SARS-CoV-2 Variants of Interest and Concern naming scheme conducive for global discourse

On behalf of the Virus Evolution Working Group of the World Health Organization (WHO) COVID-19 Reference Laboratory Network, representatives of GISAID, Nextstrain, Pango, and additional experts in virological and microbial nomenclature

Frank Konings[1*], Mark D. Perkins[1], Jens H. Kuhn[2], Mark Pallen[3], Erik Alm[4], Brett N. Archer[1], Amal Barakat[1], Trevor Bedford[5], Jinal N. Bhiman[6,7], Leon Caly[8], Lisa L. Carter[1], Ann Cullinane[9], Tulio de Oliveira[10], Julian Druce[8], Ihab El Masry[11], Roger Evans[1], George F. Gao[12], Alexander E. Gorbalenya[13,14], Esther Hamblion[1], Belinda L. Herring[1], Emma Hodcroft[15], Edward C. Holmes[16], Manish Kakkar[1], Shagun Khare[1], Marion P.G. Koopmans[17], Bette Korber[18], Juliana Leite[1], Duncan MacCannell[19], Marco Marklewitz[1], Sebastian Maurer-Stroh[20,21], Jairo Andres Mendez Rico[1], Vincent Munster[22], Richard Neher[23], Bas Oude Munnink[17], Boris I. Pavlin[1], Malik Peiris[24], Leo Poon[24], Oliver Pybus[25], Andrew Rambaut[26], Paola Resende[27], Lorenzo Subissi[1], Volker Thiel[15,28], Suxiang Tong[19], Sylvie van der Werf[29], Anne von Gottberg[6,7], John Ziebuhr[30], and Maria D. Van Kerkhove[1]

1. World Health Organization, 2. Integrated Research Facility at Fort Detrick, Division of Clinical Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Fort Detrick, Frederick, Maryland, USA, 3. University of East Anglia, United Kingdom, 4. European Centre for Disease Prevention and Control, 5. Fred Hutchinson Cancer Research

Center, Seattle, Washington, USA, 6. National Institute for Communicable Diseases, Johannesburg, South Africa, 7. School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, 8. Victorian Infectious Diseases Reference Laboratory (VIDRL), Melbourne, Australia, 9. World Organisation for Animal Health (OIE), 10. University of KwaZulu-Natal, South Africa, 11. Food and Agriculture Organization (FAO), 12. Chinese Center for Disease Control and Prevention, Beijing, P.R. China, 13. Leiden University Medical Center, Leiden, The Netherlands, 14. Faculty of Bioengineering and Bioinformatics, Lomonosov Moscow State University, Moscow, Russia, 15. University of Bern, Bern, Switzerland, 16. The University of Sydney, Sydney, Australia, 17. Erasmus University, Rotterdam, The Netherlands, 18. Los Alamos National Laboratory, USA, 19. United States Centers for Disease Control and Prevention, Atlanta, USA, 20. The Global initiative on sharing all influenza data (GISAID) Initiative, 21. Bioinformatics Institute, Agency for Science, Technology and Research, Singapore, 22. Virus Ecology Unit, NIAID, USA, 23. Biozentrum, University of Basel, Switzerland Swiss Institute of Bioinformatics, Basel, Switzerland, 24. The University of Hong Kong, Hong Kong, 25. University of Oxford, United Kingdom, 26. Institute for Evolutionary Biology Ashworth Laboratories, University of Edinburgh, Edinburgh, UK 27. Laboratory of Respiratory Viruses and Measles (LVRS), Oswaldo Cruz Institute, Fiocruz, Rio de Janeiro, Brazil, 28. Institute of Virology and Immunology, Mittelhäusern, Switzerland, 29. Institut Pasteur, Paris, France, 30. Institute of Medical Virology, Justus Liebig University Giessen, Giessen, Germany.

*Corresponding author: Mark Perkins, WHO: perkinsm@who.int

STANDFIRST

A group convened and led by the Virus Evolution Working Group of the World Health Organization (WHO) reports on its deliberations and announces a naming scheme that will enable clear communication about SARS-CoV-2 variants of interest and variants of concern.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19), has a linear, unsegmented, positive-sense RNA genome. In common with all viruses, SARS-CoV-2 continuously adapts to changing environments in real-time via random genome mutations that are subject to natural selection. Most mutations are neutral or detrimental to the virus. However, a small number of mutations may provide a selective advantage, such as escape from the host immune system or antiviral drugs or vaccines. Such mutations may also lead to increased fitness for transmissibility. As mutated forms of viruses or variants spread from person-to-person, they will eventually be detected at the population level.

