# National Immunisation Advisory Committee

RECOMMENDATIONS REGARDING BIVALENT mRNA COVID-19 VACCINES

NIAC | 15.09.2022

## About NIAC

NIAC membership includes nominees from the RCPI, its Faculties and Institutes, the RCSI, the ICGP, the National Immunisation Office, the Nursing and Midwifery Board of Ireland, the Infectious Diseases Society of Ireland, the Travel Medicine Society, the National Virus Reference Laboratory and lay members. Meetings are attended by representatives from the Department of Health and the HSE. Representatives of the Health Products Regulatory Agency attend to provide regulatory advice in relation to vaccines.

NIAC considers new evidence about vaccines and provides advice to the Chief Medical Officer and the Department of Health. The Department and the Minister for Health make policy decisions on vaccines which are implemented by the HSE.

## RECOMMENDATIONS

1. Efforts to increase primary and booster vaccination uptake remain a public health priority. Original mRNA vaccines (Comirnaty and Spikevax) are the recommended vaccines for the primary vaccination course.

2. Those who are due booster vaccination should receive an mRNA COVID-19 vaccine. Timely booster vaccination, regardless of the vaccine used, is the most important factor in sustaining protection, particularly for those at risk of more severe disease.

3. Authorised bivalent mRNA vaccines are preferentially recommended for all those aged 12 years and older eligible for a booster vaccination.

4. An interval of four to six months is recommended from the time of the last COVID-19 vaccine or confirmed SARS-COV-2 infection. In exceptional circumstances an interval of three months may be used (e.g., in a person scheduled to commence chemotherapy). Giving booster vaccination just before or at the beginning of high viral circulation (e.g., autumn/winter) is desirable.

5. The bivalent mRNA booster vaccines should be given as follows:
   a) Bivalent BA.1 vaccines
      - aged 12-29 years: Comirnaty Original/ Omicron BA.1 (0.3ml/30 mcg)
      - aged 30 years and older: Comirnaty Original/ Omicron BA.1 (0.3ml/30 mcg) or Spikevax bivalent Original/Omicron BA.1 (0.5ml/50 mcg)

   b) Comirnaty Original/ Omicron BA.4-5 vaccine
      - aged 12 years and older: Comirnaty Original/ Omicron BA.4-5 (0.3ml/30 mcg).

6. Booster vaccination may be given at the same time as influenza vaccine, with one vaccine administered in each arm.

7. If bivalent vaccine supplies are limited, priority should be given to the following groups to maintain high levels of immunity in those most at risk of severe disease:
   - those aged 65 years and older
   - those aged 12 years and older with immunocompromise associated with a sub optimal response to vaccines at the time of their primary or booster vaccination
   - those with underlying medical conditions with a higher risk of severe COVID-19
   - those who are pregnant, at 16 weeks gestation or later, and who have not received a booster vaccine in the current pregnancy.

8. Those for whom a bivalent mRNA vaccine is contraindicated or declined should be offered an alternative vaccine.

These recommendations reflect a dynamic vaccination programme. Scientific evidence is emerging and being refined. Recommendations may be updated when more information becomes available. There is significant uncertainty regarding the emergence and nature of future variants, which makes it difficult to predict with certainty the effectiveness of available vaccines.

# 1. EXECUTIVE SUMMARY

- Booster COVID-19 vaccination results in a high level of protection against severe disease that is maintained for 4 months or longer.
- Protection following vaccination and infection (hybrid immunity) is even more durable.
- Waning of protection gradually ensues, with the risk of hospitalisation and severe disease higher in those aged 65 years and older, those with immunocompromise and those with underlying medical conditions with a higher risk of severe COVID-19.
- Booster doses of a COVID-19 vaccine restore protection following previous vaccination or infection. A booster can be administered after a minimum interval of three months, however a longer interval between doses increases immunogenicity. Thus, booster dose timing is a balance between the need to optimise immunogenicity and the risk incurred by delaying the booster dose.
- A surge in COVID-19 infections is expected in the autumn/winter season. Timing of booster vaccination to reduce severe disease in those at risk and to mitigate the impact of rising case numbers on the health care service is an important additional consideration.
- Timely use of boosters, regardless of specific vaccine used, is an important factor in sustaining protection, particularly for those at risk of more severe disease.
- While a booster dose of any authorised COVID-19 vaccine will provide short term protection against infection, it will provide much more durable protection against hospitalisation and severe disease including that caused by Omicron variants.
- mRNA bivalent COVID-19 vaccines have been authorised by the European Medicines Agency (EMA) for use as booster vaccines in those aged 12 years and older.
- These adapted vaccines are similar to the original mRNA COVID-19 vaccines. They include mRNA based both on the spike protein of the ancestral virus, as in the original vaccine, and mRNA based on the spike protein of either Omicron BA.1 or Omicron BA.4-5. These modifications have been likened to the routine adjustments to the annual influenza vaccines to counter the changeable nature of the influenza virus.
- These bivalent vaccines are adapted to better match circulating variants and are expected to give broader protection against different variants, although their impact on future variants is unpredictable.
- Limited clinical trial data on BA.1 bivalent vaccines show local and systemic reactogenicity profiles similar to that associated with the original vaccines. Long term follow up data are not available. The limited numbers of participants in the studies means that very rare side effects cannot be excluded. Myocarditis and pericarditis are recognised as very rare risks of mRNA vaccination, predominantly in males aged under 30 years after the second dose of the primary vaccination course. However, the risk is lower following booster doses.
- In authorising the BA.4-5 bivalent vaccine, the EMA based their recommendations on safety of the bivalent BA.1 mRNA COVID-19 vaccine and large body of cumulative data on original mRNA vaccines that are very similar and whose safety profile is well established.

