HTAC EVALUATION FRAMEWORK FOR COVID-19 VACCINES UNDER EMERGENCY USE AUTHORIZATION

I. Background

Pursuant to Republic Act No. 11223, otherwise known as the Universal Health Care UHC Act, the Health Technology Assessment Council (HTAC) shall provide financing and coverage recommendations on health technologies to be funded by the Department of Health (DOH) and the Philippine Health Insurance Corporation (PhilHealth). The HTAC is mandated to perform the following functions: oversee HTA process implementation and assess existing and new health technologies for funding decisions. In the evidence appraisal and recommendation development, in general, the HTAC is guided by the following criteria: responsiveness to magnitude, severity, and equity; safety and effectiveness; household financial impact; cost-effectiveness; and affordability and viability.

Under the UHC Act, the HTAC shall assess a health technology's safety and effectiveness using the results of Phase IV clinical trials. This also implies that prior to HTA, the health technology must have passed the regulatory requirements of the Food and Drug Administration (FDA) through the issuance of its market authorization. However, in Republic Act No. 11494; otherwise known as the Bayanihan to Recover As One Act, the requirement for Phase IV clinical trials of COVID-19 medications and vaccines, as stipulated in the UHC Act, was waived to expedite the procurement process provided that such vaccine is recommended and approved by the WHO and/or other internationally recognized health agencies. The law also highlights the role of HTAC in evidence appraisal of health technologies that guides the development of comprehensive guidelines and approaches to address COVID-19.

II. Policy Question

The HTAC aims to answer the policy question: What COVID-19 vaccines should be used to reduce COVID-19 cases, severe infection, and deaths? In doing so, streams of continuous work to assess the clinical, economic, and ethical, legal, social, and health system implications of COVID-19 vaccine are on the way to guide the recommendation for selection among candidate vaccines.

III. Purpose of the Document

This framework was designed by the HTAC to describe how the Council intends to evaluate the vaccines by setting the criteria, framing the questions that they aim to answer per criterion, and describing the type of evidence that they will consider in answering the questions per criterion. This document shall be posted publicly through the HTA website to gather inputs and comments from different stakeholders. This is aligned with our commitment to embed principles of transparency, accountability, inclusiveness, and due process in the implementation of HTA under the work of the HTA Council.

However, in Bayanihan to Recover as One Act, the HTAC can only issue a recommendation using data from at least completed Phase III clinical trials. Consideration based on an Emergency Use Authorization (EUA) issued by the FDA, which utilizes interim analysis of ongoing Phase III clinical trials, will require amendment of the relevant laws. Thus, an HTAC recommendation based on the framework below can be done and officially submitted only when the amendments of relevant laws have been made.

In the meantime, recognizing the importance of responding to the decision of policymakers, the HTAC has begun early assessments using publicly available peer-reviewed sources as well as consultations that will involve all affected stakeholders.

This framework and the HTAC specifications indicated will be reviewed and revised as new scientific evidence becomes available.

IV. HTAC Evaluation Framework

EVALUATION CRITERIA	QUESTION	EVIDENCE TO BE CONSIDERED	SOURCE OF EVIDENCE	HTAC SPECIFICATIONS
Responsiveness to magnitude and severity The health intervention must address the top medical conditions that place the heaviest burden on the population, including dimensions of magnitude or the number of people affected by a health problem, and severity or health loss by an individual as a result of the disease such as death, handicap, disability or pain.	Can the vaccine being assessed significantly reduce the magnitude and severity of COVID 19?	Current epidemiological data on COVID-19 Data on excess deaths and morbidities Data on the disruption of essential health services (look at international groups on their data) Changes in budget allocation Impact of vaccine on reduction of disease burden • Disease modelling (local and international) showing that the vaccine can reduce the number of cases, hospitalization and deaths Economic impact of COVID-19 Note: During a public health emergency, Phase IV studies requirement is waived in accordance with the Bayanihan 2 or Republic Act 11494. The HTAC will use the current best available Phase III data to review clinical evidence of COVID-19 vaccines.	DOH Epidemiology Bureau (DOH-EB), PhilHealth claims, Secretary of Health (SOH), and Office of the President (OP) declarations on COVID-19 as PHE DOH, Philippine Statistics Authority (PSA) Disease Prevention and Control Bureau (DPCB), World Health Organization Health Policy Development and Planning Bureau (HPDPB) - Planning Division Burden of disease Model estimates from published local and international data PhilHealth claims, National Economic and Development Authority (NEDA) for local data, World Bank for international data	The vaccine can potentially reduce the COVID-19 disease burden (health, social and economic impact).

