Evidence Summary on *COVID-19 mRNA Vaccine (Nucleoside Modified)* for children 6 to 11 years old

Service Line	Evidence Summary
Publication Date	22 July 2022
Summary Length	63 Pages
Prepared by	Health Technology Assessment Council Health Technology Assessment Division
Contact details	hta@doh.gov.ph

Background

On 07 May 2021, the Philippine FDA released the initial Emergency Use Authorization (EUA) for the use of *COVID-19 mRNA Vaccine (Nucleoside Modified) [Spikevax]* in adults ages 18 years and older. The target age group of the vaccine was eventually expanded to include individuals aged 12 to 17 years old on 28 December 2021. On 20 March 2022, the Philippine Food and Drug Administration (FDA) further updated its Emergency Use Authorization (EUA) for the use of *Moderna* to include children ages 6-11 years old. According to the Philippine FDA, the use of *Moderna* will be given to children aged 6 to 11 years old as a half dose, 28 days apart (i.e., 2 doses of 0.25 mL per dose, 28 days apart compared to the adult and adolescent dose of 2 doses of 0.5 mL per dose).

On 25 January 2021, the World Health Organization (WHO) issued their interim recommendations for the use of *Moderna* among individuals 18 years of age and above. On 19 November 2021, the recommendation was updated to include children aged 12 to 17 years old. Further, on 23 February 2022, the WHO updated their interim recommendations to reflect new evidence on vaccine effectiveness, booster dose, and heterologous schedules. However, as of this writing, the WHO does not recommend *Moderna* for children ages 6 to 11 years old.

On the other hand, *Moderna* has been granted EUA for use in children aged 6-11 years old in 10 other countries (US, Switzerland, Colombia, Peru, Taiwan, Saudi Arabia, Thailand, Canada, Australia, and Vietnam). The European Medicines Agency also recommended this vaccine for the aforementioned age group. The UK Medicines and Healthcare products Regulatory Agency (MHRA) also approved the use of *Moderna* for children aged 6 to 11 years old. However, the UK Joint Committee on Vaccination and Immunisation (JCVI) has not released its recommendation on the use of this vaccine for this age group.

Table 1.1 Characteristics of *Moderna*

Trade name	COVID-19 mRNA-1273 (nucleoside modified) [SPIKEVAX]
Other name	COVID-19 Vaccine *Moderna*
Manufacturer/s	*Moderna* Biotech Spain S.L.
Vaccine platform	mRNA Vaccine (nucleoside modified)
Dose strength and administration	● Individuals aged 12 years and older : 2 doses of 100 mcg dispersion for injection ● Children aged 6 to 11 years old: 2 doses of 50 mcg dispersion for injection ● Severely immunocompromised aged 12 years and older: 3 doses of 100 mcg dispersion for injection
Route of administration	Intramuscular (IM)
Drug delivery system	Multi-dose vial (MDV) containing 10 doses of 0.5 mL per vial or a maximum of 20 doses of 0.25 mL each (Half dose of the same formulation as adults)
Storage condition	● Unopened vial: Store at -25°C to -15°C (Shelf life: 9 months) ● Thawed, unopened vial: Store at 2°C to 8°C. Protect from light for a maximum of 30 days. ● After removal from refrigerated conditions: Store at 8°C to 25°C upto 24 hours
Mechanism of action	The nucleoside-modified mRNA in the COVID-19 Vaccine *Moderna* is formulated in lipid particles, which enable delivery of the nucleoside-modified mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.
Contraindications	Do not administer the COVID-19 Vaccine *Moderna* to individuals with a known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the COVID-19 Vaccine *Moderna*.
PHL EUA status	Updated on 20 May 2022 to expand the indication to individuals aged 6 to 11 years old
PHL FDA EUA indication	For active immunization for the prevention of COVID-19 caused by SARS-CoV-2 in individuals 6 years of age and older

The product information/fact sheet is available here.

Pursuant to the role of the Health Technology Assessment Council (HTAC) which is to develop recommendations in the selection and financing of COVID-19 vaccines for the COVID-19 Vaccine Implementation for 2022, this assessment follows the HTAC evaluation framework to assess COVID-19 vaccines using the following criteria: (1) responsiveness to magnitude and severity; (2) clinical efficacy and safety; (3) affordability, viability and feasibility; (4) household financial impact; (5) social impact; and (6) responsiveness to equity.

Policy Question

The HTAC aims to answer the policy question:

Should the DOH finance ***Moderna as primary series vaccines for the pediatric population ages 6 - 11 years old*** as part of the 2022 COVID-19 Vaccination Program to reduce COVID-19 cases, severe infection, and deaths?

Recommendations *(as of 05 July 2022)*

The HTAC reviewed the evidence on the use of *Moderna* as primary series for the pediatric population ages 6 to 11 years based on the HTAC criteria of (a) responsiveness to disease magnitude and severity, (b) clinical efficacy and safety, (c) affordability, viability, and feasibility, (d) household financial impact, (e) social impact, and, (f) responsiveness to equity.

The overall burden of COVID-19 contributed by children aged 6 to 11 years old cannot be determined as children experience fewer and milder symptoms and asymptomatic presentations leading to less probability of being tested and more unreported cases (WHO, 2021). Evidence for the clinical efficacy of Moderna in children is inconclusive but it can be inferred that this vaccine has a high potential for protection for this population based on immunobridging data young adults ages 18 to 25 years old. Moderna is safe for children 6 to 11 years old based on short term data. Long term safety data is still lacking.

HTAC recognizes that the potential for protection of children will have an impact in terms of supporting the attainment of occupations of children which include social learning achieved through peer interaction. This could also contribute to the improvement of the quality of life within the households when caregivers of children are relieved of the anxiety of dealing with the consequences of COVID-19 infection and sequelae.

However, the HTAC is not recommending additional procurement of Moderna for the implementation of the current primary vaccination series for children aged 6 to 11 years old because of its higher cost relative to a similar product in the market. If existing supplies will be used for the implementation of the primary vaccination series for children aged 6 to 11 years old, then the use of Moderna can be justified.

With regard to the legal requirement of a WHO recommendation for HTAC to provide recommendation to the DOH, the WHO advised HTAD on 04 July 2022 via electronic mail that “countries may also refer the decisions from advanced levels of public health authorities and regulatory authorities.” Without the explicit WHO recommendation on Moderna as primary series for the pediatric population ages 6 to 11 years**, the HTAC cannot release its recommendation** based on the Republic Act no. 11525 otherwise known as the “COVID-19 Vaccination Program Act of 2021.”

Finally, these recommendations are interim and HTAC is actively on the watch for evidence as it is rapidly evolving. We thank you for the opportunity to be of assistance to the Department of Health.

Details of the body of evidence considered by HTAC in assessing *Moderna* as primary series for the pediatric population ages 6 to 11 years can be found below:

Criteria	HTAC Judgment *(as of 05 July 2022)*
What is the magnitude and severity of COVID-19 in children ages 6 to 17 years old? *Is COVID-19 a public health priority?*	The burden of COVID-19 contributed by children aged 6 to 11 years old cannot be ascertained as children experience milder symptoms and asymptomatic presentations leading to less probability of being tested and more unreported cases (WHO, 2021). Local evidence (SALVACION registry) shows that of the 191 children aged 6 to 11 years old who were hospitalized, 53.93% had comorbidities while 46.07% did not have comorbidities. DOH data show that CFR in children ages 6 to 11 years old (6-11 yo: 0.15%; vs <6 yo: 0.67%; 12-17 yo: 0.18%; 18 to 59 yo: 0.78%; >60 yo: 7.53%) is the lowest among age groups. This is similar with US data showing that CFR and ICU admissions in children aged 0-4 years old and adolescents aged 12-17 years old are likely greater compared to that of children aged 5 to 11 years old (US CDC, 2022). Currently, the effect of variants on hospitalization in this age group cannot be established due to limited sequencing capacity in the country. Internationally, studies from the US and UK show varying results. In addition, based on US data, the incidence of MIS-C is highest in the 5-11 age group compared to the other age groups. This is similar to the local data where 12 out of the 26 MIS-C cases (46.15%) reported, were from the 6 to 11 year age group (SALVACION Registry, as of 20 June 2022). Lastly, in terms of post COVID-19 conditions, US data shows that this condition appears to be less common in children than in adults. There are no local studies on POST COVID-19 conditions.
Is Moderna safe and efficacious for the pediatric population ages 6 to 11 years old? *Can Moderna significantly reduce the magnitude and severity of COVID-19 in children ages 6 to 11 years old?*	**Yes,** short-term safety of *Moderna* in children 6-11 years old is acceptable. No case of myocarditis was reported in the clinical trial. Further follow-up data is needed to establish longer-term safety. Currently, there is inconclusive evidence on the clinical efficacy of a 2-dose primary series of *Moderna* (50 mcg per dose) in children aged 6 to 11 years old. However, on the basis of the same Phase II/III trial, the efficacy of 2 doses of 50 mcg of *Moderna* in children can be inferred from successful immunobridging data to young adults ages 18 to 25 years old who had received the 100 mcg dose in the Phase III COVE trial, which showed high efficacy (Creech et al.). Meanwhile, in terms of protection against variants of concerns (VoCs), the efficacy and effectiveness of *Moderna* in children 6 to 11 years old against VoCs cannot be assessed due to lack of studies measuring clinical outcomes. However, immunogenicity outcomes from one study showed that children aged 6 to 11 years old had higher antibody titers against Omicron compared to adults (Girard et al.). In terms of immunogenicity against the Delta variant, data from the Phase II/III trial showed a similar immune response to Delta compared to adults (Creech et al.).

Is Moderna affordable and feasible to use in a national immunization program for the pediatric population ages 6 to 11 years old?	**Yes,** primary series vaccination in children aged 6 to 11 years old using *Moderna* is considered affordable. The HTAC is not recommending procurement of *Moderna* in the implementation of the primary vaccination series for children aged 6 to 11 years old because of its higher cost relative to a similar product in the market. However, at this time that the existing supplies will be used for the implementation of the primary vaccination series for children aged 6 to 11 years old, there will be no additional cost to the government if *Moderna* is used.
Does Moderna reduce out-of-pocket (OOP) expenses of households due to COVID-19?	**Yes**, *Moderna* has the potential to reduce out-of-pocket expenses due to averted costs of isolation and treatment of mild, moderate, and severe COVID-19 in the pediatric population ages 6 to 11 years old. Other non-medical costs, productivity loss of the parents/ caregiver of these children, and treatment cost of other family members within the household who will likely contract COVID-19 further increase the potential of the vaccine to reduce out-of-pocket expenses of households due to COVID-19.
Does Moderna possess the characteristics that are desired by key stakeholders?	**Yes,** on the basis of short-term outcomes, *Moderna* possesses most of the characteristics desired by key stakeholders for its use among children aged 6 to 11 years old. Given that there are no local studies to determine acceptability of vaccination among children 6 to 11 years old, HTAC can only recognize the social impact of vaccination in this age group in terms of supporting the attainment of occupations of children which include social learning achieved through peer interaction. This could also contribute to the improvement of the quality of life within the households when caregivers of children are relieved of the anxiety of dealing with the consequences of COVID-19 infection and sequelae.
Does Moderna reduce or not further add to existing inequities in the health system?	Pediatric vaccination poses inherent challenges because of pre-existing inequities in the healthcare system. These include inequitable access to information and capacity to diagnose co-morbidities in children (e.g., pediatric specialists), inaccessibility to vaccination sites and inadequate logistical capacity, and the general deficiency in infrastructure, transportation modalities, and health human resources across the different areas in the country. These challenges can be translated to opportunities to improve the vaccination coverage of priority groups (e.g., encouraging unvaccinated parents and/or guardians accompanying pediatric vaccinees to get vaccinated as well, improvement of information, education, and communication (IEC) campaigns, and increasing vaccination sites by deploying mobile vaccination teams and utilization of established public-private partnerships with malls, pharmacies, churches, gyms and other establishments as vaccination sites, among others). To ensure the success of the implementation of COVID-19 vaccination for children ages 6 to 11 years old, emphasize must be placed on the importance of free and prior informed consent, supporting the autonomy of parents, guardians, and the pediatric population towards vaccination, and ensuring that IEC materials are accessible and comprehensible (i.e., translated into the local language of the target population) Given that *Moderna* can be stored in 2-8 degrees Celsius for 30 days which is available in most RHUs, this does not aggravate health inequities. However, in terms of long term storage, *Moderna* still requires a low storage temperature, which might pose difficulties in distribution from warehouse to RHUs.

In the development of this recommendation, the HTA Council has appraised and considered the evidence review of the International Vaccine Access Center (IVAC) of the Johns Hopkins Bloomberg School of Public Health and World Health Organization review, COVID-NMA living review and review of global and local data pertaining to the epidemiology of 6 to 11 year-old children with COVID-19.

The HTA Council further emphasizes the need to enforce strict conditions for the emergency use of health products to safeguard against eventualities:

- Transparency and accountability in the processes of allowing emergency use of health products, especially for the public health response;
- Continuous collection of safety and effectiveness data in the context of clinical trials and actual use in the real world;
- Close monitoring of recipients and safeguards for expected and unexpected adverse events that may arise from the use of health products under an EUA;
- National coordination of the emergency use under the Philippine FDA and the DOH;
- Cascading of complete information to vaccinees and healthcare providers on potential risks and benefits, and securing of informed consent with regard to receiving the intervention; and

Finally, the HTAC recommends the conduct of research to address the current gaps in evidence with regard to the use of *Moderna*:

- Real-world effectiveness in the Philippine context particularly focused on the following knowledge gaps:

    - Effectiveness in reducing COVID-19 cases, hospitalizations and deaths, and preventing outbreaks and transmission of disease across the population
    - Effectiveness in reducing asymptomatic infection
    - Duration of protection
    - Impact of the timing and number of doses received
    - Probable need for booster dosing
    - Differences in the effectiveness of the vaccine among special populations (i.e., individuals with comorbidities, immunocompromised patients)
    - Effectiveness of the vaccine against emerging SARS-CoV-2 viral strains
- Continuous safety surveillance and monitoring of all adverse events especially severe allergic reactions, Bell's palsy, serious adverse events such as thrombosis thrombocytopenia syndrome (TTS), myocarditis and other adverse events of special interest (AESI) following vaccination
- Best practices, challenges, and barriers in implementation across different localities
- Monitoring of unexpected or additional costs associated with vaccine implementation.

Current Evidence on *Moderna COVID-19 Vaccine*

The table below summarizes the appraisal of available evidence on *Moderna* based on the HTAC evaluation framework.

In addition, the following appendices are provided for further details:

- Appendix 1: Trends in hospitalization in the Philippines, by age group
- Appendix 2A: Risk of Bias Assessment Methodology
- Appendix 2B: Risk of Bias Assessment Results by HTAC
- Appendix 3: GRADE Table
- Appendix 4: Costing Table

Table 1.2 Key Findings in the Current Evidence Considered for the HTAC Evaluation of *Moderna* for children aged 6 to 11 years old

<table>
<tr><th>Evaluation Criteria</th><th>Question</th><th>Current Evidence</th><th>HTAC specification</th></tr>
<tr><td colspan="4">CRITERION 1</td></tr>
<tr><td>1. Responsiveness to magnitude and severity</td><td>What is the magnitude and severity of COVID-19 in children ages 6 to 11 years old?

Is COVID-19 a public health priority?</td><td>
Local epidemiologic data on children ages 6 to 11 years old versus older age groups
In the pediatric population, the DOH Philippines recorded 261,990 COVID-19 cases in children (111,024 cases in 6-11 years old) and adolescents (150,966 cases in 12-17 years old) as of 18 June 2022. The case fatality rate (CFR) in children aged 6-11 (0.15%) is the lowest across different age groups CFR [below 6 years (0.67%), adolescents aged 12-17 (0.18%), and the adult population (18-59 years old: 0.78%; ≥ 60 years old: 7.53%].

In addition, children aged 6 to 11 years old with pulmonary disease, chronic kidney disease, liver disease, chronic obstructive pulmonary disease (COPD), and down syndrome have CFRs reported at around 79.41% to 100%. However, this is based on a limited number of cases as presented in Table 1.1. (as of 24 May 2022).

Table 1.1. Cases, deaths, and fatality rates per comorbidity in children aged 6 to 11 years old
<table>
<tr><th>Comorbidity</th><th>Total Cases</th><th>Deaths</th><th>CFR</th></tr>
<tr><td>Chronic Kidney Disease</td><td>7</td><td>7</td><td>100.00%</td></tr>
<tr><td>Chronic Obstructive Pulmonary Disease</td><td>1</td><td>1</td><td>100.00%</td></tr>
<tr><td>Down Syndrome</td><td>1</td><td>1</td><td>100.00%</td></tr>
<tr><td>Liver Disease</td><td>7</td><td>6</td><td>85.71%</td></tr>
<tr><td>Other Pulmonary Disease</td><td>68</td><td>54</td><td>79.41%</td></tr>
<tr><td>Other Cardiovascular and Cerebrovascular Disease</td><td>66</td><td>44</td><td>66.67%</td></tr>
<tr><td>Genito-urinary Disease</td><td>28</td><td>16</td><td>57.14%</td></tr>
<tr><td>Blood Disease</td><td>14</td><td>8</td><td>57.14%</td></tr>
<tr><td>Tuberculosis</td><td>16</td><td>8</td><td>50.00%</td></tr>
<tr><td>Obesity (BMI of 30 kg/m2 or higher)</td><td>2</td><td>1</td><td>50.00%</td></tr>
<tr><td>Immunodeficient State (HIV, HBV, HCV, on chemotherapy or steroid treatment, autoimmune disease</td><td>7</td><td>3</td><td>42.86%</td></tr>
</table>
</td><td>The magnitude and severity of the disease to the subpopulation is comparably high compared to the general population and other subpopulations.</td></tr>
</table>

Malignancy	44	17	38.64%
Diabetes Mellitus	13	1	7.69%
Hypertension	30	2	6.67%
Asthma	211	5	2.37%
Allergy	38	0	0.00%

Cumulative data from the DOH COVID-19 data drop (as of 18 June 2022) recorded a total of 3,692,746 cases of COVID-19 across all age groups. Of these, 3.33% (122,818) were hospitalized, 34.47% (1,273,039) were not hospitalized and 62.20% (2,296,889) had unknown admission status.

- Of the 122,818 confirmed COVID-19 hospitalized cases, patients aged 6 to 11 years old had the lowest proportion of hospitalization to the overall hospitalized cases at 1.64% among the pediatric age groups. Meanwhile, children less than 6 years old accounted for 3.01% and adolescents 12-17 years old accounted for 2.62% of hospitalizations. Majority of the confirmed hospitalized cases were adults ages 18 to 59 years old (62.95%) and the elderly (29.78%).
- Similarly, the plotted number of hospitalized cases over time from January 2021 to April 2022, disaggregated by age group showed that adults ages 18 to 59 years and the elderly ≥60 years were at higher risk for COVID-19 hospitalization compared to the younger age groups (i.e., <6 years, 6-11 years, 12-17 years). Trends of hospitalized cases over time, by age group are presented in Appendix 1.

However, note that according to the DOH Epidemiology Bureau, hospitalization data by age group may be underestimated due to limitations on the actual data collected in case information forms (CIF) and encoding of information to the online platform from hard copies of CIFs.

Evidence on risk of hospitalization, severe disease, MIS-C and death among children ages 6 -11 years old

The SALVACION REGISTRY had a total of 3,209 cases in children aged less than 18 years old with 689 cases (21.47%) from the 6 to 11 age group (as of 21 June 2022). In terms of severity, the majority of cases in the 6-11 age group were mild cases (45.86%), followed by asymptomatic (24.09%) and moderate cases (17.85%) while the remaining were severe (5.52%), critical (4.35%) and MIS-C (1.74%) cases. Meanwhile, 4 cases (0.58%) in the 6 to 11 age group had unknown severity. Of the 689 cases reported, 600 cases were hospitalized (87.08%) and 38 deaths occured (5.52%). Limitations of this registry include: (1) the registry is a voluntary, passive surveillance database, as such not all cases in children and adolescents are accounted for, and (2) cases reported may be confirmed or probable COVID-19 cases.

- In children who may have been hospitalized (n = 191) (i.e., moderate, severe, critical), 53.93% (103/191) had comorbidities while 46.07% (88/191) had no comorbidities. The following are the proportion of hospitalized cases with and without comorbidities out of the total hospitalized cases , by severity:

Severity	% of cases with comorbidities out of the total hospitalized (n/N)	% of cases without comorbidities out of the total hospitalized (n/N)
Moderate	47.15% (58/123)	52.84% (65/123)
Severe	63.16% (24/38)	36.84% (14/38)
Critical	70% (21/30)	30% (9/30)

- In terms of MIS-C, 12 out of the total 26 cases reported were among the 6 to 11 age group. Among these 12 cases in children ages 6 to 11 years old, only 2 cases had comorbidities (i.e., obesity) while the remaining 10 had no comorbidities. It is important to note, however, that the reports of MIS-C were most likely underestimated compared to the actual cases.

		- Among the 38 deaths recorded in patients 6 to 11 years old in the SALVACION registry:
		  - 22 had critical disease (73.33% of 30 critical cases)
		  - 8 had severe disease (21.05% of 38 severe cases)
		  - 1had MIS-C (8.33% of 12 MIS-C cases)
		  - 3 had moderate disease (2.44% of 123 moderate cases)
		  - 4 had mild disease (1.27% of 316 mild cases)
		  There was no information on the probable cause of death one the 3 moderate cases and 1 mild case who progressed to death. Meanwhile, the 3 other mild cases which progressed to death were due to septic shock secondary to ventriculitis, severe traumatic brain injury secondary to vehicular accident, and acute respiratory failure with hyperleukocytosis.
		
		The WHO stated in their COVID -19 vaccination advice on who should get vaccinated (17 May 2022) that most individuals in the pediatric (children and adolescents) age group are at low risk of serious disease and vaccination would primarily be for the reduction of transmission. They also stated that children with comorbidities have a significant risk of severe COVID-19. However, children are still at risk of experiencing prolonged symptoms (or long COVID-19) and the rare multisystem inflammatory syndrome in children (MIS-C) which has been reported to occur and complicate recovery from COVID-19 in this population (WHO interim statement dated 24 Nov 2021).
		
