Detection of mutant SARS-CoV-2 variants with nal von minden COVID-19 antigen rapid tests

Status: 06.08.2021

Background Information:

Since the outbreak of the SARS-CoV-2 pandemic, various mutations have occurred in this virus, resulting in a large number of variants. The majority of these mutations have no discernible effect on the virus, its infectivity or the course of COVID-19. Recently, however, some virus variants proved to be more infectious and less susceptible to the immune response of both vaccinated and recovered people [1-4]. Those viruses are termed "V*ariants of Concern* (VOC)" and "*Variants of Interest* (VOI)", respectively.

These mutants (VOC, VOI) usually show an abundance of characteristic mutations in the spike protein (S-protein), whereas the nucleocapsid protein (N-protein) is only affected sporadically (see Table 1). Since our COVID-19 antigen rapid tests detect the N-protein of SARS-CoV-2, we can currently assume that mutations of the S-protein have no effect on the detectability of the viruses by COVID-19 antigen rapid tests of nal von minden GmbH.

Table 1: Mutations in *Variants of Concern* (VOC) and *Variants of Interest* (VOI) of SARS-CoV-2 [3, 8, 9].

Status	WHO-Nomenclature	Lineage	Identifier	First Detection	Mutations in the S-Protein	Mutations in the N-Protein
VOC	Alpha	B.1.1.7	VOC-20DEC-01 (20I/501Y.V1)	UK	Δ69/70, Δ144, (E484K*), (S494P*), N501Y, A570D, D614G, P681H, T716I, S982A, D1118H (K1191N*)	D3L, R203K, G204R, S235F
VOC	Beta	B.1.351	VOC-20DEC-02 (20H/501.V2)	South Africa	D80A, D215G, Δ241/242/243, K417N, E484K, N501Y, D614G, A701V	T205I
VOC	Gamma	P.1	VOC-21JAN-02 (20J/501Y.V3)	Japan/ Brazil	L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y, T1027I, (V1176F*)	P80R, (R203K*), (G204R*)
VOC	Delta	B.1.617.2	VOC-21APR-02 (20A/S:478K)	India	T19R, (G142D*), 156del, 157del, R158G, L452R, T478K, D614G, P681R, D950N	D63G, R203M, D377Y, (R385K*)
VOI	Kappa	B.1.617.1	VUI-21APR-01 (20A/S:154K)	India	(T95I*), G142D, E154K, L452R, E484Q, D614G, P681R, Q1071H	R203M, D377Y
VOI	n.v.	B.1.617.3	VUI-21APR-03 (20A)	India	T19R, G142D, L452R, E484Q, D614G, P681R, D950N	P67S, R203M, D377Y

* Those mutations were only found in some isolates, thus they are not deemed to be "variant-defining mutations".

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Methods:

Different LOTs (minimum n=3) of the individual nal von minden COVID-19 Ag tests were tested with the following recombinant nucleocapsid proteins (see Table 2). For this purpose, different concentrations of the respective protein solution were prepared in the test specific buffer and applied directly to the COVID-19 Ag tests. After an incubation of 15 minutes at room temperature, the test result was interpreted with the aid of the Rapid Slide Scanner (RSS).

Table 2: Recombinant SARS-CoV-2 nucleocapsid proteins tested with nal von minden COVID-19 Ag rapid tests.

Lineage	Product	Manufacturer	Cat. No.
wild type	SARS-CoV-2 (COVID-19) Nucleocapsid protein, His Tag	ACROBiosystems	NUN-C5227
B.1.1.7	SARS-CoV-2 Nucleocapsid protein (D3L, R203K, G204R, S235F), His Tag	ACROBiosystems	NUN-C52H8
B.1.351	SARS-CoV-2 Nucleocapsid protein (T205I), His Tag	ACROBiosystems	NUN-C52Hd
P.1	SARS-CoV-2 Nucleocapsid protein (P80R), His Tag	ACROBiosystems	NUN-C52Hc
B.1.617.1	SARS-CoV-2 Nucleocapsid protein (R203M, D377Y), His Tag	ACROBiosystems	Nun-C52Hn
B.1.617.2	SARS-CoV-2 Nucleocapsid protein (D63G, R203M, D377Y, R385K),His Tag	ACROBiosystems	NUN-C52Hp

Results:

