

Strengthening Domestic Vaccine Development and Manufacturing in Vietnam as part of Post-COVID-19 Health Security Response

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- 1. Background and Contextualizing Global Health Security in Viet Nam**
- 2. National Expanded Program on Immunization and Declarations on Domestic Vaccine Manufacturing and Introduction of New Vaccines**
- 3. Existing Local Capacity for Vaccine Development and Manufacturing in Viet Nam**
- 4. Strategic Framework for the Strengthening of Viet Nam's Vaccine Development and Manufacturing**

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Background

- The COVID-19 pandemic exposed vaccine access issues for upper-middle-income (UMIC) and low-and-middle-income (LMIC) countries as high-income countries dominated vaccine research, development, and purchasing, limiting access for UMICs and LMICs.
- Recently, there are global calls and initiatives to invest in and expand local vaccine manufacturing to improve pandemic preparedness and ensure equitable and sustainable vaccine supply.
- On similar lines, Vietnam is taking steps to strengthen its domestic vaccine production and supply

Contextualizing Health Security in Vietnam

- **Pandemic Threats:** In addition to the general threat posed by an unknown pandemic, Vietnam is recognized as a hotspot for influenza virus evolution, affecting both human seasonal influenza strains and zoonotic variants with pandemic potential
- **Vaccine Self-Reliance:** The government plans to enhance self-reliance in vaccine supply for its national immunization program, with several new vaccines scheduled for introduction over the next decade
- **Health Security Framework:** This analysis includes both known and unknown diseases with epidemic or pandemic potential that can be treated with vaccines, as well as select priority vaccine-preventable diseases identified by the Vietnamese government, all within the broader framework of post-pandemic health security in Vietnam.

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National Expanded Program on Immunization (EPI) and Sources of Vaccine Supply

National Expanded Program on Immunization (EPI) and Vaccine Supply

- The national EPI **launched in 1985 with 6 traditional vaccines expanded to 14 vaccines by 2022**, providing vaccines **against 11 diseases nationwide** with some other vaccines available in high-risk areas or for high-risk populations only
 - Tuberculosis (BCG); polio (IPV and bOPV); diphtheria, pertussis, tetanus, hepatitis B and Haemophilus Influenzae Type b (pentavalent vaccine), Hep B (birth dose), measles and rubella (Measles, MR), Japanese B encephalitis (JE), cholera and typhoid (high-risk areas), and tetanus toxoid (pregnant women).
- The **domestic manufacturers supply all but two vaccines**, namely the pentavalent vaccine and IPV, to the national EPI

Key Political Declarations

- **Decision 68/QD-TTg (2014)**: Aim to meet 100% of EPI vaccine demand domestically by 2020.
- **Resolution 20 (2017)**: Improve research and production capacity for new generation vaccines.
- **Decision 1286/QD-TTg (2022)**: Targets for domestic production of pentavalent vaccine by 2025 and mastering production technology for 15 vaccines by 2030.
- **Resolution No. 104/NQ-CP (2022)**: Roadmap for introducing new vaccines (Rota, PCV, HPV, Seasonal Influenza) by 2030.

Progress on Political Declarations (as of end-2023)

- **Domestic Vaccines Manufacturing:** No clarity on concrete actions taken or plans to materialize the political declarations on the strengthening of vaccine manufacturing in the country
- **New Vaccines Introduction:**
 - Rota and Seasonal Influenza vaccines are produced domestically, while PCV and HPV vaccines are not part of any domestic manufacturer's plans.
 - Rota vaccine, initially planned for 2022, is being introduced (status as of late 2023) with Gavi support. Initially imported, it is expected to later transition to domestic sourcing.
 - GDPM and UNICEF have prepared budget estimates (2023-2030)^A for the procurement of all four vaccines.

Table. Budget Forecast for the Procurement of Rota, PCV, HPV and Seasonal Influenza Vaccines (2023-2030 and 2040)

Vaccines	2023	2024	2025	2026	2027	2028	2029	2030	2040
Rota	\$ 956,926	\$ 7,075,621	\$ 7,148,828	\$ 7,222,787	\$ 7,296,747	\$ 7,371,465	\$ 7,446,951	\$ 7,523,209	\$ 8,330,092
Provinces		63	63	63	63	63	63	63	63
PCV (Unicef Lowest Price)	\$ -	\$ -	\$ 393,027	\$ 847,456	\$ 1,259,320	\$ 1,483,869	\$ 1,691,612	\$ 1,928,918	\$ 4,050,727
PCV (Unicef Highest Price)	\$ -	\$ -	\$ 648,495	\$ 1,398,302	\$ 2,077,878	\$ 2,448,384	\$ 2,791,160	\$ 3,121,786	\$ 6,555,751
Provinces			5	10	15	20	25	30	63
HPV (Unicef Lowest Price)	\$ -	\$ -	\$ -	\$ 131,228	\$ 168,652	\$ 200,010	\$ 223,634	\$ 252,900	\$ 1,991,590
HPV (Unicef Highest Price)	\$ -	\$ -	\$ -	\$ 203,630	\$ 261,702	\$ 310,361	\$ 347,018	\$ 392,432	\$ 3,090,398
Provinces				4	5	6	7	8	63
Seasonal Influenza	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ 11,050,499	\$ 34,809,071
Provinces								8	63

A. Draft budget estimates (2023-2030) prepared by GDPM and Unicef (August 2023). 2040 estimated developed as part of this exercise.