- Clinical trial data shows that, compared to the original vaccines, neutralising antibody levels after BA.1 bivalent vaccines are similar against the ancestral COVID-19 strain and higher against Omicron variants including the BA.1, BA.2, BA.2.75 and BA.5. Antibody levels against BA.5, while higher than those achieved with the original vaccines, are lower than those against the other variants.
- In two small preclinical studies antibody levels against BA.5 were higher following vaccination with a BA.4-5 bivalent vaccine than with the BA.1 vaccines.
- Protection against COVID-19 is correlated with the level of neutralising antibodies present. While a defined cutoff level is not known, higher antibody levels are associated with increased protection.
- In clinical studies compared with the original vaccine, neutralising antibody levels induced by BA.1 bivalent vaccines were similar against the ancestral COVID-19 strain and higher against Omicron.
- The extent to which the higher antibody levels induced by the adapted vaccines will increase protection against COVID-19 variant disease is not known. It is expected that the higher antibody levels against BA.5 will afford some clinically meaningful benefit, especially for those at risk at this time when BA.5 is dominant.
- Current evidence indicates that the bivalent vaccines will offer protection similar to or better than the original vaccines. It is expected that additional protection against variant disease may be provided. As with all vaccines, vaccination with bivalent COVID-19 vaccines may not protect all recipients.
- While bivalent mRNA booster vaccines may offer some advantage compared with the original vaccine, timely booster vaccination is more important than which vaccine is administered.
- A booster dose of original mRNA COVID-19 vaccine offers significant protection against hospitalisation, severe illness and death. In the event of bivalent vaccine supply constraints the original vaccines should be offered to those for whom a booster is recommended.

## 2. INTRODUCTION

COVID-19 vaccines based on the spike protein of the ancestral strain are effective in reducing the risk of hospitalisations, severe COVID-19 disease and death. Booster COVID-19 vaccination results in a high level of protection against severe disease that is maintained for 4 months or longer. Protection following vaccination and infection (hybrid immunity) is even more durable. Waning protection gradually ensues with risk for hospitalisation and severe disease higher in those aged 65 years and older, those with immunocompromise and those with underlying medical conditions.

Waning protection is the result of a gradual slow decline in immunity over time coupled with the emergence of immune evasive variants such as Omicron. To sustain protection for those at risk of severe disease booster vaccinations have been recommended.

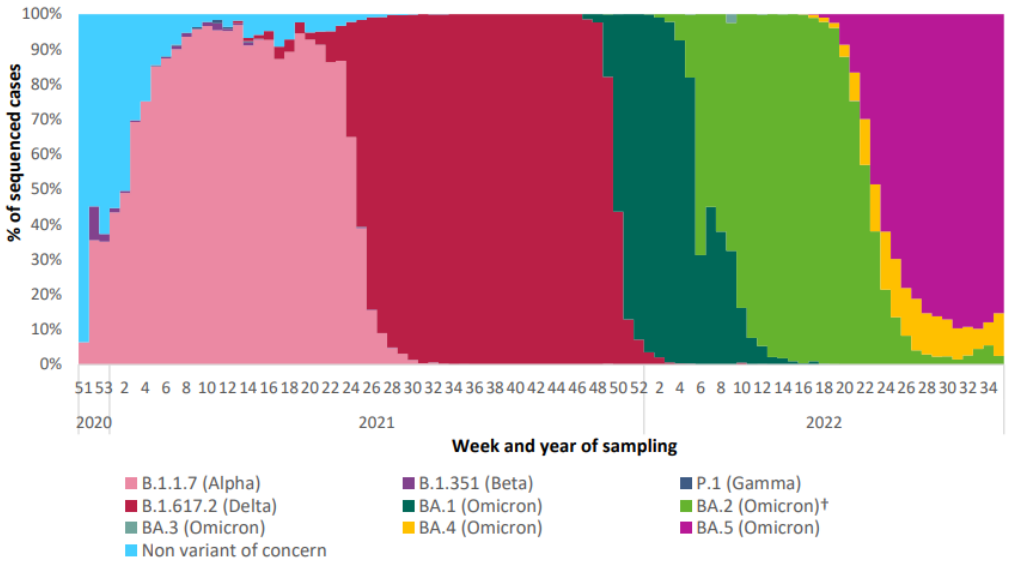
In an effort to improve effectiveness and increase protection against variants, new vaccines have been developed. These adapted vaccines are similar to the original mRNA COVID-19 vaccines. They include mRNA based both on the spike protein of the ancestral virus, as in the original vaccine, and mRNA based on the spike protein of either Omicron BA.1 or Omicron BA.4-5. These modifications have been likened to the routine adjustments to the annual influenza vaccines to counter the changeable nature of the influenza virus. They are adapted to better match circulating variants and are expected to give broader protection against different variants, although their impact on future variants is unpredictable.

