BV-BRC SARS-CoV-2 Emerging Variant Report
January 03, 2023

Details of the emerging variants analysis can be found in "BV-BRC SARS-CoV-2 Emerging Variant Report – 20230103.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 December in order to identify early signs of novel variants emerging.

The key findings are summarized below.

USA – VOC

OMICRON

- Based on CDC Nowcast estimates (https://covid.cdc.gov/covid-data-tracker/#variant-proportions) for the week ending 12/31/22 in the US in order of prevalence:
  - ***XBB.1.5 has rapidly emerged and become the predominant variant over the last month and is currently estimated at 40.5% in the U.S., a rapid rise from 21.7% last week***
  - **BQ.1.1** is currently estimated at 26.9%, down from last week's 33.2%
  - **BQ.1** is currently estimated at 18.3%, down from last week's 24.1%
  - **BA.5** is currently estimated at 3.7%, down from last week's 6.5%
  - The original **XBB** is currently estimated at 3.6%, down slightly from last week's 4.2%
  - **BN.1** is currently estimated at 2.4%, down from last week's 3.1%
  - **BF.7** is currently estimated at 2.1%, down from last week's 3.4%
  - **BA.2.75** is currently estimated at 0.9%, down from last week's 1.1%
  - **BA.5.2.6** is currently estimated at 0.6%, down from last week's 1.0%
  - **BA.4.6** is currently estimated at 0.3%, down from last week's 0.6%
- ***XBB.1.5***
  - ***Appears to have emerged in the northeastern U.S. (NY & CT) in October 2022***
  - ***Recombinant between two different BA.2 subvariants - BJ.1 and BA.2.75***
  - ***Differs from parent XBB by an F486P substitution in S instead of the F486S in XBB***
  - ***Likely founder differs from ancestral Wuhan 1 by the following substitutions in S:***
    - ***T19I,L24-,P25-,P26-,A27S,V83A,G142D,Y144-,H146Q,Q183E,V213E,G339H,R346T,L368I,S371F,S373P,S375F,T376A,D405N,R408S,K417N,N440K,V445P,G446S,N460K,S477N,T478K,E484A,F486P,F490S,Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K***

        - ***Note that the***
    - ***The XBB.1.5 sub-lineage predominant in December has also acquired the G252V substitution***
    - ***Note that the Y144-, H146Q annotation from GISAID is equivalent to Y145Q, H146- at the amino acid level, but the latter is probably the correct translation from the nucleotide sequence***
    - ***The F486P substitution likely increases affinity for ACE2 receptor***
    - ***Neutralization of XBB and XBB.1 (and likely XBB.1.5) by sera from vaccinees and infected persons was markedly impaired - https://www.biorxiv.org/content/10.1101/2022.11.23.517532v1.full.pdf***
    - ***Monoclonal antibodies capable of neutralizing the original Omicron variant, including those with Emergency Use Authorization, were largely inactive against the XBB and XBB.1 subvariants (and likely XBB.1.5) - https://www.biorxiv.org/content/10.1101/2022.11.23.517532v1.full.pdf***
- ***XBB***
    - ***Likely founder differs from ancestral Wuhan 1 by the following substitutions in S: T19I,L24-,P25-,P26-,A27S,V83A,G142D, Y144-,H146Q,Q183E,V213E,G339H,R346T,L368I,S371F,S373P,S375F,T376A,D405N, R408S,K417N,N440K,V445P,G446S,N460K,S477N,T478K,E484A,F486S,F490S, Q498R,N501Y,Y505H,D614G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969 K***
    - ***The XBB sub-lineage predominant in December has acquired the additional G252V substitution***
    - ***Note that the Y144-, H146Q annotation from GISAID is equivalent to Y145Q, H146- at the amino acid level, but the latter is probably the correct translation from the nucleotide sequence***
- Based on BV-BRC analysis of comprehensive data from GISAID, listed below are lineages with sequence prevalence >2.0% or a growth rate >3 fold and count >30 in December so far (ranked in order of sequence prevalence). Lineages with fold growth >3 from November to December so far are highlighted in ***bold italic***:
    - **BQ.1.1** - 16%, 1.4 fold growth
    - **BQ.1** – 9.3%, 1.2 fold growth
    - **BA.2.75** – 4.4%, 1.2 fold growth
    - ***XBB.1.5 – 3.9%, 12 fold growth***
    - ***XBB – 3.6%, 3.0 fold growth***
    - ***BA.2 – 2.7%, 5.9 fold growth (Note, the majority of these are misclassified XBB* genomes by GISAID)***
    - **BQ.1.1.22** – 2.2%, 2.8 fold growth
    - **BQ.1.1.4** – 2.2%, 1.5 fold growth
    - **BF.7** – 2.1%, 0.67 fold growth
    - **BQ.1.3** – 2.1%, 1.2 fold growth
    - **BQ.1.2** – 2.0%, 1.3 fold growth
    - ***BQ.1.26 - 0.26%, 3.7 fold growth***

