

VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test Package Insert

REF VCD16-01-011/VCD16-01-012/VCD16-01-013/VCD16-01-014/ VCD16-01-015/VCD16-01-016/VCD16-01-017	English
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PRINCIPLE AND INTENDED USE

VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test is for the rapid, qualitative detection of the nucleocapsid protein antigen from SARS-CoV-2 in human nasal swab, oropharyngeal swab or nasopharyngeal swab specimen.^[1] The test is for *in vitro* diagnostic use only. For professional use only. It is intended for clinical laboratories and healthcare professional use only for point-of-care testing^[3]. It provides only an initial screening test result. More specific alternative diagnosis methods (molecular diagnostic and / or CT) should be performed in order to obtain the confirmation of SARS-CoV-2 infection. Not for at-home testing.

VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test is based on immunochromatography technology. Each test device has one line of anti-SARS-CoV-2 antibody on the detection line (T line) and one line of anti-mouse IgG antibody on the quality control line (C line). When extracted specimen is added to the specimen well, it will react with the labeled antibody to form a complex, the mixture then migrates through the membrane by capillary action and interacts with the coated anti-SARS-CoV-2 antibody on the detection line. If the specimen contains SARS-CoV-2 antigen, the detection line will appear red indicating the SARS-CoV-2 antigen is positive. Otherwise, the test result will be negative. The test device also contains a quality control line C which should appear red for all valid tests. If the quality control line C does not appear, the test result will be invalid even if the detection line appears.

COMPOSITION

Each test kit contains test devices, sealed pouches (prefilled with extraction solution), extraction tubes, extraction tube tips, tube stand, sterile swabs and package insert.
Materials required but not provided: timer.

STORAGE AND HANDLING

- Store the test kit in a cool, dry place between 2-30°C. Keep away from light. Exposure to temperature and / or humidity outside the specified conditions may cause inaccurate results.
- Do not freeze or refrigerate. Use the test kit at temperatures between 15-30°C.
- Use the test kit between 10-90% humidity.
- Do not use the test kit beyond the expiration date (printed on the foil pouch and box).
- Note:** All expiration dates are printed in Year-Month-Day format. 2022-06-18 indicates June 18, 2022.

WARNINGS, PRECAUTIONS AND LIMITATIONS

- Results from SARS-CoV-2 antigen testing should not be used as the sole basis to diagnose or exclude SARS-CoV-2 infection or to inform infection status^[2].
- Negative results do not rule out SARS-CoV-2 infection, particularly in those who have been in contact with the virus. Follow-up testing with a molecular diagnostic and / or CT should be considered to rule out infection in these individuals.
- Positive results may be due to present infection with SARS-coronavirus strains, see "cross-reactivity" for details. Follow-up testing with a molecular diagnostic and / or CT should be considered to confirm the testing result.
- False positive results may be due to sticky specimen, insufficient specimen volume or bubbles during applying.
- Please take a new swab to draw the specimen if the swab is damaged or cannot use.
- Do not use unverified UTM, which may lead to false positive or false negative results.
- For *in vitro* diagnostic use only. Not for at-home testing.
- Further molecular diagnostic and / or CT is recommended to identify the actual physical situation.
- Do not open the foil pouch of the test device exposing it to the ambient environment until the test device is ready for immediate use.
- Do not use any damaged test device or material.
- Do not reuse the test device.
- Handle extraction solution with caution, do not contact with eyes or skin. If spilled on eyes or skin, wash thoroughly with water.
- Do not use test kit beyond the expiration date.
- Specific training or guidance is recommended if operators are not experienced with specimen collection and handling procedures.
- Only use nasal swab, oropharyngeal swab or nasopharyngeal swab as specimen. Follow the package insert to obtain accurate results.
- Wear protective gears such as laboratory coats, disposable gloves, and eye protection when specimens are collected and evaluated.
- Wash hands thoroughly after handling.
- All parts of kit are considered biohazardous and can potentially transmit infectious diseases from blood borne pathogens, even after you have performed cleaning and disinfection. Follow proper precautions and all local regulations when disposing of the used test kits.
- Since the outbreak of the pandemic, the SARS-CoV-2 variant with D614G mutations in the spike protein has replaced the original form in the most regions all over the world^[4]. In December 2020, a novel strain of the virus, named 'VUI-202012/01', was identified in the England with a set of 17 mutations^[5]. Another mutant strain 501Y.V2 of SARS-CoV-2, originally detected in South Africa, shares the same key mutation N501Y. The N501Y mutation locates the receptor-binding domain (RBD) of the spike protein that the virus uses to bind to the human ACE2 receptor, which might be associate with increased transmissibility^[6]. The nucleocapsid phosphoprotein (N Protein), linking the viral envelope to the viral RNA, plays a central role in the packaging signal RNA recognition and subsequent RNA encapsidation^[7]. Based on its vital role in transcription and replication of the virus, the N protein is suggested to be more sensitive for the early detection of infections^[8]. SARS-CoV-2 Ag rapid tests produced by VivaChek employ the interaction with antigen sites in N protein. Till now, there is no clear evidence indicating that mutations found in Spike protein can affect the performance of N protein based antigen tests.

