Annex A. HTAC Judgment per HTAC decision framework criterion for the assessment of second booster for individuals ages 18 to 49 years without comorbidities

<table>
<tr><th rowspan="2">Criteria</th><th colspan="7">HTAC Judgment
(08 September 2022)</th></tr>
<tr><th>Pfizer</th><th>Moderna</th><th>AstraZeneca</th><th>CoronaVac</th><th>Janssen</th><th>Sinopharm</th><th>Sputnik Light</th></tr>
<tr><td>What is the rate of breakthrough infection or hospitalizations among individuals 18 to 49 years old without comorbidities?

Is COVID-19 a public health priority for individuals 18 to 49 years old without comorbidities?</td><td colspan="7">There is an observed increase in COVID-19 cases, weekly positivity rates, and severe and critical hospital admissions from June 2022 to mid- August 2022. Cases, positivity rates, and severe and critical hospital admissions then decreased in late August 2022 to early September 2022. Meanwhile, CFRs in adults aged 18 to 49 years old remained relatively the same.

The emergence of new COVID-19 variants poses the potential threat of reduced protection and more rapid waning of immunity, thus the need to evaluate the potential impact of introducing a second booster of vaccines. Apart from the risk of COVID-19 disease, the burden of COVID-19 also includes non-clinical impact such as the possible disruption of livelihood and the additional burden to the healthcare system.

Booster vaccination can reduce the disease burden by averting a significant number of infections including any SARS-CoV-2 infection, symptomatic COVID-19, hospitalization due to COVID-19, severe COVID-19 and death due to COVID-19.</td></tr>
<tr><td>Does the first booster work for individuals 18 to 49 years old without comorbidities? How long does protection from the first booster of COVID-19 vaccines last?</td><td colspan="5">Among the general population, most studies show that there is sustained protection for severe infection/hospitalization, and death due to COVID-19 caused by the Omicron variant for 3 to 6 months. In terms of symptomatic COVID-19, most studies showed that there is a more pronounced waning of protection observed at 3 to 6 months after the first booster.</td><td colspan="2">Cannot be assessed due to current lack of evidence</td></tr>
<tr><td>Is the second booster efficacious for individuals 18 to 49 years old without comorbidities?</td><td colspan="2">Based on limited evidence:
● Absolute VE against SARS-CoV-2 infection of 2nd booster of Pfizer-BioNTech and Moderna in the general population aged 18 years and older compared to the unvaccinated population passed the HTAC specifications for VE against symptomatic COVID-19</td><td>Based on very limited evidence, the absolute VE of 2nd booster of AstraZeneca against any SARS-CoV-2 infection in the</td><td colspan="4">Cannot be assessed due to current lack of evidence</td></tr>
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	(Chariyalertsak et al. 2022). ● In terms of relative effectiveness, 2nd booster of *Pfizer-BioNTech* and *Moderna* has inconclusive VEs against any SARS-CoV-2 infection in the general population aged 16 to 54 years old compared to the first booster (Kiss et al. 2022).		general population aged 18 years and older compared to the unvaccinated population passed the HTAC specifications for VE against symptomatic COVID-19 (Chariyalertsak et al. 2022). However, given that there are only a few participants who received *AstraZeneca*, more studies are needed to establish its effectiveness.	
Is the second booster of COVID-19 vaccine safe for individuals 18 to 49 years old without comorbidities?	Short-term safety of 2nd booster *Pfizer- BioNTech* is acceptable based on real world post-marketing safety surveillance (Instituto de Salud Publico Chile; 18 years old and above). However, further follow-up data is needed to	Short-term safety of 2nd booster *Moderna* is acceptable based on post-marketing safety report (ModernaTx; 18 years old and above). However, further follow-up data is needed to establish longer-term	Based on limited use of AstraZeneca in Australia, short term safety in terms of thrombotic thrombocytopenia syndrome (TTS) is considered acceptable. However,	Cannot be assessed due to current lack of evidence

	establish longer-term safety. HTAC notes that myocarditis and pericarditis, rare adverse events of interest that are associated with mRNA vaccines, are most prevalent in male individuals aged 18 to 29 years old. Moreover, rates of myocarditis and pericarditis have been reported to be greater after the primary series, compared to boosters (UK MHRA, 2022; US ACIP, 2022). In terms of autoimmunity, a systematic review by Jara et al. noted that incidence of autoimmune events are low.	safety. HTAC notes that Myocarditis and pericarditis, rare adverse events of interest that are associated with mRNA vaccines, are most prevalent in male individuals aged 18 to 29 years old. Moreover, rates of myocarditis and pericarditis have been reported to be greater after the primary series, compared to boosters (UK MHRA, 2022; US ACIP, 2022). In terms of autoimmunity, a systematic review by Jara et al. noted that incidence of autoimmune events are low.	further follow-up data is needed to establish longer-term safety.	
Does the second booster of COVID-19 vaccines provide a highly favorable benefit/risk profile in the context of observed vaccine efficacy,	Among individuals aged 18 to 49 years old, a second booster of *Pfizer-BioNTech* or *Moderna* has an acceptable benefit-risk profile based on limited evidence on effectiveness, immunogenicity and short term safety data.		Given the very limited evidence on the effectiveness of *AstraZeneca*, more studies are needed to	Risk benefit profile cannot be assessed due to current lack of evidence on efficacy, effectiveness, and safety.

