

World Health Organization

Interim statement on the composition of current COVID-19 vaccines

17 June 2022

Key messages:

- The primary goals of COVID-19 vaccination using currently licensed vaccines continue to be to reduce hospitalization, severe disease and death, and to protect health systems. The use of currently licensed vaccines based on the index virus (i.e. the virus that was identified from the first cases of COVID-19 in December 2019) confers **high levels of protection against severe disease outcomes** for all variants, including Omicron with a booster dose.
- There has been continuous and substantial virus evolution since SARS-CoV-2 emerged in late 2019 and it is likely that this evolution will continue, resulting in the emergence of new variants, particularly those with changes in the spike protein. The trajectory of SARS-CoV-2 evolution remains uncertain and the genetic and antigenic characteristics of future variants cannot yet be predicted.
- Given the uncertainties of further evolution, it may be prudent to pursue an additional objective of COVID-19 vaccination of **achieving broader immunity** against circulating and emerging variants while **retaining protection against severe disease and death**.
- Available data (see Annex) indicate that the **inclusion of Omicron**, as the most antigenically distinct SARS-CoV-2 Variant of Concern, in **an updated vaccine composition may be beneficial if administered as a booster dose** to those who have already received a COVID-19 vaccination primary series.

The Technical Advisory Group on COVID-19 Vaccine Composition (TAG-COVAC) is an independent group of experts that has continued to assess the public health implications of emerging SARS-CoV-2 Variants of Concern (VOC) on the

1 performance of COVID-19 vaccines in order to issue timely recommendations on
2 potential modifications to vaccine strain composition. Since the designation of the
3 Omicron VOC by the World Health Organization (WHO) in November 2021, the
4 TAG-CO-VAC has closely followed the impact of Omicron on the performance
5 of currently licensed COVID-19 vaccines to consider whether a change in
6 COVID-19 vaccine composition may be warranted---. Further to the interim
7 statement published on 8 March 2022, this TAG-CO-VAC statement is intended
8 to offer Member States, vaccine developers and regulatory authorities
9 considerations as to whether a modified vaccine composition may be warranted
10 and, if so, how this may be achieved to fulfil the public health objectives of
11 COVID-19 vaccination.

12

13 **Is a modified COVID-19 vaccine composition warranted?**

14 Since the classification of Omicron as a VOC, there has been rapid and relatively
15 synchronous displacement of other circulating variants by Omicron that has
16 caused substantial epidemic waves in all 6 WHO regions. Omicron is
17 characterized by a large number of mutations, including many in antigenically
18 important regions of the spike (S) protein. Its transmission advantage over other
19 variants has largely been driven by immune escape properties, and Omicron has
20 infected many who had been previously vaccinated and/or infected. Several
21 sublineages within Omicron, notably BA.1, BA.2, BA.3, BA.4 and BA.5, have been
22 identified, which share many of the same S protein mutations.

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24 In this context, the primary goals of COVID-19 vaccination using currently
25 licensed vaccines continue to be to reduce hospitalization, severe disease and
26 death, and to protect health systems. A primary series of currently licensed
27 vaccines based on the virus that was identified from the first cases of COVID-19
28 in December 2019 (termed the index virus e.g. GISAID: hCoV-
29 19/Wuhan/WIV04/2019) confers lower levels of protection against severe disease
30 outcomes for Omicron, compared to prior VOCs. However, a booster dose of the
31 currently licensed COVID-19 vaccines based on the index virus appears to restore
32 protection against severe disease and death against currently circulating variants

1 (1) at levels that remain acceptable (2).

2
3 Nevertheless, there has been substantial virus evolution, particularly in the S
4 protein, since the first cases of COVID-19 and it is likely that this evolution will
5 continue, resulting in the emergence of new variants in the future. There is
6 uncertainty about the timing of the emergence, extent of global circulation and
7 antigenic characteristics of future variants. In this context, immunity elicited
8 against as broad a range of SARS-CoV-2 S protein antigens as possible may be
9 desirable to retain and potentially improve protection against future variants.
10 Therefore, it may be prudent to pursue an additional objective of COVID-19
11 vaccination to achieve immune responses that both:

- 12 • elicit a greater breadth in the immune response against circulating and emerging
13 variants, to enhance protection against these variants; and
- 14 • retain protection against hospitalization, severe disease and death, and
15 protecting health systems.

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17 As such, a modified COVID-19 vaccine composition may be warranted to broaden
18 immune protection against divergent SARS-CoV-2 S protein antigens.

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20 **If a modified COVID-19 vaccine composition is deemed to be necessary, what is**
21 **the recommended strain composition of the vaccine?**

22 The TAG-CO-VAC has considered the comparative epidemiological and
23 virological characteristics of VOCs to date, including Omicron. This included, but
24 was not limited to, published and unpublished data on the antigenic
25 characteristics and antibody escape of various VOCs including Omicron, the
26 cross-protection of Omicron specific responses following vaccination or infection
27 with prior VOCs, and following Omicron infection and/or Omicron-specific
28 vaccine candidates (see Annex). Importantly, the TAG-CO-VAC acknowledges
29 that at this time, limited animal model and human data have been published on
30 Omicron-specific vaccine candidates, and these will continue to be reviewed as
31 more data become available.

