

## Terms of reference for the Technical Advisory Group on Virus Evolution (TAG-VE)

The COVID-19 pandemic was characterized by an unprecedented use of genomics for real-time tracking of the evolution of SARS-CoV-2. This was followed by a multi-country outbreak of mpox in 2022-2023, caused by a new subclade (clade IIb), and the subsequent discovery of another new monkeypox virus subclade (clade Ib), circulating in Eastern Congo. These examples have highlighted the importance of strengthening coordination around the use and interpretation of sequencing to study the molecular epidemiology of priority viruses with epidemic and pandemic potential. To inform prevention and control measures, it is critical to regularly review the available evidence on variants of viruses of epidemic and pandemic potential to determine if specific mutations and combinations of mutations alter the behavior of the virus. The evolution of viruses and the emergence of new variants may result in changes in transmission and clinical presentation or severity, or the performance of countermeasures, such as diagnostics, therapeutics and vaccines.

In June 2020, the World Health Organization (WHO) established an informal Virus Evolution Expert Working Group (VEWG) to specifically assess SARS-CoV-2 evolution, mutations and variants. The work of the VEWG supports a larger WHO-coordinated global risk monitoring and assessment framework for SARS-CoV-2 variants. This independent group of experts was then formalized under the name Technical Advisory Group on SARS-CoV-2 Virus Evolution (TAG-VE), which will continue to meet regularly to discuss and analyze the impact of SARS-CoV-2 variants on transmissibility, disease severity, diagnostics, and therapeutics and determine whether a given variant constitutes a variant of interest (VOI) or a variant of concern (VOC) according to WHO definitions.

The recommendations of the TAG-VE have been used to inform WHO on global, regional, and national COVID-19 prevention and control strategies and will be utilized by other WHO advisory groups, such as the Expert Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC), and the Strategic Advisory Group of Experts on Immunization (SAGE).

In 2024, the scope of the TAG-VE will be expanded to include other priority viruses with epidemic and pandemic potential. This will be achieved through the establishment of a group of members with cross-cutting expertise, which will be supported by Observers with virus-specific expertise.

The TAG-VE will act as an advisory body to WHO in this field.

### **I. Functions**

In its capacity as an advisory body to WHO, the TAG-VE shall have the following functions:

1. Advise WHO on strengthening mechanisms to identify and prioritize (potential) relevant mutations of priority viruses of epidemic and pandemic potential, including the strengthening of global capacity to assess newly emerging variants;
2. Develop and apply a framework for analyzing and assessing variants of priority viruses of epidemic and pandemic potential and their impact on transmissibility, severity of the disease, antigenicity and diagnostics or therapeutics;

3. Provide regular and updated recommendations to WHO on the global characterization of circulating variants of viruses of epidemic and pandemic potential. Alert WHO on relevant mutations/variants, and advise on their potential impact related to viral characteristics (e.g., in virulence, transmission) and countermeasures (e.g., diagnostics, vaccines and therapeutics);
4. Recommend to WHO specific investigations on the impact of specific mutations (including the laboratory controlled *in vitro* and *in vivo* studies of mutants);
5. Advise WHO on mitigation strategies to reduce the negative effect of such mutations, that might impact virus behavior or countermeasures; and
6. Advise WHO on how/if to communicate to the scientific community and the general audience as needed
7. Advise WHO, as appropriate, on other relevant topics related to this area of work.

## II. Composition

The TAG-VE shall have up to a maximum of 25 Members<sup>1</sup>, who shall serve in their personal capacities to represent the broad range of disciplines relevant to the production of evidence and the assessment of the impact of variants of priority viruses of epidemic and pandemic potential on transmission, clinical evolution of infection and the effectiveness of public health and social measures, diagnostics, therapeutics and vaccines in relation to strains/variants. The Members of the TAG-VE will have expertise in bioinformatics, clinical management, evolutionary biology, epidemiology, laboratory sciences, outbreak preparedness and response, public health microbiology/virology, and other relevant disciplines. In the selection of the TAG-VE Members, consideration shall be given to attaining an adequate distribution of technical expertise, geographical representation and gender balance.

1. Members of the TAG-VE, including the Chairperson, shall be selected and appointed by WHO. The Chairperson's functions include the following:
  - to chair the meeting of the TAG-VE;
  - to liaise with the WHO Secretariat between meetings.

In appointing a Chairperson, consideration shall be given to gender and geographical representation.

2. Members of the TAG-VE shall be appointed to serve for a period of 3 years and shall be eligible for reappointment. A Chairperson is eligible for reappointment as a Member of the TAG-VE, but is only permitted to serve as Chairperson for one term. Their appointment and/or designation as Chairperson may be terminated at any time by WHO if WHO's interest so requires or, as otherwise specified in these terms of reference or letters of appointment. Where a Member's appointment is terminated, WHO may decide to appoint a replacement Member.

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<sup>1</sup> Members serve as full participants and partake in the decision-making process of the meeting in which they are involved.