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

- No Delta sequences in the US in December so far; three in November

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

- None

USA – Recombinants

- **XBB.1.5** - 943 sequences in December so far; 240 sequences in November
- **XBB** - 875 sequences in December so far; 916 sequences in November
- **XBB.1** - 308 sequences in December so far; 953 sequences in November
- **XBB.2** - 45 sequences in December so far; 211 sequences in November
- **XBB.4** - 5 sequences in December so far; 10 sequences in November
- **XBB.3** - 4 sequences in December so far; 55 sequences in November
- **XBF** - 2 sequences in December so far; 1 sequences in November
- **XBB.1.3** - 1 sequences in December so far; 3 sequences in November
- **XBB.1.4** - 1 sequences in December so far; 1 sequences in November
- **XBB.1.1** - 1 sequences in December so far; 45 sequences in November
- **XBD** - 1 sequences in December so far; 28 sequences in November

World – VOC

OMICRON

- Omicron remains dominant globally. Listed below are lineages showing the highest sequence prevalence (> 2.0%) or a fold growth > 3 fold and count >50 in December so far. Lineages with fold growth >3 from November to December are highlighted in ***bold italic***:
  - **BQ.1.1** - 12%, 1.2 fold growth
  - **BA.2.75** – 9.2%, 1.4 fold growth
  - **BQ.1** – 4.6%, 1.1 fold growth
  - **BF.7** – 3.5%, 0.74 fold growth
  - **XBB** – 3.1%, 2.4 fold growth
  - **BQ.1.1.22** – 2.7%, 2.4 fold growth
  - **BA.5.2** – 2.2%, 0.32 fold growth
  - ***XBB.1.5 – 1.4%, 12 fold growth***
  - ***BA.2 – 1.3%, 3.4 fold growth (Note, the majority of these are misclassified XBB* genomes by GISAID)***
  - ***BQ.1.1.20 – 1.3%, 3.1 fold growth***
  - ***BA.5.11 - 0.69%, 3.3 fold growth***

- Substitutions in spike that we are monitoring (>3 fold growth from November to December with counts >50) include those listed below (but note that the numbers are still relatively small for some of these). Substitutions with sequence prevalence >1.0% in December so far are highlighted in ***bold italic***::
  - ***Y144L – 1.0%, 5.4 fold growth***
  - ***Y145P – 1.0%, 5.4 fold growth***
  - ***N148Q – 1.0%, 5.1 fold growth***
  - ***N149Q – 1.0%, 5.1 fold growth***
  - L18F - 0.25%, 5 fold growth
  - R21G - 0.24%, 4.8 fold growth
  - T19R - 0.24%, 4.8 fold growth
  - ***H146K – 1.1%, 4.8 fold growth***

- ***F486P – 3.8%, 4.2 fold growth***
- N149T - 0.08%, 4 fold growth
- V1133A - 0.08%, 4 fold growth
- Y145T - 0.08%, 4 fold growth
- F186L - 0.27%, 3.9 fold growth
- A684V - 0.14%, 3.5 fold growth
- V608I - 0.07%, 3.5 fold growth
- A706V - 0.29%, 3.2 fold growth
- K147- - 0.47%, 3.1 fold growth
- N148-0.47%, 3.1 fold growth

