DHS SCIENCE AND TECHNOLOGY Supplemental Reference for SARS-CoV-2 Omicron Variant

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DHS Science and Technology Directorate | MOBILIZING INNOVATION FOR A SECURE WORLD

Overview – What is the Omicron variant and why are scientists concerned?

- The Omicron variant of the SARS-CoV-2 virus emerged in South Africa in November 2021,¹ and has since spread to at least 27 countries and territories.² On December 1, 2021, the U.S. confirmed its first COVID-19 case with the Omicron variant.³⁻⁴
- Very early reports suggest that the Omicron variant is more transmissible than other variants (e.g., Delta).
- Given a high number of mutations in the viral Spike protein, it is anticipated that Omicron will be resistant to existing antibodies and may lead to a higher rate of reinfection, ⁶⁻⁷ but confirmation is needed.
- Currently, very little is known about its transmissibility, ability to evade the immune system, clinical severity, and susceptibility to vaccines and other medical therapeutics.

Genomics - How does the Omicron variant compare to previous SARS-CoV-2 strains and variants?

- Current SARS-CoV-2 PCR diagnostic testing can successfully identify this variant. Several labs have reported a phenomenon termed S gene dropout. This test can thus be used to distinguish cases of Omicron from other variants. This S gene dropout is the result of a 2-amino deletion at locations 69/70. These deletions are also seen in Alpha and Eta variants.
- Omicron has 30 amino acid changes, 3 small deletions, and 1 insertion in the spike protein.9
- Mutations present in Omicron were previously studied *in vitro* and demonstrated 4-50 times greater binding affinity to ACE2 than wildtype SARS-CoV-2,^{8, 10} which may confer increased transmissibility.
- Nucleocapsid (N) mutations in Omicron have been linked to increased RNA expression¹¹ and increased viral loads.

Transmissibility – How does it spread from one host to another? How easily is it spread?

- Mutations in the spike protein furin cleavage site (H655Y, N679K, and P682H) may be linked to higher transmissibility.^{8, 13-15}
- The rate of new cases in particular areas of South Africa have increased recently, consistent with a transmission advantage for the newly-discovered Omicron variant. ¹⁶ Early reports indicate that Omicron has become the dominant variant in the Gauteng province of South Africa in a short period of time, which is also consistent with elevated transmissibility compared to other circulating variants. ¹⁷
- As of November 25, 2021, the effective reproduction number (R_e), defining the average number of new infections caused by a single infectious individual, was 1.47 for South Africa nationally, where the Delta variant is dominant, but 1.93 in the Gauteng province, which is dominated by the Omicron variant.⁵
- The European Center for Disease Control recommends that existing non-pharmaceutical interventions, such as masks and social distancing, be maintained or reintroduced, even in countries with high vaccination levels. 18

Vaccines - Are there effective vaccines? How common are breakthrough infections?

- The exact impact on efficacy is unknown, but the mutation profile of the spike protein, which is what the antibodies recognize, has been determined and suggests reduced antibody recognition. Tests are underway to determine vaccine effectiveness, with results expected in mid-December. 9, 19
- Several sequence mutations observed in Omicron have been associated with increased transmissibility and immune escape.
 Scientists are concerned because a prior, synthetic variant with 20 mutations similar to Omicron in the spike protein was almost entirely resistant to serum from previously infected and previously vaccinated individuals.
 20
- Moderna is currently testing booster candidates against the Omicron variant, including two that were designed against Beta and Delta variants which have some of the same mutations as Omicron. They are also designing a new booster candidate specifically against Omicron which they anticipate will be ready in three months.²¹

Protective Immunity - How long does the immune response provide protection from reinfection?

- The level of protection in previously infected individuals is unknown. However, preliminary evidence indicates Omicron may cause an increased risk of reinfection.²² Concern regarding the ability of the Omicron variant to escape immunity induced by the Pfizer, Moderna, and Johnson & Johnson vaccines remains high.⁹ Currently available vaccines may offer some level of protection against hospitalization and death, potentially through memory T cells directed at non-surface proteins.²³
- Convalescent patients likely will have some level of protection to neutralize the Omicron variant, however a drop in protection is expected based on the combination of mutations.¹⁹

Medical Treatments – Are there effective treatments?

