

# Global HPV Vaccine Market Study

## Demand Forecasting Methodology

September 2019

### Glossary

*Supply, as mentioned in this document, is defined as available supply for commercialization:* The number of doses available for sale at global level in one typical year with normal production facilities utilization across the various vaccines (not factoring in special market, regulatory or technical events) – this value is different from bulk or final product manufacturing capacity or from supply availability in a specific year.

*Future demand, as mentioned in this document, is defined as programmatic doses required:* The average estimated number of doses a country would need to procure to meet its immunization program needs, whether these are routine or campaign. This requirement includes wastage (depending on the presentation) and buffer.

### Background

Market Information for Access to Vaccines (MI4A) is a WHO initiative launched in 2018 (pilot phase 2017) and funded by the BMGF to enhance understanding of global vaccine supply and demand dynamics towards enhanced policy making for immunization and increased access to timely and affordable supply. The initiative specifically focuses on filling an information gap on dynamics in self-procuring and self-financing countries, complementing existing information from key partners such as UNICEF, PAHO Revolving Fund, Gavi, BMGF, PATH and CHAI.<sup>1</sup> In September 2018, MI4A developed a baseline forecast for HPV vaccine demand and supply requirements and published a market study.<sup>2</sup> The work was used to inform WHO actions towards increased access to HPV vaccines in context of a call for action towards elimination of cervical cancer. Results were shared with leadership of WHO and immunization agencies. The 2018 HPV market analysis – as well as any other MI4A market study - has been vetted by the MI4A Advisory Group of Experts.<sup>3</sup>

The 2018 HPV market study incorporated as set of demand scenarios based on elimination strategy options under discussion at SAGE at the time.<sup>4</sup> It also included supply scenarios built on the knowledge of manufacturers' supply as available at that point in time.

Since the publication of the market study, new information has become available requiring an update. In addition, the last SAGE discussion on HPV requested a review of dose allocation scenarios to inform use of scarce supply towards cervical cancer elimination. This document provides an overview of the assumptions and scenarios used to inform market shaping partners and SAGE

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<sup>1</sup> More info available in project intro document.

<sup>2</sup> [https://www.who.int/immunization/programmes\\_systems/procurement/v3p/platform/module2/WHO HPV market study public summary.pdf](https://www.who.int/immunization/programmes_systems/procurement/v3p/platform/module2/WHO HPV market study public summary.pdf)

<sup>3</sup> ToRs of the group available upon request.

<sup>4</sup> MI4A Demand Scenarios from July 2018: Base Case, Elimination, 1-dose and Gender Neutral. Refer to MI4A HPV Market Study Methodology document for all details.

discussions (October 2019) based on guidance by the SAGE HPV WG and MI4A Advisory Group of Experts.

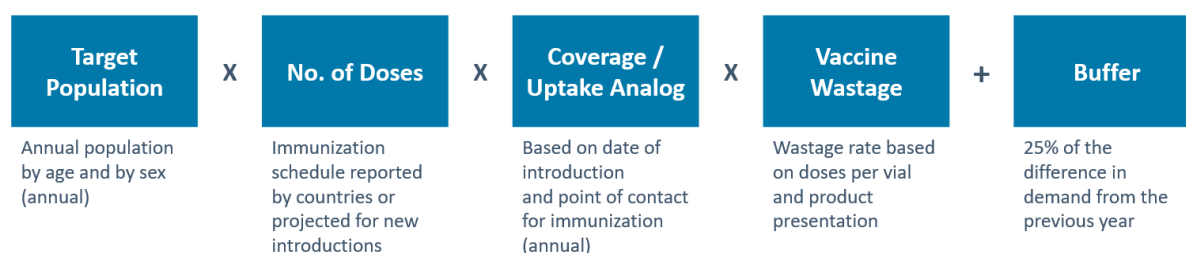
## Base Demand Assumptions:

### Building Blocks of the Global\* Demand Forecast



\* In specific cases, existing partner demand forecasts (Gavi, UNICEF SD, PAHO RF) are leveraged and demand is only forecast per the MI4A methodology for specific country groups – e.g. for HPV and MenA, the Gavi SDS served as the point of reference for forecasting demand for Gavi countries.