The World Health Organization (WHO) COVID-19 Reference Laboratory Network (1) has been tracking SARS-CoV-2 mutations since the beginning of the pandemic. In June 2020, the WHO Virus Evolution Working Group (VEWG) was established with a specific focus on SARS-CoV-2 variants, their phenotype, and impact on countermeasures. WHO has developed a global risk-monitoring framework to coordinate components of an international system for monitoring and assessing SARS-CoV-2 variants and their impacts. Specifically, this framework aims to collect, analyse and share data to identify crucial priorities, set triggers for decision-

making, and enable and improve the capacities of laboratories, technical networks, and expert groups.

WHO has provided working definitions of variants of interest (VOIs) and variants of concern (VOCs) that will be updated as and when needed (2). These working definitions also consider changes that lead to an altered phenotype which are harder to reflect in genotype-based classifications. Additionally, WHO advised how VOIs and VOCs should be reported to national health authorities and to WHO. Initial cases or clusters associated with VOC infection should be reported to WHO through the International Health Regulations (2005) mechanism. WHO has outlined actions required by WHO Member States, reference laboratories, and the WHO secretariat to assess the impact of VOIs and VOCs on the epidemiology and severity of COVID-19, and on performance of available diagnostics, therapeutics, vaccines, and public health and social measures. At the time of writing, several VOIs and VOCs are being tracked (3).

Current naming systems for SARS-CoV-2 variants

Three nomenclature systems for naming and tracking SARS-CoV-2 genetic lineages are currently in use: GISAID (4), Nextstrain (5), and Pango (6). Each system has its own scientific approach to classify and name lineages, and all three systems had been introduced before VOIs and VOCs were recognized. The existence of different nomenclature systems can mean that the same variant has multiple names, often at the same time and without regard of the properties of VOIs and VOCs. Lack of clarity on naming for VOCs makes it difficult for those who are not experts in the field to link such variants to scientific publications. Of similar concern, the use of multiple nomenclature systems is confusing for health officials, the media, and the public, and

undermines effective liaison between all the actors that must communicate easily to reach swift decisions on matters of public health concern.

It has become clear that naming of SARS-CoV-2 variants is not trivial for several reasons. First, there is no centralized authority or process responsible for VOI and VOC naming, or consensus on their designating criteria, and as a result different groups have assigned different names to the same variant. Second, a name that includes the location where a VOI or VOC was first detected can stigmatize places, countries, and locals, and could negatively impact surveillance and reporting of VOIs or VOCs. Plus, using the name of a place where a VOI or VOC was first detected is misleading because a VOI or VOC may have originated elsewhere as some countries are more engaged in sequencing than others. Finally, alphanumeric naming schemes have resulted in complex names that are liable to misreporting and misunderstanding. Even a small mistake – for instance, accidentally typing "1" instead of "2" or placing dots incorrectly – in a numerical variant name or list of names can create confusion.

Outputs of the discussion to improve naming of VOIs and VOCs

Only some of the variants that are named differently in the three existing systems are VOIs or VOCs, and new names need to be prioritised for these. To formulate an improved naming scheme for VOI and VOC, WHO invited groups that have published phylogenetics-based classification and nomenclature systems for SARS-CoV-2 variants, and experts in virological and microbial nomenclature, to find possible solutions to these challenges. Participants drew the following conclusions:

- Existing naming systems are based on genetic information and do not always consider changes in biological properties of variants. Currently, no VOI and VOC naming has

been standardized to enable straightforward communication. The existence of multiple, technical VOI and VOC names results in confusion among political decision-makers and the public.

- A mechanism using a prefix (e.g. “V” or “VAR”) combined with a consecutive number assigned to each new variant is unsuitable because it would result in names like those used by existing nomenclature systems, i.e. a combination of letters and numbers. Using neutral names produced by an algorithm that takes existing words, extracts useful syllables, and recombines them in a combinatorial fashion was also explored. However, using this method, it was not possible to easily generate sufficient numbers of two or three syllable words that were at the same time easy to pronounce and not already taken as a name of a person, location or company or otherwise registered in the World Intellectual Property Organization (WIPO) Global Brand Database, and acceptable to the majority of experts consulted.
- Having a label that is less scientific would be useful. This includes avoiding a label that uses a combination of letters and numbers such as the existing naming systems based on genomic changes are using. Mechanisms that use any kind of geographic reference – even those using an approach with coded locations that could be traced back – were discarded. All parties present agreed to create and use a new WHO labelling mechanism primarily for VOIs and VOCs.

