Evidence Summary on *SARS-CoV-2 Vaccine (Vero Cell), Inactivated [CoronaVac]* for the prevention of COVID-19

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Prepared by	Health Technology Assessment Council Health Technology Assessment Unit
Contact details	hta@doh.gov.ph

Background

The COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has led to more than two million deaths worldwide, global economic and social disruption, and unprecedented challenges in the health system. As the world continues to face these challenges, several efforts, such as developing and implementing different health technologies that will ultimately lead us to our exit strategy from the crisis, were undertaken. Among these health technologies are vaccines against COVID-19 which are currently in different phases of trials around the world. Similar to other countries, the Philippine government has been exploring all means to access these vaccines and to prepare the country for its upcoming implementation within the coming months.

On February 22, 2021, the Philippine Food and Drug Administration (FDA) released the Emergency Use Authorization (EUA) for *SARS-CoV-2 Vaccine (Vero Cell), Inactivated [CoronaVac]* and was updated as of April 7, 2021.

To date, at least twenty countries have issued an EUA for this product in their respective jurisdictions and have started vaccine implementation.

Basic information on *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* is provided below:

Table 1.1 Characteristics of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*

Trade name	CoronaVac
Other name	COVID-19 Vaccine (Vero cell), inactivated
Manufacturer/s	Sinovac Life Sciences Co., Ltd.
Vaccine platform	Inactivated vaccine
Dose strength and administration	Consists of 2 doses of 0.5 mL per dose containing 600 SU of indicated SARS-CoV-2 inactivated virus as antigen; Dose 2 should be administered after four weeks from the first dose
Route of administration	Suspension for injection, Intramuscular (IM)
Drug delivery system	Opalescent aqueous suspension in single dose vials. Each vial must contain 0.5mL per dose containing 600 SU of indicated SARS-CoV-2 inactivated virus as antigen
Storage condition	2-8°C; do not freeze; protect from light; shelf life: 6 months
Mechanism of action	Inactivated whole virion vaccine with aluminum hydroxide as the adjuvant (Hong Kong Food and Health Bureau, 2021)

PHL EUA status	Released as of 22 February 2021 https://www.fda.gov.ph/wp-content/uploads/2021/03/EUA-SINOVAC-WEBSITE-3.pdf Updated as of 07 April 2021 https://doh.gov.ph/doh-press-release/DOH-FDA-GREEN-LIGHT-CORONAVAC-FOR-SENIOR-CITIZENS
PHL FDA EUA indication	For clinically healthy people (aged 18 years old and above) susceptible to the virus. This product is not recommended for use among healthcare workers with exposure to COVID-19 patients.
WHO EUL status	Not yet approved

The package insert is available via: https://www.fda.gov.ph/wp-content/uploads/2021/03/Package-Insert-v.10.pdf

Pursuant to the role of the Health Technology Assessment Council (HTAC) to develop coverage recommendations particularly in the selection and financing of COVID-19 vaccines using the Evaluation Framework set by the HTAC, this report presents all currently available evidence considered in the assessment of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*. 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 and viability; (4) household financial impact; (5) social impact; and (6) responsiveness to equity.

Policy Question

The HTAC aims to answer the policy question:

Should ***SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*** be recommended for emergency use to reduce COVID-19 cases, severe infection, and deaths?

Recommendation *(as of 08 April 2021)*

The HTAC maintains its **recommendation for the emergency use of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*** to reduce the burden of COVID-19 in a healthy population, 18-59 years of age, with low risk of exposure to COVID-19 infection.

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

Criteria	HTAC Judgment
Can *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* significantly reduce the magnitude and severity of COVID-19?	**Yes**. *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* has the potential to reduce the disease burden by averting a significant number of symptomatic infections assuming sufficient vaccine coverage.
Is *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* efficacious and safe?	Based on a report of an interim results of unpublished Phase III trial on *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac] in Brazil* [Palacios, 2021) *(cut-off analysis: date: 16 December 2020)]*. **Yes**, it is efficacious for preventing symptomatic COVID-19 based on moderate certainty of evidence. It may reduce the risk of severe cases and hospitalization due to COVID-19, based on very low certainty of evidence. The duration of protection cannot be assessed given the current data. **Yes**, it is safe in the known short-term safety outcomes, based on moderate certainty of evidence. Meanwhile, its long term safety outcomes cannot be determined given the short duration of observation at the time of the reports. It should not be given to individuals below 18 years old and to those with a known history of severe allergic reaction to any component of the vaccine, and who is febrile, patient in acute illness period and acute attack of chronic disease.

	The product insert also highlights precaution among the following special populations: immunocompromised patients, people with neurological conditions and, people with bleeding disorders.
Is *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* affordable and feasible to use in a national immunization program (viability)?	**Yes.** It is affordable but the total budget allocation is not proportionate to the target vaccinees. The share of the cost to implement vaccination using *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* will constitute 47.83% of the total allocated budget for vaccination and will cover 36% of the 70 million target vaccinees for 2021. According to the Department of Finance, the price of SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac] offered to the Philippine government is equal to or better than the price offered in other Southeast Asian countries. **Yes**, it is feasible as there are no significant barriers in vaccine implementation using *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* in terms of storage, transport, and handling. However, there is still a need for training of vaccinators to ensure product integrity across the entire supply chain and close monitoring of adverse events.
Does *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* reduce out-of-pocket (OOP) expenses of households due to COVID-19?	**Yes**. Based on interim results of the Brazil trial, *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* may reduce the risk of hospitalization due to COVID-19. Thus, *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* has the potential to reduce out-of-pocket expenses of Filipino households due to averted costs of isolation, treatment and hospitalization costs.
Does *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* possess the characteristics desired by key stakeholders? (Social Impact)	**Yes.** Based on short term outcomes, *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* possesses most of the characteristics desired by key stakeholders.
Does *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* reduce or not further add to existing inequities in the health system?	**Yes.** Because of non-stringent logistic requirements, *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* does not aggravate health inequities related to inoculation of recipients residing in isolated and disadvantaged locations. The trial population did not include important vulnerable groups such as individuals with impaired immune

	systems, and pregnant and lactating women. Further, the vaccine is contraindicated to those with a known history of severe allergic reaction to any component of the vaccine, and who is febrile, patient in acute illness period and acute attack of chronic disease.

The evidence review on efficacy and safety included the following:

- Zhang et al., 2021 (18-59 years old), (published manuscript) - China Phase I/II trial
- Wu et al., 2021 (60 years old and above), (published manuscript) - China Phase I/II trial
- Palacios et al., 2021 (sponsor submission) - Brazil Phase III trial, interim results
- Unal et al., 2021 (personal communication) Turkey Phase III trial, interim results
- Rusmil et al., 2021 (sponsor submission) - Indonesia Phase III trial, interim results
- Bueno et al, 2021 (preprint article) - Chile Phase III trial

Of these trials, the HTA Council found that only the data from the Brazil trial (Palacios et al, 2021) are useful for the following reasons:

- The study reached at least 50% of their target sample size with at least 2 months median follow up after the 2nd dose. Based on the interim report dated February 2021, the proportion of trial subjects analyzed after receiving two doses was 79.87% in the vaccine arm and 78.46% in the placebo arm;
- The methodology was well-described;
- Patients included in the observation are well-accounted for;
- Data showed acceptable safety based on short term follow up period; and
- The study reported clinically meaningful outcomes on the prevention of COVID-19 infection, severe cases and hospitalization

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 on potential risks and benefits, and securing of informed consent with regard to receiving the intervention; and
- Just compensation mechanisms and provisions for medical management of adverse events for patients and vaccinees assured by the national government

Finally, the HTAC recommends the conduct of research to address the current gaps in evidence with regard to the use of the *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*:

- Real-world effectiveness in the Philippine context particularly focused on the following:
    - 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., elderly, individuals with comorbidities, pregnant and lactating women, 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 and adverse events of special interest (AESI) following vaccination
    - Across the general population
    - In special populations: elderly, patients with comorbidities, pregnant and lactating women, immunocompromised individuals
- Randomized controlled trials should also be done among populations not currently included in clinical trials: children below 18 years of age
- Best practices, challenges, and barriers in implementation across different localities
- Monitoring of unexpected or additional costs associated with vaccine implementation.

Current Evidence on *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*

The table below summarizes the appraisal of available evidence on *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* against the HTAC evaluation framework.

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

- Appendix 1. Evidence on evaluation criterion 2 - Clinical Efficacy and Safety
- Appendix 2. Evidence on evaluation criterion 3 - Affordability and Viability
- Appendix 3. References
- Appendix 4. Acknowledgment

Table 1. Key Findings in the Current Evidence Considered for the HTAC Evaluation of ***SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]***

Evaluation Criteria	Question	Current Evidence	HTAC specification
1. Responsiveness to magnitude and severity	*Can the SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac] significantly reduce the magnitude and severity of COVID-19?*	As of 08 April 2021, the total number of cases has exceeded more than 132.7 million cases and breached the 2.8 million mark in terms of the total number of deaths globally. In the Philippines, the cumulative number of laboratory-confirmed COVID-19 cases has already exceeded 828,366 cases with total deaths reported at 14,119 as of 08 April 2021. Based on the latest DOH-Epidemiology Bureau data (as of 18 March 2021), the young and productive age groups (20-49 years old) have the most exposure and highest prevalence of the disease. However, the most vulnerable are the senior citizens (>60 years) who have the highest case fatality rate (CFR) at 10.2% and comprise around 63% of COVID-19 deaths. In addition, individuals with existing comorbidities such as chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), other pulmonary, cardiovascular and blood diseases are also vulnerable with CFR reported at around 64 to 91%. COVID-19 has led to significant disruptions not only in the delivery of other priority health services (e.g., immunization, maternal and child health, noncommunicable diseases) but also in the social and economic life of the nation by arresting the growth of the economy, displacing migrant and local workers, loss of jobs, and food insecurity (NEDA, 2020; PSA 2020; TESDA, 2020). Social safety nets for the poorest and other vulnerable sectors have not been enough to compensate for these losses (TESDA, 2020). The lockdowns and community quarantines have also been shown to have an impact on the mental health of Filipinos and have affected how common Filipino households adjust under the new normal, unable to visit and freely enjoy quality time with members of their families, as captured in	The vaccine can potentially reduce the COVID-19 disease burden (health, social and economic impact).

		some focus group discussions conducted by the HTAC and the HTA Unit. **HTAC Judgment**: *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* has the potential to reduce the disease burden by averting a significant number of symptomatic infections assuming sufficient vaccine coverage.	

