

EG.5 Updated Risk Evaluation, 21 September 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. On 9 August 2023, WHO published its [first risk evaluation of EG.5](#) and designated 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.

As of 19 September 2023, 31 712 sequences of Omicron EG.5 have been submitted to GISAID from 71 countries. Within the EG.5 lineage, the subvariant EG.5.1.1 represents 41.7% of the available sequences for EG.5 and its descendent lineages (1). The largest portion of EG.5 sequences are from the United States of America (25.2%, 7979 sequences), China (18.4%, 5826 sequences), and Japan (10.2%, 3241 sequences). Among other countries with at least 200 sequences are the Republic of Korea (8.2%, 2608 sequences), Canada (6.8%, 2153 sequences), the United Kingdom (5.6%, 1764 sequences), France (4.8%, 1517 sequences), Spain (3.0%, 952 sequences), Singapore (1.6%, 519 sequences), Australia (1.6%, 517 sequences), Sweden (1.6%, 501 sequences), Denmark (1.3%, 409 sequences), , Italy (1.3%, 399 sequences), Germany (1.1%, 350 sequences), Portugal (1.1%, 344 sequences), Ireland (1.0%, 325 sequences), and Israel (0.9%, 282 sequences).

Globally, there has been a steady increase in the proportion of EG.5 reported, with its global prevalence at 33.10% in epidemiological week 36 (4 to 10 September 2023). This is an increase from the data reported four weeks prior (week 32, 7 to 14 August 2023), when the global prevalence of EG.5 was 26.3%.

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 compared to other currently circulating variants, there have been no reported changes in disease severity to date. While concurrent increases in the proportion of EG.5 and COVID-19 hospitalizations have been observed in some countries, no direct associations have been made between these hospitalizations and EG.5, and current hospitalizations are lower when compared to previous waves. However, due to its growth advantage and immune escape characteristics, EG.5 has caused a rise in case incidence and has become the most prevalent variant 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:

- Conduct neutralization assays using human sera, representative of the affected community(ies), and EG.5 live virus isolates (from two to four weeks, see table below for the results from previously conducted studies)
- Perform a comparative evaluation to detect changes in rolling or ad-hoc indicators of severity (from four to 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 21 August to 17 September 2023, EG.5 and its descendent lineages are most reported at 51.8%, compared to other VOI and VUM including XBB.1.16 (10.0%), FL.1.5.1 (7.5%), HK.3 (4.6%), XBB.1.5 (4.2%), EG.6.1 (3.2%), DV.7.1 (2.7%), HV.1 (2.5%), and GK.2 (2.4%), . The prevalence of the rest was less than one percent (3).

<p>Overall risk evaluation:</p> <p>Low</p>	<p>Genetic features, immune escape characteristics, and growth rate estimates suggest that EG.5 can spread globally and contribute to a surge in case incidence, and several countries with rising EG.5 prevalence have seen increases in cases and hospitalizations. However, 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 Omicron 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 36 (4 to 10 September 2023) to week 32 (7 to 14 August 2023), the global proportion of EG.5 relative to other circulating variants showed a notable increase, rising from 26.3% to 33.1%. Similarly, among countries with over 1000 EG.5 sequences, the prevalence of EG.5 rose to 25.2% (7979/31 712) for the United States of America, 18.4% (5826/31 712) for China, 10.2% (3241/31 712) for Japan.</p> <p>Based on WHO's internal variant growth rate analysis, whose methodology is similar to the methods used by the United Kingdom 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 (4).</p> <p>The UK HSA has estimated EG.5.1 and EG.5.1.3 to have the highest growth rate in the country, with an estimated prevalence of 15.6% (95% confidence interval [CI]: 12.4-19.4) and 5.2% (95% CI: 3.2-8.3) by 19 August 2023 (5).</p> <p>The United States Centers for</p>	<p>Moderate</p>	<p>High</p>

	<p>Disease Control and Prevention (US CDC) Nowcast model-based projections predict a national rise of EG.5 to 21.5% (95% predictive interval: 19.0-24.3) between 20 August to 2 September 2023 (6).</p> <p>* see footnote for more explanations</p>		
Antibody escape	<p>EG.5 has the mutation F456L, which is located within epitopes of many class-1 mABs directed at the receptor-binding domain and predicts antibody evasion. Results from several laboratories show that EG.5/EG.5.1 are significantly more resistant to neutralization by sera from individuals vaccinated and with or without breakthrough infections (BTI) with other subvariants, such as BQ or XBB, when compared to BA.1, BA.2, BA.4, and BA.5 (7-10).</p> <p>In the animal model, the 50% neutralization titer (NT50) of XBB BTI sera against EG.5.1 was comparable to those against XBB.1.5, XBB.1.9.2 and XBB.1.16, and the sensitivity of EG.5.1 to convalescent sera of hamsters infected with XBB.1 and XBB.1.5 was similar to XBB.1.5, XBB.1.9 and XBB.1.16 (11).</p> <p>** see footnote for more explanations</p>	Moderate	Moderate
Severity and clinical considerations	<p>There are currently no reports of increased disease severity due to EG.5. A laboratory-based study using Syrian hamsters reported no obvious differences in growth ability and pathogenicity between XBB.1.5 and EG.5.1 (12).</p> <p>Regarding the transmissibility, the same study revealed some differences in transmissibility and virus tropism between EG.5.1 and XBB.1.5: a slightly higher transmission efficacy was found for EG.5.1 (five of six pairs of hamsters: 83%) compared with that of XBB.1.5</p>	Low	Low

	<p>(56% transmission) and most of the EG.5.1-exposed animals (four of six exposed animals: 67%) had detectable virus in the lungs (as well as in nasal samples) as opposed to XBB.1.5-exposed animals, that only had detectable virus in nasal samples (12).</p> <p>Further evaluation is required to confirm these differences and determine what factors contribute to them.</p> <p>In addition, a number of countries have observed a rise in hospitalization following an increase in cases. However, all observed trends should be interpreted cautiously due to a reduction in surveillance activities for human cases, including a decreased in the volume of testing, a shift in testing strategies and delays in reporting.</p> <p>*** see footnote for more explanations</p>		
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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 globally. Since the first risk evaluation of EG.5 was published on 9 August 2023, the variant has maintained steady growth rates over time, becoming the dominant variant globally.

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: Moderate, as immune escape results are based on work from multiple laboratories which used pseudo-typed viruses.

*** 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 work on characterizing virus tropism in the laboratory is needed, as only one study reported subtle differences (as compared to XBB.1.5) in Syrian hamsters, and the significance of those findings are unclear. Additional studies in humans would be needed to further assess the impact of this variant on clinical outcomes.

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