• There are currently no data suggesting this variant is resistant to any current COVID-19 treatments. Experimental research is in progress to understand the capabilities.

Incubation Period and Acute Clinical Presentation - How long until symptom onset? What are initial symptoms?

• Preliminary information from South Africa reports that there are no unusual symptoms associated with Omicron and that some individuals are asymptomatic.²⁴⁻²⁶

What else do we know?

- Other aspects of the Omicron variant are either presumed or confirmed to agree with those of previously identified SARS-CoV-2 strains. Additional information can be found in the DHS S&T Master Question List (MQL) for COVID-19.²⁷
- Currently, there are key gaps in our understanding of Omicron's ability to infect previously infected and vaccinated individuals, its transmission rate in unvaccinated and vaccinated populations, and its clinical disease severity in patients of different ages and comorbidities. Additional research is needed to fill these key gaps.

References:

- 1. WHO, Classification of Omicron (B.1.1.529): SARS-CoV-2 Variant of Concern. **2021**. https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern
- 2. Picheta, R., These countries have found cases of the Omicron Covid-19 variant so far. *CNN* **2021**. https://www.cnn.com/2021/11/29/world/covid-omicron-variant-countries-list-cmd-intl/index.html
- 3. Edwards, E. a. F., E., First U.S. case of omicron variant is found in California. *NBC* **2021**. https://www.nbcnews.com/news/us-news/omicron-variant-found-california-rcna6909
- 4. Kimball, S., Kopecki, D., and Bursztynsky, J., U.S. confirms nataion's first case of omicron Covid variant in California. *CNBC* **2021**.
- 5. Health, S. A. D. o., Urgent briefing on latest developments around the Covid-19 vaccination programme. News24: 2021. https://www.youtube.com/watch?v=Vh4XMueP1zQ
- 6. HSA, U., SARS-CoV-2 variants of concern and variants under investigation in England: Technical Briefing 29; UK Health Security Agency: 2021.
- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/10 36501/Technical_Briefing_29_published_26_November_2021.pdf
- 7. WHO, Enhancing Readiness for Omicron (B.1.1.529): Technical Brief and Priority Actions for Member States; World Health Organization: 28 November 2021, 2021.
- https://www.who.int/publications/m/item/enhancing-readiness-for-omicron-(b.1.1.529)-technical-brief-and-priority-actions-for-member-states
- 8. CoVariants.org, Variant: 21K (Omicron), also known as B.1.1.529. **2021**. https://covariants.org/variants/21K.Omicron
- 9. Callaway, E., Heavily mutated Omicron variant puts scientists on alert. *Nature* **2021**. https://www.nature.com/articles/d41586-021-03552-w
- 10. Zahradník, J.; Marciano, S.; Shemesh, M.; Zoler, E.; Harari, D.; Chiaravalli, J.; Meyer, B.; Rudich, Y.; Li, C.; Marton, I., SARS-CoV-2 variant prediction and antiviral drug design are enabled by RBD in vitro evolution. *Nature microbiology* **2021**, *6* (9), 1188-1198.
- 11. Leary, S.; Gaudieri, S.; Parker, M. D.; Chopra, A.; James, I.; Pakala, S.; Alves, E.; John, M.; Lindsey, B. B.; Keeley, A. J., Generation of a novel SARS-CoV-2 sub-genomic RNA due to the R203K/G204R variant in nucleocapsid. *bioRxiv* **2021**, 2020.04. 10.029454.
- 12. Mourier, T.; Shuaib, M.; Hala, S.; Mfarrej, S.; Alofi, F.; Naeem, R.; Alsomali, A.; Jorgensen, D.; Subudhi, A.; Ben Rached, F., Saudi Arabian SARS-CoV-2 genomes implicate a mutant Nucleocapsid protein in modulating host interactions and increased viral load in COVID-19 patients. **2021**.
- 13. Gong, S. Y.; Chatterjee, D.; Richard, J.; Prévost, J.; Tauzin, A.; Gasser, R.; Bo, Y.; Vézina, D.; Goyette, G.; Gendron-Lepage, G., Contribution of single mutations to selected SARS-CoV-2 emerging variants spike antigenicity. *Virology* **2021**, *563*, 134-145.
- 14. Liu, Y.; Liu, J.; Plante, K. S.; Plante, J. A.; Xie, X.; Zhang, X.; Ku, Z.; An, Z.; Scharton, D.; Schindewolf, C.; Widen, S. G.; Menachery, V. D.; Shi, P.-Y.; Weaver, S. C., The N501Y spike substitution enhances SARS-CoV-2 infection and transmission. *Nature* **2021**. https://doi.org/10.1038/s41586-021-04245-0
- 15. Liu, Y.; Liu, J.; Johnson, B. A.; Xia, H.; Ku, Z.; Schindewolf, C.; Widen, S. G.; An, Z.; Weaver, S. C.; Menachery, V. D., Delta spike P681R mutation enhances SARS-CoV-2 fitness over Alpha variant. *bioRxiv* **2021**.
- 16. Torjesen, I., Covid-19: Omicron may be more transmissible than other variants and partly resistant to existing vaccines, scientists fear. *BMJ* **2021**, *375*, n2943.
- https://www.bmj.com/content/bmj/375/bmj.n2943.full.pdf
- 17. ECDC, Threat Assessment Brief: Implications of the emergence and spread of the SARS-CoV-2 B.1.1. 529 variant of concern (Omicron) for the EU/EEA; European Centre for Disease Prevention and Control:

