XBB.1.16 Initial Risk Assessment, 17 April 2023

XBB.1.16 is a descendent lineage of XBB, a recombinant of two BA.2 descendent lineages. XBB.1.16 was first reported on 09 January 2023, and designated a variant under monitoring (VUM) on 22 March 2023. On 17 April 2023, XBB.1.16 was designated a variant of interest (VOI). XBB.1.16 has a similar genetic profile as the VOI XBB.1.5, with the additional E180V and K478R amino acid mutations in the spike protein compared to their parent XBB.1.

As of 17 April 2023, 3648 sequences of the Omicron XBB.1.16 variant have been reported from 33 countries (GISAID, XBB.1.16 searched using variant defining nucleotide mutations T12730A, T28297C, A28447G). The majority of the XBB.1.16 sequences are from India (63.4%, 2314 sequences). The other countries with at least 50 sequences include the United States of America (10.9%, 396 sequences), Singapore (6.9%, 250 sequences), Australia (3.9%, 143 sequences), Canada (2.6%, 94 sequences), Brunei (2.4%, 89 sequences), Japan (2.0%, 73 sequences) and the United Kingdom (2.1%, 75 sequences).

Globally, there has been a weekly rise in the prevalence of XBB.1.16. During epidemiological week 13 (27 March to 2 April 2023), the global prevalence of XBB.1.16 was 4.15%, an increase from 4 weeks prior (epidemiological week 9, 27 February to 5 March 2023), when the global prevalence was 0.52%.

Following a sustained increase in the prevalence of XBB.1.16 and sustained growth advantage reported from several countries, and following the advice of the WHO Technical Advisory Group on SARS-CoV-2 Viral Evolution (TAG-VE) on a meeting convened on 17 April 2023, XBB.1.16 has been designated as a VOI.

The global risk assessment for XBB.1.16 is low as compared to XBB.1.5 and the other currently circulating variants, at this current time and with available evidence (see risk assessment table below). While growth advantage and immune escape properties are observed in different countries and immune backgrounds, including in countries where XBB.1.5 has become the dominant variant recently, no changes in severity have been reported in countries where XBB.1.16 are reported to be circulating. In India and Indonesia, there has been a slight increase in bed occupancy numbers. However, the levels are much lower than seen in previous variant waves.

Taken together, available information does not suggest that XBB.1.16 has additional public health risk relative to XBB.1.5 and the other currently circulating Omicron descendent lineages. However, XBB.1.16 may become dominant in some countries and cause a rise in case incidence due to its growth advantage and immune escape characteristics.

WHO and its Technical Advisory Group on SARS-CoV-2 Evolution (TAG-VE) continue to recommend Member States prioritize the following studies to better address uncertainties relating to antibody escape, and severity of XBB.1.16. The suggested timelines are estimates and will vary from one country to another based on national capacities:

- Share information on growth advantage for XBB.1.16 in your country and/or share sequence information (1-4 weeks)
- Neutralization assays using human sera, representative of the affected community(ies), and live XBB.1.16 virus isolates (2-4 weeks, see below table for results of studies that were performed so far)
- Comparative assessment to detect changes in rolling or ad hoc indicators of severity (4-12 weeks, see below table for results of studies that were performed)

The WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) continues to regularly assess the impact of variants on the performance of COVID-19 vaccines to inform decisions on updates to vaccine composition.(1)

1

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

2

Overall risk assessment: Low	Based on its genetic features, immune escape characteristics and growth rate estimates, XBB.1.16 may spread globally and drive an increase in case incidence. From reports from India and other countries, no early signals of increases in severity have been observed. As XBB.1.16 has spread to 33 countries, disease severity is being monitored carefully. Taken together, available evidence does not suggest that XBB.1.16 has additional public health risks relative to the other currently circulating Omicron descendent lineages.		
Indicator	Evidence	Level of Risk	Level of Confidence
Growth advantage	Comparing the month of February and the month of March 2023 in India, the proportion of XBB1.16 relative to other circulating variants rose from 15.3% (137/895) to 58.6% (2130/3636). Similarly for countries with more than 100 sequences, the prevalence of XBB.1.16 rose from 0.04 to 1.09 for the United States of America (USA), 1.2% (12/992) to 11.6% (223/1929) for Singapore, and 0.07% (2/3331) to 3.7% (154/4180) for Australia. From WHO's internal variant growth rate analysis, similarly used by the UKHSA, XBB.1 family of variants, which includes XBB.1.16, have the fastest growth over other circulating variants in AMRO, EURO, SEARO and WPRO (2). US CDC Nowcast model-based projections predict a rise of the XBB.1.16 variant to 7.2% (95% predictive interval 4.5- 1.3%) by 15 Apr 20236 (3). Nextstrain has designated XBB.1.16 a new clade 23B based on a criteria of ">0.05 per day growth in frequency and >5% regional frequency", whereby from their estimates XBB.1.16 represented ~10% of all sequences collected mid-March in Asia, had a simple logistical growth rate advantage of ~9% in all of Asia, and relative growth against all of XBB* variants of ~5% in India (4). * see footnote for more explanations	Moderate	High
Antibody escape	Similar to XBB.1 and XBB.1.5, XBB.1.16 neutralization assays have demonstrated resistance to BA.2 and BA.5 breakthrough infection sera (5) The sensitivity of XBB.1.16 to convalescent sera of XBB.1-infected hamsters was comparable to those of XBB.1 and XBB.1.5, which points at a similar ability of these variants to evade immunity (5). ** see footnote for more explanations	Moderate	Low

Severity and clinical considerations	An analysis of infections from India did not report any differences in hospitalization and oxygen requirement for XBB.1.16 as compared to other circulating lineages (Dr. Rajesh Karyakarte's, BJ Government Medical College, Pune). In terms of clinical considerations, there has been a slight rise in bed occupancy in some states in India (2-4%). However, these levels are much lower compared to the level recorded during the Delta wave or Omicron BA.1/BA.2 wave (6). Disease severity is not higher compared to previously circulating variants. In India, >70% of the population have received a booster vaccine dose (7). The antiviral sotrovimab exhibits antiviral activity against XBB.1.16, similar to other XBB subvariants (5). *** see footnote for more explanations	Low	Moderate

Annex:

*** Growth advantage**
Level of risk: Moderate, as since the first report of the emergence of XBB.1.16 on 09 January 2023, more than 3 months since, the variant has not led to a global sweep as some previous variants did. However, 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 a similar immune evasion profile as XBB.1.5, the current dominant variant globally.

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

***** Severity and clinical considerations**
Level of risk: Low, as three months into the emergence of XBB.1.16, and from sustained and detailed variant and epidemiological surveillance in India, severity indicators have not increased across the Indian states, and neither are there any reports of severity in any of the other countries that have detected XBB.1.16.

Confidence: Moderate, as there is regular coordination and data sharing with all WHO Regional colleagues, countries and partners continue, and as such we continue to receive early signals from countries if and when severity is rising.

World Health Organization

References

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5. Daichi Yamasoba, Keiya Uriu, Arnon Plianchaisuk, Yusuke Kosugi, Lin Pan, Jiri Zahradnik, et al. Virological characteristics of the SARS-CoV-2 Omicron XBB.1.16 variant. bioRxiv. 2023 Jan 1;2023.04.06.535883.

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