World Health Organization

MI4A
MARKET INFORMATION FOR ACCESS TO VACCINES

GLOBAL MARKET STUDY
MEASLES-CONTAINING VACCINES (MCV)

Key Takeaways

- All **194 WHO Member States** have introduced at least one dose of measles-containing vaccine (MCV) and 179 countries have introduced a second dose. 173 countries have introduced at least one dose of rubella-containing vaccine (RCV) as per WHO recommendations. Supplementary immunization activities (SIAs) are still required to increase coverage and reach older age groups.
- Of the total demand for MCVs, approximately two thirds of demand is for **Routine Immunization** (RI) activities and one third is for outbreak response and **SIAs**. RI demand is expected to remain stable over the next decade, with increases in coverage being offset by new dose-sparing presentations. SIA demand is concentrated in UN-procuring countries and has higher variability.
- **Supply is currently sufficient** to meet demand across all vaccine types. However, supply concerns remain:
  - » Few large manufacturers provide the majority of supply across all combinations.
  - » For **MR**, the timing of SIAs, particularly for large countries, requires early signalling and appropriate cross-country synchronization to avoid supply-demand imbalances.
  - » For **MMR/MMRV**, switches to these combinations will require early signals to manufacturers, given the limited supply flexibility.
- All MCV products show high price variance with opportunities for improved price tiering. For MMR and MMRV, since price is quoted as a barrier to introduction, advantages of higher dose presentations could be further investigated.
- Projected supply can support the MR strategy in the context of **IA2030**, even in the more aggressive scenarios. If more aggressive approaches are taken, accurate planning and dialogue with manufacturers will be critical.

QUICK STATS

NUMBER OF VACCINE TYPES

4

2020 ESTIMATED GLOBAL DEMAND

M: 80M doses

MR: 260M doses

MMR/MMRV: 115M doses

2020 NUMBER OF MANUFACTURERS

15

2020 DEMAND/SUPPLY RATIO*

- M
- MR
- MMR / MMRV

2018 REPORTED PER DOSE PRICE

M: US $0.24 – $6.60

MR: US $0.55 – $10.30

MMR/MMRV: US $1.08 – $123.40

*The colours indicate the health of the demand/supply ratio. See page 4 for a detailed legend.

Disclaimer: This market study was completed before the impact of the COVID-19 pandemic was fully ascertained. Demand projections are based on the assumption that any delay or disruption will be absorbed and resolved in the second part of the year or, at the latest, in 2021. Uncertainty on the progression of the pandemic raises the risk that disruptions will extend beyond 2021. This will require an updated analysis of overall MCV supply-demand balance.

Context and Rationale

Measles-containing vaccines (MCVs) are available in four different types: standalone measles (M), combination measles-rubella (MR), measles-mumps-rubella (MMR) and measles-mumps-rubella-varicella (MMRV).[1] WHO recommends two doses of MCV in all children and SIAs to achieve population immunity in countries where routine coverage of the first and second dose of MCV (MCV1 and MCV2) is less than 90-95% or when immunity gaps are detected in older age groups.[2]

At the time of this analysis, all countries have introduced at least one dose of MCV and only 15 do not have MCV2 in routine schedules.[3] Despite broad introduction, global coverage for MCV1 is 87% and for MCV2 is 72%.[4] Figure 1 shows the MCV schedules used by countries as of 2020.[5]

1 There is one additional combination MCV – measles-mumps (MM) – whose use is limited to two countries with domestic production. Supply and demand for the MM vaccine is not covered in this analysis.
2 WHO Measles Position Paper, April 2017
3 Planned MCV2 introductions in 2020 are considered to be introduced. The remaining countries to introduce MCV2 are Benin, Central African Republic, Chad, Comoros, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea (non-Gavi), Gabon (non-Gavi), Guinea, Guinea-Bissau, Mauritania, Somalia, South Sudan, Uganda, Vanuatu (non-Gavi)
4 WUENIC 2018
5 The *2, MMR* group in figure 1 also contains five countries that use other 2-dose schedules that cover measles, mumps, and rubella, such as one dose of MMR and one dose of MR. The *2, MR* group also contains one country that uses M for one dose and MR for the second dose.

