BV-BRC SARS-CoV-2 Emerging Variant Report August 16, 2022

Details of the emerging variants analysis can be found in "BV-BRC SARS-CoV-2 Emerging Variant Report – 20220816.xlsx" based on sequence data from GISAID.

Keep in mind that the information provided reflects sequence counts and sequence proportions and, as such, is impacted by sampling bias in the sequence databases and should not be interpreted as the prevalence of disease caused by these variants.

In addition, due to sequence anomalies (e.g., ambiguous nucleotides in many sequence records) and other issues, the absolute counts of Variants of Concern sequences are likely to be underestimates of the true sequence prevalence.

This report includes preliminary/incomplete stats for the month of August in order to identify early signs of novel variants emerging.

The key findings are summarized below.

USA – VOC

OMICRON

- In the US, virtually all sequences reported to date in June, July, and August are **Omicron**, with **BA.2.12.1** displaced by **BA.5** and **BA.4** and their sub-lineages.
 - The CDC Nowcast for the week ending 08/13/22 estimates that BA.5 proportions are now dominating in the United States at 88.8% (95% PI: 87.5-90.0%). Significant regional differences exist: <u>https://covid.cdc.gov/covid-data-tracker/#variantproportions</u>.
 - The CDC Nowcast has split BA.4 and BA.4.6; estimates for BA.4 proportions are now at 5.4% (95% PI: 4.9-5.7%); estimates for BA.4.6 proportions are now at 5.1% (95% PI: 4.1-6.4%)
 - The US CDC Nowcast estimates that **BA.2.12.1** proportions are now at 0.8% (95% PI: 0.7-0.9%)
- Lineages with sequence prevalence >0.5% in August so far are (ranked in order of sequence prevalence):
 - **BA.5.2.1** 29%, 1.2 fold growth
 - **BA.5.1** 12%, 1.1 fold growth
 - **BA.5.2** 9.7%, 1.1 fold growth
 - **BA.5.5** 8.6%, 0.84 fold growth
 - **BA.5** 8.1%, 2.1 fold growth
 - **BA.5.6** 5.2%, 0.88 fold growth
 - **BA.4.1** 4.2%, 0.66 fold growth
 - **BA.4.6** 3.9%, 1.4 fold growth
 - **BA.5.1.1** 2.9%, 1.5 fold growth
 - **BA.4** 2.9%, 0.81 fold growth
 - **BE.3** 2.7%, 1.6 fold growth
 - **BA.2.12.1** 2.5%, 0.25 fold growth
 - **BE.1** 1.7%, 1.0 fold growth

- BF.5 0.92%, 0.91 fold growth (7.5 fold growth in Nebraska)
- **BA.2** 0.89%, 0.75 fold growth
- **BE.1.1** 0.81%, 0.76 fold growth
- In aggregate, BA.5.x sequences constitute 65% in July and 77% in August so far in the US
- In aggregate, BA.4.x sequences constitute 14% in July and 12% in August so far in the US
- Many sub-lineage variants appear to carry ancestral reversion in comparison to the original Omicron consensus, including inconsistent occurrence of A67V, H69-, V70-, G142D, V143-, Y144-, Y145-, N211-, L212I, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, N764K. However, these changes are likely due to sequencing artifacts caused by inefficient amplification by certain PCR primers affected by Omicron substitutions.
- Notable substitutions present within the top ten BA.5 sub-lineages in August so far in the US:
 - One **BA.5** sub-lineage carries the T76I substitution only
 - One **BA.5** sub-lineage carries the Y144- substitution only *(new)*
 - One **BA.5** sub-lineage carries the R346T substitution only
 - One **BA.5** sub-lineage carries the V289I substitution only *(new)*
- Notable substitutions present within the top ten BA.4 sub-lineages in August so far in the US:
 - Two **BA.4** sub-lineages (including the most prevalent) carry the V3G substitution only
 - One BA.4 sub-lineage carries the R346T and N658S substitutions
 - One **BA.4** sub-lineage carries the N658S substitution only
 - One **BA.4** sub-lineage carries the V3G and I670V substitutions
 - One **BA.4** sub-lineage carries the V3G and R346T substitutions
 - One **BA.4** sub-lineage carries the R346T, N658S, and V445A substitutions (*V445A is new*)
 - One **BA.4** sub-lineage carries the V3G and R346I substitutions
 - One BA.4 sub-lineage carries the R346T, N658S, and P521Q substitutions (*P521Q is new*)
- Several Omicron sub-lineages appear to carry a recurring mutation at position 346 in the S proteins (S:R346T in BA.2.74, BA.2.76, BA.4, BA.4.1, BA.4.6, BA.4.7, BA.5, BA.2.12.1, BA.2, S:R346S in BA.5.2.1or S:R346I in BA.4.1) and show growth rates > 1 fold from June and July
- Clusters of BA.2 sub-lineage (BA.2.13, BA.2.56, BA.2.81) genomes from June and July carry the L452M substitution at the same position as L452Q, including the most prevalent BA.2.12.1 sublineage present at 6.0% in July
- Several Omicron sub-lineages appear to carry a recurring mutation at position 444 in the S proteins (K444R in BA.5.2.1 with 5 fold growth rate, K444N in BA.5.2.1 with 4 fold growth rate, and K444T in BA.5.6 with 4 fold growth rate in July)
- BG.2 had 41 sequence in July and 3 in August so far in the US, and is similar to BA.4/5 except that it lacks the H69-,V70- deletion and the F486V substitution and contains the Q493R, S740L, and V1264L substitutions

