**Supplementary Information 1: Hemagglutination-inhibition immunogenicity in the per-protocol immunogenicity cohort by seasonal influenza vaccination history**

|  | **Previous Vaccination†** | **A/H1N1** | | **A/H3N2** | | | **B/Yamagata** | | | **B/Victoria** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Day 0** | **Day 21** | **Day 0** | **Day 21** | | **Day 0** | | **Day 21** | **Day 0** | **Day 21** |
| **Seropositivity‡ rate, % (95% CI)** | | | | | | | | | | | |
| Adult, N=62 | Yes | 96.8  (83.3, 99.9) | 100  (88.8, 100) | 96.8  (83.3, 99.9) | | 100  (88.8, 100) | | 100  (88.8, 100) | 100  (88.8, 100) | 100  (88.8, 100) | 100  (88.8, 100) |
| No | 67.7  (48.6, 83.3) | 100  (88.8, 100) | 71.0  (52.0, 85.8) | | 100  (88.8, 100) | | 90.3  (74.2, 98.0) | 100  (88.8, 100) | 90.3  (74.2, 98.0) | 100  (88.8, 100) |
| Older adult, N=57 | Yes | 91.3  (79.2, 97.6) | 100  (92.3, 100) | 93.5  (82.1, 98.6) | | 100  (93.7 100) | | 100  (92.3, 100) | 100  (92.3, 100) | 100  (92.3, 100) | 100  (92.3, 100) |
| No | 90.9  (58.7, 99.8) | 100  (71.5, 100) | 81.8  (48.2, 97.7) | | 100  (71.5, 100) | | 100  (71.5, 100) | 100  (71.5, 100) | 100  (71.5 100) | 100  (71.5, 100) |
| **GMT, value (95% CI)** | | | | | | | | | | | |
| Adult, N=62 | Yes | 86.5  (56.7, 132.0) | 276.7  (206.8, 370.3) | 41.3  (26.1, 65.5) | 342.2  (240.9, 486.1) | | 133.7  (89.2, 200.4) | | 306.0  (223.4, 419.0) | 95.6  (68.7, 133.0) | 282.9  (207.7, 385.3) |
| No | 25.9  (14.4, 46.5) | 765.3  (499.0, 1174.0) | 24.7  (14.5, 42.2) | 334.6  (215.2, 520.3) | | 52.9  (29.5, 94.6) | | 374.2  (257.8, 543.1) | 49.5  (30.7, 79.6) | 473.2  (341.5, 655.7) |
| Older adult, N=57 | Yes | 33.9  (23.4, 48.9) | 151.8  (111.2, 207.0) | 44.8  (30.1, 66.5) | 281.6  (196.3, 403.9) | | 88.2  (70.2, 110.8) | | 194.6  (157.6, 240.3) | 114.9  (82.7, 159.5) | 259.2  (196.3, 342.3) |
| No | 22.0  (11.0, 43.9) | 248.7  (115.6, 534.9) | 31.0  (11.1, 87.1) | 438.5  (229.9, 836.4) | | 45.4  (24.7, 83.5) | | 425.0  (267.3, 675.7) | 54.8  (29.3, 102.8) | 452.5  (236.2, 867.1) |
| **SPR, % (95% CI)** | | | | | | | | | | | |
| Adult, N=62 | Yes | 87.1  (70.2, 96.4) | 100  (88.8, 100) | 51.6  (33.1, 69.8) | 100  (88.8, 100) | | 90.3  (74.2, 98.0) | | 100  (88.8, 100) | 87.1  (70.2, 96.4) | 100  (88.8, 100) |
| No | 41.9  (24.5, 60.9) | 100  (88.8, 100) | 41.9  (24.5, 60.9) | 96.8  (83.3, 99.9) | | 58.1  (39.1, 75.5) | | 100  (88.8, 100) | 67.7  (48.6, 83.3) | 100  (88.8, 100) |
| Older adult, N=57 | Yes | 58.7  (43.2, 73.0) | 93.5  (82.1, 98.6) | 60.9  (45.4, 74.9) | 95.7  (85.2, 99.5) | | 89.1  (76.4, 96.4) | | 100  (92.3, 100) | 89.1  (76.4, 96.4) | 100  (92.3, 100) |
| No | 36.4  (10.9, 69.2) | 100  (71.5, 100) | 45.5  (16.7, 76.6) | 100  (71.5, 100) | | 54.5  (23.4, 83.3) | | 100  (71.5, 100) | 63.6  (30.8, 89.1) | 100  (71.5, 100) |
| **SCR, % (95% CI)** | | | | | | | | | | | |
| Adult, N=62 | Yes | – | 45.2  27.3, 64.0 | – | 80.6  (62.5, 92.5) | | – | | 25.8  (11.9, 44.6) | – | 45.2  (27.3, 64.0) |
| No | – | 77.4  (58.9, 90.4) | – | 77.4  (58.9, 90.4) | | – | | 74.2  (55.4, 88.1) | – | 77.4  (58.9, 90.4) |
| Older adult, N=57 | Yes | – | 56.5  (41.1, 71.1) | – | 71.7  (56.5, 84.0) | | – | | 26.1  (14.3, 41.1) | – | 28.3  (16.0, 43.5) |
| No | – | 81.8  (48.2, 97.7) | – | 72.7  (39.0, 94.0) | | – | | 72.7  (39.0, 94.0) | – | 63.6  (30.8, 89.1) |
| **MGI, value (95% CI)** | | | | | | | | | | | |
| Adult, N=62 | Yes | – | 3.2  (2.3, 4.5) | – | 8.3  (5.4, 12.7) | | – | | 2.3  (1.7, 3.0) | – | 3.0  (2.1, 4.1) |
| No | – | 29.6  (13.5, 64.8) | – | 13.5  (8.3, 22.2) | | – | | 7.1  (4.4, 11.3) | – | 9.6  (5.6, 16.4) |
| Older adult, N=57 | Yes | – | 4.5  (3.2, 6.3) | – | 6.3  (4.5, 8.8) | | – | | 2.2  (1.8, 2.6) | – | 2.3  (1.8, 2.9) |
| No | – | 11.3  (4.1, 31.1) | – | 14.1  (4.9, 40.8) | | – | | 9.4  (4.2, 21.0) | – | 8.3  (3.1, 21.9) |

†Received seasonal influenza vaccine during the preceding season; ‡Seropositive defined as titer ≥1:10; GMT, geometric mean titer; SCR, seroconversion rate defined as the proportion with antibody titer <1:10 at baseline and with post-vaccination titer of ≥1:40, or pre-vaccination titer of ≥1:10 and a ≥4-fold post-vaccination increase in titer; SPR, seroprotection rate, defined as proportion of subjects with titer ≥1:40; MGI, mean geometric increase, defined as the fold increase in GMT after vaccination compared with pre-vaccination; CI, confidence interval; Adult, aged 18–60 years; Older, aged >60 years