2. Clinical efficacy and safety	*What is the efficacy of the SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac] in terms of reducing the incidence and/or severity of COVID-19 in the general and vulnerable populations?*	The Brazil trial (Palacios et al, 2021) is an on-going multicenter, randomized, double-blind, placebo-controlled phase III clinical trial among healthcare professionals aged 18 years and above, who work in direct contact with suspected or confirmed cases of COVID-19 in their daily work and are fully exposed to the risk of infection. Of the 12,408 participants who were enrolled in the trial, 9,823 received two doses of either the vaccine or placebo, with 4,953 participants belonging to the vaccine arm (two doses of 0.5 mL inactivated COVID-19 vaccine with 600 SU of the SARS-CoV-2 antigen) and 4,870 participants belonging to the placebo arm, following a 0, 14-day vaccination schedule. Based on personal communication with Sinovac Life Sciences Co., Ltd., a median follow-up period of 73 days after dose 2 was observed for this trial. Based on the interim results of this clinical trial: **<u>Critical efficacy outcomes:</u>** ● Using *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac],* compared to placebo, reduces the risk of: ○ Symptomatic COVID-19 (≥ Score 2, symptomatic-independent) at least 14 days after 2nd dose by **50.65% (95% CI: 35.94 to 61.98),** based on moderate certainty of evidence ○ COVID-19 (≥ Score 3, symptomatic-needs help) at least 14 days after 2nd dose by **83.70% (95% CI: 57.99 to 93.67),** based on moderate certainty of evidence ● For its efficacy against hospitalization due to COVID-19 (≥ Score 4), 14 days after dose 2, there were zero events in 4,953 participants in the intervention group versus 10 events in 4,870 participants in the control group. Protection against hospitalization due to COVID-19 remains to be demonstrated. The certainty of evidence is very low. ● For its efficacy against severe COVID-19 (≥ Score 6), 14 days after	The vaccine achieves the following efficacy parameters: **Preferred VE: ≥70% reduction** in the risk of symptomatic infection with vaccination versus no vaccination **Minimum acceptable VE: 50% reduction** in the risk of symptomatic infection with vaccination versus no vaccination The following factors were taken into consideration upon setting the minimum acceptability of 50% efficacy: pandemic situation, no standard COVID-19 vaccine, limited production from each manufacturer, and the need for multiple sources of vaccines in the Philippines.

		dose 2, there were zero events in 4,953 participants in the intervention group versus 6 events in 4,870 participants in the control group. Protection against severe COVID-19 remains to be demonstrated. The certainty of evidence is very low. **<u>Important efficacy outcomes:</u>** ● Using *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac],* compared to placebo, reduces the risk of: ○ Symptomatic COVID-19 (≥ Score 3, symptomatic-needs help) at least 14 days after 1st dose by **85.10% (95% CI: 61.85 to 94.19)**, based on moderate certainty of evidence ○ Symptomatic COVID-19 (≥ Score 2, symptomatic-independent) up to 56 days after at least one dose by **60.39% (95% CI: 56.54 to 63.9)**, based on moderate certainty of evidence ○ Symptomatic COVID-19 (≥ Score 2, symptomatic-independent) up to 98 days after at least one dose by **52.47% (95% CI: 51.88 to 53.05)**, based on moderate certainty of evidence ○ Symptomatic COVID-19 in a population with stable comorbidities 14 days after 2nd dose *(N = 6,925; 55.86% of the trial population)* **[VE: 48.93 (95% CI: 26.57 to 64.49)]**, based on low certainty of evidence. ○ Symptomatic COVID-19 in a population with obesity 14 days after 2nd dose *(% of the trial population not reported)* **[VE: 74.86 (95% CI: 53.73 to 86.35)]**, based on moderate certainty of evidence ● *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*, compared to placebo, shows inconclusive VE against the following: ○ Symptomatic COVID-19 (≥ Score 2, symptomatic-independent) 14 days after 2nd dose in elderly age 60 yrs and	Adapted from WHO, US FDA, other stringent regulatory authorities

		above *(N = 632; 5.10% of the trial population)* **[VE: 51.11 (95%CI: -166.93 to 91.04)]**, based on low certainty of evidence ○ Symptomatic COVID-19 in Asian population 14 days after 2nd dose *(N = 311; 2.51% of the trial population)* **[VE: 66.02 (95% CI: -226.82 to 96.47)]**, based on very low certainty of evidence ● For its efficacy against hospitalization due to COVID-19 (≥ Score 4), at least 14 days after at least one dose, there were zero events in 5,717 participants in the intervention group versus 10 events in 5,714 participants in the control group. Protection against hospitalization due to COVID-19 remains to be demonstrated. The certainty of evidence is very low. ● For its efficacy against severe COVID-19 (≥Score 6), at least 14 days after at least one dose, there were zero events in 5,717 participants in the intervention group versus 6 events in 5,714 participants in the control group. Protection against severe COVID-19 remains to be demonstrated. The certainty of evidence is very low. **HTAC Judgment**: *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* passed the minimum acceptable VE threshold against symptomatic COVID-19.	

	What is the duration of protection of the SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac] in terms of reducing the incidence and/or severity of COVID-19?	Current interim evidence shows protection against laboratory-confirmed symptomatic COVID-19 infection based on a minimum median follow up period of two months after receiving two doses. Data on the duration of protection will be reassessed as more evidence becomes available. **HTAC Judgment:** Cannot be assessed based on current data	**Minimum acceptable duration of protection:** confers at least 6 months protection **Preferred:** ≥1-year protective immunity *Reference: WHO Target Product Profile for COVID-19 Vaccines, 2020*

	What are the safety issues and incidence of adverse events caused by the SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]?	The evidence review on safety was based as well on the Brazil Trial (Palacios et al, 2021) as previously described, and real world data. Of the 12,396 enrolled participants, 6,202 and 6,194 were included in the vaccine and placebo, respectively, for the analysis of safety outcomes serious adverse events and death. Meanwhile for reactogenicity outcomes: 6,196 and 6,200 participants were included in the vaccine and placebo, respectively, for the analysis after the 1st dose; while 5,481 and 5,453 participants were included in the vaccine and placebo respectively, for the analysis after the 2nd dose. ***EVIDENCE FROM TRIAL*** **Short term outcomes:** Using *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*, compared to placebo increases the risk of: ● Systemic reactogenicity after dose 1 by **1.02** times **(95% CI: 1.01 to 1.03)** based on moderate certainty of evidence ● Systemic reactogenicity after dose 2 by **1.03** times **(95% CI:1.01 to 1.06)** based on moderate certainty of evidence ● Local reactogenicity after dose 1 by **1.95** times **(95%CI: 1.86 to 2.04)** based on moderate certainty of evidence ● Local reactogenicity after dose 2 by **2.47** times **(95%CI: 2.34 to 2.60)** based on moderate certainty of evidence **Long term outcomes:** *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* shows inconclusive safety for the following: ● Serious adverse events **[RR: 1.06 (95% CI:0. 65-1.73)]**, based on very low certainty of evidence ● Death (all-cause mortality) **[RR: 0.50 (95% CI: 0.05 to 5.51)]**, based on very low certainty evidence	Local and systemic reactions are tolerable, self-limiting and do not require hospitalization. No serious adverse events were caused by the vaccine. **Short term outcomes** (e.g., reactogenicity and allergic reactions): at least 2 months **Long term outcomes** (e.g., serious AEs): at least 1 year

		<u>Safety analysis for elderly population, N = 632</u> A subgroup safety analysis by age group was included in the latest interim report included. However, it did not report specifically for deaths. ● Using *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*, compared to placebo increases the risk of: ○ Local AEs by **1.70** times **(95%CI: 1.34 to 2.15),** based on moderate certainty of evidence. This is comparable to the risk relative for local AEs among age groups 18-59 years old **[RR: 1.76 (95% CI: 1.69 to 1.83)].** ● *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* shows inconclusive safety for the following: ○ AEs related to vaccination **[RR: 1.13 (95% CI: 0.97 to 1.31)]**, based on low certainty of evidence. This is comparable to the relative risk of AEs related to vaccination among age group 18-59 years old **[RR: 1.16 (95% CI:1.14 to 1.19)]** ○ Systemic AEs **[RR: 0.97 (95% CI: 0.80 to 1.17)]**, based on low certainty of evidence. This is comparable to the relative risk of local AE among age group 18-59 years old **[RR: 1.03 (95% CI: 1.00 to 1.06)]** ● In terms of Grade 3 and 4 AEs, there were zero events in 316 participants in the intervention group versus 2 events in 316 participants in the control group. The certainty of evidence is very low. ***REAL WORLD DATA*** ● **Philippines** *(as of 6 April 2021)* - 5,885 adverse event reports were collected. Of these, 5,751 are non-serious, 129 serious adverse events other than deaths, and 5 reports involving death were reported among recipients of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac].* Seventy of the 5,885 reports occurred in individuals aged 60 years old and above. (Source: FDA Philippines, 2021).	

		● **China** *(collected from 14 April 2020 to 5 February 2021)* - 4,240 cases of adverse events and 46 serious adverse events reported (incidence rate = 0.39/100,000). There were 4,194 cases of general AEs reported (incidence rate = 35.54/100,000). (Source: Personal communication with IP Biotech from Chinese CDC data, 2021). ● **Brazil** *(as of 18 March 2021)* - 2,984 adverse events reported among participants of emergency use of the vaccine. (Source: Brazil ANVISA, 2021) ● **Hong Kong** *(as of 30 March 2021)* ○ 69 adverse events reported ○ In 20 of the adverse events associated with *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac],* the three most commonly reported are: headache (5 events), dizziness (3 events), and urticaria (3 events). ○ Last March 28, the Hong Kong Department of Health had received a total of 13 death case reports with history of COVID-19 immunization from the HA. Eight of these reported deaths were concluded to be not directly associated with COVID-19 vaccination. Assessment of the remaining reported deaths are ongoing. (Source: Hong Kong Department of Health, 2021). ● **Chile** *(as of 2 March 2021)* ○ 1,911 notifications of Events Supposedly Attributable to Vaccination or Immunization (ESAVI) is associated with *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac].* ○ Of the 124 ESAVI notifications reported classified as serious, 90 occurred after vaccination with *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* (2.67 reports per 100,000 doses). ○ 11 post-vaccination notifications which resulted in death occurred with *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac].* However, after evaluation, there are no patterns	

		in causes of death that may indicate a vaccine safety problem against SARS- CoV- 2. (Source: Chile ISP, 2021) **HTAC Judgment:** Short-term safety of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* is acceptable. However, further follow-up data is needed to establish longer-term safety.	

