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ECDC-EMA statement on updating COVID-19 vaccines composition for new SARS-CoV-2 virus variants

The European Centre for Disease Prevention and Control (ECDC) and the European Medicines Agency (EMA) are providing an update on the proposed adaptation of the authorised COVID-19 vaccines and reinforcing interim public health considerations[1] on the use of such vaccines during the upcoming autumn 2023 vaccination campaigns.

The currently authorised COVID-19 vaccines in the EU/EEA include the following strain(s): bivalent Wuhan and Omicron BA.1, bivalent Wuhan and Omicron BA.4/5, monovalent Wuhan, monovalent Beta (B.1.351), and bivalent Beta (B.1.351) and Alpha (B.1.1.7). Available effectiveness data show that currently approved COVID-19 vaccines, including those based on the index virus, continue to provide protection against severe disease[1,2,3]. However, protection declines as virus mutates to immunologically distant variants from strains included in the vaccines[4].

Members of the International Coalition of Medicines Regulatory Authorities (ICMRA) including WHO met on 8 May and the WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) met on 11-12 May and issued a statement on 18 May[5,6]. In both meetings the conclusion has been that there is a need to update COVID-19 vaccine composition. Both groups concluded that the SARS-CoV-2 virus appears to evolve, diverging from the index virus. The conclusion of these bodies has been that, while waiting for more data, monovalent XBB-containing vaccines could be considered a reasonable choice for the autumn 2023 vaccination campaign to enhance vaccine-induced immune responses to circulating SARS-CoV-2 variants based on current epidemiology and the high level of immunity already present against ancestral and previously circulating strains.

Based on surveillance and sequencing data, the XBB.1 descendent lineages currently predominate globally (i.e., XBB.1.5, XBB.1.16, XBB.1.9) including in the EU/EEA countries.

Recommendations and considerations to Marketing Authorisation Holders regarding updates to vaccine composition

Having considered the WHO TAG advice as well as the ICMRA position statement on this matter, the EMA Emergency Task Force (ETF) is of the opinion that:

[1] https://www.ecdc.europa.eu/en/publications-data/interim-public-health-considerations-covid-19-vaccination-roll-out-during-2023
[2] https://www.medrxiv.org/content/10.1101/2023.01.19.23284764v1.full.pdf
[3] https://www.nejm.org/doi/pdf/10.1056/NEJMc2215471?articleTools=true
[4] https://www.medrxiv.org/content/10.1101/2023.03.02.23286561v1
[5] https://www.who.int/news/item/18-05-2023-statement-on-the-antigen-composition-of-covid-19-vaccines
[6] ICMRA COVID-19 Omicron variant workshop | International Coalition of Medicines Regulatory Authorities (ICMRA)

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- a monovalent vaccine composition is suitable to ensure adequate immunogenicity against circulating SARS-CoV-2 in both primed and naïve individuals. Since the ancestral strain or previous variants of concern account for an extremely small proportion of circulating strains in the EU/EEA countries, and given the high level of pre-existing immunity against them, it is not necessary to keep them in the vaccine formulation going forward;
- the inclusion of a strain belonging to the XBB family of Omicron subvariants is adequate to ensure cross-reactivity against current dominant and emerging strains, and XBB.1.5 is considered as a reasonable choice to increase the breadth of immunity also against XBB descendent lineages. Vaccine compositions containing other XBB strains (e.g. XBB.1.16) could be considered based on adequate justification;
- Such monovalent vaccines could be used for revaccination. They could also be used for primary vaccinations in younger children below 5 years of age, who are more likely to be naïve to the virus and never vaccinated. This age cut off is conservatively based on epidemiological data indicating that children older than 5 years have largely been exposed to SARS-CoV-2, either by infection, vaccination, or both and therefore have already mounted an immune response specific to SARS-COV2[7,8];
- using a platform approach, as already experienced for adapted mRNA vaccines in 2022, is considered acceptable to approve strain change variations. Approvals can be based on manufacturing/quality and non-clinical data only, provided the vaccine platform can demonstrate predictability of clinical immunogenicity and reactogenicity. Such clinical data can be based on different variants of concerns[9] (VOCs) that have been previously investigated. Moreover plans for post-authorisation monitoring of effectiveness and immunogenicity/safety will have to be discussed at the time of evaluation with the Committee for Medicinal Products for Human Use (CHMP).

Timing of recommendations to update vaccine composition has an impact on some platform technologies that require longer time for manufacturing, and this aspect needs to be considered. This ETF position is intended to provide guidance to vaccine Marketing Authorisation Holders on the next steps to update vaccine composition for the upcoming winter season. Alternative vaccine compositions could be discussed on ad-hoc basis. For investigational vaccines whose development is based on a different composition than what is recommended by ETF, applicants should discuss their strategy for authorisation with EMA.

