

BV-BRC SARS-CoV-2 Emerging Variant Report December 20, 2022

Details of the emerging variants analysis can be found in “BV-BRC SARS-CoV-2 Emerging Variant Report – 20221220.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 12/17/22 in the US in order of prevalence:
 - ***BQ.1.1 has overtaken BQ.1 and is currently estimated at 38.4%, up from last week's 36.8***
 - ***BQ.1 is currently estimated at 30.7%, level from last week's 31.1%***
 - ***BA.5*** proportions continue to drop in the United States, down from 11.5% last week to 10.0% this week
 - ***BF.7 has been added to the Nowcast tracker and is currently estimated at 4.9%, slightly down from last week***
 - ***XBB has been added to the tracker and is currently estimated at 7.2%, up from last week's 4.7%***
 - ***BN.1 has been added to the tracker and is relatively steady from last week at 4.1%***
 - ***BA.5.2.6*** is steady at 1.6%
 - ***BA.4.6*** continues to decrease in proportions, now at 1.1%
- Based on BV-BRC analysis of comprehensive data from GISAID, listed below are lineages with sequence prevalence >1.0% or a growth rate >3 fold and count >10 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 - 13%, 1.1 fold growth
 - ***XBB.1 – 9.9%, 9.5 fold growth***
 - BQ.1 – 9.7%, 1.0 fold growth
 - XBB – 3.9%, 2.1 fold growth
 - BF.7 – 3.8%, 1.2 fold growth
 - BA.2.75 – 3.5%, 0.96 fold growth
 - BQ.1.12 – 3.4%, 1.9 fold growth

- BQ.1.3 – 3.2%, 1.8 fold growth
- BA.5.2.1 – 2.9%, 0.48 fold growth
- BQ.1.1.4 – 2.8%, 2 fold growth
- **BQ.1.1.15 – 2.5%, 5.2 fold growth**
- BA.5.2 – 2.0%, 0.38 fold growth
- BQ.1.1.3 – 1.9%, 1.5 fold growth
- BQ.1.10 – 1.8%, 1.9 fold growth
- **CQ.2 – 1.6%, 3.7 fold growth**
- BQ.1.14 – 1.6%, 1.3 fold growth
- BQ.1.1.5 – 1.5%, 1.2 fold growth
- BQ.1.13 – 1.5%, 1.8 fold growth
- BQ.1.18 – 1.3%, 1.2 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** - 78 sequences in December so far; 612 sequences in November
- **XBB** - 31 sequences in December so far; 1108 sequences in November
- **XBB.2** - 5 sequences in December so far; 65 sequences in November
- **XAZ** - no sequences in December so far; 12 sequences in November
- **XBB.3** - no sequences in December so far; 10 sequences in November
- **XBD** - no sequences in December so far; 8 sequences in November
- **XBE** - no sequences in December so far; 7 sequences in November
- **XBB.1.3** - no sequences in December so far; 3 sequences in November
- **XBB.4** - no sequences in December so far; 3 sequences in November
- **XAY.1** - no sequences in December so far; 2 sequences in November
- **XAV** - no sequences in December so far; 1 sequence in November
- **XBB.1.1** - no sequences in December so far; 1 sequence in November

World – VOC

OMICRON

- Omicron remains dominant globally. Listed below are lineages showing the highest sequence prevalence (> 1.0%) or a fold growth > 3 fold and count >10 in December so far. Lineages with fold growth >3 from November to December are highlighted in **bold italic**:
 - BA.2.75 - 13%, 2.0 fold growth
 - BQ.1.1 - 12%, 1.1 fold growth
 - **XBB – 5.2%, 1.9 fold growth**
 - BQ.1 – 4.3%, 0.82 fold growth
 - BQ.1.18 – 4.2%, 2.6 fold growth
 - BF.7 – 3.2%, 0.69 fold growth