The EMA has recently authorised new adapted bivalent vaccines for use as booster vaccination in those aged 12 years and older. This paper reviews the evidence base to inform the recommendations for the use of the new adapted bivalent COVID-19 vaccines in Ireland.

## 3. COVID-19 EPIDEMIOLOGY IN IRELAND

Since the onset of the COVID-19 pandemic SARS-CoV-2 has evolved to produce several variants of concern (VOC). Five VOCs have been identified in Ireland to date; B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), B.1.617.2 (Delta) and most recently B.1.1.529 (Omicron). (Figure 1)

Figure 1. Percentage of sequenced specimens, by variant of concern or interest, specimen collection dates from 13 December 2020 to 30 August 2022. Source: HPSC.[1]



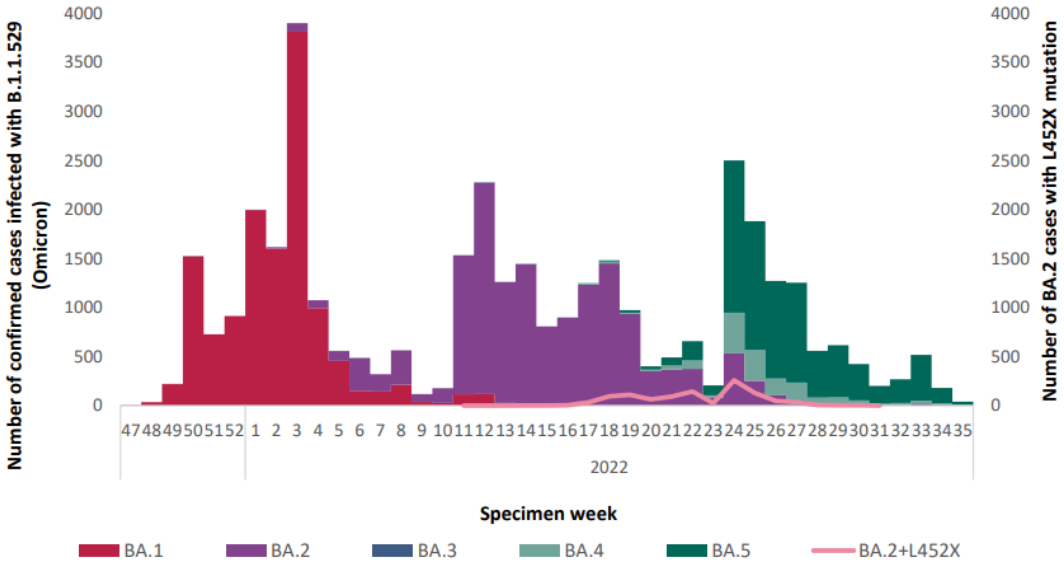

## The Omicron lineage

Omicron strains have more mutations than previous VOCs. Omicron has been notable for increased transmissibility. With more than 30 mutations in the spike protein they have enhanced ability to escape from neutralising antibodies elicited either by vaccination or prior infection. This has contributed to the waves of infection in populations with high vaccination coverage.

Omicron is associated with decreased disease severity compared to previous variants. This may be due to a combination of factors including lower virulence, and vaccine and infection induced immunity.

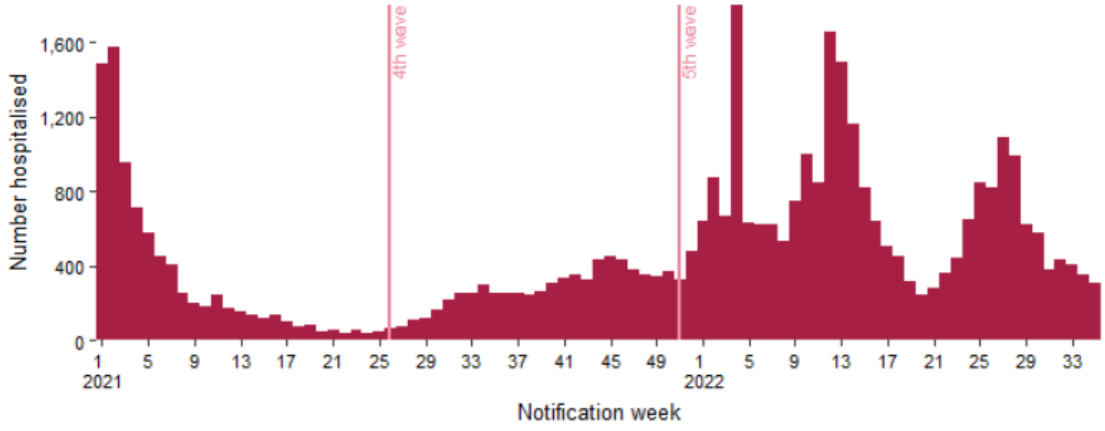
In November 2021 the first case of the Omicron variant was reported in Ireland. Since then more than 38,000 cases of Omicron have been detected. Five sublineages of Omicron (BA.1-5) have been identified, BA.1 dominated in early 2022 followed by BA.2 in March and April and the most recent upsurge has been caused by BA.4 and BA.5 strains since June 2022. (Figure 2)