1 Omicron is the most antigenically distinct SARS-CoV-2 VOC to have spread
2 globally - much more so than Alpha, or Delta, which are more antigenically similar
3 to the index virus. This has been demonstrated by the substantially reduced
4 neutralization activity against Omicron as compared to earlier VOCs, both in
5 vaccinated individuals and in those who had been previously infected with earlier
6 VOCs. Furthermore, antibody responses in previously naive (unprimed)
7 individuals exposed to Omicron are strong, but they do not cross-react well with
8 previous variants, including other VOCs. In contrast, in individuals who have been
9 previously primed by SARS-CoV-2 infection (i.e., index virus, Alpha, Delta) or
10 COVID-19 vaccination (based on the index virus), infection with Omicron elicits
11 a broadly cross-reactive antibody response. Similar observations have also been
12 seen in animal models and preliminary clinical data in humans assessing Omicron-
13 specific vaccine candidates. Collectively, the data show that repeated exposure to
14 SARS-CoV-2 antigens (either through breakthrough infection, vaccination
15 following infection, or \cong 3 vaccine doses) enhances the magnitude of the
16 antibody response and an increase in breadth is observed after Omicron infection
17 in previously primed humans.

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19 Therefore, available data indicate that the inclusion of Omicron in an updated
20 vaccine composition is likely to be beneficial in populations that have already
21 received a COVID-19 vaccination primary series. For an Omicron-specific
22 vaccine product, the TAG-CO-VAC recognizes that viruses or viral genetic
23 sequences very closely related to hCoV/South Africa/NICD-N21668/2021 or
24 hCoV/USA/CA-CDC-4358237-001/2021 are some of the most antigenically
25 distant from the index virus to date and are likely to enhance the magnitude and
26 breadth of the antibody response.

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28 Importantly, the TAG-CO-VAC considers that the protection offered by an
29 Omicron-specific vaccine product is likely to differ in those who have already
30 received a COVID-19 vaccine primary series (primed), as compared to those who
31 have not (unprimed). Based on the data to date, it is inferred that **an Omicron-**
32 **specific monovalent vaccine product administered as a booster dose for those who**

1 **have already received a primary vaccine series may elicit greater breadth in the**
2 **immune response.** In contrast, an Omicron-specific monovalent vaccine product
3 as a standalone formulation for the primary series is **not** advised as it is not yet
4 known whether Omicron-specific vaccines will offer similar cross-reactive
5 immunity and cross-protection from severe illness caused by other VOCs in
6 unprimed individuals as the index virus-based vaccines have done.

7
8 Although bi- or multivalent products have yet to be approved by regulatory
9 authorities, vaccines containing index virus and Omicron in a single product may
10 be able to achieve similar outcomes as the proposed sequential approach. However,
11 at this time, only limited data are available to assess whether the cross-reactive
12 immune responses in humans using an Omicron-containing bi/multivalent
13 product will be equivalent to those elicited with a sequential vaccine approach.

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15 The TAG-CO-VAC recognizes that the inclusion of Omicron, as the most
16 antigenically distinct VOC to date, in a variant-specific formulation and
17 administered as a booster dose, does not preclude the consideration of other
18 variant-specific formulations by regulatory authorities. The key additional
19 objective of modified COVID-19 vaccine formulations is to achieve breadth of
20 cross-reactive immunity to previous, currently circulating and/or emerging
21 variants.

22 23 **Conclusion**

24 The use of currently licensed vaccines based on the index virus confers high levels
25 of protection against severe disease outcomes for all variants, including Omicron
26 with a booster dose. As such, the continued use of currently licensed vaccines for
27 primary vaccination and as a booster dose is appropriate to achieve the primary
28 goals of COVID-19 vaccination. Given the uncertainties of the genetic and
29 antigenic characteristics of future SARS-CoV-2 variants, it may be prudent to
30 pursue an additional objective of COVID-19 vaccination of achieving a greater
31 breadth in the antibody response against circulating and emerging variants, while
32 retaining protection against severe disease and death. In this context, available

1 data indicate that the inclusion of Omicron, as the most antigenically distinct
2 SARS-CoV-2 VOC, in an updated vaccine composition may be beneficial.
3 Available data also indicate that this would be best administered as a booster dose
4 to those who have already received a COVID-19 vaccination primary series, if
5 such vaccines were to be made available.

6
7 The TAG-CO-VAC acknowledges that this position is based on limited data from
8 animal models, inference from Omicron infection in primed and unprimed
9 individuals, and preliminary clinical data in humans vaccinated with an Omicron
10 vaccine candidate. The TAG-CO-VAC therefore recognizes that considerable
11 uncertainties remain. Firstly, uncertainty in the trajectory of SARS-CoV-2
12 evolution is such that there is a risk that this update may not align with variants
13 that emerge in the future. However, a modified vaccine composition that includes
14 Omicron will likely broaden the antibody response in primed individuals.
15 Secondly, there are assumptions as to the potential performance of variant-
16 specific vaccines, including Omicron-containing vaccines. It is assumed that the
17 safety, reactogenicity and immunogenicity of the updated vaccine composition
18 will be comparable to those of the currently licensed vaccines based on the index
19 virus. The TAG-CO-VAC therefore strongly encourages the generation of clinical
20 data on immune responses in humans to a primary series and/or booster dose of
21 Omicron-specific vaccines, across different vaccine platforms. These additional
22 data may then be considered by TAG-CO-VAC and will allow the Strategic
23 Advisory Group of Experts (SAGE) on Immunization and its COVID-19 Vaccines
24 Working Group to issue policy recommendations on the use and timing of
25 Omicron-specific vaccines.

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27 The statement reflects the current vaccine performance and landscape of licensed
28 COVID-19 vaccines as of June 2022. The statement will therefore be updated as
29 further data become available.

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32 1. WHO. COVID-19 Weekly Epidemiological Update. 8 June 2022. Available

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