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

Details of the emerging variants analysis can be found in "BV-BRC SARS-CoV-2 Emerging Variant Report – 20220802.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 July 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 and July are **Omicron.** In the last month, the predominant BA.2 sublineage in the United States, BA.2.12.1, has been displaced by BA.5 and BA.4 lineages.
    - The CDC Nowcast for the week ending 7/30/22 estimates that **BA.5** proportions are now dominating in the United States at 85.5% (95% PI: 83.8-87%). Significant regional differences exist: https://covid.cdc.gov/covid-data-tracker/#variant-proportions.
    - The CDC Nowcast has split BA.4 and BA.4.6; estimates for **BA.4** proportions are now at 7.7% (95% PI: 7-8.5%); estimates for **BA.4.6** proportions are now at 4.1% (95% PI: 3.2-5.4%)
    - The US CDC Nowcast estimates that **BA.2.12.1** proportions are 2.6% (95% PI: 2.4-2.8%)
- A major re-organization of PANGO lineage nomenclature in mid-July impacted some of the earlier sequence prevalence data.
- BA sub-lineages with sequence prevalence > 0.5% in July so far are (ranked in order of sequence prevalence)(note that a major re-organization of PANGO lineage nomenclature has occurred which has impacted some of these data):
    - **BA.5.2.1** - 22%, 2.6 fold growth
    - **BA.2.12.1** - 14%, 0.30 fold growth
    - **BA.5.5** - 11%, 1.4 fold growth
    - **BA.5.1** – 9.1%, 2.8 fold growth
    - **BA.5.2** – 7.3%, ***3.3 fold growth***
    - **BA.4.1** – 7.1%, 1.1 fold growth
    - **BA.5.6** – 5.6%, 2.1 fold growth
    - **BA.4** – 4.0%, 1.2 fold growth
    - **BA.5** – 4.0%, ***3.0 fold growth***

  - **BA.4.6** – 2.4%, ***3.6 fold growth (carries R346T and N658S)***
  - **BA.5.1.1** – 2.0%, 2.0 fold growth
  - **BA.2** – 1.7%, 0.24 fold growth
  - **BE.3** – 1.6%, 1.9 fold growth
  - **BE.1** – 1.6%, 2.2 fold growth
  - **BE.1.1** - 0.92%, ***3.7 fold growth***
  - **BF.5** - 0.74%, 2.3 fold growth (carries A1020S)

- ***In aggregate, BA.5.x sequences constitute 17% of sequences in June and 61% in July in the US***
- ***In aggregate, BA.4.x sequences constitute 5.8% of sequences in June and 14% in July 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 July so far in the US:
  - One **BA.5** sub-lineage (second most prevalent) carries the T76I substitution only
  - One **BA.5** sub-lineage carries the A701S substitution only
  - One **BA.5** sub-lineage carries the P1162L substitution only
  - One **BA.5** sub-lineage carries the L5F substitution only
- Notable substitutions present within the top ten BA.4 sub-lineages in July 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 N658S and R346T substitutions
  - Two **BA.4** sub-lineages carry the N658S substitution only
  - One **BA.4** sub-lineage carries the V3G and I670V substitutions
  - One **BA.4** sub-lineage carries the N658S and A701V substitutions
  - One **BA.4** sub-lineage carries the V3G and R346T substitutions
  - One **BA.4** sub-lineage carries the R346T and D936N substitutions
- ***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.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 sublineage present at 8.4% 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.5.2.1with 4-fold growth rate, and K444T in BA.5.6 with 3.5 fold growth rate in July)***
- ***BG.2 had 41 sequence in July 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)*

- One Delta sequences in the US in July.

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

- None in July.

USA – Recombinants

- **XE** – 6 sequences in the US in July
- **XM** – 1 sequences in the US in July
- **XAA** – 1 sequences in the US in July
- 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 July:
    - **BA.5.1** - 18%, 1.50 fold growth
    - **BA.5.2.1** - 17%, 2.2 fold growth
    - **BA.5.2** - 11%, 2.3 fold growth
    - **BA.2.12.1** – 6.2%, 0.30 fold growth
    - **BA.4.1** – 5.3%, 1.1 fold growth
    - **BA.4** – 4.4%, 1.1 fold growth
    - **BA.5.5** – 4.2%, 1.4 fold growth
    - **BE.1.1** – 3.5%, 1.3 fold growth
    - **BA.5** – 3.5%, 1.7 fold growth
    - **BA.2** – 3.2%, 0.27 fold growth
    - **BF.5** – 2.9%, ***3.0 fold growth (carries A1020S)***
    - **BA.5.6** – 2.5%, 2.0 fold growth
    - **BE.1** – 2.2%, 1.8 fold growth
    - **BA.4.6** – 1.4%, ***3.1 fold growth (carries R346T and N658S)***
    - **BA.5.1.1** - 0.89%, 1.7 fold growth
    - **BF.1** - 0.78%, 1.0 fold growth
    - **BE.3** - 0.63%, 1.6 fold growth
    - **BA.5.3.1** - 0.63%, 1.3 fold growth
    - **BA.5.1.3** - 0.57%, 1.2 fold growth
    - **BA.5.2.3** - 0.53%, 2.3 fold growth