Convergent mutations in the N-Terminal Domain (NTD) of the Spike protein: (more information here)

- We noticed a sharp increase in mutations located in the NTD in the past two months (November and December 2022)
- The majority of these mutations occur in structural loops know as N1-N5 loops, especially the N3 loop
- Evidence exists that these NTD mutations are highly convergent
- Evidence suggest that these mutations result in antigenic escape
- These NTD mutations also occur in other VOCs and long-term infections
- NTD mutations may occur sequentially after RBD escape mutations occur

The following summarizes the information:

Positions in N1 Loop (14 - 26)

- L18F (~0.25%), 5-fold increase
- T19R (~0.25%), 5-fold increase
- T19I (occurs in 98% genomes - signature Omicron mutation)
- R21G (~0.24%), 5-fold increase
- L24-, P25-, P26-, A27S are signature Omicron mutations that occur in > 97% circulating November genomes.

Positions in N2 Loop (67 - 79)

- No significant increase in mutations in this region although H69- and Y70- are predominant in BA.4/5* derived sublineages (>79% December genomes).

Positions between 144 and 157 (N3 loop: 141 - 156)

- Y144L (only 207 genomes, ~1%). Y144L increased by 5-fold.
- Y144- (from ~2% to ~22% prevalence in the past 3 months)
- Y145P (~1%, Y145P has increased by 5.4-fold in the past month.
- Y145T (~0.08%, 4-fold increase)
- Y145H (~0.3%)
- Y145- (~0.3%)
- H146K (~1%), (4.8-fold increase)
- H146L (~0.3%), (~1.8-fold increase)
- H146Q (~6%)
- H146- (~0.8%)
- K147-(~0.47%), (3-fold increase)
- K147E (~11.4% mainly from BA.2.75 lineages)
- K147Q(~0.2%), (~3-fold increase)
- K147I(~0.27%)

- K147N(~0.6%)
- K147T (~0.04%)
- N148Q(~1.2%), 5-fold increase
- N148-(~0.47%), 3-fold increase
- N148T(~0.11%), 2.8-fold increase
- N149Q (1%), 5-fold increase; removes the N149 glycan.
- N149T (0.08%), 4-fold increase
- K150E (~0.45%)
- S151G (~0.09%), 3-fold increase
- W152R (~11%, BA.2.75 lineages); steady.
- M153V (~0.12%), 3-fold increase
- M153I (~0.4%), 2-fold increase
- M153T (~0.6%)
- E154S (~0.09%, 3-fold increase

156, 157, 158: moderate increase (2-3-fold in November) in mutations at these positions, including E156G, E156-, F157-, F157L, and R158-.

Delta like mutations attributable to recent increases in Delta/Omicron recombinant lineages such as XBC and XAY (and a few XBA).
Some BA.2.75 sub-lineages with E156-, F157- (mainly from Turkey), and of course most BA.2.75 already have F157L. But it's an interesting pattern.
Positions in N4 Loop (177 - 186)

- M177T (~0.16%), no longer increasing
- M177L (~0.04%), 2-fold increase
- G181V (~0.4%), no increase
- K182I (~0.18%), no increase
- Q183E (~7.2%), no increase
- N185T (0.08%), 2.7-fold
- N185D (0.52%), 2.3-fold
- F186L (0.27%), 3.9-fold

Positions between 243 and 253 (N5 loop: 246 - 260)

- 242: L242F (0.2%, 2-fold increase)
- 243: A243S (0.02%, 2-fold increase)
- 244: Deletions (A243-,L244-) occur simultaneously at both these positions in XBC* lineages (~0.14%, 1.4-fold increase)
- 245: H245N, H245Y (0.6% and 0.2% respectively, no increase)
- 248: Y248D, Y248S (0.04 and 0.16% respectively, 4-fold & 2.7-fold increase)
- 249: L249S, (0.03%, 3-fold increase)
- 251: P251H/L (0.15%, 0.23%; 1.4, 1.6-fold increase)
- 252: G252V (5.6%, 2-fold increase)
- 253: G253G (1%, no increase)
- 255: S255F (0.7%, no increase)
- 256: S256A/P (0.6% and 0.02% respectively, 2-fold increase)
- 257: G257S and G257D found in BA.2.75 and BA.2.3.20* (>11%)
- 260: A260V (0.04%, 4-fold increase)