		In the US, the surveillance data of COVID-19- Associated Hospitalization Surveillance Network (COVID-NET) as of 04 June 2021, reported that the weekly rates of COVID-19-associated hospitalization among children aged 5-11 was lower (0.6 hospitalizations per 100,000) compared to children aged 0-4 years old (2.9 hospitalizations per 100,000), adolescents 12-17 (0.8 hospitalizations per 100,000) and adults 18 years old and above (5.5 hospitalizations per 100,000). In addition, the weekly hospitalization rate trend of the 5-11 years old age group has been the lowest among all age groups from March 2020 to June 4 2022. In terms of severity among hospitalized cases in children aged 5-11 years old during the Omicron surge (December 19,2021 to March 31, 2022), 19.6% of hospitalized cases were admitted in the intensive care unit (ICU), 6.8% used high flow nasal cannula, 5.8% used bilevel positive pressure or continuous positive pressure and 5.2% were placed on mechanical ventilation. Lastly, in terms of COVID-19 associated deaths, based on the data from the National Center for Health Statistics, COVID-19 is one of the leading causes of death among children aged 1- 19 years old. In terms of multisystem inflammatory syndrome in children (MIS-C), a total of 8,525 cases were recorded in individuals aged 21 years and younger from March 2020 to May 2022. Of these, 69 deaths were recorded (US CDC, 2022)
		
		In a joint position paper (2022), the Israeli Pediatric Association and Israeli Society for Pediatric Infectious Disease discussed the disease burden of COVID-19 in Israeli children. As of late October 2021, there were 512,613 reported cases of COVID-19 in children and adolescents. About 43% of these cases (223,850) were in children ages 5-11 years old. They observed that the relatively high incidence rate of the age group was inversely related to the immunization rate of the general population (adults and adolescents) - as the immunization coverage of the older age groups increased and the relative proportion of all new COVID-19 cases in these age groups decreased, cases in the 5-11 age group increased. They also asserted that although COVID-19 morbidity and mortality are significantly lower in children than in adults, the risk of severe COVID-19 is not negligible, even among healthy children without pre-existing comorbidities. Of the 5-11 age group in Israel, 54% of patients with moderate-to-severe COVID-19 and 88% with MIS-C were previously healthy. In addition, they were able to estimate the rate at which severe clinical outcomes of COVID-19 disease occur in children:
		  ● COVID-19 associated hospitalization - 1:200 SARS-CoV2 positive children
		  ● Moderate-to-critical COVID-19 - 1:825 confirmed cases
		  ● COVID-19 associated myocarditis - 1:1600 SARS-CoV-2-positive cases in males at the age of maximum risk
		  ● MIS-C - 1:3000 SARS-CoV-2 positive children and adolescents
		  ● MIS-C associated death - 1-2% of children diagnosed with MIS-C
		  ● Long COVID - at least 1% of proven COVID-19 cases
		
		Meanwhile, a retrospective cohort review of COVID-19 hospitalization cases of children and adolescents aged 0 to 19 years in six (6) African countries from March 1 to December 31, 2020 revealed a high morbidity and mortality among this population, with greater likelihood of severe clinical outcomes among children <1 year and children with hypertension, chronic lung disease, and/or hematologic disease. Almost half of hospitalized patients (47.5%; 223 of 469 patients) presented with severe or critical COVID-19 disease with only 24.5% of the study population	

		who had at least 1 pre-existing comorbidity. While the most frequently reported symptoms were cough, fever, rhinorrhea, and respiratory distress, 18 of 297 cases (6.1%), were clinically suspected (6 patients) or confirmed (12 patients) to have MIS-C. Among the cohort, 418 patients (89.3%; 95%CI, 86.2% to 92.0%) were eventually discharged while 39 patients died (8.3%; 95% CI, 6.0%-11.2%). Of the 69 patients admitted to the ICU, 22 died. Of the 26 deaths with information on the presence or absence of clinical features of MIS-C, 4 had confirmed or suspected MIS-C. The study did not include data during the Delta and Omicron surge in Africa which occured in July 2021 and November 2021, respectively. A systematic review by Hoste et al., 2021 which included observational studies from the US, UK, Europe, India, Iran, Saudi Arabia, Turkey, and Israel, observed that MIS-C was seen among children with a median age of 8 to 8.4 years old (n=953). This was notably higher than the mean age for COVID-19 patients who did not develop MIS-C (2 years old). In general, the presence of comorbidities were infrequent in MIS-C cases and mainly consisted of asthma (4.1%; 39/953), chronic lung disease (1.5%; 14/953), cardiovascular disease (1.3%; 12/953), and immunodeficiencies (1.0%; 10/953). A systematic review for articles and national reports by Kitano et al., 2021 found that the impact on COVID-19 fatality among children ages 0 to 19 years was larger in low and middle income countries (LMICs) compared to high income countries (HICs). Of the 3,788 pediatric COVID-19 deaths gathered from the review, 91.5% were reported from LMICs and 8.5% were reported from HICs. The deaths per 1 million children and case fatality rate were significantly higher in LMICs at 2.77 and 0.24%, respectively compared to HICs at 1.32 and 0.01%, respectively ($p<0.001$). It was noted; however, that 83.5% of the pediatric population included in the study were from LMICs. Meanwhile, only 28.3% of ICU admissions included in the review were from LMICs. A systematic review and meta-analysis of early studies (search date as of 04 July 2020) looking at susceptibility, severity and transmissibility of COVID-19 in children by Gaythorpe et al., 2021 found that in general, children are susceptible to SARS-CoV-2 infection, but to a lesser extent than adults. Among the included studies in the review, varying conclusions were observed. Depending on study setting, results of studies show either comparable, lower, or higher attack rates in children (aged 18 years and younger) compared to older age groups. In terms of proportion of asymptomatic cases to SARS-CoV-2 positive children, the pooled estimate from 13 studies was 21.1% (95% CI: 14.0–28.1%) [I^2: 90.94% (95% CI: 77.44 to 97.70)]. Meanwhile, for the proportion of COVID-19 positive children who were defined as severe or critical, the pooled estimate from 14 studies was 3.8% (95% CI: 1.5–6.0%) [I^2: 91.30% (95% CI: 72.83 to 97.47)]. In terms of underlying medical conditions of children aged <18 years old which are more likely to develop severe COVID-19, a surveillance study in the US from March 2020 to May 2021 (Woodruff et al. 2021) showed that the risk of severe COVID-19 was higher among children with feeding tube dependence (aRR: 2.0, 95% CI: 1.5-2.5), diabetes mellitus (aRR: 1.9, 95% CI: 1.6-2.3), and obesity (aRR: 1.2, 95% CI: 1.0-1.4). ***Post-COVID-19 conditions in children*** Data presented to the Vaccines and Related Biological Products Advisory Committee (VRBPAC, 14 June 2022) showed that post-COVID-19 conditions in children appear to be less common in children compared to adults. A national survey in the UK reported that around 7-8% of children infected with COVID-19 had continued symptoms for more than 12 weeks. They can appear after mild to severe infections and after MIS-C. The most common post-COVID-19 symptoms are similar to adults (e.g. fatigue, headache, insomnia, trouble concentrating, muscle and joint pain, and cough). These conditions have an impact on the quality of life of children (i.e., limitations of physical activity, feeling distressed about symptoms, mental health challenges, and decreased school attendance/participation). ***Evidence on variants of concern*** In the latest WHO Weekly Epidemiological Update for COVID-19 (29 June 2022), the dominant variant across the globe remains to be the Omicron variant, accounting for 94% all sequences reported to the Global Initiative on Sharing Avian Influenza Data (GISAID) within the last 30 days. Data from the DOH Data Drop showed that between December 2021 to 18 June 2022, the number of confirmed COVID-19 cases peaked in January 2022, which was the period of Omicron surge for all age groups (i.e., <6 years, 6-11 years, 12-17 years, 18-59 years, and 60 and above),	

with 81.12% of cases during this period coming from the 18-59 years age group. Meanwhile, children less than 6 years accounted for 3.17% of the cases; children ages 6-11 years accounted for 2.62%; adolescents ages 12-17 years accounted for 2.63% and the elderly accounted for 10.46%. Across all age groups, the number of cases started to decrease in February and March 2022.

Cumulatively, as of 25 May 2022, 635 samples taken by convenience and purposive sampling tested positive for VoCs among the pediatric population ages 6 to 11 years old (total number of samples tested was not available). Of these, 40% (254 samples) was Delta, 33.54% (213 samples) was Omicron, 14.02% (89 samples) was Alpha, and 12.44% (79 samples) was Beta. Majority of the COVID-19 cases caused by VoCs have already recovered.

Three published studies (i.e. UK MHRA, 2021, Nyberg et al., 2022, Marks et al., 2022) conducted in the US and the UK reported the risk of hospitalization due to COVID-19 caused by the Omicron and Delta variants in children and adolescents. The technical briefing of the UK Health Security Agency on variants of concern estimated a lower risk of hospitalization among Omicron cases compared to the risk of hospitalization associated with the Delta variant [HR: 0.42 (95% CI 0.28-0.63)] in children ages 5-17 years old. Meanwhile, the study of Nyberg et al., 2022 concluded that COVID-19 related hospital admission rate did not differ between the Delta and Omicron variant in children <10 years old (adjusted HR: 1.10 [95% CI: 0.85 - 1.42]) or adolescents aged 10-19 years [HR: 0.83 (95% CI: 0.64-1.08)]. As for the risk of death, Nyberg et al. (2022) did not estimate the relative risk due to the small number of deaths in the populations aged <10 years and 10-19 that occurred due to both the Omicron and Delta variants. Lastly, in their published CDC report, Marks et al. (2022) reported that risk ratios (RRs) of hospitalization during the peak week of the Omicron period in the US (January 8, 2022) increased among children 5-11 years old compared to during the Delta period (Delta = 1.1; Omicron = 2.4; RR = 2.3; 95% CI = 1.5–3.6).

Evidence on seroprevalence and transmission among children
Despite the local and global epidemiologic data presented above, the burden of COVID-19 disease among children ages 6 to 11 years may still be largely underestimated.

In the US, the CDC conducted a national commercial laboratory seroprevalence study to evaluate trends in SARS-CoV-2 seroprevalence during September 2021-February 2022, by age group. During the December 2021-February 2022 period, the seroprevalence increased among children aged 0-11 years from 44.2% (95% CI = 42.8–45.8) to 75.2% (95% CI = 73.6–76.8) which is the highest increase across age groups (See Table 1.2). Moreover, as of February 2022, approximately 75% of children and adolescents had serologic evidence of previous infection with SARS-CoV-2, with approximately one third becoming newly seropositive since December 2021. The greatest increases in seroprevalence during September 2021–February 2022, occurred in the age groups with the lowest vaccination coverage. Limitations of the study, however are, (1) convenience sampling which might limit generalizability; (2) lack of race and ethnicity data which might affect the weighting for this variable; (3) overrepresentation of people with greater access to health care or those who more frequently seek care; and lastly there might be underestimation of cumulative number of infections since infections after vaccination might result in lower antibodies and anti-N seroprevalence cannot account for reinfections.

Table 1.2. Seroprevalence increases across age groups in the US December 2021 to February 2022

Age Group	December 2021 Seroprevalence	February 2022 Seroprevalence
Overall	33.5% (33.1 to 34.0)	57.7% (57.1 to 58.3)
0-11 years old	44.2% (42.8 to 45.8)	75.2% (73.6 to 76.8)
12-17 years old	45.6% (44.4 to 46.9)	74.2% (72.8 to 75.5)
18-49 years old	36.5% (35.7 to 37.4)	63.7% (62.5 to 64.8)
50-64 years old	28.8% (27.9 to 29.8)	49.8% (48.5 to 51.3)

≥65 years old	19.1% (18.4 to 19.8)	33.2% (32.2 to 34.3)

In a recent systematic review (Chen et al., 2022) evaluating the role of children in household transmission across 18 different countries, it was found that although lower transmission rates were reported in households that have children as index cases than compared to adults, an increased transmissibility of COVID-19 in children were observed as new variants such as Delta and Omicron emerged. In addition, there was no significant difference in secondary attack rates between children and adults as new variants became dominant.

Social and Economic Impact of COVID-19 in children

In the US, the Kaiser Family Foundation (KFF) COVID-19 Vaccine Monitor assessed the effects of the pandemic on children's academic and emotional development.The survey was conducted from 15 July to 2 August 2021 via telephone and online, in English and Spanish, among a nationally representative sample of 1,259 adults who are parents or guardians of a child under the age of 18 living in their household. Thirty-nine percent of the parents of children ages 5 and above responded that at least one of their children fell behind academically. Fifty one percent of these parents were from lower income households. Meanwhile, 36% of parents said that their child fell behind in their social and emotional development and 29% responded that their child experienced mental health or behavioral problems due to the pandemic. When asked about more specific problems that may indicate mental health concerns among children, 42% reported that their children experienced at least one new mental health symptoms in the past 12 months that they had not been experiencing before the pandemic which includes difficulty concentrating on schoolwork (27%), problems with nervousness or being easily scared or worried (19%), trouble sleeping (18%), poor appetite or overeating (15%), and frequent headaches or stomach aches (11%). Other factors such as household employment disruptions were also analyzed. Nearly 4 in 10 of parents reported that they or another adult in their household left a job or changed work schedules to take care of their children in the past year.

Just like in the US, the pandemic may also have a significant impact on the mental health of Filipino parents and children and has affected how common Filipino households adjust under the new normal. This is supported by a survey by Tee et al. among Filipinos (N = 1,879) during the start of the pandemic (28 March 2020 to 12 April 2022) which showed that concern for family members was significantly associated with greater psychological impact of the pandemic and higher levels of stress, anxiety and depression ($p<0.05$) while having grown-up children was significantly associated with lesser psychological impact of the pandemic and lower levels of stress, anxiety and depression ($p<0.05$).

HTAC Judgment: The burden of COVID-19 contributed by children aged 6 to 11 years old cannot be ascertained as children experience milder symptoms and asymptomatic presentations leading to less probability of being tested and more unreported cases (WHO, 2021).

Local evidence (SALVACION registry) shows that of the 191 children aged 6 to 11 years old who were hospitalized, 53.93% had comorbidities while 46.07% did not have comorbidities. DOH data show that CFR in children ages 6 to 11 years old (**6-11 yo: 0.15%**; vs <6 yo: 0.67%; 12-17 yo: 0.18%; 18 to 59 yo: 0.78%; >60 yo: 7.53%) is the lowest among other age groups. This is similar with US data showing that CFR and ICU admissions in children aged 0-4 years old and adolescents aged 12-17 years old are likely greater compared to that of children aged 5 to 11 years old (US CDC, 2022). Currently, the effect of variants on hospitalization in this age group cannot be established due to limited sequencing capacity in the country. Internationally, studies from the US and UK show varying results.

In addition, based on US data, the incidence of MIS-C is highest in the 5 to 11 age group compared to the other age groups. This is similar to the local data where 12 out of the 26 MIS-C cases (46.15%) reported, were from the 6 to 11 year age group (SALVACION Registry, as of 20 June 2022). Lastly, in terms of post COVID conditions, US data shows that this condition appears to be less common in children than in adults. There are no local studies on post COVID-19 conditions.

CRITERION 2

2. Clinical efficacy, effectiveness, and safety

*What is the **efficacy and effectiveness** of Moderna in terms of: reducing the incidence of symptomatic and severe COVID-19, hospitalization due to COVID-19, and death due to COVID-19 in children ages 6 to 11 years old?*

For the evidence on the efficacy, effectiveness or immunogenicity of the primary series of *Moderna* among children ages 6 to 11 years, the following latest available reviews were considered: International Vaccine Access Center (IVAC) of the Johns Hopkins Bloomberg School of Public Health and World Health Organization review of COVID-19 vaccines in general as of 17 June 2022; and, COVID-NMA review of COVID-19 vaccines in general as of 17 June 2022. Additionally, trial report from the Vaccines and Related Biological Products Advisory Committee (VRBPAC) briefing document for the meeting on the EUA amendment on the use of *Moderna* in children ages 6 months to 17 years old (with a separate analysis for children aged 6 to 11 years old) was reviewed. Trial reports and real world evidence from the manufacturer dossier submission to the Philippine FDA and independently retrieved publications and preprints from PubMed and medRxiv were also considered.

Overall, there was one published study of a Phase II/III RCT (Creech et al., 2022) identified which evaluated the efficacy of *Moderna* as a primary series among children ages 6 to 11 years. The result published in Creech et al. was also reported in the VRBPAC briefing document with additional vaccine efficacies reported after the second dose. Note, however, that the results reported herein only had a median follow up period of 51 days after dose 2.

In terms of immunogenicity, two publications of a Phase II/III RCT (Creech et al., 2022; VRBPAC 2022) reported different immunogenicity outcomes.

EVIDENCE FROM TRIALS

Efficacy outcomes

Description of Evidence

There is one ongoing trial using *Moderna* for children ages 6 to 11 years old being conducted in the US and Canada (NCT04796896 or KidCOVE, published in Creech et al. 2022 and VRBPAC briefing document). The trial is an ongoing two-part Phase II/III trial. Part 1 is an open-label dose selection study (2 doses of 50 mcg per dose of *Moderna* vs 2 doses of 100 mcg per dose of *Moderna*) while Part 2 is an observer-blinded, placebo-controlled, randomized clinical trial. Only Part 2 reported efficacy outcomes as Part 1 mainly focused on immunogenicity outcomes. From the results of Part 1, the 50 mcg dose of the *Moderna* vaccine was selected for evaluation in Part 2 of the trial because of lower reactogenicity compared to the 100 mcg dose level and comparable immunogenicity results of 50 mcg to 100 mcg dose.

The Creech et al. 2022 only reported efficacy outcomes after the first dose, while the VRBPAC briefing document focused on outcomes after the second dose. The unblinded data cut off was November 10, 2021 which corresponded to a median follow up of 82 days (IQR: 14 to 94) after the first dose, and 51 days (IQR: 45 to 57) after the second dose. Other details of Part 2 of the trial are detailed below. Meanwhile, details of Part 1 will be discussed in the immunogenicity section.

Table.2.1. Study characteristics of the Phase II/III RCT on *Moderna* (50mcg/dose)

Author Year Country Study Design	Population	Intervention	Comparator	Outcomes
Creech et al. 2022/ VRBPAC 2022 [Published] US and Canada Phase II/III RCT	Children ages 6-11 years old N= 4,016	*Moderna*, 2 doses (50mcg per dose), 28 days apart Assigned: n=3,012 Dose 1: n=3,005 Dose 2: n=2,988	Placebo, 2 doses, 28 days apart Assigned: n=1,004 Dose 1: n=997 Dose 2: n=973	*Reported by the Creech et al.:* ● VE against symptomatic COVID-19 (CDC definition) after dose 1 ● VE against symptomatic COVID-19 (COVE trial definition) 14 days after dose 1 ● VE against SARS-CoV-2 infection 14 days after dose 1

The vaccine achieves the following efficacy parameters:

Symptomatic COVID-19
- Preferred: At least 70% (point estimate), lower 95% confidence interval ≥50%
- Minimum/Critical: At least 50% (point estimate) and lower 95% confidence interval ≥30%.

Severe COVID-19 and Hospitalization due to COVID-19
- Preferred: At least 90% (point estimate) and 70% lower bound
- Minimum/Critical: At least 70-80% (point estimate) and 50% lower bound

Death due to COVID-19
- Preferred: None
- Minimum/Critical: None

				● VE against asymptomatic infection 14 days after dose 1 Follow up: 82 days after first dose *<u>Reported by VRBPAC Briefing Document:</u>* ● VE against symptomatic COVID-19 (CDC definition) after dose 2 ● VE against symptomatic COVID-19 (COVE trial definition) 14 days after dose 2 ● VE against SARS-CoV-2 infection 14 days after dose 2 ● VE against asymptomatic infection 14 days after dose 2 Follow up: 51 days after second dose

The following efficacy outcomes were defined as follows:

- VE against symptomatic COVID-19 (CDC definition) 14 days after dose 1 and dose 2
  - *CDC definition: One systemic or respiratory symptom AND a positive reverse transcriptase polymerase chain reaction (RT-PCR) assay for SARS-CoV-2 (less stringent criteria)*
- VE against symptomatic COVID-19 (COVE trial definition) 14 days after dose 1 and dose 2
  - *Phase III COVE trial definition: At least two prespecified systemic symptoms or at least one respiratory symptom AND a positive RT-PCR assay*
- VE against SARS-CoV-2 infection (regardless of symptoms) 14 days after dose 1 and dose 2
  - *definition: Negative SARS-CoV-2 status at baseline in participants who later had a positive RT-PCR assay at a scheduled nasal-swab test or at a visit prompted by SARS-CoV-2 symptoms or exposure or by the detection of SARS-CoV-2–binding antibody levels against SARS-CoV-2 nucleocapsid protein measured by means of the Elecsys (Roche) serologic assay at a scheduled post baseline visit*
- VE against asymptomatic infection 14 days after dose 1 and dose 2
  - *Phase II/III KidCOVE trial definition: Absence of COVID-19 symptoms AND bAb level against SARS-CoV-2 nucleocapsid protein negative (as measured by Roche Elecsys) at Day 1 that becomes positive (as measured by Roche Elecsys) post-baseline or positive RT-PCR test post baseline (at scheduled or unscheduled/illness visits*

Key Findings

<u>Risk of Bias</u>

The HTAC rated the ROB of the Phase II/III RCT (published in Creech et al. and VRBPAC briefing document) as *low* for efficacy outcomes after the first dose since the clinical trial was randomized with allocation concealment and blinding of participants, investigators and assessors. Moreover, the reported outcomes in the study and its supplementary appendix match the endpoints declared in the protocol. Meanwhile, for efficacy outcomes after the second dose, the RoB was deemed to be *high* due to a short follow-up period of 51 days after second dose (<2 months.

Results

Critical efficacy outcomes:

Moderna showed inconclusive efficacy against symptomatic COVID-19 14 days after the second dose:

- CDC case definition: **76.8% (95% CI: -37.3 to 96.6)** (VRBPAC, 2022) based on very low certainty of evidence
- COVE trial definition: **69.0% (95% CI: -131.4 to 95.8)** (VRBPAC, 2022) based on very low certainty of evidence

Important efficacy outcomes:

The following important efficacy outcomes were measured at ≥14 days after the first and second dose.

- Using *COVID-19 Vaccine Moderna* (≥14 days after dose 2) among children ages 6-11 years old, compared to placebo, **reduces the risk for:**
  - **Any SARS-CoV-2 infection : 73.6% (95% CI: 38.5 to 88.8)** (VRBPAC, 2022) based on very low certainty of evidence
  - **Asymptomatic infection: 72.3% (95% CI: 24.1 to 90.0)** (VRBPAC, 2022) based on very low certainty of evidence
- Using *COVID-19 Vaccine Moderna* (≥14 days after dose 1) among children ages 6-11 years old, compared to placebo, **reduces the risk for:**
  - **Symptomatic COVID-19 (CDC definition)** by **88.0% (95% CI: 70.0 to 95.8)** (Creech et al., 2022) based on moderate certainty of evidence
  - **Symptomatic COVID-19 (COVE trial definition)** by **91.8% (95% CI: 74.2 to 98.0)** (Creech et al., 2022) based on moderate certainty of evidence
  - **Any SARS-CoV-2 infection** by **74.0% (95% CI: 57.9 to 84.1)** (Creech et al., 2022) based on moderate certainty of evidence
  - **Asymptomatic infection** by **62.5% (95% CI: 30.9 to 79.4)** (Creech et al., 2022) based on low certainty of evidence

There were no reports of severe COVID-19, hospitalization due to COVID-19 and death due to COVID-19 among children ages 6-11 years old for both the intervention and control groups in the trial.

Immunogenicity outcomes

Description of evidence

Overall, the reference reviews identified two publications (Creech et al.; VRBPAC 2022) of a Phase II/III trial assessing different immunogenicity outcomes of the primary series of *Moderna* for children ages 6 to 11 years old. Detailed characteristics of the study is presented below:

Table.2.2. Study characteristics of the Phase II/III RCT on *Moderna* (50mcg/dose)

	Creech et al. 2022/ VRBPAC 2022 [Published] US and Canada
Study design	Phase II/III RCT (Immunobridging study)
Population	Children ages 6-11 years old and young adults ages 18-25 years old Part 1: N=362 Part 2: N= 615
Intervention	*KidCOVE Trial: Part 1:* Children ages 6-11 years old *Moderna*, 2 doses (50 mcg per dose), 28 days apart n=67

	KidCOVE Trial: Part 2 Children ages 6-11 years old *Moderna*, 2 doses (50 mcg per dose), 28 days apart n= 320
Comparator	*COVE Trial* Young adults 18-25 years old *Moderna*, 2 doses (100 mcg per dose), 28 days apart n=295
Outcome	Part 1 and Part 2 ● Neutralizing Antibody Titers and Seroresponse Rate ● Binding Antibody and Seroresponse Rate ● Binding Antibody Specific to SARS-CoV-2 Spike Protein
Follow up	1 month after second dose

Key findings

Results of the immunogenicity trials

Creech et al, 2022

Creech et al., measured the pseudovirus neutralizing antibody (PsVNA) ID_{50} titer, PsVNA ID_{80} titer and binding antibody specific to SARS-CoV-2 spike protein levels in both Part 1 and Part 2 of the trial. According to the protocol, if the accepted serum neutralizing antibody threshold of protection against COVID-19 is not available, then immune response measure in geometric mean titers and seroresponse rate, 1 month after second dose in children aged 6 to 11 years old (2 doses, 50 mcg per dose of *Moderna*, 28 days apart) will be compared to immune response results of young adults aged 18-25 years old (2 doses, 100 mcg per dose of *Moderna*, 28 days apart) in COVE trial. The prespecified non-inferiority criteria set in the trial protocol, which is also aligned with the US FDA specifications, is shown in Table.2.3. below.

Table.2.3. Non inferiority criteria for immunogenicity outcomes set in the trial protocol of Phase II/III RCT on Moderna (50mcg/dose)

Coprimary endpoint	Formula	Non inferiority Criteria
Geometric mean ratio (GMR)	$\frac{GM\ value\ of\ nAb\ in\ children\ (KidCOVE\ )}{GM\ value\ of\ nAb\ in\ young\ adults\ (COVE)}$	1. Lower boundary of the 95% CI for the geometric mean titer ratio is >0.67, AND 2. Point estimate of the GMR > 0.8
Seroresponse rate (SRR) difference	SRR in children (KidCOVE) - SRR in young adults (COVE)	1. Lower boundary of the 95% CI for the difference in serologic response is > −10 %, AND 2. Seroresponse rate difference point estimate > -5%

For Part 1 and Part 2 of the Phase II/III RCT, the neutralizing antibody titers of children aged 6 to 11 after 1 month after receiving dose 2 had a GMR of 0.93 (0.74 to 1.16) and 1.2 (1.1 to 1.4) respectively, relative to the titers of young adults aged 18 to 25 years old after 1 month after dose 2 from the main COVE trial. This was deemed by the US FDA as meeting the non-inferiority criteria for this endpoint.

The same conclusion can be drawn from the binding antibody titers, one month after dose 2 [Part 1 GMR: 1.03 (1.0 to 1.6); Part 2 GMR: 1.2 (0.98 to 1.33)].

In terms of seroresponse rates for neutralizing antibody titers, the seroresponse in children aged 6 to 11 years old from Part 1 and Part 2 of the Phase II/III RCT met the non-inferiority for neutralizing antibody [SRR Part 1: 1.0 (-4.4 to 3.0); SRR Part 2: 0.1 (-1.9 to 2.1)] according to the US FDA. Same conclusion can also be drawn for the binding antibodies [SRR Part 1: 0.7 (-4.7 to 2.6); SRR Part 2: -0.3 (-2.3 to 1.7)]. Geometric mean titers of neutralizing antibodies, binding antibodies and the corresponding seroresponse rates are enumerated in Table.2.4.

The efficacy of 2 doses of 50 mcg of *Moderna* in children is then inferred by successful immunobridging to data in young adults who had received the 100 mcg dose level of the vaccine in the COVE trial, which had shown high efficacy (Creech et al.).