Clinical efficacy and safety In a PHE, each intervention must at least be at Phase 3 trial with interim results from at least 2 months of median follow-up. (Pending legal provision allowing HTAC). The benefits of the intervention should outweigh any potential harm to the users and health care providers.	What is the efficacy of COVID-19 vaccines in terms of reducing the incidence and/or severity of COVID-19 in the general and vulnerable populations?	Phase III interim clinical trial data (pending provision allowing HTAC to consider this level of evidence) Vaccine efficacy (VE)/ effectiveness measured in terms of: ● Reduction in mortality ● Reduction of symptomatic cases ● Reduction of asymptomatic cases ● Reduction of hospitalization Among subgroups: age (include elderly, children), pregnant, patients with comorbidities, immunocompromised patients, COVID-19 survivors, frontliners	Stringent peer-reviewed reports (e.g., websites of stringent regulatory authorities, such as US FDA, European Medicines Agency, Health Canada, Japan Pharmaceutical and Medical Device Agency (PMDA), UK Medicines and Healthcare Products Regulatory Agency (MHRA), Australia Therapeutic Goods Agency (TGA), The French Agency for Food, Environmental and Occupational Health and Safety (ANSES), Germany Federal Institute for Drugs and Medical Devices (BfArM), The Pharmaceutical Service Ministry of Health Republic of Italy and Swissmedic Switzerland, Singapore Health Sciences Authority (HSA), South Korea Ministry of Food and Drug Safety (MFDS) Published Phase I to III studies in peer-reviewed journals	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 for the Philippines Note: Pending legal provision allowing the use of evidence based on Phase III interim results Adopted from WHO, US FDA, other stringent regulatory authorities
	What is the duration of protection of COVID-19 vaccines to reduce the incidence and/or severity of COVID-19?	Phase III RCT interim results (pending provision allowing HTAC to consider this level of evidence)	Phase III trial data, real-world evidence	Minimum acceptable: confers at least 6 months Ideal/Preferred: ≥1 year protective immunity Adopted from WHO Target Product Profile for COVID-19 Vaccines (2020)
	What are the safety issues and incidence of adverse events caused by COVID-19 vaccines?	All adverse events ● Local and systemic reactions, serious adverse events (AEs) ● Adverse Events of special interest	Phase III trial data, real-world evidence from DOH, Philippine FDA and National Regulatory Authorities	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

		(Reference: Preliminary list of Vaccine Adverse Event Reporting System (VAERS) AEs of special interest, publication date: Oct 30, 2020): COVID-19 disease, death, vaccination during pregnancy and adverse pregnancy outcomes, Guillain-Barre syndrome (GBS), seizures/convulsions, stroke, narcolepsy/cataplexy, anaphylaxis, acute myocardial infarction, myocarditis/pericarditis, thrombocytopenia, disseminated intravascular coagulation (DIC), venous thromboembolism (VTE), Kawasaki disease, multisystem inflammatory syndrome (MIS-C, MIS-A)		reactions): at least 2 months Long term outcomes (e.g., serious AEs): at least 1 year
	Does the vaccine provide a highly favorable benefit/risk profile in the context of observed vaccine efficacy?	Phase III RCT interim results (pending provision allowing HTAC to consider this level of evidence) Description of the balance of benefits and harms	Phase III trial results	Favorable benefit/risk profile The benefit of preventing morbidity of at least a 50% reduction in the risk of COVID-19 outweighs the reported risk of adverse events Note: Pending legal provision allowing the use of evidence based on Phase III interim results
Affordability and viability The intervention must be affordable, and the cost thereof must be viable to the financing agents. The intervention must be feasible to implement and adopt given existing health care resources at the local or national level.	Is the intervention affordable?	Costing analysis (resource requirements) • Unit cost of the vaccine, cost of full vaccination course per individual • Cost of vaccine implementation (logistics, human resource/training, information systems, safety and effectiveness monitoring, etc.)	DOH and PhilHealth	Affordability will be measured using the sufficiency of the allocated amount to achieve vaccination targets.