- **BQ.1.1.10 – 2.4%, 4.4 fold growth**
 - BA.5 – 2.4%, 2.5 fold growth
 - BA.5.2 – 1.9%, 0.28 fold growth
 - BA.5.1 – 1.9%, 0.64 fold growth
 - XBB.1 – 1.6%, 2.0 fold growth
 - BQ.1.8 – 1.5%, 2.1 fold growth
 - BA.5.2.1 – 1.4%, 0.26 fold growth
 - BQ.1.2 – 1.2%, 1.1 fold growth
 - BQ.1.1.18 – 1.0%, 0.92 fold growth
 - **BN.1.3.1 - 0.79%, 4.6 fold growth**
 - **BQ.1.1.8 - 0.73%, 3.2 fold growth**
 - **BN.1.4 - 0.49%, 4.5 fold growth**
 - **BQ.1.1.2 - 0.35%, 3.2 fold growth**
 - **BQ.1.1.19 - 0.24%, 3.4 fold growth**
 - **BA.4.6.3 - 0.16%, 3.2 fold growth**
- Substitutions in spike that we are monitoring (>3 fold growth from November to December with counts >10) 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**::
 - I1232V - 0.23%, 23 fold growth
 - **L24S – 1.1%, 22 fold growth**
 - A684V - 0.59%, 15 fold growth
 - **V70I – 1.3%, 14 fold growth**
 - N481K - 0.24%, 12 fold growth
 - R21G - 0.46%, 7.7 fold growth
 - T19R - 0.46%, 7.7 fold growth
 - D215Y - 0.3%, 7.5 fold growth
 - **N148- - 1.4%, 7.4 fold growth**
 - **K147- - 1.4%, 7 fold growth**
 - L18F - 0.48%, 6.9 fold growth
 - F186L - 0.53%, 6.6 fold growth
 - V1133A - 0.17%, 5.7 fold growth
 - D215G - 0.43%, 5.4 fold growth
 - S673G - 0.71%, 5.1 fold growth
 - **P1162S – 1.6%, 4.9 fold growth**
 - A1078S - 0.29%, 4.8 fold growth
 - A706V - 0.48%, 4.8 fold growth
 - P621S - 0.62%, 4.4 fold growth
 - N185D - 0.85%, 4.0 fold growth
 - L368J - 0.19%, 3.8 fold growth
 - T1117I - 0.53%, 3.8 fold growth
 - E156G - 0.56%, 3.7 fold growth
 - N148Q - 0.86%, 3.4 fold growth
 - N149Q - 0.86%, 3.4 fold growth
 - Y144L - 0.85%, 3.4 fold growth
 - Y145P - 0.85%, 3.4 fold growth

- R158- - 0.5%, 3.3 fold growth
- N211- - 0.42%, 3.2 fold growth
- T470N - 0.3%, 3 fold growth
- L212I - 0.42%, 3 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 from last week's report:

Positions in N1 Loop (14 - 26)

- L18F (~0.01%), 3.5-fold increase
- T19R (~0.07%), 3.5-fold increase
- T19V(~0.02%), 2-fold increase
- T19I (occurs in 96% genomes – signature Omicron mutation)
- R21G (~0.06%), 6-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 (>83% November genomes).

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

- Y144L (only 207 genomes, ~0.2%); increased by 12-fold in past month
- Y144- (from ~2% to ~19% prevalence in the past 3 months) 2-fold increase
- Y145P (~0.2%), Y145P has increased by 12-fold in the past month
- Y145H (~0.5%)
- Y145- (~0.4%)
- H146K (~0.3%), (4.6-fold increase)
- H146L (~0.2%), (~3-fold increase)
- H146Q (~0.4%), (~2.3-fold increase)
- H146- (~0.1%)
- K147- (~0.1%), (4-fold increase)
- K147Q (~0.2%), (~3-fold increase)
- K147E (~9% mainly from BA.2.75 lineages),
- K147I (~0.2%)
- K147N (~0.4%)
- K147T (~0.07%)
- N148Q (~0.2%), 12-fold increase
- N148- (~0.2%), ~4.4-fold increase

- N148T (~0.05%), ~2-fold increase
- N149Q (0.2%), 12-fold increase; removes the N149 glycan.
- K150E (~0.4%), 4-fold increase
- S151G (~0.03%), 3-fold increase
- W152R (BA.2.75 lineages); steady
- M153V/T sporadic increases in October and November.
- moderate increase (2-3-fold in November) in mutations in positions 156 - 158, 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 (~0.13%), 4-fold increase
- M177L (~0.02%), 2-fold increase
- G181V (~0.4%), no increase
- K182I (~0.1%), 4.5-fold increase
- Q183E (~4%), 2.4-fold increase
- Q183P (~0.02%), 2-fold increase
- F186L (~0.08%), 2-fold increase

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

- 243 & 244: deletions (A243-,L244-) are paired in XBC* lineages (~0.1%, 1.8-fold increase)
- 245: H245N, H245Y (0.9% and 0.1% respectively, no increase)
- 247: S247N (0.2%, 1.7-fold increase, BF*)
- 248: Y248- (0.1%, 1.6-fold increase)
- 251: P251S/L/H (0.03%, 0.2%, 0.1% ; 3-, 2.4, 1.5-fold increase)
- 252: G252V (2.6%, 3-fold increase)
- 253: G253G (0.7%, 3-fold increase)
- 255: S255P, S255F (0.05% and 0.8%, 2.5-fold and 1-fold respectively)
- 257: G257S and G257D found in BA.2.75 and BA.2.3.20*

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

- 2 Delta genomes in December so far

World (other VOIs)

- none in December so far

World – Recombinants

- **XBB** - 361 sequences in December so far; 5277 sequences in November
- **XBB.1** - 112 sequences in December so far; 1503 sequences in November
- **XBB.2** - 7 sequences in December so far; 246 sequences in November
- **XBC.1** - 3 sequences in December so far; 137 sequences in November
- **XAY.1** - 1 sequence in December so far; 8 sequences in November
- **XBC** - 1 sequence in December so far; 4 sequences in November
- **XAY.2** - 1 sequence in December so far; 2 sequences in November