Table.2.4. Immunogenicity Outcomes of *Moderna* in Children 6 to 11 years old from KidCOVE trial versus Young Adults aged 18 to 25 years old from COVE trial (Creech et al.)

Immune response Outcomes	**Timepoint**	**KidCove Trial: Part 1 Children (6-11 years old) 50 mcg *Moderna*** N=67	**COVE Trial: Part 1 Young adults (18-25 years old) 100 mcg *Moderna*** N=295	**KidCove Trial: Part 2 Children (6-11 years old) 50 mcg *Moderna*** N=320	**COVE Trial: Part 2 Young adults (18-25 years old) 100 mcg *Moderna*** N=295
Neutralizing antibody titers					
GMT	Baseline	9.3 (Not estimable) n=67	9.5 (9.2-9.4) n=295	9.3 (Not estimable) n=317	9.3 (9.2-9.4) n=295
	28 days after Dose 1	Not measured	Not measured	108.1 (93.1-125.5) n=97	96.7 (86.7-107.9) n=294
	1 month after Dose 2	1,204.6 (986.7 - 1,470.8) n=67	1,299.9 (1181.8-1429.7) n=295	1,610.2 (1456.6-1780.0) n=319	1,299.9 (1170.6-1443.4) n= 295
GMR	1 month after Dose 2	**0.93 (0.74 to 1.16)**		**1.2 (1.1 to 1.4)**	
Seroresponse rate (n/N)	28 days after Dose 1	Not measured	Not measured	66.7 (56.3-76.0) 64/96	66.3 (60.6-71.7) 195/294
	1 month after Dose 2	100.0 (94.6-100.0) 67/67	99.0 (97.1-99.8) 292/295	99.1 (97.3-99.8) 313/316	99.0 (97.1-99.8) 292/295
Seroresponse rate difference (percentage points)	1 month after Dose 2	**1.0 (-4.4 to 3.0)**		**0.1 (−1.9 to 2.1)**	
Binding antibody titers					
GMT	Baseline	30.4 (23.9 - 38.5) n=67	48.4 (42.4-55.3) n=279	32.8 (28.7 - 37.5) n=303	48.4 (42.4 - 55.3) n=279
	28 days after Dose 1	Not measured	Not measured	Not measured	Not measured

	1 month after Dose 2	333,103 (237,621 - 405,517) n=67	257,788 (234,099-283,875) n=279	295,106 (265,273 - 328,295) n=318	257,788 (230,064-288,854) n=279
GMR	1 month after Dose 2	**1.3 (1.0 to 1.6)**		**1.2 (0.98 to 1.33)**	
Seroresponse rate (n/N)	28 days after Dose 1	Not measured	Not measured	Not measured	Not measured
	1 month after Dose 2	100.0 (94.6 - 100.0) 67/67	99.3 (97.4-99.9) 277/279	99.0 (97.1 - 99.8) 299/302	99.3 (97.4 - 99.9) 277/279
Seroresponse rate difference (percentage points)	1 month after Dose 2	**0.7 (-4.7 to 2.6)**		**-0.3 (-2.3 to 1.7)**	

EVIDENCE FROM REAL WORLD STUDIES

Vaccine Effectiveness outcomes

Description of evidence

The reference reviews and systematic search did not identify any real world studies on the clinical effectiveness (VE against symptomatic and severe COVID-19, hospitalization due to COVID-19, and death due to COVID-19) and immunogenicity of *Moderna* for the pediatric population ages 6 to 11 years old.

HTAC Judgment: Currently, there is inconclusive evidence on the clinical efficacy of a 2-dose primary series of *Moderna* (50 mcg per dose) in children aged 6 to 11 years old. However, on the basis of the same Phase II/III trial, the efficacy of 2 doses of 50 mcg of *Moderna* in children can be inferred from immunobridging data to young adults ages 18 to 25 years old who had received the 100 mcg dose in the Phase III COVE trial, which showed high potential for protection (Creech et al.).

*What is the **efficacy and effectiveness** of Moderna in terms of: reducing incidence of symptomatic and severe COVID-19, hospitalization due to COVID-19 and death due to COVID-19 caused by **variants of concern** in children ages 6 to 11 years old?*	For the evidence on the efficacy, effectiveness or immunogenicity against variants of concerns (VoCs) of the primary series of *Moderna* among children ages 6 to 11 years, the following latest available reviews were considered: International Vaccine Access Center (IVAC) of the Johns Hopkins Bloomberg School of Public Health and World Health Organization review of COVID-19 vaccines in general as of 17 June 2022; and, COVID-NMA review of COVID-19 vaccines in general as of 17 June 2022. Additionally, trial report from the Vaccines and Related Biological Products Advisory Committee (VRBPAC) briefing document for the meeting on the EUA amendment on the use of *Moderna* in children ages 6 months to 17 years old (with a separate analysis for children aged 6 to 11 years old) was reviewed. Trial reports and real world evidence from the manufacturer dossier submission to the Philippine FDA and independently retrieved publications and preprints from PubMed and medRxiv were also considered. There were no studies identified which evaluated the clinical efficacy or effectiveness of *Moderna* against VoCs among children ages 6 to 11 years old. In terms of immunogenicity, two publications (Creech et al., 2022; VRBPAC 2022) and one preprint (Girard et al. 2022) from the same Phase II/III RCT reported different immunogenicity outcomes against VoCs relative to different comparator groups. **EVIDENCE FROM TRIALS** ***Efficacy outcomes*** The reference reviews and independent search did not detect trials assessing efficacy of *Moderna* against VoCs among children ages 6 to 11 years old. ***Immunogenicity outcomes*** ***Description of evidence*** Overall, the reference reviews identified two publications (Creech et al., 2022; VRBPAC 2022) and one preprint (Girard et al.) of one Phase	The vaccine achieves the following efficacy parameters: **Symptomatic COVID-19** ● Preferred: At least 70% (point estimate), lower 95% confidence interval ≥50% ● Minimum/Critical: At least 50% (point estimate) and lower 95% confidence interval ≥30%. **Severe COVID-19 and Hospitalization due to COVID-19** ● Preferred: At least 90% (point estimate) and 70% lower bound ● Minimum/Critical: At least 70-80% (point

II/III trial assessing immunogenicity outcomes against VoCs of the primary series of *Moderna* for children ages 6 to 11 years old. For Creech et al., only Part 1 reported outcomes against VoCs. Detailed characteristics of the study are presented below:

Table.2.5. Study characteristics of Immunogenicity Studies of *Moderna* primary series for children aged 6 to 11 years old.

Author Year Country Study Design	Population	Intervention	Control	Outcomes
Creech et al. 2022/VRBPAC 2022 [Published] Phase II/III RCT US and Canada *Delta*	Children ages 6-11 years old Part 1 (dose finding, open label): N= 429 Part 2 (observer-blinded, placebo-controlled): No outcomes against VoCs	Children ages 6-11 years old *Moderna*, 2 doses (50 mcg per dose), 28 days apart n=134	Young adults 18-25 years old *Moderna*, post booster dose (50 mcg booster dose) n=295	Creech et al.: Neutralizing antibody titers and seroresponse rate against Delta variant (children vs adults) VRBPAC et al.: Neutralizing antibody titers and seroresponse rate against Ancestral (D614G) and Delta variant (children only) Follow-up: 1 month after second dose
Girard et al. 2022 [Preprint] US and Canada Phase II/III RCT *Omicron*	Children: 6-11 years old Adolescent: 12-17 years old Adults: ≥ 18 years old N=60	Children: 6-11 years old *Moderna*, 2 doses (50 mcg per dose), 28 days apart n=20	Adolescent: 12-17 years old *Moderna*, 2 doses (100 mcg per dose), 28 days apart n=20 Adults: ≥ 18 years old *Moderna*, 2 doses (100 mcg per dose), 28 days apart n=20	Neutralizing antibody geometric mean ID50 titers (GMT) against Omicron and wild-type (D614G) strain Follow-up : 1 month after second dose

Key findings

Results of the immunogenicity trials

Study on Omicron

Girard et al. also reported neutralizing antibody titers and seroresponse rate against the Omicron variant and in comparison to the wild-type (D614G) strain. Immunogenicity results of Girard et al. were also presented in the VRBPAC Meeting. Results showed that 1 month after the second dose, neutralizing antibody titers against Omicron increased from 5 (95% CI not reported) to 95 (95% CI not reported). As compared with neutralizing antibodies against wild-type (D614G) strain, neutralizing antibody titers against Omicron was 22.1-fold lower. Between age groups, neutralizing antibody titers against Omicron and against wild-type (D614G) strain were numerically higher in children (*Moderna* 50 mcg) and adolescents (*Moderna* 100 mcg) as compared to adults (100 mcg). Omicron neutralization titers were also lower than wild-type (D614G) strain neutralization titers.

estimate) and 50% lower bound

Death due to COVID-19

- Preferred: None
- Minimum/Critical: None

Table.2.6. Geometric mean titers of neutralizing antibodies and seroresponse rate against Omicron and wild type (D614G) strain (Girard et al., 2022)

Age Group	Time Point	Omicron	Ancestral
Children (6-11 years old) 50 mcg *Moderna*	**Neutralizing antibody (GMT)**		
	Baseline	5	5
	1 month after second dose	95	2,102
	Fold difference *(Omicron vs wild-type/D614G)*	22.1-fold	
	Seroresponse rate (%)		
	Baseline	0	0
	1 month after second dose	100	100
Adolescents (12-17 years old) 100 mcg *Moderna*	**Neutralizing antibody (GMT)**		
	Baseline	5	5
	1 month after second dose	135	1,594
	Fold difference *(Omicron vs wild-type/D614G)*	11.8-fold	
	Seroresponse rate (%)		
	Baseline	0	0
	1 month after second dose	100	100
Adults (≥ 18 years old) 100 mcg *Moderna*	**Neutralizing antibody (GMT)**		
	Baseline	5	5
	1 month after second dose	36	1,039
	Fold difference *(Omicron vs wild-type/D614G)*	22.8-fold	
	Seroresponse rate (%)		
	Baseline	0	5
	1 month after second dose	95	100

Study on Delta

Creech et al. reported seroresponse rate and geometric mean titers of neutralizing antibodies against the Delta variant of children aged

		6 to 11 years old and young adults aged 18 to 25 years old. One month after the second dose, a total of 99.3% (133/134) of the children had a serologic response which is similar to the seroresponse rate in young adults aged 18 to 25 years old (92.2% i.e. 270 of 293). In terms of neutralizing titers, a GMT of 756.4 (651.0-878.8) was measured in children which corresponds to a geometric mean fold ratio (GMFR) of 81.8 (95% CI 70.4 to 95.0) from the baseline of 9.3 (not estimable). Similar GMT was reported in young adults [GMT: 803.5 (95% CI: 731.4 to 882.7)]. Meanwhile, the VRBPAC briefing document reported seroresponse rate and geometric mean titers of neutralizing antibodies against the ancestral (D614G) and Delta variant of children aged 6 to 11 years old. One month after the second dose, a total of 99.3% (133/134) of the children had a serologic response against the Delta variant. The same seroresponse rate was observed against the ancestral (D614G) strain [193/194 or 99.3% seroresponse rate (95%CI: 95.9 to 100.0)]. In terms of neutralizing titers, a GMT of 756.4 (651.0-878.8) was measured against the Delta strain which corresponds to a geometric mean fold ratio of 81.8 (95% CI 70.4 to 95.0) from the baseline of 9.3 (not estimable). This is lower compared to the GMT measured against the ancestral (D614G) strain at 1964.6 (no 95% CI reported) which corresponds to a GMFR of 209.5 (182.9 to 329.8) from baseline of 9.4 (no 95% CI reported). **EVIDENCE FROM REAL WORLD STUDIES** ***Vaccine Effectiveness outcomes*** ***Description of evidence*** The reference reviews and systematic search did not identify any real world studies on the clinical effectiveness (VE against symptomatic and severe COVID-19, hospitalization due to COVID-19, and death due to COVID-19) and immunogenicity of *Moderna* against VoCs for the pediatric population ages 6 to 11 years old. **HTAC Judgment**: The clinical efficacy and effectiveness of *Moderna* in children 6 to 11 years old against VoCs cannot be assessed due to lack of studies measuring clinical outcomes. However, immunogenicity outcomes from one study showed that children aged 6 to 11 years old had higher antibody titers against Omicron compared to adults (Girard et al.). In terms of immunogenicity against the Delta variant, data from the Phase II/III trial showed a similar immune response compared to adults (Creech et al.).	
	*What is the **duration of protection** of the Moderna in terms of reducing the incidence of symptomatic and severe COVID-19, hospitalization due to COVID-19 and death due to COVID-19 in children ages 6 to 11 years old?*	Creech et al./VRBPAC 2022, the only study which reported clinical efficacy outcomes only had a median follow-up of 51 days after second dose (i.e <2 months), thus duration of protection cannot be determined due to a short follow-up period. Data on the duration of protection of *Moderna* among children ages 6-11 years will be assessed as more evidence becomes available. **HTAC Judgment**: Cannot be assessed based on current limited evidence.	Minimum acceptable duration of protection: confers at least 6 months protective immunity Preferred: ≥1-year protective immunity
	*What is the **safety** of Moderna in children ages 6 to 11 years old in terms of: serious adverse events, all-cause mortality systemic*	For the evidence on the safety of the primary series of *Moderna* among children ages 6 to 11 years, the following latest available reviews were considered: International Vaccine Access Center (IVAC) of the Johns Hopkins Bloomberg School of Public Health and World Health Organization review of COVID-19 vaccines in general as of 17 June 2022; and, COVID-NMA review of COVID-19 vaccines in general as of 17 June 2022. Additionally, trial reports and real world evidence from the VRBPAC briefing document and manufacturer dossier submission to the Philippine FDA were reviewed. Independently retrieved publications and preprints from PubMed and medRxiv were also considered. A targeted search in Ministry of Health (MOH) and National Regulatory Authority (NRA) websites were also conducted to detect real world safety reports in countries implementing *Moderna* for children ages 6 to 11 years old.	Local and systemic reactions are tolerable, self-limiting and do not require hospitalization. No serious adverse events were caused by the vaccine.

reactogenicity local reactogenicity special adverse events of interest (i.e. Bell's palsy, Myocarditis/Pericarditis, Thrombosis with Thrombocytopenia Syndrome, Capillary *Leak Syndrome, Immune Thrombocytopenia, Multisystem Inflammatory Syndrome in Children [MIS-C] Post Vaccination)*

Overall, 1 Phase II/III RCT (Creech et al. 2022/VRBPAC 2022) and 3 reports on real world evidence that evaluated the safety of *Moderna* among children ages 6 to 11 years were identified.

SAFETY DATA FROM CLINICAL TRIALS

Description of Evidence

The reference reviews identified one Phase II/III RCT with results published as Creech et al., 2022 and in VRBPAC briefing document which reported safety outcomes of *Moderna* among children ages 6-11 years from one two-part Phase II/III trial. This trial is the same trial mentioned in the efficacy section of this Evidence Summary which has reported its safety within 7 days after each dose for local and systemic AEs and within 28 days after each dose for unsolicited AEs. Safety data after the unblinding of the trial was reported during the ACIP meeting on *Moderna* among children ages 6-11 years (blinded follow up period: 5.6 months after the second dose)

The safety outcomes were analysed using (1) Safety Set which consists of all enrolled participants in Part 1 (open label, dose-finding phase) and all randomly assigned participants in Part 2 (observer blinded randomized placebo controlled) who received at least 1 dose of the vaccine, and (2) Solicited Safety Set which consists of participants in the Safety Set who contributed any had at least 1 postbaseline solicited safety assessment. Safety outcomes in Part 1 are only reported in Creech et al. while all safety outcomes in Part 2 are reported by Creech et al. and VRBPAC. Both references reported safety outcomes that were assessed using the safety set, except for the solicited adverse reactions which were evaluated using the solicited safety sets. Creech et al. only reported unsolicited serious adverse events while the VRBPAC briefing document reported all serious AEs. Thus, Creech et al. was used as the reference for Part 1 safety outcomes and VRBPAC document was used as the reference for the Part 2 trial safety outcomes. Details of the study are presented in Table.2.7. below.

Table.2.7. Study characteristics of clinical trials that reported the safety of *Moderna* among children ages 6 to 11 years.

Author, Year Country Study Design	Population	Intervention	Comparator	Outcomes
VRBPAC 2022 / Creech et al., 2022/ACIP 2022 US and Canada Phase II/III	Children ages 6 to 11 years Part 1: N=751 (open label, dose-finding phase) Part 2: n= 4,016 (observer blinded randomized placebo controlled)	PART 1: (Safety Set) *Moderna*, 2 doses (50 mcg per dose), 28 days apart n= 380 *Moderna*, 2 doses (100 mcg per dose), 28 days apart n= 371 (Solicited Safety Set) *Moderna* (50 mcg) dose 1; n=378 dose 2; n=379 *Moderna* (100 mcg) dose 1; n=369 dose 2; n=371	PART 1: None	• Solicited Local and Systemic Adverse Reactions • Unsolicited Adverse Events • Serious adverse events • Fatal Adverse events Blinded follow up: 51 days after dose 2 Unblinded follow up: 5.6 months after dose 2
		PART 2: (Safety Set) *Moderna*, 2 doses (50 mcg per dose), 28 days	PART 2: (Safety Set) Placebo, 2 doses, 28 days apart	• Solicited local and systemic adverse reactions

Short term outcomes (e.g., reactogenicity and allergic reactions, AESI): at least 2 months
Long term outcomes (e.g., serious AEs, all-cause mortality, AESI, Vaccine-associated enhanced disease): at least 1 year

		apart n=3007 (Solicited Safety Set) *Moderna* (50 mcg) dose 1; n=3004 dose 2; n=2988	n=995 (Solicited Safety Set) Placebo dose 1; n=993 dose 2; n=969	• Unsolicited adverse events • Serious adverse events • Fatal Adverse events • Adverse events of special interest

Key findings

Risk of bias

The HTAC rated the RoB of the Phase II/III RCT published in the VRBPAC document as *low* for the short term safety outcomes [i.e., any systemic adverse events; any local adverse events; unsolicited adverse events (regardless of relationship to the vaccine); and unsolicited adverse events (related to the vaccine)]. However, long term safety outcome (i.e. serious adverse events) was rated *high* RoB due to a short follow up period of 51 days after the second dose.

Results of clinical safety

Part 1: Open label, dose finding phase [Creech et al.; Comparator: 100mcg Moderna]

In Part 1, the safety of *Moderna* at dose levels 50 mcg and 100 mcg were evaluated. In general, in terms of both solicited (local and systemic) and unsolicited adverse events related to the vaccine, the reported events were lower in the 50 mcg-arm than in the 100 mcg-arm, with an exemption of unsolicited adverse events regardless of relationship to vaccination, where the events reported in the 50 mcg-arm were slightly higher than those in the 100 mcg-arm. The most common local reaction for both arms was pain at the injection site, followed by erythema while the most common systemic reactions for both arms were fatigue, followed by headache. Serious AEs were reported by 7 participants: 5 in the 50-mcg group and 2 in the 100-mcg group. None were assessed as related to study vaccination. Lastly, there were no reported adverse events of special interest after vaccination of both 50 mcg and 100 mcg doses. Table.2.8. shows the actual reported events per safety outcome.

Table.2.8. Actual reported events per safety outcome in Part 1 of Creech et al. (2022).

Safety Outcome	50 mcg *Moderna*		100 mcg *Moderna*	
	after dose 1 (%)	after dose 2 (%)	after dose 1 (%)	after dose 2 (%)
Any solicited local adverse reactions (solicited safety set)	339/378 (89.7)	355/379 (93.7)	347/369 (94.0)	348/371 (93.8)
Any solicited systemic adverse reactions (solicited safety set)	207/378 (54.8)	284/379 (74.9)	223/369 (60.4)	313/371 (84.4)
Unsolicited Adverse events regardless of relationship to vaccination (safety set)	119/380 (31.3)		100/371 (27.0)	

Unsolicited Adverse events related to the vaccine (safety set)	44/380 (11.6)	47/371 (12.7)	

Part 2: Observer-blinded, placebo-controlled expansion evaluation of the selected dose [VRBPAC 2022; Comparator: Placebo]

Short-term safety outcomes:

Based on the computed risk ratio (RR) from the Phase II/III RCT (Creech et al.), *Moderna* for children ages 6-11 years compared to placebo increases risk for:

- any systemic adverse events by:
  - **1.11 times more (95% CI 1.04 to 1.19)** within 7 days after dose 1, based on high certainty of evidence
  - **1.56 times more (95% CI 1.46 to 1.67)** within 7 days after dose 2, based on high certainty of evidence
- any local adverse events by:
  - **1.94 times more (95% CI 1.82 to 2.07)** within 7 days after dose 1, based on high certainty of evidence
  - **1.89 times more (95% CI 1.77 to 2.01)** within 7 days after dose 2, based on high certainty of evidence
- any unsolicited adverse events (regardless of relationship to the vaccine) by:
  - **1.18 times more (95% CI 1.05 to 1.33)** within 28 days after any dose, based on high certainty of evidence
- any unsolicited adverse events (related to the vaccine) by:
  - **2.11 times more (95% CI 1.58 to 2.82)** within 28 days after any dose, based on moderate certainty of evidence

Long-term safety outcomes:

Meanwhile, *Moderna,* shows inconclusive safety data on the risk for:

- **serious AEs (regardless of relationship to the vaccine) [RR: 0.99 (0.20 to 4.91)]** within 28 days after any dose, based on very low certainty of evidence.

During the blinded period of the trial, all serious AEs in both the vaccine and placebo arms were considered by the investigators as unrelated to the vaccine or the placebo. Meanwhile, after unblinding, 1 related serious AE (ileus) was reported in a participant with a complex gastrointestinal medical history. This participant was from the placebo group which crossed over to the intervention after unblinding. There were no deaths reported in the blinded and unblinded period of the study (up to 5.6 months after dose 2).

Adverse events of special interest:

As of data-cutoff date (November 10, 2022), there were no observed adverse events of special interest (e.g. MIS-C, myocarditis or pericarditis) related to the vaccine. No AESI was also reported during the follow up period after the unblinding.

SAFETY DATA FROM REAL WORLD EVIDENCE

For the real world evidence on the safety of the primary series of *Moderna* among children ages 6 to 11 years old, two safety surveillance reports were identified via a targeted search in MOH and NRAs of countries currently implementing *Moderna* for this age group: one from EudraVigilance of the European Medicines Agency and one from the Government of Canada. ModernaTX, Inc. also provided a global summary safety report for the *Moderna* vaccine which included safety data for children 6 to 11 years old.

Description of Evidence

Three safety surveillance studies on *Moderna* for the pediatric population (6-11 years old) were included: one from the EudraVigilance website, and one from the Government of Canada, and one from a glocal safety summary report from ModernaTX, Inc. ModernaTX, Inc. provided their safety report with data from the company's global safety database which includes cases received from health care professionals (HCPs), health authorities (HA), consumers, and worldwide literature. Reports were retrieved using search strategies that

used customized Medical Dictionary for Regulatory Activities (MedDRA) preferred terms to include specific safety outcomes with cases only for *Moderna* vaccine among the 6 to 11 age group. The report included cumulative safety data from 18 December 2020 to 15 April 2022 and new cases for the reporting period of 16 February 2022 to 15 April 2022. The characteristics of these surveillance reports are indicated in Table.2.9. below:

Table.2.9. Characteristics of safety surveillance reports from countries implementing pediatric vaccination and ModernTX, Inc.

Agency [Period of Observation]	Reporting system	Population (N)	Intervention	Limitations
European Medicines Agency (as of 28 May 2022) **Period of observation not indicated*	EudraVigilance	Children 3-11 years old	*Moderna* (dose strength not mentioned) **number of doses administered not reported*	• The information relates to suspected side effects, i.e. medical events that have been observed following the administration of the COVID-19 vaccines, but which are not necessarily related to or caused by the vaccine. • AEs for children ages 6-11 years old were not disaggregated. Only information on children aged 3-11 years old was available. However, it was noted that *Moderna* is approved in the EU for 6-11 years old only. • There was no disaggregation of AEs after the first and second dose. • The number of doses of *Moderna* administered was not reported.
Government of Canada (as of 13 May 2022) **Period of observation not indicated*	Canada's infobase on reported side effects following COVID-19 vaccination in children 5-11 years old	Children 5-11 years old	*Moderna* (2 doses, 50 mcg) **number of doses administered not reported*	• Since the date of implementation of vaccine authorization of *Moderna* for children 5-12 just started last 17 March 2022, safety data may be limited since less than two months have passed since the administration of the first dose. • The number of doses of *Moderna* administered was not reported
ModernaTX, Inc. Bimonthly Safety Report (BSSR) (as of 15 April 2022) [from 16 February 2022 to 15 April 2022]	Global safety database of ModernaTX, Inc.	Children 6-11 years old	*Moderna* (2 doses, 50 mcg), 1 month apart	• The safety review covered data from the company's global safety database from 18 December 2020 to 15 April 2022 and new cases for the reporting period of 16 February 2022 to 15 April 2022. Some countries started *Moderna* pediatric vaccination in the later months of the first quarter of 2022, thus data from countries that started pediatric vaccination (6-11 years old) later than 15 April 2022 were not included in the safety report. Only short-term safety can be assessed from this report.