Based on decades of experience with influenza and discussions with different developers, it can be foreseen that a recommendation on the potential need to adapt vaccine composition should be issued at regular intervals to allow stakeholders to deliver a timely vaccination campaign. For example, a recommendation around April/May each year should ensure sufficient time for most developers to adapt their manufacturing process and generate the necessary data in support of vaccine approval by the end of summer. Public Health Authorities would then have the necessary authorisations to prepare for vaccination campaigns to start in autumn depending on the local epidemiological situation. This plan should be considered as indicative as it is based on the current situation and understanding of the virus seasonality, but it may be further revised as evidence and data are accumulated.

[7] https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-changes-simplify-use-bivalent-mrna-covid-19-vaccines

[8] Eurosurveillance | Seroprevalence of antibodies against SARS-CoV-2 and risk of COVID-19 in Navarre, Spain, May to July 2022

[9] https://www.ecdc.europa.eu/en/covid-19/variants-concern

Proposed revision of Product Information of newly adapted vaccines

Marketing authorisation holders of the authorised COVID-19 vaccines should discuss with EMA a revision of the respective Product Information to reflect a simplified approach to vaccination as follows.

For individuals above 5 years of age, when vaccination is recommended according to national guidelines, a single dose of the newly adapted vaccine is indicated. For children below 5 years of age, without history of vaccination or prior SARS-CoV-2 infection, a primary series composed of 2 or 3 doses depending on the specific vaccine to be administered is recommended. Use in paediatric population is expected to follow national guidelines.

In people with compromised immunity, additional doses might be necessary. The number of doses and intervals should be tailored to the individual patient depending on the severity of the condition and in line with national recommendations.

COVID-19 vaccines regulatory approval allows revaccination with an interval as short as 3 months after the previous dose[10], if deemed needed. However, the time interval between doses may vary depending on the epidemiology and the targeted population. Longer intervals of at least 4 months may be considered in vaccination campaigns, based on real-world evidence of high level of protection against severe disease maintained for at least 4 months following revaccination.

Final decision on approval and wording of indication will be taken by the CHMP following assessment of submitted data.

Recommended population groups for vaccination in 2023

Vaccination campaigns for COVID-19 are expected to take place in the EU in 2023 ahead of the cold season, during the autumn.

According to public health considerations recently issued by ECDC, for the upcoming autumn vaccination campaigns a priority should be targeting individuals that are at risk of progression to severe disease once infected because of risk factors, such as older adults (e.g. above 60 years of age), immunocompromised individuals, those with underlying medical conditions irrespective of age, and pregnant women.

Healthcare workers should also be considered by public health authorities as a priority for COVID-19 revaccination[11]. The purpose of vaccinating healthcare workers would be to provide protection against new infection, given their increased exposure to the virus, and to maximise the ability of healthcare systems to operate in case of a significant wave of SARS-CoV-2 in the colder months.

Individuals in the previously described risk groups that received their last vaccine dose one year ago or longer could be particularly at risk of severe COVID and need to be specifically targeted as a priority. In addition, particularly vulnerable groups such as elderly above 80 years of age or immunocompromised individuals might require an additional dose of the new updated vaccine at a time interval of at least 4 months since the previous dose, a decision that could be made at a national level based on the evolution of the epidemiological situation.

Concomitant vaccination for COVID-19 and influenza can be done considering vaccine specific available information on the co-administration with influenza vaccines.

[10] Comirnaty, INN-tozinameran, tozinameran/riltozinameran, tozinameran/famtozinameran (europa.eu)
[11] https://www.who.int/publications/i/item/WHO-2019-nCoV-Vaccines-SAGE-Roadmap

Once authorised, and without prejudice to the CHMP scientific opinion and subsequent EC authorisation of these monovalent XBB-adapted vaccines, they could also be used for primary vaccination of young children below 5 years of age who are at risk of complications or severe disease.

Overall, the decisions at country level related to COVID-19 vaccination for 2023 will continue to depend on a number of key evolving factors, such as the specific national epidemiological situation, possible virus evolution, availability of vaccines, vaccine effectiveness and protection over time, evidence on the effect of repeated boosters, degree of hybrid immunity[12]across the population, projected vaccine uptake in different age groups, vaccine acceptance and the capacity of health systems to deliver vaccinations in the context of other competing public health priorities during the post-pandemic phase. Based on these factors, National Immunisation Technical Advisory Groups (NITAGs) will make national recommendations on the use of COVID-19 vaccines. Ultimately, responsibility for national decisions on the best strategies lies with Ministries of Health, taking into account the relevant advice and/or recommendations given by NITAGs.

[12] Hybrid immunity is defined as the immune protection in individuals who have had one or more doses of a COVID-19 vaccine and experienced at least one SARS-CoV-2 infection before or after the initiation of vaccination.