

THE EXTERNALITIES OF GAVI MARKET SHAPING: FINDINGS FROM FIRST MONITORING

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This document summarises the findings of Gavi’s first “market shaping externalities” monitoring exercise. The exercise has been undertaken to assess whether Gavi’s market shaping activities have resulted in any unintended consequences, or “externalities”, particularly for countries, manufacturers or other key partners. We tested for evidence of the following pre-identified potential externalities: reduced investment in vaccine R&D with a low-income countries (LICs) focus; compromised supply security for Gavi and non-Gavi-funded vaccines in Gavi and non-Gavi geographies; dwindling product & manufacturer diversity; price increases in ex-Gavi and non-Gavi geographies to compensate for lower Gavi prices, including price volatility. The project was conducted by an external agency and the methodology was set to be rigorous, data-driven and inclusive of partner, country and manufacturer consultations. Conclusions are based on quantitative evidence strengthened by qualitative input gathered from consultations reflecting different views.

There was no clear evidence of definite negative externalities deriving from Gavi’s market shaping work. Although two important potential negative impacts were identified, in each case the evidence was mixed.

First, although the number of suppliers to the pentavalent market grew from 2006-14, the market saw a manufacturer exit in 2018. This could be interpreted as attrition in a market in which competition became intense and where prices have fallen, and the current number of suppliers remains healthy. Nevertheless, many stakeholders interviewed noted that the price level achieved could result in further exits from the market, raising potential future risks to supply security.

Second, the human papillomavirus (HPV) market saw a supply shortfall in 2017. This was more closely associated with Gavi policy shifts (resulting in rapid demand increases) than with Gavi’s market shaping interventions.

Positive outcomes of Gavi’s market shaping activities (as opposed to positive externalities per se) were identified for pneumococcal and measles-rubella supply security and manufacturer diversity for oral cholera, yellow fever, rotavirus and pentavalent. The pentavalent market also appears to have seen benefits to middle-income countries (MICs) in terms of lower prices – potentially a positive spillover effect of Gavi’s market shaping work.

The next steps will be to: instigate regular monitoring of the 2018 findings; continue our alertness to potential manufacturer exits; and improve input data in particular with regards to MIC vaccine pricing (in conjunction with WHO/Market Information for Access (MI4A)), global supply & demand dynamics and “country preference” analysis with partners.

1. Introduction

Gavi has contributed to remarkable progress in the roll-out of new and underused vaccines and increasing immunisation coverage in lower income countries over the last 18 years, and this is partly attributable to its market shaping activities that have fostered improvements in vaccine market dynamics. While Gavi has been highly effective in achieving its core objectives, questions have arisen about the extent to which Gavi’s market shaping work may have had any unintended consequences for manufacturers, Gavi-supported and non-Gavi-supported countries and other Gavi partners, as on occasion, tools which Gavi utilises to reduce short-term risk might have negative long-term consequences. These unintended consequences, which may be positive or negative, are referred to as externalities. Risks and consequences must be weighed against the potential benefits and it is therefore important to fully understand which externalities exist and to measure their impact to assess their relative importance. As set out in Gavi’s Supply and Procurement Strategy 2016-2020, Gavi conducted a project to identify and monitor any potential positive or negative externalities that may be arising from its market shaping work.

2. Project approach

The project was conducted in two phases: the development of a framework to monitor externalities in 2017 and its first application carried out from June 2018 to March 2019. Both phases have been conducted independently by external agencies.

The framework¹ was developed in close collaboration with market stakeholders, including 28 interviews with manufacturers, Gavi partners, countries, academia and independent experts, as well as a stakeholder workshop. It identified eight potential externalities that should be closely monitored relating to three overarching categories: i) investments in research and development; ii) supply security for countries and sustainability for manufacturers; and iii) affordability for countries. Additionally, a process was developed through which these externalities could be monitored, including the identification of relevant quantitative indicators, counterfactuals and available data sources.