Key Findings

Safety results

The results from the safety surveillance studies among the vaccinated pediatric population with ages ranging from 6 years old to 11 years old in Europe and Canada are reported in Table.2.10 below. These surveillance databases only summarized the number of adverse events reported and not rates. Both databases did not report the total number of doses of *Moderna* administered in children ages 6-11 years old.

The Government of Canada did report on cases of death and AESIs, (e.g., myocarditis) but did not disaggregate between age groups and vaccine brands. Cases of deaths due to COVID-19 and AESIs were also not reported in the EudraVigilance report.

Table.2.10. Results of safety surveillance reports from countries implementing pediatric vaccination.

	EudraVigilance EU (EMA, 2022)	Health Canada (Government of Canada, 2022)
Number of Adverse events (AE) reported	52	*Not reported*
Number of Serious Adverse Events (SAE) reported	*Not reported*	0
Number of Non-serious AEs reported	*Not reported*	1

Meanwhile, global safety data from ModernaTX, Inc (18 December 2020 to 15 April 2022) reported 107 cases of adverse events among children ages 6 to 11 years old. Of these, 85 were medically-confirmed, 5 were serious and none had fatal outcomes. Among the reported serious cases, 3 cases were nervous system disorders (e.g., seizures, paraparesis, and facial cranial nerve disorders), 1 case was respiratory depression and 1 case was related to injury, poisoning and procedural complications. However, it was not specified whether these serious cases were vaccine-related. Most of the cases were from the United States while in Asia, only two 2 cases were reported and both were non serious. No deaths or cases of myocarditis in children less than 12 years old were also reported. Overall, the global safety report concluded that there were no safety issues identified involving myocarditis or pericarditis in children aged <12 years old who received *Moderna*. Tabulation of cases by severity and region is shown in Table.2.11.

Table.2.11. Reported cases in children ages 6 to 11 years old by severity and region from 18 December 2020 to 15 April 2022

Region	Non-Serious Cases (%)	Serious Cases (%)
Asia	2 (2.0%)	0 (0.0%)
Canada	8 (7.8%)	0 (0.0%)
European Economic Area	28 (27.5%)	1(20.0%)
United Kingdom	3 (2.9%)	0 (0.0%)
United States	41 (40.2%)	4 (80.0%)
Unknown	20 (19.6%)	0 (0.0%)
Total cases	**102**	**5**

HTAC Judgment: Short-term safety of Moderna in children 6-11 years old is acceptable. No case of myocarditis was reported in the clinical trial. Further follow-up data is needed to establish longer-term safety.

	Does Moderna	The following table summarizes the evidence on efficacy, effectiveness, and safety of a *Moderna* half dose (50 mcg) among children ages 6 to	Favorable benefit/risk profile

<table>
<tr><td></td><td>provide a highly favorable benefit/risk profile in the context of observed vaccine effectiveness and safety?</td><td>11. Given that Moderna was observed to have protection against symptomatic and asymptomatic COVID-19 after the first dose, as well as passing the non-inferiority criteria in terms of immunogenicity, Moderna has an acceptable risk-benefit profile based on limited evidence on effectiveness and short-term safety data.

<table>
<tr><th>Outcomes</th><th>Moderna (50 mcg)</th></tr>
<tr><td>Efficacy</td><td>Currently, there is inconclusive evidence on the efficacy of a 2-dose primary series of Moderna (50 mcg per dose) in children aged 6 to 11 years old.</td></tr>
<tr><td>Effectiveness</td><td>No evidence</td></tr>
<tr><td>Immunogenicity</td><td>On the basis of the same Phase II/III trial, the efficacy of 2 doses of 50 mcg of Moderna in children can be inferred from immunobridging data to young adults ages 18 to 25 years old who had received the 100 mcg dose in the Phase III COVE trial, which showed high potential for protection (Creech et al.).</td></tr>
<tr><td>Safety</td><td>Short-term safety of Moderna in children 6-11 years old is acceptable. No case of myocarditis was reported in the clinical trial. Further follow-up data is needed to establish longer-term safety</td></tr>
</table>

HTAC Judgment: Among children aged 6 to 11, Moderna (50 mcg) has an acceptable risk-benefit profile based on limited evidence on efficacy.</td><td></td></tr>
<tr><td colspan="4">CRITERION 3</td></tr>
<tr><td>3. Affordability, viability and feasibility</td><td>What are the current best practices, challenges and measures used to address challenges related to the implementation of COVID-19 Vaccines in the pediatric population (5-11 years old), which can be applicable to the implementation of Moderna in children ages 6 to 11 years old?

What are the lessons learned from the current implementation of COVID-19 Vaccines in the pediatric</td><td>Based on a series of consultations with the National Vaccine Operations Center (NVOC) and selected DOH Centers for Health Development (CHDs), information on real world experience during the current roll out of COVID-19 vaccines in children ages 5-11 years old using Pfizer-BioNTech and plans for the future roll out of Moderna for children 6-11 years old were gathered.

<u>Best Practices in the Current Implementation of COVID-19 Vaccination for Children (5 to 11 years old)</u>

Available and accessible vaccination sites: Vaccinations were conducted at the mega-sites such as malls, temporary posts, mobile buses, and house visits to accommodate the vaccinees and their guardians, to ensure that standard public health measures are maintained, and to actually encourage children, especially the younger ones, to get vaccinated. These strategies also allowed parents and children to be vaccinated together at one site.
Utilizing festive strategies in vaccination sites: Regional offices noted the use of mascots and playgrounds to encourage children to get vaccinated. Incentives such as food and free accommodations to park were also given
Vaccination rollout during weekends: Vaccination was extended until weekends in some vaccination sites to accommodate children with parents/guardians who are unavailable during weekdays.
Coordination with the Department of Education (DepEd): Schools were also used as vaccination sites for children. DepEd’s plan to conduct face-to-face classes encouraged parents to have their children vaccinated for safety reasons.
Availability of guidelines: According to regional offices, implementers find it helpful that the pediatric vaccination guidelines were readily available which contributed to the clarity of implementation and a well prepared roll-out.
Transparent reporting of AEFIs: According to NVOC, side effects for the pediatric population were less as compared to adults and these AEFIs were documented and properly reported.
Presence of medical specialists at the vaccination site: Aside from the usual AEFI teams present in vaccination sites, the on-site supervision of pediatricians and allergologists during vaccination of the pediatric population facilitated the timely and appropriate management of AEFIs (vs the on-call visit of the specialists for the adult vaccination).
Confidence to get vaccinated: Unlike adults, children are used to getting vaccinated as they are the target population of routine EPI
</td><td>There are no significant barriers and if there are, the plans to address the barriers are clearly reflected in the vaccine roadmap and other relevant documents.</td></tr>
</table>

	population (5-11 years old)? *How will the vaccination for the pediatric population be DIFFERENT with the use of Moderna compared to other vaccines for the pediatric population?* *Are there any foreseen advantages and barriers specific to the use of Moderna in the pediatric population? How are these foreseen barriers planned to be managed?*	immunization. ● ***Confidence of healthcare workers:*** Healthcare workers were also more confident because of their experience with the adolescent roll-out. ● ***Experts, healthcare workers and LGUs encouraging the vaccination of the pediatric population***: Testimonials from experts and DOH personnel who got their children vaccinated were used to promote pediatric vaccination efforts. Ceremonial giving of vaccines to pediatric family members of health workers and local chief executives were conducted to encourage parents to have their children vaccinated as well. The Philippine Pediatric Society (PPS) and private sectors also supported the roll-out. ● ***Stringent documentary requirements:*** Documentation from the accompanying parent/guardian was required to provide proof of affiliation to the pediatric vaccinee. Obtaining informed consent from the parent/guardian and assent from the child were strictly implemented prior to vaccination. ● ***Stringent screening process:*** The rollout for the pediatric population was tailored to ensure that vaccinees with comorbidities, including those with a history of conditions that were considered AESIs associated with vaccination (e.g. myocarditis and pericarditis) are identified and educated properly. ***Challenges in the Current Implementation of COVID-19 Vaccination for Children (5 to 11 years old)*** *General Challenges* ● ***Low Vaccination Turnout****:* The NVOC reported that some factors might have lowered the turnout of vaccinees. These factors include conflict with the schedule of guardians since vaccination is usually held on weekdays, and diminished sense of urgency to vaccinate children due to DepEd's non requirement of vaccination for face to face classes. The DOH explained though that we cannot require vaccination for face to face classes until sustainable supply of vaccines for the pediatric population is ensured. ● ***Vaccine Hesitancy:*** NVOC experienced an unexpected increase in vaccine hesitancy during the rollout of vaccination for children ages 5 to 11 years compared to when they were rolling out for adolescents. Identified causes of hesitancy include the spread of fake news, including authenticity of AEFI reporting, and resurfacing of the *Dengvaxia* controversy. An increased presence of anti-vaccine groups was also noticed, with some going as far as picketing outside vaccination sites. These circumstances have also made public communication difficult. ● ***Lengthier Vaccination Time for Pediatric Populations:*** NVOC noted that vaccination time is longer for the pediatric population compared to adult vaccination time. This was attributed to the following reasons: more complicated obtainment of children's assent; and the need for a more exhaustive assessment and screening prior to vaccination, which take longer to perform. ● ***Refusal of children to get vaccinated:*** During vaccination, some children refuse to give assent to get vaccinated, and to some extent cry loudly while at the vaccination site. Implementers express that in these certain situations, the children were sent home without getting the vaccine and may have to return some other time. These types of scenarios might also affect other children waiting when they see others in distress. ● ***Compliance to stringent documentary requirements in certain situations:*** Compliance was difficult with regard to the documentary requirements (e.g. proof of affiliation to the child) and the presence of the parent/guardian. This was especially true for children of OFWs. ● ***Inadvertent vaccination using vaccines with no EUA for pediatric use:*** The NVOC previously received a few reports of inadvertent vaccination using vaccines that do not have an EUA for pediatric use at the time (e.g., *AstraZeneca* and *CoronaVac*). This administration error happened during the National Vaccination Days (NVDs) where there were no special lanes for the pediatric age group. ● ***Cold chain requirement:*** Most LGUs, particularly in Region VI, still do not have the capacity to store *vaccines* that require ultra-low temperatures. The central storage of this vaccine is still at the Provincial Health Offices (PHO) or municipalities that have ultra-low temperature freezers (ULTFs). This causes delays and complications in the delivery of vaccines to the LGUs and vaccination sites. ● ***Insufficient human resource:*** Vaccination teams were limited which caused HCWs to become more fatigued leading to more errors toward the end of the day. This was observed especially during the NVDs where the turnout was twice or thrice the crowd when the rollout started. ● ***Limited vaccine supply and delays in delivery****:* Vaccine manufacturers cannot keep up with the high demand due to global rollout of	

vaccination for children leading to 3 days to 1 week delay in the delivery of vaccines.

Challenges in the Current Implementation of Moderna half-dose During Booster Vaccination for age group 18 years and older

- ***Difficulty in vaccine utilization reporting:*** The NVOC highlighted that at the beginning of their booster implementation, there was difficulty in reporting the utilization of *Moderna* due to the change in dosage from full to half dose. Half dose (50 mcg) of *Moderna* will also be implemented for the upcoming *Moderna* primary series vaccination in children ages 6 to 11 years old.

Measures to Address Challenges in the Current Implementation of COVID-19 Vaccination for Children

The key informants have noted the following observed measures to address these challenges. These will be carried on for the *Moderna* rollout in children ages 6-11 years old :

- ***Fast dissemination of accurate information on vaccines:*** Different mechanisms of proper information dissemination were promptly implemented in both local level (e.g. conduct of town hall meetings, prompt release of communications) and national level (e.g. use of social media) to counter the spread of fake news.
- ***Providing Incentives:*** Different incentivization mechanisms were given to children who got vaccinated (e.g. giving candies and lollipops, seeing dogs while being vaccinated, festive mall environment, free access to a waterpark). This strategy also helped to encourage other children to get vaccinated.
- ***Improving health education to lessen vaccine hesitancy among parents and their children:*** Implementers produce more public-friendly and easy to understand information materials to help explain to parents and children the need to get vaccinated and what to expect.
- ***Ensuring fast response to AEFIs:*** All principals concerned are informed such that all directives to address concerns, manage, and finance AEFI cases related to COVID-19 vaccination were quick.
- ***Require assent from children****:* Assent of children who will be vaccinated and consent from their parents is included in the guidelines. Crying and hesitation of the child is considered dissent. Parents are encouraged to get their children vaccinated however they also advised not to force their children to get vaccinated. According to the regional offices, hesitant children are encouraged to stay on site and observe to see that the process is easy.
- ***Online pre-registration:*** Online pre-registration systems were utilized to facilitate more efficient assessment of children at the vaccination site and shorten waiting time in the administration of multi-dose vials.
- ***Rollout during weekends***: Weekend schedules for vaccinations were made available to avoid conflicts with the parents' work schedule during the weekdays.
- ***Testimonials from health experts, DOH officials, and parents***: Testimonials from health experts, DOH officials, and parents who got their children vaccinated were published to encourage other parents to get their children vaccinated.
- ***Allowing use of alternatives for required documents****:* Requirements prior to vaccination were tweaked during the rollout to facilitate compliance. As an alternative to proof of affiliation, certification from the barangay captain was also accepted. A different guardian (e.g. neighbor, grandparent) was allowed to take the child to the vaccination site provided that they present an informed consent form and authorization note signed by the parent.
- ***Hiring of additional pharmacist****:* To prevent errors in the preparation and administration, additional pharmacists were hired to ensure dedicated roles wherein the pharmacist is in charge of dilution and preparation of the vaccine while the vaccinator is solely in charge of administration.
- ***Timely strategic planning and forecasting with implementers***: NVOC is constantly communicating with implementers (CHDs, LGUs and PHOs) to provide guidance in managing the distribution of vaccines given the limited vaccine supply and delays in delivery. Updates on new arrivals of supply and match with stocks on hand to consider possible readjustment of implementation are regularly provided. Alternative scenarios for adjusted vaccine arrival are also explained.

NVOC Plans for the Implementation of Moderna as a primary series vaccine for children ages 6-11 years old

For the implementation of *Moderna as a primary series* in children ages 6 to 11 years old, the NVOC expressed that this roll out will be implemented similar to the ongoing 5-11 years old vaccination. Roll-out for this age group will still require informed consent of the guardian or parent and assent from the vaccine recipient. Vaccination will be school-based and will also include outreach and fixed vaccination

		strategies. On the other hand, the following are the **foreseen implementation barriers** in the previous pediatric vaccination roll-out that may be considered in the upcoming *Moderna* vaccination in children ages 6-11 years and the proposed measures to manage them: ● ***Confusion in half dose administration:*** Implementation of half dose of *Moderna* in children aged 6 to 11 years old may pose confusion in dose administration of the vaccine. However, the current experience in administering half dose of *Moderna* as a booster in adults may lessen half dose administration difficulties. ● ***Inadvertent vaccine administration:*** Currently**,** *Pfizer-BioNTech* and *Moderna* are the vaccines included in the roll-out to the pediatric population with *Pfizer-BioNTech* being administered in children ages 5 to 17 years old and *Moderna* being administered in adolescents aged 12 to 17 years old. Should *Moderna* be implemented in children aged 6 to 11 years old, there will be a slight difference in their target pediatric population (i.e., *Moderna* for 6 to 17; Pfizer for 5 to 17). Inadvertent administration might occur. ○ *Management measures:* Separate schedules for each vaccine brand will be implemented to prevent administration errors. ● ***Vaccine hesitancy (for vaccine brands for the pediatric population):*** Previous controversy with the Dengvaxia vaccine as well as anti-vaccination groups contributed to the challenges in pediatric vaccination roll out. ○ *Management measures:* Implementers plan to produce more public-friendly and easy to understand information materials. NVOC also publishes testimonials from health experts, DOH officials, and parents who got their children vaccinated to encourage other parents to get their children vaccinated. **HTAC Judgment:** The challenges noted in the COVID-19 vaccine implementation for the pediatric population ages 5 to 11 years old can be mitigated and addressed. The best practices and control measures shall be noted and carried over in the upcoming implementation of Moderna roll-out in the 6 to 11 year old population.	
	Is Moderna for pediatric vaccination (6 to 11 years old) affordable?	According to the UNICEF COVID-19 Vaccine Market Dashboard, the price per dose of *Moderna* offered to the Philippine government is lower than the price range for which it is available among middle income countries (i.e., USD 21.50 to 40.00). According to the NVOC target population and considering the current vaccination coverage as of 24 April 2022, about 10.50 million children ages 6 to 11 years old are still unvaccinated. According to the DPCB, existing doses of *Moderna* will be used to vaccinate this population thus there will be no additional procurement for this roll out. To determine if there will be enough stocks to be used for the rollout, an analysis was done to compute the remaining stocks using the vaccine supply inventory (as of 22 April 2022) and vaccination coverage report (as of 24 April 2022) which are parts of the National Government procurement portfolio as disclosed by the NVOC. In this analysis, a total of six (6) scenarios were simulated to determine the **remaining supply** of *Moderna* vaccines after the implementation of all planned vaccination strategies, or the number of *Moderna* vaccines **needed to be procured** to achieve the target for all planned vaccination strategies (in case the scenario analysis shows that no supplies will be left available), depending on the following: (1) vaccine coverage (varied to incorporate ideal versus actual coverage based on willingness to be vaccinated); and the (2) population and vaccination strategy that will be prioritized for the consumption of the current supply of COVID-19 vaccines. Scenarios 1a and 1b assumes 100% target vaccination coverage, while scenarios 2a, 2b assumes a relatively lower vaccine coverage at 80.41% for all vaccination strategies (referred from the highest achieved coverage among the vaccination policies across all age groups) to reflect actual coverage based on willingness to be vaccinated. Meanwhile, scenarios 3a and 3b also use the 80.41% coverage but compounds it across vaccination strategies i.e. 80.41% of the target population will receive a primary series and 80.41% of the primary series recipient will receive the first booster dose and so on. Scenarios 1a, 2a, and 3a assume that vaccinees aged 12 years and older will be prioritized to receive the existing COVID-19 vaccine supplies, while scenarios 1b, 2b, and 3b assume that children aged 5 to 11 years old will be prioritized to receive the existing COVID-19 vaccine supplies. Details of the analysis are found in Appendix 5. Table.3.1. Description of scenarios used for the comparison of current existing stocks and expected demand of COVID-19 vaccines for the adolescent and adult vaccination policies.	Affordability will be measured using the sufficiency of the allocated amount to achieve vaccination targets. **The vaccine unit cost is comparable with those in other ASEAN countries.* **The vaccine implementation cost is a reasonable and acceptable allocation of resources.*

Scenario	*Assumed vaccine coverage*	*Population and vaccination strategy that will be prioritized for the current supply of COVID-19 vaccines*
1a	100% for all vaccination strategies	Adult Primary Adult 1st booster/3rd dose Adult 2nd booster/4th dose Adolescents Primary Adolescents Booster/3rd Dose
1b	100% for all vaccination strategies	Children 6 to 11 years Primary
2a	80.41% for all vaccination strategies	Adult Primary Adult 1st booster/3rd dose Adult 2nd booster/4th dose Adolescents Primary Adolescents Booster/3rd Dose
2b	80.41% for all vaccination strategies	Children 6 to 11 years Primary
3a	80.41% for each succeeding vaccination policy of the vaccination series (i.e., 80.41% will receive the primary series and 80.41% who received the primary series will receive the booster; and 80.41% of the target population for 2nd boosters)	Adult Primary Adult 1st booster/3rd dose Adult 2nd booster/4th dose Adolescents Primary Adolescents Booster/3rd Dose
3b	80.41% for each succeeding vaccination policy of the vaccination series (i.e.,80.41% will receive the primary series and 80.41% who received the primary series will receive the booster; and 80.41% of the target population for 2nd boosters)	Children 6 to 11 years Primary

Key Findings of the analysis comparing the supply and demand

- Based on the costing analysis, if current *Moderna* stocks will be prioritized for the primary vaccination of the pediatric 5-11 years old population [Scenarios 1b, 2b, 3b], then current stocks are enough and no additional procurement of *Moderna* will be necessary to cover the primary vaccination for children aged 6 to 11 years old**.** However, if the current stocks of *Moderna* will be prioritized for the remaining doses needed for the adolescent and adult vaccination policies (i.e., primary series, booster vaccination, and 2nd booster/4th dose) [Scenarios 1a, 2a, 3a], then additional procurement of COVID-19 vaccines [*Moderna, Pfizer-BioNTech* (10 mcg), or mix of both assuming only these brands will be allowed and implemented for pediatric use] is necessary in order to meet the demands for primary series of the remaining unvaccinated children aged 6 to 11 years old.

- For scenario 1a and 1b which assumes 100% coverage for all vaccination strategies, regardless of the prioritized population, additional doses of *Moderna* and other vaccine brands for vaccination policies need to be procured. For scenario 1a which prioritized adolescents and adult population for the existing *Moderna* supplies, existing supply of all COVID-19 vaccines will not be enough even for these populations; thus there is a need to procure for adolescents, adults, and children. Meanwhile, for scenario 1b which prioritized the children for the existing *Moderna* supplies, the additional COVID-19 vaccine doses needed to be procured will only be for the adolescent and adult population.

- For scenarios 2a and 3a which assume lower vaccination coverage but will prioritize existing stocks of *Moderna* and other vaccine brands for vaccination policies for the adolescent and adult populations, there will be a surplus of COVID-19 vaccines of other brands,

while *Moderna* and *Pfizer-BioNTech* will all be consumed. In addition, for children aged 6 to 11 years old, assuming that only *Moderna* and *Pfizer-BioNTech* will be allowed and implemented for use, additional procurement of these vaccines will still be needed to meet the demand for primary series of unvaccinated children aged 6 to 11 years old.

- For scenarios 2b and 3b which assume lower vaccination coverage but will prioritize existing stocks of *Moderna* for children aged 6 to 11 years old, there will be a surplus of *Moderna* on top of existing stocks of other brands of COVID-19 vaccines for the adolescent and adult population. Although the excess supplies may be used in future vaccination policies, these will not be enough to cover the entirety of any of the pediatric, adolescent or adult population.

Table.3.2. Summary of results of the costing scenarios comparing the current existing stocks and the expected demand of COVID-19 vaccines for the pediatric, adolescent and adult vaccination policies.[See Annex 3 for the detailed calculations]

Scenario	Availability of *Moderna* COVID-19 vaccines to cover the pediatric population	Excess supply of COVID-19 vaccines	Additional COVID-19 vaccines needed to be procured
1a	Supply of *Moderna* is **NOT enough** to cover the target pediatric population for primary vaccinations.	No excess supply of vaccines for all vaccination policies (children, adolescent, adult)	Need to procure for all vaccines for vaccination policies for **adults, adolescents, and children**
1b	Supply of *Moderna* is **enough** to cover the target pediatric population for primary vaccination.	Excess supply of vaccines for children which can be allotted for adolescent and adult vaccination strategies No excess supply of vaccines for all vaccination policies for adolescent and adult population	No additional procurement needed for **children** Need to procure for all vaccines for vaccination policies for the **adult** and **adolescent** population
2a	Supply of *Moderna* is **NOT enough** to cover the target pediatric population for primary vaccination	With an excess supply of vaccines for the adolescent and adult population. No excess supply of vaccines for all vaccination policies for children.	No additional procurement needed for the **adolescents and adults** Need to procure for primary series of **children**
2b	Supply of *Moderna* is **enough** to cover the target pediatric population for primary vaccination	Excess supply of vaccines for children which can be allotted for adolescent and adult vaccination strategies Excess supply of vaccines for all vaccination policies for adolescent and adult population	No additional procurement needed for **adult, adolescent, and children**
3a	Supply of *Moderna* is **NOT enough** to cover the target pediatric population for primary vaccination	Excess supply of vaccines for the adolescent and adult population. No excess supply of vaccines for all vaccination policies for children.	No additional procurement needed for the **adolescents and adults** Need to procure for primary series of **children**
3b	Supply of *Moderna* is **enough** to cover the target pediatric population for primary vaccination	Excess supply of vaccines for children which can be allotted for adolescent and adult vaccination strategies	No additional procurement needed for **adult, adolescent, and children**

		<table><tr><td></td><td></td><td>Excess supply of vaccines for all vaccination policies for adolescent and adult population</td><td></td></tr></table> Further, a costing analysis was conducted for the implementation of primary series vaccination of children ages 6 to 11 years using *Moderna* for scenarios where existing stocks will be used for adult vaccination policies, which may require procurement of doses of *Moderna* (details of the costing assumptions and scenarios are provided in Appendix 5). The unit cost of the vaccine used in the analysis was based on the latest price offered to the government as disclosed by the DOH Bureau of International Health Cooperation (BIHC). The additional cost of consumables were sourced from the DOH National Immunization Program (NIP) in January of 2022, while the updated cost of logistics for both vaccines and consumables were consulted with the DOH Supply Chain Management Services (SCMS). The operations (i.e. human resource mobilization and training cost) will not incur additional cost to the DOH since COVID-19 vaccinations are now incorporated in the routine vaccination programs of the LGUs. For scenarios prioritizing the vaccination policies for the adolescent and adult population that will need procurement of *Moderna* vaccines for children, the total cost of the primary series vaccination roll-out with *Moderna* for pediatric vaccinees will range from Php **6.06 B to Php 9.17 B,** depending on the target vaccine coverage scenario. **HTAC Judgment:** Based on the costing analysis, *Moderna* is considered affordable.	
	What are the budget implications of using Moderna in children ages 6 to 11 years old?	Based on the calculations, no additional procurement will be necessary to cover the primary series vaccination for children aged 6 to 11 years if the existing stocks of *Moderna* will be prioritized for this vaccination policy over the vaccination policies of adolescents and adults. The total cost of the primary series vaccination roll-out with *Moderna* for 10,503,096 pediatric vaccinees (100% of the PSA population) ages 6 to 11 years old is at around Php **10.77 B**. Details of this costing analysis (e.g., inputs) are provided in Appendix 5. The actual proportionality of the budgetary requirement of using *Moderna* as primary series to the target number of doses cannot be computed since it is affected by factors such as the brands that will be available in the facilities (supply side) and actual brand preference of the vaccinees among the available brand supplies at the facility (demand side). **HTAC Judgment:** HTAC is not recommending procurement of *Moderna* in the implementation of the primary vaccination series for children aged 6 to 11 years old because of its higher cost relative to a similar product in the market. However, at this time that the existing supplies will be used for the implementation of the primary vaccination series for children aged 6 to 11 years old, there will be no additional cost to the government if *Moderna* is used.	Proportionality of the size of the population to be vaccinated versus the cost. The share of the cost to implement the COVID-19 vaccine within the total vaccination budget is not too disproportionate to the share of the population to be vaccinated using the said vaccine in the total population to be vaccinated.
	Does Moderna represent good value for money in terms of preventing COVID-19 morbidity and mortality in the pediatric population (6 to 11 years old)?	*Moderna* in a primary series for children ages 6 to 11 years old represents good value for money in terms of reducing the incidence of symptomatic COVID-19 based on an immunobridging Phase II/III trial. Rough estimates of the vaccination cost per case averted are high. However, HTAC has bases to conclude that these will be offset by averted healthcare costs (i.e., total COVID-19-related PhilHealth claims, out of pocket expenditures), economic gains (i.e., in terms of recovery in GDP), and social gains. **HTAC Judgment:** The HTAC deems that the health, economic, and social benefits of using *Moderna* in children 6 to 11 years old can outweigh the cost of its introduction and implementation.	The HTAC deems that the health, economic, and social benefits of the vaccination program outweigh the costs. The vaccine is a cost-effective/ efficient allocation of resources.

