	• Immunocompromised population aged 18 years old and above: 3 doses of 600 SU/0.5 mL suspension for injection (IM)
Route of administration	Intramuscular (IM)
Drug delivery system	Opalescent aqueous suspension in one-dose or two-dose vials.
Storage condition	Store at 2° to 8°C. Protect from light. Do not freeze. One dose vial: 12 months; Two-dose vial: 6 months
Mechanism of action	*Inactivated strain of SARS-CoV-2 created from vero -cells to induce immune response (Mascellino et al., 2021)*
Contraindications	• People with history of allergic reaction to *CoronaVac* or other inactivated vaccine, or any component of CoronaVac (active or inactive ingredients, or any material used in the process); • Previous severe allergic reactions to the vaccine (e.g. acute anaphylaxis, angioedema, dyspnea, etc); • People with severe neurological conditions (e.g. transverse myelitis, Guillain-Barre syndrome, demyelinating diseases, etc); • Patients with uncontrolled chronic diseases
PHL EUA status	• Released on 22 February 2021 • Updated on 07 April 2021 to include senior citizens in the target population • Updated on 15 November 2021 to include its indication for booster vaccination among adults 18 years and above • Updated on 11 March 2022 to expand the indication to individuals aged 6 and above
PHL FDA EUA indication	This product is suitable for clinically healthy people aged 6 years old and above susceptible to virus.

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 ***CoronaVac COVID-19 Vaccine for the pediatric population ages 6 - 17 years old*** as part of the 2022 COVID-19 Vaccination Program to reduce COVID-19 cases, severe infection, and deaths?

Recommendations *(as of 05 October 2022)*

The **HTAC is not recommending government financing of *CoronaVac* for primary vaccination series for children aged 6 to 11 years old because of the unsatisfactory benefit-risk profile** based on currently available evidence on clinical efficacy and effectiveness against Omicron variant and short term safety data.

However, for children ages 6 to 11 years old with contraindications to receiving currently available mRNA vaccines (eg. anaphylaxis to the first dose of mRNA vaccine or previous allergy to PEG), the HTAC recommends using available supplies of *CoronaVac* as an alternative based on the evidence that *CoronaVac* shows lower risk of having severe adverse events (SAEs) compared to mRNA vaccines.

Meanwhile, **for children ages 12 to 17 years, the HTAC recommends using available supplies of *CoronaVac* as an alternative for mRNA vaccines due to its acceptable benefit-risk profile** based on currently available clinical effectiveness against the Omicron variant and short-term safety data.

The HTAC considered the following criteria in formulating its recommendation for the vaccine:

Criteria	HTAC Judgment for 6 to 11 years old *(as of 05 October 2022)*	HTAC Judgment for 12 to 17 years old *(as of 05 October 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 global burden of COVID-19 contributed by children aged 6 to 17 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). In the Philippines, trends of cases in children are similar to other age groups, with a rise in cases from July to August 2022. A decrease in cases was observed in early September 2022 but an increase is being observed again in late September 2022. Meanwhile, Case Fatality Rates (CFRs) in children remained relatively the same over time, which is consistent in other age groups as well. In terms of hospitalization, currently, the effect of variants in this age group cannot be established due to limited sequencing capacity in the country. Only one (1) new case of MIS-C was reported in the 12-17 year-old age group from March to July 2022 and no new case of MIS-C was then reported from July to August 2022 based on passive surveillance of the SALVACION registry. It is noted that studies of hospitalized children with SARS-CoV-2 Omicron infection in Hong Kong showed more severe illness with neurologic manifestations and croup compared to children with influenza and parainfluenza. In terms of transmission, children have significantly lower possibility to transmit SARS-CoV-2 to their family members. Specifically for Omicron, there is no significant difference in the household secondary attack rate between child and adult contacts. There are no local studies on post-COVID-19 conditions. US data shows that this post-COVID-19 condition appears to be less common in children than in adults. Based on the above, there is no apparent increase in the burden of COVID-19 among children aged 6 to 17 years old, as of the writing of this report (07 September 2022).	
Is CoronaVac safe and efficacious for the pediatric population ages 6 to 17 years old? *Can CoronaVac*	**Yes,** based on limited trial data and real-world post-marketing safety surveillance, the short-term safety of 2-dose primary series of *CoronaVac* in children aged 6-17 years is acceptable. However, further follow-up data is needed to establish longer-term safety. Evidence on clinical efficacy of C*oronaVac* in children aged 6 to 17 years old showed that VEs against the Omicron variant did not pass HTAC specifications, based on very low certainty of evidence (Sinovac Life Sciences Co., Ltd., 2022). • **Symptomatic COVID-19 (6 to 11 yo):** 22.11% (95% CI: -26.74 to 52.52) • **Symptomatic COVID-19 (12-17 yo):** 19.97% (95% CI: -77.45 to 64.59)	

significantly reduce the magnitude and severity of COVID-19 in children ages 6 to 17 years old?	• **Severe COVID-19(6 mo to 17 yo):** 75.29% (95% CI: -149.70 to 99.50)
	
