

4 The Market Shaping Goal

Shape vaccine markets to ensure adequate supply of appropriate, quality vaccines at low and sustainable prices for developing countries.

Combined Supply and Procurement Roadmap

Pentavalent (DTwP-HepB-Hib)

Inactivated Polio Vaccine (IPV)

Hexavalent (DTwP-HepB-Hib-IPV)

Booster 2nd Year of life (DTwP, Pentavalent, Hexavalent)

PUBLIC SUMMARY

This supply and procurement roadmap was developed before the COVID-19 pandemic. The long-term market strategy shared in this document is believed to remain valid. The impact of COVID-19 on demand will be shared at a later stage.

Public Summary

This roadmap integrates analyses and market shaping considerations on four interrelated markets where Gavi Partners are involved in market shaping: Pentavalent, IPV, Hexavalent, and DTwP-containing boosters during the second year of life (Booster2ndY). It replaces the updates of the Pentavalent and IPV roadmaps and creates the first Booster2ndY roadmap.

The intention is to ensure that market-to-market issues are integrated into a portfolio view that is relevant both to Gavi Partners and to vaccine manufacturers with the following benefits:

- Reach a better understanding of potential future dynamics between markets,
- Consider implications related to market or portfolio opportunities and risks,
- Seek the best outcome short-, mid-, and long-term for the interrelated portfolio of vaccines,
- Deliver clear and consistent market signals that help manufacturers decide and prioritise investments, with the aim to contribute to better future market health.

The Pentavalent vaccine (DTwP-HepB-Hib) is the bedrock of the expanded program on immunization and of Gavi's engagement in childhood vaccination. It represents Gavi's most significant public health achievement to date: during 2011-2020, it is estimated that Gavi investments in Pentavalent vaccination will have helped avert a total of 6.5 million future deaths¹. DTwP-based vaccination is also the main health intervention on which Gavi-supported countries build childhood prevention strategies; the quality of its implementation influences the build-up of key country health systems and of equity.

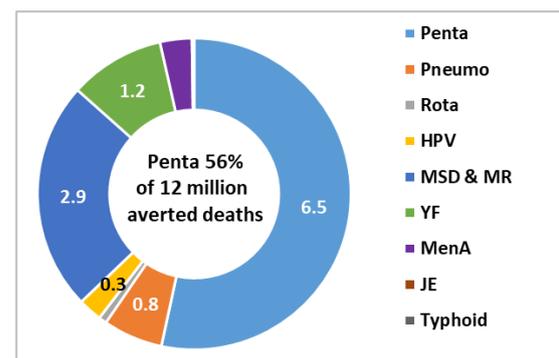
The inactivated poliomyelitis vaccine (IPV) is essential to the successful completion of the effort to eradicate polio. The current plan is to stop using OPV and replace it by at least 2 doses of IPV, one year after wild polio virus (WPV) eradication has been certified. The Gavi Board approved support of IPV post-2020 in November 2018 and its co-financing mechanism in June 2019.

The Hexavalent vaccine combines Pentavalent and IPV antigens (DTwP-HepB-IPV-Hib). The Gavi Board approved in-principle support for Hexavalent in November 2018, subject to the availability of WHO prequalified products and conditions² supporting its successful implementation.

DTwP-containing vaccines are currently used for booster dose vaccination in 24³ out of the Gavi 73 countries. Gavi catalytic support for booster dose vaccination will start in 2021 and is expected to increase uptake across Gavi countries. DTwP-containing boosters have the potential to avert approximately 106,000 deaths (of which 82% in children under age 5) during the period 2021-2035. Such vaccination can be provided during the second year of life, through DTwP or Pentavalent vaccines, and potentially through future Hexavalent vaccines if immunogenically, operationally relevant and economically feasible.

During the period 2021-2025, [Penta-IPV-Hexa-Booster2ndY] represents 24% of Gavi's total forecasted expenditure for vaccine purchasing or USD 1.2Bn, 30% of Gavi's forecasted volume for vaccine purchasing or 800 million doses, and 2.8 million future deaths averted.

