Gavi's Role in a Future COVID-19 Vaccine Programme

Annex B – COVID-19 Vaccine Investment Assessment

Gavi Alliance Board

26-27 June 2023

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Gavi The Vaccine Alliance

Disease context and uncertainties

Disease and epidemiological context

Coronavirus disease (COVID-19) is a respiratory infectious disease caused by the SARS-CoV-2 virus; **high potential for transmissibility, immune escape and severity, especially for vulnerable populations** (e.g., ages 60+, pregnant persons, immuno-compromised, adults with significant comorbidities)[1]

COVID-19 was recognized as the **fifth leading cause of death globally**, accounting for nearly one in twenty deaths worldwide since the beginning of 2020[2]. As of March 2023, **762M confirmed cases** and **6.8M deaths** have been officially reported. Several variants continue to co-circulate, although vaccination has helped reduce burden of severe disease and death[3].

Individuals recovered from acute COVID-19 illness may experience persistent symptoms or Post-COVID Condition (PCC). By the end of 2021, an estimated **3.7%** of SARS-CoV-2 patients had developed post-COVID condition and **15.1%** had persistent symptoms at 12 months[4]

Continued uncertainties

Predictability of **surges and seasonality**

New variants that could be more severe and/or more transmissible

Continued demand for COVID-19 vaccines

Long term protection against severe disease and death

Evolution of products and implications on efficacy, durability and programmatic feasibility and country product preferences

Evolution of the **future supplier base**

Recognising the **need to start planning**, the Secretariat is proposing to move forward using the **best information available**, understanding that our **assumptions can change** with new information

SOURCE: 1) WHO (Link), 2) Think Global Health (Link), 3) Data as of 9 April 2023 - WHO epidemiological update (Link), 4) WHO

Several safe and efficacious COVID-19 vaccines are available through COVAX to protect vulnerable groups

Vaccine effectiveness during Omicron period[1]

			Nucleic acid (RNA or DNA)		Viral vector		Protein subunit		Inactivated or attenuated	
Measure	**Schedule**	**Outcome**	**Pfizer**	**Moderna**	**AZ**	**J&J**	**Novavax**	**SP/GSK**	**Sinovac**	**Sinopharm**
Effectiveness (<3 months following last dose)	Booster dose (homologous)	**Severe disease**	74-94%	82-99%	82%*	67-85%	TBC	TBC	74%	TBC
	Booster dose (homologous)	**Infection/ Symptomatic disease**	35-81%	44-70%	45-53%	54%	TBC	TBC	54%	TBC

Durability of protection[2]

- **Vaccine effectiveness (VE) has been observed to wane over time, in particular in the context of emerging variants.**
- **In adults, VE declines for all outcomes between 1 and 6 months following a first booster dose.**
- **A second booster at 6 or 12 months can restore VE against severe disease.**

	Severe disease/ hospitalization	Symptomatic disease	Infection
VE % decrease between 1 and 6 months after vaccination	↓15.7%	↓ 32%	↓ 47%
VE at 12 months (modelling)	~35%	NA	NA

R&D pipeline and innovations[3]

- There are currently **183 COVID-19 vaccines** in clinical development.
- Innovations in the pipeline include (i) **vaccines targeting mucosal immunity** (intranasal, inhaled, oral), (ii) **combination vaccines** (with influenza and/or RSV), (iii) **microarray patches**, and (iv) **optimised formulations** to improve temperature stability.

1. Efficacy and effectiveness estimates obtained from WHO SAGE product-specific guidance documents: https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials
   *Estimate for homologous booster dose VE against severe disease for AZ: Kirsebom et al 2022 (link)
2. Durability of protection and hybrid immunity data obtained from March 2023 SAGE session on COVID-19: https://www.who.int/news-room/events/detail/2023/03/20/default-calendar/sage_meeting_march_2023
3. R&D pipeline data are sourced from ongoing COVAX internal monitoring of the vaccines landscape

COVID-19 programme vaccination strategy for 2024-2025 focuses on booster doses for high priority groups

Programme eligibility

- Focus on **boosters for high priority group only** as recommended by latest SAGE Prioritization Roadmap[1]
- **Provision** for providing **primary doses for high priority groups only**
- **New entrants** into the high priority groups will be eligible for the above
- 2024-2025 C19 programme will NOT include medium or low priority groups[2] based on the health impact assessment

High priority groups	Schedule
1) Oldest adults (>80) 2) Older adults (>60) with significant comorbidities	2 doses, 6 months apart
1) Older adults (>60) 2) Younger adults with significant comorbidities/ obesity	1 dose per year
Immunocompromised individuals 6 months and older	2 doses, 6 months apart
Pregnant persons	Once during pregnancy (2nd trimester)
Frontline health workers	1 dose per year

The WHO SAGE prioritization roadmap published in March 2023 has been indicated for planning 2023 and 2024. The Gavi programme will be adapted in accordance with any subsequent SAGE recommendations

1. WHO prioritization roadmap (March 2023): https://www.who.int/publications/i/item/WHO-2019-nCoV-Vaccines-SAGE-Roadmap
2. Medium priority group includes healthy younger adults and children/ adolescents aged 6 months to 17 with severe obesity or comorbidities.

Health and economic impact (1/2)