### Routine Immunization Demand Forecast Methods



### For the HPV Global Market Study

- **Target population** for future demand is 9-14 year-old girls (one age cohort for routine, all five for most<sup>5</sup> MACs). Boys are included for countries with an existing gender-neutral immunization policy.<sup>6</sup> No gender-neutral HPV vaccine use is forecasted for new introductions<sup>7</sup> for the base case or any of the scenarios below. Opportunistic catch-up (immunization of older adolescents and adults) is incorporated into the forecast via the coverage estimate (see details below).
  - **Source:** UNPD WPP<sup>i</sup> population projections by age, by sex is used for each country. The Indian census<sup>ii</sup> for population by state is also leveraged as demand is forecasted by state for India.
- **Immunization schedule** of two doses (single dose or extended interval schedules are demand scenarios – see below). China is forecasted to use 3-doses, sub-nationally, with domestically produced product, from 2020 through 2024 (then 2-dose schedule nationwide in 2025).
  - **Sources:** JRF country-reported immunization schedules<sup>iii</sup>; WHO MI4A Vaccine Purchase Data<sup>iv</sup>; ECDC Vaccine Schedules<sup>v</sup>
- **Introduction date:** Planned introduction dates are as reported by countries or partners (WHO, PAHO, Gavi, Gates Foundation, PATH, CHAI). Where no plans are available, regional offices and experts are consulted to advise on potential introduction dates and ultimately review the MI4A

<sup>5</sup> Some Gavi-supported countries are planning MACs for 2-3 cohorts as their MAC is delayed, due to the current supply constraint. MACs for five non-Gavi countries included to represent potential targeting of multiple cohorts for an introduction (three cohorts used for forecasting).

<sup>6</sup> Countries currently recommending immunization of boys, along with girls: Antigua, Argentina, Australia, Austria, Bahamas, Barbados, Brazil, Canada, Croatia, Czech Republic, Germany, Grenada, Ireland, Israel, Italy, New Zealand, Norway, Panama, St. Lucia, Switzerland, Trinidad, Turkmenistan, UK, USA. WHO intel also suggests Netherlands will soon, so they are included.

<sup>7</sup> One exception is Slovakia. Introduction of HPV with a gender-neutral policy is forecast, based on input from WHO.

proposed introduction year. Countries with domestic products in the pipeline (China<sup>8</sup>, India<sup>9</sup>) projected introductions are assumed to coincide with forecasted date of national product licensure. Continuous refinement of introduction dates is possible; assumptions and supply information are, and will be, the latest available at time of presentation.

- Source: JRF<sup>3</sup>, WHO Immunization Repository<sup>vi</sup>, Gavi, HPV partners and experts<sup>vii</sup>, WHO Regional Offices, final review by MI4A advisory group of experts
- **Coverage:** The Gavi Strategic Demand Base 2-dose Scenario (SDS)<sup>10</sup> assumptions/approach were leveraged to estimate coverage for Gavi-supported countries. Country-specific and regional coverage estimates are applied to non-Gavi countries. Country-specific estimates are sourced from WHO HPV coverage data (shared as of May 2019) and are the midpoint of the first and second dose. This coverage data from countries with more than one year of national introduction is averaged by region to develop the regional coverage estimates that are applied to future introductions or countries for which coverage data is not available (per tables below).

Existing coverage data leveraged to place the country in a “coverage band”. These “coverage bands” are in increments of 5%, e.g. 65%, 70%, 75% coverage. For most countries, coverage is forecasted to remain steady over time. Select countries that have had a crisis greatly reducing their HPV coverage in recent years are forecast to achieve the same coverage as their highest historical by 2030. e.g. if they are in the 50% coverage band for 2019 but once had 75% coverage, we forecast a ~2.3% annual increase from 50% in 2019 reaching 75% in 2030. This seemed appropriate given the context of the cervical cancer elimination initiative. For countries with a gender-neutral schedule male coverage data is used OR one coverage band lower is applied to males.