Fig. 1: Estimated number of future deaths averted vs. no vaccination in Gavi73, 2011-2020



¹ Number of children immunised, and deaths averted in the 2011–2015 period also include children vaccinated with Hib- and HepB-containing vaccines outside of Pentavalent vaccine (includes Tetravalent DTP-HepB)

² Conditions for support include: Hexavalent vaccines achieve polio immunogenicity targets with the least number of doses (3 doses in primary series +/- booster during the 2nd year of life), Hexavalent prices are in line with value-based principles, supply security of IPV standalone and DTP-containing vaccines is not compromised by Hexavalent, Gavi Partners define a policy for country access to manage the potential mismatch between demand and supply, two or more Hexavalent manufacturers (with different bulk sources) can supply the market with a capacity of at least 20% of Gavi71 demand each when Hexavalent demand matures.

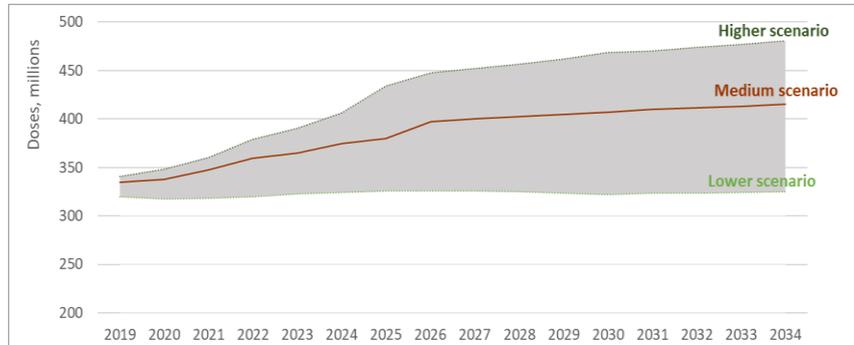
³ 20 Gavi countries use DTP as a booster during the 2nd year of life, 3 countries use Pentavalent and one country uses DT

Market overview

Market volumes:

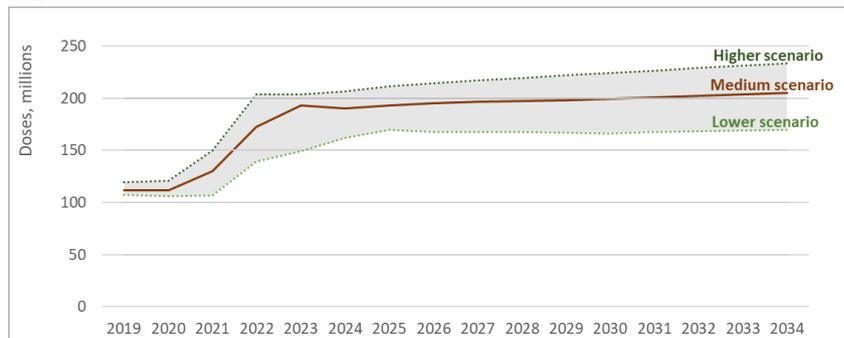
Population growth is the main growth driver in the Pentavalent market where global demand in primary series is expected to increase from approximately 290M doses in 2019 to approximately 320M doses in 2030, excluding the potential impact of Hexavalent. Global demand for DTwP-containing boosters during the 2nd year of life is expected to increase from approximately 50M doses in 2020 to approximately 90M doses in 2030. Overall, the DTwP/Pentavalent demand may reach approximately 410M doses by 2030 (range according to scenario = 320-470M doses in 2030).

Fig. 2: Estimated global demand for DTP/Pentavalent (primary series and 2nd year of life booster) without Hexavalent, 2019 to 2034



In 2018, for the first time since the introduction of IPV standalone in 126 OPV only-using countries, IPV supply was sufficient to cover demand for a one-dose schedule in countries procuring through UNICEF. As of April 2019, all countries have completed introduction of one dose of IPV standalone. Countries that had to stop or delay IPV introduction are set to immunize their missed

Fig. 3: Estimated global demand⁴ for IPV standalone without Hexavalent, 2019 to 2034



cohorts by 2021 which will require approximately 50M doses. Following this, the ramp-up to a 2-dose schedule of IPV recommended by SAGE will likely take place over a period of three years between 2021-2023 and should be finalized prior to OPV withdrawal once polio eradication is certified. Overall, global IPV demand could increase from approximately 100M doses in 2020 up to 200M doses in 2030 (range according to scenario = 170-230M doses in 2030).