Figure 2. Confirmed Omicron cases identified in Ireland to 5 September 2022, by specimen week and Omicron lineage. Source: HPSC.[1]



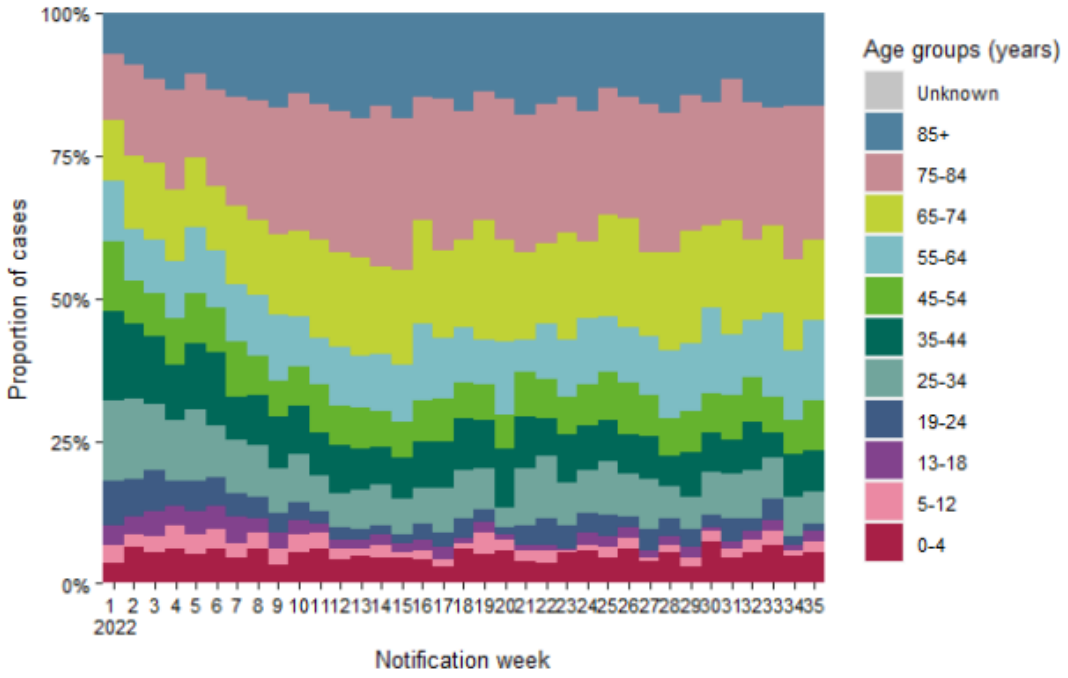

Between 21-27 August 2022 there were 1,822 new confirmed COVID-19 cases in Ireland, a decrease of 11.7% compared to the previous week. (Figure 3)

Figure 3. Hospitalisations among confirmed COVID-19 cases notified in Ireland between 1 January 2021 and 3 September 2022. Source: HPSC.[2]




Of those, 332 were hospitalised, of whom most were aged 65 years and older. (Figure 4)

Figure 4: Age distribution of hospitalised confirmed COVID-19 cases notified on CIDR in Ireland between 1 January 2022 and 3 September 2022. Source: HPSC.[2]




The incidence of respiratory viruses increases in autumn and winter months. It is anticipated that there will also be a surge in COVID-19 infections. This will likely coincide with an increase in circulating levels of influenza and other respiratory viruses with significant clinical impact and will increase the burden on the healthcare service.

## 4. COVID-19 VACCINATION COVERAGE IN IRELAND

In Ireland as of 4 September 2022, 99% of those aged 18 years and older had completed their primary COVID-19 vaccination course and 72% of those aged 12 years and older had received a first booster. The uptake rate of subsequent booster doses has declined with only 66% of those aged 65 years and older having received a second booster. (Table 1)[3]

Table 1: COVID-19 vaccination uptake of eligible population by age group and vaccination status. Source: Adapted from HPSC.[3]

| Age group | Primary course completed | 1st booster dose received | 2nd booster dose received |
|---|---|---|---|
| 65+ years | 99.9% | 99.9% | 66.3% |
| 18+ years | 99.1% | 77.3% | 16.4% |
| 12+ years | 96.8% | 72.3% | 14.8% |
| 12-17 years | 74.8% | 26.6% | <1% |
| 5-11 years | 24.2% | <1% | n/a |

## 5. VACCINE EFFECTIVENESS

Emergence of the Omicron lineage has resulted in a reduction of vaccine effectiveness against infection with protection waning rapidly over time.[4,5] However, current mRNA vaccines provide high and more durable protection against hospitalisation, severe disease and death.[6-8] Protection following vaccination and infection (hybrid immunity) is even more long lasting than following either alone.[9] However, waning of protection gradually ensues with the risk of hospitalisation and severe disease higher in those aged 65 years and older, those with immunocompromise and those with underlying medical conditions with a higher risk of severe COVID-19.[8]

