



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Emergency Task Force

## ETF statement on use of recently updated COVID-19 vaccines

Since the declaration of the COVID-19 pandemic in early 2020, multiple vaccines have been approved in the European Union and elsewhere for the prevention of COVID-19. Early deployment of the first of these vaccines, which were based on the ancestral strain of SARS-CoV-2, played a significant role in curbing the pandemic's effects.<sup>1</sup>

As SARS-CoV-2 circulates and evolves, new SARS-CoV-2 variants continue to emerge with the ability to evade immunity induced by prior infection or vaccination. Consequently, COVID-19 vaccines require regular strain updates, a situation very similar to the regularly updated influenza vaccines.<sup>2</sup>

### **SARS-CoV-2 evolution**

After a lag phase during which the D614G substitution was the most significant change, SARS-CoV-2 evolved further in the human population. Many variants of concern (VOCs) emerged and replaced prior VOCs.<sup>3,4</sup> Some of the new VOCs harboured more than 30 amino acid mutations in the spike protein, with 15 mutations in the receptor-binding domain alone.<sup>5</sup> These changes affected virus transmission (ACE2 receptor binding) and resulted in reduced virus neutralization by pre-existing antibodies,<sup>6</sup> allowing new global waves of infections to occur. The ancestral virus as well as the first variant lineages are no longer circulating in the human population to any meaningful extent.

### **Immune response to SARS-CoV-2 variants**

Updated vaccines expand the breadth of the neutralizing antibody response, targeting emerging variants and boosting the immune response to the ancestral variant.<sup>7</sup> Furthermore preferential re-direction of the neutralizing antibody response towards currently circulating variants could be achieved by repeated exposure to the variants in the absence of simultaneous boosting with the ancestral virus.<sup>8</sup>

T-cell immunity appears to be directed mostly to conserved epitopes still present in the most recent VOCs.<sup>9</sup> To what extent boosting of T-cell immunity by the recently updated or previous versions of the COVID vaccines contributes to protection from the currently circulating strains is not established.



## Updated vaccines and vaccine effectiveness

In a population largely exposed to the virus and/or vaccines, the main focus of vaccination programmes is on single dose re-vaccination. Initially immune responses were boosted by re-vaccination with the ancestral virus vaccine but subsequent campaigns in Europe have used updated vaccines. The first of these updated vaccines were bivalent vaccines targeting a newly emerged Omicron VOC in addition to the ancestral virus. The latest updated vaccines are monovalent vaccines targeting only a more recent VOC, i.e. XBB1.5.

Vaccine effectiveness data have shown that updated vaccines are effective in preventing disease caused by contemporary viral strains. In a head-to-head comparison of ancestral virus vaccines and bivalent ancestral plus Omicron vaccines, recipients of bivalent vaccines had a 12 to 39% additional protection (depending on age) against SARS-CoV-2 Omicron disease.<sup>10</sup> In the same study, extended to include over 2 million participants, the relative vaccine effectiveness of a booster dose of the bivalent vaccines versus a booster dose of ancestral virus vaccines was 42.4% against SARS-CoV-2 infection and 81 to 85% against severe disease or death.<sup>11</sup> Emerging effectiveness data also show evidence of the protection against COVID-19 with the updated XBB.1.5 vaccines.<sup>12,13,14</sup>

### In conclusion

EU Member States are recommending that people in the EU/EEA at increased risk for severe COVID-19 disease should be offered vaccination. To provide optimal protection against circulating strains, ETF recommends that the most recently updated COVID-19 vaccines should be used.

The ETF recognizes that, in the future, new COVID-19 vaccines may initially be authorised with a composition that does not match circulating VOCs but reflects the composition of the vaccines used in pre-licensure clinical trials. Whenever this occurs, similarly to influenza, the vaccines are expected to be updated before deployment to reflect recent and/or circulating SARS-CoV-2 variants.

The ETF will continue to evaluate SARS-CoV-2 epidemiological data and provide updated vaccine composition recommendations as appropriate.

### References

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