CRITERION 4

4. Household Financial Impact

Will vaccination with Moderna for children ages 6 to 11 years reduce or not add further to the out-of-pocket expenses of Filipino households?

As mandated by Philhealth Circular 2021-0014 and Philhealth Circular 2020-0009, the following benefit packages with corresponding case rates related to COVID-19 are available for the general population. Note that these also cover the pediatric population as there are no separate benefit packages for this subgroup:

1. Home Isolation Package for asymptomatic and mild cases (C19HI) = Php 5,917.00
2. Community Isolation Package for symptomatic and confirmed cases (C19CI): Case rate= Php 22,499.00
3. Admissions that were referred to the Community Isolation Units (CIU) from higher level facilities for step-down care (C19IS) = Php 22,499.00
4. Mild COVID-19 pneumonia for elderly and with comorbidities (C19IP1): Case rate= Php 43,997.00
5. Moderate COVID-19 pneumonia (C19IP2): Case rate= Php 143, 267.00
6. Severe COVID-19 pneumonia (C19IP3): Case rate= Php 333,519.00
7. Critical COVID-19 pneumonia (C19IP4): Case rate= Php 786,384.00

Meanwhile, children of healthcare workers are eligible to the full financial risk protection (i.e. no cap in terms of case rate) for hospitalization due to COVID-19 (C19FRP) as mandated by PhilHealth Circular 2020-0011.

Based on Philhealth data, there were a total of 321 hospitalization claims for the pediatric population ages 6 to 11 years old from the first quarter of 2020 to the second quarter of 2022. The table below summarizes the cost of COVID-19 illness (inferred from total hospital bill) and out-of-pocket expenses incurred by patients belonging to the pediatric population 6 to 11 years old at different levels of severity. The average financial coverage for hospitalization across the different levels of severity ranged from 70.64% (mild COVID-19) to 83.59% (severe COVID-19).

Table.4.1. Philhealth data on COVID-19 Hospitalization Costs and Claims in the Pediatric Population 6-11 years old

Severity *[Benefit package]*	**Case Rate**	**Total Number of Paid Claims**	**Total Hospital Cost**		**Out-of-Pocket Payment**		**Average % of Financial Coverage** *[proportion of financial coverage out of the total bill]*
			Range of Hospitalization Cost *[PHP]*	**Median Hospitalization Cost** *[PHP]*	**Range of Out-of-Pocket Payment** *[PHP]*	**Median Out-of-Pocket Payment** *[PHP]*	
Mild COVID-19 *[C19IP1]*	₱ 43,997.00	136	₱3,764.50 to ₱386,039.35	₱57,107.76	₱0.00 to ₱342,042.35	₱13,110.76	70.64%
Moderate COVID-19 *[C19IP2]*	₱ 143, 267.00	150	₱0.00 to ₱1,192,054.04	₱146,002.44	₱0.00 to ₱1,048,787.04	₱10,149.33	81.07%
Severe COVID-19 *[C19IP3]*	₱ 333,519.00	22	₱102,775.70 to ₱1,345,333.85	₱335,963.50	₱0.00 to ₱1,011,814.85	₱6,420.21	83.59%
Critical COVID-19 *[C19IP4]*	₱ 786,384.00	7	₱346,460.30 to ₱1,564,458.38	₱512,117.50	₱0.00 to ₱778,074.38	₱0.00	82.85%
Full Financial Risk Protection *[C19FRP]*	No cap	6	₱21,300.68 to ₱3,236,743.07	₱133,806.06	₱0.00 to ₱1,095,392.87	₱42,912.50	73.76%

The adoption of the vaccine can reduce out-of-pocket spending of individuals and families due to averted COVID-19 disease and/or hospitalization.

		Meanwhile, there were a total of 449 community isolation claims recorded by PhilHealth for asymptomatic and mild cases for pediatric patients 6 to 11 years old, using the same dataset. The median cost of community isolation based on bills recorded was ₱22,254.68 while the median claims cost was at Php 22,449.00. Therefore, the median out-of-pocket expenses for community isolation is at Php 0.00 (Php 0.00 to Php ₱310,778.92). The mean financial coverage is at 95.53%. The out-of-pocket expenses reflected above only represents medical costs shouldered by patients and their families. Other non-medical costs such as transportation, food, and productivity loss of the parents of these children were not incorporated due to lack of data. In addition, the above costing of household costs did not include the treatment/ management cost of other family members within the household who had likely contracted COVID-19. Considering these other incurred costs shouldered by households further increases the potential of the vaccine to reduce out-of-pocket expenses of households due to COVID-19. **HTAC Judgment**: Based on current evidence, *Moderna* has the potential to reduce out-of-pocket expenses due to averted costs of isolation and treatment of mild, moderate, and severe COVID-19 in the pediatric population ages 6 to 11 years old.	
CRITERION 5			
5. Social Impact	*Does vaccination with Moderna for children ages 6 to 11 years possess the characteristics desired by key stakeholders (i.e., policy- and decision-makers, health workers, program managers and/or implementers, patient groups, CSOs, communities, general public)?* • *Safety* • *Efficacy* • *Transparency in the regulatory/approval process and information on the vaccines* • *Availability* • *Potential for high and equitable coverage* • *Ease in logistical and*	Based on the results of the focus group discussions conducted in the context of vaccinating the adult population by the HTAC among *healthcare workers, patient groups, civil society organizations and community leaders* from low- and high-prevalence areas, the results from the deliberations in congressional inquiries on the COVID-19 vaccination roadmap, public hearings, and consultations with government decision-makers and implementers, the following are the important and desirable attributes of COVID-19 vaccines and the corresponding evidence for *Moderna as a primary series vaccine* specifically in children ages 6 to 11 years old. 1) **Safe and efficacious** - Evidence: Currently, there is inconclusive evidence on the clinical efficacy of a second dose of *Moderna* (50 mcg per dose) in children aged 6 to 11 years old. On the basis of the same Phase II/III trial which showed immunobridging results with young adults aged 18 to 25 years old from a Phase III trial (COVE), the immune response in children aged 5 to 11 years old passed the non-inferiority criteria according to the US FDA. The efficacy of 2 doses of 50 mcg of *Moderna* in children is then inferred by successful immunobridging to data in young adults who had received the 100-µg dose level of the vaccine in the COVE trial, which had shown high efficacy (Creech et al.). - The efficacy and effectiveness of *Moderna* in children 6 to 11 years old against VoCs cannot be assessed due to lack of evidence. However, immunogenicity from the Phase II/III trial showed a similar immune response to VoCs compared to adults (Creech et al., Girard et al., Bartch et al.). One study showed that there is a consistent loss of binding to Omicron in both children and adults. Based on trial and real world evidence, short-term safety of *Moderna* (50 mcg/dose) among children ages 6-11 years is acceptable. No case of myocarditis was reported in the clinical trial. Further follow-up data are needed to establish longer-term safety. Further evidence is needed to establish the vaccine's effectiveness in preventing COVID-19 in children ages 6-11 years old in the real world setting. 2) Underwent a **transparent regulatory process** of being evaluated and approved by health authorities - Evidence: *Moderna* underwent the usual regulatory process of the FDA Philippines. The Philippine FDA updated the EUA for the vaccine on 20 May 2022 to expand its use among children 6 to 11 years old. 3) **Potential for high and equitable coverage across the population** - Evidence: *Moderna* has a lower storage temperature requirement for long term storage which makes distribution more difficult. However, given that *Moderna* can be stored in 2-8 degrees Celsius for 30 days which is available in most RHUs, which facilitates storage at the vaccinations site. - The Philippine Pediatric Society (PPS) and Pediatric Infectious Disease Society of the Philippines (PIDSP) released a joint position	The vaccine possesses all or most of the characteristics desired by key stakeholders Qualitative responses will contextualize the Filipino experience and may impact on implementation strategy

	implementation requirements • *Cost-efficiency to the government* • *Public acceptability* • *Availability of mechanisms to compensate vaccine recipients for any untoward event following vaccination* • *Appropriateness of the vaccine to special at-risk groups and patients with comorbidities*	statement (published 4 February 2022) reiterating its recommendation last 17 January 2022 for the vaccination of children ages 5 to 11 years old against COVID-19. The PPS and PIDSP did not recommend any specific brand for this vaccination strategy. The updated statement emphasizes the risk of children from acquiring severe illnesses due to COVID-19 such as Multisystem Inflammatory Syndrome in Children (MIS-C) and post-COVID-19 conditions such as "long COVID". Prioritization of children in the age group who have comorbidities and children of healthcare frontliners was also recommended. 4) **Ease in logistics and administration** - Evidence: *Moderna* once thawed can be stored at temperatures of 2°C to 8°C for 30 days which can be catered by most RHUs. However, *Moderna* has a lower storage temperature requirement for a longer period of time (-25°C to -15°C: up to 9 months) and requires more stringent logistical requirements which are available in limited areas and RHUs. Based on previous vaccination roll-out, the NVOC implements measures and ensures proper training and preparation prior to the rollout of *Moderna* to mitigate challenges in logistics. ***NVOC Plans for the Implementation of Moderna for children ages 6-11 years old*** For the implementation of *Moderna* in children ages 6 to 11 years old, the NVOC expressed that this roll out will be implemented similar to the ongoing 5-11 years old vaccination. Roll-out for this age group will still require informed consent of the guardian or parent and assent from the vaccine recipient. Vaccination will be school-based and will also include outreach and fixed vaccination strategies. ***Best Practices in the Current Implementation of COVID-19 Vaccination for Children (5 to 11 years old)*** • ***Available and accessible vaccination sites:*** Vaccinations were conducted at the mega-sites such as malls, temporary posts, mobile buses, and house visits to accommodate the vaccinees and their guardians, to ensure that standard public health measures are maintained, and to actually encourage children, especially the younger ones, to get vaccination. These strategies also allowed parents and children to be vaccinated together at one site. • ***Utilizing festive strategies in vaccination sites:*** Regional offices noted the use of mascots and playgrounds to encourage children to get vaccinated. Incentives such as food and free accommodations to park were also distributed. • ***Vaccination rollout during weekends:*** Vaccination was extended until weekends in some vaccination sites to accommodate children with parents/guardians that are unavailable during weekdays. • ***Coordination with the Department of Education (DepEd):*** Schools were also used as vaccination sites for children. DepEd's plan to conduct face-to-face classes encouraged parents to have their children vaccinated for safety reasons. • ***Availability of guidelines:*** According to regional offices, implementers find it helpful that the pediatric vaccination guidelines were readily available which contributed to the clarity of implementation and a well prepared roll-out. • ***Transparent reporting of AEFIs:*** According to NVOC, side effects for the pediatric population were less as compared to adults and these AEFIs were documented and properly reported. • ***Presence of medical specialists at the vaccination site:*** Aside from the usual AEFI teams present in vaccination sites, the on-site supervision of pediatricians and allergologists during vaccination of the pediatric population facilitated the timely and appropriate management of AEFIs (vs the on-call visit of the specialists for the adult vaccination). • ***Confidence to get vaccinated***: Unlike adults, children are used to getting vaccinated as they are the target population of routine EPI immunization. • ***Confidence of healthcare workers:*** Healthcare workers were also more confident because of their experience with the adolescent roll-out. • ***Experts, healthcare workers and LGUs encouraging the vaccination of the pediatric population***: Testimonials from experts and DOH personnel who got their children vaccinated were used to promote pediatric vaccination efforts. Ceremonial giving of vaccines to pediatric family members of health workers and local chief executives were conducted to encourage parents to have their children vaccinated as well. The pediatric society such as the Philippine Pediatric Society (PPS) and private sectors also supported the roll-out. • ***Stringent documentary requirements:*** Documentation from the accompanying parent/guardian was required to provide proof of affiliation to the pediatric vaccinee. Obtaining informed consent from the parent/guardian and assent from the child were strictly implemented prior to vaccination.	

- ***Stringent screening process:*** The rollout for the pediatric population was tailored to ensure that vaccinees with comorbidities, including those with a history of conditions that were considered AESIs associated with vaccination (e.g. myocarditis and pericarditis) are identified and educated properly.

On the other hand, the following are the **foreseen implementation barriers** in the previous pediatric vaccination roll-out that may be considered in the upcoming *Moderna* vaccination in children ages 6-11 years and the **proposed measures** to manage them:

- ***Confusion in half dose administration:*** Implementation of half dose of *Moderna* in children aged 6 to 11 years old may pose confusion in dose administration of the vaccine. However, the current experience in administering half dose of *Moderna* as a booster in adults may lessen half dose administration difficulties
- ***Inadvertent vaccine administration:*** Currently**,** *Pfizer-BioNTech* and *Moderna* are the vaccines included in the roll-out to the pediatric population with *Pfizer-BioNTech* being administered in children ages 5 to 17 years old and *Moderna* being administered in adolescents aged 12 to 17 years old. Should *Moderna* be implemented in children aged 6 to 11 years old, there will be a slight difference in their target pediatric population. Inadvertent administration might occur.
  - *Management measures:* Separate schedules for each vaccine brand will be implemented to prevent administration errors.
- ***Vaccine hesitancy:*** Previous controversy with the Dengvaxia vaccine as well as anti-vaccination groups contributed to the challenges in pediatric vaccination roll out.
  - *Management measures:* Implementers plan to produce more public-friendly and easy to understand information materials. NVOC also publishes testimonials from health experts, DOH officials, and parents who got their children vaccinated to encourage other parents to get their children vaccinated.

5) **Cost-effective**

- Evidence:The health, economic, and social benefits of implementing the vaccination program with primary series of *Moderna* in children aged 6 to 11 years old outweigh the negative impact of COVID-19 such as deaths due to COVID-19, medical costs, social disruption, and unprecedented challenges in the health system. Its cost is within the range of current new vaccines that are also part of the National Immunization Program (NIP).

6) **Public acceptability**

- Evidence:

General Public's Acceptability of Administration of COVID-19 Vaccination for the Pediatric Population *Global and Regional View of Vaccine Acceptance and Related Behaviors (Johns Hopkins Center for Communication Programs, WHO GOARN)*

A living global survey being conducted by Johns Hopkins Center for Communication Programs and the World Health Organization's (WHO) Global Outbreak Alert and Response Network (GOARN) on the acceptability of pediatric vaccination across different countries (which included data specific to the Philippines) was found. The survey asks parents of children under 18 years old if they will choose to vaccinate their oldest child under age 18 when eligible.

Table.5.1. Responses from Filipino parents surveyed over time showed the following rates of willingness:

Time Period	% Willingness to definitely or probably allow their children to get vaccinated once they are eligible for COVID-19 vaccine
January 1-15, 2022	81%
January 16-31, 2022	76%
February 1-15, 2022	71%
February 16-28, 2022	72%

March 1-15, 2022	65%
March 16-31, 2022	66%
April 1-15, 2022	70%
April 16-30, 2022	70%
May 1-15, 2022	67%

Starting January 2022, the percentage of vaccine willingness ranged from 65% to 81%. This vaccine willingness was generally lower compared to Filipino parents' willingness to get their oldest child vaccinated last 2021 which ranged from 82% to 91%.

Meanwhile, a study by Skjefte et al. (2021) on COVID-19 vaccine acceptance among pregnant women (n=5,282) and mothers of children younger than 18 years old (n=12,562) among 16 countries revealed that vaccine acceptance was generally highest in the Philippines, India, and sampled countries in Latin America. Specifically, mothers and mothers-to-be in the Philippines are very likely to get their child vaccinated if the vaccine has an efficacy of 90%.

The COVID-19 pandemic in children and young people during 2020-2021: A complex discussion on vaccination (Rudan et al. 2021)
An editorial paper by Rudan et al. published on 25 December 2021, presented the complex debate on the COVID-19 vaccination of children and young people.

As cited in Rudan et al. (2021) the European Center for Disease Prevention and Control suggested that decisions on pediatric vaccination should consider the vaccine uptake in older age groups, the incidence of COVID-19 in the general population, and practical issues concerning availability and access to vaccines globally.

Meanwhile, Rudan stated that proponents of mass vaccination in children suggest that vaccinating children will improve children and adolescent's well-being and mental health allowing them to resume education and social interactions which are important to their development. They suggested that this will also prevent the pediatric population from becoming a pocket of the population wherein COVID-19 would continue to circulate freely leading to mutation of the virus into new variants.

Rudan et al.'s paper also highlighted that ethical concerns would need to be carefully documented and addressed. Notable concerns include specific situations and needs of children with developmental disorders and chronic conditions, health inequities and vaccine hesitancy. Vaccination willingness and hesitancy should first be assessed before attempting vaccination. The following surveys were conducted among caregivers of minors to assess caregiver's willingness to vaccinate their minor children.

Table.5.2. Surveys on Willingness to Vaccinate Children Cited in Rudan et al. 2021

Author (Year)	Study Period	Country	Survey participants	Vaccination willingness and hesitancy
Goldman et al. (2020)	26 to 31 March 2020	US, Canada, Israel, Japan, Spain , and Switzerland *COVID-19 Parental Attitude Study (COVIPAS)*	1,541 caregivers Median age of children: 7.5 years old	● Willing to vaccinate their children once vaccine is available: 65% ○ Most common reason for willingness: Protection of their child (62%) ○ Most common reason for hesitancy:

					Vaccine's novelty (52%)
		Teasdale et al. (2021)	9 March, 2021 to 2 April 2021	US *(nationwide)*	2,074 parents/ caregivers of children ≤12 years	● Willing to vaccinate their children once vaccine is available: 49% ○ Primary reasons for hesitancy: Safety and lack of need for vaccines ● Lower income and less education were associated with greater parental vaccine hesitancy.
		Ruggiero et al. (2021)	November 2020 to January 2021	US *(nationwide)*	427 parents of children (aged 1–18 years; 34.1% have children ages 4 to 8 yo; 25.1% have children ages 8 to 12 yo)	● Willing to vaccinate their children: 49.45%
		Szilagyi et al. (2021)	February to March 2021	US *(nationwide)*	1,745 parents of children (<5 years: 24%, 5 to 10 years: 36%, 11 to 18 years: 40%)	● Likelihood of child COVID-19 vaccination: ○ Very likely : 28% ■ High among parents of older children ■ High among parents with bachelor's degree or higher education ■ Among those had already received or were likely to receive a COVID-19 vaccine ■ Had Democratic affiliation ○ Somewhat likely : 18% ○ Somewhat unlikely: 9% ○ Very Unlikely: 33% ○ Unsure 12% ● Concerns were centered around vaccine safety and side effects
		Teasdale et al. (2021)	9 March to 11 April 2021	US *(New York City)*	1,119 primary caregivers of a child ≤ 12 years of age	● Plans to vaccinate their children (≤12 years): 61.9% ● Unsure: 23.3% ● No plans to vaccinate their children:14.8% ○ Most common reason for hesitancy: Vaccine safety and effectiveness (81.2%) ● Vaccinated parents and parents intended to get themselves vaccinated: 67.3% ○ Pediatric vaccine hesitancy is strongly tied to parental vaccine hesitancy.
		Zhang et al. (2020)	1 to 7 September 2020	China	2,053 factory workers, guardians of	● Willing to vaccinate their children: 72.6%

			children <18 years old	
Yang et al (2021)	7 to 19 February 2020	China	12,872 questionnaires guardians of children aged 0–6 years old	● Willing to vaccinate their children: 70.87%
Wan et al. (2021)	December 2020 to February 2021	China	468 parents of 3–6 year old children	● Willing to vaccinate their children: 86.75% ○ Most common reason for willingness: Worried about their children being infected in the future (78.57%) ● Hesitant to vaccinate their children: 13.25% ○ Most common reason for hesitancy: Did not believe in the safety of vaccines (67.74%)
Feng et al. (2021)	30 November, 2020 to 31 January 2021	China	3,703 guardians of children <18 years old	● Willing to vaccinate their children: 84.0%
Wang et al. (2021)	September 2020 to April 2021	China	914 guardians of children with special disease (congenital heart disease, preterm birth, others) Mean age of children: 1.4 years old *Face-to-face questionnaire interview*	● Willing to vaccinate their children with special diseases: 49.9%
Brandstetter et al. (2021)	5 to 28 May 2020	Europe *(Data used is from KUNO-Kids health study which is a multipurpose birth cohort study situated in Germany)*	612 parents with children ages 1.5 - 5 years old	● Intended to vaccinate their children: 51% ● Parents intended to get themselves vaccinated: 58%
Montalti et al. (2021)	December 2020 to January 2021	Italy	5054 parents/ guardians of children aged <18 years old	● Willing to vaccinate their children: 60.4% ● Considering: 29.6% ● Hesitant to vaccinate their children: 9.9%
Choi et al. (2021)	25 May to 3 June 2021	South Korea	226 parents of children ≤18 years old and 117 children 10 -18 years old	● Children willing to get vaccinated: 49.6% ● Parents willing to have their children be vaccinated: 64.2% ○ Factors associated intention to vaccinate: ■ High confidence in the safety of the vaccines

				■ Willingness to vaccinate themselves ■ Awareness of the need to vaccinate children against COVID-19

Social impact of the COVID-19 pandemic and pandemic response on children and adolescents

According to the WHO Interim Statement on COVID-19 vaccination for children and adolescents (24 November 2021), vaccinating children may help minimize school disruptions. Prolonged school closure can result in education loss and exacerbation of pre-existing inequalities and marginalization of learning. This also leads to loss of access to a wide range of school-provided services which include school meals, health, nutrition, water, sanitation and hygiene.

Further, social isolation places children at risk of :

- potential for predatory behavior from adults related to spending more time online
- cyberbullying from other children
- disruption in physical activities and routines
- increased emotional distress
- mental health problems

In general, vaccination for children and adolescents may contribute in advancing highly valued societal goals as maintaining education for school-aged children should be a priority during this pandemic. Being able to attend school is important for the well-being and life prospects of children as well as for parental participation in the economy.

7) Availability of mechanisms to manage any untoward serious adverse reactions following vaccination

- Evidence: Evidence: Republic Act 11525 or the COVID-19 Vaccination Program Act of 2021 establishes the COVID-19 National Vaccine Indemnity Fund to provide funds and authorize PhilHealth to pay compensation to any person inoculated through the vaccination program, in the case of death and permanent disability. In response to RA 11525, PhilHealth released PhilHealth Circular No. 2021-0007 last 17 June 2021. The circular, otherwise known as the "Implementing Guidelines on the Coverage of COVID-19 Vaccine Injury due to Serious Adverse Effects (SAEs) following immunization resulting in hospitalization, permanent disability or death under the COVID-19 National Vaccine Indemnity Fund (The COVID-19 Vaccine Injury Compensation Package), aims to provide coverage for cases of hospital confinement, permanent disability, or death due to SAEs from the use of COVID-19 vaccines administered through the COVID-19 vaccination program.