Department of Homeland Security Science and Technology Directorate – SARS-CoV-2 Omicron (B.1.1.529) Variant Update – 12/1/2021

- 26 November 2021, 2021. https://www.ecdc.europa.eu/en/publications-data/threat-assessment-brief-emergence-sars-cov-2-variant-b.1.1.529
- 18. EU/EEA, Implications of the emergence and spread of the SARS-CoV-2 B.1.1. 529 variant of concern (Omicron) for the EU/EEA. **2021**.
- https://www.ecdc.europa.eu/sites/default/files/documents/Implications-emergence-spread-SARS-CoV-2%20B.1.1.529-variant-concern-Omicron-for-the-EU-EEA-Nov2021.pdf
- 19. Kupferschmidt, K., 'Patience is crucial': Why we won't know for weeks how dangerous Omicron is. *Science* **2021**. https://www.science.org/content/article/patience-crucial-why-we-won-t-know-weeks-how-dangerous-omicron
- 20. Schmidt, F.; Weisblum, Y.; Rutkowska, M.; Poston, D.; Da Silva, J.; Zhang, F.; Bednarski, E.; Cho, A.; Schaefer-Babajew, D. J.; Gaebler, C., High genetic barrier to SARS-CoV-2 polyclonal neutralizing antibody escape. *Nature* **2021**, 1-9.
- 21. Moderna, Moderna Announces Strategy to Address Omicron (B.1.1.529) SARS-CoV-2 Variant. **2021**. https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-strategy-address-omicron-b11529-sars-cov-2
- 22. WHO, Update on Omicron. 2021. https://www.who.int/news/item/28-11-2021-update-on-omicron
- 23. Tarke, A.; Sidney, J.; Methot, N.; Yu, E. D.; Zhang, Y.; Dan, J. M.; Goodwin, B.; Rubiro, P.; Sutherland,
- A.; Wang, E., Impact of SARS-CoV-2 variants on the total CD4+ and CD8+ T cell reactivity in infected or vaccinated individuals. *Cell Reports Medicine* **2021**, *2* (7), 100355.
- 24. Africa, N. I. f. C. d.-d. o. t. N. H. L. S.-S., Frequently asked questions for the B.1.1.529 mutated SARS-COV-2 lineage in South Africa. *NCID/NHLS*. https://www.nicd.ac.za/frequently-asked-questions-for-the-b-1-1-529-mutated-sars-cov-2-lineage-in-south-africa/
- 25. Schnell, M., 13 omicron cases detected in Portuguese pro soccer team. *The Hill* 2021. https://thehill.com/policy/international/583328-13-omicron-cases-detected-in-portuguese-pro-soccer-team
- 26. BBC, Omicron symptoms mild so far, says South African doctor who spotted it. *BBC* 2021. https://www.bbc.com/news/av/uk-59450988
- 27. DHS, Master Question List for COVID-19 (caused by SARS-CoV-2). https://www.dhs.gov/publication/st-master-question-list-covid-19.

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