As more manufacturers successfully develop Hexavalent and conditions for support are met, the Gavi Board may open a funding window allowing Gavi countries to start introducing Hexavalent (most likely starting 2024). The Hexavalent schedule based on 3 doses in the primary series and a booster dose during the 2nd year of life is expected to provide programmatic advantages by reducing the total number of injections and delivery costs, potentially improving IPV coverage, reducing the risk of premature discontinuation of IPV and enhancing the likelihood of DTP boosters' implementation in the 2nd year of life. Hexavalent demand uptake will mainly depend on supply availability and relative affordability versus a "base schedule" which includes 3 doses of Pentavalent and 2 doses of IPV in the primary series and a DTP-containing booster during the 2nd year of life. If favorable conditions are met, global demand could reach 150M doses in 2030 which would account for 35% of the DTwP-containing⁵ vaccines volume and 55% of the IPV-containing⁴ vaccines volume.

Supply landscape:

The Pentavalent market is competitive, the global production capacity of prequalified vaccines is approximately 500M doses per year largely concentrated in India, the buffer capacity is above 30% of demand and the supply base is diverse with six prequalified suppliers. The weighted average price (WAP)

⁴ Demand numbers do not include doses to be used for catch-up in 2019-2021, estimated at 50M doses in total.

⁵ DTwP-containing vaccines in this roadmap are limited to DTwP, Pentavalent and Hexavalent, and IPV-containing vaccines are IPV standalone and Hexavalent.

decreased by about 50% in 2017-2019 for countries procuring through UNICEF. As a result of the strong competition that continued to play out outside of the UNICEF market (e.g. India), some manufacturers have voiced concerns around the long-term price sustainability. The need for market and price stability is carefully considered when developing the Pentavalent market strategy.

Three suppliers offer WHO prequalified DTwP vaccines and they also supply Pentavalent that shares the same antigen bulk, so available capacity of DTwP standalone is substantially above demand. The market is small compared to Pentavalent, but manufacturers are not expected to have a challenge in meeting the anticipated increase in demand.

Two suppliers offer WHO prequalified IPV vaccines. During 2014-2018, only 46% of UNICEF-contracted quantities were supplied due to technical challenges in scaling up production capacity. In the UNICEF tender for supply covering 2019-2022, prices offered increased 60-140%. New manufacturers are expected to have IPV vaccines prequalified starting 2020. Together with increased capacity from some current manufacturers, this will increase competition and should reduce the WAP. Overall, IPV bulk capacity may increase from approximately 180M doses in 2020 to approximately 350M doses in 2030.

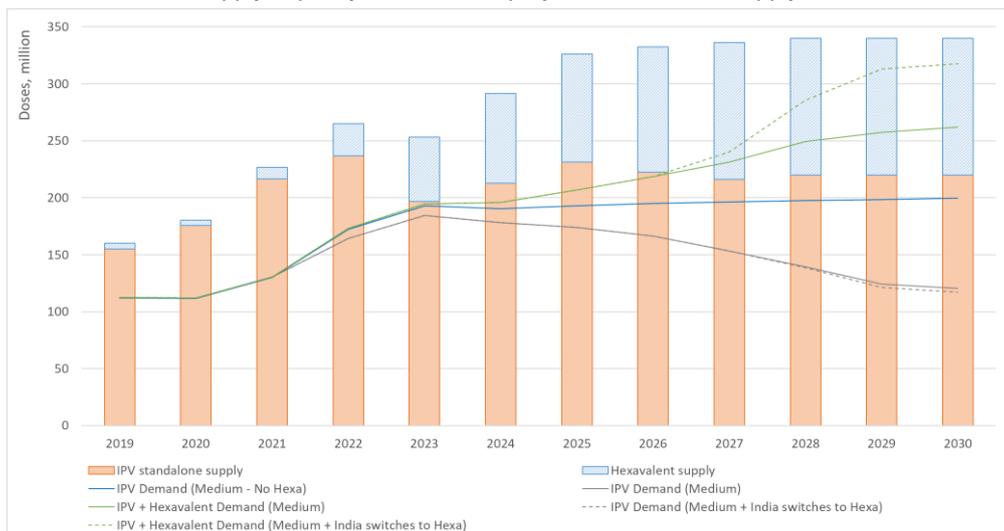
One wP-Hexavalent vaccine is approved in India and used predominantly in the private market but aiming for WHO prequalification. Four other manufacturers have products in development with the intent to obtain WHO prequalification. Hexavalent supply capacity in the global market may reach 20-70M doses in 2023 and 60-200M doses in 2030, depending on the number of successful manufacturers, the availability and decisions to allocate bulk antigens between Pentavalent, IPV, and Hexavalent.