Currently, 173 countries have introduced at least one dose of RCVs. The remaining mostly Gavi countries and three non-Gavi countries still use only M for RI (figure 1).[6] All countries that have not yet introduced rubella vaccine and provide two doses of M in RI should consider including rubella-containing vaccines (RCVs) in their immunization programme, starting with a catch-up campaign targeting a wide age range (e.g. 9 months to 15 years).[7] All countries have immunization plans or are expected to introduce MCV2 and/or RCV by 2030, except for two.[8]

In recent years, national stock-outs in high-income countries (HICs) and upper-middle-income countries (UMICs) have raised some questions on the health of the global MCV market. In addition, the refinement of the MR Strategic Framework (MRSF) 2021-2030 in the context of the Immunization Agenda 2030[9] required a better understanding of supply flexibility and availability for different vaccination strategies and for all countries irrespective of their procurement channel and income level. MCV market efforts have historically focused on specific market segments, particularly UN-procuring countries and the 47 priority countries for the Measles & Rubella Initiative (M&RI),[10] or on specific vaccine types: M standalone and MR. Supply and demand dynamics in more than 70 self-procuring countries and for MMR/MMRV were not well understood.

A global understanding across all combinations is critical, given that measles bulk is shared across all products, supply is concentrated and demand is highly variable due to SIAs; unexpected demand increases to perform SIAs in a few large countries can trigger global imbalances, affecting other countries and other products.[11]

Demand

Global demand[12] for MCV is estimated to be 450 million doses in 2020 (figure 2), with coverage for MCV1 and MCV2 expected to reach 89% and 85% by 2030, respectively, under base case assumptions.

Demand for RI is expected to remain steady over the forecasted period, with the anticipated growth from increased coverage for MCV2 offset by wider adoption of lower-wastage 5-dose presentations in lieu of current higher dose presentations (10-dose vials).[13]

Non-priority M&RI countries comprise almost half of global demand in 2020 (44% or 200 million doses),[14] primarily for MMR/MMRV. Demand in these countries is expected to remain relatively stable across the analysis period – with lower and less variable SIA demand than in the M&RI priority countries – but still could have fluctuations of up to ~50 million doses from year to year. Some switches from MR to MMR/MMRV are expected to occur by 2030 and would add approximately 15 million doses of routine MMR demand. Just over half of non-priority M&RI countries are self-procuring, but they contribute 75% of the demand volume.

FIGURE 1: MCV ROUTINE USE (AS OF 2020)

Most countries (114) use MMR/MMRV for RI, but this only corresponds to 25% of total demand in 2020.