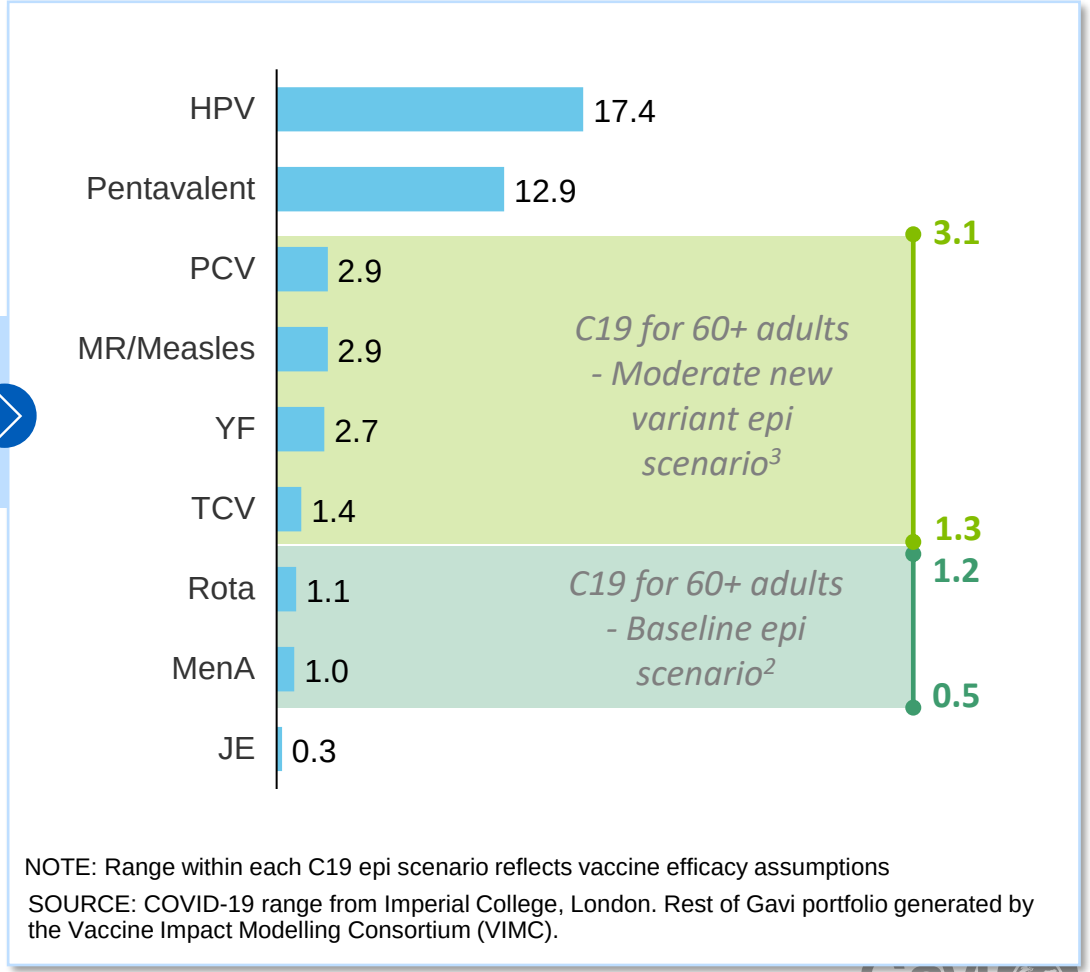
Key takeaways

- Modelling is challenging given **uncertainties**, evidence gaps and **complex assumptions**. (e.g., Continuing to use Years of Life Lost rather than Disability Adjusted Life Years; unable to produce estimates for all priority population groups)
- Modelling across a range of scenarios and age groups demonstrates **greatest impact in terms of deaths averted per fully vaccinated person is seen among priority 60+ group**[1]
- Initial projections from Imperial College, London, for the proposed 2024-2025 programme (i.e., for high priority group) show **deaths averted per FVP ranges comparable** to **current Gavi core routine immunization portfolio**
- Imperial projects the following for **total deaths averted in 60+ age population during 2024-2025 per country group**

Gavi 54	AMC 37
45K – 281K deaths averted	**28K – 182K** deaths averted

- **The Institute for Disease Modelling** (BMGF) generated similar estimates to those of Imperial, with a range of 1.54-3.1 deaths averted per 1,000 FVP for 60+ age group. All estimates are **subject to change** as more evidence is generated.

Deaths averted per 1,000 FVP for Gavi supported vaccinations



NOTE: Range within each C19 epi scenario reflects vaccine efficacy assumptions

SOURCE: COVID-19 range from Imperial College, London. Rest of Gavi portfolio generated by the Vaccine Impact Modelling Consortium (VIMC).

1. 0.2 to 1.2 deaths averted per 1,000 FVP for broader adults compared with 0.5-3.1 deaths averted for 60+ age population
2. Baseline epi scenario: Small drift and increase in transmissibility and immune escape
3. Moderate new variant epi scenario: Slightly more transmissible, slightly increased severity and some immune escape

Health and economic impact (2/2)

Key takeaways

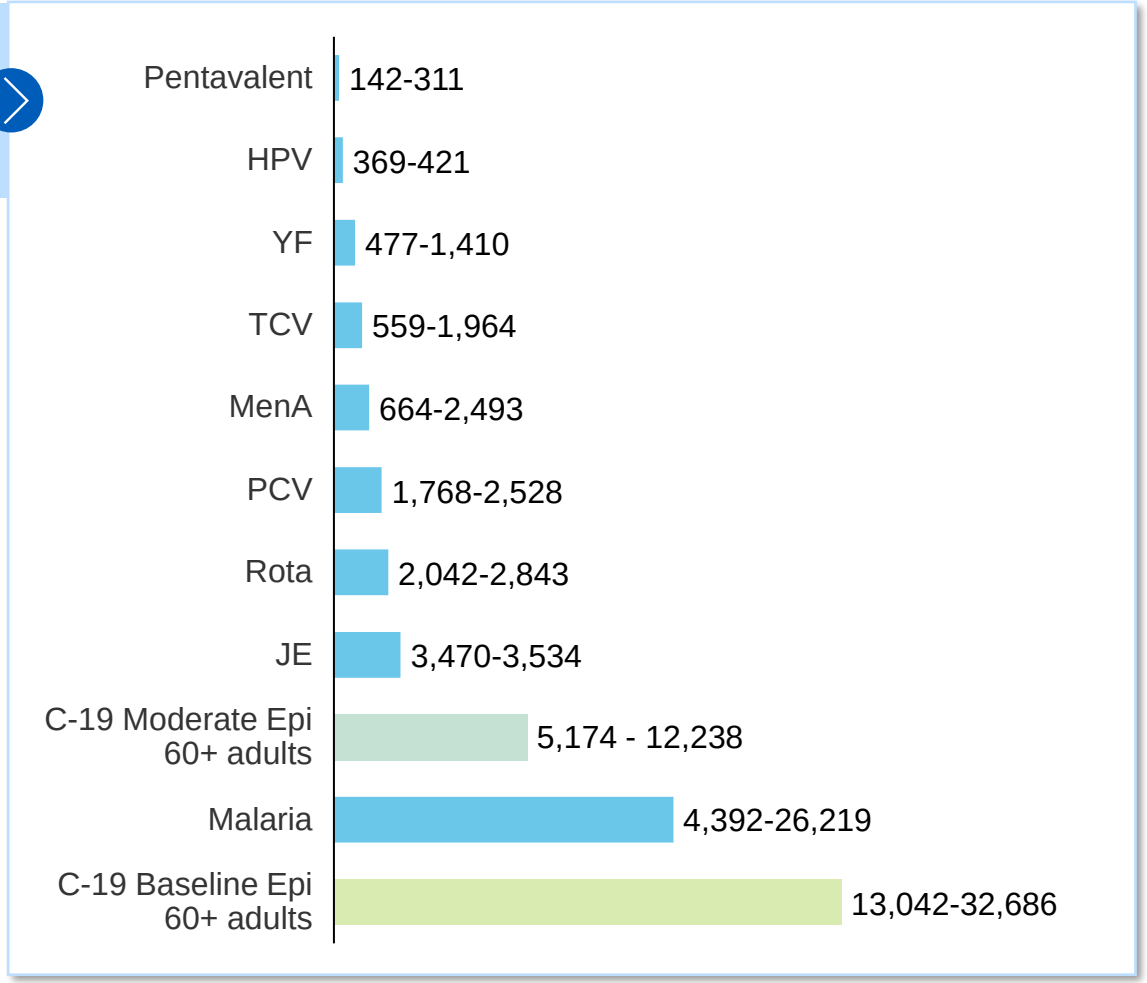
- The proposed programme appears to **compare relatively less favourably on value for money** than Gavi core supported programmes, although ranges are broad and do overlap with current Gavi RI portfolio (broader adult boosting even less favorable)

- Modelling also shows considerable impact in terms of cases and **hospitalisations averted**. Hospitalisations averted are particularly pertinent given the significant impact of the COVID-19 pandemic on health systems and health workforce in particular.
  - In a baseline COVID-19 scenario, current estimates project **360K-880K hospitalisations** among 60+ could be averted
  - In a moderate COVID-19 scenario, estimates increase to **665K-1.6M** hospitalisations among 60+ could be averted

- Estimates by the IHME suggest that by the end of 2021, **3.7%** of individuals infected with SARS-CoV-2 developed PCC which met the WHO definition and **15.1% had persistent symptoms at 12 months – this is not yet accounted for in modelling**

- The COVID-19 pandemic has resulted in wide **socioeconomic impact**. Literature[2] suggests clinical management costs alone had a catastrophic impact on annual health expenditure in some LMICs

Cost[1] (USD) per death averted for Gavi supported vaccinations



SOURCE: COVID-19 range from Imperial College, London. Rest of Gavi portfolio generated by the Vaccine Impact Modelling Consortium (VIMC).