While a booster of any authorised COVID-19 vaccine provides short term protection against infection, it will provide more durable protection against hospitalisation and severe disease including that caused by Omicron variants.[8] Booster vaccination results in a high level of protection against severe disease that is maintained for 4 months or longer.[6,8] Booster vaccination also restores protection following infection. A booster can be administered after a minimum interval of three months following vaccination or infection, however a longer interval between doses increases immunogenicity.[10-14] Thus, booster dose timing is a balance between the need to optimise immunogenicity and the risk incurred by delaying the booster dose. Booster vaccines following a primary series increases protection against Omicron COVID-19 disease.[7] Timing of boosters with respect to prior vaccination or infection, regardless of specific vaccine used, is an important factor in sustaining protection, particularly for those at risk of more severe disease.

Timing of booster vaccination to optimise protection when levels of circulating virus are high and to mitigate the impact of rising case numbers on the health care service is an important additional consideration. Vaccination prior to or at the beginning of autumn/winter is desirable.

## 6. ADAPTED BIVALENT VACCINES

mRNA bivalent COVID-19 vaccines have been authorised by the European Medicines Agency (EMA) for use as booster vaccines in those aged 12 years and older.

These vaccines are adapted to better match circulating variants and are expected to give broader protection against different variants, although their impact on future variants is unpredictable. The rapid development of bivalent COVID-19 vaccines reflects the ability to quickly adapt mRNA vaccines to meet a current need.

They are very similar to the original mRNA COVID-19 vaccines. They include mRNA based both on the spike protein of the ancestral virus, as in the original vaccine, and mRNA based on the spike protein of either Omicron BA.1 or, noting that the spike protein on BA.4 and BA.5 is identical, Omicron BA.4-5. These modifications have been likened to the routine adjustments to the annual influenza vaccines to counter the changeable nature of the influenza virus.

Limited clinical trial data on BA.1 bivalent vaccines show local and systemic reactogenicity profiles similar to those associated with the original vaccines. Long term follow up data are not available. The limited numbers of participants in the studies means that very rare side effects cannot be excluded. Myocarditis and pericarditis are recognised as very rare risks of mRNA vaccines, reported predominantly in males aged under 30 years and after the second primary dose. The risk is lower following booster doses.

In authorising the BA.4-5 bivalent vaccine, the EMA based their recommendations on safety of the bivalent BA.1 mRNA COVID-19 vaccine and a large body of cumulative data on original mRNA vaccines that are very similar to the adapted vaccines and whose safety profile is well established. [15,16]

Higher antibody levels against Omicron variants can be induced by adapted bivalent vaccines.[17,18] Protection against COVID-19 correlates with the level of neutralising antibodies present. While a defined cut-off level is not known, higher antibody levels are associated with increased protection. The extent to which the higher antibody levels will increase protection is not known. Current evidence on immunogenicity and safety of the bivalent mRNA vaccines is presented below.

## Spikevax Bivalent Original/Omicron BA.1

Spikevax bivalent Original/Omicron BA.1 vaccine contains 50 micrograms (mcg) of mRNA (25mcg based on the ancestral strain and 25mcg based on Omicron BA.1). This is the same overall quantity of mRNA as in the Spikevax Original booster dose.

The immunogenicity of a booster dose of the Spikevax bivalent Original/Omicron BA.1 vaccine was compared to a booster dose the original vaccine in healthy adults (mean age 57 years) who had already received three doses of the original vaccine. The vaccines were given at a median of 4.5 (range 2.9-13.4) months after previous vaccination. One month following booster vaccination, the bivalent BA.1 containing booster elicited higher BA.1 neutralising antibodies than the original vaccine, both in those with and without prior SARS-CoV-2 infection. (Figure 5)

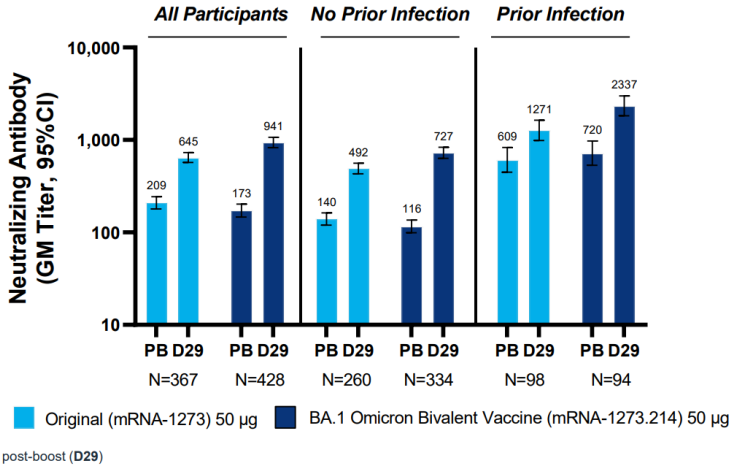
Neutralising antibodies against the ancestral strain were also found to be slightly higher in those who received the bivalent vaccine compared to the original vaccine, meeting non inferiority criteria. (Figure 5)