	Does the SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac] provide a highly favorable benefit/risk profile in the context of observed vaccine efficacy?	The current evidence shows that likely clinical benefits in terms of decreased occurrence of symptomatic COVID-19 infection after 2nd dose [VE: 50.65% (95% CI: 35.94 to 61.98)] outweigh the known short-term risks based on data available at the time of evaluation. Current evidence from the Brazil trial are inconclusive in terms of the following: ● Vaccine efficacy against: - COVID-19 infection among older adults (60 years and above) *(N = 632; 5.10% of the trial population)*, VE: 51.11 % (95%CI: -166.93 to 91.04) - COVID-19 infection in the Asian population *(2.51% of trial population),* VE: 66.02 % (95% CI: -226.82 to 96.47) - asymptomatic COVID-19 infection (not reported) ● Safety in terms of: - long term safety outcomes: - serious adverse event, RR: 1.06 (95% CI:0. 65-1.73) - death (all-cause mortality), RR: 0.50 (95% CI: 0.05 to 5.51)] - safety outcomes for elderly subgroup: - adverse events related to vaccination, RR: 1.13 (95% CI: 0.97 to 1.31) - systemic adverse reactions, RR: 0.97 (95% CI: 0.80 to 1.17) Thus, we cannot determine the benefit/risk profile specifically for these subgroups. **HTAC Judgment:** PASSED	Favorable benefit/risk profile The benefit of preventing morbidity of at least 50% far outweighs the reported risk of adverse events

3. Affordability and viability	*Is SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac] affordable?*	Based on the projected calculations, the total cost of rolling out vaccination with *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* for **25M Filipinos in 2021** (i.e., target vaccinees for this vaccine profile identified in the vaccination roll out plan) will amount to **Php 39,457,905,333.33.** According to the Department of Finance, the price of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* offered to the Philippine government is equal to or better than the price offered in other Southeast Asian countries. **HTAC Judgment:** The vaccine is affordable since the budget for the purchase and use of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* for the target number of vaccinees has been allocated.	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.*

	What are the budget implications of using the SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]?	The total cost of vaccination per individual, which accounts for other costs such as consumables, hauling and storage, and operations, was computed at Php 1,578.32. The potential budget impact of the use of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* to the national government to cover 25 million Filipinos was calculated at about Php 39,457,905,333.33 It is estimated that **47.83% of the total allocated budget for vaccination will go to 36% of the 70 million target vaccinee**s for 2021. **HTAC Judgment:** The share of the cost of the *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* to the total vaccine budget is considered not proportionate to the share of the population to be vaccinated using the said vaccine.	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 the SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac] represent good value for money in terms of: *a. preventing COVID-19 mortality* *b. lowering hospitalization (moderate, severe and critical cases)* *c. lowering incidence of symptomatic (mild) and asymptomatic cases (RT-PCR confirmed cases)*	Whether *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* represents good value for money in terms of preventing COVID-19 mortality, lowering hospitalization (moderate, severe, and critical cases), and lowering the incidence of symptomatic (mild) and asymptomatic cases (RT-PCR confirmed cases) cannot be fully assessed at the moment. 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 the vaccination program using *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* outweigh the negative impacts such as deaths due to COVID-19, medical costs, loss of productivity, social disruption and unprecedented challenges in the health system.	The health, economic, and social benefits of the vaccination program outweigh the costs. The vaccine is likely cost-effective. *Note: A full-blown cost-effectiveness analysis is currently not done for rapid reviews under a pandemic situation due to its emergency nature. A full-blown cost-effectiveness analysis that takes on a societal perspective (i.e., including the economic and social impacts) will be performed once sufficient evidence is available and when full market authorization has been granted.*

	Are there significant barriers to vaccine implementation in terms of vaccine storage and transport, handling; adequacy, skills and training of vaccinators; and access of the target population to the health care facility? Are there plans to overcome significant barriers?	The vaccine can be readily stored in a refrigerator at 2 to 8 degrees Celsius. Given this, it is expected that the *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* can be widely distributed to facilities with the said equipment. Like any vaccine implementation, there is still a need for training on vaccine storage and handling to ensure product integrity across the entire supply chain. Trained personnel in handling unreported or rare adverse reactions that could occur following vaccination should also be in place. **HTAC Judgment:** There are no significant barriers in vaccine implementation using *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* in terms of storage, transport, and handling. However, there is still a need for training to: ensure product integrity across the entire supply chain; and, close monitoring of adverse events.	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.
4. Household Financial Impact	*Will the SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac] reduce or not add further to the out-of-pocket expenses of Filipino households?*	**<u>For mild COVID-19 pneumonia:</u>** ● PhilHealth has issued the following packages and case rates related to mild COVID-19: - Isolation Package (C19CI): Php 22,499.00 - Mild COVID-19 pneumonia for elderly and with comorbidities (C19IP1): Php 43,997.00 ● Looking at the actual PhilHealth claims as of January 2021, the isolation package amounted to a median cost of **Php 22,499,** while claims for mild COVID-19 pneumonia for elderly and those with comorbidities amounted to a median cost of **Php 43,997.** ● Reviewing the hospital bills data collected by PhilHealth as of January 2021, the median amount spent by patients for isolation is at **Php 22,499** while mild cases among elderly and	The adoption of the vaccine can reduce out-of-pocket spending of individuals and families due to averted COVID-19 disease and/or hospitalization.

		those with comorbidities is at **Php 60,020.25.** ● From the same dataset, the calculated median out-of-pocket spending for patients with mild COVID-19 pneumonia is at **Php 16,023.25.** Meanwhile, the median out-of-pocket reported for patients availing an isolation package is 0. **<u>For moderate COVID-19 pneumonia:</u>** ● PhilHealth has issued benefit package C19IP2 for moderate COVID-19 pneumonia with a case rate of Php 143, 267. ● Looking at the actual PhilHealth claims for moderate COVID-19 pneumonia as of January 2021, they amounted to a median of **Php 143, 267.00**. ● Reviewing the hospital bills data collected by PhilHealth as of January 2021, the median amount spent by patients with moderate COVID-19 is at **Php 234, 925.13**. ● From the same dataset, the calculated median out-of-pocket spending for patients with moderate COVID-19 pneumonia is at **Php 63,371.3**. **<u>For severe COVID-19 pneumonia:</u>** ● PhilHealth has issued benefit package C19IP3 for severe COVID-19 pneumonia with a case rate of Php 333,519. ● Looking at the actual PhilHealth claims for severe COVID-19 pneumonia as of January 2021, they amounted to a median of **Php 333,519.00**. ● Reviewing the hospital bills data collected by PhilHealth as of January 2021, the median amount spent by patients with severe COVID-19 pneumonia is at **Php 388,904.20**. ● From the same dataset, the calculated median out-of-pocket spending for patients with severe COVID-19 pneumonia is at **Php 388,903.20**. Interim results from the clinical trials have shown its clinical benefit in	

		decreasing the risk of symptomatic COVID-19. It may reduce the risk of hospitalization due to COVID-19. **HTAC Judgment**: Based on current evidence, *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* has the potential to reduce out-of-pocket expenses of Filipino households due to averted isolation, treatment and hospitalization costs.	
5. Social Impact	*Does the SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac] 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*	Based on the results of the focus group discussions conducted 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 evidences for the *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*: 1) Safe and efficacious for the general population (18 years old and older) and for some vulnerable groups like the older population and individuals with comorbidities. - Evidence: Clinical trial shows acceptable safety profile for known short-term risks and efficacy to reduce risk of symptomatic COVID-19, and may reduce the risk of severe COVID-19 and hospitalization due to COVID-19. There is insufficient efficacy and safety data for populations aged 60 and older and the Asian population. Trials are ongoing to provide more conclusive evidence on the efficacy and safety for these special populations. 2) Underwent a transparent regulatory process of being evaluated	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

	and information on the vaccines ● *Availability* ● *Potential for high and equitable coverage* ● *Ease in logistical and 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*	and approved by health authorities - Evidence: The *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* underwent the usual regulatory process of the FDA Philippines. However, this review had to consider unpublished, non-peer reviewed data. To date, no stringent regulatory agency has issued EUA on this vaccine. 3) Potential for high and equitable coverage across the population - Evidence: *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* can be made more available since vaccine handling and storage are within the capacity of the RHUs. 4) Ease in logistics and administration - Evidence: *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* can be stored at 2 to 8 degrees Celsius which is present in most RHUs. 5) Cost-effective - Evidence: The health, economic, and social benefits of implementing vaccination program using *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* outweigh the negative impact of COVID-19 such as deaths due to COVID-19, medical costs, loss of productivity, social disruption and unprecedented challenges in the health system. 6) Public acceptability - Evidence: No brand-specific study has been conducted to provide evidence for this characteristic. Based on a series of focus group discussions (FGD) conducted by HTAC, there were expressed reservations towards China-produced vaccines. However, in the concluding discussion, the participants emphasized the transparency of regulatory process and consideration for shortage of supply.	

		7) Availability of mechanisms to compensate vaccine recipients for any untoward event following vaccination - Evidence: The 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. 8) Appropriateness of the vaccine to special at-risk groups and patients with comorbidities - Evidence: The Phase III clinical trial conducted in Brazil included healthcare workers 18 years and older, who are healthy and/or have underlying medical conditions that can be controlled by medication. - <u>Elderly population</u>: - The *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* shows inconclusive vaccine efficacy in the older population of 60 years and above [VE: 51.11% (95% CI: -166.93 to 91.04)] *(N = 632; 5.10% of the trial population)*, based on very low certainty of evidence. - In terms of safety, using SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac], compared to placebo increases the risk of local AEs by 1.70 times (95%CI: 1.34 to 2.15), based on moderate certainty of evidence. However, its safety profile for the following outcomes are inconclusive: AEs related to vaccination [RR: 1.13 (95% CI: 0.97 to 1.31)], based on low certainty of evidence; and systemic AEs [RR: 0.97 (95% CI: 0.80 to 1.17)], based on low certainty of evidence.	

		- With stable comorbidities: The reported vaccine efficacy for the population with stable comorbidities is 48.93% (95% CI: 26.57 to 64.49) *(N = 6.925; 55.86% of the trial population),* based on low certainty of evidence. The reported vaccine efficacy for the obese population is 74.86% (95%CI: 53.73 to 86.35) *(proportion in the trial population not mentioned),* based on moderate certainty of evidence. The trial did not report specific safety analysis for this subpopulation. Evidence for efficacy and safety are insufficient for the following populations: individuals aged below 18 years and 60 years and above, individuals with uncontrolled comorbidities, and those who are immunocompromised, pregnant, and lactating women. **HTAC Judgment:** Based on short-term outcomes, *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* possesses most of the characteristics desired by key stakeholders.	
6. Responsiveness to equity	*How will the SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac] and its use impact pre-COVID and COVID-generated health and*	*SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* has been shown to have an efficacy against symptomatic COVID-19 at 50.65% (95%CI: 35.94 to 61.98) in healthcare workers who have direct contact with suspected or confirmed cases of COVID-19, based on the interim results of the Brazil Phase III trial. There may be issues/gaps in access for special and vulnerable populations such as individuals below 18 years old and those with allergy to one of the components of the vaccine.	Ideally, health interventions can be fairly adopted and distributed/ implemented for eligible populations without aggravating existing health inequities especially for

	socioeconomic inequities? *Which groups might be unfairly disadvantaged in relation to the COVID-19 disease burden and delivery of the SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]?*	*SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* can be stored at normal cold storage conditions (2 to 8 degrees Celsius). This will make vaccine distribution more logistically feasible which in turn does not aggravate inequities for patients living in geographically isolated and disadvantaged areas. Compared to other new vaccines, the price per dose and the logistical and operational cost of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* allow it to be utilized widely. **HTAC Judgment:** Because of non-stringent logistic requirements, *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* does not aggravate health inequities related to inoculation of recipients residing in isolated and disadvantaged locations. However, the evidence on the efficacy and safety of the vaccine among individuals aged 60 years and above are insufficient. Trials are ongoing to provide more conclusive evidence on the efficacy and safety for older adults. The trial population also did not include important vulnerable groups such as individuals with impaired immune systems, and pregnant and lactating women.	vulnerable sectors of our society.

