU/mL	3/3	0/3	No
<i>Legionella pneumophila</i> subsp. <i>pneumophila</i>	1.0×10^6 CFU /mL	3/3	0/3	No
<i>Staphylococcus aureus</i> (Strain MRSA; COL)	1.0×10^6 CFU/mL	3/3	0/3	No
<i>Staphylococcus epidermidis</i> (Strain MRSE; RP62A)	1.0×10^6 CFU/mL	3/3	0/3	No
Pooled human nasal wash	N/A	3/3	0/3	No
Coronavirus HKU1 was not tested for cross-reactivity due to lack of availability. Twenty (20) clinical specimens containing Coronavirus HKU1 were tested, and all resulted as negative, additional cross-reactivity wet testing was not required.				

The study results showed that the Nano-Check™ COVID-19 Antigen Test would not react with nor be interfered by listed pathogens, high prevalence disease agents, and normal or pathogenic flora that are reasonably likely to be encountered in the clinical specimen.

b) Endogenous/Exogenous Interference

The Endogenous/Exogenous interference study of the Nano-Check™ COVID-19 Antigen Test was conducted using medically relevant endogenous and exogenous interferents. The SARS-CoV-2 Omicron Variant (hCoV-19/USA/MD-HP20874/2021) was diluted in negative clinical matrix to 3x LoD and the potentially interfering substance was spiked to the concentration presented in Table 5 below. The effects of the substances were evaluated by the agreement with the expected negative or positive results. Three (3) replicates were tested for each sample prepared.

Table 5. Results of Endogenous/Exogenous Interference Study

Substances	Active ingredients	Interferent Conc.	Interference
Beclomethasone dipropionate	Beclomethasone dipropionate	$5.04 \times 10^0 \mu\text{g/mL}$	No
Budesonide Nasal Spray	Budesonide	15% v/v	No
Dexamethasone	Dexamethasone	$1.20 \times 10^1 \mu\text{g/mL}$	No
Flunisolide	Flunisolide	$8.70 \times 10^1 \mu\text{g/mL}$	No
Hand Sanitizer Gel	Ethyl alcohol 70%	1% v/v	No
Hand Soap Fresh Breeze Scent	N/A	10% v/v	No
Histaminum 30C	Histaminum hydrochloricum, HPUS	5% w/v	No
Homeopathic Allergy Nasal Spray	N/A	15% v/v	No
Molnupiravir	Molnupiravir	$4.20 \times 10^4 \mu\text{g/mL}$	No
Mucin (Bovine submaxillary Glands, Type I-S)	Mucin protein	2.5 mg/mL	No
Mupirocin	Mupirocin	$1.50 \times 10^0 \mu\text{g/mL}$	No
Nasacort Allergy 24HR	Triamcinolone acetonide	15% v/v	No
Nasal Allergy Relief	Cardiospermum, Galphimia glauca, Luffa operculata Sabadilla	15% v/v	No
Nasal Drops	Xylometazoline	15% v/v	No
Nasal Spray 1	Oxymetazoline	15% v/v	No
Nasal Spray 2	Cromolyn sodium	15% v/v	No
Nasal Spray 3	Fluticasone propionate	15% v/v	No
Nasal Spray 4	Phenylephrine HCl	15% v/v	No
NasoGEL (Gel Spray)	Sodium Hyaluronate, Allantoin, Sodium chloride, Methylparaben, Propylparaben	15% v/v	No

Nasonex 24 hr Allergy	Mometasone furoate monohydrate	15% v/v	No
Oseltamivir Phosphate	Oseltamivir Phosphate	$3.99 \times 10^{-1} \mu\text{g/mL}$	No
Human Neutrophils	N/A	$5 \times 10^6 \text{ cells/mL}$	No
Remdesivir	Remdesivir	$2.40 \times 10^3 \mu\text{g/mL}$	No
Sore Throat (Oral Pain Reliever spray)	Phenol, Menthol	15% v/v	No
Sore throat Lozenges	Benzocaine, Menthol	15% w/v	No
Tobramycin	Tobramycin	$3.30 \times 10^1 \mu\text{g/mL}$	No
Whole Blood	N/A	2.5%	No
ZICAM® Oral mist	Zincum aceticum, Zincum gluconicum	15% v/v	No
Zinc Lozenges	Zincum gluconicum	5% w/v	No

The study results showed no interference with positive or negative results for the Nano-Check™ COVID-19 Antigen Test at the concentrations tested in the presented study.

c) Biotin Interference

The samples containing 3 x LoD concentrations of SARS-CoV2 (2019-nCoV/USA-WA1/2020) at different concentrations of biotin were tested in 5 replications. The Biotin Interference Study for Nano-Check™ COVID-19 Antigen Test showed that there was no interference up to 3,500 ng/mL of biotin in the samples so no limitation in the labeling regarding the biotin interference was necessary.