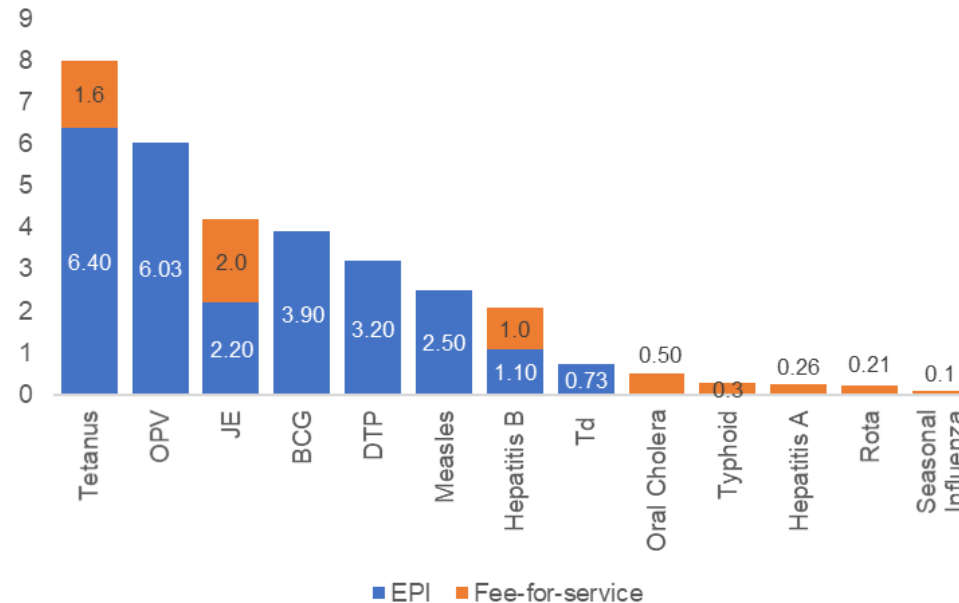
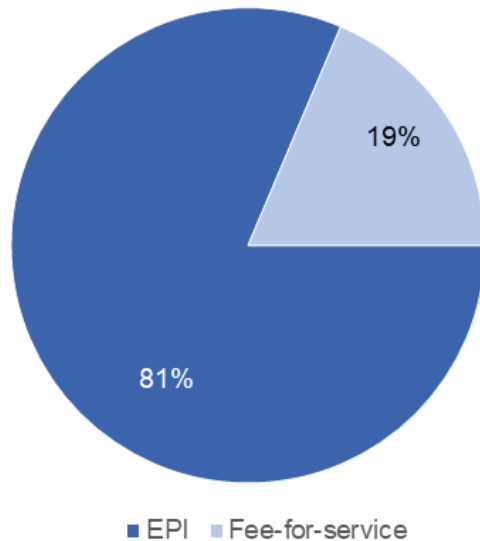
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Domestic Manufacturers: Supply

- **Strong history of domestic vaccine production history, led** by four state-owned vaccine manufacturers - IVAC, POLYVAC, VABIOTECH, and DAVAC.
- These manufacturers have a total annual production capacity of 40 million doses for 13 vaccines, while 2023 consumption was around 32 million doses
- **~81% of these vaccines by volume are for the national EPI** (2023) and the rest are used in the private sector (including fee-for-service at public health facilities)
- Two new private companies, VinBioCare (now ceased operations), and Nanogen, emerged during Covid-19



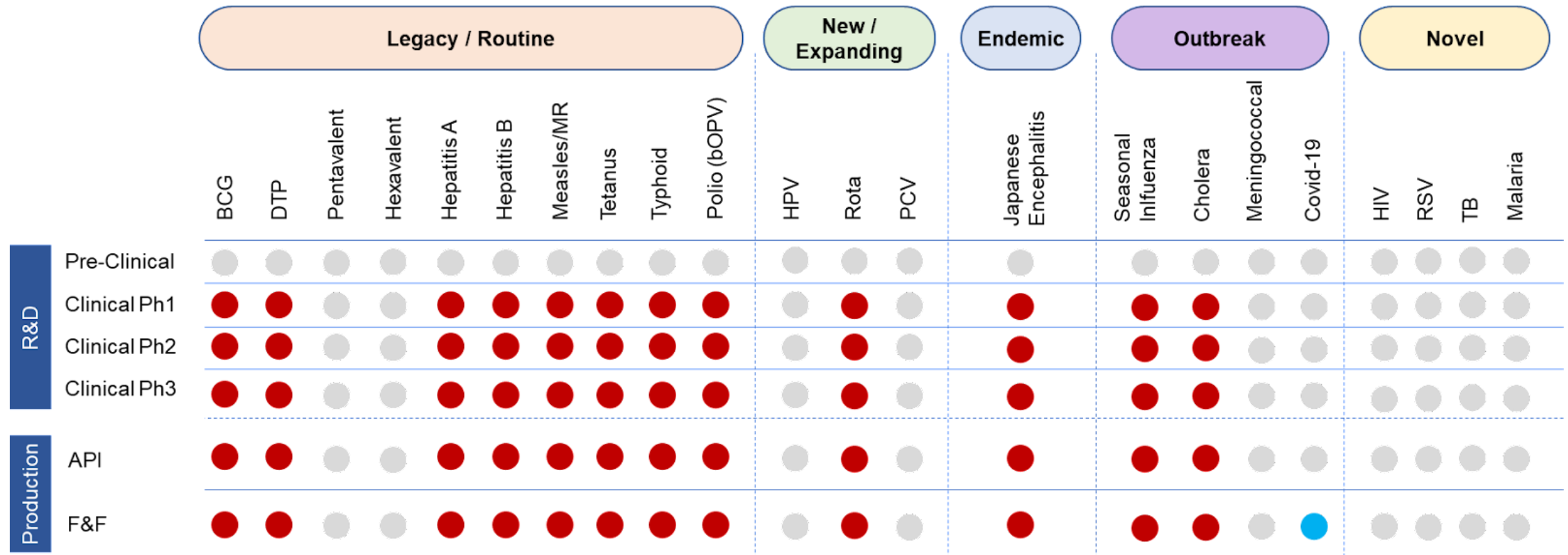
Domestic Manufacturers: Manufacturing Capabilities, Estimated Production Capacity and R&D Portfolio of Vaccines (2023)

