World Health Organization

# Addendum to the recommended composition of influenza virus vaccines for use in the 2019–2020 northern hemisphere influenza season

**21 March 2019**

On 21 February 2019 WHO announced a recommendation on the composition of three of the four components of influenza vaccines for use in the 2019-2020 northern hemisphere influenza season (https://www.who.int/influenza/vaccines/virus/recommendations/2019_20_north/en/). The decision on the A(H3N2) component was postponed to allow more time to better understand the distribution and proportions of recently circulating antigenically and genetically diverse A(H3N2) viruses and to develop and fully characterize appropriate candidate vaccine viruses. This addendum provides the recommendation and supporting data for the A(H3N2) component of 2019-2020 northern hemisphere influenza vaccines.

Additional data obtained in recent weeks has confirmed the wide regional differences in the relative proportion of A(H3N2) viruses belonging to the phylogenetic subclade 3C.2a1b and clade 3C.3a. The majority of A(H3N2) viruses collected and genetically characterised from September 2018 to February 2019 belonged to the phylogenetic subclade 3C.2a1b; however, the proportion of viruses falling into clade 3C.3a has increased substantially since November 2018 in several countries in western Europe, Israel and especially in the United States of America.

HI and virus neutralisation assays with ferret antiserum panels showed that viruses from subclade 3C.2a1b and clade 3C.3a were antigenically distinct. The majority of recent viruses from subclade 3C.2a1b were inhibited well by post-infection ferret antisera raised against cell culture-propagated A/Singapore/INFIMH-16-0019/2016-like viruses of subclade 3C.2a1 (Table 1). In contrast, ferret antisera raised against egg-propagated A/Singapore/INFIMH-16-0019/2016-like and egg-propagated A/Switzerland/8060/2017-like viruses of subclade 3C.2a2 inhibited a much smaller proportion of recently circulating viruses (Table 2). Viruses from clade 3C.3a were poorly inhibited by post-infection ferret antisera raised against cell culture-propagated A/Singapore/INFIMH-16-0019/2016-like viruses, but were well inhibited by ferret antisera raised against recent 3C.3a cell culture-propagated reference viruses such as A/Kansas/14/2017 (Table 1). Ferret antisera raised against egg-propagated A/Kansas/14/2017 inhibited recent viruses from clade 3C.3a but showed little inhibition against viruses from clade 3C2a1b. Current vaccines containing A/Singapore/INFIMH-16-0019/2016-like antigens induced antibodies in humans that cross-reacted with recent 3C.2a1b viruses but reacted poorly with clade 3C.3a viruses.

**Accordingly, it is recommended quadrivalent vaccines for use in the 2019-2020 northern hemisphere influenza season contain the following:**

**- an A/Brisbane/02/2018 (H1N1)pdm09-like virus;**
**- an A/Kansas/14/2017 (H3N2)-like virus;**
**- a B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage); and**
**- a B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage).**

**It is recommended that the influenza B virus component of trivalent vaccines for use in the 2019-2020 northern hemisphere influenza season be a B/Colorado/06/2017-like virus.**

Lists of egg- or cell culture-propagated candidate vaccine viruses (CVVs) suitable for use in human vaccine production are available on the WHO website[1]. Lists of reagents for vaccine standardisation, including those for this recommendation, can be found on the same WHO website[1].