1. These costs reflect procurement costs only without considering dose donations; Preliminary C19 impact estimates as generated by Imperial College
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8640196/#:~:text=Without%20mitigation%20policies%2C%20average%20COVID,to%20US%241.10%E2%80%93US%241.32.

Delivery strategy considerations

In accordance with the WHO/ UNICEF guidance on integration, the Gavi will focus on sustainable integration of COVID-19 vaccination with RI, PHC and other healthcare services

Differentiated delivery strategies will be needed for each of the high priority sub-groups in 2024-25 and depending on **country capacity and context**, countries **may need to complement these integration efforts with campaigns** to reach certain high priority sub-groups.

The **experience of reaching high priority groups through a multitude of delivery strategies is still new** and will be particularly important opportunities to learn and to strengthen the antenatal care platform to reach pregnant persons and platforms to reach health care workers, both of which may be critical in the delivery of future vaccines under consideration in Gavi's 2018 and 2024 Vaccine Investment Strategies.

Recommended strategies (not exhaustive)

All high priority user groups: leveraging routine health care and outreach services to provide COVID-19 vaccination

Elderly persons: integrated into outreach activities and social services that target the elderly; likely requires supplementary campaigns

Persons with comorbidities: leveraging specialised clinics e.g., HIV & TB, as well as integrating into outreach activities

Pregnant persons: integrating as part of antenatal care (ANC) services

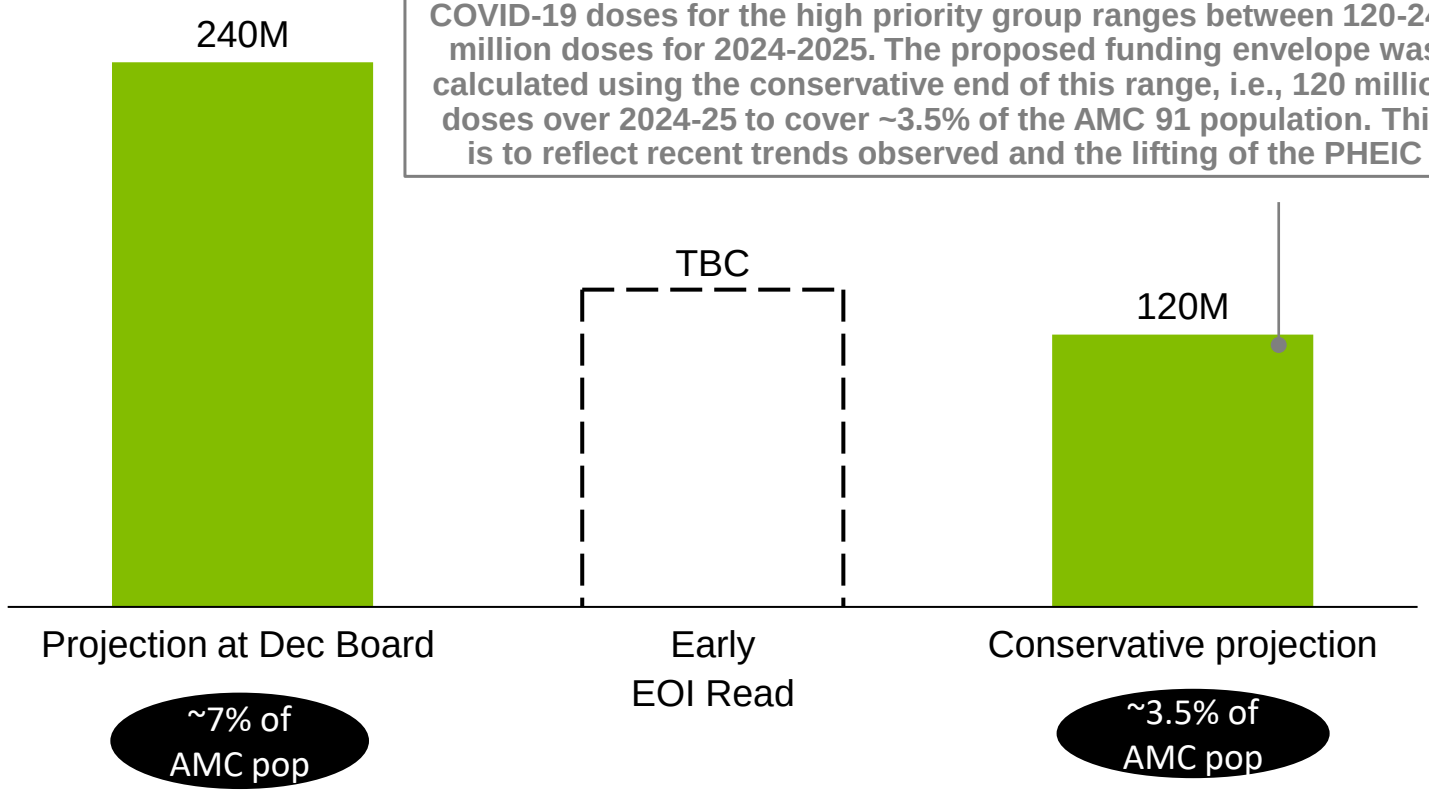
Healthcare workforce: encourage COVID-19 vaccination delivery to health workforce at fixed sites as well as during training opportunities; countries will also be encouraged to integrate and offer other vaccinations for HCWs during these key opportunities

Volume projections for 2024-25 based on received 2024 EoI submissions

As of 7 June 2023

Projected Gavi supported C19 vaccine volumes in AMC 91 over 2024-25, in millions of doses

Based on EoI responses, the projected demand for Gavi supported COVID-19 doses for the high priority group ranges between 120-240 million doses for 2024-2025. The proposed funding envelope was calculated using the conservative end of this range, i.e., 120 million doses over 2024-25 to cover ~3.5% of the AMC 91 population. This is to reflect recent trends observed and the lifting of the PHEIC



EOI = Expression of Interest (Demand & Preferences forecast from countries)