Manufacturer	Vaccine	Platform Technology	Status				Annual Demand in Vietnam (in million doses)	
			Currently Produced (API + F&F)	API* Only	F&F Only	Annual Capacity of API + F&F Production (million doses)		In R&D
Vabiotech	1. Hepatitis B	Subunit	✓	X	X	20	2-2.5 (EPI + Private)	
	2. Hepatitis A	Inactivated	✓	X	X	0.3		0.35-0.40 (EPI + Private)
	3. JE (mouse brain)	Inactivated	✓	X	X	6		
	4. Oral Cholera	Killed whole cell	✓	X	X	8		
	5. JE (cell-based)	Inactivated					✓	2 (EPI) + 2 (Private)
	6. Hib conjugate	Subunit					✓	6-9 (EPI + Private)
IVAC	1. DTP* (includes Td vaccine capacity)	Inactivated	✓	X	X	6	3-4 (EPI)	
	2. TT	Toxoid	✓	X	X	10		6-9 (EPI + Private)
	3. BCG	Inactivated	✓	X	X	2-3		
	4. Seasonal Flu	Inactivated	✓	X	X	0.3		2-4 (EPI + Private)
	1. Pandemic Flu	Inactivated					✓	2-3 (EPI + Private)
POLYVAC	1. OPV	Live-attenuated	✓	X	X	10	6 (EPI)	
	2. Measles	Live-attenuated	✓	X	X	3		2-3 (EPI)
	3. Measles and Rubella	Live-attenuated	✓	X	X	3		
	4. Rota	Live-attenuated	✓	X	X	0.2-0.3		2-3 (EPI)
20 (EPI)								
DAVAC	1. Typhoid fever Vi polysaccharide	Subunit	✓	X	X	3-5	0.3 (Private)	

Despite producing adequate supply for the national EPI and private sector, none of the vaccine manufacturers in Vietnam have reached maximum production capacity due to: (1) export limitations, as most vaccines have not been pre-qualified by WHO, and (2) smaller domestic market coupled with preference to purchase imported vaccines among higher-income populations in the country.

Current Capacity among Vietnamese Manufacturers for Different Vaccines and Value Chain Steps

- **Established in the space of monovalent vaccines**, with limited presence in new (second-generation) and pandemic vaccines
- No in-country capacity for pre-clinical research



Number of manufacturers 0 1 2

Current Capacity among Vietnamese Manufacturers by Vaccine Platforms

- Strongly rooted in traditional vaccine platform technologies, with limited capacity in select modern platforms and nascent capacity in novel vaccine platforms

	Traditional / Classical		Modern		Novel / Next Generation			
	Live-Attenuated	Killed or Inactivated	Toxoid	Sub-unit	Nucleic acid (mRNA)	Viral Vector	Virus-like Particles	Antigen-presenting Cells
Vabiotech	●	●	●	●	●	●	●	●
IVAC	●	●	●	●	●	●	●	●
POLYVAC	●	●	●	●	●	●	●	●
DAVAC	●	●	●	●	●	●	●	●
Nanogen	●	●	●	●	●	●	●	●
VinBioCare*	●	●	●	●	●	●	●	●

*VinBioCare shut its business operations in 2023 due to lack of orders from the government

● R&D and manufacturing capacity

● Growing capacity at the R&D level

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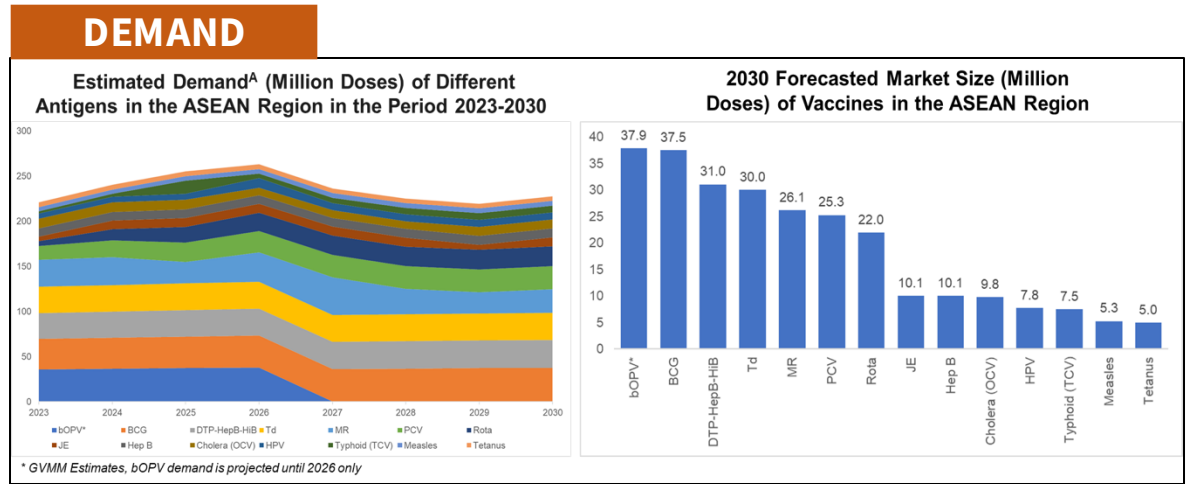
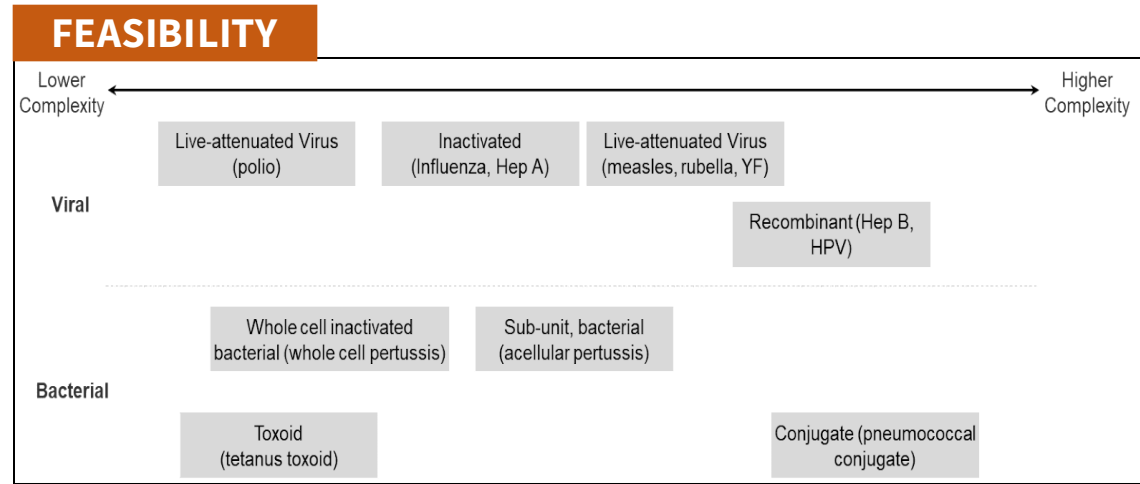
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Strategic framework for strengthening Vietnam's vaccine development and manufacturing industry

