Statement on the detectability of mutated SARS-CoV-2 virus variants with nal von minden GmbH COVID-19 antigen rapid tests

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Since the outbreak of the SARS-CoV-2 pandemic, various mutations have arisen in this virus, resulting in a large number of variants and subvariants. The majority of these mutations has 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 "*Variants of Concern* (VOC)", "*Variants of Interest* (VOI)" and "*Variants under Monitoring* (VUM)", respectively.

These mutants (VOC, VOI, VUM) 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 the **nal von minden NADAL® COVID-19 Ag (plus) test** and the **nal von minden dedicio® COVID-19 Ag plus/pro test** detect the N-protein of SARS-CoV-2, we can 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), *Variants of Interest* (VOI), *Variants under Monitoring* (VUM) and De-escalated Variants[1)] of SARS-CoV-2 [3-6].

Status	WHO-Nomenclature	Lineage	First Detection	Mutations in the N-Protein
VOC	Alpha	B.1.1.7	UK	D3L, R203K, G204R, S235F
VOC	Beta	B.1.351	South Africa	T205I
VOC	Gamma	P.1	Japan/ Brazil	P80R, R203K, G204R
VOC	Delta	B.1.617.2	India	D63G, R203M, G215C, D377Y
VOC	Omicron	B.1.1.529	South Africa	P13L, del31/33, R203K, G204R
VOC	Omicron BA.1	B.1.1.529	South Africa	P13L, del31/33, R203K, G204R
VOC	Omicron BA.2	B.1.1.529	India/ South Africa	P13L, del31/33, R203K, G204R, S413R
VOC	Omicron BA.5	B.1.1.529	South Africa	P13L, del31/33, R203K, G204R, S413R
VOI	Lambda	C.37	Peru	P13L, R203K, G204R, G214C
VOI	Mu	B.1.621 B.1.621.1	Columbia	T205I
VUM	n.a.	C.1.2	South Africa	P13L, R203K, G204R, Q384H
VUM	Eta	B.1.525	UK / Nigeria	S2Y, A12G, T205I, del3/3
VUM	Iota	B.1.526	USA	None
VUM	Kappa	B.1.617.1	India	R203M, D377Y
VUM	n.a.	B.1.617.3	India	P67S, R203M, D377Y
VUM	Theta	P.3	Philippines	R203K, G204R
VUM	B.1.1.318-related	B.1.1.318	UK	R203K, G204R, A208G, del209/209
VUM	C.36.3-related	C.36.3	Egypt	R203K, G204R, G212V
de-escalated	Epsilon	B.1.427 B.1.429	USA	T205I

[1)] *"These former VOCs and/or VOIs have been de-escalated by public health agencies based on at least one of the following criteria: (1) the variant is no longer circulating, (2) the variant has been circulating for a long time without any impact on the overall epidemiological situation, (3) scientific evidence demonstrates that the variant is not associated with any concerning properties.[5]"*

In the meantime, several studies have been published that show that there is no evidence of negative effects of the virus variants Alpha (B.1.1.7), Beta (B.1.351), P.1 (Gamma), B.1.617.2 (Delta) and B.1.1.529 (Omicron) on the results of COVID-19 antigen rapid tests [2, 4, 7-10].

Our previous laboratory results with recombinant proteins show that the mutations in the N-protein of the following variants have no influence on the test performance of the nal von minden NADAL® COVID-19 Ag (plus) test and the nal von minden dedicio® COVID-19 Ag plus/pro test: Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2), Lambda (C.37), Mu (B.1.621), Epsilon (B.1.427/B.1.429), Kappa (B.1.617.1), Iota (B.1.526), Theta (P.3) and Omicron (B.1.1.529). All of these variants are unrestrictedly detectable with all nal von minden COVID-19 antigen rapid tests. This also applies to the Omicron subtypes **BA.1**, **BA.2** and **BA.5**. Further subtypes are currently under investigation.

At this time, not all mutations affecting the N-protein of the **Eta (B.1.525), C.1.2, B.1.617.3, B.1.1.318-related** and **C.36.3-related** variant have been tested with our nal von minden COVID-19 Ag Test. Based on our previous studies with mutations at very close positions to the aforementioned variants of the N-protein, we currently do not anticipate any limitations in the detection of the these variants with our rapid tests.

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, 04.10.2021, *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 08.12.2021.

[6] https://cov-lineages.org/global_report.html, reviewed 08.12.2021.

[7] SARS-CoV-2 lateral flow antigen tests: evaluation of VUI-202012/01, 23.12.2020, *Public Health England.*

[8] Jungnick S., Hobmaier B., Mautner L. *et al.*; Bavarian SARS-CoV-2-Public Health Laboratory Team; Bavarian SARS-CoV-Public Health Laboratory Team. Detection of the new SARS-CoV-2 variants of concern B.1.1.7 and B.1.351 in five SARS-CoV-2 rapid antigen tests (RATs), Germany, March 2021. *Euro Surveill*. 2021 Apr; 26(16):2100413. doi: 10.2807/1560-7917.ES.2021.26.16.2100413.

[9] Jungnick S., Hobmaier B., Mautner L. *et al.*; *In Vitro* Rapid Antigen Test Performance with the SARS-CoV-2 Variants of Concern B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), and B.1.617.2 (Delta). *Microorganisms*. 2021 Sep; 9(9):1967. doi: 10.3390/microorganisms9091967.

[10] Frequently asked questions for the B.1.1.529 mutated SARS-CoV-2 lineage in South Africa, 26.11.2021, *National Institute for Communicable Diseases (NICD).*