WHO naming mechanism for VOIs and VOCs

As soon as variants are designated as VOIs and VOCs according to the WHO working definitions, labels will be chosen and applied. When working definitions are revised, e.g. other characteristics are included, the labelling mechanism will follow the new

definitions. Labels will be selected by WHO using names of letters of the Greek alphabet, i.e. Alpha, Beta, Gamma, etc. These will be easier to remember and more practical to use than alphanumerical designations. The Greek alphabet is well-established as generic as the names of its individual letters have already been used for so many different purposes. While some of these names may also be the name of a person, place or company at present, there is no intent to establish a link with these and the mechanism is purely to label the SARS-CoV-2 variants for ease of communication. Once all 24 letters have been assigned to VOIs or VOCs, other lists of names will be considered.

Labels for VOIs and VOCs, their links to existing phylogenetics-based SARS-CoV-2 classification and nomenclature systems and their key scientific and medical features will be published and updated continuously by WHO at https://www.who.int/activities/tracking-SARS-CoV-2-variants. It is recommended that all interested parties, especially journalists, visit this site frequently. Examples of VOI and VOC labels, along with their scientific designations in three different classification systems based on phylogenetics, are shown in Table 1.

Finally, SARS-CoV-2 variants that do not meet WHO definitions for VOI or VOC may not be labelled via this scheme, unless deemed necessary by WHO in consultation with the VEWG, but can be tracked using the classification systems of GISAID, Nextstrain, and Pango. The WHO labelling mechanism is independent of the existing SARS-CoV-2 lineage nomenclature systems but informed by the available classifications and will be cross-linked with them. Countries will inform WHO through established WHO Country or Regional Office reporting channels, with supporting information about cases associated with VOIs or VOCs, using WHO working definitions. When a VOI or VOC is confirmed by WHO, a label

will be issued by WHO. This label will anchor the three different names arising from the three existing naming systems.

Conclusion

We emphasize that the existing phylogenetics-based nomenclature systems of SARS-CoV-2 lineages convey important information and continue to inform research. This new naming system is intended to facilitate sharing of research advancements with a broader audience and aims to provide a platform to enable clear global discourse around VOIs and VOCs.

Acknowledgements

The authors thank Dr. Dmitriy Pereyaslov of the WHO Global Influenza Programme for his critical review of the manuscript.

Disclaimer

The views and conclusions contained in this document are those of the authors and should not be interpreted as necessarily representing the official policies, either expressed or implied, of the United States government, including those of the National Institutes of Health (NIH), the National Institute of Allergy and Infectious Diseases (NIAID) or the United States Centers for Disease Control and Prevention (US CDC), or of the institutions and companies affiliated with the authors.

Competing interests

The authors declare no competing interests.

Table 1. WHO naming mechanism for SARS-CoV-2 VOIs and VOCs. SARS-CoV-2 VOCs with their labels along with their scientific designations in three different classification systems based on phylogenetics: GISAID, Nextstrain, and Pango. A continuously updated list of names can be found at https://www.who.int/activities/tracking-SARS-CoV-2-variants.

WHO label	Variant type	Country of first detection	Date of designation	Earliest documented samples	GISAID clade/variant	Nextstrain clade	Pango lineage
Alpha	VOC	United Kingdom	18 December 2020	September 2020	GRY (formerly GR/501Y.V1)	20I/501Y.V1	B.1.1.7
Beta	VOC	South Africa	18 December 2020	May 2020	GH/501Y.V2	20H/501Y.V2	B.1.351
Gamma	VOC	Brazil	11 January 2021	November 2020	GR/501Y.V3	20J/501Y.V3	P.1
Delta	VOC	India	VOI: 4 April, VOC: 11 May 2021	October 2020	G/452R.V3	21A/S:478K	B.1.617.2

References:

1. World Health Organization. WHO reference laboratories providing confirmatory testing for COVID-19 2020 [Available from: https://www.who.int/publications/m/item/who-reference-laboratories-providing-confirmatory-testing-for-covid-19.

2. World Health Organization. COVID-19 weekly epidemiological update, 25 February 2021. 2021 2021-02-25.

3. World Health Organization. Coronavirus disease (COVID-19) Weekly Epidemiological Update 2021 [Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.

4. GISAID. Clade and lineage nomenclature aids in genomic epidemiology studies of active hCoV-19 viruses 2021 [updated 2nd March 2021. Available from: https://www.gisaid.org/references/statements-clarifications/clade-and-lineage-nomenclature-aids-in-genomic-epidemiology-of-active-hcov-19-viruses/.

5. Bedford BH, E.; Neher, R. Updated Nextstrain SARS-CoV-2 clade naming strategy 2021 [updated 2021-01-06. Available from: https://nextstrain.org/blog/2021-01-06-updated-SARS-CoV-2-clade-naming.

6. Rambaut A, Holmes EC, O'Toole Á, Hill V, McCrone JT, Ruis C, et al. A dynamic nomenclature proposal for SARS-CoV-2 lineages to assist genomic epidemiology. Nat Microbiol. 2020;5(11):1403-7.