

## Recommendations for reporting and notification of SARS-CoV-2 Variants of Concern and Variants of Interest

27 Julio 2021

Since the initial genomic characterization of SARS-CoV-2, the virus has been divided into different genetic groups. The occurrence of mutations is a natural and expected event within the evolution process of the virus.<sup>[1]</sup>

Some specific mutations define the viral genetic groups or lineages that are currently circulating globally. Due to various microevolution processes and selection pressures, some additional mutations may appear, generating differences within each genetic group (called variants).<sup>[2,3]</sup>

However, some mutations can improve the virus ability to spread, change the clinical manifestations, or even affect the effectiveness of vaccines, antivirals or diagnostic tools. Since late 2020, these variants that could pose an increased risk to global public health have been emerging<sup>[4]</sup> On 25 February 2021, the World Health Organization (WHO) provided operational definitions for SARS-CoV-2 variants of interest (VOI) and variants of concern (VOC). These definitions are available at <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/>.

Although the variants have assigned systematic nomenclature according to their genomic and phylogenetic patterns (e.g. those assigned by GISAID, Nextstrain and Pango), in order to make naming easier and simplify public communications, and to avoid nourishing stigma toward specific countries or places where new variants arise, WHO has assigned simple, easy to say and remember labels for de VOC and VOI of SARS-CoV-2, using letters of the Greek alphabet.<sup>[4]</sup>

Currently 4 VoCs are recognized by the World Health Organization: Alpha (linage B.1.1.7); Beta (linage B.1.351); Gamma (linage B.1.1.28/P.1) and Delta (linage B.1.617-2). The full list of SARS-CoV-2 variants, according to the WHO is available at: <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/>, being reviewed and updated periodically.

Due to the potential impact in public health surveillance, notification to PAHO/WHO under the International Health Regulations is required when a VOC or VOI is detected for the first time.

However, the initial detection of a VOC or a VOI can be either by sequencing or targeted RT-PCR, relying on relatively complex laboratory analysis. In this sense, this interim guideline provides operational recommendations for reporting and notification of VOC and VOI through IHR official channels.

## Screening and identification of VOC or VOI

Different approaches are available for detecting VOC or VOI of SARS-CoV-2 based on genomic sequencing or real-time RT-PCR.

### Real-time RT-PCR strategy for VOC screening and identification.

Through the COVID-19 Genomic Surveillance Network (COVIGEN), PAHO has been supporting the countries providing reagents and supporting the implementation of different real-time RT-PCR protocols for either VOC screening and VOC preliminary identification.

These molecular screening test targets a specific mutation shared by the Alpha, Beta and Gamma VOC. However, this mutation is not present on the Delta VOC, thus cannot be detected through this assay.

The Alpha, Beta and Gamma VOC molecular identification PCR, targets a specific sequence position where Alpha, Beta and Gamma VOC have specific single mutation.

Since the VOC screening and identification for **Alpha, Beta and Gamma VOC are based on a point mutation, the result is presumptive as additional mutations in different positions of the genome are necessary for classifying the viral lineage.** Likewise, Delta virus circulation cannot be discharged since it is not detected through this methodology. So far, there is not a reliable PCR for Delta discrimination.

### Genomic Sequencing for detecting VOC or VOI

The determination of the lineage of a circulating variant of SARS-CoV-2 is possible only through phylogenic analysis of the virus whole genomic sequencing data. Several protocols are made available for full genome sequencing of SARS-CoV-2, specially the one on Next Generation Sequencing.<sup>[1]</sup>

Although some circulating SARS-CoV-2 can present specific mutations associated to VOC or VOI, a point mutation by itself is not sufficient for classifying the virus as one of the recognized VOC or VOI. In this sense, like the-PCR strategies for detecting VOC, **if Sanger sequencing is used and the sequence of only a specific fragment is available instead of the whole genome, the result should also be considered as preliminary.**

Thus, the whole genome sequencing is the gold standard methodology for identifying a VOC or VOI. This also applies for the detection of the **Delta VOC that at this moment can only be confirmed through genomic sequencing.**

