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Executive Summary

XEC is currently the only SARS-CoV-2 variant under monitoring (VUM) with increasing prevalence globally. Considering the available evidence, the additional public health risk posed by XEC is evaluated as low at the global level. The recommended COVID-19 vaccines are expected to remain cross-reactive to this variant against symptomatic and severe disease, as there is limited immune escape from JN.1 or KP.2 mRNA booster vaccines. Therefore, the continued spread of this variant alone is unlikely to increase the burden on national public health systems compared to other Omicron sub-lineages.

Initial Risk Evaluation of XEC, 09 December 2024

XEC is a recombinant SARS-CoV-2 variant derived from the JN.1 descendent lineages KS.1.1 and KP.3.3, with the earliest sample collected on 26 June 2024. XEC is one of six VUMs tracked by the WHO, and was designated as a VUM on 24 September 2024 [1,2].

As of 09 December 2024, there were 13 331 XEC sequences submitted to GISAID [3] from 50 countries, representing 36.8% of the globally available sequences in epidemiological week 47, (18 to 24 November 2024). This is a significant rise in prevalence from 26.9% four weeks prior in epidemiological week 44 (28 October to 3 November 2024), Table 1. The XEC variant is the only SARS-CoV-2 variant with increasing prevalence in all the three WHO regions with consistent sharing of SARS-CoV-2 sequences between epidemiological weeks 44 and 47, i.e. an increase from 14.3% to 35.6% for the Western Pacific region (WPR), from 37.0% to 48.0% for the European region (EUR), and from 22.7% to 32.8% for the region of the Americas (AMR). There are only four XEC sequences each from the African Region (AFR) and the East Mediterranean Region (EMR), and seventeen sequences from the South East Asia region.

Table 1: Global proportions of SARS-CoV-2 Variants, epidemiological week 44 to 47 of 2024

Lineage*	Countries§	Sequences§	2024-44	2024-45	2024-46	2024-47
VOIs						
JN.1	146	294307	11.7	12.5	12.0	12.1
VUMs						
KP.2	87	33287	1.3	1.3	1.2	0.9
KP.3	77	56177	8.4	7.7	8.2	6.1
KP.3.1.1	65	65234	48.8	47.2	43.7	41.8
JN.1.18	100	7962	1.1	1.0	1.2	0.9
LB.1	83	16166	0.9	0.9	0.6	0.6
XEC	50	13331	26.9	27.8	31.7	36.8
Recombinant	146	494028	0.8	1.3	0.9	0.7
Unassigned	68	4095	0.0	0.0	0.0	-
Others	119	37149	0.1	0.2	0.4	0.2

Figures by WHO, data from GISAID, extracted on 07 December 2024.

§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 orange, 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 XEC:

- Conduct neutralization assays using human sera, representative of the affected community(ies), and sera from naive animal models infected with XEC 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 [4].

The risk evaluation below follows the WHO framework [5] and is based on currently available evidence. It 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 decided on 29th November 2024 to begin attaching risk evaluations to VUM designations in addition to VOI designations, starting with the current document that refers to the latest designated VUM (XEC).

To support member states in addressing the 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 WHO Director General's latest standing recommendations remain in effect from 9 August 2023 until 30 April 2025 [6].

Overall risk evaluation: **Low**	XEC is growing rapidly but possesses minimal antigenic advantage in evading previous immunity. There is a significant increase in cases attributable to XEC infections, but there are no reports to suggest that the associated disease severity is higher as compared to other circulating variants. The available evidence on XEC 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 13 331 XEC sequences available from 50 countries, representing 36.8% of the globally available sequences in epidemiological week 47, (11 to 17 November 2024). (18 to 24 November 2024). This is a significant rise in prevalence from 26.9% four weeks prior in epidemiological week 44 (28 October to 3 November 2024). While XEC is increasing in prevalence, the most prevalent SARS-CoV-2 variant KP.3.1.1 is gradually declining globally and across the WHO regions. In August 2024, the relative effective reproduction number (R_e) of XEC was estimated to be 1.13-fold higher than that of KP.3.1.1 [7], the most prevalent SARS-CoV-2 variant globally then and at present. * see footnote for more explanations	High	Moderate

Immune escape	Using pseudoviruses, XEC was shown to have enhanced humoral immune evasion and receptor-binding domain-targeting antibody escape capabilities, which is thought to arise from the receptor-binding domain conformational dynamics induced by additional N-terminal domain glycosylation (T22N) [8,9]. Similarly using live viruses, there was a significant reduction in antibody titre from B.1 and XBB.1.5 to KP.3.1.1 and XEC in individuals aged 68 - 82 years from Norway [10]. Studies with either monovalent JN.1 or monovalent KP.2 mRNA vaccines suggest that these vaccines enhance neutralising antibody responses against XEC as compared to the pre-vaccination titres. However, neutralisation titres against XEC are typically lower than those against the homologous JN.1 or KP.2 immunising antigen [11–13]. ** see footnote for more explanations	Low	Moderate
Severity and clinical/diagnostic considerations	Recent data suggests continued activity for the monoclonal antibody pemivibart and pemivibart-like antibodies against KP.3.1.1 and XEC [14]. There are no reported or published studies on the impact of XEC on clinical outcomes. *** see footnote for more explanations	Low	Low

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Annex:

*** Growth advantage**

Level of risk: High, as the variant is growing substantially across all WHO regions with consistent SARS-CoV-2 sequence data sharing, and the most prevalent SARS-CoV-2 variant KP.3.1.1 starting to decline.

Confidence: Moderate, as even though we are seeing growth in three WHO regions, data is inconsistent in the other three regions.

**** Antibody escape**

Level of risk: Low, as it is estimated that XEC has limited immune evasion relative to co-circulating variants.

Confidence: Moderate, as there are increasing data on cross neutralization of XEC. Additional laboratory studies from different regions of the world would be needed to further assess the risk of antibody escape in settings with different population immunity backgrounds.

***** Severity and clinical considerations**

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

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 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.

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