Figure 5: Primary immunogenicity analysis of ancestral SARS-CoV-2 and Omicron BA.1 after Spikevax bivalent Omicron/Omicron BA.1 and Original Spikevax administered as a second booster. Source: Chalkias et al.[17]

| | Ancestral SARS-CoV-2 (D614G) | | Omicron | |
|---|---|---|---|---|
| | 50 µg mRNA-1273.214 Booster Dose | 50 ug mRNA-1273 Booster Dose | 50 µg mRNA-1273.214 Booster Dose | 50 ug mRNA-1273 Booster Dose |
| | N=334 | N=260 | N=334 | N=260 |
| Pre-booster n† | 334 | 260 | 334 | 260 |
| Observed GMT (95% CI)§ | 1266.7 (1120.2-1432.5) | 1521.0 (1352.8-1710.2) | 298.1 (258.8-343.5) | 332.0 (282.0-390.9) |
| Day 29, n† | 334 | 260 | 334 | 260 |
| Observed GMT (95% CI)§ | 5977.3 (5321.9-6713.3) | 5649.3 (5056.8-6311.2) | 2372.4 (2070.6-2718.2) | 1473.5 (1270.8-1708.4) |
| GMFR (95% CI)§ | 4.7 (4.4-5.1) | 3.7 (3.4-4.0) | 8.0 (7.2-8.8) | 4.4 (4.0-5.0) |
| Estimated GMT (95% CI)¶ | 6422.3 (5990.1-6885.7) | 5286.6 (4887.1-5718.9) | 2479.9 (2264.5-2715.8) | 1421.2 (1283.0-1574.4) |
| GMR (97.5% CI)¶‖ | 1.22 (1.08, 1.37) | | 1.75 (1.49-2.04) ¶¶ | |
| Day 29 SRR, n/N1 %‡ | 334/334, 100 | 260/260-100 | 333/333, 100 | 256/258, 99.2 |
| (95% CI) | (98.9-100) | (98.6-100) | (98.9-100) | (97.2-99.9) |
| Difference (97.5% CI)‖†† | 0 | | 1.5 (-1.1- 4.0) | |

While the bivalent vaccine effectively boosted levels of neutralising antibody to BA.4-5 by a 5.4 fold rise compared to pre booster levels, the antibody titres were lower than against Omicron BA.1. (Figure 6)

Figure 6. Omicron BA.4-5 neutralising antibody titres following Spikevax bivalent Omicron/Omicron BA.1 and Original Spikevax administered as a second booster. Source: ACIP, 1-2 September 2022.[19]




Pre-booster (**PB**), Day 29 post-boost (**D29**)

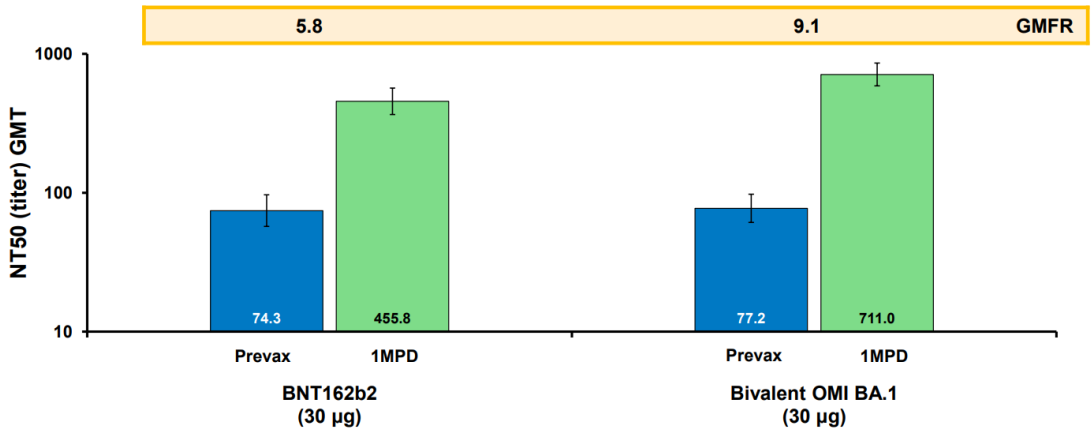
Spikevax bivalent Original/Omicron BA.1 was found to have similar reactogenicity and safety profiles to the original Spikevax. The most commonly reported symptoms were mild to moderate injection site pain, fatigue, headache, myalgia and arthralgia. No serious adverse events related to the vaccine were reported in either group, specifically no myocarditis, pericarditis or death. However, it should be noted that the study was not powered to detect rare events with only 437 participants receiving the new bivalent vaccine.[17,20]

An independent randomised controlled trial, the COVAIL trial, reported the immunogenicity of different vaccine combinations of the original (prototype) and a variety of adapted monovalent vaccines administered at separate sites. The combination of the Omicron BA.1 adapted vaccine and Spikevax gave comparable antibody responses to those of the original vaccine for all variants except for Omicron BA.1 for which they were superior.[21]