Region	Coverage/Uptake Analog
AFR	85%
AMR <sup>11</sup>	70%
EMR	65%
EUR	75%
SEAR	80%
WPR	80%

The coverage estimate incorporates the additional coverage achieved from **opportunistic catch-up of older populations** (particularly relevant for HICs with lower coverage in the target age cohort). This is to say that we do not include a separate forecast of demand for opportunistic older age group catch-up, but rather attempt to account for this additional demand in the coverage analog that we use. For example: coverage of the target cohort in the USA is 65%; opportunistic catch-up of older adolescents and adults is 8.6%; thus, the coverage analog used in forecasting USA’s annual demand is 75%.

#### Sources:

- WHO IVB HPV coverage estimates (May 2019)

<sup>8</sup> Subnational, non-reimbursed EPI use of HPV in China is projected to start in 2020 (at 5% of the population). National introduction is projected for 2026.

<sup>9</sup> Introduction year forecasted by state for India.

<sup>10</sup> January 2019

<sup>11</sup> PAHO RF input on annual procurement taken into account to estimate coverage for AMR

- Country-specific estimates<sup>viii</sup> (US CDC, Public Health England, Australian DOH, Spain MOH, ECCMID, Norwegian Institute of Public Health and more)
  - Available papers that report on HPV coverage<sup>ix</sup>
  - [HPV Information Centre](#)
  - Assumptions approved by MI4A advisory group
- **Uptake:** Factor applied to coverage to indicate that in the first few years after new HPV vaccine introduction, full coverage goal (value outlined above) is not achieved. For new introductions in non-Gavi countries, uptake is: Year 1: 100%, Y2: 80%, Y3:90%, Y4+:100%. For Gavi countries, the SDS was referenced to determine the uptake assumption.
  - **Routine Wastage:** 5% for 1-dose vials, 10% for 2-dose (wastage for MACs is 5%)
  - **Private Market:** Estimated for MICs where HPV is not available in the EPI schedule. Private market use in other countries is acknowledged, but where HPV is in the country's EPI schedule, this demand is not distinguished from public market demand and is captured in the overall forecast for a country. MICs without HPV in EPI have been identified as a key missing segment; hence this MICs private market estimate is included.
    - Sources: Lot release data from China.<sup>x</sup> For India and other MICs, MI4A estimates the private market based on the portion of the population in the wealthiest tier (5-10%). (Private market data was purchased, but found to be insufficient)

## Demand Scenarios:

Table: Comparison of Scenario Assumptions

	Scenario	Countries Affected by Scenario	No. of Routine Doses	MAC/Catch-up	No. of MAC/Catch-up Doses	Coverage
1	2-dose	-	2 <sup>*</sup>	✓ (3-5 cohorts 9-14 yo)	2	MI4A Base Case
2					-	
3	1-dose	LICs & MICs	1 (from 2022)	✓ (3-5 cohorts 9-14 yo)	1	1-dose 2022+: 1.15X the base case coverage, up to 90%
4					-	
5	Extended Interval	Gavi-supported & PAHO RF**	1+1 (3-year interval)		-	For 1+1 countries: 1.15X 1st dose, 0.7X 2nd dose coverage
6			1+1 (5-year interval)	✓ (14yo)	2	For 1+1 countries: 1.15X 1st dose, 0.6X 2nd dose coverage; base case coverage for 14y 2-dose
7	14yo, Later Switch to 9yo	Gavi, PAHO RF & LMICs	2	✓ (14yo)	2	MI4A Base Case

*\* In the forecast, China introduces sub-nationally with 3 doses then changes to 2 doses in 2025. This is the only exception to use of 2 doses in the target cohort for HPV; \*\* Plus Mexico*