The first monitoring exercise then followed the approach set out in the monitoring framework. The relevant data were gathered from secondary sources and the limitations and robustness of the data sources were assessed. The quantitative analysis then focused on the identification of key trends in the data, i.e. whether there were clear upward or downward movements in the analysed indicators. Where feasible, trends were compared to a counterfactual to understand how the indicator might have developed in the absence of Gavi's market shaping activities. This included analysing trends on non-Gavi funded vaccine markets. Where this was not possible, assumptions were made on what might have taken place in markets in the absence of Gavi support. Quantitative evidence was complemented and strengthened by consultations with 22 different stakeholders including the Gavi Secretariat, Alliance partners such as the Gates Foundation, UNICEF Supply Division, WHO including Pan-American Health Organisation (PAHO), manufacturers, country governments, academia and independent experts. These consultations were used to determine whether trends were linked to Gavi market shaping activities or were driven by non-Gavi factors such as broader market dynamics, specific events such as disease outbreaks or changes in immunisation policy. Impacts that Gavi intended to deliver through its market shaping work, or the consequences of work done by Gavi partners outside the scope of Gavi's market shaping work were not considered to be externalities and part of this exercise.

It should be noted that findings are based on the evidence available. In many cases, data does not fully capture the entire market or sample for the indicator being analysed. As such, findings should be interpreted as an indication of what the available evidence suggests, as opposed to a definitive conclusion of whether externalities exist.²

3. Key findings

To date, the evidence does not indicate any clear negative externalities from Gavi's market shaping work. However, two potential negative externalities were identified based on mix evidence:

- The pentavalent market has recently seen a manufacturer exiting the market. This was the result of supply capacity surpassing global demand (demand through Gavi and for non-Gavi-supported countries) with the consequence that the higher cost competitors could no longer be

¹ For more details on the framework: <https://www.gavi.org/library/gavi-documents/supply-procurement/gavi-market-shaping-externalities-framework---public-summary/>

² Key examples of data limitations include the limited historical and consistent data for investments in R&D related to improved product characteristics and cold chain equipment (CCE), and limited historical and consistent data to analyse price trends for self-procuring MICs. Some vaccines could also not be analysed for the different externalities due to data not being available (including Japanese encephalitis (JE) and yellow fever for R&D spending, JE, cholera and typhoid for national stock-outs and cholera, measles, meningitis A for price trends in non-Gavi-supported countries), but this did not prevent the overall analysis for other externalities being undertaken.

competitive. The remaining number of manufacturers remains sufficient, and so this exit should not be interpreted as a negative outcome of competition (discussed further in Section 4.2.1). However, it will be important to keep balancing the need for affordable and sustainable prices with healthy market dynamics, and potentially managing the risks of future market exits.

- There have recently been temporary supply shortages in the human papillomavirus (HPV) vaccine market for Gavi-supported countries. These, however, were associated more with Gavi policy shifts, combined with global supply shortages, than with Gavi’s market shaping interventions (discussed further in Section 4.2.2). The degree of disruption caused was mitigated by delaying the proposed rapid roll-out schedule, and any negative impacts need to be set against the positive impacts resulting from HPV vaccine introduction.

A clear and significant positive externality was found in the pentavalent market, where available evidence suggests Gavi’s market shaping activities contributed to stimulating competition, resulting in increased access at more affordable prices for non-Gavi-supported countries that receive no Gavi funding support. Additionally, although the monitoring exercise focused on unintended consequences, it also added to the evidence base regarding several positive *intended* outcomes of Gavi market shaping work.

An overview of the findings is presented in Table 1 below.

Table 1: Findings of the first monitoring exercise

Externality ³	Key findings
1A. Investment in vaccine R&D	No evidence of externality
2A. Manufacturer diversity for Gavi-funded vaccines	Potential negative externality for pentavalent (post 2016)
	Positive outcomes for cholera, rotavirus, yellow fever and pentavalent (pre 2014)
	No evidence of externality for others
2B. Supply security for Gavi-funded vaccines	Potential negative externality for HPV
	Positive outcomes for pneumococcal conjugate vaccine (PCV) and measles/ measles-rubella (MR)
	No evidence of externality for others
2C. Supply security for non-Gavi-funded vaccines	No evidence of externality
2D. Product diversity	Many positive outcomes and no evidence of negative externality
3A. Price trends and price volatility for non-Gavi supported countries	Positive externality for pentavalent
	No externality for other markets