## Comirnaty original/ Omicron BA.1 bivalent vaccine

Comirnaty Original/Omicron BA.1 contains 15mcg of mRNA based on the ancestral strain and 15mcg of mRNA based on Omicron BA.1. A phase 3 clinical trial included healthy adults aged over 55 years who had received three doses of the original vaccine (Comirnaty). Participants received a booster dose of either Comirnaty or Comirnaty Original/Omicron BA.1 bivalent vaccine (n=305 per group). The median interval between third and fourth doses was 6.3 (range 4.7-12.9) months. Omicron BA.1 neutralising antibody responses were 1.56 fold higher in Comirnaty Original/Omicron BA.1 bivalent vaccine recipients than in those who received the original vaccine. (Figure 7)[18]

Figure 7. Omicron BA.1 neutralizing antibody titres following Comirnaty Original (BNT162b2)/ Omicron BA.1 bivalent vaccine in those aged over 55 years without evidence of prior infection. Source: ACIP, 1-2 September 2022.[18]




Ancestral strain neutralising antibody titres were comparable for bivalent and original vaccines meeting non-inferiority criteria. The bivalent vaccine was also found to produce higher BA.4-5

neutralising antibodies however titres were approximately 3-fold lower than BA.1 antibody titres.[18]

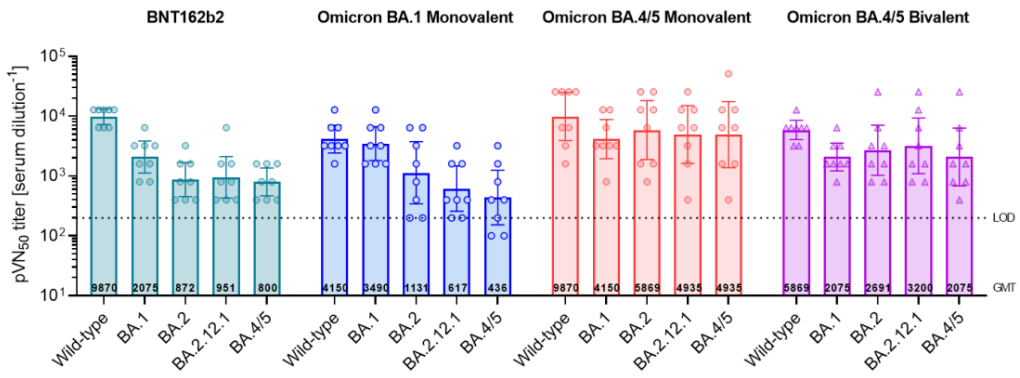
The reactogenicity and safety profile of Comirnaty Original/Omicron BA.1 was similar to that of Original Comirnaty in those aged over 55 years. The most frequent adverse reactions were injection site pain, fatigue, headache and myalgia. No new adverse reactions were identified. This study was not powered to capture rare events. In authorising Comirnaty Original/Omicron BA.1 the EMA extrapolated safety data in those aged 18-55 years from clinical trial where 315 adults aged 18-55 years received the Omicron BA.1 30mcg monovalent vaccine. Reactogenicity and safety profiles again were similar to the Original Comirnaty. No serious adverse events were noted in either trial.[22]

## Comirnaty Original/ Omicron BA.4-5

In authorising the BA.4-5 bivalent vaccine, Comirnaty Original/Omicron BA.4-5, the EMA based their recommendations on safety of the bivalent BA.1 mRNA COVID-19 vaccine and large body of cumulative data on original mRNA vaccines that are very similar and whose safety profile is well established. To date reactogenicity and safety profiles of all adapted versions of Comirnaty (Beta and Omicron BA.1) have been similar. The change in mRNA sequence in Comirnaty Original/Omicron BA.4-5 is not expected to result in a change in safety or side effect profile. In authorising the BA.4-5 bivalent vaccine, the EMA based their recommendations on safety of the bivalent BA.1 mRNA COVID-19 vaccine and large body of cumulative data on original mRNA vaccines that are very similar and whose safety profile is well established.[22]

In a preclinical immunogenicity study in mice, booster vaccination with Omicron BA.4-5 bivalent vaccine increased neutralisation responses to all Omicron variants, including a 2.6 fold increase in BA.4-5 antibody titre compared to that following a booster dose of Comirnaty Original (BNT162b2) vaccine. (Figure 8)[18]

Figure 8: Neutralisation responses to ancestral and omicron variants of SARS-CoV-2 in mice given a booster dose of either Original, Omicron BA1 monovalent, Omicron BA4/5 Monovalent or Omicron BA.4-5 Bivalent vaccines. Source: ACIP, September 1-2 2022.[18]



Clinical trials on Comirnaty Original/Omicron BA.4-5 are ongoing. Data are not yet available.

### Spikevax Bivalent Original/Omicron BA.4-5 vaccine

This vaccine has been authorised by the FDA and is now in clinical use in the US. Submission for assessment to the EMA is anticipated. Similar to Comirnaty Original/Omicron BA.4-5, available preclinical immunogenicity data for the Spikevax Bivalent Original/Omicron BA.4-5 vaccine show enhanced BA.5 antibody responses following vaccination.[19]

### Bivalent vaccines and pregnancy

The COVID-19 bivalent vaccines are approved for use in pregnancy.[23] Differences between original mRNA vaccines and the new bivalent vaccines are confined to the spike protein sequence and there are no clinically meaningful differences in reactogenicity.