	What are the budget implications of using COVID-19 vaccines?	Budget impact analysis Consider in the analyses the purchases of LGUs and private sectors	COVID-19 International Modelling (CoMo) Consortium	The share of the cost to implement the COVID-19 vaccine in 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. Note: The vaccine unit cost is comparable with those in other ASEAN countries.
	Does the vaccine represent good value for money in terms of: a. preventing COVID-19 mortality b. lowering hospitalization (moderate, severe and critical cases) c. lowering the incidence of symptomatic (mild) and asymptomatic cases (RT-PCR confirmed cases)	Economic evaluation based on Disease Modeling (CoMo Model)	DOH DPCB and other relevant offices, Department of Finance (DOF) and the NEDA	The health, economic, and social benefits of the vaccination program outweigh the costs. The vaccine is likely cost-effective and represents an efficient allocation of resources. Note: A full-blown cost-effectiveness analysis (CEA) 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, skills and training of vaccinators/vaccine providers, and access of the target population to the health care facility? Are there plans to overcome significant barriers?	Manufacturer reports on handling and distribution Reports from DOH-Supply Chain Management Office and Public Health Services Team	DOH, SCMO	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.

Household Financial Impact The intervention must be affordable, and the cost thereof must be viable to the financing agents. The intervention must be feasible to implement and adopt given existing health care resources at the local or national level.	Will the vaccine reduce or not add further to the out-of-pocket (OOP) expenses of Filipino households?	Transportation costs Averted testing/treatment, isolation costs Averted loss of income	PhilHealth claims, PSA data on employment	The adoption of the vaccine can reduce out-of-pocket spending of individuals and families due to averted COVID-19 disease and/or hospitalization.
Social impact Social, cultural, religious, and other factors which affect the acceptability of the adoption and use of the health technology in the Philippines for the general population and/or specific subgroups of the population. Patient preferences and values that need to be considered by decision-makers, such as the acceptability of the health intervention and its convenience of use, which may impact various aspects of the lives of patients as well as their families and caregivers	Does the vaccine possess the characteristics desired by key stakeholders (i.e., policy- and decision makers, health workers, program managers/implementers, patient groups, CSOs, communities, general public)? • Safety • Efficacy • Availability • Transparency in the regulatory/approval process and information on the vaccines • Cost-efficiency to the government • Potential for high and equitable coverage • Ease in logistical and implementation requirements • 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	Assessment of stakeholders' acceptability of the intervention	Evidence from FGD, national surveys and consultations	The vaccine possesses all or most of the characteristics desired by key stakeholders. Qualitative responses will contextualize the Filipino experience, and may impact implementation strategy.

Responsiveness to equity The health intervention must address the poorest and most vulnerable population's conditions and must reduce or not aggravate the existing disparities.	How will the vaccine and its use impact pre-COVID and COVID-generated health and socioeconomic inequities? Which groups might be unfairly disadvantaged in relation to the COVID-19 disease burden and delivery of COVID-19 vaccines?	Assessment to identify groups that might be disadvantaged (PROGRESS PLUS) Sociodemographic profile of those who have been greatly affected by COVID-19 (clinically, economically) Epidemiology by area and subgroups	DOH EB, regional health offices (CHDs), scientific and gray literature	Ideally, health interventions can be fairly adopted and distributed/ implemented for eligible populations without aggravating existing health inequities, especially for vulnerable sectors of our society.

IV. References

ACIP slides

- Public Health Problem, Resource Use, and Equity Domains (presented during ACIP Meeting, November 23, 2020): https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2020-11/COVID-02-Oliver.pdf
- Values, Acceptability, and Feasibility Domains (presented during ACIP Meeting, November 23, 2020): https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2020-11/COVID-03-Oliver.pdf

Handbook *(Version 1.2, November 1, 2013)*: https://www.cdc.gov/vaccines/acip/recs/grade/downloads/handbook.pdf

Worksheet (Last updated 7 June 2018): https://www.cdc.gov/vaccines/acip/recs/grade/downloads/ACIP-evidence-rec-frame-508.pdf

WHO Target Product Profiles for COVID-19 Vaccines *(Version 3, 29 April 2020)*: https://www.who.int/publications/m/item/who-target-product-profiles-for-covid-19-vaccines

WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination (14 September 2020): https://apps.who.int/iris/bitstream/handle/10665/334299/WHO-2019-nCoV-SAGE_Framework-Allocation_and_prioritization-2020.1-eng.pdf?sequence=1&isAllowed=y