[1] http://www.who.int/influenza/vaccines/virus/candidates_reagents/home

**Table 1. Antigenic Analysis of A(H3N2) Viruses – Focus Reduction Neutralisation Assay**

| | | REFERENCE FERRET ANTISERA | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 2a1 | | | 3a | | | | |
| | REFERENCE VIRUSES | EGG SN/X307A | SIAT SN/16 | QMC NC/4 | EGG KS/14 | SIAT KS/14 | 3C Clade | DATE COLLECTED | PASSAGE |
| 1 | A/Singapore/INFIMH-16-0019/2016 X-307A | **5120** | 640 | 640 | 80 | 160 | 2a1 | 2014/09/24 | E5E2E9/E1 |
| 2 | A/Singapore/INFIMH-16-0019/2016 | 640 | **1280** | 2560 | 320 | 320 | 2a1 | 2016/06/14 | C1S3/S4 |
| 3 | A/North Carolina/04/2016 | 640 | 1280 | **2560** | 320 | 640 | 2a1 | 2016/01/13 | QMC*X |
| 4 | A/Kansas/14/2017 | <80 | 40 | <40 | **2560** | 160 | 3a | 2017/12/14 | E7 |
| 5 | A/Kansas/14/2017 | 80 | 80 | 80 | 640 | **1280** | 3a | 2017/12/14 | S3 |
| **TEST VIRUSES** | | | | | | | | | |
| 6 | A/Bulgaria/1534/2018 | 640 | 1280 | 2560 | <80 | 80 | 2a1b | 2018/12/28 | S2 |
| 7 | A/Santiago/103164/2018 | 640 | 1280 | 2560 | 160 | 320 | 2a1b | 2018/12/06 | S2 |
| 8 | A/Delaware/07/2019 | 640 | 2560 | 2560 | <80 | 160 | 2a1b | 2019/01/20 | S1 |
| 9 | A/Virginia/07/2019 | 320 | 1280 | 1280 | 160 | 160 | 2a1b | 2019/01/14 | S2 |
| 10 | A/California/127/2018 | 320 | 640 | 640 | <80 | 320 | 2a1b | 2018/12/31 | S1 |
| 11 | A/California/08/2019 | 1280 | 2560 | 2560 | <80 | 320 | 2a1b | 2019/01/04 | S1 |
| 12 | A/Hawaii/78/2018 | 640 | 2560 | 2560 | <80 | 160 | 2a1b | 2018/12/31 | S1 |
| 13 | A/Montana/04/2019 | 640 | 1280 | 2560 | <80 | 160 | 2a1b | 2019/01/10 | S1 |
| 14 | A/Kuwait/6419/2018 | 640 | 2560 | 2560 | <80 | 160 | 2a1b | 2018/07/11 | S2 |
| 15 | A/North Carolina/04/2019 | 640 | 1280 | 2560 | 80 | 320 | 2a1b | 2019/01/22 | S2 |
| 16 | A/Hong Kong/3217/2018 | 80 | 640 | 640 | 80 | 40 | 2a1b | 2018/12/12 | S1 |
| 17 | A/Pennsylvania/08/2019 | 80 | 40 | 40 | 640 | 1280 | 3a | 2019/01/23 | S1 |
| 18 | A/Texas/11/2019 | 160 | 80 | 80 | 640 | 640 | 3a | 2019/01/23 | S2 |
| 19 | A/Indiana/05/2019 | 80 | 80 | 80 | 640 | 1280 | 3a | 2019/01/23 | S2 |
| 20 | A/Missouri/06/2019 | 80 | 80 | 40 | 640 | 1280 | 3a | 2019/01/28 | S1 |
| 21 | A/Minnesota/08/2019 | 80 | 40 | <40 | 320 | 320 | 3a | 2019/01/26 | S1 |
| 22 | A/Arkansas/09/2019 | <80 | 40 | <40 | 640 | 640 | 3a | 2019/01/30 | S1 |
| 23 | A/Wisconsin/24/2019 | 80 | 80 | 40 | 640 | 640 | 3a | 2019/01/27 | S1 |
| 24 | A/Massachusetts/07/2019 | 80 | 40 | 80 | 640 | 640 | 3a | 2019/01/24 | S1 |
| 25 | A/Florida/14/2019 | <80 | 80 | <40 | 640 | 640 | 3a | 2019/01/25 | S1 |

*Qualified MDCK cells 33016 PF approved for use for human vaccine manufacturing

**Table 2. Antigenic Analysis of A(H3N2) Viruses – Haemagglutination Inhibition Assay**
(with 20nM Oseltamivir, 4 HA units/50 microliters)