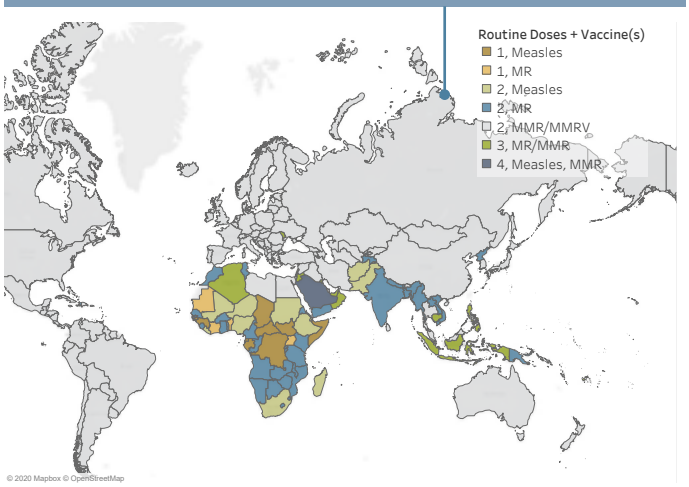


FIGURE 2: GLOBAL MCV BASE DEMAND BY VACCINE AND RI/SIA

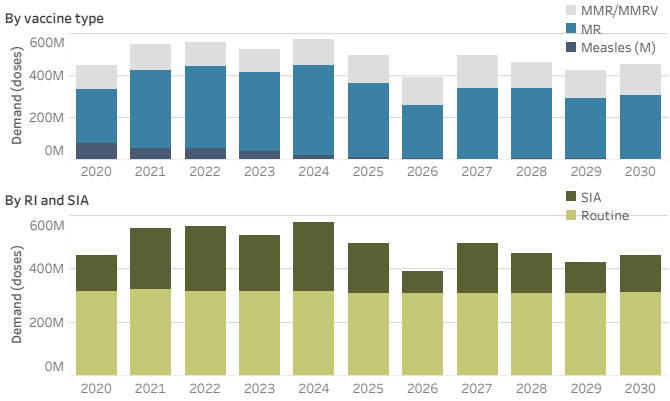
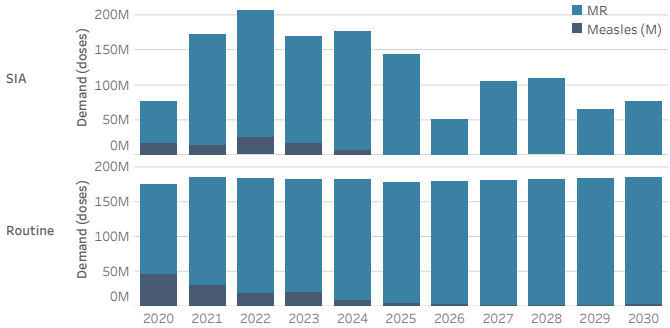


FIGURE 3: M&RI PRIORITY COUNTRIES: MCV BASE DEMAND BY VACCINE



6 Equatorial Guinea, Gabon and South Africa
7 WHO Rubella Position Paper, July 2020
8 Only CAR and South Sudan are not expected to introduce MCV2 prior to 2030, based on intel provided by partners.
9 https://www.who.int/immunization/immunization_agenda_2030/en/ – accessed on June 23, 2020
10 Global Measles & Rubella Strategic Plan 2012-2020
11 Different strains of measles vaccine exist. Based on currently available information, those differences do not influence manufacturers' ASC or country product preferences.
12 Demand is defined as estimated programmatic doses required: for future years, the average estimated number of doses a country would need to procure to meet its immunization program needs, whether these are routine – national or subnational – campaigns/SIAs, or for special risk groups only. This requirement includes wastage (depending on the presentation) and buffer.
13 Wastage rate is assumed to reduce from 40% for the 10-dose presentation to 15% for the 5-dose presentation for routine use.
14 China accounts for 16% (or 32 million doses) of this demand.

Demand from non-priority self-procuring countries totals 145 million doses in 2020. SIAs make up 15-35% of demand each year. Routine demand decreases slightly from 2020 to 2030 to hit 100 million doses.

MCV demand in priority M&RI countries is approximately 250 million doses in 2020 and is highly variable from year to year, depending on the timing and size of SIAs (figure 3). SIA demand is expected to decline after 2025, once the remaining countries introduce RCV and conduct large catch-up campaigns with MR as part of that introduction: from 47% of total demand between 2020-2025 to 31% of demand from 2026-2030. All priority M&RI countries are UN-procuring except for three (India, Indonesia and Viet Nam).

Finally, measles standalone (M) demand is expected to significantly reduce as countries introduce RCV.

To inform the development of the 2021-2030 MRSF and assess the supply feasibility of an aggressive measles and rubella control strategy, a high-demand scenario was developed with ambitious coverage growth reaching nearly 95% and larger, more frequent SIAs (figure 4). Additionally, a low-demand scenario was developed to compare the relative impact of various drivers of demand.[15]

The timing and scope of SIAs were found to be the most significant cause of variation for MR demand and, consequently, for overall MCV demand (figure 4). More frequent and larger SIAs can add up to 984 million doses of demand between 2020-2030. Increases in routine programme coverage could also contribute to shifts in global demand, but changes are modest compared to demand variance caused by SIAs.