3. TAG-VE Members must respect the impartiality and independence required of WHO. In performing their work, Members may not seek or accept instructions from any Government or from any authority external to the Organization. They must be free of any real, potential or apparent conflicts of interest. To this end, proposed Members/Members shall be required to complete a declaration of interests form and their appointment, or continuation of their appointment, shall be subject to the evaluation of completed forms by the WHO Secretariat, determining that their participation would not give rise to a real, potential or apparent conflict of interest.
4. Following a determination that a proposed Member's participation in the TAG-VE would not give rise to a real, potential or apparent conflict of interest, the proposed Member will be sent a letter inviting them to be a Member of the TAG-VE. Their appointment to the TAG-VE is subject to WHO receiving the countersigned invitation letter and memorandum of agreement. Notwithstanding the requirement to complete the WHO declaration of interest form, TAG-VE Members have an ongoing obligation to inform WHO of any interests real or perceived that may give rise to a real, potential or apparent conflict of interest.
5. As contemplated in paragraph II.4 above, WHO may, from time to time, request TAG-VE Members to complete a new declaration of interest form. This may be before a TAG-VE meeting or any other TAG-VE-related activity or engagement, as decided by WHO. Where WHO has made such a request, the TAG-VE Member's participation in the TAG-VE activity or engagement is subject to a determination that their participation would not give rise to a real, potential or apparent conflict of interest.
6. Where a TAG-VE Member is invited by WHO to travel to an in-person TAG-VE meeting, WHO shall, subject to any conflict of interest determination as set out in paragraph II.6 above, issue a letter of appointment as a temporary adviser and accompanying memorandum of agreement (together 'Temporary Adviser Letter'). WHO shall not authorize travel by an TAG-VE Member, until it receives a countersigned Temporary Adviser Letter.
7. TAG-VE Members do not receive any remuneration from the Organization for any work related to the TAG-VE. However, when attending in-person meetings at the invitation of WHO, their travel cost and per diem shall be covered by WHO in accordance with the applicable WHO rules and policies.

### **III. Operation**

1. The TAG-VE shall meet on a quarterly basis. However, WHO may convene additional meetings. TAG-VE meetings will be held virtually, via video or teleconference, or in person (at WHO headquarters in Geneva or another location, as determined by WHO).
1. TAG-VE meetings may be held in open and/or closed session, as decided by the Chairperson in consultation with WHO:

(a) Open sessions: Open sessions shall be convened for the sole purpose of the exchange of information and views, and may be attended by Observers (as defined in paragraph III.3 below).

(b) Closed sessions: The sessions dealing with the formulation of recommendations and/or advice to WHO shall be restricted to the Members of the TAG-VE and essential WHO Secretariat staff.

2. The quorum for TAG-VE meetings shall be two thirds of the Members.
3. WHO may, at its sole discretion, invite external individuals with disease-specific expertise to attend the open sessions of the TAG that focus on the disease (or disease group) they are expert in, or parts thereof, as “Observers”. Similarly, external individuals from international agencies contributing to the virus evolution space (e.g. European CDC, Africa CDC, FAO, WOAHA etc.) may be invited from time to time also as Observers. Observers may be invited either in their personal capacity, or as representatives from a governmental institution / intergovernmental organization, or from a non-state actor. WHO will request Observers invited in their personal capacity to complete a confidentiality undertaking and a declaration of interests form prior to attending a session of the TAG-VE group. Invitations to Observers attending as representatives from non-state actors will be subject to internal due diligence and conflict of interest considerations in accordance with FENSA. Observers invited as representatives may also be requested to complete a confidentiality undertaking. Observers shall normally attend meetings of the TAG-VE at their own expense and be responsible for making all arrangements in that regard. Up to 15 Observers can be invited for each TAG-VE meeting. At the invitation of the Chairperson, Observers may be asked to present their personal views and/or the policies of their organization. Observers will not participate in the process of adopting decisions and recommendations of the TAG-VE.
4. The TAG-VE may decide to establish smaller working groups (sub-groups of the TAG-VE) to work on specific issues. Their deliberations shall take place via teleconference or video-conference. For these sub-groups, no quorum requirement will apply; the outcome of their deliberations will be submitted to the TAG-VE for review at one of its meetings.
5. TAG-VE Members are expected to attend meetings. If a Member misses two consecutive meetings, WHO may end his/her appointment as a Member of the TAG-VE.
6. Reports of each meeting shall be submitted by the TAG-VE to WHO (the Assistant Director-General for Emergency Preparedness). All recommendations from the TAG-VE are advisory to WHO, who retains full control over any subsequent decisions or actions regarding any proposals, policy issues or other matters considered by the TAG-VE.

7. The TAG-VE shall normally make recommendations by consensus. If, in exceptional circumstances, a consensus on a particular issue cannot be reached, minority opinions will be reflected in the meeting report.
8. Active participation is expected from all TAG-VE Members, including in working groups, teleconferences, and interaction over email. TAG-VE Members may, in advance of TAG-VE meetings, be requested to review meeting documentation and to provide their views for consideration by the TAG-VE.
9. WHO shall determine the modes of communication by the TAG-VE, including between WHO and the TAG-VE Members, and the TAG-VE Members among themselves.
10. TAG-VE Members shall not speak on behalf of, or represent, the TAG-VE or WHO to any third party.

#### **IV. Secretariat**

WHO shall provide the secretariat for the TAG-VE, including necessary scientific, technical, administrative and other support. In this regard, the WHO Secretariat shall provide the Members in advance of each meeting with the agenda, working documents and discussion papers. Distribution of the aforesaid documents to Observers will be determined by the WHO Secretariat. The meeting agenda shall include details such as: whether a meeting, or part thereof, is closed or open; and whether Observers are permitted to attend.

#### **V. Information and documentation**

1. Information and documentation to which Members may gain access in performing TAG-VE related activities shall be considered as confidential and proprietary to WHO and/or parties collaborating with WHO. In addition, by counter signing the letter of appointment and the accompanying terms and conditions referred to in section II(5) above, TAG-VE Members undertake to abide by the confidentiality obligations contained therein and also confirm that any and all rights in the work performed by them in connection with, or as a result of their TAG-VE-related activities shall be exclusively vested in WHO.
2. TAG-VE Members and Observers shall not quote from, circulate or use TAG-VE documents for any purpose other than in a manner consistent with their responsibilities under these Terms of Reference.
3. WHO retains full control over the publication of the reports of the TAG-VE, including deciding whether or not to publish them.