SPECIMEN COLLECTION AND HANDLING

1) Specimen collection

Nasal swab specimen

It is important to obtain as much secretion as possible. Insert the sterile swab into one nostril. The swab tip should be inserted up to 2.5 cm (1 inch) from the edge of the nostril. Roll the swab 5 times along the mucosa inside the nostril to ensure that both mucus and cells are collected. Repeat this process for the other nostril to ensure that an adequate specimen is collected from both nasal cavities (use the same swab).

Oropharyngeal swab specimen

It is important to obtain as much secretion as possible. Insert the sterile swab into throat that presents the most secretion from the red area of the throat wall and maxillary tonsils to collect throat swab specimen. Rub the bilateral throat tonsils and throat wall moderately to obtain the specimen. Please do not touch the tongue when remove the swab.

Nasopharyngeal swab specimen

It is important to obtain as much secretion as possible. Insert the sterile swab into the nostril that presents the most secretion under visual inspection. Keep the swab near the septum floor of the nose while gently pushing the swab into the posterior nasopharynx. Rotate the swab 5 times then remove it from the nasopharynx.



Nasal swab



Oropharyngeal swab



Nasopharyngeal swab

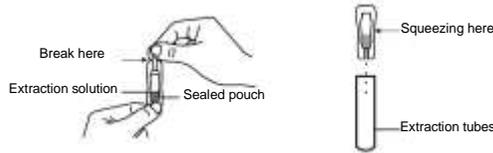
2) Specimen handling

Freshly collected specimens should be tested as soon as possible. It is essential that correct specimen collection and preparation methods are followed.

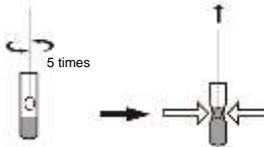
TEST PROCEDURE

Allow the Test Devices and Extraction Solution to equilibrate to 15-30°C prior to testing.

- Hold the sealed pouch vertically and let all extraction solution flow into the bulb. Break the tip and squeeze the bulb to dispense all extraction solution into the extraction tube.



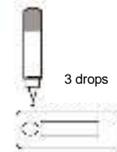
- Collect specimen refer to **Specimen Collection**.
- Insert the swab with collected specimen into the extraction tube filled with extraction solution. Roll the swab 5 times while pressing the head against the bottom and side of the extraction tube. Remove the swab while squeezing the sides of the tube to extract the liquid from the swab. Try to release as much liquid as possible. Dispose the used swab as a biohazard waste.



- Put on the tube tip.



- Take out a test device from sealed foil pouch and put it on a clean and level surface.
- Apply 3 drops of the extracted specimen into the specimen well. Please avoid bubbles during applying.



- Read the test result at 15 minutes. Don't read the result after 20 minutes.



15 min



Note:

- Do not interchange or mix extraction solution from different lots.
- Handle extraction solution with caution, do not contact with eyes or skin. If spilled on eyes or skin, wash thoroughly with water.
- Please follow local regulations to handle the used materials.

INTERPRETATION OF TEST RESULTS

1. Positive Result:

Both the quality control line C and the detection line T appear.

2. Negative Result:

Only the quality control line C appears, with no other line appearing on the detection line.

3. Invalid Result:

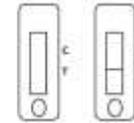
Quality control line C fails to appear indicating the test is invalid, no matter if the detection line appears or not. Collect a new specimen and perform another test with a new test device.



Positive: Both the quality control line C and the detection line T appear.



Negative: Only the quality control line C appears, with no other line appearing on the detection line.



Invalid: Quality control line C fails to appear indicating the test is invalid, no matter if the detection line appears or not.

QUALITY CONTROL

Internal procedural controls are included in the test. A colored line appearing in the control region (C) is the internal procedural control. It confirms sufficient specimen volume and correct procedural technique. Control standards are not supplied with this kit; however, it is recommended that positive and negative controls be tested as a good laboratory practice to confirm the test procedure and to verify proper test performance.

PERFORMANCE

1. Limit of Detection

The LoD for the VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test was established using dilutions of an inactivated virus culture. The starting material was supplied at a concentration of 1.51X10⁸ TCID₅₀/mL. Studies were designed to estimate the LoD of the assay using nasal swab specimens, the starting material was spiked into a volume of pooled human nasal matrix obtained from healthy donors and confirmed negative for SARS-CoV-2 to obtain a series of different concentrations.