Supply

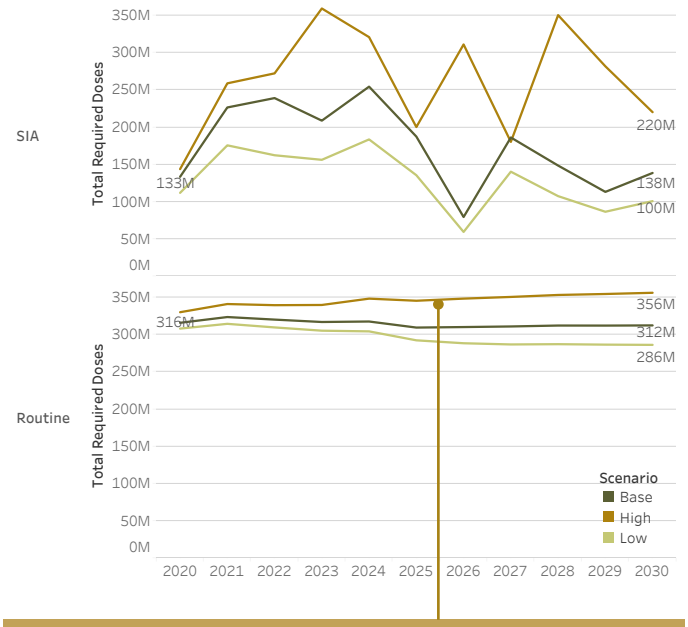
The MCV supply is concentrated, with two M and MR products and three MMR and MMRV products representing 80% or more of the global available supply for commercialization (ASC).[16] The MCV manufacturing base is a complex and heterogeneous ecosystem comprising 15 manufacturers and affiliates,[17] with commercialized vaccines across the four vaccine types, as represented in the table below:

TABLE 1: NUMBER OF PRODUCTS PER VACCINE TYPE

	M	MR	MMR	MMRV
Marketed	6	7	7	3
WHO-prequalified	2	3	3	0

Ten of the 15 manufacturers have multiple vaccines; five have WHO-prequalified vaccines and supply internationally to a large number of countries (Bio Farma from Indonesia, Biological E and SII from India, GSK from Belgium and Merck from the United States of America).

FIGURE 4: MCV DEMAND BY RI/SIA AND SCENARIO



Higher wastage resulting from reduced adoption of the 5-dose presentation and higher coverage account for up to a 346 million dose difference between the base and high RI demand scenarios from 2020-2030 (~30 million doses per year of additional demand).

MCVs are available in single- and multi-dose vials (from 1 to 20 doses); pre-filled syringes are also available but are not WHO-prequalified. All of these vaccines share common sources of measles bulk; consequently, significant changes in supply of one combination can be expected to have an impact on the supply availability of the others.

Three more vaccines are in development from manufacturers that are already supplying other combinations. In addition, between 2020 and 2025, at least two additional manufacturers are expected to license MCVs, and at least one is anticipated to seek prequalification and concentrate on providing vaccine internationally to lower- and middle-income countries, including their local markets.

In the short- to mid-term, the global ASC for all MCVs combined is expected to remain stable above 800 million doses with a substitution of M with MR in response to the evolving demand. MMR/MMRV's global ASC is expected to show a very modest increase.