- ***BA.2.75:*** *sometimes nicknamed "Centaurus", this sublineage shows a high growth rate in India (123 fold in June and 3.1 fold in July), and is present in 14 other countries, including the United States (CA, IL, NY, NC, WA, WI, AZ, IA, VA). Preliminary signs of increasing growth rates for July in Australia, Indonesia, Japan and Nepal.*
- ***BA.2.76:*** *this sublineage showed a high growth rate globally in June (9.6 fold) but has slowed down in July (0.60 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 July:
    - One **BA.5** sub-lineage carries the T76I substitution
    - One **BA.5** sub-lineage lacks the R408S substitution
    - One **BA.5** sub-lineage lacks the N440K substitution
    - One **BA.5** sub-lineage carries the P1162L substitution
- Notable substitutions present within the top ten **BA.4** sub-lineages globally in July:
    - One **BA.4** sub-lineage carries the V3G only
    - One **BA.4** sub-lineage carries the N658S substitution only
    - One **BA.4** sub-lineage carries the R346T and N658S substitutions (BA.4.6)
    - One **BA.4** sub-lineage carries the V3G and lacks the N440K substitution
    - 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 R408S substitution
    - One **BA.4** sub-lineage carries the V3G and C1235F substitutions

- Substitutions in spike that we are monitoring (> 3 fold growth from June to July) include the following (but note that the numbers are still relatively small for most of these):
    - **V70L** - 0.08%, 4 fold growth
    - **D1163Y** - 0.04%, 4 fold growth
    - **K444T** - 0.07%, 3.5 fold growth
    - **D1084E** - 0.03%, 3 fold growth
    - **E583D** - 0.03%, 3 fold growth
    - **F486I** - 0.06%, 3 fold growth
    - **G1099D** - 0.03%, 3 fold growth
    - **G1099S** - 0.03%, 3 fold growth
    - **I1225V** - 0.03%, 3 fold growth
    - **I68-** - 0.03%, 3 fold growth
    - **K444M** - 0.03%, 3 fold growth
    - **Q218E** - 0.03%, 3 fold growth
    - **Q675L** - 0.03%, 3 fold growth
    - **S221L** - 0.03%, 3 fold growth
    - **T1006I** - 0.03%, 3 fold growth
    - **G252D** - 0.03%, 3 fold growth

DELTA (**B.1.617.2** and **AY** sub-lineages)

- One Delta isolate globally in July so far
- The AY.57 sub-lineage of the Delta variant appears to have spiked in Viet Nam in June, showing a prevalence of 23.44% (n=15) and a growth rate of 21.5 fold.
- Five (5) AY.45 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 NGS-SA report and on this github designation issue here.

World (other VOIs)

- None in July

World – Recombinants

- **XE** – 7 sequences in July
- **XAF** – 5 in July
- **XAG** – 5 in July
- **XM** – 2 in July
- See a summary of recombinant lineages at the end of this report.

World – Other Omicron variants

- **BG.2** – 108 in July
- **BG.4** – 18 in July
- **BG.1** – 7 in July so far
- **BG.3** – 6 in July so far

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

- Neutralization of SARS-CoV-2 Omicron sublineages by 4 doses of mRNA vaccine
- COVID Cases USA: NYC Hospitalizations, BA5 Variant Infections Boom
- Reinfection, severe outcome more common with BA.5 variant; virus spike protein toxic to heart cells
- Australia nears 12,000 Covid deaths with hospitals 'heaving' under caseload
- CanSino's inhaled booster vaccine stronger against Omicron BA.1 subvariant than Sinovac

Recombinant lineages:

Four new recombinant lineages have been designated this week (XAL and XAP). 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	#189	B.1.634	B.1.631	N. America
XC	25	#263	Delta (AY.29)	B.1.1.7	Japan
XD	28	#444	Delta (AY.4)	BA.1	France
XE	2787	#454	BA.1	BA.2	UK
XF	34	#445	Delta	BA.1	UK
XG	477	#447	BA.1	BA.2	Denmark