8) Appropriateness of the vaccine in special at-risk groups and patients with comorbidities

- Evidence: The results from the Phase II/III clinical trial (NCT04796896 or KidCOVE) enrolled children ages 6 months to 11 years of age. However, to date, only the interim results for the 6-11 year age group with a short follow up period (median follow up of 51 days after the second dose) have been published. *Moderna* (50 mcg/dose) which showed immunobridging results with young adults aged 18 to 25 years old from a Phase III trial (COVE), the immune response in children aged 5 to 11 years old passed the non-inferiority criteria according to the US FDA. Eligible participants in this trial included healthy children and those with chronic diseases (eg., asthma, diabetes mellitus, cystic fibrosis, human immunodeficiency virus [HIV] infection). However, as specified in the protocol, disease should be stable which is defined as no change in their status or in the medications required to control them in the 6 months prior to screening visit. No sub-analysis was performed specific to children with comorbidities and in special at-risk groups. It is noted from selective scoping that an additional dose of *Moderna* (50 mcg) in children ages 6 to 11 years old was recommended in immunocompromised children by NRAs and MOHs (EMA, Australia ATAGI and Canada NACI).
- The updated WHO interim recommendations (19 November 2021) reflected the extension of the population eligible to receive *Moderna* to include children aged 12 to 17 years old. However, as of writing the latest WHO SAGE interim recommendation for *Moderna* (23 February 2022), the WHO does not recommend *Moderna* for children ages 6 to 11 years old.
- Further, in the updated WHO SAGE Roadmap for prioritizing uses of COVID-19 vaccines, the WHO recommends vaccinating children only when high vaccine coverage (i.e., 40 to 70%) both for primary series and booster vaccination has been achieved in higher priority-use

<table>
<tr><td></td><td></td><td>groups (i.e., older adults, healthcare workers, immunocompromised persons, adults with comorbidities, pregnant women, teachers and other essential workers, disadvantaged sociodemographic subpopulations at higher risk of severe COVID-19, and remaining adults). The WHO also recommended for countries to consider the individual and population benefits of vaccinating this age group based on country-specific epidemiologic and social context.

HTAC Judgment: On the basis of short-term outcomes, Moderna possesses most of the characteristics desired by key stakeholders for its use among children aged 6 to 11 years old. Given that there are no local studies to determine acceptability of vaccination among children 6 to 11 years old, HTAC can only recognize the social impact of vaccination in this age group in terms of supporting the attainment of occupations of children which include social learning achieved through peer interaction. This could also contribute to the improvement of the quality of life within the households when caregivers of children are relieved of the anxiety of dealing with the consequences of COVID-19 infection and sequelae.</td><td></td></tr>
<tr><td colspan="4">CRITERION 6</td></tr>
<tr><td>6. Responsiveness to equity</td><td>How will Moderna and its use impact pre-COVID-19 and COVID-generated health and socioeconomic inequities?

Which groups might be unfairly disadvantaged, in relation to the COVID-19 disease burden and delivery of Moderna?</td><td>As of this writing, there are three vaccines with EUA from the Philippine FDA for children aged 6 to 11 years old - Pfizer-BioNTech, CoronaVac and Moderna. Of these three vaccines, only Pfizer-BioNTech is currently rolled out by the National Vaccines Operations Center (NVOC) which also includes 5-year old children.

Moderna once thawed can be stored at temperatures of 2°C to 8°C for 30 days which can be catered by most RHUs. However, Moderna has a lower storage temperature requirement for a longer period of time (-25°C to -15°C: up to 9 months) and requires more stringent logistical requirements which are available in limited areas and RHUs.

As of 20 June 2022, 3,251,129 individuals (23.21%) out of the 14,007,875 individuals currently eligible among children ages 5 to 11 years old have already received a full regimen of COVID-19 vaccines (i.e., Pfizer-BioNTech).

The overall vaccination coverage in the Philippines for the primary series and booster dose, by age group as of 20 June 2022, are as follows:

<table>
<tr><th rowspan="2">WHO Prioritization groups</th><th rowspan="2">Age Group</th><th colspan="3">Philippine COVID-19 Vaccination Coverage</th></tr>
<tr><th>Primary Series</th><th>1st Booster Dose</th><th>2nd Booster Dose</th></tr>
<tr><td></td><td>Across all age groups</td><td>77.94%</td><td>16.42%</td><td>0.91%</td></tr>
<tr><td rowspan="2">Highest to Medium Priority Use</td><td>18-59 years old</td><td>90.76%</td><td>22.49%</td><td>0.71%</td></tr>
<tr><td>60 years and older</td><td>77.48%</td><td>25.63%</td><td>4.31%</td></tr>
<tr><td rowspan="2">Medium to Lowest Priority Use</td><td>5 to 11 years old</td><td>23.21%</td><td>0% (not yet eligible)</td><td>0% (not yet eligible)</td></tr>
<tr><td>12 to 17 years old</td><td>82.83%</td><td>0% (not yet eligible)</td><td>0% (not yet eligible)</td></tr>
</table>

In terms of coverage by regions, there is an observed disparity in the vaccination coverage for primary series and first booster dose. As of 20 June 2022, NCR reported the highest vaccination coverage for the primary series at 107.84% (12,282,151 out of 11,389,534) and for the first booster dose at 36.24% (4,127,419 out of 11,389,534). The higher number of vaccinated individuals versus the targets is likely due to individuals who are residents of nearby provinces who were vaccinated in NCR. Meanwhile, the Bangsamoro Autonomous Region in Muslim Mindanao (BARMM) recorded the lowest vaccination coverage for the primary series at 33.27% (1,169,857 out of 3,516,278), and for the first booster dose at 3.64% (128,035 out of 3,516,278). Vaccination coverage of primary series (i.e., 63.02% to 85.32%) in other regions were considered high to</td><td>Ideally, health interventions can be fairly adopted and distributed/ implemented for eligible populations without aggravating existing health inequities especially for vulnerable sectors of our society.</td></tr>
</table>

		very high (i.e. 40% and above) based on WHO vaccination coverage classification; while the vaccination coverage for the first booster dose for other regions (i.e., 7.50% to 21.39%) remains to be low to moderate (i.e. 0 to <40%) based on WHO vaccination coverage classification. According to the revised WHO SAGE Roadmap for prioritizing uses of COVID-19 vaccines (21 January 2022), vaccination in medium priority-use groups which includes children and adolescents with comorbidities should only be initiated when at least moderate vaccination coverage has been achieved for both primary series and booster doses of higher priority-use groups (i.e, 10-40%). Meanwhile, for lowest priority-use groups which include healthy children and adolescents, vaccination should be initiated when at least high vaccination coverage (40-70%) has been achieved for both primary series and booster doses of higher priority-use groups. Both of these conditions have already been met as of the latest vaccination coverage. **HTAC Judgment:** Pediatric vaccination poses inherent challenges because of pre-existing inequities in the healthcare system including: - inequitable access to information in order for parents to provide informed consent and for children to provide assent; - inequitable capacity (e.g., pediatric specialists) to diagnose co-morbidities in children, especially for marginalized sectors, - inaccessibility to vaccination sites and inadequate logistical capacity among geographically isolated and disadvantaged areas (GIDAs); - general deficiency in infrastructure, transportation modalities, and health human resources across the different areas in the country. These challenges can be translated to opportunities to improve the vaccination coverage of priority groups (e.g., encouraging unvaccinated parents and/or guardians accompanying pediatric vaccinees to get vaccinated as well, improvement of information, education, and communication (IEC) campaigns, and increasing vaccination sites by deploying mobile vaccination teams and utilization of established public-private partnerships with malls, pharmacies, churches, gyms and other establishments as vaccination sites among others). The HTAC reiterates the importance of the following measures in the success of the implementation of COVID-19 vaccination for children ages 6 to 11 years old: ● emphasize the importance of free and prior informed consent ● emphasize the need for supporting the autonomy of parents, guardians, and the pediatric population towards vaccination ● ensure that IEC and other vaccination-related documents are accessible and comprehensible (i.e., translated into the local language of the target population) Pediatric vaccination shall be rolled out following the country's prioritization criteria, cognizant of the following: ● burden of COVID-19 in the pediatric population, especially those with comorbidities; ● sufficient supply to cover the pediatric population in addition to the higher priority-use groups Given that *Moderna* can be stored in 2-8 degrees Celsius for 30 days which is available in most RHUs, this does not aggravate health inequities. However, in terms of long term storage, *Moderna* still requires a lower temperature which might pose difficulties in distribution from warehouse to RHUs.	

References

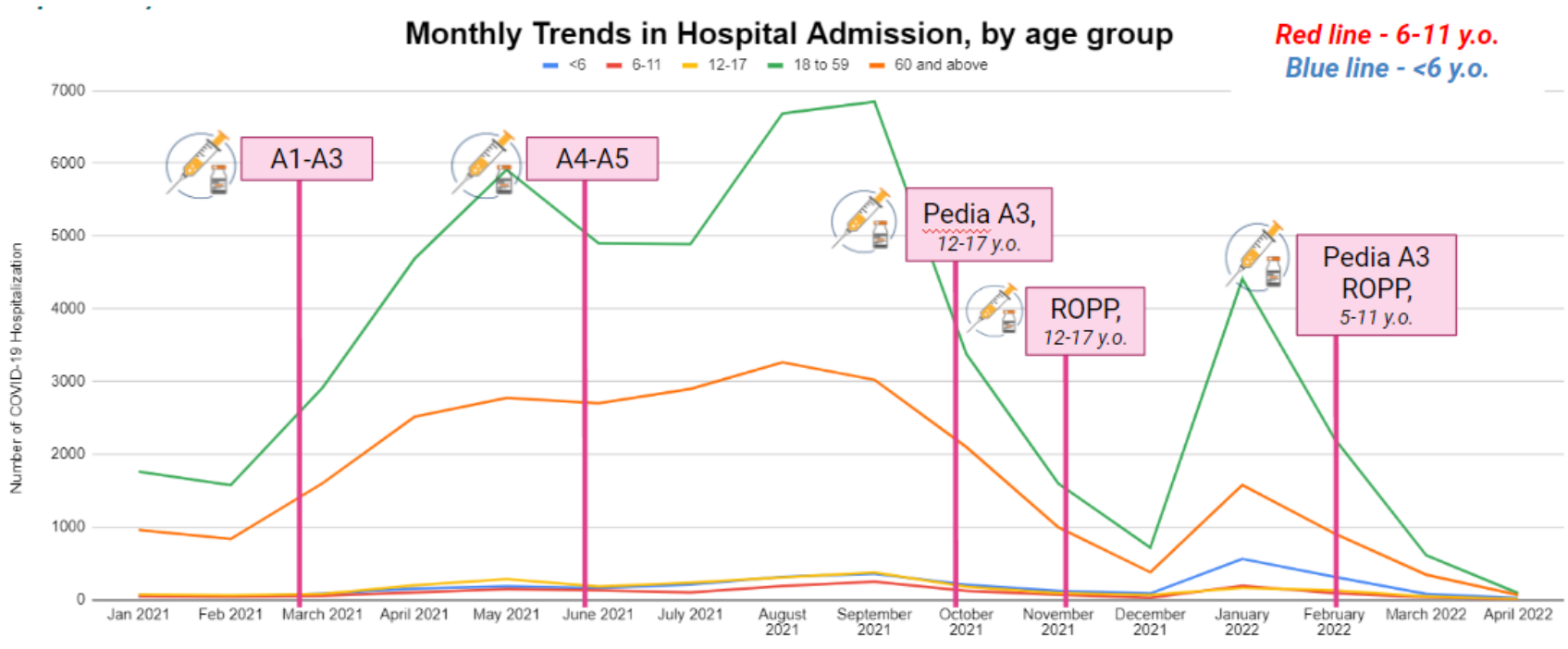
1. Chen, F., Tian, Y., Zhang, L., & Shi, Y. (2022). The role of children in household transmission of COVID-19: a systematic review and meta-analysis. International Journal of Infectious Diseases, 122, 266–275. https://doi.org/10.1016/j.ijid.2022.05.016
2. Clarke KE, Jones JM, Deng Y, et al. Seroprevalence of Infection-Induced SARS-CoV-2 Antibodies — United States, September 2021–February 2022. MMWR Morb Mortal Wkly Rep 2022;71:606-608. DOI: http://dx.doi.org/10.15585/mmwr.mm7117e3
3. COVID-19- Associated Hospitalization Surveillance Network (COVID-NET). (2022). COVID-NET: A Weekly Summary of US COVID-19 Hospitalization Data. Retrieved 15 June 2022 from https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html
4. COVID-NMA. A living mapping and living systematic review of COVID-19 trials. https://covid-nma.com/vaccines/vaccines . Accessed 17 June 2022.
5. Creech, C.B., Anderson, V., Berthaud, I, Yildirim, A.M., Atz, I., Melendez Baez, D., Finkelstein, P. ,..Schnyder Ghamloush, S. (2022). Evaluation of mRNA-1273 Covid-19 Vaccine in Children 6 to 11 Years of Age. *The New England Journal of Medicine*, 386(21). doi: 10.1056/NEJMoa2203315.
6. Department of Health (2022). COVID-19 DOH Data Drop. Retrieved 17 June, 2022 from https://drive.google.com/drive/folders/1ZPPcVU4M7T-dtRyUceb0pMAd8ickYf8o
7. Department of Health Epidemiology Bureau. (25 May 2022). Comorbidities Data COVID-19 Cases and Epidemiological Data on Variants of Concern among the Pediatric Population (6 to 11 years old). [Personal communication]
8. European Medicines Agency (2022). EudraVigilance for COVID-19 mRNA vaccine Moderna (CX-024414). Retrieved 30 May 2022 from https://dap.ema.europa.eu/analytics/saw.dll?PortalPages
9. Fleming-Dutra, K. (14 June 2022). COVID-19 epidemiology in children and adolescents ages 6 months - 17 years. *Presentation.* Retrieved June 15, 2022 from https://www.fda.gov/media/159222/download
10. Food and Drug Administration Philippines. (2021). Emergency Use Authorization (EMA) for COVID-19 mRNA Vaccine (Nucleoside Modified) (COVID-19 Vaccine Moderna), Zuellig Pharma Corporation. Retrieved 27 May 2022 from https://drive.google.com/file/d/12W3_j5jDZzc8EfMtcZzxqwL4brwQT7XD/view
11. Food and Drug Administration Philippines. (2021). Fourth Amendment to the Emergency Use Authorization (EUA) for COVID-19 mRNA Vaccine (Nucleoside Modified) Dispersion for Injection [SPIKEVAX], Zuellig Pharma Corporation. Retrieved on 20 March 2022 from https://www.fda.gov.ph/wp-content/uploads/2022/01/EUA-Fourth-Amendment-Moderna-Booster-w.pdf
12. Food and Drug Administration Philippines. (2022). Sixth Amendment to the Emergency Use Authorization (EUA) for COVID-19 mRNA Vaccine (Nucleoside Modified) Dispersion for Injection [SPIKEVAX], Zuellig Pharma Corporation. Retrieved on XX June 2022 from https://drive.google.com/file/d/1Y32hNqawAPiWz2fj8MY3BgJNQvkxpwlo/view
13. Gaythorpe, K.A., Bhatia, S., Mangal, T., Unwin. J.T.m Imai, N., Cuomo-Dannenburg, G., Walters, C.E., Jauneikaite, E., Bayley, H., Kont, M.D., Mousa, A., Whittles, L.K., Riley, S. & Gerguson, N.F. (2021). Children's role in the COVID-19 pandemic-: a systmatic review of early surveillance data on susceptibility, severity, and transmissiblity. Retrieved 24 June 2022 from https://www.nature.com/articles/s41598-021-92500-9
14. Girard, B., Tomassini, J.E., Deng, W., Maglinao, M., Zhou H., Figueroa, A., Ghamloush, S.S., Montefiori, D.C., Das, R., Pajon, R. (2022). mRNA-1273 Vaccine-elicited Neutralization of SARS-CoV-2 Omicron in Adolescents and Children. Retrieved 26 May 2022 from https://pubmed.ncbi.nlm.nih.gov/35118475/
15. Government of Canada (2022). Reported side effects following COVID-19 vaccination in Canada. Retrieved 30 May 2022 from https://health-infobase.canada.ca/covid-19/vaccine-safety/#a3
16. Hoste, L., Van Paemel, R. & Haerynck, F. Multisystem inflammatory syndrome in children related to COVID-19: a systematic review. Eur J Pediatr 180, 2019–2034 (2021). https://doi.org/10.1007/s00431-021-03993-5
17. International Vaccine Access Center (IVAC), Johns Hopkins Bloomberg School of Public Health. (2022). Results of COVID-19 Vaccine Effectiveness Studies: An Ongoing Systematic Review. Retrieved 17 June 2022 from https://view-hub.org/sites/default/files/2022-01/COVID19%20Vaccine%20Effectiveness%20Transmission%20Studies%20-%20Summary%20Tables_20220113.pdf
18. Kitano, T., Kitano, M., Krueger, C., Jamal, H., al Rawahi, H., Lee-Krueger, R., Sun, R. D., Isabel, S., García-Ascaso, M. T., Hibino, H., Camara, B., Isabel, M., Cho, L., Groves, H. E., Piché-Renaud, P. P., Kossov, M., Kou, I., Jon, I., Blanchard, A. C., . . . Morris, S. K. (2021). The differential impact of pediatric COVID-19 between high-income countries and low- and middle-income countries: A systematic review of fatality and ICU admission in children worldwide. *PLOS ONE*, *16*(1), e0246326. https://doi.org/10.1371/journal.pone.0246326
19. Johns Hopkins Center for Communication Programs (2022). Global and Regional View of Vaccine Acceptance and Related Behaviors. https://covidbehaviors.org/. Accessed: 9 June 2022
20. Lopes, L., Stokes, M., & 2021. (2021, August 19). KFF COVID-19 Vaccine Monitor: The Impact Of The Coronavirus Pandemic On The Wellbeing Of Parents And Children. KFF. https://www.kff.org/coronavirus-covid-19/poll-finding/kff-covid-19-vaccine-monitor-the-impact-of-the-coronavirus-pandemic-on-the-wellbeing-of-parents-and-children/
21. Marks KJ, Whitaker M, Anglin O, et al. Hospitalizations of Children and Adolescents with Laboratory-Confirmed COVID-19 — COVID-NET, 14 States, July 2021–January 2022. MMWR Morb Mortal Wkly Rep 2022;71:271–278. DOI: http://dx.doi.org/10.15585/mmwr.mm7107e4
22. McLean, H. Q., Grijalva, C. G., Hanson, K. E., Zhu, Y., Deyoe, J. E., Meece, J. K., Halasa, N. B., Chappell, J. D., Mellis, A. M., Reed, C., Belongia, E. A., Talbot, H. K., & Rolfes, M. A. (2022a). Household Transmission and Clinical Features of SARS-CoV-2 Infections. Pediatrics, 149(3). https://doi.org/10.1542/peds.2021-054178
23. ModernaTX, Inc (2022). Bimonthly Summary Safert Report (BSSR). [Personal communications]
24. Nachega, J. B., Sam-Agudu, N. A., Machekano, R. N., Rabie, H., van der Zalm, M. M., Redfern, A., Dramowski, A., O'Connell, N., Pipo, M. T., Tshilanda, M. B., Byamungu, L. N., Masekela, R., Jeena, P. M., Pillay, A., Gachuno, O. W., Kinuthia, J., Ishoso, D. K., Amoako, E., Agyare, E., . . . Adirieje, C. (2022). Assessment of Clinical Outcomes Among Children and Adolescents Hospitalized With COVID-19 in 6 Sub-Saharan African Countries. *JAMA Pediatrics*. https://doi.org/10.1001/jamapediatrics.2021.6436
25. National Vaccine Operations Center (2022). COVID-19 vaccination coverage as of 30 May 2022. [Personal communication].
26. Nyberg, T., Ferguson, N.M., Nash, S.G., Webster, H.H., Flaxman, S., Andrews, N., Hinsley, W., … Thelwall, S. (2022). Comparative analysis of the risks of hospitalisation and death associated with SARS-CoV-2 omicron (B.1.1.529) and delta (B.1.617.2) variants in England: a cohort study. *The Lancet.* Retrieved 24 March 2022 from https://doi.org/10.1016/S0140-6736(22)00462-7
27. PhilHealth (2020). PhilHealth Circular 2020-0009: Benefit packages for inpatient care of probable and confirmed COVID-19 developing severe illness/outcomes. Retrieved 1 June 2022 from: https://www.philhealth.gov.ph/circulars/2020/circ2020-0009.pdf
28. PhilHealth (2020). PhilHealth Circular 2020-0012: Guidelines on the COVID-19 Community Isolation Benefit Package (CCIBP). Retrieved 1 June 2022 from: https://www.philhealth.gov.ph/circulars/2020/circ2020-0012.pdf

29. PhilHealth (2021). PhilHealth Circular 2021-0007: Implementing Guidelines on the Coverage of COVID-19 Vaccine Injury due to Serious Adverse Effects (SAEs) Following Immunization Resulting in Hospitalization, Permanent Disability, or Death under the COVID-19 National Vaccine Indemnity Fund (The COVID-19 Vaccine Injury Compensation Package). Retrieved 1 June 2022 from: https://www.philhealth.gov.ph/circulars/2021/circ2021-0007.pdf
30. PhilHealth (2021). PhilHealth Circular 2021-0014: COVID-19 Home Isolation Benefit Package (CHIBP). Retrieved 1 June 2022 2022 from: https://www.philhealth.gov.ph/circulars/2021/circ2021-0014.pdf
31. Philippine Pediatric Society (PPS) and Pediatric Infectious Disease Society of the Philippines (PIDSP). (2022). PPS-PIDSP Statement on COVID-19 Vaccination in Children. Retrieved from 9 June 2022 http://www.pidsphil.org/home/wp-content/uploads/2022/02/1643963420943449.pdf
32. Philippine Pediatric Society (PPS) and Pediatric Infectious Disease Society of the Philippines (PIDSP). (2022). PPS-PIDSP Joint Position Statement on COVID-19 Vaccination for Children ages 5 to 11 years old. Retrieved from 9 June 2022 http://www.pidsphil.org/home/wp-content/uploads/2022/01/1642312046361888.pdf
33. Pediatric COVID-19 Working Group of the Pediatric Infectious Disease Society of the Philippines (PIDSP). (May 26, 2022). Surveillance and Analysis of COVID-19 in Children Nationwide - SALVACION Registry Interim Data Analysis. [Personal communication]
34. Rudan, I., Adeloye, D. Katikreffi, V., Murray, J., Simpson, C., Shah, S.A., Robertson, C., Sheikh, A. (2021). The COVID-19 pandemic in children and young people during 2020-2021: a complex discussion on vaccination. Retrieved 16 March 2022 from https://jogh.org/2021/jogh-11-01011
35. Skjefte, M., Ngirbabul, M. , Akeju, O., Escudero, D., Hernandez-Diaz, S., Wyszynski, D.F., Wu, J.W. (2021). COVID-19 vaccine acceptance among pregnant women and mothers of young children: results of a survey in 16 countries. Eur J Epidemiol. 36(2), 197-211. Retrieved 9 June 2022 from https://doi.org/10.1007/s10654-021-00728-6.
36. Stein, M., Ashkenazi-Hoffnung, L., Greenberg, D., Dalal, I., Livni, G., Chapnick, G., … Grossman, Z. (2022). The Burden of COVID-19 in Children and Its Prevention by Vaccination: A Joint Statement of the Israeli Pediatric Association and the Israeli Society for Pediatric Infectious Diseases. Vaccines, 10(1), 81. doi:10.3390/vaccines10010081 Retrieved from https://www.mdpi.com/2076-393X/10/1/81
37. The City Paper News Article. (2021) Retrieved from: https://thecitypaperbogota.com/news/colombia-starts-covid-19-vaccination-campaign-for-children-age-3-or-older/28389
38. UK Health Security Agency. (31 December 2021). SARS-CoV-2 variants of concern and variants under investigation in England Technical briefing: Update on hospitalisation and vaccine effectiveness for Omicron VOC-21NOV-01 (B.1.1.529). Retrieved from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1045619/Technical-Briefing-31-Dec-2021-Omicron_severity_update.pdf
39. United Nations Children's Fund. (2022). COVID-19 Vaccine Market Dashboard. Retrieved 25 May 2022 from: https://www.unicef.org/supply/covid-19-vaccine-market-dashboard
40. Vaccines and Related Biological Products Advisory Committee (2022). FDA Briefing Document EUA amendment request for use of the Moderna COVID-19 vaccine in children 6 months through 17 years of age. Retrieved 15 June 2022 from https://www.fda.gov/media/159189/download
41. Woodruff, R.C., Campbell, A.P., Taylor, C.A., Chai, S.J., Kawasaki, B., Meek, J., Anderson, E.J., Weigel, A., Monroe, M.L., Reeg, L., Bye, E., Sosin, D., Muse, A., Bennett, N.M.m Billing, L.M., Sutton, M., Talbot, H.K., McCaffrey, K., Pham, K….McMorrow, M. (2021). Risk factors for severe COVID-19 in children. Retrieved 29 June 2022 from https://publications.aap.org/pediatrics/article/149/1/e2021053418/183463/Risk-Factors-for-Severe-COVID-19-in-Children?autologincheck=redirected
42. World Health Organization (2021). Interim statement on COVID-19 vaccination for children and adolescents. Retrieved from 9 June 2022 from: https://www.who.int/news/item/24-11-2021-interim-statement-on-covid-19-vaccination-for-children-and-adolescents
43. World Health Organization (2021). Interim recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19. Retrieved on 27 May 2022 from https://apps.who.int/iris/bitstream/handle/10665/338862/WHO-2019-nCoV-vaccines-SAGE_recommendation-mRNA-1273-2021.1-eng.pdf?sequence=5&isAllowed=y
44. World Health Organization (2021). Interim recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19. Retrieved from 1 June 2022 from https://apps.who.int/iris/bitstream/handle/10665/349300/WHO-2019-nCoV-vaccines-SAGE-recommendation-mRNA-1273-2021.3-eng.pdf?sequence=5&isAllowed=y
45. World Health Organization. (2022). COVID-19 questions and answers: Who should get vaccinated against COVID-19?. Retrieved 25 May 2022 from https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-(covid-19)-vaccines
46. World Health Organization (2022). COVID-19 advice for the public: Getting vaccinated. Retrieved 16 March 2022 from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines/advice
47. World Health Organization. (2022). Weekly epidemiological update on COVID-19 - 12 June 2022. Retrieved 17 June 2022 from https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---15-june-2022
48. World Health Organization. (2022).WHO SAGE Roadmap for prioritizing uses of COVID-19 vaccines. Retrieved 16 March 2022 from https://www.who.int/publications/i/item/who-sage-roadmap-for-prioritizing-uses-of-covid-19-vaccines

Acknowledgements

- DOH-Bureau of International Health Cooperation (BIHC)
- DOH- Centers for Health Development (CHD)
- DOH-Disease Prevention and Control Bureau (DPCB)
- DOH-Epidemiology Bureau (EB)
- DOH-Health Promotion Bureau (HPB)
- DOH- National Immunization Program (NIP)
- DOH- Supply Chain Management Service (SCMS)
- Department of Foreign Affairs (DFA)
- Department of Finance (DOF)
- National COVID-19 Vaccination Operations Center (NVOC)
- Philippine Living Clinical Practice Guidelines Group (LCPG Group)
- Salvacion Gatchalian Registry
- Philippine Insurance Corporation (PhilHealth)

Appendix 1: Trends in Hospitalization in the Philippines, by age group



Appendix 2A: Risk of Bias (RoB) Assessment Methodology

RoB for RCTs

The Cochrane RoB1 tool was used in the RoB of the included RCTs. Therefore, the overall RoB rating of RCTs corresponds to its overall rating using the Cochrane ROB1 tool. Figure A4.1 below summarized the ROB1 method on assessment of overall RoB.