Appendix 1. Evidence for criterion 2 - Clinical Efficacy and Safety

Evidence from trials were considered on the review of efficacy, while evidence from both trials and available real world data were considered on the review of the safety of this vaccine.

The evidence review on efficacy and safety included the following:

- Zhang et al., 2021 (18-59 years old), (published manuscript) - China Phase I/II trial
- Wu et al., 2021 (60 years old and above), (published manuscript) - China Phase I/II trial
- Palacios et al., 2021 (sponsor submission) - Brazil Phase III trial, interim results
- Unal et al., 2021 (personal communications) Turkey Phase III trial, interim results
- Rusmil et al., 2021 (sponsor submission) - Indonesia Phase III trial, interim results
- Bueno et al, 2021 (preprint article) - Chile Phase III trial

Of these trials, the HTA Council found that only the data from the Brazil trial (Palacios et al, 2021) are useful for the following reasons:

- The study reached at least 50% of their target sample size with at least 2 months median follow up after the 2nd dose. Based on the interim report dated February 2021, the proportion of trial subjects analyzed after receiving two doses was 79.87% in the vaccine arm and 78.46% in the placebo arm;
- The methodology was well-described;
- Patients included in the observations are well-accounted for;
- Data showed acceptable safety based on short term follow up period; and
- The study reported clinically meaningful outcomes on the prevention of COVID-19 infection, severe cases and hospitalization.

The HTAC's clinical research question elements are as follows:

Population: General and vulnerable population

Intervention: SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]

Comparator: Placebo (Saline) OR Active Control

Outcomes: Vaccine efficacy (VE) and safety (see table below for details)

Table 1.1 Definitions and rating of importance of efficacy outcomes of interest

Name of outcome	Definition	HTAC rating of outcome importance
Vaccine efficacy (VE) against symptomatic	Positive Nucleic Acid Amplification Test (NAAT) and the following symptoms after dose 2:	**CRITICAL** to decision making

COVID-19 after dose 2	● Acute onset of any of three or more signs and symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status ● Anosmia (loss of smell), ageusia (loss of taste) in the absence of any other identified cause *Reference: WHO COVID-19 case definitions*	Subgroup analyses: **IMPORTANT** but not critical to decision-making
VE against Hospitalization due to COVID-19	Hospital admission for the management of COVID-19	**CRITICAL** to decision making
VE against Severe COVID-19 Occurrence after at least dose 1	Symptomatic COVID-19 after dose 1 with the addition of the following clinical manifestations: pneumonia, severe acute respiratory syndrome, multi-organ failure, and death *Reference: US FDA*	**CRITICAL** to decision making
VE against Severe COVID-19 Occurrence after dose 2	Symptomatic COVID-19 after dose 2 with the addition of the following clinical manifestations: pneumonia, severe acute respiratory syndrome, multi-organ failure, and death *Reference: US FDA*	**CRITICAL** to decision making
VE against symptomatic COVID-19 after at least Dose 1	Positive Nucleic Acid Amplification Test (NAAT) and the following symptoms after dose 1: ● Acute onset of any of three or more signs and symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status ● Anosmia (loss of smell), ageusia (loss of taste) in the absence of any other identified cause *Reference: WHO COVID-19 case definitions*	**IMPORTANT** but not critical to decision-making
VE against symptomatic COVID-19 among older adults after dose 2	Positive Nucleic Acid Amplification Test (NAAT) and the following symptoms after dose 2 in older adults as defined in the trials: ● Acute onset of any of three or more signs and symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea,	**IMPORTANT** but not critical to decision-making

	anorexia/nausea/vomiting, diarrhea, altered mental status ● Anosmia (loss of smell), ageusia (loss of taste) in the absence of any other identified cause *Reference: WHO COVID-19 case definitions*	
VE against symptomatic COVID-19 among population with comorbidities after dose 2	Positive Nucleic Acid Amplification Test (NAAT) and the following symptoms after dose 2 in population with comorbidities: ● Acute onset of any of three or more signs and symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status ● Anosmia (loss of smell), ageusia (loss of taste) in the absence of any other identified cause *Reference: WHO COVID-19 case definitions*	**IMPORTANT** but not critical to decision-making
VE against symptomatic COVID-19 among Asians, after dose 2	Positive Nucleic Acid Amplification Test (NAAT) and the following symptoms after dose 2 in Asian population: ● Acute onset of any of three or more signs and symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status ● Anosmia (loss of smell), ageusia (loss of taste) in the absence of any other identified cause *Reference: WHO COVID-19 case definitions*	**IMPORTANT** but not critical to decision-making
VE against asymptomatic COVID-19	Absence of COVID-19 symptoms but with positive NAAT results	**IMPORTANT** but not critical to decision-making

Table 1.2 Definitions and rating of importance of safety outcomes of interest

Name of outcome	Definition	HTAC rating of outcome importance
Serious adverse events	An adverse event is any undesirable experience associated with the use of a vaccine. The event is serious when the patient outcome is: ● Death ● Life threatening ● Hospitalization (initial or prolonged) ● Disability of permanent damage	**CRITICAL** to decision making

	• Congenital anomaly/ birth defect • Required intervention to prevent permanent impairment of damage • Other serious events which may jeopardize the patient and may require medical or surgical intervention to prevent one of the other outcomes *Reference: US FDA*	
Death (All-cause mortality)	Reported deaths regardless of cause	**CRITICAL** to decision making
Systemic reactogenicity (Dose 1) Systemic reactogenicity (Dose 2)	General systemic reactions to injectable products such as vaccines include nausea/vomiting, diarrhea, headache, fatigue, and myalgia *Reference: US FDA*	**CRITICAL** to decision making
Local reactogenicity (Dose 1) Local reactogenicity (Dose 2)	Local reaction to injectable products such as vaccines include pain, tenderness, erythema/redness, and induration/ swelling *Reference: US FDA*	**IMPORTANT** but not critical to decision-making
Adverse Events, Unsolicited	Any untoward medical occurrence associated with the use of a vaccine in humans, whether or not considered vaccine-related. *Reference: US FDA*	**IMPORTANT** but not critical to decision-making

EVIDENCE FROM TRIALS

Brazil Phase III trial (Palacios et al, 2021)

Study characteristics

The *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* trial conducted in Brazil is an on-going, multi-center, randomized, double-blind, placebo-controlled phase III clinical trial. The participants of this trial were healthcare professionals aged 18 years and above who work in direct contact with suspected or confirmed cases of COVID-19 in their daily work and are fully exposed to the risk of infection. The trial was designed to enroll 13,060 participants, including 11,800 adults aged 18-59 years and 1,260 elderly aged over 60 years. The trial excluded pregnant and breastfeeding women, patients with uncontrolled chronic conditions, patients with impaired immune system, patients undergoing treatment with immunosuppressive therapies, patients with behavioral, cognitive, or psychiatric illness, those with history of alcohol or drug abuse 12 months

prior to inclusion in the study, those with severe allergic reactions to the vaccine or its components, possible or confirmed cases of COVID-19 on the day of vaccination, participants of another clinical trial, those who have been vaccinated with a live attenuated virus in the last 28 days or inactivated vaccine in the last 14 days prior to inclusion in the study, or patients with a history of bleeding disorders. Participants were randomly assigned to either the vaccine or placebo group in a 1:1 ratio to receive two doses of 0.5 mL inactivated COVID-19 vaccine with 600 SU of the SARS-CoV-2 antigen or placebo in a 0, 14-day schedule. Based on personal communication with Sinovac Life Sciences Co., Ltd., a median follow-up period of 73 days after dose 2 was observed for this trial. A total of 12,408 participants were enrolled in the trial and of these participants, 9,823 received two doses of either the vaccine or placebo, with 4,953 participants belonging to the vaccine arm and 4,870 participants belonging to the placebo arm.

The primary efficacy endpoint of the study was measured using the cumulative incidence of symptomatic individuals with virologically (RT-PCR) confirmed COVID-19 two weeks after the second vaccination. Secondary efficacy endpoints were measured using cumulative incidence of symptomatic RT-PCR confirmed COVID-19 two weeks after second vaccination according to previous exposure to SARS-CoV-2, cumulative incidence of RT-PCR confirmed symptomatic COVID-19 cases two weeks after first vaccination, and cumulative incidence of RT-PCR confirmed symptomatic COVID-19 cases two weeks after the second vaccination according to severity of COVID-19 progression. Meanwhile, primary safety endpoints were measured using the frequency of solicited and unsolicited local and systemic adverse reactions 7 days after vaccination stratified by age group. The secondary safety endpoints were measured using the incidence rate of adverse reactions four weeks after each vaccination, and the incidence rate of adverse events of special interest (AESI) in participants who received at least one dose of the investigational product.

Table 1.3 presents the HTAC outcomes of interest and the corresponding outcomes reported by Palacios et al., 2021. The interim results in this trial did not report VE against asymptomatic COVID-19.

Table 1.3. HTAC outcomes of interest and the corresponding outcomes reported by Palacios et al., 2021

HTAC outcome of interest	**Matching reported outcome from the *SARS-CoV-2 Vaccine***	**Definition of outcome from the *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* trial** (Palacios et al., 2021)

	***(Vero cell), Inactivated [CoronaVac]* trial** (Palacios et al., 2021)	
Efficacy outcomes		
VE against symptomatic COVID-19 after dose 2	VE against symptomatic COVID-19 (≥ Score 2, symp independent) at least 14 days after 2nd dose *(PP)* *Case definition 1*	Individuals with at least two type A symptoms, or at least one type B symptom, or radiologic characteristics of COVID-19 vaccine, with positive PCR test of COVID-19 (including saliva sample). Symptom A (for at least 2 days: Fever (Axillary temperature ≥37.5ºC), chills, sore throat, fatigue, nasal congestion or runny nose, muscle pain, headache, nausea or vomiting, diarrhea. Symptom B: Cough (for at least 2 days), loss of smell or taste (for at least 2 days), shortness of breath or difficulty breathing.
No matching HTAC outcome of interest	VE against symptomatic COVID-19 (≥ Score 3, symp need help) at least 14 days after the 2nd dose *(PP)* *Case definition 1* VE against symptomatic COVID-19 (≥ Score 3, symp need help) at least 14 days after the 1st dose *(ITT)* *Case definition 1*	● Symptomatic; assistance needed ● Hospitalized, no oxygen therapy ● Hospitalised; oxygen by mask or nasal prongs ● Hospitalised; oxygen by NIV or high flow ● Intubation and mechanical ventilation, pO2/FiO2≥150 or SpO2/FiO2≥200 ● Mechanical ventilation, pO2/FiO2<150 (SpO2/FiO2<200) or vasopressors ● Mechanical ventilation, pO2/FiO2<150 and vasopressors, dialysis, or ECMO ● Dead
VE against hospitalization due to COVID-19	VE against hospitalized due to COVID- 19 (≥ Score 4) *at least 14 days after 2nd dose (PP)* *Case definition 1* VE against hospitalized) COVID-19 (≥ Score 4) *at least 14 days after 1st dose (ITT)* *Case definition 1*	● Hospitalized, no oxygen therapy ● Hospitalised; oxygen by mask or nasal prongs ● Hospitalised; oxygen by NIV or high flow ● Intubation and mechanical ventilation, pO2/FiO2≥150 or SpO2/FiO2≥200 ● Mechanical ventilation, pO2/FiO2<150 (SpO2/FiO2<200) or vasopressors ● Mechanical ventilation, pO2/FiO2<150 and vasopressors, dialysis, or ECMO ● Dead