Therefore, **even if detected and identified previously by real-time PCR or sequencing of a genome fragment/region, additional full genomic sequencing of the SARS-CoV-2 variant is required for confirming the VOC.**

## Validation of VOC and VOI results

Because of the methodology used and proficiency among laboratories facilities can vary across a country, PAHO recommends **the first VOC or VOI detection to be validated by the National Public Health Laboratory (NPHL) or National Influenza Center (NIC) as the reference for COVID-19 laboratory diagnostic and surveillance inside the country.**

These laboratories are the official reference laboratories for the Ministry of Health surveillance network, usually being the National Influenza Center or National Public Health Laboratory. These laboratories are constantly assessed for quality control, undergo proficiency testing and follows strict and standard guidelines that ensures reliable results.

Therefore, the **validation of the results obtained at a laboratory outside of the official public health network by the NPHL guarantees the quality of the results** and provides strengthen to the national public health system avoiding any reporting of mistaken results during the ongoing COVID-19 pandemic response.

**The validation of the VOC and VOI results by the NPHL responsible/reference of the Ministry of Health for the COVID-19 surveillance before the notification through IHR official channels should be considered.**

## Main actions by a Member State, when a VOC or VOI is identified for the first time:

- Immediately report to PAHO/WHO initial cases/clusters associated with VOC or VOI infection through the IHR mechanism.
- Submit complete genome sequences and associated metadata to a publicly available database, such as GISAID.
- Where capacity exists and in coordination with the international community, perform field investigations to improve understanding of the potential impacts of the VOC or VOI on COVID-19 epidemiology, severity, effectiveness of public health and social measures, or other relevant characteristics.
- Perform laboratory assessments or contact WHO for support to conduct laboratory assessments on the impact of the VOC or VOI on diagnostic methods, immune responses, antibody neutralization or other relevant characteristics.

## SARS-CoV-2 Genomic Surveillance

PAHO encourages laboratories to timely sequence COVID-19 positive samples and share genetic information through the global platform GISAID.

In addition, PAHO is working to strengthen SARS-CoV-2 genomic sequencing in the Region of the Americas, so that genomic data is available in a timely manner through GISAID. The **COVID-19 Genomic Surveillance Regional Network** is open to all the countries of the Americas through the National Public Health Laboratories. This network also includes 6 Regional Sequencing Laboratories (CDC-USA; Fiocruz-Brazil; GORGAS-Panama; InDRE-Mexico; ISP-Chile; UWI-Trinidad and Tobago), which provide external sequencing for the participating laboratories without such capacity<sup>[5]</sup>. For additional information, the PAHO Regional Office can be contacted at the email addresses [leitejul@paho.org](mailto:leitejul@paho.org), [ricoj@paho.org](mailto:ricoj@paho.org).

## References

1. World Health Organization. Genomic sequencing of SARS-CoV-2: a guide to implementation for maximum impact on public health, 8 January 2021. 2021. Available at <https://apps.who.int/iris/handle/10665/338480>
2. Pan American Health Organization. Technical Note: SARS-CoV-2 genomic characterization and circulating variants in the Region of the Americas. 2020 Oct 8. Available at <https://www.paho.org/en/documents/technical-note-sars-cov-2-genomic-characterization-and-circulating-variants-region>
3. Pan American Health Organization. Guidance for SARS-CoV-2 samples selection for genomic characterization and surveillance. 2021 Feb 9. Available at <https://www.paho.org/en/documents/guidance-sars-cov-2-samples-selection-genomic-characterization-and-surveillance>
4. Konings F., Perkins MD, Kuhn JH., et al. SARS-COV-2 VARIANTS OF INTEREST AND CONCERN NAMING SCHEME CONDUCIVE FOR GLOBAL DISCOURSE. Nat Microbiol. 2021. 6(7):821-823.
5. Pan American Health Organization. COVID-19 Genomic Surveillance Regional Network. 2021 Available at: <https://www.paho.org/en/topics/influenza/covid-19-genomic-surveillance-regional-network>