SARS-CoV-2 Titer	1.51X10 ⁸ TCID ₅₀ /mL							
Dilution	1/10	1/100	1/1000	1/2500	1/5000	1/10000	1/20000	1/40000
Concentration in Dilution tested (TCID ₅₀ /mL)	1.51X 10 ⁵	1.51X 10 ⁴	1.51X 10 ³	6.04X10 ²	3.02X10 ²	1.51X10 ²	75.5	37.8
Detection rates of 5 replicates	100% (5/5)	100% (5/5)	100% (5/5)	100% (5/5)	100% (5/5)	100% (5/5)	100% (5/5)	80% (4/5)
Detection rates of 20 replicates near cut-off	NA	NA	NA	NA	100% (20/20)	100% (20/20)	95% (19/20)	75% (15/20)
Lowest Concentration with Uniform Positivity per Analyte	75.5 TCID ₅₀ /mL							
Limit of detection (LoD) per inactivated Virus Culture	75.5 TCID ₅₀ /mL							

2. Clinical Sensitivity/Clinical Specificity

A total of 566 specimens were tested using the VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test. These specimens were obtained by nasal swabs from symptomatic patients. The performance of the VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test was compared to a commercialized molecular assay.

Table Summary of sensitivity/specificity of the VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test compared to PCR.

VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test	PCR		
	Positive	Negative	Total
Positive	131	0	131

Negative	4	431	435
Total	135	431	566
Sensitivity	97.04% (131/135, 95%CI, 92.63%–98.84%)		
Specificity	>99.99% (431/431, 95%CI, 99.12%–100.00%)		
Accuracy	99.29% (562/566, 95%CI, 98.20%–99.72%)		

The VivaDiag™ Pro SARS-CoV-2 Ag Test for nasal swab specimens showed a clinical sensitivity of 97.04%.
The VivaDiag™ Pro SARS-CoV-2 Ag Test for nasal swab specimens showed a clinical specificity of >99.99%.
The VivaDiag™ Pro SARS-CoV-2 Ag Test for nasal swab specimens showed a clinical accuracy of 99.29%.

A total of 379 specimens were tested using the VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test. These specimens were obtained by oropharyngeal swabs from symptomatic patients. The performance of the VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test was compared to a commercialized molecular assay.

Table Summary of sensitivity/specificity of the VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test compared to PCR

VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test	PCR		
	Positive	Negative	Total
Positive	99	0	99
Negative	4	276	280
Total	103	276	379
Sensitivity	96.12% (99/103, 95%CI, 90.44%–98.48%)		
Specificity	>99.99% (276/276, 95%CI, 98.63%–100.00%)		
Accuracy	98.94% (375/379, 95%CI, 97.3%–99.59%)		

The VivaDiag™ Pro SARS-CoV-2 Ag Test for oropharyngeal swab specimens showed a clinical sensitivity of 96.12%.

The VivaDiag™ Pro SARS-CoV-2 Ag Test for oropharyngeal swab specimens showed a clinical specificity of >99.99%.

The VivaDiag™ Pro SARS-CoV-2 Ag Test for oropharyngeal swab specimens showed a clinical accuracy of 98.94%.

A total of 379 specimens were tested using the VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test. These specimens were obtained by nasopharyngeal swabs from symptomatic patients. The performance of the VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test was compared to a commercialized molecular assay.

Table Summary of sensitivity/specificity of the VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test compared to PCR

VivaDiag™ Pro SARS-CoV-2 Ag Rapid Test	PCR		
	Positive	Negative	Total
Positive	99	0	99
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Sensitivity	96.12% (99/103, 95%CI, 90.44%–98.48%)		
Specificity	>99.99% (276/276, 95%CI, 98.63%–100.00%)		
Accuracy	98.94% (375/379, 95%CI, 97.3%–99.59%)		

The VivaDiag™ Pro SARS-CoV-2 Ag Test for nasopharyngeal swab specimens showed a clinical sensitivity of 96.12%.

The VivaDiag™ Pro SARS-CoV-2 Ag Test for nasopharyngeal swab specimens showed a clinical specificity of >99.99%.

The VivaDiag™ Pro SARS-CoV-2 Ag Test for nasopharyngeal swab specimens showed a clinical accuracy of 98.94%.

CROSS-REACTIVITY

1. Cross-Reactivity: there was no cross-reaction with potential cross-reactive substances except SARS-coronavirus.

1) Cross-reaction with SARS-coronavirus.

Virus	Strain	Concentration
SARS-coronavirus	Urbani	1X10 ⁶ PFU/mL

2) No cross-reaction with potential cross-reactive substances.