- 1 Strategic prioritization of the existing portfolio based on **manufacturing complexity, demand and supply constraints**
- 2 **Market access** for sustainable vaccine manufacturing
- 3 **Capabilities required** in the context of a threat of a **pandemic**
- 4 Collaboration for **technology transfer** and product development
- 5 **Local enabling ecosystem** in Vietnam to support the domestic vaccine industry – national regulatory authority (NRA) strengthening, talent pool upgrading, commitment from the government on the purchasing of vaccines from local manufacturers

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Strategic prioritization based on manufacturing complexity, demand and supply constraints



- ✓ Though complex vaccines generate higher profit in general, considering existing capacities is important in terms of self-sufficiency
- ✓ Two ways to group vaccines by complexity - Valency - Monovalent vs multivalent (more complex); Technology: Traditional vs modern/novel platforms (more complex)

- ✓ Low volume domestic sales would struggle to turn itself economically viable and invest profits in expanding capacities
- ✓ The ASEAN region potentially represents a sizable market demand for some vaccines in order to achieve economies of scale

SUPPLY

Vaccine	Volume Purchased by Gavi (2021)	No. of WHO-prequalified Manufacturers (Jun 2023)	No. of Gavi Suppliers (2021)	Potentially Needing Additional Suppliers for Increased or Diversified Supply*?
Hexavalent**	0	0	0	
Pentavalent	137	5	5	
IPV	83	5	5	
Rota	82	4	3	✓
PCV	132	3	3	
HPV	15	2	2	
Yellow Fever	67	4	4	
Measles-Rubella	132	2	2	✓
Measles	82	2	2	✓
JE	0	3	1	
OCV (Cholera)***	27	3	2	✓
Typhoid Conjugate	28	2	1	
Malaria****	0	1	1	✓

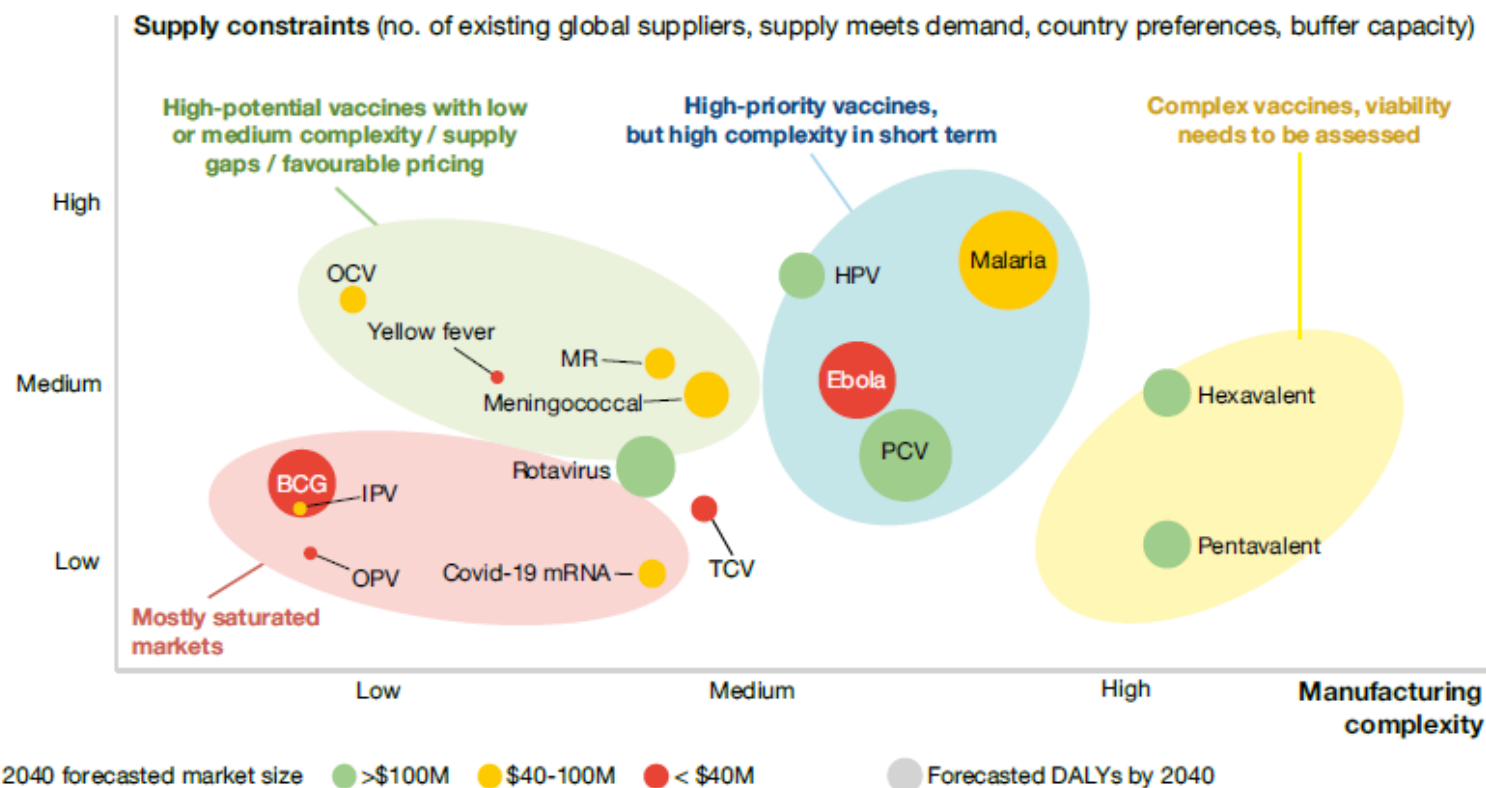
- ✓ For many vaccines, the market is already saturated, and prices are extremely low.
- ✓ In short-to-medium term, the efforts should rather concentrate on supply-constrained vaccines. For instance,
 - BCG and pentavalent vaccines have large market size, but there is fierce competition, prices are low and no shortage in supply
 - A promising candidate could be OCV, which still suffer supply shortages (despite having a smaller market) and has relatively low manufacturing complexity. Similar case can be made for Rota, Measles and Measles-Rubella vaccines.