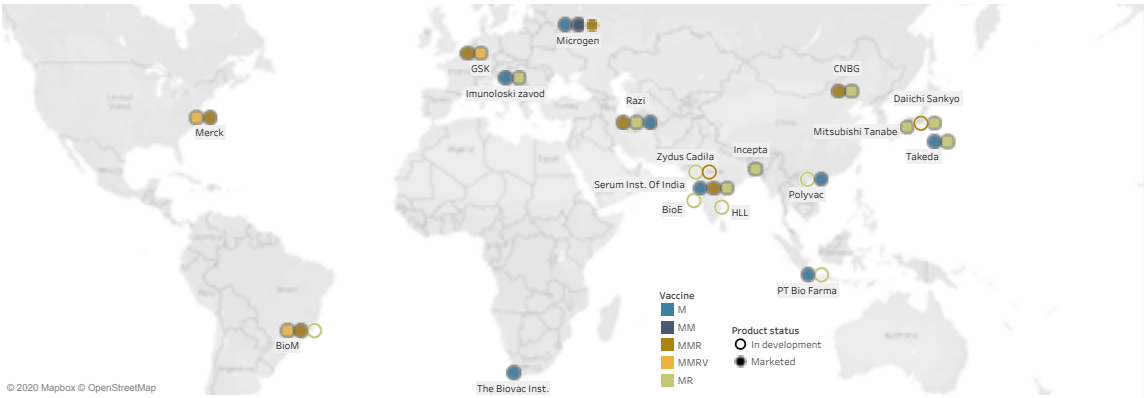
In the second part of the decade, the combined ASC for all MCVs is expected to slightly reduce, adjusting to the M and MR demand dynamics. The magnitude of these adjustments, limited to M and MR, will depend on the timing of completion of the large SIAs (all

15 The base scenario assumes continuation of historical coverage growth rates, half of countries using MR will adopt the 5-dose vial for RI, all countries introduce RCV by 2030, and all countries introduce MCV2 by 2030 (except for two countries that are unlikely to introduce by this time). SIAs are assumed to occur with the same frequency (3-5 years), scope, and target age groups as historically performed by each country. India is assumed to only perform one more national SIA between 2022 and 2024. The high-demand scenario assumes higher coverage, more rapid coverage growth, lower adoption of 5-dose vial MR, accelerated introduction of MCV2 and RCV, more frequent national SIAs, wider target age ranges for SIAs, and national SIAs in India every three years. The low-demand scenario assumes no coverage growth, higher adoption of 5-dose vial MR, and subnational SIAs.

16 In this analysis supply is defined as ASC: the number of doses available for sale globally in one typical year, with normal production facility utilization across the various vaccines and not factoring in special market, regulatory or technical events.

17 Affiliations can take the form of a technology transfer that is progressive, starting with fill/finish and leading to also include bulk manufacturing or a simpler distribution agreement, but always represent a dependent relationship with another manufacturer and not one that will increase the total ASC.

FIGURE 5: MCV MANUFACTURERS (MARKETED & IN DEVELOPMENT)



performed with MR). The ASC of M will progressively reduce, and, if all countries switch their RI demand to MR, will completely disappear, with the measles bulk dedicated to the other combinations.

Successful completion of the current clinical development programmes from new and existing manufacturers could lead to up to 20% additional ASC, mostly for MR, most likely replacing other existing suppliers.

Demand and Supply Balance

In recent years, country shortages of MCVs have been reported, particularly in HICs and UMICs. Those shortages have been investigated and are not due to global supply-demand imbalances but rather to localized procurement issues. The overall demand-supply balance is positive, albeit with some areas of risk as indicated below.

For M, the current ASC is more than sufficient to support a declining demand. Continued production of measles bulk – used across all combinations – guarantees long-term supply security if the need for M supply is clearly communicated.

MR's global ASC is also sufficient to support demand; however, the timing and size of SIAs – in particular for the very high populous countries – may cause time-limited, geographically specific imbalances in the coming years when most of the SIAs are planned.

Careful global monitoring of SIA planning should help identify risks that may result from the synchronization of delayed and planned SIAs and allow for their mitigation by fine-tuning demand and supply. In the long run, ASC is expected to be more than sufficient, given the reduced number of SIAs.

For MR, one area requiring special attention is the concentration of ASC. While the situation has recently improved with the addition of a second large supplier, two manufacturers (SII and BioE), both released by the same national regulatory authority, still represent the major source of global supply (the other five products are only registered in a limited number of markets). Additional international suppliers of this key combination will be critical to further improve the security of MR supply.

