

WHO TAG-VE Risk Evaluation for SARS-CoV-2 Variant Under Monitoring: XFG

Executive Summary

XFG has been designated a SARS-CoV-2 variant under monitoring (VUM) with increasing proportions globally. Considering the available evidence, the additional public health risk posed by XFG is evaluated as low at the global level. Currently approved COVID-19 vaccines are expected to remain effective to this variant against symptomatic and severe disease. Several countries in the South-East Asia Region have reported a simultaneous rise in new cases and hospitalisations, where XFG has been widely detected. Current data do not indicate that this variant leads to more severe illness or deaths than other variants in circulation.

Initial Risk Evaluation of XFG, 25 June 2025

XFG is a SARS-CoV-2 variant that is a recombinant of the lineages LF.7 and LP.8.1.2, with the earliest sample collected on 27 January 2025. XFG is one of seven VUMs tracked by the WHO and was designated as a VUM on 25 June 2025 [1,2]. In comparing JN.1 with XFG and NB.1.8.1, the currently dominant SARS-CoV-2 variant, distinct mutational profiles in the Spike protein can be identified; however, some amino acid changes are held in common:

NB.1.8.1 = JN.1 + [T22N, F59S, G184S, A435S, **F456L**, T478I, **Q493E**] - [T478K]

XFG = JN.1 + [T22N, S31P, K182R, R190S, R346T, K444R, V445R, **F456L**, N487D, **Q493E**, T572I] - [V445H]

Spike mutations at amino acids 478 and 487 have been shown to enhance the evasion of Class 1/2 antibodies [3]. Using pseudoviruses and plasma from BA.5 breakthrough infections with JN.1 or XDV+F456L infection, XFG showed 1.9-fold reduction in neutralization compared to LP.8.1.1 [3]. In mice previously immunized with SARS-CoV-2 variant vaccines, further immunisation using monovalent KP.2 or monovalent LP.8.1 mRNA vaccines elicited similar or modestly lower neutralising antibody titres against XFG than those elicited by immunising KP.2 or LP.8.1 antigens [3,4].

As of 22 June 2025, there were 1648 XFG sequences submitted to GISAID [5] from 38 countries, representing 22.7% of the globally available sequences in epidemiological week (EW) 22 of 2025 (26 May to 1 June 2025). This is a significant rise in proportion from 7.4% four weeks prior in EW19 of 2025 (5 to 11 May 2025), Table 1. Between EW 19 and EW 22 of 2025, XFG increased in proportion in all the three WHO regions that are consistently sharing SARS-CoV-2 sequences, i.e. an increase from 1.6% to 6.0% for the Western Pacific region (WPR), from 7.8% to 26.5% for the Region of the Americas (AMR), and from 10.6% to 16.7% for the European Region (EUR). Albeit with fewer sequence submissions, XFG proportion increased from 17.3% to 68.7% in the South-East Asia Region (SEAR), where NB.1.8.1 had rapidly gained dominance earlier in the Spring. In India, XFG has been the dominant variant throughout the Spring and NB.1.8.1 remained very rare. There are only 2 XFG sequences from the African Region (AFR), and 65 from the East Mediterranean Region (EMR).

Table 1: Global proportions of SARS-CoV-2 Variants, epidemiological week 19 to 22 of 2025

Lineage*	Countries§	Sequences§	2025-19	2025-20	2025-21	2025-22
VOIs						
JN.1	144	342221	9.2	9.0	10.7	15.3
VUMs						
KP.3	86	61946	1.9	1.2	1.4	0.8
KP.3.1.1	91	119109	5.0	3.9	3.9	3.8
LB.1	99	25816	0.6	0.5	0.9	0.3
XEC	78	54778	11.0	9.9	6.1	5.2
LP.8.1	60	21618	33.5	30.1	30.0	22.6
NB.1.8.1	37	4176	25.1	29.6	26.4	24.9
XFG	38	1649	7.4	9.5	15.7	22.7
Recombinant	145	514376	6.2	6.1	5.2	4.4
Others	111	35307	0.1	0.1	-	-

Figures by WHO, data from GISAID, extracted on 22 June 2025.

§Number of countries and sequences are since the emergence of the variants.

*The variants listed include descendant lineages, except those individually specified elsewhere in the table.

The VOI and the VUMs that have shown increasing trends are highlighted in yellow, those that have remained stable are highlighted in blue, while those with decreasing trends are highlighted in green.

WHO and its Technical Advisory Group on Virus Evolution (TAG-VE) continue to recommend that Member States prioritize specific actions to better address uncertainties relating to antibody escape and severity of XFG:

- Conduct neutralization assays using human sera, representative of the affected community(is), and sera from naive animal models infected with XFG live virus isolates.
- Perform a comparative evaluation to detect changes in rolling or ad hoc indicators of severity.

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. In the latest recommendation published on 15 May 2025, the WHO TAG-CO-VAC advised that monovalent JN.1 or KP.2 remain appropriate COVID-19 vaccine antigens; monovalent LP.8.1 is a suitable alternative vaccine antigen [6].