Update on 2024 Demand EoIs

- **58 countries submitted 2024 EoIs** representing almost ~60% of AMC91 pop.
  - **55 expressed interest in C19 doses in 2024;** 3 confirmed they are NOT interested (Burundi, Mozambique, Indonesia)
    - 42 explicitly asked for a cumulative of ~92M doses in 2024, reduced to **~72M[1] if capped to est. high-risk pop.**
    - 13 confirmed they require doses in 2024, but have not provided a dose estimate; **conservative top-down projections for these countries is ~17M**
- **33 countries pending submission** among which the most populous are:
  - *Gavi 54: Bangladesh, Uganda, Tanzania*
  - *AMC 37: Morocco, Philippines, Vietnam*

NOTE: 2024 demand EoIs represent total demand numbers, however Gavi will provide only 50% procurement support for AMC 37 for 1 year

1. 51M for Gavi 54 and 21M for AMC 37
2. 10M for Gavi 54 and 7M for AMC 37

Risks and mitigation

Risks	Mitigation measures
Policy: Updated SAGE roadmap merits an expansion or a reduction of the programme scope	▪ Regular monitoring and dialogue with WHO/ SAGE to anticipate updates; updates to the Board, incl. decisions for substantial adjustments, if needed
Demand and wastage	▪ Demand data monitoring, regular demand and uptake review and dialogue with countries though Country Teams, strong collaboration and data exchange with UNICEF ▪ LTA's good-faith contracting approach inherently have more flexibility (vs APAs) on adjusting volumes based on how demand and product preferences manifest ▪ Encourage manufacturers to continue their potential shelf-life extension
Supply: ▪ Prices/ mRNA overdependence/ supplier drop offs ▪ Uncertainty on donations – balancing with LTAs ▪ Reduction/ lack of effectiveness of vaccines against emerging new variants	▪ Leverage the UNICEF/PAHO tender, an established Alliance model, and explore interventions to maintain sustainable supplier base ▪ Ensure flexibility in LTAs with manufacturers to access updated VCVs ▪ Continued and regular dialogue with donors to monitor the supply situation ▪ Continued monitoring of epidemiological situation and vaccine effectiveness data
In country delivery: ▪ Inability to reach high priority population ▪ Risk of not integrating/use only of campaigns ▪ Vaccines used for broader population groups ▪ Lack of funding after the extension of CDS funding ▪ Simultaneous Gavi/ RI/ health emergencies deprioritise C19 delivery	▪ Regular programmatic monitoring by Country Teams ▪ TA support (WHO/UNICEF/Expanded partners) to ensure appropriateness of delivery activities to reach high priority populations ▪ Risk mitigating measures for vaccine delivery under COVAX to continue through 2024-2025 ▪ Possibility to request funding to the Board in case of surge ▪ Activate TA/surge support
Impact on other RI priorities like new introductions, catch up vaccination, reaching zero dose children	▪ Development of robust communication strategy ▪ Leverage of existing collaboration/ partnerships with local partners (e.g., CSOs)

Financial implications

		As presented to Board in December 2022	**Updated with updated demand estimate based on EoIs**
Assumptions	Estimated proc. cost	[redacted]	[redacted]
Assumptions	Estimated delivery cost	~$1.6/ dose[1]	~$1.6/ dose[1]
Assumptions	Eligible pop cohorts	5 high priority groups as per SAGE; which represent ~20% of AMC population	
Assumptions	Est. coverage of population	~35% coverage x 20% eligibility = ~7% of total AMC pop	**~18% coverage** x 20% eligibility = **~3.5% of total AMC pop**
Assumptions	Procurement doses	240Md	80Md
Assumptions	Dose donations #	0	**~40Md**
Scope	Extent of Gavi support – Gavi 54	Proc: 100% Delivery: 70% of estimated costs	Proc: 100% Delivery: Proposal to cover thru **extension of CDS** funding
Scope	Extent of Gavi support – AMC 37	Proc: 50% in 2024, 0% in 2025 Delivery: 0%	Proc: 50% in 2024, 0% in 2025 Delivery: Proposal to cover thru **extension of CDS** funding
Scope	SEC+PEF	$60m for 2yrs	$37m for 2yrs
	2024-25 Total Doses funded incl. donations	~240Md	~120Md
	2024-25 Total Cost Estimate	**~$1.9B**	**~$0.82B**

Key changes since Dec 2022 Board

Product mix with **higher mRNA share** based on country preferences indicated in the 2024 EoIs

Projected demand between 120-240 Md for 2024-2025; early read on country EoIs closer to conservative end of the range, i.e., **120 Md**

Latest estimate on **dose donations**; 2024-25 donations **not yet secured** and are **subject to uncertainty**

CDS rephasing ($320m) over 2024-25 should be **sufficient to cover delivery support** for C19 programme

$0.71B incremental ask. No new delivery funding needed

1. Calculated with Delivery Costing Working Group in Sept. 2022: incl. CoVDP, UNICEF, BMGF, Harvard School of Public Health, Mgmt. Sciences for Health, WHO & Gavi; Calcs are based on reaching higher priority user group size for 1 dose per year over 2024-25 through fixed, outreach & mass vax delivery methods; considers higher cost for adult, non-RI vaccine; Costing incl. HR for delivery, PPE, hand hygiene, per diems, transportation for outreach, training, planning & coordination, social mobilization, cold chain maintenance, waste mgmt., vax certificates, pharmacovigilance; Costing excludes ancillaries (syringes & safety boxes), TA & cost of vial.

APPENDIX

C19 Vaccine Investment Assessment

Developing a VIS-like assessment framework for COVID-19

Combination of key elements from Gavi's Endemic and Epidemic VIS frameworks to create a hybrid VIS-like framework to assess a future COVID-19 vaccination programme given current uncertainties

Endemic VIS framework

- For endemic diseases with outbreak or epidemic potential (e.g. Measles)
- **Used as the basis** for C19 framework with key elements including:
  - Health impact
  - Value for money
  - Economic impact
  - Gavi comparitive advantange

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Epidemic VIS framework

- For diseases with sporadic outbreaks only
- **Additional parameters** considered relevant for C19 across themes of:
  - Disease risk and burden
  - Long-term benefits of the vaccine
  - Relevance (e.g., burden in Gavi countries, country demand)
  - Gavi comparative advantage[1] (e.g., complement. with other initiatives)
  - Risk (e.g., Risk of action & inaction)

C19 2024-25 hybrid evaluation framework

1. Disease Burden & Risk	E.g. Total cases/ hospitalisations/ deaths, impact on health systems
2. Vaccine Impact & Feasibility	E.g. Health impact, value for money, implementation feasibility
3. Fit for Gavi & Partners	E.g. Relevance, country demand, comparative advantage, risk
4. Financial Implications	E.g. Vaccine, delivery and operational costs

1 Additional indicators under Gavi comparative advantage added

1

Disease risk & burden

Disease risk and health burden

Number of C19 deaths and cases per annum

- The table below reflects officially reported cases and deaths due to COVID-19[1*]. WHO estimates of excess deaths due to COVID-19 are substantially higher, particularly among lower-income settings where reporting of official disease burden faced greater challenges.