VE against severe COVID-19	VE against Severe) COVID- 19 (≥ Score 6) at least 14 days after 2nd dose *(PP)* *Case definition 1*	A laboratory confirmed case of SARS-CoV-2 infection that has one or more of the following conditions : ● Clinical signs at rest indicating severe systemic disease (respiratory rate ≥ 30 per minute, heart rate ≥ 125 per minute, oxygen saturation ≤ 93% at room temperature at sea level or PaO2 / FiO2 <300 mm Hg); ● Respiratory failure (defined as the need for high-flow supplemental oxygen, non-invasive ventilation, mechanical ventilation or extracorporeal oxygenation); ● Evidence of shock (Systolic BP <90 mm Hg, Diastolic BP <60 mm Hg, or need for vasopressors); ● Major acute renal, hepatic or neurological dysfunction; ● Admission to the Intensive Care Unit; ● Death.
	VE against Severe) COVID- 19 (≥ Score 6) at least 14 days after 1st dose *(ITT)* *Case definition 1*	
VE against symptomatic COVID-19 after dose 1	VE against Confirmed COVID-19 cases (≥Score 3, symp needs help), 14 days after 1st dose *(ITT)* *Case definition 1*	Individuals with at least two type A symptoms, or at least one type B symptom, or radiologic characteristics of COVID-19 vaccine, with positive PCR test of COVID-19 (including saliva sample). Symptom A (for at least 2 days: Fever (Axillary temperature ≥37.5ºC), chills, sore throat, fatigue, nasal congestion or runny nose, muscle pain, headache, nausea or vomiting, diarrhea. Symptom B: Cough (for at least 2 days), loss of smell or taste (for at least 2 days), shortness of breath or difficulty breathing.
	VE against Confirmed COVID-19 cases (≥Score 2, symp independent) up to 56 days after 1st dose *(ITT)* *Case definition 1*	
	VE against Confirmed COVID-19 cases (≥Score 2, symp independent) up to 98 days after 1st dose *(ITT)* *Case definition 1*	
VE against symptomatic COVID-19 after dose 2 in older adults	VE against symptomatic COVID-19 in the older population, >60 years (≥Score 2, symp independent) at least 14 days after 2nd dose *(PP)*	Individuals with at least two type A symptoms, or at least one type B symptom, or radiologic characteristics of COVID-19 vaccine, with positive PCR test of COVID-19 (including saliva sample). Symptom A (for at least 2 days: Fever (Axillary temperature ≥37.5ºC), chills, sore throat, fatigue, nasal congestion or runny nose, muscle pain, headache, nausea or vomiting, diarrhea.

	Case definition 1	Symptom B: Cough (for at least 2 days), loss of smell or taste (for at least 2 days), shortness of breath or difficulty breathing.
VE against symptomatic COVID-19 after dose 2 in population with comorbidities	VE against symptomatic COVID-19 in population with precondition, 14 days after 2nd dose *(PP)* *Case definition 1*	Individuals with at least two type A symptoms, or at least one type B symptom, or radiologic characteristics of COVID-19 vaccine, with positive PCR test of COVID-19 (including saliva sample). Symptom A (for at least 2 days: Fever (Axillary temperature ≥37.5ºC), chills, sore throat, fatigue, nasal congestion or runny nose, muscle pain, headache, nausea or vomiting, diarrhea. Symptom B: Cough (for at least 2 days), loss of smell or taste (for at least 2 days), shortness of breath or difficulty breathing.
	VE against symptomatic COVID-19 in obese population, 14 days after 2nd dose *(PP)* *Case definition 1*	
VE against COVID-19 infection in Asians	VE against symptomatic COVID-19 in Asian population, 14 days after 2nd dose *(PP)* *Case definition 1*	Individuals with at least two type A symptoms, or at least one type B symptom, or radiologic characteristics of COVID-19 vaccine, with positive PCR test of COVID-19 (including saliva sample). Symptom A (for at least 2 days: Fever (Axillary temperature ≥37.5ºC), chills, sore throat, fatigue, nasal congestion or runny nose, muscle pain, headache, nausea or vomiting, diarrhea. Symptom B: Cough (for at least 2 days), loss of smell or taste (for at least 2 days), shortness of breath or difficulty breathing.
VE against asymptomatic COVID-19	Not Reported	Not Reported
Safety outcomes		
Serious adverse events	Serious adverse events (ITT)	Adverse events that results in following serious outcomes:need hospitalization treatment, prolong hospitalization time, disability, endanger life or death, cause congenital malformation, etc
Death (all-cause mortality)	Deaths (ITT)	Deaths due to all causes
Systemic reactogenicity	Systemic adverse events after dose 1 (ITT)	Occurrence of the ff solicited local adverse events: pain, induration, swelling, erythema and pruritus, 7 days after each dose, and unsolicited AEs up to 28 days after each dose
	Systemic adverse events after dose 2 (ITT)	

Local reactogenicity	Local adverse events after dose 1(ITT)	Occurrence of the ff solicited systemic adverse events (including vital signs): Fever (axillary temperature), acute allergic reaction, rash, diarrhea, loss of appetite, vomiting, nausea, myalgia, headache, cough, fatigue, joint pain, chills, and pruritus, 7 days after each dose, and unsolicited AEs up to 28 days after each dose
Adverse events	Local adverse events after dose 2 (ITT)	

Below are the details of the analysis sets used by the Brazil trial.

Table 1.4. Analysis Set definitions used in the report by Palacios et al., 2021

Analysis Set	Population
Intention-to-treat (ITT) set	All participants who have been randomized and have completed **at least one dose.** Incorrectly vaccinated participants were analyzed according to the group which the participants were randomized to.
Per-protocol (PP) set	All randomized participants who meet the inclusion criteria, did not meet any exclusion criteria, ***received two doses*** of the investigational vaccine or placebo, **do not use drugs prohibited by the protocol, and without major protocol deviations.** It will also exclude: - *Subjects who drop out within 14 days after second dose vaccination and do not enter the case surveillance period;* - *Subjects who test PCR-positive during the period from the first dose vaccination to within 14 days after the second dose vaccination;* - *Subjects who are confirmed of COVID-19 during the period from the first dose vaccination to within 14 days after the second dose vaccination.*
Modified intention-to-treat set (mITT)	All randomized participants who ***received two doses*** of the investigational vaccine or placebo, excluding: - *Subjects who drop out within 14 days after second dose vaccination and do not enter the case surveillance period;* - *Subjects who test PCR-positive during the period from the first dose vaccination to within 14 days after the second dose vaccination;* - *Subjects who are confirmed of COVID-19 during the period from the first dose vaccination to within 14 days after the second dose vaccination.*
Safety analysis set	All subjects enrolled in the study who complete at least one dose of the test product and provide relevant safety data. For incorrectly vaccinated subjects, they will be included in the vaccine group for analysis if the subject has received at least one dose of the investigational vaccine. Otherwise, they will be included in the placebo group for analysis.

We performed risk bias assessment for each outcome using Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB2 tool). Two reviewers independently

appraised the risk of bias. Any disagreements between reviewers were resolved through consensus. Quality of evidence was then appraised by two reviewers through the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) Approach.

Findings from the trial

The interim results of the Brazil trial covered data gathered from 21 July 2020 to 16 December 2020. There were a total of 12,408 participants enrolled in the trial. Among these participants, 9,823 belonged to the per-protocol set with 4,953 and 4,870 participants belonging to the vaccine and placebo arm respectively. The per-protocol set was used as the main analysis set for the efficacy analysis of this study. Of the nine efficacy outcomes and the five safety outcomes of interest to the HTAC, the current trial was able to measure and report all outcomes except vaccine efficacy against asymptomatic COVID-19.

For the efficacy of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*, the point estimate was computed using the formula 100 x (1-HR), where HR is the risk ratio. The vaccine was reported to have an efficacy of 50.65% (95%CI: 35.94 to 61.98) against symptomatic COVID-19 at least 14 days after the second dose, based on moderate certainty of evidence. Meanwhile, its efficacy against hospitalization due to COVID-19 and severe COVID-19 are at 100%, based on very low certainty of evidence. For its efficacy against hospitalization due to COVID-19 (≥ Score 4), 14 days after dose 2, there were zero events in 4,953 participants in the intervention group versus 10 events in 4,870 participants in the control group. For its efficacy against severe COVID-19 (≥ Score 6), 14 days after dose 2, there were zero events in 4,953 participants in the intervention group versus 6 events in 4,870 participants in the control group. Protection against hospitalization due to COVID-19 and severe COVID-19 remains to be demonstrated.

For its efficacy against symptomatic COVID-19 in the older population of 60 years or older, it was reported to be at 51.11% (95%CI: -166.93 to 91.04) based on low certainty of evidence as the elderly were not adequately represented in the trial, with only 5% of the trial population being aged 60 years and older. For its efficacy against symptomatic COVID-19 in populations with stable comorbidities, it was reported to be at 48.93% (95%CI: 26.47 to 64.69) based on low certainty of evidence. For the vaccine efficacy against symptomatic COVID-19 in the Asian population, it was found to be at 66.02%

(95%CI: -226.82 to 96.47) based on very low certainty of evidence as Asians were not adequately represented in the trial, with only 3% of the trial population being Asian.

As for the safety of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac],* the relative risks were calculated based on the reported number of participants that experienced adverse events. Based on the moderate certainty of evidence, there is minimal risk of systemic reactogenicity after dose 1 and after dose 2 of the vaccine while the risk of local reactogenicity after dose 1 and after dose 2 is higher in the vaccine group compared to placebo. For the critical outcome systemic reactogenicity, the relative risk after dose 1 is 1.02 times higher (95% CI: 1.01 to 1.03) and after dose 2 is 1.03 times higher (95% CI: 1.01 to 1.06) in participants who received the vaccine compared to participants who received placebo. As for the important outcome local reactogenicity, the relative risk after dose 1 is 1.95 times higher (95%CI: 1.86 to 2.04) and after dose 2 is 2.47 times higher (95%CI: 2.34 to 2.60) in the vaccine group compared to the placebo group.

Based on very low certainty of evidence for long-term critical outcomes, the relative risk of serious adverse events (RR: 1.06, 95% CI: 0.65 to 1.73) and death (all-cause mortality), (RR: 0.50, 95% CI: 0.045 to 5.51) remain inconclusive as the confidence intervals crossed the null-value. Two deaths (one due to cardiorespiratory arrest and one due to suicide) were reported in the Brazil trial, one occurred in the vaccine group and one occurred in the placebo group. Both deaths were deemed not related to the vaccination. A longer follow-up period is needed to ascertain the safety of the vaccine for these outcomes.