Figure A4.1. *Possible approach for summary assessments of the risk of bias for each important outcome (across domains) within and across studies (Higgins, et al., 2017)*

OVERALL Risk of bias of the study	Interpretation	RoB rating per domain
Low risk of bias	Plausible bias unlikely to seriously alter the results	Low risk of bias for all key domains
Unclear risk of bias	Plausible bias that raises some doubt about the results	Unclear risk of bias for one or more key domains
High risk of bias	Plausible bias that seriously weakens confidence in the results	High risk of bias for one or more key domains

RoB for Observational studies

Meanwhile, the appraisal of real world evidence (i.e., observational studies) is composed of two parts as adopted from the LCPG assessment method: (1) Cochrane RoB1 tool as (2) some additional questions to appraise an additional domain - control of prespecified confounders by LCPG, namely, age, exposure risk, and comorbidities.

DESCRIPTION OF THE TOOLS AND RATING ALGORITHM

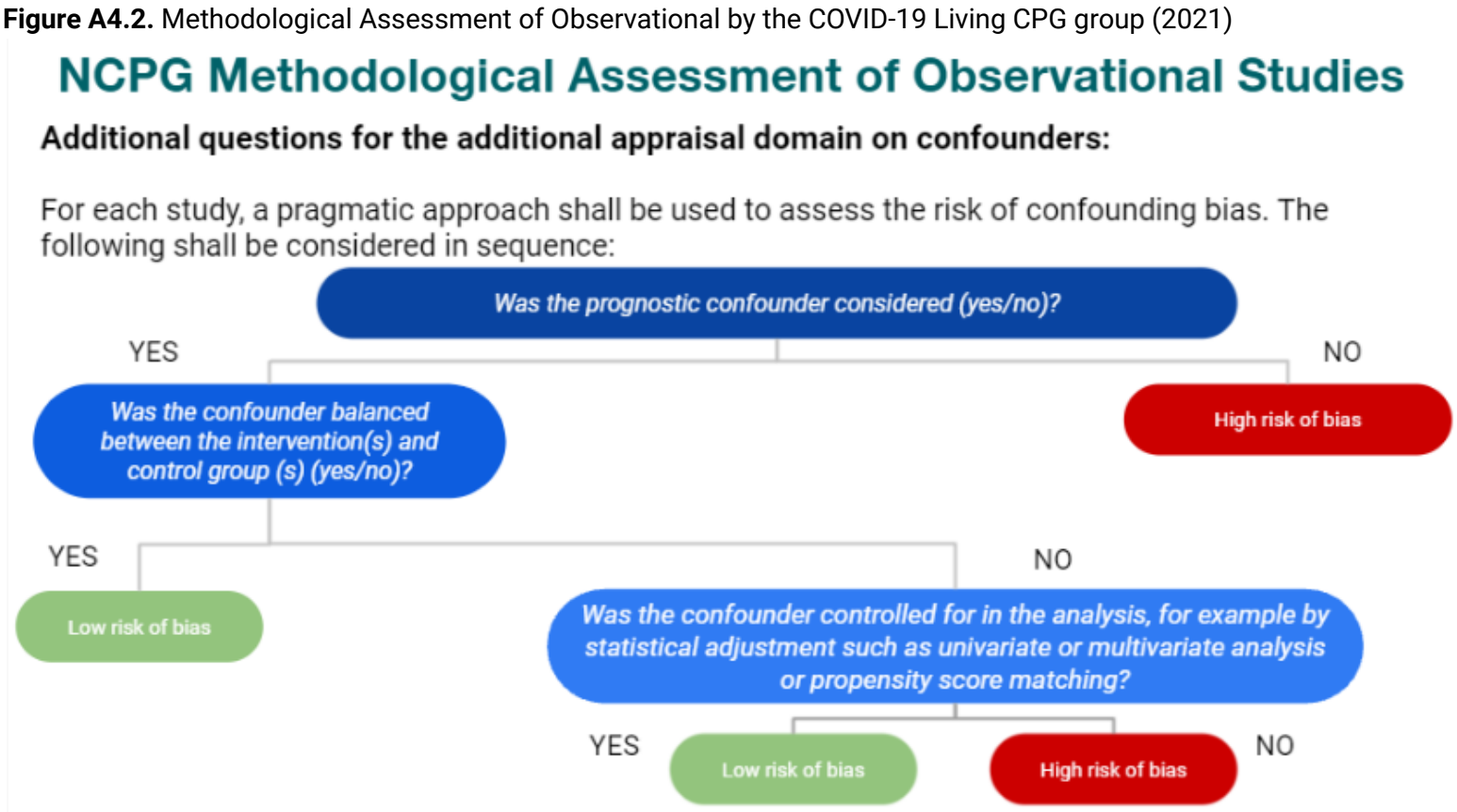
Part 1: Cochrane RoB1 Tool

- please refer to algorithm in the RoB for RCT section

Part 2: Control for Confounders

- please refer to Figure A4.2 below for the set of questions in assessment control for confounders.

Figure A4.2. Methodological Assessment of Observational by the COVID-19 Living CPG group (2021)



Note: Assessment for control of confounders should be performed for each pre-specified confounding variable (i.e., age, comorbidities, exposure risk).

ALGORITHM FOR OVERALL CONTROL OF CONFOUNDERS for RWE

Confounder Variables Controlled (i.e. age, comorbidity, exposure risk)	Overall RoB rating for Control on Confounders
3 Low RoB, 0 High RoB	**LOW**
2 Low RoB, 1 High RoB *	**LOW ***
1 Low RoB, 2 High RoB	**HIGH**
0 Low RoB, 3 High RoB	**HIGH**

** Note: LCPG follows the majority rather than the worst case for the assessment of overall RoB on confounders.*

OVERALL RoB RATING ALGORITHM FOR EACH RWE STUDY

Overall RoB rating in RoB1 tool	Overall RoB rating for Control on	Overall RoB of RWE

	Confounders	
High	High	Very Serious
High	Low	Serious
Unclear	High	Very Serious
Unclear	Low	Serious
Low	High	Serious
Low	Low	Not Serious

Appendix 2B: Risk of Bias (RoB) Assessment Results

Appraisal of RCTs

RCTs on efficacy outcome

Author Year	Study Design	ROB1 Domains							
		Randomization	Allocation concealment	Blinding of Participants	Blinding of Investigators	Blinding of Assessors	Incomplete Outcome Data	Selective reporting	OVERALL ROB1 ASSESSMENT
VRBPAC 2022 [published] *efficacy after the second dose*	Phase II/III RCT	Low	Low	Low	Low	Low	High	Low	**HIGH**
Creech et al. 2022 [unpublished] *efficacy after the first dose*	Phase II/III RCT	Low	Low	Low	Low	Low	Low	Low	**LOW**

RCTs on safety outcomes

Author Year	Study Design	ROB1 Domains							
		Randomization	Allocation concealment	Blinding of Participants	Blinding of Investigators	Blinding of Assessors	Incomplete Outcome Data	Selective reporting	OVERALL ROB1 ASSESSMENT
VRBPAC 2022 [published] *long term safety*	Phase II/III RCT	Low	Low	Low	Low	Low	High	Low	**HIGH**
VRBPAC 2022 [published] *short term safety*	Phase II/III RCT	Low	Low	Low	Low	Low	Low	Low	**LOW**

Appraisal of observational Studies

Observational studies on effectiveness outcomes

No identified real world studies

Observational studies on safety outcomes

Not applicable

Appendix 3: GRADE TABLE for the Assessment of Phase II/III RCT (Creech et al. and VRBPAC Briefing Document) [published]

Efficacy Outcome		Quality Assessment					Summary of Findings			Certainty	IMPORTANCE
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vaccine n/N (%)	Control n/N (%)	Vaccine Efficacy (CI)		
EFFICACY OUTCOMES											
Symptomatic COVID-19 (CDC definition) *at least 14 days after the 2nd dose* *VRBPAC briefing document*	1 RCT	Serious (Short follow up period)	Cannot be assessed	Not Serious	Very Serious (Wide CI, crosses null, unclear if powered to conclude for efficacy/descriptive analysis only)	None	3/2,644 (0.1%)	4/853 (0.5%)	VE: 76.8 (-37.3 to 96.6)	⊕◯◯◯ **VERY LOW**	CRITICAL
Symptomatic COVID-19 (COVE trial definition) *at least 14 days after the 2nd dose* *VRBPAC briefing document*	1 RCT	Serious (Short follow up period)	Cannot be assessed	Not Serious	Very Serious (Wide CI, crosses null, unclear if powered to conclude for efficacy/descriptive analysis only)	None	3/2,644 (0.1%)	3/853 (0.4%)	VE: 69.0 (-131.4 to 95.8)	⊕◯◯◯ **VERY LOW**	CRITICAL
Any SARS-CoV-2 infection *at least 14 days after the 2nd dose* *VRBPAC briefing document*	1 RCT	Serious (Short follow up period)	Cannot be assessed	Not Serious	Very Serious (Wide CI, unclear if powered to conclude for efficacy/descriptive analysis only)	None	12/2,644 (0.5%)	14/853 (1.6%)	VE: 73.6 (38.5 to 88.8)	⊕◯◯◯ **VERY LOW**	IMPORTANT
Asymptomatic COVID-19 *at least 14 days after the 2nd dose* *VRBPAC briefing document*	1 RCT	Serious (Short follow up period)	Cannot be assessed	Not Serious	Very Serious (Wide CI, unclear if powered to conclude for efficacy/descriptive analysis only)	None	9/2,644 (0.3%)	10/853 (1.2%)	VE: 72.3 (24.1 to 90.0)	⊕◯◯◯ **VERY LOW**	IMPORTANT
Symptomatic COVID-19 (CDC definition) *at least 14 days after the 1st dose* *Creech et al.*	1 RCT	Not serious	Cannot be assessed	Not serious	Serious (unclear if powered to conclude for efficacy/descriptive analysis only)	None	7/2,687 (0.3%)	18/880 (2.1%)	VE: 88.0 (70.0 to 95.8)	⊕⊕⊕◯ **MODERATE**	IMPORTANT
Symptomatic COVID-19 (COVE trial definition) *at least 14 days after the 1st*	1 RCT	Not serious	Cannot be assessed	Not serious	Serious (unclear if powered to conclude for efficacy/descriptive analysis only)	None	4/2,687 (0.1%)	15/880 (1.7%)	VE: 91.8 (74.2 to 98.0)	⊕⊕⊕◯ **MODERATE**	IMPORTANT

dose *Creech et al.*											
Any SARS-CoV-2 infection *at least 14 days after the 1st dose* *Creech et al.*	1 RCT	Not serious	Cannot be assessed	Not serious	Serious (unclear if powered to conclude for efficacy/descriptive analysis only)	None	34/2,687 (1.3%)	40/880 (4.6%)	VE: 74.0 (57.9 to 84.1)	⊕⊕⊕◯ **MODERATE**	IMPORTANT
Asymptomatic COVID-19 *at least 14 days after the 1st dose* *Creech et al.*	1 RCT	Not Serious	Cannot be assessed	Not Serious	Very Serious (Wide CI, unclear if powered to conclude for efficacy/descriptive analysis only)	None	22/2,687 (0.8%)	27/880 (3.1%)	VE: 62.5 (30.9 to 79.4)	⊕⊕◯◯ **LOW**	IMPORTANT
SAFETY OUTCOMES											
Serious AEs (regardless of relationship to the vaccine) *≤28 days after any dose* *VRBPAC briefing document*	1 RCT	Serious (Short follow up period)	Cannot be assessed	Not Serious	Very Serious (crosses null, wide CI)	None	6/3,007 (0.2%)	2/995 (0.2%)	RR: 0.99 (0.20 to 4.91)	⊕◯◯◯ **VERY LOW**	CRITICAL
Any systemic AE *≤ 7 days after 2nd dose* *VRBPAC briefing document*	1 RCT	Not serious	Cannot be assessed	Not serious	Not serious	None	2,335/2,988 (78.1%)	485/969 (50.1%)	RR: 1.56 (1.46 to 1.67)	⊕⊕⊕⊕ **HIGH**	IMPORTANT
Any systemic AE *≤ 7 days after 1st dose* *VRBPAC briefing document*	1 RCT	Not serious	Cannot be assessed	Not serious	Not serious	None	1,740/3,004 (57.9%)	518/993 (52.2%)	RR: 1.11 (1.04 to 1.19)	⊕⊕⊕⊕ **HIGH**	IMPORTANT
Any local AE *≤ 7 days after 2nd dose* *VRBPAC briefing document*	1 RCT	Not serious	Cannot be assessed	Not serious	Not serious	None	2,849/2,988 (95.3%)	490/969 (50.6%)	RR: 1.89 (1.77 to 2.01)	⊕⊕⊕⊕ **HIGH**	IMPORTANT
Any local AE *≤ 7 days after 1st dose* *VRBPAC briefing document*	1 RCT	Not serious	Cannot be assessed	Not serious	Not serious	None	2,814/3,004 (93.7%)	480/993 (48.3%)	RR: 1.94 (1.82 to 2.07)	⊕⊕⊕⊕ **HIGH**	IMPORTANT
Unsolicited AE (regardless of relationship to the vaccine)	1 RCT	Not Serious	Cannot be assessed	Not serious	Not serious	None	891/3,007 (29.6%)	250/995 (25.1%)	RR: 1.18 (1.05 to 1.33)	⊕⊕⊕⊕ **HIGH**	IMPORTANT

≤28 days after any dose											
Unsolicited AE (related to the vaccine) *≤28 days after any dose*	1 RCT	Not Serious	Cannot be assessed	Not serious	Serious (Wide CI)	None	319/3,007 (10.6%)	50/995 (5.0%)	RR: 2.11 (1.58 to 2.82)	⊕⊕⊕◯ **MODERATE**	IMPORTANT

Appendix 4: Costing analysis

Part A: Cost of implementing *Moderna for age group 6 to 11 years old*

In projecting the costs for implementing the COVID-19 Vaccination program in 2022 using *Moderna* for age group 6 to 11 years old, the following cost items were identified in calculating for the total resource requirement: *Moderna* and vaccine consumables; logistics (hauling and storage); and operations (mobilization and training of vaccinators). The source of these costs were derived from the DOH - Disease Prevention and Control Bureau's (DPCB) overall vaccine budget plan. Overall, the projected cost of vaccine and consumables, logistics and operations to vaccinate 10.5 million pediatric Filipinos 6 to 11 years old with *Moderna* is **Php 10.77 B**.

For the sources of cost value inputs, we used the unit cost of vaccines based on the price offered to the government (as disclosed in confidence by the DOH-BIHC). Meanwhile, the cost inputs (i.e., cost items, cost values, and resource utilization) to estimate the cost of consumables, logistics, and operations were all referenced from the DOH-NIP, and DOH-SCMS.

The paragraphs below will detail the costing calculation for cost components.

Vaccine and Consumables

The total cost of vaccines and consumables for 10.5 million pediatric Filipinos 6 to 11 years old with *Moderna* is Php 10.69 B. This amount accounts for the cost of two half doses of *Moderna* for every vaccinee, with 1% estimated wastage of vaccines, and 10% estimated wastage for vaccine consumables. Vaccine consumables include AD syringes, and safety collector boxes. As for personal protective equipment (PPE) of the vaccination team, these costs will be incurred by the LGU as this will be incorporated in their routine vaccination program.

Logistics

Included under logistics are hauling and storage costs of vaccines and consumables related to *Moderna*. Hauling cost includes the transport cost using transport/shipper boxes that can contain 10 to 560 vials each. The rental cost for these transport boxes are waived assuming that the procured transport boxes arrived last April 2022 (DOH-SCMS, 2022). Given an assumed weight of 42.9 kg per transport box sized 0.12 cubic meter containing 560 *Moderna* vials, the total cost for hauling 21 million half doses of *Moderna* by land and air is estimated at Php 49.41 M. In addition, an estimated amount of Php 32.37 M will also be incurred for the transport of vaccine consumables giving a total of Php 81.78 M for hauling. This amount includes 1% valuation cost for air transport and 0.5% valuation cost for land transport of both vaccine and consumables to the vaccination sites. For the cold-chain storage of vaccines, it is estimated to cost Php 504.00 per cubic meter per month, resulting in a total storage cost of Php 49,722.47 per month. The overall cost for logistics is estimated to be at Php 81.83 M.

Operations

Operations cost includes mobilization, hiring costs, as well as training for vaccine implementation. However, since COVID-19 Vaccination in 2022 has been incorporated in the routine immunization program of LGUs, operations costs shall be incurred by the LGU.

Table A3.1 summarizes the resource requirement costs and assumptions in the roll-out of *Moderna* for pediatric Filipinos ages 6-11 years old in the Philippines in 2022.

Table A4.1. Resource requirement costs in the roll-out of *Moderna vs Pfizer [10 mcg]* in Filipinos 6 to 11 years old in 2022

Description	Cost *Moderna* for Filipinos 6 to 11 years old	Cost of *Pfizer [10 mcg]* for Filipinos 6 to 11 years old	Assumptions/Notes	Source
Vaccine and Vaccine Consumables	**₱10,692,698,177.79**	**₱7,235,133,529.26**	For two doses, with 1% wastage for vaccines; consumables include syringes, and safety collector boxes, with 10% wastage for vaccine consumables *(estimated costs spent for the 21 million half doses that will be used in the rollout of Moderna in Filipinos 6 to 11 years old in 2022)*	DOH-BIHC, 20212 NIP, 2021
Logistics	**₱81,879,023.05**	**₱84,570,936.00**	This includes hauling and storage costs of vaccines and hauling of ancillaries.	NIP, 2021 SCMS, 2022

			(estimated costs for vaccinating 10.5 million pediatric Filipinos based on identified target for Moderna in 6-11 year-olds in 2022)	
Operations	**Php 0**		Operations cost will be incurred by the LGUs as this will be incorporated in their routine vaccination program.	DPCB
TOTAL COST	**Php 10.77 B**	**Php 7.5B**		

Acronym: **DPCB:** Disease Prevention and Control Bureau | **DOF:** Department of Finance | **NIP:** National Immunization Program | **SCMS:** Supply Chain Management Service

Part B. Costing analysis on the net supply/demand of COVID-19 vaccines based on the current vaccine supply and anticipated coverage for COVID-19 vaccination policies

In determining the remaining supplies of COVID-19 vaccines after the implementation of the different COVID-19 vaccination policies for children ages 6-11, adolescents ages 12 to 17 years, and adults ages 18 years and above, the following data were considered: 1) the current stocks of COVID-19 vaccines in the Philippines as of 22 April 2022 and, 2) the COVID-19 vaccination coverage as of 24 April 2022. The following COVID-19 vaccination policies were considered for the expected demand of COVID-19 vaccines in 2022: 1) primary series vaccination among children 5 years of age, 2) primary series vaccination among children ages 6 to 11, 3) primary series vaccination among adolescents ages 12 to 17 years, 4) booster dose/additional dose vaccination among adolescents ages 12 to 17 years, 5) primary series vaccination among adults ages 18 years and above, 6) first booster/third dose vaccination among adults 18 years and above, and 7) second booster/4th dose vaccination among HCWs, elderly, and immunocompromised population aged 18 years and older.

In this costing analysis, a total of six (6) scenarios were simulated to determine the remaining supply of vaccines after implementation of the planned vaccination strategies or the number of vaccines needed to be procured to achieve the target vaccination strategies planned, depending on the following: (1) target vaccine coverage; (2) and the population and vaccination strategy that will be prioritized for the current supply of COVID-19 vaccines.

The following target vaccine coverage scenarios were simulated:

Scenario 1: 100% vaccination coverage for all policies (i.e., 100% of the PSA population for children aged 5 to 11 years old will receive the primary series; 100% of the PSA population for adolescents will receive the primary series and booster; 100% of the PSA population for adults will receive the primary series and 1st booster/third ; and 100% of the HCWs, elderly and adult ICPs will receive the 2nd booster/4th dose)

Scenario 2: 80.41% vaccination coverage for all policies (i.e., 80.41% of the PSA population for children ages 5 to 11 years old will receive the primary series; 80.41% of the PSA population for adolescents will receive the primary series and booster; 80.41% of the PSA population for adults will receive the primary series and 1st booster/third ; and 80.41% of the HCWs, elderly and adult ICPs will receive the 2nd booster/4th dose)

Note: 80.41% was used as the reference target vaccine coverage since this is the highest coverage among the vaccination policies across all age groups (i.e., 80.41% primary series coverage among adults 18-59 years)

Scenario 3: 80.41% vaccination coverage for each succeeding vaccination policy of the vaccination series (i.e., 80.41% of the PSA population for children ages 5 to 11 years old will receive the primary series; 80.41% of the PSA population for adolescents will receive the primary series and 80.41% of adolescents who received the primary series will receive the booster; 80.41% of the PSA population for adults will receive the primary series and 80.41% of adults who received the primary series will receive the booster; and 80.41% of HCWs, elderly and adult ICPs will receive the 2nd booster/4th dose).

The data inputs used for the expected demand for all COVID-19 vaccination policies and the current supply of COVID-19 vaccines are detailed in Table A5.2 and A5.3 while the comparison of the existing supply of COVID-19 vaccines and the expected demand for vaccination policies for the pediatric, adolescent, and adult population are detailed in Tables A5.4 to A5.6.