DELTA (**B.1.617.2**, **AY** sub-lineages and some **X** recombinants)

- 31 Delta genomes in December so far (mostly XAY.2 in Denmark)

World (other VOIs)

- none in December so far

World – Recombinants (count >5 in December)

- **XBB** - 2193 sequences in December so far; 3196 sequences in November
- **XBB.1.5** - 980 sequences in December so far; 261 sequences in November
- **XBB.1** - 696 sequences in December so far; 4816 sequences in November
- **XBB.2** - 97 sequences in December so far; 1136 sequences in November
- **XBB.1.4.1** - 60 sequences in December so far; 256 sequences in November
- **XBC.1** - 45 sequences in December so far; 204 sequences in November
- **XBB.1.1** - 28 sequences in December so far; 289 sequences in November
- **XAY.2** - 27 sequences in December so far; 91 sequences in November
- **XBB.1.4** - 16 sequences in December so far; 64 sequences in November
- **XBB.3** - 10 sequences in December so far; 242 sequences in November
- **XBB.4** - 7 sequences in December so far; 62 sequences in November
- **XBF** - 6 sequences in December so far; 18 sequences in November
- **XAZ** - 6 sequences in December so far; 67 sequences in November

Variants that have been mentioned in the media and/or social media (*from last weeks report*):

- New coronavirus subvariant, XBB, now widespread in New England
- CDC tracking rise of new XBB.1.5 COVID variant, already more than 40% of U.S. cases
- XBB is highly contagious, evades vaccines and monoclonal antibodies
- Belgium to test wastewater on airliners from COVID-hit China
- Flu and RSV on the Decline But COVID Hospitalizations Rise
- China Has No New Covid Variants as Sequencing Efforts Strengthen
- Early Estimates of Bivalent mRNA Vaccine Effectiveness in Preventing COVID-19-Associated Emergency Department or Urgent Care Encounters and Hospitalizations Among Immunocompetent Adults
  Prior infection- and/or vaccine-induced protection against Omicron BA.1, BA.2 and BA.4/BA.5-related hospitalisations in older adults: a test-negative case-control study in Quebec, Canada

Recombinant lineages:

One new recombinant lineage has been added this week. A summary table of recombinant lineages can be found below with more details. 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-XBK are Omicron/Omicron or Omicron/Delta recombinants. With the exception of XBB, the majority of these recombinant lineages do not appear to have taken off and several have not been detected in recent weeks. The XBB 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	33	#444	Delta (AY.4)	BA.1	France
XE	2836	#454	BA.1	BA.2	UK
XF	34	#445	Delta	BA.1	UK
XG	479	#447	BA.1	BA.2	Denmark
XH	174	#448	BA.1	BA.2	Denmark
XJ	256	#449	BA.1	BA.2	Finland
XK	25	#460	BA.1	BA.2	Belgium
XL	120	#464	BA.1	BA.2	UK
XM	526	#472	BA.1.1	BA.2	Multiple EU
XN	288	#480	BA.1	BA.2	UK
XP	57	#481	BA.1.1	BA.2	UK
XQ	145	#468	BA.1.1	BA.2	UK
XR	183	#469	BA.1.1	BA.2	UK
XS	60	#471	Delta	BA.1.1	USA
XT	17	#478	BA.2	BA.1*	S. Africa
XU	16	#522	BA.1*	BA.2	India
XV	42	#463	BA.1*	BA.2*	Denmark
XW	195	#591	BA.1*	BA.2*	JP, DE, SI, CA, UK, US
XY	126	#606	BA.1*	BA.2*	FR, IL, UK, US
XZ	49	#636	BA.2*	BA.1*	Multiple
XAA	965	#664	BA.1*	BA.2*	US, IL
XAB	131	#665	BA.1*	BA.2*	IT, FR, DE, CH, DK
XAC	16	#590	BA.1*	BA.2*	IL, DE, CA, IR, NL, JP, UK, US
XAD	51	#607	BA.2*	BA.1*	CZ,DE,UK
XAE	6	#637	BA.2*	BA.1*	CA,US,NL,CH