effectiveness and safety in individuals 18 to 49 years old without comorbidities?		establish the benefit-risk profile of this vaccine.		
Is the second booster of COVID-19 affordable, feasible, and viable to use in a national immunization program for individuals 18 to 49 years old without comorbidities?	Rollout of second boosters among healthy population aged 18 to 49 yo is viable and feasible.	Viability and feasibility was not further assessed due to very limited clinical evidence as a second booster.	Viability and feasibility was not further assessed due to lack of clinical evidence as a second booster.	Viability and feasibility was not further assessed due to lack of clinical evidence as a second booster and its non-inclusion in the WHO EUL listing
Is the second booster of COVID-19 affordable, feasible, and viable to use in a national immunization program for individuals 18 to 49 years old without comorbidities?	*Pfizer-BioNTech and Moderna* are considered affordable and within the range of price at which it is available in other countries. Further, implementing 2nd boosters of *Pfizer-BioNTech* and *Moderna* for the healthy population aged 18 to 49 yo will not incur additional budget impact. These vaccines may represent good value for money as it is likely to be effective/efficacious.	Affordability, budget impact, and value for money was not further assessed due to very limited clinical evidence as a second booster.	Affordability, budget impact, and value for money was not further assessed due to lack of clinical evidence as a second booster.	Affordability budget impact, and value for money was not further assessed due to lack of clinical evidence a second booster and its non-inclusion in the WHO EUL listing
Does the second booster reduce out-of-pocket (OOP) expenses of households due to COVID-19?	Based on current evidence, 2nd booster *Pfizer-BioNTech* or *Moderna* has the potential to reduce out-of-pocket expenses due to averted costs of isolation and treatment of mild, moderate, and severe COVID-19.	Potential to reduce out-of-pocket expenses was not further assessed due to	Potential to reduce out-of-pocket expenses was not further assessed due to lack of clinical evidence as a second booster.	Potential to reduce out-of-pocket expenses was not further assessed due to

		very limited clinical evidence as a second booster.		lack of clinical evidence as second booster and its non-inclusion in the WHO EUL listing
Does the second booster possess the characteristics that are desired by key stakeholders?	Given the available clinical evidence, ease in logistics, ability to allow for equitable coverage, cost effectiveness, and availability of mechanism to manage any untoward serious adverse reactions following vaccination, *Pfizer-BioNTech* and *Moderna* possess **some** of the characteristics desired by key stakeholders for its use as a second booster booster dose for the healthy population aged 18 to 49 years old. However, the WHO has not yet recommended a 2nd booster for the general healthy population. In addition, the Philippine FDA has not yet issued an EUA for 2nd boosters for the healthy population aged 18 to 49 years old. Further, local acceptability showed a general hesitancy towards getting boosters in general as they think that they will not be infected by the COVID-19 since they are already vaccinated with the primary series (DOH HPB, 2022).	Social impact was not further assessed due to very limited clinical evidence as a second booster.	Social impact was not further assessed due to lack of clinical evidence as a second booster.	Social impact was not further assessed due to lack of clinical evidence as a second booster and its non-inclusion in the WHO EUL listing.
Does a second booster of COVID-19 vaccine reduce or not further add to existing inequities in the health system?	The HTAC reiterates the importance of the following measures in the success of the implementation of COVID-19 second booster vaccination: ● emphasis on strategies to increase primary series for children < 12 yo and first booster vaccination coverage among	The appropriateness of the use of *AstraZeneca*, second booster was not further assessed due to very limited	The appropriateness of the use of *CoronaVac, Sinopharm,and Janssen* as second booster was not further assessed due to lack of clinical evidence as a second booster.	The appropriateness of the use of Sputnik Light as second booster was not further assessed due to

	priority groups ● ensure that IEC and other vaccination-related documents are accessible and comprehensible (i.e., translated into the local language of the target population) Second booster vaccination shall be rolled out following the country's prioritization criteria, cognizant of the following: ● burden of COVID-19 in the priority groups, especially those with comorbidities; ● sufficient supply to cover the all other vaccination strategies in the pipeline (remaining primary for adult and pediatric population, remaining first booster/3rd dose for adults, booster for pediatric population) ● high first booster vaccination coverage (40-70%, per WHO criteria) for the general population aged 18 years and above We note that the National Vaccination Operations Center (NVOC) has started implementing alternative vaccination sites to increase access to vaccines.	clinical evidence as a second booster.		lack of clinical evidence as second booster and its non-inclusion in the WHO EUL listing.