1

Strategic prioritization based on manufacturing complexity, demand and supply constraints (contd.)

- Given that Vietnam's domestic companies are mostly concentrated in the production of monovalent vaccines, the potential of the existing monovalent vaccines for overseas business should be assessed in short—to-medium term while the capabilities to produce other new vaccines (mono or multivalent vaccines) on modern or novel platforms are developed in the medium-to-long term.
- As indicative analysis for short-to-medium term: potential vaccine candidates from Vietnamese manufacturers include OCV (by Vabiotech), and Measles, Measles-Rubella, and Rota vaccines (by POLYVAC).

Figure. Strategic Prioritization of Vaccines Based on Manufacturing Complexity, Demand and Supply Constraints



*Source: BCG-Wellcome-Biovac Study

2 Market access for sustainable vaccine manufacturing

- **Market access is essential** for sustainable vaccine manufacturing. Procurement commitments from governments or global vaccine procurement coordinators (e.g., Gavi, UNICEF) have been key to the growth of the vaccine industry in India, China, Indonesia, and Brazil.
- If the demand for Vietnamese vaccine can translate into predictable pooled procurement volumes, investments in manufacturing could be significantly de-risked.
- Vietnamese manufacturers should leverage pull mechanisms (e.g., Gavi, UNICEF) for global expansion of strategically identified vaccines in their portfolio
- As many ASEAN countries phase out Gavi support, direct procurement commitments from ASEAN governments will be key. In the absence of such commitments, innovative regional mechanisms may be needed (e.g., ADB's Asia Pacific Vaccine Access Facility - APVAX for COVID-19 vaccines).
- In addition to pull mechanisms, various push mechanisms can also be explored to drive growth.

3 Capabilities required in the context of a threat of a pandemic

- Vietnam faces a significant risk of pandemics from seasonal influenza strains alongside general threats from unknown pathogens
- Recently, the decision was made to include the seasonal influenza vaccine in the national EPI starting in 2030. However, current production capacity is **only 0.3 million doses**, with no long-term government plans for R&D and manufacturing preparedness.
- Expanding seasonal influenza vaccine production capacity is also essential for enabling manufacturers to quickly shift to pandemic vaccine production when necessary.
- Current **vaccine platform technology** in Vietnam is insufficient for rapid study initiation and large-scale manufacturing during an outbreak

Suitability of Vaccine Platforms for Rapid Response*

Platform	Description	Minimal time until first batch ¹	Ability to pre-optimize processes prior to outbreak	CD independent of immunogen knowledge	Key limitations	Example vaccines
RNA	Delivery of RNA of antigen using lipid nanoparticles (LNPs)	3+ weeks	✓ Similar process (assuming use of same LNP)		Plasmid DNA can be rate-limiting raw material	COVID-19
Viral vector	Delivery of DNA or RNA of antigen using viral vectors	10-12 weeks	⊗ Unique viral banks required	⊗	↑ Long release assays required (e.g., replication competent virus)	COVID-19, Ebola, Zika, influenza, HIV
Recombinant protein	Protein vaccine based on viral antigens	Similar to viral vector	⊗ Optimize cell growth, protein folding & formulation w/ adjuvant	Viral antigen needs to be known & targetable	Protein folding and formulation difficult to standardise	COVID-19, hepatitis B, shingles HPV
Virus-like Particles	Virus-resembling molecules with multiple surface antigens	Longer than recombinant proteins	⊗ Optimize cell growth, protein folding, complex assembly and formulation		Protein folding and formulation difficult to standardise; complex molecules due to need for self-assembly	Hepatitis B, HPV
Inactivated vaccine	Inactivated or altered replication-deficient virus	Speed determined by ability to use high BSL facilities, cell line availability & scalability and viral doubling time	⊗ Relatively simple to manufacture but growth may be virus-specific	✓ Whole virus vaccines requires limited knowledge of specific antigens	Weaker immune response / multiple doses; release test to ensure full inactivation	COVID-19, influenza (shot), hepatitis A, polio (shot), rabies
Live attenuated vaccine	Genetically modified virus which does not cause disease		⊗ Genetic manipulation unique to virus		Not suitable for people with compromised immune system	MMR, rotavirus, smallpox, shingles, yellow fever

- Safeguarding against pandemics requires targeting manufacturing platforms with proven abilities to quickly scale up production of appropriate vaccines.
- **mRNA technology** shows the best potential for immediate initiation of human studies during outbreaks, followed by viral vector platform.