Finally, the ASC of MMR/MMRV is sufficient to support current and future expected moderate increases in demand. However, if an unexpectedly large number of countries were to switch to these combinations, advance warning would be required to ensure that ASC can be scaled-up.

Sizeable increases in demand, as depicted in the high-demand scenario, may lead to an increase in the risk of shortages for the MR combination. These demand changes will occur only in the mid to long term, allowing sufficient lead time for suppliers to adapt registration strategies and adjust critical production and capacity allocation plans.

FIGURE 6: MCV SUPPLY/DEMAND BALANCE[18]

Comparison of total high- and base-demand scenarios with base supply scenario

Base supply versus base demand

	Current	Short-Term	Mid-Term	Long-Term
Measles standalone (M)	🟢	🟢	🟢	🟢
MR	🟢	🟡	🟢	🟢
MMR / MMRV	🟢	🟢	🟢	🟢

Base supply versus high demand

	Current	Short-Term	Mid-Term	Long-Term
Measles standalone (M)	🟢	🟢	🟢	🟢
MR	🟢	🟡	🟢	🔴
MMR / MMRV	🟢	🟢	🟡	🟢

Thresholds	< 1.1	> 1.1 and < 1.3	> 1.3

18 Colors are defined based on thresholds comparing the ratio of ASC to demand, where red represents insufficient ASC compared to demand; yellow represents low supply risk; and green represents sufficient ASC compared to demand.

Pricing

M and MR are the lowest priced MCVs. In 2018, self-procuring MICs reported median prices of $0.75 for M and $1.10 for MR (prices are per dose for the 10-dose vial size). However, prices for both of these vaccines vary widely. The range in 2018 prices reported by self-procuring MICs was $0.20-$6.60 for 10-dose M and $0.50-$10.30 for 10-dose MR. The cost of the 9 month-15 year catch-up campaign with MR is known to be a barrier to introducing MR for at least one self-procuring MIC.

MMR represents a large leap in price compared to MR, particularly for MICs, and has been reported as a barrier to introduction. Compared to $1.10 for 10-dose MR, the reported median price for the single-dose vial of MMR by self-procuring MICs was nearly six times higher, and the HIC price for the same product is only slightly higher (figure 8). The price for a higher-dose presentation of MMR is much lower for self-procuring MICs ($1.60 for the 10-dose vial), but this presentation has more limited availability (only available from one of the three suppliers) and was only procured by five countries in 2018.

MMRV is more expensive than MMR and was only procured by a few HICs in 2018. The median reported price for HICs was $11.10. The CDC reported price is $123.