XAF	39	#676	BA.1*	BA.2*	CR
XAG	35	#709	BA.1.1	BA.2.23	BR
XAH	88	#755	BA.2*	BA.1*	SI
XAJ	273	#826	BA.2.12.1	BA.4	UK
XAK	96	#823	BA.1*	BA.2*	DE
XAL	2	#757	BA.1.1	BA.2*	DE
XAM	51	#759	BA.1.1	BA.2.9	Panama
XAN	167	#771	BA.2*	BA.5.1	Multiple
XAP	173	#789	BA.2*	BA.1*	US
XAQ	3	#798	BA.1*	BA.2*	Canada
XAR	70	#860	BA.1*	BA.2*	Reunion/France
XAS	633	#882	BA.5*	BA.2*	N. America
XAT	20	#885	BA.2.3.13	BA.1*	Japan
XAU	21	#894	BA.1.1*	BA.2.9*	Multiple
XAV	131	#911	BA.2*	BA.5*	France
XAW	48	#895	BA.2*	AY.122	Russia
XAY*	395	#844	BA.2	AY.45	S. Africa
XAZ	2166	#797	BA.2.5, BA.5	BA.2.5	Multiple
XBA	1	#844	AY.45	BA.2	S. Africa
XBB*	22673	#1058	BJ.1	BM.1.1.1	Singapore/US
XBC*	650	#1100	Delta	BA.2	Philippines
XBD	502	#1137	BA.2.75.2	BF.5	Multiple
XBE*	6725	#1246	BA.5.2	BE.4	USA
XBF	1854	#1259	BA.5.2.3	CJ.1	Australia
XBG	125	#896	BA.2.76	BA.5.2	UK
XBH	~128	#1229	BA.2.3.17	BA.2.75.2	Multiple
XBJ	~247	#1268	BA.2.3.20	BA.5.2	Multiple
XBK	~50	#1381	CJ.1	BA.5.2	Denmark

Newly designated Pango lineages:

Few new lineages designated last week:

- BA.5.2.47: Undesignated BA.5.2+orf1b:1050N+S:R346T lineage with S:K147N
- DF.1.1: DF.1 + S:V445A, ORF8:A51V
- BQ.1.1.32: BQ.1.1 sublineage(s) with S:Y144-, S:M153I

- BQ.1.28: BQ.1 Sublineage with ORF3a:R68I, ORF1a:V2157I, ORF1b:P2321L
- BA.5.2.46: New BA.5.2 +Orf1b:1050N + C26681T with Orf1a:K510E, S:K444T and S:N460K
- CK.1.1: CK.1 Sublineage with S:N856S, S:Y144del
- BF.5.2: BF.5 sublineage with S:V445A circulating in Japan
- BF.5.1: BF.5 sublineage with S:346T circulating in Japan
- DN.1.1: DN.1 sublineage with ORF1a:R2159W
- DJ.1.3: DJ.1 with additional mutations ORF1ab:T6098A, Nuc:T9070C, A22924G mutations circulating mostly in Peru
- BN.1.3.2: BN.1.3 with S:V445A
- BQ.1.25.1: BQ.1.25 Sublineage with S:L858I, ORF1a:A54V
- BF.10.1: BF.10 Sublineage with S:V445A, S:G446S, ORF8:ins18NG*
- CR.1.3: CR.1 + S:144del + Orf1a:D2592G + S:H146Q - 16 sequences
- XBB.1.6: XBB.1 sublineage with S:L216F
- CH.1.1.3: Potential CH.1.1 with Spike S255P mainly from Australia and New Zealand
- XBK: BA.5.2/CJ.1 recombinant, 46 samples from Denmar
- BE.10: Another BA.5.3.1 sublineage with S:K444T and S:N460K
- CN.2: BA.5.2.21 sublineage with S:R346T and S:Y28H circulating in USA