Timelines until first batch vary between platforms but so does their immune response & side effect profile and need for immunogen identification

*Source: CEPI

4 Collaboration for technology transfer and product development

- Vietnamese manufacturers have strong experience in technology transfer and product development.
- However, no sustainable R&D capacity or long-term agreements for modern technology platforms have been established.
- For vaccines like HPV and PCV, expected to be introduced in Vietnam, technology transfer partnerships are essential for self-reliance and present business opportunities in ASEAN.
- To address pandemic threats, partnerships for novel platforms (e.g., mRNA, viral vectors) are also crucial.

Table. Vaccine Technology Transfer Partnerships in Vietnam

Vaccine	Technology Platform	Vietnam Manufacturer	Technology Partner	Value Step Chain	Rolled Out by EPI
Hep B	Subunit	Vabiotech	Green Cross (S. Korea)	API + F&F	Yes
Typhoid Vi Polysaccharide	Subunit	DAVAC	NIH (USA)	API + F&F	No
Seasonal Influenza	Inactivated	IVAC	WHO and PATH	API + F&F	No
Measles	Live-attenuated	POLYVAC	Kitasato Institute (Japan)	API + F&F	Yes
Measles-Rubella	Live-attenuated	POLYVAC	Daiichi Sankyo Biotech (Japan)	API + F&F	No
Covid-19*	mRNA	VinBioCare	Arcturus Therapeutics (US)	F&F	No

*The agreement didn't materialize into local production due to a lack of orders from the government

5

Local enabling ecosystem in Vietnam for the support of the vaccine industry

Local Enabling Environment

Short-term

Clarity and Commitment from the Vietnam Government on Purchasing

- Vaccine procurement is annual, but manufacturers face uncertainty about when or if their vaccines will be purchased by the government.
- Domestic vaccine prices, set by the Ministry of Finance, have remained unchanged since 2008.
- Clear, long-term government demand signals and purchase agreements are crucial to incentivizing local investment and attracting global partnerships for future vaccines.

Medium-term

Vietnam National Regulatory Authority (NRA) Strengthening

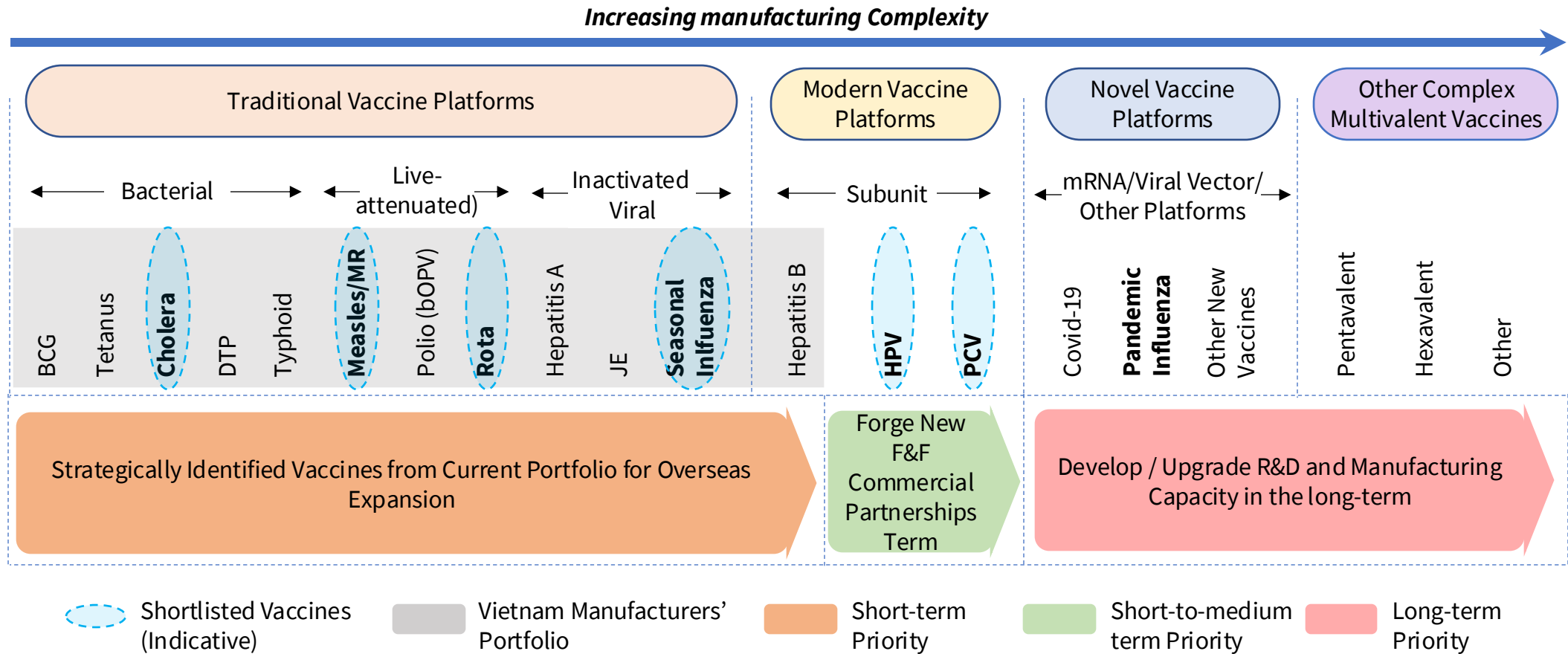
- No domestically produced vaccines in Vietnam currently have WHO PQ approval, limiting manufacturers' ability to export internationally..
- Although Vietnam's NRA is WHO Level 3 certified, it lacks the resources and capacity to expedite WHO PQ processes for new technology vaccines

Long-term

Talent Upskilling of Workforce

- Facilitate practical learning through secondments with experienced manufacturers and global experts working at local sites in Vietnam.
- Emphasize capacity building during technology transfers and address gaps in tertiary and vocational education for vaccine manufacturing.