1. **Routine 2 doses with MACs 9-14 years old:** Country forecasted demand (programmatic doses required) is based on planned and projected new introductions with all countries introducing HPV vaccine by 2030. Coverage for new countries is based on MI4A coverage methodology (as detailed above). The scenario includes MACs for Gavi-supported countries with 2 doses since these are planned per Gavi policy. MACs for some non-Gavi countries are also projected, given pattern of introductions historically (five countries represent ~350M doses for across 2020 and 2021).
  - a. **Unconstrained:** as specified above
  - b. **Supply constrained “real world”:** as a first step new introductions are ordered based on country plans and readiness. Subsequently, introductions are delayed based on the following rule: (a) HICs and UMICs with GNI > \$6,000 are assumed to be served first due to market forces; in case supply is insufficient for all of them they will be ordered in decreasing order of GNI. (b) PAHO RF countries next, ordered by disease burden, then (c) Gavi-supported countries and non-Gavi MICs < \$6,000 GNI are ordered in by disease burden and supplied accordingly. India and China will introduce as planned when domestic supply is available
    - i.e. if a higher burden country is forecasted to introduce in 2028, their introduction date stays in 2028 and does not move to more near term. If a HIC is projected to introduce it does not get pushed to a later year by a higher burden LIC or LMIC.
2. **Routine 9 years old, 2 -doses (No MACs):** Same as #1, but no MACs.
  - a. **Unconstrained:** as specified above
  - b. **Supply constrained “real world”:** as specified in scenario #1
3. **Routine 1 dose with MACs 9-14:** Current country use continues with planned and projected new introductions for all countries by 2030. Starting in 2022<sup>12</sup>, new introductions in LICs, LMICs and UMICs are for a single dose schedule (1-dose); new introductions in HICs remain at 2-doses<sup>13</sup>. Countries with 2023+ planned/projected introductions are forecasted to move their introduction forward by one year, given the programmatic benefits of the single dose schedule.<sup>14</sup> Additionally, LICs and MICs that introduced HPV vaccine prior to 2022 reduce their schedule to 1-dose starting in 2022<sup>15</sup> (HICs remain at 2-doses). Coverage is forecasted to increase (compared to the base case) by 1.15X (up to 90%) if a country switches to or introduces with 1-dose. The scenario includes MACs as described in #1 but with only 1-dose if the country is modeled to introduce with 1-dose per the scenario rules.

<sup>12</sup> Assumes 1-dose provisional policy measure from SAGE in 2021.

<sup>13</sup> Note: Only five HICs that have not yet introduced HPV, and are thus forecasted for 2020+ – Bahrain, Oman, Poland, Qatar, Slovakia

<sup>14</sup> Except China and India, as their introduction dates are related to domestic supply availability timelines

<sup>15</sup> Non-Gavi, Non-PAHO MICs > \$6K GNI forecasted to delay one year and make the change to 1-dose in 2023.

*[The 1-dose scenarios (#s 3 and 4) are NOT meant to inform discussion on HPV schedule but, rather, to provide some further background information as part of discussions on time-limited supply allocation coping strategies given ongoing review of 1 dose evidence.]*

- a. **Unconstrained:** as specified above
  - b. **Supply constrained “real world”:** as specified in scenario #1
4. **Routine 1 dose (No MACs):** Same as #3 above, but no MACs.
  - a. **Unconstrained:** as specified above
  - b. **Supply constrained “real world”:** as specified in scenario #1
5. **Three-year Extended interval:** Dates for planned and projected new introductions for all countries by 2030 also based on the base case. A 1+1 schedule (3-year interval between first and second dose) is assumed for all new introductions (2020+) in Gavi-supported and PAHO RF countries; new introductions in other MICs and HICs remain at 2-doses (current schedule). Gavi-supported and PAHO RF countries that have already introduced, as well as Mexico, are forecasted to adopt the 1+1 schedule in 2020 as well. Coverage is forecasted to be higher for the first dose (compared to the base case) by 1.15X (up to 90%) but much lower for the second dose (0.70X) given the extended interval. Other assumptions are same as #2.
  - a. **Unconstrained:** as specified above
  - b. **Supply constrained “real world”:** as specified in scenario #1 (noting that even if countries are introducing with just one dose in the first year, supply will need to be sufficient three years later [when they introduce their second dose] to allow for their introduction)
6. **Five-year Extended Interval + 14 year-old catch-up:** Dates for planned and projected new introductions for all countries by 2030 based on the base case. A 1+1 schedule (5-year interval between first dose at 9 years and second dose at 14 years) is assumed for all new introductions (2020+) in Gavi-supported and PAHO RF countries; new introductions in other MICs and HICs remain at 2-doses (current schedule). To catch-up girls that would never be reached, all newly introducing countries implementing the 1+1 schedule do an annual catch-up at 14 years with 2-doses (first five years is: 1-dose at 9, 2-doses at 14; starting in year six, there is 1-dose at 9 years and 1-dose at 14 years). Gavi-supported and PAHO RF countries that have already introduced, as well as Mexico, are forecasted to adopt the 1+1 schedule in 2020 as well. Those countries that introduced in 2016 or later will target 14 years with 2-doses for the required number of years, to ensure no cohort between 9 and 14 is missed. Coverage is forecasted to be higher for the first dose (compared to the base case) by 1.15X (up to 90%) but lower for the second dose (0.60X) given the 5-year extended interval. Coverage for the 2-dose catch-up at 14years is per the base case.
  - a. **Unconstrained:** as specified above
  - b. **Supply constrained “real world”:** as specified in scenario #1
7. **14-year-old, later switch to 9 year old:** Dates for planned and projected new introductions for all countries by 2030 based on the base case. HICs and UMICs stay the same as the Base Case. Gavi, PAHO RF and LMICs that have already introduced HPV and have caught up all cohorts through 14 years old (yo) by virtue of time in their immunization schedule or a MAC experience