| | | REFERENCE FERRET ANTISERA | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 2a1 | 2a1b | | 2a2 | 3C.3a | | | | |
| | REFERENCE VIRUSES | EGG SN/X307A | EGG UE/240 | EGG NL/10260 | EGG SZ/8060 | SIAT KS/14 | EGG KS/14 | 3C Clade | DATE COLLECTED | PASSAGE |
| 1 | A/Singapore/INFIMH-16-0019/2016 X-307A | **2560** | 320 | 160 | 160 | 80 | 80 | 2a1 | REASS | E5E2E9/E1 |
| 2 | A/Abu Dhabi/240/2018 | 640 | **10240** | 5120 | 160 | 80 | 40 | 2a1b | 2018/01/01 | E6 |
| 3 | A/Netherlands/10260/2018 | 1280 | 10240 | **5120** | 160 | 160 | 80 | 2a1b | 2018/02/15 | E4/E2 |
| 4 | A/Hong Kong/681/2018 | 2560 | 5120 | 5120 | 320 | 640 | 640 | 2a1b | 2018/04/09 | E6/E2 |
| 5 | A Switzerland/8060/17 | 640 | 80 | 80 | **2560** | 40 | 40 | 2a2 | 2017/12/21 | E5/E2 |
| 6 | A/Kansas/14/2017 | 80 | 80 | 80 | 80 | **160** | 80 | 3a | 2017/12/14 | S3 |
| 7 | A/Kansas/14/2017 | 160 | 160 | 320 | 40 | 640 | **1280** | 3a | 2017/12/14 | E7 |
| **TEST VIRUSES** | | | | | | | | | | |
| 8 | A/Florida/15/2019 | 80 | 160 | 160 | 80 | 160 | 20 | 2a1b | 2019/02/04 | S2 |
| 9 | A/Hawaii/09/2019 | 80 | 320 | 40 | 40 | 80 | <20 | 2a1b | 2019/02/09 | S1 |
| 10 | A/California/127/2018 | 160 | 320 | 160 | 40 | 80 | <20 | 2a1b | 2018/12/31 | S1 |
| 11 | A/Hawaii/08/2019 | 160 | 320 | 80 | 80 | 160 | <20 | 2a1b | 2019/02/01 | S1 |
| 12 | A/New Mexico/09/2019 | 160 | 160 | 160 | 80 | 160 | <20 | 2a1b | 2019/02/05 | S1 |
| 13 | A/New Mexico/10/2019 | 160 | 160 | 160 | 80 | 160 | <20 | 2a1b | 2019/02/10 | S1 |
| 14 | A/Delaware/12/2019 | 40 | 80 | 80 | 20 | 80 | <20 | 2a1b | 2019/02/04 | S1 |
| 15 | A/Vermont/06/2019 | 40 | 80 | 80 | 40 | 160 | <20 | 2a1b | 2019/02/06 | S1 |
| 16 | A/Vermont/09/2019 | 80 | 160 | 160 | 80 | 80 | <20 | 2a1b | 2019/02/11 | S2 |
| 17 | A/Brisbane/34/2018 | 40 | 40 | 160 | 40 | 320 | 320 | 3a | 2018/03/17 | E2/E1 |
| 18 | A/Lousiana/14/2019 | 40 | 40 | 20 | 20 | 320 | 160 | 3a | 2019/02/06 | S1 |
| 19 | A/Maine/08/2019 | 40 | 80 | 40 | 20 | 320 | 160 | 3a | 2019/02/06 | S1 |
| 20 | A/New Hampshire/13/2019 | 40 | 40 | 40 | 20 | 320 | 160 | 3a | 2019/02/15 | S1 |
| 21 | A/North Dakota/12/2019 | 80 | 80 | 80 | 40 | 320 | 160 | 3a | 2019/02/10 | S1 |
| 22 | A/South Dakota/10/2019 | 40 | 40 | 40 | 20 | 320 | 160 | 3a | 2019/02/18 | S1 |
| 23 | A/Tennessee/09/2019 | 20 | 20 | 40 | 20 | 320 | 160 | 3a | 2019/02/04 | S1 |
| 24 | A/Texas/45/2019 | 40 | 40 | 20 | 20 | 320 | 160 | 3a | 2019/02/07 | S1 |
| 25 | A/Iowa/11/2019 | 40 | 40 | 40 | 40 | 640 | 320 | 3a | 2019/02/07 | S1 |
| 26 | A/Wyoming/06/2019 | 80 | 80 | 160 | 40 | 2560 | 640 | 3a | 2019/02/04 | S1 |