Balance of supply and demand:

Overall bulk capacity of DTP and IPV-based vaccines is expected to sufficiently cover demand.

- DTP/Pentavalent supply covers demand with a buffer of 30-65%.
- In case half of the Gavi71 countries decide to switch to Hexavalent (excluding India) at least four Hexavalent manufacturers are needed to cover demand until 2028 and a fifth manufacturer is needed from 2029 (based on market intelligence about supply production plans as of April 2020).
- Global supply of IPV standalone is expected to cover demand in the 2019-2023 period during which countries should implement catch-up immunization (2017-2021) and switch to a 2-dose schedule as recommended by SAGE (2021-2023). However, as manufacturers start producing Hexavalent, a close engagement is needed with them on demand forecasts and production planning to avoid low buffer situations.

Fig. 4: Global IPV-based vaccine supply capacity and demand projections, medium supply and demand scenarios, 2019-2030



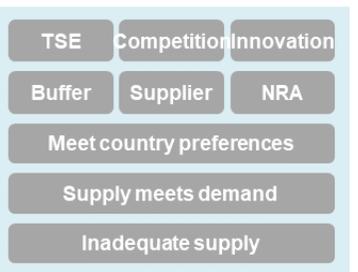
Price: The UNICEF weighted average price (WAP) per dose for Pentavalent vaccines decreased from USD 1.55 in 2016 to USD 0.86 in 2019 while the WAP per dose for DTwP remained stable at approximately USD 0.20 until 2018 and dropped to USD 0.17 in 2019. The UNICEF WAP per dose for IPV vaccines increased from USD 1.26 in 2017 to 2.35 in 2019.

Market value: The market value of IPV and DTwP-combination vaccines for Gavi70 countries (Gavi73 less India, Georgia, Armenia) reached approximately USD 260M in 2019.

Market Health Framework Evaluation (2019-2023)

The health of Pentavalent market is moderate to high with most market attributes either met or partially met. The health of the IPV market is low to moderate with years of supply constraints but new manufacturers are expected to improve supply and WAP. The first Hexavalent vaccines are expected to be prequalified towards 2021-23 and interactions between the three markets will be limited before then but manufacturers with Hexavalent development plans are expected to make strategic decisions during this period.

Dynamic market health assessment – period 2019 – 2023 (colour code : green = met, orange = partially met, red = unmet)

	DTP/Pentavalent: moderate to high	IPV: low to moderate	Hexavalent: n/a
Market health framework*			
Attributes	<ul style="list-style-type: none"> Supply meets demand, country preferences and buffer capacity are met (over 50% buffer). NRA partially met: about 90% of available supply is from Indian manufacturers. This high concentration is considered a risk. Individual supplier risk and Long-term competition are partially met as some quality and financial issues may impact future supply. TSE is met even though prices may evolve unfavorably. Innovation is met thanks to one manufacturer having launched Hexavalent and four others with Hexavalent in their pipeline 	<ul style="list-style-type: none"> Supply will meet demand for a 2-dose schedule starting 2021, if at least two new products are available to UNICEF-SD. Buffer capacity is partially met due to some risk of low buffer capacity in 2023. Country preferences are partially met because of limited availability of 10-dose vials. Individual supplier risk is high due to important hurdles faced by manufacturers and the difficulties of IPV development. NRA mix is met: suppliers are dependent on a wide range of NRAs (France, South Korea, The Netherlands, India, China). TSE is partially met due to the important price increase in the 2019-2022 tender which is expected to be improved with the arrival of new suppliers starting 2020. Innovation is met: new manufacturers with Sabin IPV are expected to reach the market in 2021 and with Hexavalent in 2023. 	<ul style="list-style-type: none"> Supply for Gavi countries may not be available before 2024.