Virus/Bacteria/Parasite	Strain	Concentration Range
Influenza A	H1N1	1X10 ⁴ –1X10 ⁶ TCID ₅₀ /mL
	H3N2	
	H5N1	
	H7N9	
Influenza B	N/A	
Adenovirus	Type1	
	Type2	
	Type3	
	Type5	
	Type7	
	Type55	

Respiratory syncytial virus	Type A	
Coronavirus	Type B	1X10 ³ ng/mL
	229E	
	OC43	
	NL63	
	HKU1	
MERS-Coronavirus	Florida/USA-2, Saudi Arabia.2014	1X10 ⁴ –1X10 ⁶ TCID ₅₀ /mL
Parainfluenza virus	Type1	
	Type2	
	Type3	
	Type4	
Rhinovirus A16	N/A	
Legionella pneumophila	Bloomington-2	1X10 ⁶ cells/mL
	82A3105	
Mycobacterium tuberculosis	K	
	Erdman	
	HN878	
	CDC1551	
	H37Rv	
Streptococcus pneumonia	475298 [Maryland(D1)6B-17]	
	178[Poland23F-16]	
	262[CIP 104340]	
	Slovakia14-10 [29055]	
Streptococcus pyrogens	Typing strain T1	
Mycoplasma pneumoniae	Mutant22	1X10 ⁶ cfu/mL
	FH strain of Eaton Agent	
	M129-B7	
Staphylococcus aureus	NCTC 8325	

2. Endogenous/Exogenous Interference Substances Studies: there was no interference for potential interfering substances listed below.

Potential Interfering Substance	Concentration	Results	Viral Strain Culture (In multiples of LoD)	Results	
Anti-viral drugs	Zanamivir (Influenza)	5 mg/mL	NEG	SARS-CoV-2 cultured virus 1/20000 dilution (75.5 TCID ₅₀ /mL)	POS
	Oseltamivir (Influenza)	10 mg/mL	NEG		POS
	Artemether-lumefantrine (Malaria)	50 µM	NEG		POS
	Doxocycline hyclate (Malaria)	70 µM	NEG		POS
	Quinine (Malaria)	150 µM	NEG		POS
	Lamivudine (Retroviral medication)	1 mg/mL	NEG		POS
	Ribavirin (HCV)	1 mg/mL	NEG		POS
Daclatasvir (HCV)	1 mg/mL	NEG	POS		
Respiratory Specimens	Mucin: bovine submaxillary gland, type I-S	100 µg/mL	NEG	POS	
	Blood (human), EDTA anticoagulated	5% (v/v)	NEG	POS	
	Biotin	100 µg/mL	NEG	POS	
Nasal sprays or drops	Neo-Synephrine (Phenylephrine)	10% (v/v)	NEG	POS	
	Afrin Nasal Spray (Oxymetazoline)	10% (v/v)	NEG	POS	
	Saline Nasal Spray	10% (v/v)	NEG	POS	
Homeopathic allergy relief medicine	Homeopathic Zicam Allergy Relief Nasal Gel	5% (v/v)	NEG	POS	
	Sodium Cromoglycate	20 mg/mL	NEG	POS	
	Olopatadine Hydrochloride	10 mg/mL	NEG	POS	

Anti-inflammatory medication	Acetaminophen	199 µM	NEG		POS
	Acetylsalicylic acid	3.62 mM	NEG		POS
	Ibuprofen	2.425 mM	NEG		POS
Antibiotic	Mupirocin	10 mg/mL	NEG	POS	
	Tobramycin	5 µg/mL	NEG	POS	
	Erythromycin	81.6 µM	NEG	POS	
	Ciprofloxacin	30.2 µM	NEG	POS	

3. High-dose Hook Effect: cultured SARS-CoV-2 virus was spiked into specimen. No hook-effect was observed at 1.51X10⁶ TCID₅₀/mL of cultured SARS-CoV-2 virus.

REFERENCES

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2. Perlman, S. Netland, J. Coronaviruses post-SARS: update on replication and pathogenesis. Nature Reviews Microbiology 7, 439-450, doi: 10.1038/nrmicro2147 (2009).
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4. B. Korber et al. Tracking Changes in SARS-CoV-2 Spike: Evidence that D614G Increases Infectivity of the COVID-19 Virus. Cell, vol. 182, no. 4, pp. 812-827.e19, Aug. 2020, doi: 10.1016/j.cell.2020.06.043.
5. Investigation of novel SARS-CoV-2 variant: Variant of Concern 202012/01, GOV.UK.
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8. J. Mariën et al. Evaluating SARS-CoV-2 spike and nucleocapsid proteins as targets for antibody detection in severe and mild COVID-19 cases using a Luminox bead-based assay. Journal of Virological Methods, vol. 288, p. 114025, Feb. 2021, doi: 10.1016/j.jviro.2020.114025.

INDEX OF SYMBOLS

	Consult instructions for use		Use by		Contains sufficient for <n> tests
	For <i>in vitro</i> diagnostic use only		Lot number		Catalog number
	Storage temperature limitations		Manufacturer		Do not reuse
	Authorized Representative				

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