FIGURE 7: 2018 MEDIAN SELF-PROCURED AND AVERAGE CDC, PAHO AND UNICEF MCV PRICES PER DOSE

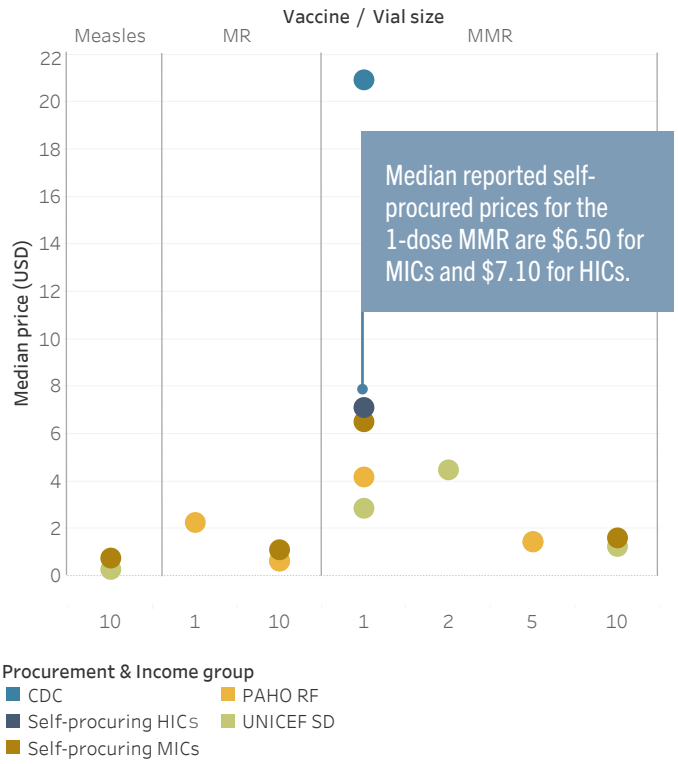
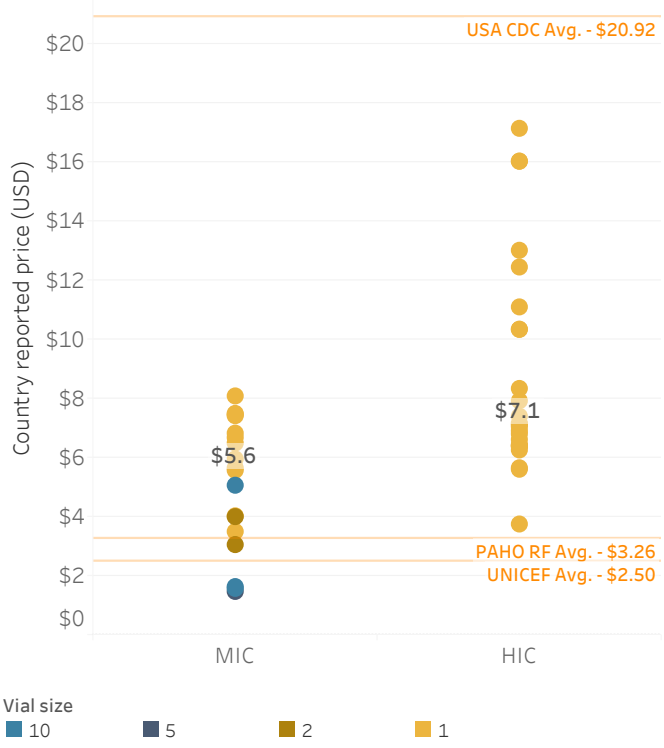


FIGURE 8: 2018 COUNTRY-REPORTED SELF-PROCURED MMR PRICES PER DOSE



Areas for Action

To enhance sustainable access to supply of MCV in coordination with immunization partners, WHO will:

- In the context of the COVID-19 pandemic, monitor the evolution of MCV demand and supply – and in particular the timing of post-pandemic catch-ups and SIAs – to ensure transparent understanding of the evolving global supply requirements and proactive identification of risk areas.
- Inform SAGE discussions on refinement of the M&RI strategy as part of the IA2030.
- Continue supporting country SIA planning and monitor decisions with regards to product preferences (e.g. MR 5- versus 10-dose presentations) and switches to MMR/MMRV to ensure timely signalling of emerging needs to suppliers.
- Enhance quality of global forecasting and ensure global coordination across market segments, leveraging existing fora, with a particular focus on the systemic impact of upcoming large MR SIAs on the global MCV supply-demand balance.
- Monitor progress of clinical development of new MR vaccines and engage with existing suppliers to explore opportunities for broader registration to enlarge the MR supplier base.
- Clarify with countries and M&RI the need for long-term supply for standalone measles (M) to ensure availability if the supply of this presentation is required.

Other Resources

WHO FAQ: Immunization in the context of COVID-19
https://apps.who.int/iris/handle/10665/331818

WHO April 2017 position paper on measles vaccines
https://apps.who.int/iris/bitstream/handle/10665/255149/WER9217.pdf?sequence=1

WHO July 2020 position paper on rubella vaccines
https://www.who.int/wer/2011/wer8629.pdf?ua=1

UNICEF August 2019 MCV supply and demand update
https://www.unicef.org/supply/reports/measles-containing-vaccines-mcvs-supply-and-demand-update

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