DELTA (B.1.617.2 and AY sub-lineages) (no significant change since previous report)

• No Delta sequences in the US in August so far.

USA – (other VOCs and VOIs) (no significant change since previous report)

• None in July or August.

<u>USA – Recombinants</u>

- XE 6 sequences in the US in July, none in August so far
- XM 1 sequence in the US in July, none in August so far
- XAA 1 sequence in the US in July, none in August so far
- XAC 1 sequence in the US in July, none in August so far
- See a summary of recombinant lineages at the end of this report.

World – VOC

OMICRON

- Omicron remains dominant globally, with the following lineages showing the highest sequence prevalence (> 0.5%) or growth rate (>3 fold) in August so far:
 - **BA.5.1** 22%, 1.2 fold growth
 - **BA.5.2.1** 20%, 1.1 fold growth
 - **BA.5.2** 18%, 1.4 fold growth
 - **BE.1.1** 5.4%, 1.4 fold growth
 - **BA.5** 4.5%, 1.3 fold growth
 - **BA.2** 4.2%, 1.3 fold growth
 - **BA.4.6** 2.4%, 1.5 fold growth
 - **BA.4** 2.4%, 0.65 fold growth
 - **BF.5** 2.3%, 0.79 fold growth
 - **BA.4.1** 2.3%, 0.49 fold growth
 - \circ **BA.5.5** 2.0%, 0.48 fold growth
 - \circ **BE.1** 2.0%, 1.0 fold growth
 - **BA.5.6** 1.6%, 0.59 fold growth
 - **BA.5.2.3** 1.1%, 2.1 fold growth
 - **BA.2.12.1** 0.91%, 0.19 fold growth
 - **BA.5.1.3** 0.88%, 1.4 fold growth
 - **BF.1** 0.79%, 1.1 fold growth
 - **BA.5.1.1** 0.73%, 0.78 fold growth
 - **BA.2.75** 0.67%, 1.3 fold growth
 - BE.3 0.62%, 0.94 fold growth
 - **BA.5.3.1** 0.61%, 0.97 fold growth
 - **BA.5.1.2** 0.59%, 1.4 fold growth
 - **BA.4.7** 0.25%, *3.6 fold growth*
- **BA.2.75:** sometimes nicknamed "Centaurus", this sublineage shows a high growth rate in India (94 fold in June, 4.2 fold in July, and 3.1 fold in August so far) and comprises 61% of sequences in India in August so far. It is also present in 21 other countries, including the United States (22 states). Preliminary signs of increasing growth rates for July and August

in Australia, Austria, USA, Japan, Nepal, Germany, New Zealand, Canada, Thailand, and Indonesia