4. Assay Reportable Range:

This section is not applicable as this test device is a qualitative assay.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

a) Internal Quality Control

The Nano-Check™ COVID-19 Antigen Test contains built in internal assay control. The appearance of the control line on the test ensures that sufficient flow of the sample occurred during the assay.

b) External Quality Controls

The Nano-Check™ COVID-19 Antigen Test kit contains one positive external control swab and one negative external control swab that allow for monitoring of the performance of the assay. The positive

control swab contains recombinant SARS-CoV-2 nucleocapsid and negative control swab contains blank Universal Viral Transport media.

c) External Controls Lot-to-Lot Reproducibility

The lot-to-lot reproducibility for the external positive and negative control swabs was evaluated using three lots of external controls with three operators. The results from the study are summarized in Table 6 below.

Table 6. External Controls Lot-to-Lot Reproducibility Study Results

External control	Lot No.	Test result (Test count / Total replication)		
		Positive count	Negative count	Agreement
Positive External Control	0804-CN-2B01-P	10 / 10	0 / 10	100%
	0804-CN-2D29-P	10 / 10	0 / 10	100%
	0804-CN-2E04-P	10 / 10	0 / 10	100%
Negative External Control	0804-CN-2B01-N	0 / 10	10 / 10	100%
	0804-CN-2D29-N	0 / 10	10 / 10	100%
	0804-CN-2E04-N	0 / 10	10 / 10	100%

All lots of external controls generated 100% agreement with the expected results.

d) Specimen Stability

Two test samples were prepared for the specimen stability study: a negative sample (consisting of pooled human nasal wash with no analyte) and a low positive sample (containing a diluted SARS-CoV-2 Omicron Variant, hCoV-19/USA/MD-HP20874/2021, sample at 2 x LoD in the negative pooled human nasal wash). Swabs were spiked with 50 µL of each sample and subjected to two different temperature conditions: room temperature (23.5°C), high room temperature (30 °C) and 2°C to 8°C. The samples were exposed for various time intervals including 0 hours, 1 hour, 2 hours, 4 hours, 8 hours, 24 hours, and 48 hours. Subsequently, the exposed sample swabs were tested using 5 replicates for each exposure time, as shown in the table 7 below.

Table 7. Specimen Stability Results

Specimen Storage Temperature	Tested Sample	Specimen Storage Time (No. of Positive/No. of Total Test)						
		0 hour	1 hour	2 hours	4 hours	8 hours	24 hours	48 hours
23.5°C	2x LoD	5/5	5/5	5/5	5/5	5/5	5/5	3/5
	Negative	0/5	0/5	0/5	0/5	0/5	0/5	0/5
30°C	2x LoD	5/5	5/5	5/5	5/5	5/5	5/5	2/5
	Negative	0/5	0/5	0/5	0/5	0/5	0/5	0/5
2°C to 8°C	2x LoD	5/5	5/5	5/5	5/5	5/5	5/5	5/5

	Negative	0/5	0/5	0/5	0/5	0/5	0/5	0/5
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The results showed that the SARS-CoV-2 positive sample swabs were stable up to 24 hours at room temperature and up to 48 hours at 2°C to 8°C. Therefore, freshly collected specimen swabs are recommended to be processed no later than one hour after specimen collection at room temperature or before 48 hours when stored at 2°C to 8°C.

6. Detection Limit:

The Limit of Detection (LoD) was determined with gamma-irradiated SARS-CoV-2 (isolate USA-WA1/2020), heat-inactivated SARS-CoV2 Omicron (isolate hCoV-19/USA/MD-HP20874/2021) and UV inactivated SARS-CoV-2 Delta (isolate USA/PHC658/2021). Contrived samples were prepared by spiking the strain into pooled negative nasal wash matrix. A preliminary LoD was determined by spiking 50 µL of serially diluted sample onto swab heads and tested using the Nano-Check™ COVID-19 Antigen Test. The preliminary LoD initially determined by testing two-fold serial dilution series of 3 replicates was confirmed by testing in 20 replicates. Based on the testing procedure for this study the LoD was determined to be 7.00×10^2 TCID₅₀/mL (USA-WA1/2020), 1.95×10^2 TCID₅₀/mL (hCoV-19/USA/MD-HP20874/2021), and 5.21×10^2 TCID₅₀/mL (USA/PHC658/2021), equating to 3.50×10^1 TCID₅₀/swab, 9.75×10^0 TCID₅₀/swab and 2.61×10^1 TCID₅₀/swab, respectively

Table 8. Limit of Detection (LoD)