Table 3: Wild type SARS-CoV-2 nucleocapsid proteins tested with nal von minden COVID-19 Ag rapid tests.

wild type	4 ng/mL	1 ng/mL	0.4 ng/mL	0.05 ng/mL
NADAL® COVID-19 Ag Test	Positive	Positive	Positive	Negative
NADAL® COVID-19 Ag plus Test	Positive	Positive	Positive	Negative
dedicio® COVID-19 Ag plus/pro Test	Positive	Positive	Positive	Negative

Table 4: B.1.1.7 SARS-CoV-2 nucleocapsid proteins tested with nal von minden COVID-19 Ag rapid tests.

B.1.1.7	4 ng/mL	1 ng/mL	0.4 ng/mL	0.05 ng/mL
NADAL® COVID-19 Ag Test	Positive	Positive	Positive	Negative
NADAL® COVID-19 Ag plus Test	Positive	Positive	Positive	Negative
dedicio® COVID-19 Ag plus/pro Test	Positive	Positive	Positive	Negative

Table 5: B.1.351 SARS-CoV-2 nucleocapsid proteins tested with nal von minden COVID-19 Ag rapid tests.

B.1.351	4 ng/mL	1 ng/mL	0.4 ng/mL	0.05 ng/mL
NADAL® COVID-19 Ag Test	Positive	Positive	Positive	Negative
NADAL® COVID-19 Ag plus Test	Positive	Positive	Positive	Negative
dedicio® COVID-19 Ag plus/pro Test	Positive	Positive	Positive	Negative

Table 6: P.1 SARS-CoV-2 nucleocapsid proteins tested with nal von minden COVID-19 Ag rapid tests.

P.1	4 ng/mL	1 ng/mL	0.4 ng/mL	0.05 ng/mL
NADAL® COVID-19 Ag Test	Positive	Positive	Positive	Negative
NADAL® COVID-19 Ag plus Test	Positive	Positive	Positive	Negative
dedicio® COVID-19 Ag plus/pro Test	Positive	Positive	Positive	Negative

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Table 7: B.1.617.1 SARS-CoV-2 nucleocapsid proteins tested with nal von minden COVID-19 Ag rapid tests.

B.1.617.1	4 ng/mL	1 ng/mL	0.4 ng/mL	0.05 ng/mL
NADAL® COVID-19 Ag Test	Positive	Positive	Positive	Negative
NADAL® COVID-19 Ag plus Test	Positive	Positive	Positive	Negative
dedicio® COVID-19 Ag plus/pro Test	Positive	Positive	Positive	Negative

Table 8: B.1.617.2 SARS-CoV-2 nucleocapsid proteins tested with nal von minden COVID-19 Ag rapid tests.

B.1.617.2	4 ng/mL	1 ng/mL	0.4 ng/mL	0.05 ng/mL
NADAL® COVID-19 Ag Test	Positive	Positive	Positive	Negative
NADAL® COVID-19 Ag plus Test	Positive	Positive	Positive	Negative
dedicio® COVID-19 Ag plus/pro Test	Positive	Positive	Positive	Negative

Conclusion:

Our laboratory results show that the virus variants from Great Britain (B.1.1.7, Alpha), South Africa (B.1.351, Beta), Brazil (P.1, Gamma) and India (B.1.617.1, Kappa and B.1.617.2, Delta) are unrestrictedly detectable in nal von minden COVID-19 antigen rapid tests with the same performance as determined with the original strain (wild type) of SARS-CoV-2.

Literature:

[1] Investigation of SARS-CoV-2 variants of concern in England, Technical Briefing 10, 07.05.2021, *Public Health England*.

[2] Risk related to spread of new SARS-CoV-2 variants of concern in the EU/EEA, Rapid Risk Assessment, 29.12.2020, *European Centre for Disease Control and Prevention (ECDC)*.

[3] SARS-CoV-2 Variant Classifications and Definitions, 15.06.2021, *National Center for Immunization and Respiratory Diseases (NCIRD).*

[4] SARS-CoV-2 variants of concern and variants under investigation in England, Technical briefing 15, 11.06.2021, *Public Health England.*

[5] https://outbreak.info/situation-reports, reviewed 22.06.2021

[6] https://cov-lineages.org/global_report.html, reviewed 22.06.2021.

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