Strategic Directions for the Strengthening of Vietnam Vaccine Manufacturing



Annex Slides

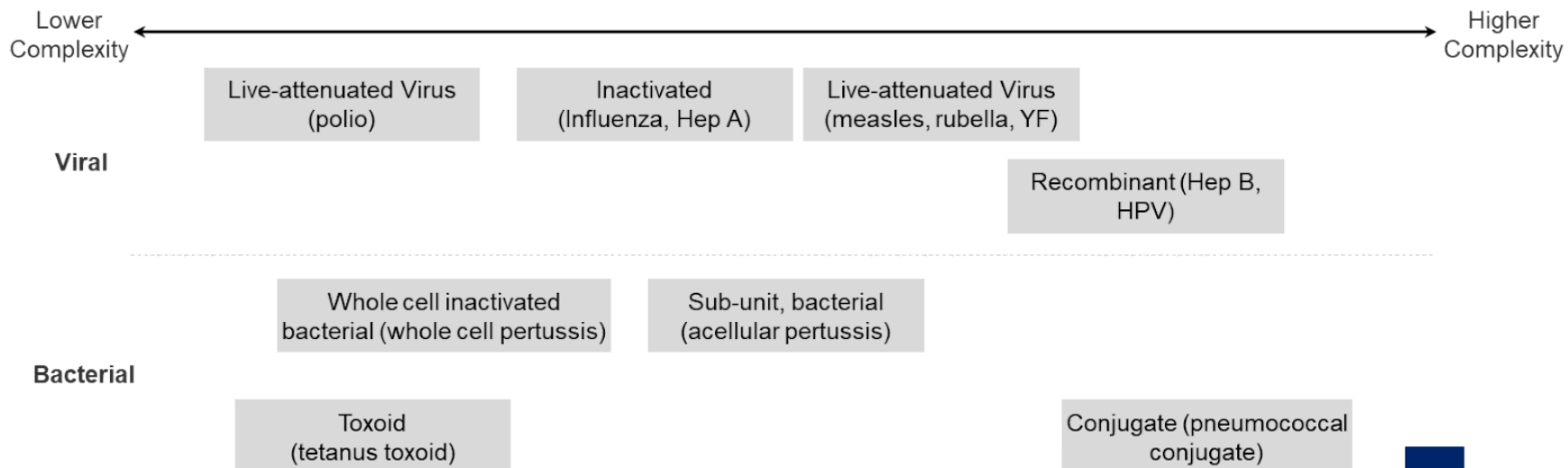
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Strategic prioritization based on manufacturing complexity, demand and supply constraints

FEASIBILITY

- The aim for domestic manufacturers must be to approach self-sufficiency in end-to-end vaccine production in long-term, so the suitability of the targeted portfolio, from pathogen type to valency (monovalent or multivalent) to technology platforms while considering the existing portfolio and capabilities, is important
- Briefly, there are two ways to group vaccines based on the complexity
 - Valency: Monovalent (Hep A, Hep B, Rota; less complex to develop/produce) v Multivalent (pentavalent, hexavalent; more complex and command a higher price/profit)
 - Technology: Traditional platforms have relatively lower production complexity in general compared to modern (subunit, recombinant) and novel platforms (mRNA) which tend to generate more profits