SARS-CoV-2 Variant	Strain	LoD (TCID ₅₀ /mL)	Positive Rate (%) (# Positive/# Tested)
Wild	2019-nCoV/USA-WA1/2020	7.00×10^2	95% (19/20)
Omicron	hCoV-19/USA/MD-HP20874/2021	1.95×10^2	95% (19/20)
Delta	USA/PHC658/2021	5.21×10^2	95% (19/20)

Furthermore, the LoD was established using the 1st WHO International Standard for SARS-CoV-2 Antigen (NIBSC 21/368) in real clinical matrix of nasal fluid. Initially, a preliminary LoD test was performed by spiking 50 µL of each diluted sample onto the sample collection swab head in three replicates. Following this, a confirmatory LoD test with 17 additional replicates was conducted at the preliminary LoD concentration, a total of 20 replications. To determine LoD concentration, additional dilutions were investigated bracketing the confirmed LoD concentration, with each dilution level undergoing 20 replications. It was determined that the LoD of the 1st WHO International Standard for SARS-CoV-2 Antigen (NIBSC 21/368) in nasal matrix was confirmed to be 889 IU/mL (44 IU/swab).

7. Analytical Reactivity (Inclusivity):

A total of 15 SARS-CoV-2 isolates were tested in the inclusivity study. 10-fold dilutions of virus stocks were prepared in pooled negative nasal wash matrix and 50 µL were pipetted onto the swabs. The swabs were tested in 5 replicates in this study. The lowest dilution of each strain that resulted in 100% detection (5/5) is presented in Table 9 below.

Table 9. Analytical Reactivity

Lineage /Variant	Strain	LoD	# Positive/ # Tested
Wild	USA-WA1/2020	4.79×10^4 TCID ₅₀ /mL	5/5
B.1.1.7 (Alpha)	USA/CA_CDC_5574/2020	6.77×10^6 genome equivalency/mL	5/5
	England/204820464/2020	7.19×10^3 TCID ₅₀ /mL	5/5
	USA/CA_CDC_5574/2020	2.39×10^4 TCID ₅₀ /mL	5/5
B.1.351 (Beta)	hCoV-19/USA/MD-HP01542/2021	7.20×10^4 genome equivalency/mL	5/5
	USA/MD-HP01542/2021	3.80×10^6 genome equivalency/mL	5/5
	South Africa/KRISP-K005325/2020	1.90×10^4 TCID ₅₀ /mL	5/5
P.1 (Gamma)	Japan/TY7-503/2021	1.58×10^4 TCID ₅₀ /mL	5/5
	USA/NY-Wadsworth-21033899-01/2021	7.85×10^3 TCID ₅₀ /mL	5/5
B.1.617.2 (Delta)	hCoV-19/USA/MD-HP05285/2021	7.20×10^7 genome equivalency/mL	5/5
	USA/PHC658/2021	5.21×10^2 TCID ₅₀ /mL	5/5
	USA/MD-HP05285/2021	5.00×10^3 genome copies/mL	5/5
B.1.617.1 (Kappa)	USA/CA-Stanford-15_S02/2021	8.48×10^4 TCID ₅₀ /mL	5/5
B.1.1.529 (Omicron)	hCoV-19/USA/MD-HP20874/2021	1.95×10^2 TCID ₅₀ /mL	5/5
	USA/GA-EHC-2811C/2021	2.11×10^4 genome copies/mL	5/5

8. High Dose Hook Effect:

High-dose hook effect study was conducted to determine if a hook effect would be observed at high concentrations of the analyte (i.e., a false negative at high concentrations of SARS-CoV-2) in a testing sample. The series of five concentrations were prepared in pooled negative nasal wash matrix and tested in three replicates on Nano-Check™ COVID-19 Antigen Test, between and including 1x LoD (7.0×10^2 TCID₅₀/mL) and to its stock concentration of 2.8×10^6 TCID₅₀/mL. All spiked samples were 100% positive, as expected, at all tested concentrations. The Nano-Check™ COVID-19 Antigen Test did not display a Hook Effect for high concentrations of SARS-CoV-2 tested herein.

Table 10. High Dose Hook Effect Test

Concentration of SARS-CoV-2 (TCID ₅₀ /mL)	# Positive/# Tested
2.8×10 ⁶	3/3
2.8×10 ⁵	3/3
2.8×10 ⁴	3/3
2.8×10 ³	3/3
7.0×10 ²	3/3

9. Assay Cut-off:

Not Applicable

10. Carry-Over:

Carry-over contamination is not applicable to this test device as each sample uses an independent, new, single-use test cassette that is discarded after each run.

B. Comparison Studies:

1. Method Comparison with Predicate Device:

Not applicable. The performance of the Nano-Check™ COVID-19 Antigen Test was evaluated in a clinical study against an FDA-cleared molecular assay.