For its safety among elderly, using *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*, compared to placebo increases the risk of local adverse events by 1.70 times (95% CI: 1.34 to 2.15), based on moderate certainty of evidence. Meanwhile, there is inconclusive safety in terms of systemic adverse events [RR: 1.03 (95% CI: 1.00 to 1.06)], based on low certainty of evidence; and adverse events related to vaccination [RR: 1.13 (95% CI: 0.97 to 1.31)], based on low certainty of evidence. In terms of Grade 3 and 4 AEs reported in the population 60 years and above, there were zero events in 316 participants in the intervention group versus 2 events in 316 participants in the control group.

The ratings of evidence based on the trial are detailed on Table 1.5 and Table 1.6.

Table 1.5. Summary of findings for efficacy outcomes

OUTCOME	Quality Assessment *Note: The study design and number of studies column were collapsed since the input for these columns are the same across all outcomes*					Summary of Findings			Certainty	Importance
	Risk of bias	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**CoronaVac n/N (incidence density)**	**Placebo n/N (incidence density)**	**Effect Size (95% CI)** *(Reported values: unvalidated and will require IPD)*		
1A. VE against COVID-19 symptomatic COVID-19 *(≥ Score 2, symptomatic-independent)* *(at least 14 days after 2nd dose, case definition 1)*	**Not serious** (Low ROB)	NA	Not serious	Not Serious	Serious (Non-published data)	85/4953 (11.03)	168/4870 (22.34)	**VE: 50.65** (35.94 to 61.98)	⨁⨁⨁◯ **Moderate**	CRITICAL
1B. VE against symptomatic COVID-19 (≥ Score 3, symptomatic- need help) *(at least 14 days after the 2nd dose, case definition undefined)*	**Not serious** (Low ROB)	NA	Not serious	Not serious	Serious (Non-published data)	5/4953 *(0.66)*	30/4870 *(4.07)*	**VE:83.70** (57.99 to 93.67)	⨁⨁⨁◯ **Moderate**	CRITICAL
2A. VE against hospitalized COVID- 19 (≥ Score 4) *(at least 14 days after 2nd dose)*	**Not serious** (Low ROB)	NA	Serious	Serious (wide CI)	Serious (Non-published data)	**0/4953 (0.00)**	**10/4870 (1.35)**	**VE: 100.00**	⨁◯◯◯ **VERY LOW**	CRITICAL
2B. VE against hospitalized COVID- 19 (≥ Score 4) *(at least 14 days, after at least one dose)*	**Not serious** (Low ROB)	NA	Serious	Serious (wide CI)	Serious (Non-published data)	0/5717 (0.00)	10/5714 (0.99)	**VE:100.00**	⨁◯◯◯ **VERY LOW**	IMPORTANT
3A . VE against Severe COVID- 19 (≥ Score 6) *(at least 14 days, after 2nd dose)*	**Not serious** (Low ROB)	NA	Serious	Serious (wide CI)	Serious (Non-published data)	0/4953 (0.00)	6/4870 (0.81)	**VE:100.00**	⨁◯◯◯ **VERY LOW**	CRITICAL
3B. VE against Severe COVID- 19 (≥ Score 6) *(at least 14 days after at least one dose)*	**Not serious** (Low ROB)	NA	Serious	Serious (wide CI)	Serious (Non-published data)	0/5717 (0.00)	6/5714 (0.59)	**VE:100.00**	⨁◯◯◯ **VERY LOW**	IMPORTANT
4A. VE against symptomatic COVID-19 (≥Score 3, symptomatic - needing help) *(at least 14 days after 1st dose)*	**Not serious** (Low ROB)	NA	Not serious	Not Serious	Serious (Non-published data)	5/5717 (0.49)	33/5714 (3.27)	**VE: 85.10 (**61.85 to 94.19**)**	⨁⨁⨁◯ **MODERATE**	IMPORTANT

4B. VE against symptomatic COVID-19 (≥ Score 2, symptomatic independent) ***(up to 56 days, after at least 1 dose)***	**Not serious** (Low ROB)	**NA**	**Not serious**	**Not serious**	Serious (Non-published data)	**63/6195 (4.021)**	**158/6201 (4.006)**	**VE: 60.39 (56.54 to 63.9)**	⨁⨁⨁◯ **MODERATE**	**IMPORTANT**
4C. VE against symptomatic COVID-19 (≥ Score 2, symptomatic- independent) ***(up to 98 days after at least one dose)***	**Not serious** (Low ROB)	**NA**	**Not serious**	**Not serious**	Serious (Non-published data)	**116/6195 (8.38)**	**241/6201 (17.63)**	**VE:52.47 (51.88 to 53.05)**	⨁⨁⨁◯ **MODERATE**	**IMPORTANT**
5. VE against symptomatic COVID-19 in the older population, >60 years (≥ Score 2, symp independent) *(at least 14 days after 2nd dose)*	**Not serious** (Low ROB)	NA	Serious (elderly not adequately represented)	Very serious	Serious (Non-published data)	2/212 (10.75)	4/207 (21.89)	**VE: 51.11** (-166.93, 91.04)	⨁⨁◯◯ **LOW**	IMPORTANT
6. VE against symptomatic COVID-19 in population with stable comorbidities(PPS) *(at least 14 days after 2nd dose) (WHO Score not reported)*	**Not serious** (Low ROB)	NA	Not serious	Serious	Serious (Non-published data)	44/2731 (10.64)	86/2730 (20.84)	**VE: 48.93** (26.57 to 64.49)	⨁⨁◯◯ **LOW**	IMPORTANT
7. VE against symptomatic COVID-19 in patients with obesity (PPS) *(at least 14 days after 2nd dose) (WHO Score not reported)*	**Not serious** (Low ROB)	NA	Not serious	Not Serious	Serious (Non-published data)	13/1099 (5.78)	50/1112 (23.02)	**VE: 74.86** (53.73 to 86.35)	⨁⨁⨁◯ **MODERATE**	IMPORTANT
8. VE against symptomatic COVID-19 in Asian population (PPS) *(at least 14 days after 2nd dose) (WHO Score not reported)*	**Not serious** (Low ROB)	NA	Serious (Asians not adequately represented (3%))	Very Serious	Serious (Non-published data)	1/125 (5.38)	3/125 (15.54)	**VE: 66.02** (-226.82 to 96.47)	⨁◯◯◯ **VERY LOW**	IMPORTANT

Table 1.6. Summary of findings for safety outcomes

OUTCOME	Quality Assessment *Note: The study design and number of studies column were collapsed since the input for these columns are the same across all outcomes*					Summary of Findings			Certainty	Importance
	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CoronaVac n/N (% risk)	Placebo n/N (% risk)	Relative Risk *(Computed)*		
1. Serious adverse events	**Not serious** (Low ROB)	NA	Serious[b]	Serious[c]	Serious (Non-published data)	33/6202 (0.53%)	31/6194 (0.5%)	**1.06** (0.65 to 1.73)	⨁◯◯◯ **VERY LOW**	CRITICAL
1A. Death (All-cause mortality)	**Not serious** (Low ROB)	NA	Serious[b]	Serious[c]	Serious (Non-published data)	1/6202 (0.02%)	2/6194 (0.03%)	**0.50** (0.045 to 5.51)	⨁◯◯◯ **VERY LOW**	CRITICAL
2A. Systemic reactogenicity (Dose 1)	**Not serious** (Low ROB)	NA	Not serious	Not serious	Serious (Non-published data)	5844/6196 (94.32%)	5709/6200 (92.08%)	**1.02** (1.01 to 1.03)	⨁⨁⨁◯ **MODERATE**	CRITICAL
2B. Systemic reactogenicity (Dose 2)	**Not serious** (Low ROB)	NA	Not serious	Not serious	Serious (Non-published data)	3955/5453 (72.53%)	3852/5481 (70.28%)	**1.03** (1.01 to 1.06)	⨁⨁⨁◯ **MODERATE**	CRITICAL
3A. Local reactogenicity (Dose 1)	**Not serious** (Low ROB)	NA	Not serious	Not serious	Serious (Non-published data)	3252/6196 (55.39%)	1671/6200 (26.89%)	**1.95** (1.86 to 2.04)	⨁⨁⨁◯ **MODERATE**	IMPORTANT
3B. Local reactogenicity (Dose 2)	**Not serious** (Low ROB)	NA	Not serious	Not serious	Serious (Non-published data)	3261/5453 (59.80%)	1328/5481 (24.19%)	**2.47** (2.34 to 2.60)	⨁⨁⨁◯ **MODERATE**	IMPORTANT
4A. AEs related to vaccination among elderly (≥60 yo)	**Not serious** (Low ROB)	NA	**Not serious**	Serious	Serious (Non-published data)	176/316 (55.70%)	156/316 (49.37%)	***1.13*** *(0.97 to 1.31)*	⨁⨁◯◯ **LOW**	IMPORTANT
4B. Grade 3 and 4 adverse events among elderly (≥60 yo)	**Not serious** (Low ROB)	NA	**Serious**	Serious	Serious (Non-published data)	0/316 (0%)	2/316 (0.63%)	**0.00**	⨁◯◯◯ **VERY LOW**	IMPORTANT
4C. Systemic AEs among elderly (≥60 yo)	**Not serious** (Low ROB)	NA	Not serious	Serious	Serious (Non-published data)	128/316 (40.51%)	132/316 (41.77%)	***0.97*** *(0.80 to 1.17)*	⨁⨁◯◯ **LOW**	IMPORTANT
4D. Local AEs among elderly (≥60 yo)	**Not serious** (Low ROB)	NA	Not serious	Not serious	Serious (Non-published data)	129/316 (40.82%)	76/316 (24.05%)	**1.70** (1.34 to 2.15)	⨁⨁⨁◯ **MODERATE**	IMPORTANT