(*): Buffer = Buffer Capacity, Supplier = Individual Supplier Risk, NRA = Risk linked to National Regulatory Agency, TSE = Total System Effectiveness, Competition = Long-term Competition

Supply and Procurement Target Outcomes

Supply and procurement objectives were analysed resulting in the following target outcomes:

- At least four medium- to large-scale prequalified DTP/Pentavalent manufacturers provide vaccines to the global market until 2026, and at least three beyond 2027. Buffer capacity is maintained $\geq 40\%$ of demand during the 2019-2034 period.
- At least four medium- to large-scale IPV manufacturers supply GPEI/Gavi markets with a combined capacity of 230M doses by 2024 and buffer capacity is maintained $\geq 30\%$ starting 2025.
- A number of medium to large scale manufacturers successfully develop and launch WHO prequalified Hexavalent vaccines:
 - At least two Hexavalent vaccines (with different bulk sources) are prequalified and launched by 2024 with a total annual supply capacity of ≥ 25 M doses
 - More Hexavalent vaccines are launched and supply capacity increases in line with expected demand materialization
- Gavi countries adopt WHO recommended immunization schedules for IPV and DTP-containing boosters.
- Market exits don't increase NRA risk in the DTP/Pentavalent, IPV and Hexavalent markets.
- The cost of immunizing one child against DTP, HepB, Hib, and IPV during the first two years of life is in line with price targets defined in accordance with value-based principles whatever the vaccine mix.
- SAGE issues clear recommendations on the use of Hexavalent (e.g. schedules).
- Hexavalent co-financing mechanism is in line with the currently reviewed policies under Gavi 5.0 and supports the Hexavalent introduction strategy that will be presented to the Board for approval alongside the request to open a funding window.
 - Co-financing policies are currently under review for Gavi 5.0 and will impact the policies defined for Hexavalent.

Supporting Stakeholder Action Plan

A concerted action plan ensures the coordination between Gavi Partners; it is designed to facilitate the achievement of the above supply and procurement target outcomes.

- Provide regular information to manufacturers on DTP/Pentavalent/IPV/Hexavalent demand and on Gavi's strategy. Develop and implement plans to prevent decisions that may jeopardize supply security.
- Support pipeline manufacturers to develop and prequalify IPV vaccines that are appropriate for the Gavi market to be available by 2022. Provide guidance to manufacturers as needed and appropriate to minimize time to prequalification. Encourage suppliers to plan for a two-dose demand scenario and for adequate long-term supply of IPV.
- Support some manufacturers with Hexavalent development plans where appropriate, share country preferences with manufacturers to ensure they develop presentations that are adapted to country needs. Monitor the switch of suppliers to Hexavalent and evaluate impact on DTP/Pentavalent and IPV supply capacity.
- UNICEF, Gavi and WHO develop and implement plans to ensure countries introduce and roll-out the 2nd dose of IPV as soon as supply is available and before bOPV withdrawal, to prevent premature abandonment of IPV by countries after polio eradication, and to ensure countries introduce D,T,P-containing boosters.
- Consider a portfolio view for all strategy development and partners' engagements with manufacturers to capitalize on portfolio efficiency, improve supply security and market sustainability.

- Prepare and implement the next procurement cycles for Pentavalent, IPV, and DTwP boosters.
- Provide SAGE with information about polio immunogenicity in Hexavalent clinical trials, to develop a recommendation on the most appropriate schedule (3-dose vs 4-dose) by 2021.
- Define a co-financing policy for Hexavalent that is based on the reviewed policies for Gavi 5.0 and takes into account the specificities of IPV's co-financing policy.

Gavi's future market shaping exit conditions: Gavi market shaping activities will not end before the [Penta-IPV-Hexa-Booster2ndY] markets are stabilized and meet the following evaluation criteria:

- Suitable DTP-based products are available to Gavi73 countries and IPV-based products are available to Gavi73 and to other countries as defined in the Polio Endgame Strategy,
- Total available supply is consistently above total demand and meets product preferences, for DTP-based products available to Gavi-supported countries, and for IPV-based products available to Gavi73 and other key countries for polio eradication,
- Products originate from a diverse supplier base,
- Prices are deemed affordable and sustainable.

Such market situation is not expected before 2029.