2. Matrix Comparison:

The Nano-Check™ COVID-19 Antigen Test is only intended for the qualitative detection of the nucleocapsid protein antigen from SARS-Co V-2 in direct anterior nasal swab specimens. As no other specimen or sample type is claimed herein.

C. Clinical Study:

The clinical performance of the Nano-Check™ COVID-19 Antigen Test was evaluated in a multi-center, prospective clinical study in the U.S. in 2022-2023, during a period when the SARS-CoV-2 Omicron variant was the predominant strain. The study only enrolled subjects with symptoms of respiratory infection consistent with a SARS-CoV-2 infection. A total of six hundred seventy (670) subjects were consecutively enrolled and tested by eleven (11) operators across four (4) different Point of Care (POC) CLIA-waived sites. Two anterior nasal swabs were collected from each study subject during the same visit. The first AN swab sample for the comparator method was collected by the operators using the swab included in a Universal Viral Transport from both sides of the nose. The collected AN swab was then added into the UVT media containing 1 mL media and stored in dry ice until it was shipped to a reference laboratory and tested with an FDA Cleared SARS-CoV-2 RT-PCR Test as comparator. The second AN swab sample was collected from both

sides of the nose using the provided swab and was tested immediately using the Nano-Check™ COVID-19 Antigen Test by an operator at the site.

There were 670 subjects evaluated, with 24.9% collected from patients aged 21 years or younger, 59.7% from patients aged 22-60 years, and 15.4% from patients aged 61 years or older. Among the subjects, 59.6% were from female patients, while 40.4% were from male patients. Results obtained with the Nano-Check™ COVID-19 Antigen Test were compared to the results obtained with the RT-PCR comparator test to determine clinical sensitivity and specificity. The study cohort included 21.1% low-positive samples. The Nano-Check™ COVID-19 Antigen Test demonstrated a Positive Percent Agreement of 83.67 % (123/147, 95% CI: 76.86-88.78%) and Negative Percent Agreement 99.62% (521/523, 95% CI: 98.62-99.90%).

Table 11. Clinical Performance of Nano-Check™ COVID-19 Antigen Test Compared to an RT-PCR Comparator

Nano-Check™ COVID-19 Antigen Test	RT-PCR Comparator		Total
	Positive	Negative	
Positive	123	2	125
Negative	24	521	545
Total	147	523	670
Positive Percent Agreement (PPA) = 83.67% (123/147, 95% CI: 76.86-88.78%)			
Negative Percent Agreement (NPA) = 99.62% (521/523, 95% CI: 98.62-99.90%)			
Positivity in Study Cohort = 21.94% (147/670; 95% CI: 18.97-25.23%)			

1. Clinical Sensitivity:

Please refer to Section VI.C (Clinical Studies) above for the clinical validation.

The PPA for the test is 83.67% (123/147, 95% CI: 76.86-88.78%).

2. Clinical Specificity:

Please refer to Section VI.C (Clinical Studies) above for the clinical validation.

The NPA for the test is 99.62% (521/523, 95% CI: 98.62-99.90%).

3. Serial Testing:

As a mitigation for low performance of the device at Day 0 of symptom onset., as indicated by these clinical study data and in other studies for test devices of a similar principle and design, the Intended Use for this test device (and associated Instructions for Use) include recommendations for repeat testing (i.e., test at least twice over three days with at least 48 hours between tests.). This mitigation is supported by data generated by the National Institutes for Health (NIH) and the University of Massachusetts Chan Medical School (in collaboration with the FDA) demonstrating that repeat testing over multiple days improves test performance and increases the likelihood that a COVID-19 antigen test will accurately detect an infection. These results have informed the FDA's general understanding that repeat testing after a negative result from a COVID-19 antigen

test reduces the risk of a false negative result. Please refer to the following studies for additional details:

- Finding a Needle in the Haystack: Design and Implementation of a Digital Site-less Clinical Study of Serial Rapid Antigen Testing to Identify Asymptomatic SARS-CoV-2 Infection - <https://www.medrxiv.org/content/10.1101/2022.08.04.22278274v1>
- Performance of Screening for SARS-CoV-2 using Rapid Antigen Tests to Detect Incidence of Symptomatic and Asymptomatic SARS-CoV-2 Infection: findings from the Test Us at Home prospective cohort study: <https://www.medrxiv.org/content/10.1101/2022.08.05.22278466v1>

D. Clinical Cut-Off:

Not Applicable since there is no clinical cutoff related to the presence of SARS-CoV-2 in patient samples.

E. Expected Value/Reference Range:

Patient Samples are expected to be negative for COVID-19 Antigen.

VIII. Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.