- **XBB.3** - no sequences in December so far; 70 sequences in November
- **XAZ** - no sequences in December so far; 53 sequences in November
- **XBB.1.1** - no sequences in December so far; 43 sequences in November
- **XBD** - no sequences in December so far; 32 sequences in November
- **XBB.4** - no sequences in December so far; 21 sequences in November
- **XBE** - no sequences in December so far; 7 sequences in November
- **XBB.1.3** - no sequences in December so far; 5 sequences in November
- **XAY** - no sequences in December so far; 2 sequences in November
- **XBB.5** - no sequences in December so far; 2 sequences in November
- **XAS** - no sequences in December so far; 1 sequence in November
- **XAV** - no sequences in December so far; 1 sequence in November
- **XBC.2** - no sequences in December so far; 1 sequence in November

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

- [Japan Logs 847,371 New COVID-19 Cases in Past Week](#)
- ['A huge burden': L.A. hospitals strained by COVID surge, very bad flu season](#)
- [Omicron subvariants that more easily dodge immunity are causing more than 70% of U.S. infections](#)
- [US flu surge continues amid jump in COVID activity](#)
- [China medical expert says COVID has mutated, should be renamed - state media](#)
- [Meta-analysis estimates 29% vaccine effectiveness against long COVID](#)
- [Duration of viral shedding of the Omicron variant in asymptomatic and mild COVID-19 cases from Shanghai, China](#)
- [Alpha to Omicron: Disease Severity and Clinical Outcomes of Major SARS-CoV-2 Variants](#)
- [BA.2 and BA.5 omicron differ immunologically from both BA.1 omicron and pre-omicron variants](#)
- Neutralising antibody potency against SARS-CoV-2 wild-type and omicron BA.1 and BA.4/5 variants in patients with inflammatory bowel disease treated with infliximab and vedolizumab after three doses of COVID-19 vaccine (CLARITY IBD)
- [Efficacy of Antiviral Agents against Omicron Subvariants BQ.1.1 and XBB](#)

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-XBJ 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
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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	217	#636	BA.2*	BA.1*	Multiple
XAA	104	#664	BA.1*	BA.2*	US, IL
XAB	114	#665	BA.1*	BA.2*	IT, FR, DE, CH, DK
XAC	207	#590	BA.1*	BA.2*	IL, DE, CA, IR, NL, JP, UK, US
XAD	99	#607	BA.2*	BA.1*	CZ,DE,UK
XAE	133	#637	BA.2*	BA.1*	CA,US,NL,CH
XAF	301	#676	BA.1*	BA.2*	CR
XAG	423	#709	BA.1.1	BA.2.23	BR

XAH	169	#755	BA.2*	BA.1*	SI
XAJ	106	#826	BA.2.12.1	BA.4	UK
XAK	149	#823	BA.1*	BA.2*	DE
XAL	122	#757	BA.1.1	BA.2*	DE
XAM	547	#759	BA.1.1	BA.2.9	Panama
XAN	213	#771	BA.2*	BA.5.1	Multiple
XAP	81	#789	BA.2*	BA.1*	US
XAQ	4	#798	BA.1*	BA.2*	Canada
XAR	10	#860	BA.1*	BA.2*	Reunion/France
XAS	190	#882	BA.5*	BA.2*	N. America
XAT	27	#885	BA.2.3.13	BA.1*	Japan
XAU	43	#894	BA.1.1*	BA.2.9*	Multiple
XAV	80	#911	BA.2*	BA.5*	France
XAW	45	#895	BA.2*	AY.122	Russia
XAY*	72	#844	BA.2	AY.45	S. Africa
XAZ	2308	#797	BA.2.5, BA.5	BA.2.5	Multiple
XBA	3	#844	AY.45	BA.2	S. Africa
XBB*	12582	#1058	BJ.1	BM.1.1.1	Singapore/US
XBC*	398	#1100	Delta	BA.2	Philippines
XBD	411	#1137	BA.2.75.2	BF.5	Multiple
XBE*	5429	#1246	BA.5.2	BE.4	USA
XBF	843	#1259	BA.5.2.3	CJ.1	Australia
XBG	50	#896	BA.2.76	BA.5.2	UK
XBH	~100	#1229	BA.2.3.17	BA.2.75.2	Multiple
XBJ	~25	#1268	BA.2.3.20	BA.5.2	Multiple

Newly designated Pango lineages:

Few new lineages designated last week:

- [DJ.1.2: DJ.1 sublineage with S:N460K \(and multiple AA substitutions\) emerged in Peru](#)
- [BQ.1.1.25: BQ.1.18 with S:Y144-, S:F490S and N:G30- in New York](#)