- **BA.2.76:** this sublineage showed a high growth rate globally in June (11 fold) but has slowed down in July (0.9 fold). Notable spike substituions in this variant include Y248N and R346T, both of which occur in antigenically important sites.
- Similar issues with variable ancestral reversion that are likely due to sequencing artifacts, as described above for US sequences
- Notable substitutions present within the top ten **BA.5** sub-lineages globally in August so far:
 - One **BA.5** sub-lineage carries the T76I substitution
 - One **BA.5** sub-lineage carries the R346T substitution
 - One **BA.5** sub-lineage lacks the T19I substitution
 - One **BA.5** sub-lineage lacks the N440K substitution
- Notable substitutions present within the top ten **BA.4** sub-lineages globally in August so far:
 - One **BA.4** sub-lineage (most prevalent) carries the R346T and N658S substitutions (**BA.4.6**)
 - One **BA.4** sub-lineages carries the V3G substitution only
 - One **BA.4** sub-lineage carries the N658S substitution only
 - One **BA.4** sub-lineage carries the R346S and N658S substitutions
 - One **BA.4** sub-lineage carries the V3G and lacks the N440K and G142D substitutions
 - One BA.4 sub-lineage carries the V3G and lacks the N440K substitution
 - One **BA.4** sub-lineage carries the V3G and I670V substitutions
 - One **BA.4** sub-lineage carries the R346T and N658S substitutions
- Substitutions in spike that we are monitoring (>3 fold growth from July to August with counts >10) include the following (but note that the numbers are still relatively small for most of these):
 - **S982A** 0.1%, 10 fold growth
 - **P1263S** 0.09%, 9 fold growth
 - **P384H** 0.33%, 4.7 fold growth
 - **K444M** 0.19%, 3.8 fold growth
 - **Q677H** 0.31%, 3.4 fold growth
 - V1228L 0.13%, 3.3 fold growth
 - **N450D** 0.58%, 3.2 fold growth

DELTA (B.1.617.2 and AY sub-lineages)

- One Delta isolates globally in August so far
- Five (5) AY.4-like genomes have been detected in the Gauteng province of South Africa in June. These are part of a larger group of viruses (n=8) that appear to have features of both Delta and Omicron (BA.5). More information can be found on slide 19 of the <u>NGS-SA</u> report and on this github designation issue <u>here</u>.

World (other VOIs)

• None in July

<u>World – Recombinants</u>

- XAG 14 in July
- **XE** 8 sequences in July
- XAF 8 in July
- XM 2 in July
- XJ 1 in July
- XAA 1 in July
- XAC 1 in July
- XAD 1 in July
- XAE 1 in July
- See a summary of recombinant lineages at the end of this report.

Variants that have been mentioned in the media and/or social media:

On BA.2.75

- Will 'Centaurus' be the next global coronavirus variant? Indian cases offers clues
- Twitter thread from Trever Bedford: What do we expect after BA.5?

Others

- High levels of COVID still circulating in Florida: new BA.4.6 is spreading quickly
- Tokyo reports 22,740 new cases of coronavirus on Sunday
- First bivalent COVID-19 booster vaccine approved by UK medicines regulator
- Shanghai to reopen all schools Sept. 1 with daily COVID testing
- Mask mandates return in New Delhi as COVID-19 cases rise
- <u>Comparative pathogenicity of SARS-CoV-2 Omicron subvariants including BA.1, BA.2, and BA.5</u>
- Further humoral immunity evasion of emerging SARS-CoV-2 BA.4 and BA.5 subvariants
- Omicron BA.4/BA.5 escape neutralizing immunity elicited by BA.1 infection
- Moderna dual-variant (Wuhan plus Omicron) vaccine approved for use in UK. https://www.theguardian.com/world/2022/aug/15/dual-variant-covid-vaccine-approved-ukbooster-programme-moderna

Recombinant lineages:

One new recombinant lineages have been designated this week (XAQ). A summary table of previously identified recombinant lineages can be found below. We have added the number of recombinants genomes for each lineage. XA, XB, and XC have not been detected in the past 6 months. XD-XAP are Omicron or Omicron/Delta recombinants. The majority of these recombinant lineages do not appear to have taken off and several have not been detected in recent weeks. The XE lineage appears to have the largest number of genomes.

| Name | number | Github# | Lineage 1 | Lineage 2 | Location first detected |
|------|--------|---------|-----------|-----------|----------------------------|
| XA | 45 | NA | B.1.1.7 | B.1.177 | UK |