Table A4.2**. Inventory of COVID-19 vaccines as of 22 April 2022 (NVOC, 2022)**

Brand	Inventory as of 22 April 2022
Vaccines for Individuals aged 12 years and older	
Pfizer (30ug) (for ≥12 y.o.)	29,126,652
Sinovac	8,995,838
Moderna	14,812,138
AstraZeneca	11,349,049
Sputnik	6,602,592

Janssen	5,017,319
Sinopharm	49,866
TOTAL	**75,953,454**
Vaccines for Individuals aged 5 to 11 years old only	
**Pfizer* (10ug)	**7,912,017**

Table A4.3. Expected demand for the 2022 COVID-19 vaccination policies for scenarios 1, 2, and 3 based on the vaccination coverage as of 24 April 2022 (NVOC, 2022)

Table A4.3a Expected demand for the 2022 COVID-19 vaccination policies for scenario 1

Priority Age Group	(A) Target Population (PSA population)	(B) Number of Partially Vaccinated Individuals	(C) =(B/A) *100 Coverage of Partially Vaccinated	(D) Number of Fully Vaccinated Individuals	(E)=(D/A)*100 Coverage of Fully Vaccinated	(F) Number of Individuals vaccinated with 1st Booster Dose or 3rd Dose	(G)=(F/A)*100 Coverage of 1st Booster or 3rd dose	(H)=A*100% Number of individuals expected to get primary series	(I)= A*100% Number of individuals expected to get 1st booster or 3rd dose*	(J) Eligible population for 2nd booster or 4th dose*100% **	(K)=[(H*2)-[B+(D*2)]+(I-F)+J Remaining demand (doses)
Scenario 1: Assuming vaccination coverage of 100% target PSA population for all policies											
5 years old	2,277,000	171,458	7.53%	294,189	12.92%	0	0.00%	2,277,000	0	0	3,794,165
6-11 years old	13,203,138	994,196	7.53%	1,705,846	12.92%	0	0.00%	13,203,138	0	0	22,000,388
12-17 years old	12,729,206	793,619	6.23%	9,165,902	72.01%	0	0.00%	12,729,206	12,729,206	0	19,062,195
18-59 years old (Adult Population)	61,994,737	2,765,280	4.46%	49,851,205	80.41%	10,866,223	17.53%	61,994,737	61,994,737	5,606,431	78,256,729
60 - above (Senior Population)	10,260,113	262,999	2.56%	6,658,468	64.90%	2,073,050	20.20%	10,260,113	10,260,113	8,721,357	23,848,711
TOTAL for individuals aged 12 and above	84,984,056	3,821,898	4.50%	65,675,575	77.28%	12,939,273	15.23%	84,984,056	84,984,056	14,327,788	121,167,635
TOTAL for all populations	100,464,194	4,987,552	4.96%	67,675,609	67.36%	12,939,273	12.88%	100,464,194	84,984,056	14,327,788	146,962,188

*As of writing, only individuals aged 18 years and older are eligible for a 1st booster/3rd dose
**As of writing, only HCWs, elderly, and immunocompetent populations are eligible for a 2nd booster/4th dose

Table A4.3b Expected demand for the 2022 COVID-19 vaccination policies for scenario 2

Priority Age Group	(A) Target Population (PSA population)	(B) Number of Partially Vaccinated Individuals	(C) =(B/A) *100% Coverage of Partially Vaccinated	(D) Number of Fully Vaccinated Individuals	(E)=(D/A)*100% Coverage of Fully Vaccinated	(F) Number of Individuals vaccinated with 1st Booster Dose or 3rd Dose	(G)=(F/A)*100 Coverage of 1st Booster or 3rd dose	(H)=A*80.41% Number of individuals expected to get primary series	(I)I= A*80.41% Number of individuals expected to get 1st booster or 3rd dose*	(J) = Eligible population for 2nd booster or 4th dose*80.41%**	(K)=[(H*2)-[B+(D*2)]+(I-F)+J Remaining demand (doses)
Scenario 2: Assuming vaccination coverage using the vaccination program with highest attained coverage (*full vaccination of the primary series among adults with 80.41% coverage*) for all policies											
5 years old	2,277,000	171,458	7.53%	294,188	12.92%	0	0.00%	1,830,982	0	0	2,902,129

6-11 years old	13,203,138	994,196	7.53%	1,705,845	12.92%	0	0.00%	10,616,907	0	0	16,827,927
12-17 years old	12,729,206	793,619	6.23%	9,165,902	72.01%	0	0.00%	10,235,809	10,235,809	0	11,582,004
18-59 years old (Adult Population)	61,994,737	2,765,280	4.46%	49,851,205	80.41%	10,866,223	17.53%	49,851,205	49,851,205	4,508,244	40,727,946
60 - above (Senior Population)	10,260,113	262,999	2.56%	6,658,468	64.90%	2,073,050	20.20%	8,250,362	8,250,362	7,013,018	16,111,119
TOTAL for individuals aged 12 and above	84,984,056	3,821,898	4.50%	65,675,575	77.28%	12,939,273	15.23%	68,337,376	68,337,376	11,521,262	68,421,069
TOTAL for all populations	100,464,194	4,987,552	4.96%	67,675,609	67.36%	12,939,273	12.88%	80,785,265	68,337,376	11,521,262	88,151,125

*As of writing, only individuals aged 18 years and older are eligible for a 1st booster/3rd dose
**As of writing, only HCWs, elderly, and immunocompetent populations are eligible for a 2nd booster/4th dose

Table A4.3c Expected demand for the 2022 COVID-19 vaccination policies for scenario 3

Priority Age Group	(A) Target Population (PSA population)	(B) Number of Partially Vaccinated Individuals	(C) =(B/A) *100% Coverage of Partially Vaccinated	(D) Number of Fully Vaccinated Individuals	(E)=(D/A)*100% Coverage of Fully Vaccinated	(F) Number of Individuals vaccinated with 1st Booster Dose or 3rd Dose	(G)=(F/A)*100 Coverage of 1st Booster or 3rd dose	(H)=A*80.41% Number of individuals expected to get primary series	(I)=H *80.41% Number of individuals expected to get 1st booster or 3rd dose*	(J) = Eligible population for 2nd booster or 4th dose*80.41%**	(K)=[(H*2)-[B+(D*2)]+(I-F)+J Remaining demand
Scenario 3: Assuming vaccination coverage using the vaccination program with highest attained coverage (*full vaccination of the primary series among adults with 80.41% coverage*) for each succeeding policy											
5 years old	2,277,000	171,458	7.53%	294,188	12.92%	0	0.00%	1,830,982	0	0	2,902,129
6-11 years old	13,203,138	994,196	7.53%	1,705,845	12.92%	0	0.00%	10,616,907	0	0	16,827,927
12-17 years old	12,729,206	793,619	6.23%	9,165,902	72.01%	0	0.00%	10,235,809	8,230,819	0	9,577,014
18-59 years old (Adult Population)	61,994,737	2,765,280	4.46%	49,851,205	80.41%	10,866,223	17.53%	49,851,205	40,086,349	4,508,244	30,963,090
60 - above (Senior Population)	10,260,113	262,999	2.56%	6,658,468	64.90%	2,073,050	20.20%	8,250,362	6,634,281	7,013,018	14,495,038
TOTAL for individuals aged 12 and above	84,984,056	3,821,898	4.50%	65,675,575	77.28%	12,939,273	15.23%	68,337,376	54,951,449	11,521,262	55,035,142
TOTAL for all populations	100,464,194	4,987,552	4.96%	67,675,609	67.36%	12,939,273	12.88%	80,785,265	54,951,449	11,521,262	74,765,198

*As of writing, only individuals aged 18 years and older are eligible for a 1st booster/3rd dose
**As of writing, only HCWs, elderly, and immunocompetent populations are eligible for a 2nd booster/4th dose

Table A4.4. Comparison of the existing supply and expected demand for the 2022 COVID-19 vaccination policies for scenarios 1a, 1b, 2a, 2b, 3a, and 3b.

Legend	
	Remaining number of vaccines that can be used for future vaccination policies
	Number of vaccines needed to be procured

Scenario 1: Target vaccinees based on entire PSA population

The table below summarizes the supply and demand scenario assuming 100% uptake (demand) in all vaccination programs.

*Table A4.4a. Summary of vaccine supply utilization for **Scenario 1a**: 100% target coverage for all vaccination policies, prioritizing the existing stocks for the adolescent and adult vaccination policies (primary series, first boosters/3rd dose, 2nd booster/4th dose)*

Supply		Demand		Net Supply	
Number of available doses of *Moderna* **(A)**	14,812,138	Doses needed for: - Remaining unvaccinated and partially vaccinated **adults** needing Primary Series - Remaining **adults** needing 1st Booster/3rd Dose, and 2nd Booster/4th Dose - Remaining unvaccinated and partially vaccinated **adolescents** needing primary series - Remaining **adolescents** needing 1st Booster/3rd Dose **(C)**	121,167,635	**NET SUPPLY OF MODERNA IF WE WILL PRIORITIZE TO USE THESE FOR ADOLESCENT AND ADULT VACCINATION POLICIES** **(D=A-C)**	Supply: 14,812,138 **<** Demand: 121,167,635 -106,355,497 ***(0 supplies left of Moderna, 106 M doses of other brands needed for adolescents and adults)***
Number of available doses of other vaccine brands **(B)**	61,141,316			**NET SUPPLY OF COVID-19 VACCINES (MIXED BRANDS) FOR VACCINATION STRATEGIES (PRIMARY AND BOOSTER) FOR ADULTS AND ADOLESCENTS** **(E=B-D)**	Supply: 61,141,316 **<** Demand: 106,355,497 -45,214,181 ***(0 supplies left for all adolescent and adult vaccine brands, 45.21 M doses of other brands needed for vaccination policies for adolescents and adults)***
Number of available doses of Pfizer 10µg for children 5-11 years old **(F)**	7,912,017	Doses needed for the remaining unvaccinated and partially vaccinated **5 year-olds** needing primary series **(G)** *Note: Assuming that 5 year olds will be prioritized for Pfizer pedia dose as it is the only vaccine with EUA for the population*	3,794,165	**NET SUPPLY FOR COVID-19 VACCINATION (PRIMARY) AMONG CHILDREN 5 TO 11 YEARS OLD** **(I=F-(G+H))**	Supply: 7,912,017 **<** Demand: 25,794,553 -17,882,536 ***(0 supplies of Pfizer BioNTech pedia left, 17.88 M doses of Moderna or Pfizer-BioNTech pedia vaccines needed for vaccination policies for children)***
		Doses needed for the remaining unvaccinated and partially vaccinated children aged **6 to 11 years old** needing primary series **(H)**	22,000,388		

				OVERALL NET SUPPLY OF COVID-19 VACCINES OF ALL BRANDS (J=E+I)	**-63,096,717** ***(0 supplies left for all vaccine brands, 63.09 M doses of mixed brand vaccines needed for children, adolescent and adult vaccination policies, assuming 100% vaccination coverage for all policies)***

*Table A4.4b. Summary of vaccine supply utilization for **Scenario 1b**: 100% target coverage for all vaccination policies, prioritizing the existing stocks childhood vaccination policies (primary series)*

Supply		Demand		Net Demand/ Supply	
Number of available doses of Pfizer 10µg for children 5-11 years old **(A)**	7,912,017	Doses needed for the remaining unvaccinated and partially vaccinated **5 year-olds** needing primary series **(B)** *Note: Assuming that 5 year olds will be prioritized for Pfizer pedia dose as it is the only vaccine with EUA for the population*	3,794,165	**NET SUPPLY OF PEDIATRIC PFIZER-BIONTECH IF WE WILL PRIORITIZE TO USE THESE FOR VACCINATION OF CHILDREN AGED 5 YEARS OLD** **(C= A-B)**	Supply: 7,912,017 **>** Demand: 3,794,165 4,117,853 ***(Surplus of 4.1 M doses of Pfizer-BioNTech pedia that can be used for other pediatric age group)***
Number of available half-doses of *Moderna* ***(D)***	29,624,276 *= 14,812,138 x 2*	Doses needed for the remaining unvaccinated and partially vaccinated children aged **6 to 11 years old** needing primary series **(E)** *Note: Assuming that all remaining unvaccinated and partially vaccinated adolescents will receive Moderna after the remaining Pfizer pediatric doses are depleted*	22,000,388	**NET SUPPLY FOR COVID-19 VACCINATION (PRIMARY) AMONG CHILDREN 6 TO 11 YEARS OLD** **(F)=(C+D)-E)**	Supply: (4,117,853 + 29,624,276) **>** Demand: 22,000,388 **11,741,740** ***(Surplus of 11.7 M half-doses (or 5.87 M full doses) of Moderna that can be used for adolescent and adult vaccination policies)***
Remaining available full-dose *Moderna* after pediatric vaccination **(G)=F/2**	5,870,870	Doses needed for: - Remaining unvaccinated and partially vaccinated **adults** needing Primary Series - Remaining **adults** needing 1st Booster/3rd Dose, and 2nd Booster/4th Dose - remaining unvaccinated and partially vaccinated **adolescents** needing primary series - Remaining **adolescents** needing 1st Booster/3rd Dose **(H)**	121,167,635	**TOTAL REMAINING SUPPLY OF *MODERNA* AFTER ADOLESCENT AND ADULT VACCINATION** **(I)=G-H**	Supply: 5,870,870 **<** Demand: 121,167,635 -115,296,766 ***(0 supplies left of Moderna, 115 M doses of other brands needed for adolescents and adults)***

Number of available doses of other vaccine brands **(J)**	61,141,316			**OVERALL NET SUPPLY OF COVID-19 VACCINES (MIXED BRANDS) FOR VACCINATION STRATEGIES (PRIMARY AND BOOSTER) FOR ADULTS AND ADOLESCENTS** **(K)=J-I**	Supply: 61,141,316 **<** Demand: 115,296,766 **-54,155,449** ***(0 supplies left for all adolescent and adult vaccine brands, 54.16 M doses of other brands needed for adolescent and adult vaccination policies, assuming 100% vaccination coverage for all policies)***

Scenario 2: Target vaccinees based on applying the proportion of fully vaccinated adults (80.41%) to entire PSA population

The table below summarizes the existing supply and demand scenario assuming the target coverage (demand) will be equal to the vaccination policy with the current highest coverage *(full vaccination of the primary series among adults with 80.41% coverage)* in all vaccination programs.

*Table A4.5a. Summary of vaccine supply utilization for **Scenario 2a**: 80.41% target coverage for all vaccination policies, prioritizing the existing stocks for the adolescent and adult vaccination policies (primary series, 1st boosters/3rd dose, 2nd boosters/4th dose)*

Supply		Demand		Net Supply	
Number of available doses of Moderna **(A)**	14,812,138	Doses needed for: - Remaining unvaccinated and partially vaccinated **adults** needing Primary Series - Remaining **adults** needing 1st Booster/3rd Dose, and 2nd Booster/4th Dose - remaining unvaccinated and partially vaccinated **adolescents** needing primary series - Remaining **adolescents** needing 1st Booster/3rd Dose **(C)**	68,421,069	**NET SUPPLY OF MODERNA IF WE WILL PRIORITIZE TO USE THESE FOR ADULT AND ADOLESCENT VACCINATION POLICIES** **(D=A-C)**	Supply: 14,812,138 **<** Demand: 68,421,069 -53,608,931 ***(0 supplies left of Moderna, 53.61 M doses of other brands needed for adolescents and adults)***
Number of available doses of other vaccine brands **(B)**	61,141,316			**NET SUPPLY OF COVID-19 VACCINES (MIXED BRANDS) FOR VACCINATION STRATEGIES (PRIMARY AND BOOSTER) FOR ADULTS AND ADOLESCENTS** **(E=B-D)**	Supply: 61,141,316 **>** Demand: 53,608,931 7,532,385 ***(Surplus of 7.53 M doses of other brands that can be used for adolescent and adult vaccination policies)***
Number of available doses of Pfizer 10µg for children 5-11 years old **(F)**	7,912,017	Doses needed for the remaining unvaccinated and partially vaccinated **5 year-olds** needing primary series **(G)** *Note: Assuming that 5 year olds will be prioritized for Pfizer pedia dose as it is the only vaccine with EUA for the population*	2,902,129	**NET SUPPLY FOR COVID-19 VACCINATION (PRIMARY) AMONG CHILDREN 5 TO 11 YEARS OLD** **(I)=F-(G+H)**	Supply: 7,912,017 **<** Demand: 19,730,056 -11,818,039 ***(0 supplies left of Pfizer-BioNTech pedia, 11.82 M doses of Moderna or Pfizer-BioNTech pedia needed for vaccination policies for children)***

		Doses needed for the remaining unvaccinated and partially vaccinated children aged **6 to 11 years old** needing primary series **(H)**	16,827,927		
				OVERALL NET SUPPLY OF COVID-19 VACCINES OF ALL BRANDS **(J)= E (adult and adolescents) and I (children)**	**7,532,385** ***(Surplus of 7.53 M doses of other brands that can be used for adolescent and adult vaccination policies)***
					-11,818,039 ***(0 supplies left of Pfizer-BioNTech pedia, 11.82 M doses of Moderna or Pfizer-BioNTech pedia needed for children)***

*Table A4.5b. Summary of vaccine supply utilization for **Scenario 2b**: 80.41% target coverage for all vaccination policies, prioritizing the existing stocks childhood vaccination policies (primary series)*

Supply		Demand		Net Demand/ Supply	
Number of available doses of Pfizer 10µg for children 5-11 years old **(A)**	7,912,017	Doses needed for the remaining unvaccinated and partially vaccinated **5 year-olds** needing primary series **(B)** Note: Assuming that 5 year olds will be prioritized for Pfizer pedia dose as it is the only vaccine with EUA for the population	2,902,129	**NET SUPPLY OF PEDIATRIC PFIZER-BIONTECH IF WE WILL PRIORITIZE TO USE THESE FOR VACCINATION OF CHILDREN AGED 5 YEARS OLD** **(C)= A-B**	Supply: 7,912,017 **>** Demand: 2,902,129 5,009,888 ***(Surplus of 5.01 M doses of Pfizer pedia that can be used for other pediatric age group)***
Number of available half-doses of *Moderna* ***(D)***	29,624,276 *=14,812,138 x 2*	Doses needed for the remaining unvaccinated and partially vaccinated children aged **6 to 11 years old** needing primary series **(E)** [Note: Assuming that all remaining unvaccinated and partially vaccinated adolescents will receive Moderna after the remaining Pfizer pediatric doses are depleted]	16,827,927	**NET SUPPLY FOR COVID-19 VACCINATION (PRIMARY) AMONG CHILDREN 6 TO 11 YEARS OLD** **(F)=(C+D)-E**	Supply: (5,009,888 + 29,624,276) **>** Demand: 16,827,927 **17,806,237** ***(Surplus of 17.81 M half-doses (8.9 M full doses) of Moderna that can be used for adolescent and adult vaccination policies)***
Remaining available full-dose *Moderna* after pediatric vaccination **(G)=F/2**	8,903,118	Doses needed for: - Remaining unvaccinated and partially vaccinated **adults** needing Primary Series - Remaining **adults** needing 1st Booster/3rd Dose, and 2nd	68,421,069	**TOTAL REMAINING SUPPLY OF *MODERNA* AFTER ADOLESCENT AND ADULT VACCINATION** **(I=(G-H))**	Supply: 8,903,118 **<** Demand: 68,421,069 -59,517,951 ***(0 supplies left of Moderna, 59.5 M doses of other brands needed for adolescents and adults)***

		Booster/4th Dose - remaining unvaccinated and partially vaccinated **adolescents** needing primary series - Remaining **adolescents** needing 1st Booster/3rd Dose **(H)**			
Number of available doses of other vaccine brands **(J)**	61,141,316			**OVERALL NET SUPPLY OF COVID-19 VACCINES (MIXED BRANDS) FOR VACCINATION STRATEGIES (PRIMARY AND BOOSTER) FOR ADOLESCENTS AND ADULTS** **(K)=J-I**	Supply: 61,141,316 **>** Demand: 59,517,951 **1,623,365** ***(Surplus of 1.6 M doses of other brands that can be used for future vaccination policies, if any)***

Scenario 3: Target vaccinees based on applying the proportion of fully vaccinated adults (80.41%) for each succeeding COVID-19 vaccination series

The table below summarizes the existing supply and demand assuming the target coverage (demand) will be equal to the vaccination policy with current highest coverage *(adult primary series)* for each succeeding vaccination series (i.e., 80.41% will receive the primary series and 80.41% of those who received the primary series will receive the booster dose).

*Table A4.6a. Summary of vaccine supply utilization for **Scenario 3a**: 80.41% target coverage for each succeeding COVID-19 vaccination policy, prioritizing the existing stocks for the adolescent and adult vaccination policies (primary series, 1st boosters/3rd dose, 2nd booster/4th dose)*

Supply		Demand		Net Supply	
Number of available doses of Moderna **(A)**	14,812,138	Doses needed for: - Remaining unvaccinated and partially vaccinated **adults** needing Primary Series - Remaining **adults** needing 1st Booster/3rd Dose, and 2nd Booster/4th Dose - remaining unvaccinated and partially vaccinated **adolescents** needing primary series - Remaining **adolescents** needing 1st Booster/3rd Dose **(C)**	55,035,142	**NET SUPPLY OF MODERNA IF WE WILL PRIORITIZE TO USE THESE FOR ADULT AND ADOLESCENT VACCINATION POLICIES** **(D=A-C)**	Supply: 14,812,138 < Demand: 55,035,142 -40,223,004 ***(0 supplies left of Moderna, 40.22 M doses of other brands needed for adolescents and adults)***
Number of available doses of other vaccine brands **(B)**	61,141,316			**NET SUPPLY OF COVID-19 VACCINES (MIXED BRANDS) FOR VACCINATION STRATEGIES (PRIMARY AND BOOSTER) FOR ADULTS AND ADOLESCENTS** **(E=B-D)**	Supply: 61,141,316 **>** Demand: 40,223,004 20,918,312 ***(Surplus of 20.92 M doses of other brands that can be used for adolescent and adult vaccination policies)***
Number of available doses of Pfizer 10µg for children 5-11 years old **(F)**	7,912,017	Doses needed for the remaining unvaccinated and partially vaccinated **5 year-olds** needing primary series **(G)** Note: Assuming that 5 year olds will be prioritized for Pfizer pedia dose as it is the only vaccine with EUA for the population	2,902,129	**NET SUPPLY FOR COVID-19 VACCINATION (PRIMARY) AMONG CHILDREN 5 TO 11 YEARS OLD** **(I)=F-(G+H)**	Supply: 7,912,017 **<** Demand: 19,730,056 -11,818,039 ***(0 supplies left of Pfizer-BioNTech pedia, 11.82 M doses of Moderna or Pfizer-BioNTech pedia vaccines needed for vaccination policies for children)***

		Doses needed for the remaining unvaccinated and partially vaccinated children aged **6 to 11 years old** needing primary series **(H)**	16,827,927		
				OVERALL NET SUPPLY OF COVID-19 VACCINES OF ALL BRANDS **(J)= E (adult and adolescents) and I (children)**	**20,918,312** ***(Surplus of 20.92 M doses of other brands that can be used for adolescent and adult vaccination policies)***
					-11,818,039 ***(0 supplies of Pfizer-BioNTech pedia left, 11.82 M doses of Moderna or Pfizer-BioNTech pedia vaccines needed for pediatric vaccination policies, assuming 80.41% vaccination coverage for all policies)***

*Table A4.6b. Summary of vaccine supply utilization for **Scenario 3b**: 80.41% target coverage for each succeeding COVID-19 vaccination policy, prioritizing the existing stocks for the childhood vaccination policies (primary series)*

Supply		Demand		Net Demand/ Supply	
Number of available doses of Pfizer 10µg for children 5-11 years old **(A)**	7,912,017	Doses needed for the remaining unvaccinated and partially vaccinated **5 year-olds** needing primary series **(B)** Note: Assuming that 5 year olds will be prioritized for Pfizer pedia dose as it is the only vaccine with EUA for the population	2,902,129	**NET SUPPLY OF PEDIATRIC PFIZER-BIONTECH IF WE WILL PRIORITIZE TO USE THESE FOR VACCINATION OF CHILDREN AGED 5 YEARS OLD** **(C)= A-B**	Supply: 7,912,017 **>** Demand: 2,902,129 5,009,888 ***(Surplus of 5.01 M doses of Pfizer pedia that can be used for other pediatric age group)***
Number of available half-doses of *Moderna* ***(D)***	29,624,276 *=14,812,138 x 2*	Doses needed for the remaining unvaccinated and partially vaccinated children aged **6 to 11 years old** needing primary series **(E)** [Note: Assuming that all remaining unvaccinated and partially vaccinated adolescents will receive Moderna after the remaining Pfizer pediatric doses are depleted]	16,827,927	**NET SUPPLY FOR COVID-19 VACCINATION (PRIMARY) AMONG CHILDREN 6 TO 11 YEARS OLD** **(F)=(C+D)-E**	Supply: (5,009,888 + 29,624,276) **>** Demand: 16,827,927 **17,806,237** ***(Surplus of 17.81 M half-doses (or 8.9 M full doses) of Moderna that can be used for adolescent and adult vaccination policies)***
Remaining available full-dose *Moderna* after pediatric vaccination **(G)=F/2**	8,903,118	Doses needed for: - Remaining unvaccinated and partially vaccinated **adults** needing Primary Series - Remaining **adults** needing 1st Booster/3rd Dose, and 2nd Booster/4th Dose	55,035,142	**TOTAL REMAINING SUPPLY OF *MODERNA* AFTER ADOLESCENT AND ADULT VACCINATION** **(I)=(G-H)**	Supply: 8,903,118 **<** Demand: 55,035,142 -46,132,024 ***(0 supplies left of Moderna, 46.13 M doses of other brands needed for adolescents and adults)***

		- remaining unvaccinated and partially vaccinated **adolescents** needing primary series - Remaining **adolescents** needing 1st Booster/3rd Dose **(H)**			
Number of available doses of other vaccine brands **(J)**	61,141,316			**OVERALL NET SUPPLY OF COVID-19 VACCINES (MIXED BRANDS) FOR VACCINATION STRATEGIES (PRIMARY AND BOOSTER) FOR ADULTS AND ADOLESCENTS** **(K)=J-I**	Supply: 61,141,316 **>** Demand: 46,132,024 **15,009,292** ***(Surplus of 15 M doses of other brands that can be used for future vaccination policies, if any)***