

EG.5 Initial Risk Evaluation, 9 August 2023

EG.5 is a descendent lineage of XBB.1.9.2, which has the same spike amino acid profile as XBB.1.5. EG.5 was first reported on 17 February 2023, and designated as a variant under monitoring (VUM) on 19 July 2023. With this risk evaluation, we are designating EG.5 and its sub-lineages as a variant of interest (VOI).

EG.5 carries an additional F456L amino acid mutation in the spike protein compared to the parent XBB.1.9.2 subvariant and XBB.1.5. Within the EG.5 lineage, the subvariant EG.5.1 has an additional spike mutation Q52H and represents 88% of the available sequences for EG.5 and its descendent lineages.

As of 7 August 2023, 7354 sequences of EG.5 have been submitted to GISAID from 51 countries. The largest portion of EG.5 sequences are from China (30.6%, 2247 sequences). The other countries with at least 100 sequences are the United States of America (18.4%, 1356 sequences), the Republic of Korea (14.1%, 1040 sequences), Japan (11.1%, 814 sequences), Canada (5.3%, 392 sequences), Australia (2.1%, 158 sequences), Singapore (2.1%, 154 sequences), the United Kingdom (2.0%, 150 sequences), France (1.6%, 119 sequences), Portugal (1.6%, 115 sequences), and Spain (1.5%, 107 sequences).

Globally, there has been a steady increase in the proportion of EG.5 reported. During epidemiological week 29 (17 to 23 July 2023), the global prevalence of EG.5 was 17.4%. This is a notable rise from the data reported four weeks prior (week 25, 19 to 25 June 2023), when the global prevalence of EG.5 was 7.6%.

Based on the available evidence, the public health risk posed by EG.5 is evaluated as low at the global level, aligning with the risk associated with XBB.1.16 and the other currently circulating VOIs (see risk evaluation table below). While EG.5 has shown increased prevalence, growth advantage, and immune escape properties, there have been no reported changes in disease severity to date. While concurrent increases in the proportion of EG.5 and COVID-19 hospitalizations (lower than previous waves) have been observed in countries such as Japan and the Republic of Korea, no associations have been made between these hospitalizations and EG.5. However, due to its growth advantage and immune escape characteristics, EG.5 may cause a rise in case incidence and become dominant in some countries or even globally.

WHO and its Technical Advisory Group on SARS-CoV-2 Evolution (TAG-VE) continue to recommend that Member States prioritize specific actions to better address uncertainties relating to antibody escape and severity of EG.5. The suggested timelines are estimates and will vary from one country to another based on national capacities:

- Share information on the growth advantage of EG.5 in your country and/or provide sequence information (1-4 weeks).
- Conduct neutralization assays using human sera, representative of the affected community(ies), and EG.5 live virus isolates (2-4 weeks, see table below for the results from previously conducted).
- Perform a comparative evaluation to detect changes in rolling or ad hoc indicators of severity (4-12 weeks, see table below for the results from previously conducted studies).

The WHO and its Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) continue to regularly assess the impact of variants on the performance of COVID-19 vaccines to inform decisions on updates to vaccine composition.(2)

The risk evaluation below is based on currently available evidence and will be revised regularly as more evidence and data from additional countries become available.

Amongst the VOIs and VUMs featuring the F456L mutation and for the period 19 June to 23 July 2023, EG.5 is most reported at 49.1%, compared to other VOI and VUM including XBB.1.16.6 (4.88%), FL.1.5.1 (4.41%), XBB.1.5.10 (4.06%), XBB.1.5.72 (3.52%), EG.6.1 (3.26%), FD.1.1 (3.07%), EG.5.2 (3.06%), FE.1.1 (2.58%), FL.15 (2.47%), FE.1.2 (2.09%), XBB.1.5.70 (1.91%), GK.1 (1.83%), FE.1.1.1 (1.68%), XBB.1.5.59 (1.31%), XBB.1.5 (1.27%), GN.1 (1.26%), XBB.1.16.9 (1.15%), FL.1.5 (1.08%), and XBB.1.9.1 (1.07%), among others with reported prevalence less than one percent.

<p>Overall risk evaluation:</p> <p>Low</p>	<p>Based on its genetic features, immune escape characteristics, and growth rate estimates, EG.5 may spread globally and contribute to a surge in case incidence. Several countries with rising EG.5 prevalence have seen increases in cases and hospitalizations, although at present there is no evidence of an increase in disease severity directly associated with EG.5. Collectively, available evidence does not suggest that EG.5 has additional public health risks relative to the other currently circulating SARS-CoV-2 descendent lineages. However, due to the prevailing unreliability of reporting and non-representative availability of sequencing, additional data outlined in this risk evaluation are needed for a more comprehensive evaluation of the risk posed by EG.5.</p>		
Indicator	Evidence	Level of risk	Level of confidence
<p>Growth advantage</p>	<p>Comparing epidemiological week 25 (19 to 25 June 2023) to week 29 (17 to 23 July 2023), the global proportion of EG.5 relative to other circulating variants showed a notable increase, rising from 7.6% (744/9762) to 17.5% (542/3093). Similarly, among countries with over 1000 EG.5 sequences, the prevalence of EG.5 rose from 24.7% to 45.0% for China, 5.6% to 12.8% for the United States of America, and 7.6% to 19.3% for the Republic of Korea.</p> <p>Based on WHO’s internal variant growth rate analysis, which is similar to the methods used by the UK Health Security Agency (UK HSA), EG.5 has the fastest growth among variants currently circulating in the Region of the Americas, the European Region, and the Western Pacific Region (3).</p> <p>The UK HSA has estimated EG.5.1 to have the highest growth rate in the country, with an estimated prevalence of 14.6% (95% confidence interval: 9.1 to 22.4) by 20 July 2023 (4).</p> <p>The U.S. Centers for Disease Control and Prevention (U.S. CDC) Nowcast model-based projections predict a national rise of EG.5 to 17.3% (95% predictive interval: 14.1- 21.0%) by 5</p>	<p>Moderate</p>	<p>High</p>

	August 2023 (5). * see footnote for more explanations		
Antibody escape	EG.5 has the mutation F456L. Using a XBB.1.5 + F456L pseudotyped virus (i.e., the same spike profile as EG.5), this mutation has been shown to escape or decrease the neutralization of most XBB.1.5-neutralizing antibodies (1). ** see footnote for more explanations	Moderate	Low
Severity and clinical considerations	There are currently no reports of increased disease severity due to EG.5. *** see footnote for more explanations	Low	Low

Annex:

* Growth advantage

Level of risk: Moderate, as the variant is the fastest growing variant in several WHO regions as well as rapidly increasing in prevalence. If the estimated growth rates are sustained, this variant may become the dominant variant in more countries and even globally over time.

Confidence: High, as the growth advantage has been estimated by several groups of experts and in several countries and WHO regions.

** Antibody escape

Level of risk: Moderate, due to immune evasion of XBB.1.5 neutralizing antibodies, the previous globally dominant variant that peaked at >50% prevalence.

Confidence: Low, as immune escape results are based on work from one laboratory, which used pseudotyped viruses. Additional laboratory studies would be needed to further assess the risk of antibody escape.

*** Severity and clinical considerations

Level of risk: Low, as currently there are no reports of elevated disease severity associated with this variant.

Confidence: Low. Although, there is regular co-ordination and data sharing between all WHO Regional colleagues, countries and partners, reporting of new hospitalizations and ICU data with the WHO has decreased substantially, therefore caution should be taken when interpreting severe cases due to this decrease in reporting. Further, additional studies would be needed to further assess the impact of this variant on clinical outcomes.

References

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