4. Detailed findings

4.1. Externality category 1: Investment in Research & Development

The first externality for investment in R&D measures whether Gavi’s market shaping activities had unintended consequences on the investment in vaccine development for antigens where the disease burden is predominately in Gavi-supported countries and middle-income countries (MICs). Two indicators were used to monitor trends: i) the total R&D funding for vaccine products for selected

³ Externality 1B on investments in existing vaccines and Externality 1C on investment in cold chain equipment have not been included here, since the analysis was not undertaken at this stage due to limitations of the available data.

neglected tropical diseases⁴; and ii) the total number of vaccine development efforts in the pipeline^{5,6}. As counterfactuals, these indicators were respectively compared with data on R&D funding for non-vaccine products for neglected tropical diseases and with vaccine development efforts for antigens where the disease burden was not predominantly in Gavi-supported countries and MICs.

There was no evidence for a negative externality resulting from Gavi's market shaping activities. The historical trends for both indicators showed no clear deviation from the trends exhibited by the counterfactuals. Instead, evidence suggests trends were determined by non-Gavi factors such as changes in market dynamics, disease outbreaks and advances in technology. Total R&D funding for neglected tropical diseases remained largely stable over time with a one-off drop in philanthropic spending in 2010, but the share of private R&D funding increased for both vaccine and non-vaccine products. There also has been an upward trend in vaccine development efforts in the pipeline regardless of whether the antigens had a disease burden in Gavi-supported countries or not.

Two additional measures were in the monitoring framework to assess externalities in R&D – i) R&D investment in improving existing vaccines in Gavi portfolio; and ii) investment in the development of new cold chain equipment. However, analysis for these externalities was not undertaken, as historic, quantifiable data was not available. The approach for these externalities and the availability of additional data will be re-assessed as part of the next monitoring exercise.

4.2. Externality category 2: Supply security for countries and sustainability for manufacturers

4.2.1. Manufacturer diversity for Gavi-funded vaccines

The first externality analysed under this category measures manufacturer diversity for Gavi-funded vaccines, including both the total number of manufacturers and their geography. This has been measured by using UNICEF supplier data. We considered measuring all WHO pre-qualified manufacturers as an alternative source but focused on the UNICEF data as the best measure of manufacturers actively supplying Gavi-supported countries specifically.

Analysis showed no clear evidence of a definite negative externality, although mixed evidence suggested the *potential* for a negative externality may exist in the pentavalent market. This is shown in Figure 1 below. Qualitative evidence gathered from consultations linked Gavi's market shaping activities to increasing numbers of pentavalent manufacturers from 2005-14 (see arrows 1 & 2 in the diagram in Figure 1) - a positive intended outcome. However, this resulted in oversupply and supply capacity surpassing global demand (both through Gavi and for non-Gavi-supported countries). The high levels of capacity and the intensification of competition following the attraction into the market of several low-cost high-volume manufacturers contributed to significant price reductions from 2008-17 (see arrow 3). This resulted in the market exit of a high-income country (HIC) manufacturer in 2018 that could no longer participate (see arrow 4).⁷