| XB | 3435 | <u>#189</u> | B.1.634 | B.1.631 | N. America |
|-----------|------|--------------|------------------|---------|--------------------------------------|
| XC | 25 | <u>#263</u> | Delta (AY.29) | B.1.1.7 | Japan |
| XD | 28 | <u>#444</u> | Delta (AY.4) | BA.1 | France |
| <u>XE</u> | 2787 | <u>#454</u> | BA.1 | BA.2 | UK |
| <u>XF</u> | 34 | <u>#445</u> | Delta | BA.1 | UK |
| XG | 477 | <u>#447</u> | BA.1 | BA.2 | Denmark |
| XH | 174 | <u>#448</u> | BA.1 | BA.2 | Denmark |
| XJ | 253 | <u>#449</u> | BA.1 | BA.2 | Finland |
| <u>XK</u> | 18 | <u>#460</u> | BA.1 | BA.2 | Belgium |
| <u>XL</u> | 119 | <u>#464</u> | BA.1 | BA.2 | UK |
| <u>XM</u> | 512 | <u>#472</u> | BA.1.1 | BA.2 | Multiple EU |
| <u>XN</u> | 158 | <u>#480</u> | BA.1 | BA.2 | UK |
| <u>XP</u> | 57 | <u>#481</u> | BA.1.1 | BA.2 | UK |
| XQ | 142 | <u>#468</u> | BA.1.1 | BA.2 | UK |
| <u>XR</u> | 181 | <u>#469</u> | BA.1.1 | BA.2 | UK |
| <u>XS</u> | 59 | <u>#471</u> | Delta | BA.1.1 | USA |
| <u>XT</u> | 13 | <u>#478</u> | BA.2 | BA.1* | S. Africa |
| <u>XU</u> | 17 | <u>#522</u> | BA.1* | BA.2 | India |
| XV | 42 | <u>#463</u> | BA.1* | BA.2* | Denmark |
| XW | 99 | <u>#591</u> | BA.1* | BA.2* | JP, DE, SI, CA, UK, US |
| XY | 118 | <u>#606</u> | BA.1* | BA.2* | FR, IL, UK, US |
| XZ | 106 | <u>#636</u> | BA.2* | BA.1* | Multiple |
| XAA | 96 | <u>#664</u> | BA.1* | BA.2* | US, IL |
| XAB | 112 | # <u>665</u> | BA.1* | BA.2* | IT, FR, DE, CH, DK |
| XAC | 204 | # <u>590</u> | BA.1* | BA.2* | IL, DE, CA, IR, NL, JP, UK, US |
| XAD | 54 | <u>#607</u> | BA.2* | BA.1* | CZ,DE,UK |
| XAE | 128 | <u>#637</u> | BA.2* | BA.1* | CA,US,NL,CH |
| XAF | 260 | <u>#676</u> | BA.1* | BA.2* | CR |
| XAG | 347 | <u>#709</u> | BA.1.1 | BA.2.23 | BR |
| XAH | 82 | <u>#755</u> | BA.2* | BA.1* | SI |
| XAJ | 35 | <u>#826</u> | BA.2.12.1 | BA.4 | UK |

| XAK | 55 | <u>#823</u> | BA.1* | BA.2* | DE |
|-----|-----|-------------|--------|--------|----------|
| XAL | 95 | <u>#757</u> | BA.1.1 | BA.2* | DE |
| XAM | 341 | <u>#759</u> | BA.1.1 | BA.2.9 | Panama |
| XAN | 35 | <u>#771</u> | BA.2* | BA.5.1 | Multiple |
| XAP | 69 | <u>#789</u> | BA.2* | BA.1* | US |
| XAQ | 74 | <u>#798</u> | BA.1* | BA.2* | Canada |

Newly designated Pango lineages:

Not many new lineages designated this week, however there are several proposed new lineages with important characteristics that should be monitored.

- <u>BE.1.2</u>: Sublineage of BE.1 with S:R346T, circulating in Costa Rica & USA
- <u>BJ.1</u>: BA.2.10(.1) sublineage with S:V83A, H146Q, Q183E, V213E, G339H, R346T, L368I, V445P, G446S, V483A, F490V, G798D, S1003I
- BA.2.75 sublineage with S:F486S, ORF1a:Q1198K (7 seq. India, Singapure, Australia)
- Proposal for a Sublineage of BA.2.75.1 with S:R346T [34 seq as of 2022-08-15, 2x non-India]
- <u>BA.2.75 lineage with S:356T [28 seq, 2022-08-15, mostly India with 2x Israel/Singapore, 1x Japan/Germany/Denmark/Australia]</u>
- Sublineage of BA.5.2.1 with S:K444R, 71 sequences, USA
- Potential BA.2.75 sublineage with S:L452R in India, Japan and Austria [37 sequences]

Variants being monitored by various public health agencies:

The ECDC has added the Omicron sublineage BA.2.75 to its list of "<u>Variants of Interest</u>" list. The latest summary table for all agencies can be found here: <u>https://docs.google.com/spreadsheets/d/1mAgO2wRJyEyGtL-</u> <u>SBe3NgOjUk7a5nZTeKmSorVkaHSU/edit#gid=0</u>