The risk evaluation below follows the published WHO framework for risk evaluation of SARS-CoV-2 variants [7] and is based on currently available evidence. This risk evaluation will be revised regularly as more evidence and data from additional countries become available. With declining prevalence of VOIs, and VUMs increasingly unable to meet the VOI definition, WHO, on 29 November 2024, began conducting risk evaluations for VUM designations in addition to VOI designations.

Considering the evolution of the global epidemiological situation in relation to COVID-19 and to support member states in addressing the continuous risk posed by COVID-19 during the transition from the response to a public health emergency of international concern to its management within broader disease prevention and control programmes, the IHR Standing Recommendations for COVID-19 issued by the WHO Director General's originally set to expire on 30 April 2025, have been extended for an additional year with the same content, until 30 April 2026 [8].

Overall risk evaluation: Low	XFG is growing rapidly compared to co-circulating variants globally. However, XFG exhibits only marginal additional immune evasion over LP.8.1. While there are reported increases in cases and hospitalizations in some of the SEAR countries, which has the highest proportion of XFG, there are no reports to suggest that the associated disease severity is higher as compared to other circulating variants. The available evidence on XFG does not suggest additional public health risks relative to the other currently circulating Omicron descendent lineages.		
Indicator	Evidence	Level of risk	Level of confidence
Growth advantage	There are currently 1648 XFG sequences from 38 countries, representing 22.7% of the globally available sequences in epidemiological week (EW) 22 of 2025 (26 May to 1 June 2025). This is a significant rise in proportion from 7.4% four weeks prior in EW19 of 2025 (5 to 11 May 2025). This increase was observed in all the three WHO regions that are consistently sharing SARS-CoV-2 sequences, i.e. WPR, AMR and EUR. Although with fewer sequence submissions, XFG had the highest increase in proportion in the SEAR. While XFG is increasing in proportion, NB.1.8.1, a recently designated VUM, has begun a decline from EW21 to EW22. However, NB.1.8.1 proportions continued to increase in the AMR and EUR, while remaining stable in the WPR. Using a logistic regression model [9], compared to LP.8.1.1, XFG was estimated to have the highest relative growth advantage than co-circulating variants BA.3.2, NB.1, NB.1.8, NB.1.8.1, LF.9, XFH and XEC.25.1 [10]. XFG pseudovirus exhibits markedly reduced engagement of soluble human ACE2, with this engagement lower than that of NB.1.8.1 [10]. * see footnote for more explanations	Moderate	Low
Immune escape	Using pseudoviruses, and plasma from BA.5 breakthrough infections with either JN.1 or JN.1/XDV+F456L infection, XFG showed 1.9-fold reduction in neutralization compared to LP.8.1.1 [10]. Neutralization data from other cohorts is not currently available.	Low	Low

	Antigenic cartography employing serum samples from naive mice immunized with two doses of spike mRNA vaccine indicates that XFG pseudovirus antigenically clusters with other JN.1 sublineages [10]. XFG pseudovirus exhibits enhanced evasion of several RBD-targeting neutralizing monoclonal antibodies from class 1/2 (likely due to Spike mutations T478K and N487D [10]. ** see footnote for more explanations		
Severity and clinical/diagnostic considerations	There are no reported or published studies on the impact of XFG on clinical outcomes. The detection of XFG is increasing across several countries in various regions that are consistently sharing SARS-CoV-2 sequences with stable to slightly increasing trend in viral activity and hospitalizations. In the SEAR, some countries, despite reporting relatively low sequencing numbers, are detecting high levels of XFG and are concurrently experiencing a rise in SARS-CoV-2-related cases and hospitalizations. However, routine clinical surveillance does not indicate any signs of increased severity associated with XFG, compared to previously circulating variants. Currently the limited information from those countries do not suggest an increase in indicators like COVID-19-related ICU admissions and deaths per hospitalizations, or all-cause mortality. XFG does not contain any additional mutations that have previously been associated with resistance to Remdesivir and Nirmatrelvir compared to these variants [11,12]. *** see footnote for more explanations	Low	Low

Annex:

*** Growth advantage**

Level of risk: Moderate, as XFG is growing substantially across all WHO regions with consistent SARS-CoV-2 sequence data sharing.

Confidence: Low, as XFG expansion has only begun recently, there are low levels of sequencing data, and NB.1.8.1 is still growing in proportion in AMR and EUR.

**** Antibody escape**

Level of risk: Low, as the immune evasion of XFG in available data is of a similar magnitude to prior JN.1 sublineages upon their emergence. Additionally, XFG clusters with other JN.1 sublineages within antigenic cartography data based on sera from immunised mice.

Confidence: Low, as XFG antigenicity has only been assessed in a single study using pseudoviruses with serological data from two cohorts. Additional laboratory studies using sera from different cohorts and regions are 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. Available evidence doesn't suggest resistance to Remdesivir and Nirmaltevir.

Confidence: Low. Currently there are no studies assessing the impact of this variant on clinical outcomes. Although, there is regular co-ordination and data sharing between all WHO Regional Offices, countries reporting of data on severe outcomes such as new hospitalizations, ICU admissions and deaths with the WHO has been decreased substantially. Therefore, caution should be taken when interpreting trends in routine surveillance of severe cases for increased severity. No studies have been conducted yet on the potential impact of the variant on the activity of antivirals like Remdesivir and Nirmaltevir.

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