XH	174	#448	BA.1	BA.2	Denmark
XJ	251	#449	BA.1	BA.2	Finland
XK	18	#460	BA.1	BA.2	Belgium
XL	119	#464	BA.1	BA.2	UK
XM	509	#472	BA.1.1	BA.2	Multiple EU
XN	158	#480	BA.1	BA.2	UK
XP	57	#481	BA.1.1	BA.2	UK
XQ	142	#468	BA.1.1	BA.2	UK
XR	181	#469	BA.1.1	BA.2	UK
XS	59	#471	Delta	BA.1.1	USA
XT	13	#478	BA.2	BA.1*	S. Africa
XU	16	#522	BA.1*	BA.2	India
XV	42	#463	BA.1*	BA.2*	Denmark
XW	99	#591	BA.1*	BA.2*	JP, DE, SI, CA, UK, US
XY	118	#606	BA.1*	BA.2*	FR, IL, UK, US
XZ	106	#636	BA.2*	BA.1*	Multiple
XAA	96	#664	BA.1*	BA.2*	US, IL
XAB	111	#665	BA.1*	BA.2*	IT, FR, DE, CH, DK
XAC	203	#590	BA.1*	BA.2*	IL, DE, CA, IR, NL, JP, UK, US
XAD	51	#607	BA.2*	BA.1*	CZ,DE,UK
XAE	126	#637	BA.2*	BA.1*	CA,US,NL,CH
XAF	257	#676	BA.1*	BA.2*	CR
XAG	333	#709	BA.1.1	BA.2.23	BR
XAH	81	#755	BA.2*	BA.1*	SI
XAJ	35	#826	BA.2.12.1	BA.4	UK
XAK	55	#823	BA.1*	BA.2*	DE
XAL	95	#757	BA.1.1	BA.2*	DE
XAM	341	#759	BA.1.1	BA.2.9	Panama
XAN	35	#771	BA.2*	BA.5.1	Multiple
XAP	69	#789	BA.2*	BA.1*	US

Newly designated Pango lineages:

- BA.2.13.1 from #785: Sublineage of BA.2.13 with Spike T941S
- BA.2.3.19 from #824: BA.2.3 sublineage with additional spike K417T
- BA.2.36.1 from #874: BA.2.36 sublineage with S:R346T circulating in Australia
- BA.2.38.2 from #828: BA.2.38 sublineage defined by S:K444N, Orf1a:T1543I, Orf1a:N3725S, Orf1a:T4355I and S:F157S circulating in India
- BA.2.81: BA.2 sublineage mainly in Brazil
- BA.2.9.5: BA.2.9 sublineage mainly in Thailand
- BA.4.1.5: BA.4.1 sublineage mainly in Israel
- BA.4.1.6 : BA.4.1 sublineage mainly in USA
- BA.4.1.7 : BA.4.1 sublineage mainly in Australia
- BA.4.1.8 from #800: Recent BA.4.1+ C28720T sublineage with S:346T
- BA.4.7 from #777: BA.4 + S:658S sublineage with S:R346S and Orf3a:I47V - emerged in South Africa
- BA.5.1.5 from #835: Sublineage of BA.5.1 with S:P1263Q
- BA.5.1.6: BA.5.1 sublineage mainly in Mexico
- BA.5.1.7 : BA.5.1 sublineage mainly in Canada
- BA.5.1.8: BA.5.1 sublineage mainly in Peru
- BA.5.2.5: BA.5.2 sublineage mainly in Indonesia
- BA.5.6.1 : BA.5.6 sublineage mainly in Peru
- BA.5.7: BA.5 sublineage mainly in Australia
- BA.5.8 from #743: BA.5 branch with G29032A, Orf1a:M2096L, Orf1b:V1271L +Orf1b:T2376I , S:P1162L
- BA.5.9 from #753: BA.5 sublineage with S:R346I
- BF.10: BA.5.2.1 sublineage, manily in the USA
- BF.11: BA.5.2.1 sublineage
- BF.12: BA.5.2.1 sublineage
- BF.3.1 from #825: Indian BF.3 sublineage with additional S:G446S
- BF.6 from #821: BA.5.2.1 sublineage with S:G181A
- BF.7 from #827: Sublineage of BA.5.2.1 with S:R346T and N:S33F
- BF.8: BA.5.2.1 sublineage mianly in the USA
- BF.9: BA.5.2.1 sublineage mainly in Canada
- BG.5 from #763: BA.2.12.1 Sublineage with T15009C, C21721T, and ORF1a:D3972G, USA

Variants being monitored by various public health agencies:

The ECDC has added the recombinant Omicron virus, XAK (spike: K147E, N460K, G339D, Δ69) to its list of "Variants under Monitoring".

The latest summary table for all agencies can be found here: https://docs.google.com/spreadsheets/d/1mAgO2wRJyEyGtL-SBe3NgOjUk7a5nZTeKmSorVkaHSU/edit#gid=0