Table 1.7. Links to Risk of Bias 2 appraisal sheets for Palacios, et al. 2021

Outcome of Interest	Link to RoB sheets
Efficacy outcomes	
VE against Confirmed COVID-19 cases 14 days after 2nd dose (case definition 1)(PP)	https://docs.google.com/document/d/1O4CiJmz-0Vg0ytqCdr0dw-A9xvQPiDAP/edit
VE against COVID-19 Score 3 or higher at least 14 days after the second dose (PP)	https://docs.google.com/document/d/1O4CiJmz-0Vg0ytqCdr0dw-A9xvQPiDAP/edit
VE against COVID-19 Score 3 or higher at least 14 days after dose 1(ITT)	https://docs.google.com/document/d/1Beb6VZyEFgccvSxGAxfqtbCm-3S_I50d/edit
VE against symptomatic confirmed COVID- 19 score 4 and above by WHO 14 days after 2nd dose (PP)	https://docs.google.com/document/d/1O4CiJmz-0Vg0ytqCdr0dw-A9xvQPiDAP/edit
VE against COVID-19 Score 4 or higher at least 14 days after 1st dose (ITT)	https://docs.google.com/document/d/1Beb6VZyEFgccvSxGAxfqtbCm-3S_I50d/edit
VE against severe COVID-19 14 days after 2nd dose (PP)	https://docs.google.com/document/d/1O4CiJmz-0Vg0ytqCdr0dw-A9xvQPiDAP/edit
VE against severe COVID-19 14 days after 1st dose (ITT)	https://docs.google.com/document/d/1Beb6VZyEFgccvSxGAxfqtbCm-3S_I50d/edit
VE against Confirmed COVID-19 cases (up to 56 days after 1st dose) (ITT)	https://docs.google.com/document/d/1iYTy8oUiLSqINz8duKfOzMEVXvzZiaEN/edit
VE against Confirmed COVID-19 cases (up to 98 days after 1st dose) (ITT)	https://docs.google.com/document/d/1iYTy8oUiLSqINz8duKfQzMEVXvzZiaEN/edit
VE against symptomatic COVID-19 in elderly age group aged 60 years and above, 14 days after 2nd dose (PP)	https://docs.google.com/document/d/1S0wYzxGEV1WDmqB7OHZknQj2iP6yCbxB/edit
VE against symptomatic COVID-19 in population with stable comorbidities, 14 days after 2nd dose (PP)	https://drive.google.com/file/d/1atTmpgklkUL12bblRDKjDM1viL7VhDBo/view?usp=sharing
VE against symptomatic COVID-19 in obese population, 14 days after 2nd dose (PP)	https://drive.google.com/file/d/1atTmpgklkUL12bblRDKjDM1viL7VhDBo/view?usp=sharing
VE against symptomatic COVID-19 in Asian population, 14 days after 2nd dose (PP)	https://drive.google.com/file/d/14HCASgRa1y6f2snDNRlSVBu9vPnBAX6-/view?usp=sharing
Safety outcomes	
Serious adverse events	https://docs.google.com/document/d/16bXOdmeOftBfYIi_RtolhWqTatrkxrxbi46CCwS7698/edit
Deaths	https://docs.google.com/document/d/16bXOdmeOftBfYIi_RtolhWqTatrkxrxbi46CCwS7698/edit
Systemic adverse events after dose 1	https://docs.google.com/document/d/16bXOdmeOftBfYIi_RtolhWqTatrkxrxbi46CCwS7698/edit
Systemic adverse events after dose 2	https://docs.google.com/document/d/16bXOdmeOftBfYIi_RtolhWqTatrkxrxbi46CCwS7698/edit
Local adverse events after dose 1	https://docs.google.com/document/d/16bXOdmeOftBfYIi_RtolhWqTatrkxrxbi46CCwS7698/edit
Local adverse events after dose 2	https://docs.google.com/document/d/16bXOdmeOftBfYIi_RtolhWqTatrkxrxbi46CCwS7698/edit

Phase I/II trial in China (≥ 60 years old), (Wu et al, 2021)

Study characteristics

The trial of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* conducted in China for adults 60 years old and older was a randomized, double-blind, placebo-controlled Phase I/II trial. Phase I targeted 72 participants in a dose escalation study. Participants were randomly assigned (2:1) to receive 3 µg vaccine (1st block) versus placebo and 6 µg of vaccines versus placebo (2nd block). Meanwhile, Phase II targeted 350 participants who were randomly assigned (2:2:2:1) into 3 vaccine arms (1.5 µg, 3 µg, and 6 µg) and 1 placebo arm. This Phase I/II trial excluded participants with high-risk epidemiological history within 14 days before enrolment, history of severe acute respiratory syndrome (SARS) or SARS-Cov-2 infection, axillary temperature of more than 37 degrees Celsius, or history of allergy to any vaccine component. The primary safety endpoint was adverse reactions within 28 days after each injection in participants who received at least 1 dose. Primary immunogenicity endpoint was seroconversion rate at 28 days after the second injection.

Findings

The Phase I/II trial reached its target 422 participants (72 in Phase I and 350 in Phase II). Of these, 421 (72 in Phase 1 and 349 in Phase II) were included in the safety population while 411 (71 in Phase I and 340 in Phase II) were included in the immunogenicity evaluation. Table 1.8 shows the seroconversion rates and geometric mean titers of neutralizing antibodies of the two arms in the Phase I and Phase II trials.

Table 1.8. Neutralizing antibody response of 3 µg dose versus placebo in the Phase I/II clinical trials on adults age 60 years and above (Day 0, 28 schedule)

	SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac] arm		**Placebo arm**	
	Seroconversion rate (95%CI)	**Geometric mean titer (95% CI)**	**Seroconversion rate (95%CI)**	**Geometric mean titer (95% CI)**
Phase I				
	N = 24		*N = 24*	
Day 28 after 1st dose	**54.2%** (32.8 to 74.5)	**6.9** (4.6 to 10.2)	**0** (0 to 14.3)	**2.0** (2.0 to 2.0)

Day 28 after 2nd dose	**100%** (85.8 to 100)	**54.9** (38.6 to 78.2)	**0** (0 to 14.3)	**2.0** (2.0 to 2.0)
Phase II				
	N = 98		*N = 47*	
Day 28 after 1st dose	Not reported	Not reported	Not reported	Not reported
Day 28 after 2nd dose	**98.0%** (92.8 to 99.8)	**42.2** (35.2 to 50.6)	**0** (0 to 7.6)	**2.1** (2.0 to 2.10)

In phase I, none of the participants had any detectable neutralising antibody response against live SARS-CoV-2 at baseline. In both phase I and phase II trials, there were no neutralizing antibodies in all placebo recipients. Participants who received the vaccine exhibited immune response. However, the trial only reported the p values across all doses but did not report the statistical difference between each dose and the placebo.

As for the safety outcomes, the combined analysis of Phase I and Phase II trials showed that the use of SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac] showed inconclusive safety in adults age 60 years old and above in terms of any adverse reactions, systemic adverse reactions and local adverse reactions based on the calculated relative risks shown in Table 1.9.

Table 1.9. Results of safety evaluation of 3 µg dose in the Phase I/II clinical trials on adults age 60 years and above

Outcomes	***SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]***	**Placebo**	**Relative risk (95% CI)**
	n/N	**n/N**	
Any adverse reaction	25/125	15/73	0.97 (0.55 to 1.72)
Systemic reactions	13/125	12/73	0.63 (0.31 to 1.31)
Local reactions	15/125	3/73	2.92 (0.87 to 9.75)

REAL WORLD DATA

As of this writing, several countries have started administering *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*, including the Philippines.

- In the Philippines, the FDA collected reports of AEFIs from 01 March 2021 to 06 April 2021. In the most recent report, 378,525 and 50,685 individuals have been vaccinated with the first dose and second dose of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac],* respectively (FDA Philippines, 2021). There were a total of 5,885 reports of AEFIs, 5,751 of which were reports of non-serious events, with 129 serious reports other than death, and 5 reports involving death. A total of 70 AEFIs were reported by individuals aged 60 years and above. Severe allergic reactions have been reported on the use of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac].* However, these are very rare and occur only in a few individuals who were vaccinated. Due to an increasing number of reports of severe allergic reactions, its causal link with the vaccine is currently being investigated.
- In China, real world safety data were collected from 14 April 2020 to 5 February 2021. A total of 11,800,000 doses of the vaccine was administered (Personal communication with IP Biotech based on Chinese CDC, 2021) with a total of 4240 cases of adverse events reported. There were 46 serious adverse events recorded.
- As of 18 March 2021, about 9.78 million doses of the *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* have been administered in Brazil (Brasil Ministério de Saúde, 2021). There were 2,984 adverse events reported among participants of emergency use of the vaccine, however, the number of participants for emergency use was not reported. The adverse event rate for Grade 1 adverse events is 4.81%, 1.04% for Grade 2, and only 0.12% for Grade 3 (Brazil ANVISA, 2021).
- As of 18 March 2021, about 201,500 individuals in Hong Kong have received their first dose of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac].* The most recent report on the safety monitoring of the vaccine rollout is as of 7 March 2021 wherein 91,818 people had received *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac].* Of these vaccinees, 69 adverse events were reported. Direct causation between the reported adverse events and the vaccination are ongoing. In 20 of the adverse events associated with *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac],* the three most commonly reported are: headache (5 events), dizziness (3 events), and urticaria (3 events). Last March 28, the Department of Health had received a total of 13 death case reports with history of COVID-19 immunization from the HA. Eight of these reported deaths were concluded to be not directly associated

with COVID-19 vaccination. Assessment of the remaining reported deaths are on-going (Hong Kong Department of Health, 2021).

- As of 02 March 2021, a total of 3,378,552 doses of the *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* have been administered in Chile. There were 1,911 notifications of Events Supposedly Attributable to the Vaccination or Immunization (ESAVI) for the *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*, 90 of which were classified as serious. The report rate for serious adverse events after vaccination of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* was 2.67 per 100,000 doses. The most reported clinical manifestation of serious adverse events for *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* were anaphylaxis, dyspnea, pruritus, manifestations in the site of injection, general discomfort, headache nausea, urticaria, erythema, and diarrhea. There were 11 deaths after vaccination with *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac].* However, after evaluation it was deemed that the deaths were not related to the vaccine (Chile ISP, 2021).

  We have requested additional real world data from Sinovac Life Sciences Co., Ltd. These data shall be incorporated in this document as soon as it is available.

Appendix 2. Evidence for Criteria 3 - Affordability and viability

Cost of Implementing *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*

The following cost items were identified in calculating for the total resource requirement in implementing *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* to the Philippine government: the *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* and vaccine consumables; logistics (hauling and storage); and operations (recruitment and training of vaccinators). The source of these costs was 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 based on the data is Php 39,457,905,333.33. The paragraphs below will detail the costing calculation for cost components.

Vaccine and Consumables

The total cost of vaccines and consumables for 25 million Filipinos will amount to Php 37,093,971,428.57. This amount takes into account 5% estimated wastage of vaccines and cost of two doses of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* for every vaccinee. Vaccine consumables include personal protective equipment (PPE) of the vaccination team and injection devices.

Logistics

Included under logistics are hauling and storage costs. Hauling cost includes the procurement of transport boxes that can contain 1,000 vials each box. Given a weight of 31.4 kg per box, the total cost for hauling *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* is estimated at Php 665,994,000. This amount also includes a 1% valuation cost. For storage, the transport boxes are assumed to be stored in warehouses with storage capacity of 100 boxes per warehouse which will be used as temporary location before distribution to vaccination sites. The storage of the vaccines is assumed to last for a month at most, and is estimated to cost Php 2,800 per warehouse occupied, resulting in a storage cost of Php 1,470,000 per month. The overall cost for logistics is estimated to be at Php 667,464,000.

Operations

Operations cost includes mobilization, hiring costs, as well as training for vaccine implementation. Since it is projected that 25,000,000 Filipino will receive *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*, it is assumed that 178,571 vaccinators will be needed for the rollout. Further, the number of supervisors needed is estimated at 59,524,

with the assumption that one supervisor is needed per three vaccinators. The duration of the activity provided by DPCB was seven (7) days. With a salary of Php 500 per day for 7 days, the cost of mobilization of these individuals is estimated to be Php 833,333,333.33. For the training of the vaccinators and supervisors, two days are allotted to train them with a cost of Php 1,200 per head per day. In the training costing, DPCB included an input quantity of 121,545 on top of the total number of trainees (i.e., 238,095) multiplied by the cost (in peso) of training per day. This input value is currently being validated with DPCB. In total, the operations cost is computed at Php 1,696,469,904.76. Excluded in the operations cost are the cost of conducting routine RT-PCR tests among vaccination teams, as well as their transportation or any other costs necessary for mobilization and service delivery. Table 2.1 elaborates the resource requirement costs and assumptions in the roll-out of the *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* in the Philippines in 2021.