Outcome	Population	2020	2021	2022	2023 (17 Feb '23)
Deaths	Global	1,928,561	3,521,920	1,243,796	149,990
	AMC	282,674	827,260	136,768	1,747
Cases	Global	82,936,185	204,173,244	443,649,916	25,822,505
	AMC	16,446,959	45,041,868	29,985,976	139,783

Severity of disease especially for vulnerable population

- Estimated **case fatality rate among adults >50 years is 19%,** compared to 1% among the general population according to a systematic review conducted by the NIH[2].
- **26% higher risk of ICU admission and an 87% increased risk of in-hospital death** for unvaccinated **immunocompromised people** compared to unvaccinated non-immunocompromised individuals according to a study by the US CDC[3].

Cases of long-term disability (e.g., Long COVID/Post COVID Condition)[4-6]

- COVID-19 has been documented to affect **wide range of organ systems**: neurologic, cardiovascular, GI, metabolic, respiratory, systemic; Most common symptoms include fatigue, shortness of breath, cognitive dysfunction
- Estimates by the IHME suggest that by the end of 2021, **3.7%** of individuals infected with SARS-CoV-2 developed PCC which met the WHO definition and **15.1% had persistent symptoms at 12 months** (challenging to ascertain 'true' prevalence of PCC following acute infection due to differences in definitions and timepoints, data sources/symptom ascertainment methods – even more so in LMIC settings)
- Potential **risk factors** include female sex, older age, severe acute illness requiring hospitalizing, certain pre-existing comorbidities, number of symptoms during acute illness
- **Vaccination** prior to SARS-CoV-2 infection is associated with **reduced long COVID**. Evidence for impact of vaccination on the trajectory of PCC is not conclusive at this stage (some studies show symptom improvement, others report no change).

* COVID-19 surveillance in AMC92 countries is not performed thoroughly and likely significantly underestimates the number of cases and deaths.

1) WHO COVID-19 vaccine dashboard as of 17 Feb 2023, 2) NIH CFR study: Alimohamadi Y, Tola HH, Abbasi-Ghahramanloo A, Janani M, Sepandi M. Case fatality rate of COVID-19: a systematic review and meta-analysis. J Prev Med Hyg. 2021 Jul 30;62(2):E311-E320. doi: 10.15167/2421-4248/jpmh2021.62.2.1627. PMID: 34604571; PMCID: PMC8451339, 3) US CDC: https://www.clinicaltrialsarena.com/comment/immunocompromised-adults-covid/, 4) PCC prevalence, clinical manifestation, risk factors: Bull-Otterson et al, Global Burden of Disease Long COVID Collaborators, Groff et al, Havervall et al, Huang et al, Menges et al, Osmanov et al, Pazukhina et al , 5) Protective effect of vaccination on risk/odds of PCC: Antonelli et al Al-Aly et al Ayoubkhani et al Senjam et al Simon et al Taquet et al , 6) Uncertain impact of vaccination on improvement of PCC: Arnold et al Ayoubkhani et al Gaber et al Kuodi et al Nehme et al Peghin et al Scherlinger et al Strain et al Tran et al Tsuchida et al Wisnivesky et al

Economic burden

Direct costs

- **LMIC**: COVID-19 clinical management costs have been found to vary by countries in LMICs and ranged between **<0.1%–12% of the GDP** and **0.4%–223% of the total annual health expenditure** (excluding out-of-pocket payments)[1].
- **Global:** Main drivers for costs included **ICU admission & in-hospital resource use** e.g. mechanical ventilation, which lead to **increased costs of $2082.65 ± 345.04 to $2990.76 ± 545.98**. On average, older patients incurred higher costs compared to younger age groups[2].
- **Long term disability:** Based on a study in Israel, over a one-year follow-up, long COVID was associated with a **doubling of the direct medical costs** compared to the cost before infection[3].

Indirect costs
(e.g., income loss, labor productivity loss)

- **LIC:** Data from Ethiopia, Malawi, Nigeria and Uganda showed that 256 million people, **77% of the population**, live in households that have lost income during COVID-19 pandemic[4]. Lost income due to the COVID-19 was associated with household food insecurity in LICs with limited social safety nets[5].
- **LIC**: There is persistence of loss-of-learning effects (from pandemic-related school closure) on labor productivity in the aftermath of pandemic in LICs[6].
- **Global**: The C19 pandemic has affected significantly the labor force. The International Labour Organization (ILO) estimated that 8.8% of global working hours, equivalent to 255 million full-time jobs, were lost in 2020 due to the pandemic. The losses were four times greater than those during the 2009 financial crisis. LMICs were most severely impacted[7].

1) Stark choices: exploring health sector costs of policy responses to COVID-19 in low-income and middle-income countries (2021): Link. 2) Richards F, Kodjamanova P, Chen X, Li N, Atanasov P, Bennetts L, Patterson BJ, Yektashenas B, Mesa-Frias M, Tronczynski K, Buyukkaramikli N, El Khoury AC. Economic Burden of COVID-19: A Systematic Review. Clinicoecon Outcomes Res. 2022 Apr 28;14:293-307. doi: 10.2147/CEOR.S338225. PMID: 35509962; PMCID: PMC9060810. 3) I Tene, T. Bergroth, A. Eisenberg, S. Shapiro Ben David G. Chodick, Risk factors, health outcomes, healthcare services utilization, and direct medical costs of patients with long COVID, December 2022,:https://doi.org/10.1016/j.ijid.2022.12.002, 4) Josephson A, Kilic T, Michler JD. Socioeconomic impacts of COVID-19 in low-income countries. Nat Hum Behav. 2021 May;5(5):557-565. doi: 10.1038/s41562-021-01096-7. Epub 2021 Mar 30. PMID: 33785897., 5) Narayan,Ambar; Cojocaru,Alexandru; Agrawal,Sarthak; Bundervoet,Tom; Davalos,Maria Eugenia; Garcia,Natalia; Lakner,Christoph; Mahler,Daniel Gerszon; Montalva Talledo,Veronica Sonia; Ten,Andrey; Yonzan,Nishant. *COVID-19 and Economic Inequality : Short-Term Impacts with Long-Term Consequences (English).* Policy Research working paper,no. WPS 9902,COVID-19 (Coronavirus),Paper is funded by the Knowledge for Change Program (KCP) Washington, D.C. : World Bank Group. http://documents.worldbank.org/curated/en/219141642091810115/COVID-19-and-Economic-Inequality-Short-Term-Impacts-with-Long-Term-Consequences, 6) Edward F Buffie ; Christopher S Adam ; Luis-Felipe Zanna ; Kangni R Kpodar, Loss-of-Learning and the Post-Covid Recovery in Low-Income Countries, February 2022, Link, 7) International Labour Organization, COVID-19 and the world of work. Seventh edition Updated estimates and analysis, January 2021, Link

2

Vaccine impact & feasibility

Health impact modelling – assumptions used[1]

Epi scenarios	**Three epi scenarios** were modelled: 1. **Baseline** scenario assumes small drift, with severity similar to omicron variant and a gradual increase in transmission and immune escape 2. **Moderate** scenario assumes a slightly more transmissible variant, with slightly increased severity and some immune escape. 3. **Worst-case** scenario assumes a new variant with substantially increased transmissibility and immune escape. Severity is assumed to be similar to Delta variant.
Vaccine scenarios	• Modelling incorporates both an "**original vaccine" scenario** (where vaccine efficacy against omicron is as currently reported, with immune escape proportional to that evidenced with omicron and wild type) and "**new vaccine" scenario** (where vaccine efficacy is set to the original vaccine efficacy reported for wild type).
Vaccine efficacy and durability of protection	• Assume that vaccination is with the Moderna vaccines, using the original mRNA.1273 vaccine effectiveness data generated from England. For the fourth dose onwards, immunogenicity data based from Chalkas et al is used for re-parameterisation purposes.

