BV-BRC SARS-CoV-2 Emerging Variant Report August 30, 2022

Details of the emerging variants analysis can be found in "BV-BRC SARS-CoV-2 Emerging Variant Report – 20220830.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 08/27/22 estimates that BA.5 proportions are now dominating in the United States at 88.7% (95% PI: 87.3-89.8%). 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 3.6% (95% PI: 3.3-3.8%); estimates for BA.4.6 proportions are now at 7.5% (95% PI: 6.4-8.8%)
 - The US CDC Nowcast estimates that **BA.2.12.1** proportions are now at 0.2% (95% PI: 0.2-0.3%)
- Lineages with sequence prevalence >0.5% or growth rate > 2 fold in August so far are (ranked in order of sequence prevalence):
 - **BA.5.2.1** 30%, 1.2 fold growth
 - **BA.5.1** 13%, 1.2 fold growth
 - **BA.5.2** 13%, 1.4 fold growth
 - **BA.5.5** 8.0%, 0.79 fold growth
 - **BA.5.6** 6.1%, 1.0 fold growth
 - **BA.4.6** 5.3%, 1.8 fold growth
 - **BA.5** 5.0%, 1.3 fold growth
 - **BA.4.1** 3.9%, 0.63 fold growth
 - **BA.4** 2.2%, 0.62 fold growth
 - **BA.5.1.1** 1.9%, 1.0 fold growth
 - **BA.2.12.1** 1.9%, 0.20 fold growth
 - **BE.1** 1.8%, 1.1 fold growth
 - **BE.3** 1.6%, 0.93 fold growth

- **BF.5** 1.4%, 1.3 fold growth
- **BE.1.1** 1.2%, 1.1 fold growth
- **BE.2** 0.31%, *2.2 fold growth*
- **BA.2.75** 0.23%, 2.9 fold growth
- 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 (BA.5.5)
 - One **BA.5** sub-lineage lacks the N440K substitution (BA.5.2.1)
 - One **BA.5** sub-lineage carries the R346S substitutions (BA.5.2.1)
- Notable substitutions present within the top six BA.4 sub-lineages in August so far in the US:
 - One **BA.4** sub-lineage carries the R346T and N658S substitutions
 - 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 V3G and R346T substitutions
 - One **BA.4** sub-lineage carries the R346T and N658S substitutions and lacks the N440K substitution
- Several Omicron sub-lineages appear to carry a recurring mutation at position 346 in the S protein (S:R346T in BA.2.74, BA.2.76, BA.4, BA.4.1, BA.4.6, BA.4.7, BA.5, BA.5.1, BA.2.12.1, BA.2, S:R346S in BA.5.2.10r S:R346I in BA.4.1)
- Several Omicron sub-lineages appear to carry a recurring mutation at position 444 in the S protein (K444R in BA.5.2.1 with 2.2 fold growth rate, and K444T in BA.5.6 with 1.7 fold growth rate in August)

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.

<u>USA – (other VOCs and VOIs)</u> (no significant change since previous report)

• None in July or August.

<u>USA – Recombinants</u>

- XE –none in August so far
- XM –none in August so far
- XY 1 sequence in the US in August so far
- XAA –none in August so far
- XAC –none in August so far
- XAF 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%) in August so far:
 - **BA.5.2.1** 23%, 1.2 fold growth
 - **BA.5.2** 18%, 1.3 fold growth
 - **BA.5.1** 18%, 0.97 fold growth
 - **BA.5** 4.0%, 1.2 fold growth
 - **BA.5.5** 3.5%, 0.85 fold growth
 - **BE.1.1** 3.3%, 0.89 fold growth
 - **BA.4.6** 3.3%, 2.0 fold growth
 - **BF.5** 3.0%, 1.0 fold growth
 - **BA.5.6** 2.9%, 1.1 fold growth
 - **BA.4.1** 2.7%, 0.61 fold growth
 - \circ **BE.1** 2.0%, 0.96 fold growth
 - **BA.4** 1.9%, 0.55 fold growth
 - **BA.2** 1.1%, 0.48 fold growth
 - **BA.2.12.1** 0.97%, 0.22 fold growth
 - **BA.5.1.1** 0.92%, 1.0 fold growth
 - **BA.2.75** 0.71%, 1.2 fold growth
 - **BE.3** 0.64%, 0.96 fold growth
 - **BA.5.3.1** 0.62%, 0.95 fold growth
 - **BA.5.1.3** 0.62%, 0.97 fold growth
 - **BA.5.2.3** 0.58%, 1.2 fold growth
- BA.2.75: shows a high growth rate in India (95 fold in June, 4.6 fold in July, and 1.4 fold in August so far) and comprises 32% of sequences in India in August so far. It is also present in 32 other countries, including the United States (22 states). Preliminary signs of increasing growth rates for July and August in Israel, Austia, Germany, UK, South Korea, Australia, Singapore, Japan, USA, Canada, Denmark, and New Zealand
- *BF.3:* shows a high growth rate in the UK (9 fold in August and 4 fold in July) but the numbers are small (n=38 in August)
- 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
- Notable substitutions present within the top five **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-lineage carries the V3G substitution only
 - One **BA.4** sub-lineage carries the N658S substitution only
 - One **BA.4** sub-lineage carries the V3G and lacks the N440K substitution