	In terms of **v**accine effectiveness during the Omicron-dominant period and the Delta-dominant period, there were varying results.
	• A real-world study in Chile during the Delta dominant period (Jara et al., 2022, preprint) showed passing VE against hospitalization due to COVID-19 [VE: 91.0% (95% CI: 87.7 to 93.4)] in children aged 6 to 16 years old, based on high certainty of evidence.
	• Meanwhile, in terms of the Omicron variant:
	  ○ Florentino, et al. 2022 (published) showed that VEs against Omicron variant in children aged 6 to 11 years old did not pass HTAC specifications based on moderate to very low certainty of evidence:
	  ■ Symptomatic COVID-19 39.8% (95% CI: 33.7 to 45.4)
	  ■ Hospitalization due to COVID-19: 59.2% (95% CI: 11.3 to 84.5)
	  ■ ICU admission due to COVID-19 20.9 (95% CI: -177.2 to 85.0)]
	  ○ Lau et al., 2022 (preprint), a test-negative design study showed that:
	  ■ In children aged 3 to 11 yo, VE against infection of *CoronaVac* at least 14 days after the second dose did not pass the HTAC specifications for symptomatic COVID-19 [VE: 40.8% (95% CI: 12.8 to 59.5)]. However, it was noted vaccination in children aged 3 to 11 yo was implemented during the Omicron variant and while the study was already being conducted. Longer follow-up period is needed to establish the effectiveness of the vaccine in this age group.
	  ■ In adolescents aged 12 to 17 yo, VE against infection of *CoronaVac* at least 14 days after the second dose passed the HTAC specifications for symptomatic COVID-19 [VE: 55% (38.2 to 67.2)].
	
	In terms of immunogenic response is acceptable:
	• Phase III trial by Soto et al., 2022 (preprint) showed that *CoronaVac* induces an immune response in children aged 6 to 17 years old. However, there was a decrease in neutralizing antibody and T-cell response against Delta variant compared to the wild-type strain. For the Omicron variant, there is a decrease in neutralizing antibodies but an increase in T-cell response.
	• Immunobridging study by Rosa Duque et al., 2022 (published, variant not specified) showed that *CoronaVac* induces an immune response in adolescents aged 11 to 17 years old that is either non-inferior or superior compared to the immune response of adults.
	• Phase II trial by Leung et al., 2022 (preprint, wild-type) showed enhanced immune response in adolescents aged 11 to 17 yo after the second dose of *CoronaVac* compared to before vaccination.	

Does CoronaVac provide a highly favorable benefit/risk profile in the context of observed vaccine efficacy, effectiveness and safety in individuals aged 6 to 17	Among children aged 6 to 11 years old, the 2-dose primary series of *CoronaVac* has an **unsatisfactory benefit-risk** profile based on currently available evidence on clinical efficacy and effectiveness against the Omicron variant and short-term safety data. However, for children aged 6 to 11 years old with mRNA vaccine contraindication (eg. anaphylaxis to the first dose of mRNA vaccine or previous allergy to PEG), *CoronaVac* may be given.	Among children aged 12 to 17 years old, the 2-dose primary series of *CoronaVac* has an acceptable benefit-risk profile based on currently available clinical effectiveness against the Omicron variant and short-term safety data.

years old?		
Is CoronaVac affordable and feasible to use in a national immunization program for the pediatric population ages 6 to 17 years old? Does CoronaVac represent good value for money in terms of preventing COVID-19 morbidity and mortality?	Implementing 2-dose primary series using *CoronaVac* for children aged 6 to 11 years old with mRNA vaccine contraindications and adolescents aged 12 to 17 years old will not incur additional budget impact as existing doses will be used for this vaccination strategy. A 2-dose primary series of *CoronaVac* for children aged 6 to 11 years old with mRNA vaccine contraindications and adolescents aged 12 to17 years old may represent good value for money as it is likely to be effective based on limited evidence.	
Does CoronaVac reduce out-of-pocket (OOP) expenses of households due to COVID-19?	Based on current evidence, 2-dose primary series of *CoronaVac* for children aged 6 to 11 years old with mRNA vaccine contraindications and adolescents aged 12 to 17 years old has the potential to reduce out-of-pocket expenses due to averted costs of isolation and treatment of mild, moderate, and severe COVID-19.	
Does CoronaVac possess the characteristics that are desired by key stakeholders?	Given the available clinical evidence, ease in logistics and ability to allow for equitable coverage, and availability of FDA EUA, *CoronaVac* possesses most of the characteristics desired by key stakeholders for its use as a 2-dose primary series for children aged 6 to 11 years old with mRNA vaccine contraindications and adolescents aged 12 to 17 years old. However, currently there is no information on public acceptability of CoronaVac as the primary series for pediatric vaccination. Furthermore, *CoronaVac* does not have a WHO EUL for the pediatric population.	
Does CoronaVac reduce or not further add to existing inequities in the health system?	The HTAC reiterates the importance of the following measures in the success of the implementation of COVID-19 primary series for the adolescent population: ● emphasis on strategies to increase primary series in children <12 years old and first booster vaccination coverage among priority groups ● ensure that information, education, and communication (IEC) and other vaccination-related documents are accessible and comprehensible (i.e., translated into the local language of the target population) Vaccination of the adolescent population shall be rolled out following the country's prioritization criteria, cognizant of the following: ● burden of COVID-19 in the priority groups, especially those with comorbidities; ● sufficient supply to cover the all other vaccination strategies in the pipeline along with second booster (remaining primary and 1st booster for adult population)	

In the development of this recommendation, the HTA Council has appraised and considered the evidence review of the Philippine COVID-19 Living Clinical Practice Guidelines Group, 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 17 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 *CoronaVac*:

- 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 *CoronaVac COVID-19 Vaccine*

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

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

- Appendix 1A: Risk of Bias Assessment Methodology

- Appendix 1B: Risk of Bias Assessment Results by HTAC
- Appendix 2: GRADE Table