Illustrative Examples of Vaccine Platforms and Relative Production Complexity



1 Strategic prioritization based on manufacturing complexity, demand and supply constraints (contd.)

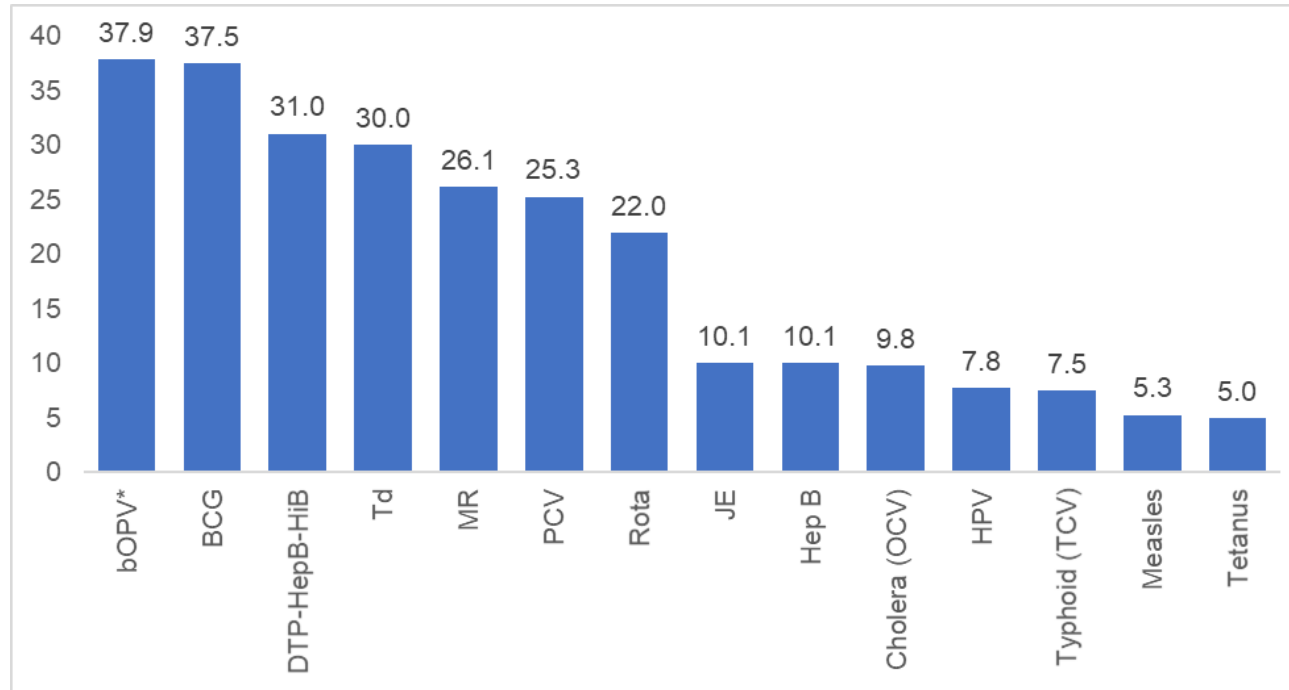
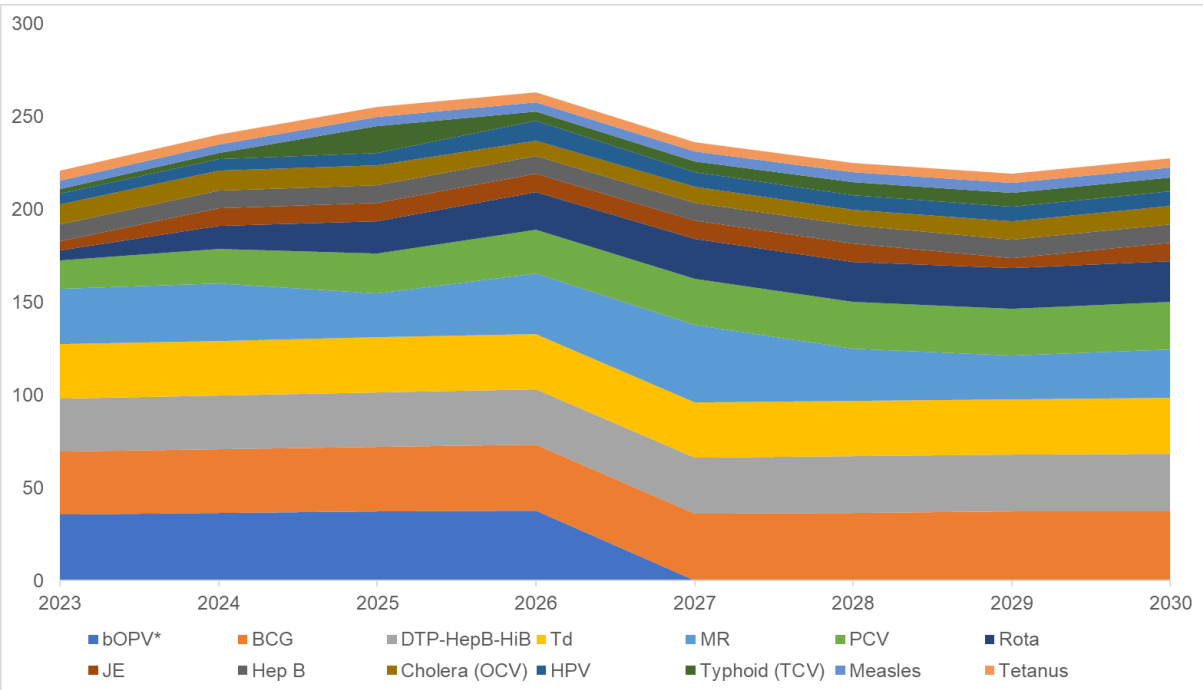
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DEMAND

- Low volume sales would struggle to turn itself economically viable
- While a huge domestic market backs Indian and Chinese manufacturers, Vietnamese manufacturers must serve beyond Vietnam to achieve economies of scale. The ASEAN region potentially represents a sizable market demand for larger volume facilities.

Estimated Demand^A (Million Doses) of Different Antigens in the ASEAN Region in the Period 2023-2030

2030 Forecasted Market Size (Million Doses) of Vaccines in the ASEAN Region



* GVMM Estimates, bOPV demand is projected until 2026 only

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Strategic prioritization based on manufacturing complexity, demand and supply constraints (contd.)

SUPPLY

- For many vaccines, the market is already saturated, and prices are extremely low. The efforts should rather concentrate on supply-constrained vaccines for the time being.
 - For instance, BCG and pentavalent vaccines might appear attractive owing to their large market size, but the markets are characterized by fierce competition, with no supply shortage and dose prices averaging in cents
 - Far more promising would be products like OCV, which still suffer supply shortages (despite having a smaller market) and which have relatively low manufacturing complexity. A similar case can be made for Rota, Measles and Measles-Rubella vaccines.

Volume Purchased and Supply Base of Relevant Vaccines (2021)

Vaccine	Volume Purchased by Gavi (2021)	No. of WHO-prequalified Manufacturers (Jun 2023)	No. of Gavi Suppliers (2021)	Potentially Needing Additional Suppliers for Increased or Diversified Supply*?
Hexavalent**	0	0	0	
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JE	0	3	1	
OCV (Cholera)***	27	3	2	✓
Typhoid Conjugate	28	2	1	
Malaria****	0	1	1	✓

*as per Gavi in 2022
 **one hexavalent vaccine manufacturer is in process to receive WHO prequalification by end of 2023
 *** one manufacturer will exit the market at the end of 2023
 **** a second malaria vaccine is currently in process of receiving WHO prequalification