see no change in this scenario and are as per the base case. Countries that introduced but have not caught all cohorts through 14yo continue with their base forecasted demand but add annual catch-ups to 14yo, 2-doses for the required number of years. For new introductions, countries are forecasted to target 14 yo to start until sufficient supply allows adding 9 yo. A “supply optimization year” (SOY) was set based on the timing of expected substantial increase to available supply (mid 2020’s) and is an inflection point in the scenario. For new introductions, 2020 until the SOY, countries target 14yo to start, then adding 9yo (2 doses for 14yo continue for five years after 9yo added). After the SOY, new introductions target both 9yo and 14yo with 2-doses (14yo for only the first five years). Other assumptions, including coverage, are the same as #2.

a. **Unconstrained:** *as specified above*

b. **Supply**

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#### Sources:

<sup>i</sup> UN Population Division World Population Prospects (WPP): <https://population.un.org/wpp/>

<sup>ii</sup> Indian census (2011), population by state, by age and sex: <http://censusindia.gov.in/>

<sup>iii</sup> JRF Country-reported immunization schedules:  
[http://apps.who.int/immunization\\_monitoring/globalsummary/schedules](http://apps.who.int/immunization_monitoring/globalsummary/schedules)

<sup>iv</sup> WHO MI4A Vaccine Purchase Data:  
[https://www.who.int/immunization/programmes\\_systems/procurement/v3p/platform/module1/en](https://www.who.int/immunization/programmes_systems/procurement/v3p/platform/module1/en)

<sup>v</sup> ECDC Vaccine Schedules: <https://vaccine-schedule.ecdc.europa.eu/>

<sup>vi</sup> WHO Immunization Repository: <https://www.who-immunization-repository.org/>

<sup>vii</sup> Experts consulted as of April 9, 2019 (*list to be updated as necessary*): Anagha Loharikar (CDC), Anissa Sidibe (Gavi), Cuauhtemoc Ruiz (PAHO RF), David Mutuerandu (UNICEF SD), John Fitzsimmons (PAHO RF), Laia Bruni (ICO Barcelona), Nicolas Theopold (Gates Foundation), Olivia Bullock (Gavi), Paul Bloem (WHO IVB), Peter Dull (Gates Foundation), Scott LaMontagne (PATH) – along with all WHO Regional Offices.

<sup>viii</sup> US CDC, Public Health England, Australian DOH, Spain MOH, ECCMID (EU/EAA countries), Norwegian Institute of Public Health – *to be updated as more sources are identified and leveraged*

<sup>ix</sup> Brotherton & Bloem, 2017; Bruni, et al., 2016

<sup>x</sup> Chinese Lot Release Data: <http://www.nifdc.org.cn/CL0108/>