1. Refers to assumptions used for impact modelling from Imperial College, London. IDM group used similar assumptions. Further details on assumptions, parameters and modelling approaches for both groups can be found in technical Appendices available on Board Effect.

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Health impact with comparators (1/3)

Direct health impact per 1,000 Fully Vaccinated Person

Deaths averted per 1,000 FVP

	Min	Max	Mean
HPV	16.2	18.5	17.4
Pentavalent	7.9	17.2	12.6
Malaria	1.0	5.9	3.5
PCV	2.3	3.6	3.0
MR/measles	2.8	2.9	2.9
YF	1.2	3.5	2.4
C-19 Moderate epi - 60+	1.3	3.1	2.2
TCV	0.6	2.1	1.4
Rota	0.8	1.5	1.2
MenA	0.4	1.6	1.0
C-19 Baseline epi - 60+	0.5	1.2	0.9
C-19 Moderate epi - all adults	0.5	1.2	0.8
C-19 Baseline epi 60+ - all adults	0.2	0.5	0.3
JE	0.3	0.3	0.3
MR/Rubella 2nd dose	0.2	0.2	0.2

YLLs averted per 1,000 FVP

	Base line epi scenario[1]	Moderate epi scenario[2]
60+ adults	4.7 - 11.1	15.5 - 33.6
Adults	2.86 - 6.91	7.64 - 19.71

- **DALYs averted per 1,000 FVPs for Gavi-supported vaccines 2021-2030 ranges from 15 – 551**
- Estimates for YLLs averted are not currently available for the Gavi core vaccine portfolio. However, estimates for YLLs represent the largest proportion / driver of DALYs, compared to the years of healthy life lost due to disability (YLD)
- For example, measles YLLs estimates breakdown as follows: 14.52m YLLs = 14.49m YLLs + 0.03m YLDs. Therefore, while a comparison of YLLs to DALYs is imperfect, it can be used to inform a relative comparison

Cases averted per 1,000 FVP

	Base line epi scenario	Moderate epi scenario
60+ adults	721 - 1,846	707 - 1,796
Adults	1,179 - 2,636	1,223 - 2,492

1. Baseline epi scenario: Small drift and increase in transmissibility and immune escape
2. Moderate new variant epi scenario: Slightly more transmissible, slightly increased severity and some immune escape

Health impact with comparators (2/3)

Value for money

Cost (USD) per death averted

	Min	Max
Pentavalent	142	311
MR/Rubella	310	320
HPV	369	421
YF	477	1,410
TCV	559	1,964
MenA	664	2,493
PCV	1,768	2,528
Rota	2,042	2,843
JE	2,470	3,534
C-19 Moderate epi - 60+ adults	5,174	12,238
Malaria	4,392	26,219
C-19 Baseline epi - 60+ adults	13,042	32,686
C-19 Moderate epi - all adults	16,772	42,479
C-19 Baseline epi - all adults	52,243	132,279

Key takeaways

The proposed programme appears to **compare relatively less favourably from a value for money perspective** than Gavi core supported vaccine programmes, although ranges are broad and do overlap with current Gavi RI portfolio.

Estimates of **cost per death averted based on 60+ adults are comparatively more favourable than for a broader adult vaccination programme**.

NOTE: These costs reflect procurement costs only; Range within each C19 epi scenario reflects vaccine efficacy assumptions

SOURCE: COVID-19 range from Imperial College, London. Rest of Gavi portfolio generated by the Vaccine Impact Modelling Consortium (VIMC).

Health impact (3/3)

Absolute numbers for AMC 91 in 2024-25

Total deaths averted

	Base line epi scenario	Moderate epi scenario
60+ adults	75K – 187K	200K – 472K
All adults	133K – 337K	337K – 854K

Total YLLs averted

	Base line epi scenario	Moderate epi scenario
60+ adults	715K – 1.6M	2.4M – 5.1M
All adults	2M – 5M	5.5M – 14.1M

Total hospitalisations averted

	Base line epi scenario	Moderate epi scenario
60+ adults	360K – 883K	654K – 1.572M
All adults	818K- 1.9M	1.4M – 3.3M

Total cases averted

	Base line epi scenario	Moderate epi scenario
60+ adults	110M – 282M	108M – 274M
All adults	846M - 1.8B	878M – 1.8B

SOURCE: From Imperial College, London

Vaccine effectiveness, durability of protection, and R&D pipeline and innovations

Vaccine efficacy and effectiveness

			Nucleic acid (RNA or DNA)		Viral vector		Protein subunit		Inactivated or attenuated	
Measure	**Schedule**	**Outcome**	**Pfizer**	**Moderna**	**AZ**	**J&J**	**Novavax**	**SP/GSK**	**Sinovac**	**Sinopharm**
Efficacy	Primary series	Severe disease	75-89%	100%	86-92%	77-88%	100%	*	100%	79%
Effectiveness (during Omicron, <3 months following last dose)	Primary series	Severe disease	43-91%	51-79%	67%	28%	TBC	TBC	56-65%	59%
	Primary series	Infection/ Symptomatic disease	26-78%	24-76%	11-89%	47-73%	TBC	TBC	28-42%	TBC
	Booster dose (homologous)	Severe disease	74-94%	82-99%	TBC	67-85%	TBC	TBC	74%	TBC
	Booster dose (homologous)	Infection/ Symptomatic disease	35-81%	44-70%	45-53%	54%	TBC	TBC	54%	TBC

Durability of protection (waning effectiveness)

Vaccine effectiveness has been observed to wane over time, in particular in the context of emerging variants.
In adults, VE declines for all outcomes between 1 and 6 months following a first booster dose.

- Waning following first booster is similar in adult age groups (18.6 vs. 11.8 % decline in younger vs older adults, respectively).
- First booster dose VE against severe disease/ hospitalization from 1 to 6 months: 15.7% decrease
- First booster dose VE against symptomatic disease from 1 to 6 months: steeper VE decrease by 32%
- First booster dose VE against any infection from 1 to 6 months: 47% decrease

Model projection suggests VE against severe disease/ hospitalization could drop to 35% by 12 months. A second booster at 6 or 12 months can restore VE against severe disease.

Hybrid immunity

Seroprevalence studies suggest that 80-90% of the population in LMICs has been exposed to COVID-19. Hybrid immunity (infection + vaccination) may confer the most durable protection.

