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Emergency Task Force

Replacement of quadrivalent seasonal influenza vaccines with trivalent vaccines in the EU

Removal of antigens from B/Yamagata lineage

Background

Influenza viruses that cause disease in humans are classified as types A, B and C. Types A and B cause most cases of influenza in humans, and the subtypes responsible for seasonal influenza are A(H1N1)pdm09, A(H3N2) and the two influenza B lineages, B/Yamagata and B/Victoria. Influenza A viruses cause approximately 75% of seasonal epidemic cases, while 25% are attributed to influenza B viruses[1]. Whilst influenza B and C circulate almost exclusively in humans, influenza A viruses also infect a wide range of other species.

Trivalent influenza vaccines (TIVs) include two influenza A antigens and one influenza B antigen from either the B/Victoria or B/Yamagata lineage depending on which lineage/strain is expected to contribute most to the next season's global annual influenza epidemic. Quadrivalent influenza vaccines (QIVs), on the other hand, contain antigens of both B/Victoria and B/Yamagata lineages. The use of quadrivalent vaccines has completely replaced the use of trivalent formulations at least in the EU, with only a few TIV marketing authorisations still valid in EU Member States.

According to data from the Global Initiative on Sharing All Influenza Data (GISAID)[2] and FluNet[3], there has been no confirmed detection of the naturally occurring B/Yamagata virus since March 2020[4,5]. Specific features of the B-Yamagata virus related to its fitness and transmission modality are believed

[1] Heikkinen, T., N. Ikonen, and T. Ziegler, Impact of influenza B lineage level mismatch between trivalent seasonal influenza vaccines and circulating viruses, 1999-2012. Clin Infect Dis, 2014. 59(11): p. 1519-24.
[2] https://gisaid.org/influenza-subtypes/
[3] https://www.who.int/tools/flunet/flunet-summary
[4] https://www.who.int/publications/m/item/recommended-composition-of-influenza-virus-vaccines-for-use-in-the-2024-2025-northern-hemisphere-influenza-season
[5] Paget J, Caini S, Del Riccio M, van Waarden W, Meijer A. Has influenza B/Yamagata become extinct and what implications might this have for quadrivalent influenza vaccines? Euro Surveill. 2022 Sep;27(39):2200753. doi: 10.2807/1560-7917.ES.2022.27.39.2200753. PMID: 36177871; PMCID: PMC9524051.

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to be partly responsible for its apparent disappearance as are the public health measures put in place to limit the spread of SARS-CoV-2.[6]

As naturally the occurring B/Yamagata virus has not been detected in the last four years, the relevance of vaccinating against this lineage has been questioned globally as the virus no longer poses a threat to public health. Moreover, live virus vaccines containing the B/Yamagata antigen could pose a remote risk of the lineage being reintroduced into humans via reassortment of B/Yamagata vaccine strain with wild type B/Victoria strain.

Taking all these considerations into account, the World Health Organization (WHO) issued recommendations in 2023 for the southern hemisphere[7] and in 2024 for the northern hemisphere[8] to switch to the manufacture of seasonal influenza vaccines without the B-Yamagata virus component as soon as possible, meaning that vaccines should only include components from three subtypes: A/(H1N1)pdm09, A/(H3N2) and B/Victoria. These recommendations apply to both live attenuated vaccines and inactivated vaccines.

Recommendation of the Emergency Task Force (ETF)

EMA's Emergency Task Force (ETF) recommends a well-planned transition to trivalent influenza vaccines given that the inclusion of antigens from B/Yamagata influenza no longer appears to be warranted. However continuous monitoring is important to confirm the disappearance of B/Yamagata. In light of the uncertainties, a cautious stepwise approach is recommended. A review of the regulatory status of all EU approved seasonal influenza vaccines has been performed to anticipate hurdles for any specific vaccine during this transition. During this exercise, EMA consulted with EU public health authorities and vaccine manufacturers.

The ETF recommends starting the process of re-authorising TIVs by prioritising the live attenuated virus vaccines for which there could be a potential risk of the re-introduction of B/Yamagata. For inactivated vaccines, there is no public health concern requiring an immediate transition, and vaccine availability is of primary importance. In the EU, most inactivated vaccines are approved at the national level and the newer vaccines have only been approved as quadrivalent formulations. The transition to TIV formulations could therefore be complex and not all companies will be able to complete this in time for the 2024/2025 vaccination campaign.

Taking the above into account, the ETF recommends that antigens of the B/Yamagata lineage should be removed from the live attenuated influenza vaccines ideally for the 2024/2025 influenza season. For all other influenza vaccines, the target for completing the transition to trivalent formulations is the 2025/2026 influenza season.

For some inactivated vaccines it may be possible to complete transition to TIVs in 2024, possibly in time for the start of the vaccination campaign in the autumn of 2024. The decision regarding which vaccine to choose for the vaccination campaign remains in the remit of the national competent authorities.

[6] Influenza vaccine shake-up, The Lancet Infectious Diseases, Volume 23, Issue 12, 2023, Page 1323, ISSN 1473-3099, https://doi.org/10.1016/S1473-3099(23)00697-7. (https://www.sciencedirect.com/science/article/pii/S1473309923006977)

[7] https://www.who.int/news/item/29-09-2023-recommended-composition-of-influenza-virus-vaccines-for-use-in-the-2024-southern-hemisphere-influenza-season

[8] https://www.who.int/news/item/23-02-2024-recommendations-announced-for-influenza-vaccine-composition-for-the-2024-2025-northern-hemisphere-influenza-season

Patients and health care professionals are reminded that both the trivalent and quadrivalent influenza vaccines that will be available for the 2024/2025 season are safe and effective against circulating strains, and that the official national vaccination recommendations of each Member State should be followed.