Annex B. Scoping of Recommendations of other National Regulatory Agencies regarding second booster (as of 08 September 2022)

A. Positive recommendation on 2nd booster for the general adult population

Country/ Territory / Organization	Vaccine Brands Recommended	Dosing Interval	Remarks
Chile	Pfizer-BioNTech, Moderna	5 months after 1st booster	also recommended for children (3-17 years old); persons with comorbidities, the elderly (60 years old and above) and health care workers
Bahrain	Pfizer-BioNTech, Valneva, Sinopharm	at least 3 months after 1st booster	also recommended for adolescents (12-17 years old), the elderly (60 years old and above) and healthcare workers
Thailand	Pfizer-BioNTech, Moderna, AstraZeneca	at least 4 months after 1st booster	also recommended for the elderly (60 years old and above) and healthcare workers.
Abu Dhabi	Pfizer-BioNTech, Sinopharm	at least 6 months after 1st booster	also recommended for the elderly (60 years old and above)
Ecuador	Pfizer-BioNTech, CoronaVac, AstraZeneca, Cansino	4 months after 1st booster	also recommended for the elderly (60 years old and above), and healthcare workers
Lebanon	Pfizer-BioNTech	6 months after 1st booster	None
Mongolia	Pfizer-BioNTech, Sinopharm	3 months after 1st booster	None
Pakistan	Not specified (may be same or different than initial doses)	4 months after 1st booster	also recommended for children (12 to 17 yo) and healthcare workers
Peru	Pfizer-BioNTech, Moderna	5 months after 1st booster	Positive recommendation of 2nd booster for 30 years and older only
Canada (NACI)	Moderna (Bivalent), Moderna, Pfizer-BioNTech	3 to 6 months after 1st booster	Positive recommendation of 2nd booster 18 to 29 years old only
Argentina	AstraZeneca, Cansino, Sputnik V, Pfizer-BioNTech	3 to 6 months after 1st booster	also recommended for persons with comorbidities, the elderly (60 years old and above), healthcare workers, and strategic government personnel

B. Discretionary recommendation on 2nd booster for the general adult population

Country/ Territory / Organization	Vaccine Brands Recommended	Dosing Interval	Remarks
Canada (NACI)	Moderna (Bivalent), Moderna, Pfizer-BioNTech	3 to 6 months after 1st booster	Discretionary recommendation for 12 to 17 yo and 30 to 59 yo
Ontario Health	No specified vaccine brand	3 to 5 months after 1st booster	Discretionary recommendation for 18 to 59 yo
Australia	Preferred: Pfizer-BioNTech, Moderna AstraZeneca	3 months after 1st booster	Discretionary recommendation for 30 to 49 yo

C. Negative recommendation on 2nd booster for the general adult population

Country/ Territory / Organization	Remarks
European CDC/ European Medicines Agency	2nd booster recommended only for individuals with comorbidities, elderly (60 years and older), healthcare workers
Israel	2nd booster recommended only for elderly (60 years and older) and healthcare workers
HongKong	2nd booster recommended only for individuals with comorbidities, elderly (50 years and older), healthcare workers
Uruguay	2nd booster recommended only for individuals with comorbidities, elderly (60 years and older), healthcare workers
Brazil	2nd booster recommended only for individuals with comorbidities, elderly (50 years and older)
Panama	2nd booster recommended only for individuals with comorbidities, elderly (50 years and older)
Colombia	2nd booster recommended only for individuals with comorbidities, elderly (50 years and older)
Malaysia	2nd booster recommended only for individuals with comorbidities, healthcare workers
Indonesia	2nd booster recommended only for healthcare workers
Morocco	2nd booster recommended only for individuals with comorbidities, elderly (60 years and older)
Trinidad and Tobago	2nd booster recommended only for elderly (60 years and older), healthcare workers
Saudi Arabia	2nd booster recommended only for elderly (50 years and older)
South Africa	2nd booster recommended only for elderly (50 years and older)
United Kingdom	2nd booster recommended only for individuals with comorbidities, elderly (50 years and older), healthcare workers

Singapore	2nd booster recommended only for individuals with comorbidities, elderly (50-59 yo discretionary; 60 yo mandatory)
WHO	2nd booster recommended only for individuals with comorbidities, elderly (age cut off should be defined by countries), healthcare workers, and pregnant women

D. Revised recommendation on 2nd booster for the general adult population

Country/ Territory / Organization	Remarks
US CDC	guidelines are simplified i.e. changing from dose counting to 1 bivalent booster for everyone (12 years old and older for *Pfizer BioNTech (Bivalent) vaccine, 18 years old and above for Moderna (Bivalent) vaccine*, regardless of number of doses received.
US FDA	monovalent mRNA vaccines are now not authorized given US FDA's authorization of bivalent Moderna and Pfizer-BioNTech as booster dose

E. Unavailable recommendations on 2nd booster for the general adult population

- United Arab Emirates
- Zambia
- Mexico
- China
- Egypt