- Severe disease: following booster vaccination protection wanes less
- Reinfection: omicron infection + vaccination sustains protection better than pre-omicron infection
- Waning of hybrid immunity protection is more substantial in older adults (age 65+)

R&D pipeline and innovations

There are currently 183 COVID-19 vaccines in clinical development.
Innovations in the pipeline include vaccines targeting mucosal immunity (intranasal, inhaled, oral), combination vaccines (with influenza and/or RSV), microarray patches, and optimized formulations to improve temperature stability.

Efficacy and effectiveness estimates obtained from WHO SAGE product-specific guidance documents: https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials
Durability of protection and hybrid immunity data obtained from March 2023 SAGE session on COVID-19: https://www.who.int/news-room/events/detail/2023/03/20/default-calendar/sage_meeting_march_2023
R&D pipeline data are sourced from ongoing internal monitoring of the vaccines landscape

183 COVID-19 vaccines in clinical development with innovations in the pipeline*

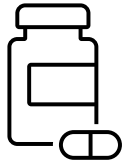
	Phase I or I/II	Phase II	Phase II/III and III	Regulatory Approval
Viral vector	N = 15 ***Combination vaccines*** *Covid-19 + influenza (Novavax)*	N = 4	N = 6	AstraZeneca: AZD1222 Bharat: iNCOVACC (**intranasal**) CanSino: Ad5-nCoV CanSino: ConvidenciaAir (**inhaled**) Gamaleya: Sputnik V Janssen: Ad26-CoV
Nucleic acid (RNA or DNA)	N = 37 ***Combination vaccines*** *COVID-19+ infuenza (Pfizer, Moderna)* *COVID-19 + influenza + RSV (Moderna)* ***Microarray patch**: Vaxxas HexaPro HD-MAP* ***Targeting non-spike protein**: Pfizer BNT162b4*	N = 3 ***Improved temperature stability**: Moderna*	N = 13	CSPC ZhongQi: SYS6006 Moderna mRNA1273 Moderna 1273.214 Moderna 1273.222 Pfizer BNT162 Pfizer WT/BA.1 Pfizer WT/BA.4/5
Protein subunit or VLP	N = 29	N = 7	N = 22	Biological E. CORBEVAX Livzon Pharm. V-01 Medicago VLP Medigen MVC-COV1901 Novavax NVX CoV2373 Sanofi / GSK Beta monovalent Sinocelltech SCTV01C
Inactivated or attenuated	N = 8	N = 0	N = 13	Bharat COVAXIN Sinopharm BIBP Sinovac CoronaVac Valneva VLA2001

WHO EUL
COVAX portfolio

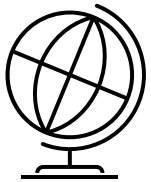
Gavi The Vaccine Alliance

* Data as of 30 March 2023

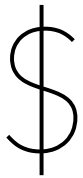
Alternative interventions are primarily therapeutic, and have limited accessibility in LMICs



- Treatments available include monoclonal antibodies, antivirals, and medical oxygen
  - Antivirals: potential reduction of mortality and hospitalization ranging from 30 to ~70% with efficacy potentially maintained against the latest subvariants[1]
  - Antivirals must be taken within 5-7 days of symptom onset, posing challenges in resource-limited settings where individuals may not seek care for early, less severe symptoms.
  - Monoclonal antibodies must be administered intravenously, limiting their large-scale use in LMICs



- Additional barriers[2] to access in LMICs include:
  - licensing challenges and lack of transparency
  - regulatory approvals in AMC countries
  - limited access to COVID-19 testing in LMICs, which is a prerequisite to use these treatments
- Several agreements have been made to increase access to antivirals through MPP[3] and the ACT-A therapeutics pilar[4], however very limited quantities of pills have reached LMICs



- Treatment cost for antivirals ranges between US$ 500 to US$ 700 per full treatment
- Treatment cost for monoclonal antibodies ranges between US$ 50 to US$ 1,250 per dose[5]

SOURCE: 1) Burdet C, Ader F. Real-world effectiveness of oral antivirals for COVID-19. Lancet. 2022 Oct 8;400(10359):1175-1176. doi: 10.1016/S0140-6736(22)01929-8. PMID: 36215994; PMCID: PMC9539533. 2) Boro E. and Stoll B. Barriers to COVID-19 Health Products in Low-and Middle-Income Countries During the COVID-19 Pandemic: A Rapid Systematic Review and Evidence Synthesis. Frontiers. 2022 July 22. Volume 10 - 2022 | https://doi.org/10.3389/fpubh.2022.928065, 3) MPP press release: https://medicinespatentpool.org/news-publications-post/pfizer-and-the-medicines-patent-pool-mpp-sign-licensing-agreement-for-covid-19-oral-antiviral-treatment-candidate-to-expand-access-in-low-and-middle-income-countries, 4) ACT-A therapeutics pilar: https://app.powerbi.com/view?r=eyJrIjoiNmE0YjZiNzUtZjk2OS00ZTg4LThlMzMtNTRhNzE0NzA4YmZlIiwidCI6Ijc3NDEwMTk1LTE0ZTEtNGZiOC05MDRiLWFiMTg5MjAyMzY2NyIsImMiOjh9&pageName=ReportSectiona329b3eafd86059a947b&pageName=ReportSectionda5c4e233b28021ed9d4&pageName=ReportSection133a58bf9d853a31e25e, 5) CGDev Summary of current evidence on costs and cost effectiveness of COVID-19 oral antivirals: https://www.cgdev.org/sites/default/files/covid-antivirals-table-one-annex.pdf

Implementation feasibility

Delivery platforms	• **In accordance with the WHO/ UNICEF guidance on integration**, Gavi will focus on sustainable integration of C19 vaccination with RI, PHC and other healthcare services. A self-assessment tool covering several topics[1] has been developed by CoVDP to assist countries to that effect. • **Differentiated delivery strategies will be needed for each of the high priority sub-groups** in 2024-25 and depending on **country capacity and context**, countries **may need to complement these integration efforts with campaigns** to reach certain high priority sub-groups in order to reach high coverage • Although C19 vaccination has already been rolled out in AMC countries and proven feasible during the pandemic, reaching high-risk groups through a multitude of delivery platforms remains new in the routine immunization context. Countries have yet to share their experiences on the feasibility of using non-traditional platforms to reach these target groups. • Countries' consultation through CDS programmatic implementation revealed that 25% of Gavi countries reported a successful delivery of vaccines via campaigns and integrated campaigns. It however requires additional resources to help support full expansion of services through fixed sites and outreach for routinization.
Demand generation/ acceptability	• Outreach/ demand generation has been more successful in countries with well-established community networks, therefore leveraging existing relationships with local partners and communities will be critical. • Vaccine confidence is potentially improving due to an increase in COVID-19 vaccination coverage in AMC countries. It is also higher with COVID-19 vaccines that have been widely used and proven to be safe (e.g., mRNAs). Continued high-level political advocacy, effective communication to health workers and managing misinformation around COVID-19 vaccines are three key elements to improve/ maintain acceptability in target populations.
Ease of supply chain integration	• Ease of supply chain integration will depend on COVID-19 vaccines selection for the C19 routine immunisation programme. • Cold chain infrastructure was put in place where needed through the pandemic response (2020-2023), however an assessment on the maintenance and/ or additional requirements related to cold chain may be needed based on implementation strategy, type of vaccine and storage volumes needed.
Capacity-building	• COVID-19 products have been the first vaccines delivered to adults at scale. Vaccinators are trained to give injectables, however they likely have minimal experience counseling and educating the highest risk groups on the value, safety, and potential AEFIs associated with COVID-19 vaccine. Capacity-building of health workers on such aspects will therefore be required.