There are no specific data regarding use of COVID-19 bivalent vaccines during pregnancy. However, a large amount of observational data from pregnant women vaccinated with initially approved vaccines during the second and third trimester have not shown an increase in adverse pregnancy outcomes. While data on pregnancy outcomes following vaccination during the first trimester are presently limited, no increased risk for miscarriage has been seen. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/fetal development, delivery, or post-natal development. Since differences between products are confined to the spike protein sequence, and there are no clinically meaningful differences in reactogenicity, bivalent vaccines can be used in pregnancy.[20,22]

### Coadministration with influenza vaccine

Concomitant administration of Omicron adapted bivalent vaccines with other vaccines has not been studied. Data are available on coadministration of influenza vaccines with original mRNA COVID-19 vaccines. Coadministration is associated with a small increase in mild side effects, such as injection site pain.[24,25] No serious safety concerns or immune interference have been identified to date.[24,25] Concomitant administration of bivalent booster vaccination with influenza vaccination will facilitate timely vaccine roll out. Concomitant administration may enhance uptake of COVID-19 boosters.

## 7. INTERNATIONAL POSITIONS

| Region | Approved bivalent vaccines as of 14 September 2022 (Date of approval) |
|---|---|
| EU/EMA | Spikevax bivalent Original/Omicron BA.1 (1 September) |
| | Comirnaty Original/Omicron BA.4-5 (12 September) |
| UK | Spikevax bivalent Original/Omicron BA.1 (15 August) |
| Switzerland | Spikevax bivalent Original/Omicron BA.1 (29 August) |
| Australia | Spikevax bivalent Original/Omicron BA.1 (31 August) |
| US | Spikevax bivalent Original/Omicron BA.4-5 (31 August)<br>Comirnaty Original/Omicron BA.4-5 (31 August) |
| Canada | Spikevax bivalent Original/Omicron BA.1 (1 September) |

| Region | Recommendations for bivalent vaccine use in those eligible for a booster dose |
|---|---|
| UK (JCVI)[26] | • Adults aged 18 years and older including pregnant women<br>• Those aged 12-17 years including pregnant women (off label use) |
| Switzerland[27] | • Those aged 18 years and older |
| Belgium | • Those aged 18 years and older |
| Australia (ATAGI)[28] | • Those aged 18 years and older |
| US (FDA)[29] | • Those aged 12 years and older including pregnant women |
| Canada (NACI)[30,31] | • Adults aged 18 years and over including pregnant women<br>• Those aged 12-17 years with risk factors for severe COVID-19 including pregnant women |

## RECOMMENDATIONS

1. Efforts to increase primary and booster vaccination uptake remain a public health priority. Original mRNA vaccines (Comirnaty and Spikevax) are the recommended vaccines for the primary vaccination course.

2. Those who are due booster vaccination should receive an mRNA COVID-19 vaccine. Timely booster vaccination, regardless of the vaccine used, is the most important factor in sustaining protection, particularly for those at risk of more severe disease.

3. Authorised bivalent mRNA vaccines are preferentially recommended for all those aged 12 years and older eligible for a booster vaccination.

4. An interval of four to six months is recommended from the time of the last COVID-19 vaccine or confirmed SARS-COV-2 infection. In exceptional circumstances an interval of three months may be used (e.g., in a person scheduled to commence chemotherapy). Giving booster vaccination just before or at the beginning of high viral circulation (e.g., autumn/winter) is desirable.

5. The bivalent mRNA booster vaccines should be given as follows:
   a) Bivalent BA.1 vaccines
      - aged 12-29 years: Comirnaty Original/ Omicron BA.1 (0.3ml/30 mcg)
      - aged 30 years and older: Comirnaty Original/ Omicron BA.1 (0.3ml/30 mcg) or Spikevax bivalent Original/Omicron BA.1 (0.5ml/50 mcg)

   b) Comirnaty Original/ Omicron BA.4-5 vaccine
      - aged 12 years and older: Comirnaty Original/ Omicron BA.4-5 (0.3ml/30 mcg).

6. Booster vaccination may be given at the same time as influenza vaccine, with one vaccine administered in each arm.

7. If bivalent vaccine supplies are limited, priority should be given to the following groups to maintain high levels of immunity in those most at risk of severe disease:
   - those aged 65 years and older
   - those aged 12 years and older with immunocompromise associated with a sub optimal response to vaccines at the time of their primary or booster vaccination
   - those with underlying medical conditions with a higher risk of severe COVID-19
   - those who are pregnant, at 16 weeks gestation or later, and who have not received a booster vaccine in the current pregnancy.

8. Those for whom a bivalent mRNA vaccine is contraindicated or declined should be offered an alternative vaccine.

These recommendations reflect a dynamic vaccination programme. Scientific evidence is emerging and being refined. Recommendations may be updated when more information becomes available. There is significant uncertainty regarding the emergence and nature of future variants, which makes it difficult to predict with certainty the effectiveness of available vaccines.

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