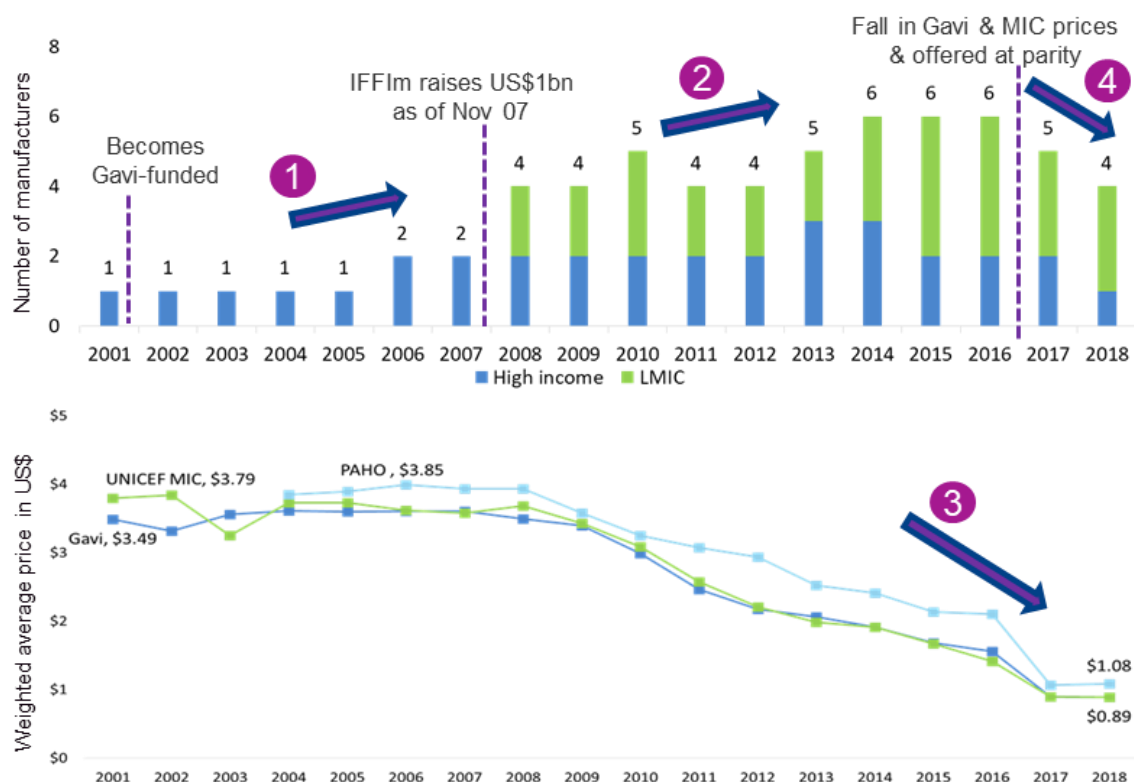
⁴ Included disease areas are diarrhoeal diseases, helminth infections, kinetoplastids, and malaria.

⁵ Vaccine development efforts for 34 diseases were included that were classified by Gavi as having a disease burden predominately in Gavi-supported countries. A number of Gavi-funded vaccines have not been included, given that R&D investment in these vaccines is often driven by trends in high-income markets, and therefore are unlikely to be directly influenced by Gavi market shaping.

⁶ Using G-Finder data and Citeline data respectively.

⁷ The graph depicts the reduction in number of UNICEF suppliers. Qualitative evidence suggested that of the two manufacturers that did not win an UNICEF award in 2018, one decided to exit the pentavalent market completely.

Figure 1: Diversity of manufacturers supplying to UNICEF and price changes for pentavalent



Source: UNICEF Supply Division data; Global Vaccine Market Model data.

Qualitative evidence suggests that the current manufacturer numbers are sufficient, and several consultees indicated that the recent reduction in manufacturers represents a healthy, maturing market. However, most consultees pointed to the risk that the low prices may lead to further market exits that could impact global supply security. This risk is being closely and proactively monitored by the Gavi Secretariat and UNICEF Supply Division through close engagement with all pentavalent manufacturers.

For other vaccines, no evidence of negative externalities resulting from Gavi’s market shaping activities was found. Qualitative evidence suggests that where manufacturer numbers have been limited or have fallen, this has generally not been linked to Gavi’s market shaping activities but rather has been caused by non-Gavi factors including:

- High barriers to market entry (particularly for more complex vaccines such as PCV and HPV);
- A declining market (measles), particularly for HIC manufacturers, given the availability of alternative vaccines (such as measles, mumps and rubella (MMR)); and
- Limited scope for competition where Gavi markets are geographically limited (meningitis A).

Qualitative evidence also suggested that there have been a range of positive intended outcomes where Gavi’s market shaping activities led to an increase in the number of manufacturers or contributed to sustaining a healthy number of suppliers that would not have occurred in the absence of Gavi’s market shaping work. This includes manufacturer numbers for cholera, rotavirus, yellow fever and the pentavalent market prior to 2014.

Additionally, several consultees said Gavi’s market shaping activities have been critical to increasing development efforts in the pipeline – for example, in PCV and rotavirus – and it is expected that more positive outcomes will be observed in these markets in the coming years.