1) Topics covered in the self-assessment tool include: governance and collaboration that is cross-sectoral/departmental within MoH; C19 included in the National Strategic Plans and MoH budgets (self-financed or donor financed); demand and community engagement activities integrating C19 as part of other comms interventions; availability and capacity of HRH; data collection and reporting mechanisms; and supply chain; availability of infrastructures to meet C19 relevant standards, multidisciplinary team approach to reach high risk populations; national health care guidelines including C19 as part of the health service package.

3

Fit for Gavi Alliance

Relevance and demand

Gavi-supported country proportion of global disease risk & burden

- The table below reflects officially reported cases and deaths due to COVID-19*. WHO estimates of excess deaths due to COVID-19 are substantially higher, particularly among lower-income settings where reporting of official disease burden faced greater challenges.

C19 cases			
Year	AMC	Global	Proportion burden in AMC
2020	16,446,959	82,936,185	20%
2021	45,041,868	204,173,244	22%
2022	29,985,976	443,649,916	7%

C19 deaths			
Year	AMC	Global	Proportion burden in AMC
2020	282,674	1,928,561	15%
2021	827,260	3,521,920	23%
2022	136,768	1,243,796	11%

Demand

- AMCs look to COVAX to supply a **large proportion** of their COVID-19 doses – with **LICs relying on COVAX for ~75% of their supply**
- **54 countries (of 56 respondents) representing more than 60% of the AMC91 population have shared their interest in continuing a COVID-19 vaccination programme in 2024** via an Expression of Interest survey that COVAX sent in March 2023. Based on the responses, the **projected demand for Gavi supported COVID-19 doses for the high priority group ranges between 120-240 million doses for 2024-2025.**
- 59% of countries (111 respondents from 36 countries) in the VIS 2024 country consultation survey identified the integration of COVID 19 vaccinations as a high priority

Fit with Gavi's mission and strategy

- Gavi's 5.1 Strategy approved by the Board in Dec 2022 recognises it is impossible to return to pre-C19 world and ways of working; Building on the lessons from the pandemic, Gavi 5.1 recognises the profound societal, geopolitical, economic and technological shifts that have transformed the environment the Alliance operates in.
- C-19 programme will contribute to **learnings on routinely reaching adult pop.** and **integration of immunisation into primary health care**, in view of Gavi 6.0 discussions on life-course vaccination, and pandemic preparedness and response

* COVID-19 surveillance in AMC92 countries is not performed thoroughly and likely significantly underestimates the number of cases and deaths.

Gavi is uniquely positioned to support a COVID-19 programme

- Gavi can leverage its COVAX experience of procuring and supporting delivery of COVID-19 vaccines for the AMC 91 countries, using well-established platforms for supplies (through APAs and donations), and its familiarity of facing uncertainty around epidemiology, duration of protection and demand while having to make timely decisions to ensure access to vaccines.
- Gavi's downstream experience via the COVDP and the extension of the CDS delivery support for the C19 vaccines into 2024-25 is an added advantage.
- Gavi support has catalyzed manufacturers' investments and maintained/enhanced the health of the Gavi- supported vaccine markets during the pandemic. While the COVID-19 market has its own unique dynamics, Gavi support has the potential to improve the health of the market for example by containing the extent of anticipated price increases or preventing negative exits of key manufacturers. Gavi Market Shaping led and completed the Alliance Covid-19 Market Shaping Roadmap in 2022 in collaboration with COVAX and other core partners, which is informing UNICEF procurement strategy. The team is therefore well-positioned to continue assessing the viability of COVID-19 vaccines market and potential risk associated.
- As part of the Alliance, Gavi will continue to coordinate with partners bringing specific expertise (supply chain, tendering, health systems integration) to deliver COVID-19 vaccines, and considering uncertain future of COVID-19 evolution, leveraging each's strengths is a strong advantage as integration of COVID-19 into health services is ongoing.
- Gavi also works closely with a multitude of stakeholders such as donors[1], NGOs, civil society organizations, academia, and implementing country governments and leveraging these relationships are key to supply and deliver vaccines and reach the target populations unique to C19.

1. Including sovereign governments, private sector foundations and corporate partners;

4

Financial implications

Financial implications

		As presented to Board in December 2022	Updated with updated demand estimate based on EoIs
Assumptions	Estimated proc. cost	[redacted]	[redacted]
	Estimated delivery cost	~$ 1.6/ dose[1]	~$ 1.6/ dose[1]
	Eligible pop cohorts	5 high priority groups as per SAGE; which represent ~20% of AMC population	
	Est. coverage of population	~35% coverage x 20% eligibility = ~7% of total AMC pop	**~18% coverage** x 20% eligibility = **~3.5% of total AMC pop**
	Procurement doses	240Md	80Md
	Dose donations #	0	**~40Md**
Scope	Extent of Gavi support – Gavi 54	Proc: 100% Delivery: 70% of estimated costs	Proc: 100% Delivery: Proposal to cover thru **extension of CDS** funding
	Extent of Gavi support – AMC 37	Proc: 50% in 2024, 0% in 2025 Delivery: 0%	Proc: 50% in 2024, 0% in 2025 Delivery: Proposal to cover thru **extension of CDS** funding
	SEC+PEF	$ 60m for 2yrs	$ 37m for 2yrs
	2024-25 Total Doses funded incl. donations	~240Md	~120Md
	2024-25 Total Cost Estimate	**~$1.9B**	**~$0.82B**

Key changes since Dec 2022 Board

Product mix with **higher mRNA share** based on country preferences indicated in the 2024 EoIs

Projected demand between 120-240 Md for 2024-2025; early read on country EoIs closer to conservative end of the range, i.e., **120 Md**

Latest estimate on **dose donations**; 2024-25 donations **not yet secured** and are **subject to uncertainty**

CDS rephasing ($320m) over 2024-25 should be **sufficient to cover delivery support** for C19 programme

$0.71B incremental ask. No new delivery funding needed

1. Calculated with Delivery Costing Working Group in Sept. 2022: incl. CoVDP, UNICEF, BMGF, Harvard School of Public Health, Mgmt. Sciences for Health, WHO & Gavi; Calcs are based on reaching higher priority user group size for 1 dose per year over 2024-25 through fixed, outreach & mass vax delivery methods; considers higher cost for adult, non-RI vaccine; Costing incl. HR for delivery, PPE, hand hygiene, per diems, transportation for outreach, training, planning & coordination, social mobilization, cold chain maintenance, waste mgmt., vax certificates, pharmacovigilance; Costing excludes ancillaries (syringes & safety boxes), TA & cost of vial.

Thank you