Table 2.1 Resource requirement costs in the roll-out of *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* in the Philippines in 2021

Description	Cost	Assumptions/Notes	Source
Vaccine and Vaccine Consumables	**Php 37,093,971,428.57**	For 2 doses, with 5% wastage; consumables include syringes, personal protective equipment, hand rub, cotton *(estimated costs for vaccinating 25,000,000 Filipinos based on identified target vaccinees for this brand)*	DPCB
Logistics	**Php 667,464,000.00**	For 2°C to 8°C vaccine storage temperature only. This includes hauling and storage costs. *(estimated costs for vaccinating 25,000,000 Filipinos based on identified target vaccinees for this brand)*	DPCB
Operations	**Php 1,696,469,904.76**	This does not include yet cost of their testing, transportation of vaccinators, or any other costs necessary for mobilization and service delivery. Note that the duration of activity provided by DPCB was 7 days. *(estimated costs for vaccinating 25,000,000 Filipinos based on identified target vaccinees for this brand)*	DPCB
TOTAL COST	**Php 39,457,905,333.33**		
TOTAL VACCINATION COST PER INDIVIDUAL	**Php 1,578.32**		

Acronym: ***DPCB:*** *Disease Prevention and Control Bureau*

Based on the projected calculations, the total cost of rolling out vaccination with *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* for 25,000,000 Filipinos would amount to Php 39,457,905,333.33 (which translates to Php 1,578.32 per individual). This would entail utilization of 47.83% of the total allocated budget for vaccination while the roll out using *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* will cover 36% of the target vaccinees for 2021.

Deployment and Feasibility

The COVID-19 Vaccine Deployment Plan outlines the prioritization of eligible populations in receiving the COVID-19 vaccine which includes *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]*. For Stage 1 of the Vaccine Deployment Plan of COVID-19 vaccines, 22.8% (24,668,128) of the Philippine population is targeted to receive the vaccine under Priority Eligible Population A. This group includes frontline health workers (1.6% or 1,762,994), indigent senior citizens (3.5% or 3,789,874), senior citizens (5.3% or 5,678,544), indigent populations (12.0% or 12,911,193), and uniformed personnel (0.5% or 525,523). On the other hand, Stage 2 of the Vaccine Deployment Plan will increase coverage to 32.95% of the population that will include teachers and social workers (0.95% or 1,179,097), other government workers (1.66% or 1,728,641), other essential workers (1.63% or 1,690,206), other socio-demographic groups with a significantly higher risk (1.72% or 1,785,000), overseas Filipino workers or OFWs (1.66% or 1,728,641), and other remaining members of the workforce (1.25% or 1,298,729) will be inoculated with the vaccine. Finally, in Stage 3 of the Vaccine Deployment Plan, the remaining Filipinos (67.05% or 73,888,198) will be vaccinated. In terms of the priority areas for the deployment of the COVID-19 vaccine, regions determined to have a higher prevalence would be prioritized for the vaccine rollout (i.e., NCR and Region III – Central Luzon).

In the rollout of the vaccine deployment plan, the logistics involved must be taken into consideration. The required storage temperature for the *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* is at 2 to 8 degrees Celsius protected from light and the shelf-life of the vaccine is estimated at 6 months. This temperature requirement can be addressed by use of refrigerators. It is expected that the *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* can be widely distributed to facilities with the said equipment; examples of which include tertiary hospitals, Rural Health Units, Municipal Health Offices, and City Health Offices. *SARS-CoV-2 Vaccine (Vero cell), Inactivated [CoronaVac]* can be accessible at the rural level.

Even though there is anticipated easier and wider distribution brought about by the storage temperature requirements, there is still a need for training on vaccine storage and handling to ensure product integrity across the entire supply chain, and a need to ensure the availability of trained personnel in handling unreported or rare adverse reactions that could occur following vaccination.

Appendix 4. References

1. Agência Nacional de Vigilância Sanitária - Anvisa. (2021). *Uso emergencial: confira votos, relatório e apresentações da reunião*. Retrieved 16 March 2021 from https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2021/confira-materiais-da-reuniao-extraordinaria-da-dico
2. Bueno, S., Abarca, K., González, P., Gálvez, N., Soto, J., & Duarte, L. et al. (2021). Interim report: Safety and immunogenicity of an inactivated vaccine against SARS-CoV-2 in healthy chilean adults in a phase 3 clinical trial. doi: 10.1101/2021.03.31.21254494
3. COVID-19 Vaccination Program Act of 2021. S10. (Philippines)
4. Chile Instituto de Salud Pública. (2021). Tercer Informe Estadístico: ESAVI serios asociados a la administración de las vacunas SARS-CoV-2 en Chile (24 diciembre 2020 - 02 marzo 2021). Retrieved 07 April 2021 from https://www.ispch.cl/wp-content/uploads/2021/03/20210319-Tercer-Informe-Estadistico-ESAVI-serias-VF-jrs-1.pdf
5. Department of Health (March 22, 2021). COVID-19 Tracker. Retrieved March 22, 2021, from https://ncovtracker.doh.gov.ph/
6. Department of Health Epidemiology Bureau. (January 16, 2021). *Average Daily Attack Rate and 2-Week Growth Rate of Cases by Region*. Retrieved March 20, 2021.
7. Department of Health- National Epidemiology Bureau (2021). *Distribution of Cases Outcomes as of 18 March 2021*. Unpublished report
8. Department of Health- Health Promotion Bureau. *Preliminary Results of the COVID-19 Vaccine Healthcare Workers Round 2 survey.* Unpublished report
9. Max Roser, Hannah Ritchie, Esteban Ortiz-Ospina and Joe Hasell (2020) - "Coronavirus Pandemic (COVID-19)". Published online at OurWorldInData.org. Retrieved from: 'https://ourworldindata.org/coronavirus' [Online Resource] National Economic and Development Authority. (December 30, 2020). LOSSES AND SETBACKS IN 2020 OFFER LESSONS TO RECOVER TOGETHER IN 2021 – NEDA. Retrieved January 15, 2021 from https://www.neda.gov.ph/losses-and-setbacks-in-2020-offer-lessons-to-recover-together-in-2021-neda/
10. Ministério da Saúde. (2021). *Doses de vacinação COVID-19 aplicadas*. Retrieved 19 March 2021 from https://viz.saude.gov.br/extensions/DEMAS_C19Vacina/DEMAS_C19Vacina.html
11. Palacios, R. (2021). *Report of a Randomized, Double-Blind, Placebo-controlled Phase III clinical trial to evaluate the efficacy and safety of the COVID-19 Vaccine (Vero Cell), Inactivated developed and manufactured by Sinovac in health care professions.* Unpublished report.
12. Personal communication with Prof. Dr. Serhat Ünal. (2021). *Randomized, Double-Blind, Placebo-Controlled Phase III Clinical Trial For Evaluation of Efficacy and Safety of SARS-CoV-2 Vaccine (Vero cell).* Unpublished report.
13. Personal communication with Sinovac Life Sciences Co., Ltd. (2021). *COVID-19 Vaccine (Vero cell), Inactivated.* Unpublished report.
14. Personal communication with Philippine Department of Foreign Affairs. (2021). *Certification of Comparability of Sinovac Price with other ASEAN countries.* Unpublished.
15. Personal communication with IP Biotech. (2021). *Analysis of Sinovac COVID-19 AEFI data from Chinese CDC.* Unpublished report.

16. Philippine Food and Drug Administration. (2021). *Emergency use authorization (EUA) for SARS-CoV-2 Vaccine (Vero Cell), Inactivated [CoronaVac], Sinovac Life Sciences Co., Ltd.* Retrieved 22 February 2021 from https://www.fda.gov.ph/wp-content/uploads/2021/03/EUA-SINOVAC-WEBSITE-3-1.pdf
17. Philippine Food and Drug Administration. (2021). Reports of Suspected Adverse Reaction to COVID-19 Vaccines (01 to 14 March 2021). Retrieved 24 March 2021 from https://www.fda.gov.ph/wp-content/uploads/2021/03/COVID-19-AEFI-Weekly-Report-as-of-14-March-2021-ver-2.1_1616139524.pdf
18. Philippine Statistics Authority. (December 3, 2020). Employment Situation in October 2020. Retrieved January 15, 2021 from https://psa.gov.ph/content/employment-situation-october-2020
19. Rusmil, K. (2021). *A Phase III, Observer-blind, Randomized, Placebo-controlled Study of the Efficacy, Safety and Immunogenicity of SARS-CoV-2 Inactivated VAccine in Health Adults Aged 18-59 years in Indonesia.* Unpublished report.
20. Technical Education and Skills Development Authority. (2020). COVID-19's Impact to the Philippine Economic Sectors: A TVET Response. Retrieved January 15, 2021 from https://www.tesda.gov.ph/Uploads/File/TVET%20Brief%202020/TVET%20Brief%20Issue%20no.%206_COVID-19s%20-Impact-to-Economic-Sectors.pdf
21. The Government of Hong Kong Special Administrative Region. *Expert Committee on Clinical Events Assessment Following COVID-19 Immunisation assesses serious adverse events relating to COVID-19 vaccination*. Retrieved 19 March 2021 from https://www.info.gov.hk/gia/general/202103/15/P2021031500828.htm?fontSize=1
22. The Government of Hong Kong Special Administrative Region. *Statistics for COVID-19 Vaccination Programme*. Retrieved 19 March 2021 from https://www.info.gov.hk/gia/general/202103/18/P2021031800838.htm
23. Ünal, S. (2020). *Protocol of Randomized, Double-Blind, Placebo-Controlled Phase III Clinical Trial For Evaluation of Efficacy and Safety of SARS-CoV-2 Vaccine (Vero cell), Inactivated.* Unpublished report.
24. Ünal, S. (2020). *Interim analysis report on Efficacy and Safety Evaluation of COVID-19 Vaccine (Vero cell), Inactivated Randomized , Double blind, Placebo controlled Phase III Clinical Trial.* Unpublished report.
25. Wong, J.Q., (2021). *Public Health Impact of CoronaVac Vaccine.* [Powerpoint slides].
26. Wu, Z., Hu, Y., Xu, M.m Chen, Z., Yang, W., Jiang, Z., Li, M., Jin, H., Cui, G., Chen, P., Wang, L., Zhao, G., Ding, Y., Zhao Y., & Yin, W. (2021). *Safety tolerability, and immunogenicity of inactivated SARS-CoV-2 vaccine (CoronaVac) in health adults aged 60 years and older: a randomised, double-blind, placebo-controlled, phase ½ clinical trial. The Lancet.* https://doi.org/10.1016/S1473-3099(20)30987-7
27. Zhang, Y., Zeng, G., Pan, H., Li, C., Hu, Y., Chu, K., Han, W., Chen, Z., Tang, R., Yin, W., Chen, X., Hu, Y, Liu, X., Jiang, C., Li, J., Yang, M, Song, Y., Wang, X, Gao, Q., & Zhu, F. (2021). *Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18-59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. The Lancet.* 10.1016/S1473-3099(20)30843-4

Appendix 5. Acknowledgement

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