4.2.2. Global capacity to produce and availability of Gavi-funded vaccines

The second supply security and sustainability externality measures supply security for Gavi-funded vaccines. Specific indicators analysed include national stock-out data collected by WHO and self-reported by countries, as well as Gavi monitoring data on vaccine markets with sufficient and uninterrupted supply. Qualitative evidence suggested that for vaccines where data showed high stock-out levels at the national level or shortages at the global level (inactivated polio vaccine (IPV) and yellow fever), this was driven by non-Gavi factors.⁸ For example, for yellow fever these have often been driven by demand variation due to outbreaks, while for IPV issues arose as a result of a rapid scale-up in routine introduction initiated at the global level. There was no evidence of a negative externality caused by Gavi's market shaping activities.

However, one exception is the recent vaccine shortages in HPV, which was brought up by several interviewees and is thus being discussed. The lack of supply in the HPV market is perceived variously as a negative outcome or a negative externality depending on perspectives, and there are different viewpoints as to how the HPV supply story played out and what could have been done differently. However, strictly speaking it was not seen as an externality of Gavi's market shaping activities, but rather as a negative outcome of a Gavi policy decision (expanding from pilot demonstration to national roll-out including multi-age cohorts) and thus rapid roll-out of HPV in Gavi-supported countries, combined with global supply shortages, not necessarily as an external consequence of market shaping interventions. It should be noted that once the shortages materialised, Gavi reacted by adapting HPV programme design, prioritising single age cohorts until supply becomes sufficient for all eligible cohorts and allowing 11 countries to introduce despite the shortages. In addition, evidence suggests that the shortages also affected MICs, with some countries that wanted to introduce the HPV vaccine not being able to access supply due to the shortages. These shortages should be considered in the wider context of the increased coverage realised through expanding the HPV programme, and the subsequent health benefits achieved. The experience has also provided valuable lessons for both the HPV programme and for expansion of other vaccine programmes.

Consultees also noted the emergence of supply issues for rotavirus in 2018, though these were not considered to have been a result of Gavi's market shaping activities and may even have been mitigated by Gavi's presence. However, this was not reflected in the quantitative data that went back to 2017 only as the exercise was done in 2018. As the process has generally tried to use the qualitative evidence to test and deepen the quantitative findings, and not as a substitute for the quantitative analysis, this will be further analysed in the next monitoring to see how these issues played out on a comparable basis to the earlier years.

Finally, there have also been some positive outcomes where Gavi's market shaping activities were seen as contributing to sufficient global capacity to produce the vaccines, including for measles/MR, PCV and rotavirus (pre-2018).

4.2.3. Global capacity to produce and availability of non-Gavi-funded vaccines

The third supply security and sustainability externality measures global capacity to produce and availability of non-Gavi-funded vaccines targeted at low- and middle-income countries. This is also based on WHO-collected data of national stock-outs, and also draws on future estimates of global supply and demand estimates made by WHO. No evidence was found for an externality caused by

⁸ The term 'stock-outs' refers to vaccine programme interruptions of at least one month that occur at the national level due to a lack of vaccine supplies. The terms 'vaccine shortages' and 'insufficient supply' are used more broadly, and also capture situations where planned vaccine activities (i.e. campaign or routine introduction) have been postponed or delayed as there were no assurances that there will be sufficient stock to carry out the activities in full.

Gavi's market shaping activities. Non-Gavi-funded products had very different trends, with bivalent OPV (bOPV) and Tetanus toxoid (TT) exhibiting low levels of supply stock-outs, while BCG has experienced several supply issues. For BCG (a non-Gavi-funded vaccine), there was no clear trend over time in the severity or frequency of stock-outs that could be linked to Gavi's market shaping activities. In recent years, qualitative evidence suggests that the stock-outs in BCG were predominately linked to funding delays, procurement delays and forecasting challenges at the national level.⁹ Prior to 2016, where manufacturing issues were reportedly a bigger driver behind stock-outs, stakeholders interviewed did not see any links between the supply issues and Gavi's market shaping activities.

4.2.4. Product diversity

The final supply security and sustainability externality measures the number of available presentations for existing products available for Gavi-funded vaccines. This draws on UNICEF Supply Division and Global Vaccine Market Model (GVMM) data. There was no evidence to suggest a negative externality. Where the number of presentations supplied to Gavi-supported countries remained relatively limited (for example in the case of HPV, JE, meningitis A and cholera), most of our interviewees suggested that this was attributable to non-Gavi factors such as low overall market demand, low manufacturer numbers and other barriers to entry such as technical complexity of vaccine development and production.

