Supplementary Materials

COVID-19 variants and vaccine development

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**Table S1.** The ingredients of Comirnaty and Spikevax COVID-19 vaccine.

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| --- | --- | --- | --- |
| **Ingredients** | **Comirnaty (original)** | **Comirnaty (updated)** | **Spikevax** |
| mRNA | Nucleoside-modified mRNA encoding the S glycoprotein of SARS-CoV-2 | Nucleoside-modified mRNA encoding the S glycoprotein of SARS-CoV-2 |
| Lipid | 2[(polyethylene glycol (PEG))-2000]-N, N-ditetradecylacetamide1,2-distearoyl-sn-glycero-3-phosphocholineCholesterol (plant derived)((4-hydroxybutyl) azanediyl) bis(hexane-6,1-diyl) bis(2-hexyldecanoate) | PEG2000-DMG1,2-distearoyl-sn-glycero-3-phosphocholineBotaniChol®SM-102 |
| OtherIngredients | Dibasic sodium phosphate dihydrateMonobasic potassium phosphatePotassium chloride (common food salt)Sodium chloride (basic table salt)Sucrose (basic table sugar) | Sucrose (table sugar)TromethamineTromethamine hydrochloride | Sodium acetateSucrose (basic table sugar)TromethamineTromethamine hydrochlorideAcetic acid (the main ingredient in white household vinegar) |

**Table S2.** Bivalent vaccines.

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| **Developers (Name)** | **Dose (mRNA)****/Volume** | **Vaccine Composition** | **Effectiveness against Omicron subvariants** |
| Pfizer and BioNTech (Comirnaty) Bivalent Booster | Original/Omicron BA.1 bivalent vaccine | 30 μg/0.3 mL | 15 μg WT+ 15 μg Omicron BA.1 (mRNA) | Higher neutralization activity against BA.2 and BA.5 compared with WT groupDecreased neutralization activity against BA.51 |
| Omicron BA.4/BA.5-adapted bivalent vaccine | 30 μg/0.3 mL | 15 μg WT+ 15 μg Omicron BA.4/BA.5(mRNA) | Higher neutralizing responses against BA.5-derived sublineages (BA.4.6, BQ.1.1, and XBB.1) and BA.2-derived sublineage (BA.2.75.2) compared with the original monovalent vaccine2 |
| Moderna (Spikevax) Bivalent Booster | BA.1 Omicron- containing vaccine (mRNA-1273.214) | 50 μg/0.5mL | 25 μg WT+ 25 μg Omicron BA.1(mRNA) | Elicited neutralizing antibody responses against omicron that were superior to those with original monovalent vaccine3 |
| BA.4/BA.5 Omicron-containing vaccine (mRNA-1273.222) | 50 μg/0.5mL | 25 μg WT+ 25 μg Omicron BA.4/BA.5(mRNA) | Enhanced neutralizing antibody responses against omicron sublineages (BA.1, BA.2.75.2 and BA.5) compared with original monovalent vaccine3 |

1 Kawasuji, H. *et al.* Efficacy of the wild-type/Omicron BA. 1 bivalent vaccine as the second booster dose against Omicron BA. 2 and BA. 5. *medRxiv*, 2022.2011. 2015.22282328 (2022).

2 Zou, J. *et al.* Improved neutralization of Omicron BA. 4/5, BA. 4.6, BA. 2.75. 2, BQ. 1.1, and XBB. 1 with bivalent BA. 4/5 vaccine. *BioRxiv*, 2022.2011. 2017.516898 (2022).

3 Scheaffer, S. M. *et al.* Bivalent SARS-CoV-2 mRNA vaccines increase breadth of neutralization and protect against the BA. 5 Omicron variant in mice. *Nature medicine* **29**, 247-257 (2023).