- 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):
 - **F486S** 0.1%, 10 fold growth
 - G261D 0.05%, 5 fold growth
 - **D1199N** 0.09%, 4.5 fold growth
 - K356T 0.09%, 4.5 fold growth
 - A264T 0.04%, 4 fold growth
 - **Q14H** 0.04%, 4 fold growth
 - **Y200C** 0.04%, 4 fold growth
 - T604N 0.07%, 3.5 fold growth
 - A626V 0.03%, 3 fold growth
 - **G142-** 0.03%, 3 fold growth
 - G252S 0.03%, 3 fold growth
 - G339Y 0.03%, 3 fold growth
 - L141- 0.03%, 3 fold growth
 - **P9L** 0.03%, 3 fold growth
 - **A243-** 0.03%, 3 fold growth
 - L244- 0.03%, 3 fold growth

DELTA (B.1.617.2 and AY sub-lineages)

- Four Delta isolates (two AY.122, one AY.23, one AY.43) globally in August so far; 29 in July.
- Countries where Delta lineages have been detected in July and August 2022: Austria, Belgium, France, India, Indonesia, Italy, Luxembourg, Philippines, Russia, South Africa, Spain, Switzerland, Ukraine, United Kingdom, USA

World (other VOIs)

• 1 Alpha genome (B.1.1.7) detected in July in the USA; none in August.

<u>World – Recombinants</u>

- XAJ 45 in July, 3 in August so far
- XAG 17 in July; none in August so far
- XAN 14 in July; 6 in August so far
- XAF 10 in July; one in August so far
- XE 8 sequences in July; none in August so far
- XM 2 in July; none in August so far
- XJ 1 in July; none in August so far
- XAA 1 in July; none in August so far
- XAC 1 in July; none in August so far
- XAD 1 in July; none in August so far
- XAE 1 in July; none in August so far
- **XY** 1 in August so far
- See a summary of recombinant lineages at the end of this report.

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

- COVID vaccines slash risk of spreading Omicron and so does previous infection
- <u>Predicting the efficacy of variant-modified COVID-19 vaccine boosters</u>
- <u>The Potential Clinical Impact of Implementing Different COVID-19 Boosters in Fall 2022 in</u> <u>the United States</u>
- <u>Nirmatrelvir Use and Severe Covid-19 Outcomes during the Omicron Surge</u>
- Relative hypercoagulopathy of the SARS-CoV-2 Beta and Delta variants when compared to the less severe Omicron variants is related to TEG parameters, the extent of fibrin amyloid microclots, and the severity of clinical illness
- <u>Bivalent Omicron vaccines (BA.4 and BA.5) could be available in the US as soon as Sept 6, according to CDC.</u>
- New Covid Variant BA.4.6 Outcompeting Dominant BA.5 In Swath Of U.S.
- Increased Disease Potential Of Covid Variant BA.5 Currently Circulating In The United States
- What is the infectivity of SARS-CoV-2 Omicron BA.2.75 variant?

Recombinant lineages:

One new recombinant lineages have been designated this week (XAR). 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-XAR 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	34	<u>#444</u>	Delta (AY.4)	BA.1	France
XE	2804	<u>#454</u>	BA.1	BA.2	UK
XF	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	254	<u>#449</u>	BA.1	BA.2	Finland
XK	18	<u>#460</u>	BA.1	BA.2	Belgium
XL	119	<u>#464</u>	BA.1	BA.2	UK

XM	533	<u>#472</u>	BA.1.1	BA.2	Multiple EU
XN	158	<u>#480</u>	BA.1	BA.2	UK
XP	57	<u>#481</u>	BA.1.1	BA.2	UK
XQ	142	<u>#468</u>	BA.1.1	BA.2	UK
XR	181	<u>#469</u>	BA.1.1	BA.2	UK
XS	60	<u>#471</u>	Delta	BA.1.1	USA
XT	13	<u>#478</u>	BA.2	BA.1*	S. Africa
XU	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	120	<u>#606</u>	BA.1*	BA.2*	FR, IL, UK, US
XZ	108	<u>#636</u>	BA.2*	BA.1*	Multiple
XAA	96	<u>#664</u>	BA.1*	BA.2*	US, IL
XAB	114	# <u>665</u>	BA.1*	BA.2*	IT, FR, DE, CH, DK
XAC	205	# <u>590</u>	BA.1*	BA.2*	IL, DE, CA, IR, NL, JP, UK, US
XAD	56	<u>#607</u>	BA.2*	BA.1*	CZ,DE,UK
XAE	130	<u>#637</u>	BA.2*	BA.1*	CA,US,NL,CH
XAF	287	<u>#676</u>	BA.1*	BA.2*	CR
XAG	358	<u>#709</u>	BA.1.1	BA.2.23	BR
XAH	82	<u>#755</u>	BA.2*	BA.1*	SI
XAJ	79	<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
XAR	49	#860	BA.1*	BA.2*	Reunion/France

Newly designated Pango lineages:

Few new lineages designated this week:

• BF.22: BA.5.2.1 sublineage with N:T49I and N:T379I in Japan

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>