The analysis did point to positive outcomes of Gavi's market shaping work in the form of increases in the number of available presentations for a range of vaccines, or changes in the composition to more favoured presentations. For example, pentavalent liquid presentations have replaced lyophilised forms and multi-dose presentations became available, with both presentations being programmatically favourable product options. Additional, more favoured presentations have also been introduced for pneumococcal, IPV, cholera and rotavirus.

Stakeholders indicated that changes in product diversity should be measured by assessing whether countries have sufficient access to their preferred presentations rather than measuring the total number of different presentations that are available in the market. This feedback will be considered and taken forward into the next monitoring round by leveraging ongoing analyses on country presentation preferences, which are being conducted by Gavi partners.

4.3. Externality category 3: Affordability for non-Gavi supported-countries

The final externality measures price trends and volatility of Gavi-funded vaccines in non-Gavi-supported countries, primarily MICs, based on UNICEF and PAHO data for non-Gavi-supported countries, and UNICEF data for Gavi-supported countries for comparison. Data was sourced from the UNICEF Supply Division, GVMM and WHO Market Information for Access (MI4A) vaccine purchase data. The available evidence suggests lower prices in Gavi markets have not been met with associated increases in non-Gavi markets. In fact, in the pentavalent market, evidence suggests Gavi and non-Gavi markets have experienced a mutually-beneficial effect, with the higher level of capacity and price competition leading to lower prices of pentavalent in both settings.

Figure 1 above illustrates how pentavalent prices in MICs procuring through UNICEF and PAHO declined in line with Gavi prices for several years, including a sharp drop during the 2017 tendering process. Qualitative evidence linked the decline in pentavalent prices to Gavi's market shaping activities, which encouraged new manufacturers to enter the market and increased price competition, benefiting Gavi-supported countries, MICs procuring through UNICEF and PAHO countries. While data for self-procuring countries was considerably less widely available and robust than for countries

⁹ *Global Vaccine Action Plan (GVAP) – Secretariat Annual Report 2017, p. 167*

procuring through UNICEF or PAHO, stakeholders interviewed noted that some key markets (particularly India) were able to access lower prices, in part due to the interrelationship between Gavi and national markets.

For other vaccines, there was no clear evidence of externalities arising from Gavi's market shaping activities. Prices for rotavirus, HPV and pneumococcal have been stable in both Gavi and non-Gavi markets in recent years, albeit at higher levels in non-Gavi markets. For example, for HPV the weighted average price (WAP) for Gavi was around US\$4.50 in 2018, for PAHO it was US\$9.04 and for MICs procuring through UNICEF WAPs were US\$13.40 (although composition of prices may differ between income groups). Qualitative evidence suggests these stabilisations are due to limited competition and manufacturer price tiering, with self-procuring countries looking at PAHO in particular as well as UNICEF procurement for MICs for a reference of what prices they should be receiving. Consequently, significant price reductions have not occurred as manufacturers are not able to supply all countries at prices offered to Gavi-supported countries. For prices to reduce, stakeholders interviewed noted competition from new manufacturers is needed in future.

Other vaccine markets, including yellow fever and MR, saw price increases for both Gavi and non-Gavi-supported countries. Interviewees generally considered that price increases in non-Gavi-supported countries were not specifically linked to Gavi's market shaping activities. For example, PAHO prices for yellow fever were driven by pricing decisions of the manufacturer for the Americas region, and the trend did not differ significantly from that observed for countries procuring through UNICEF. These are low margin markets where the similarity of price trends across different markets indicates that more general factors, such as inflation, were at play. For IPV, price trends fluctuated over time, with market dynamics changing significantly after 2012 where expansion in use and significant investments in production scale up and production issue resolution, not specifically linked to Gavi, were key drivers of pricing.

5. Next monitoring phase

Gavi Secretariat and Alliance Partners remain committed to monitoring for potential negative or positive externalities that could arise from its market shaping activities going forward. Next steps will be to instigate regular monitoring of the 2018 findings, continuing our alertness to potential manufacturer exits, and improving input data with regards to MICs vaccine pricing (in conjunction with WHO/MI4A), global supply & demand dynamics and "country preference" analysis with partners.