Analysis and Critique of the Advance Market Commitment (AMC) for Pneumococcal Conjugate Vaccines (PCVs) and Impact on Access

EXECUTIVE SUMMARY

This briefing document provides a critical analysis of Gavi, the Vaccine Alliance's Advance Market Commitment (AMC) pilot for Pneumococcal Conjugate Vaccines (PCVs) and its impact on access to pneumonia vaccines for populations in need. A close and critical review of issues with the AMC model is needed because of the replication of its use for global access to other important vaccines, such as the new COVAX Facility for COVID-19 vaccines, which draws heavily from the AMC mechanism.[1,2]

Touted as an innovative financial mechanism to incentivize pharmaceutical corporations to address developing-country health needs, the AMC pilot for PCVs (heretofore referred to as "the AMC") achieved some success but also had shortcomings. Drawing from two evaluations commissioned by the Gavi AMC Secretariat,[3,4] as well as Gavi's Pneumococcal AMC Annual Reports,[5] this document aims to give a critical assessment of the AMC to highlight for stakeholders and Gavi the lessons learned from the practical application of the AMC model, and offers recommendations for reflection and debate in implementation of the AMC model going forward.

Launched in 2009 and scheduled to close in 2020, the overarching goal of the PCV AMC was to reduce morbidity and mortality from pneumococcal diseases, aiming to prevent an estimated 7 million childhood deaths by 2030.[6] The AMC aspired to achieve four objectives:

1. **Accelerate research and development (R&D)** of pneumococcal vaccines that meet developing-country needs, as specified in the Target Product Profile (TPP), which defined the minimal technical criteria that PCVs must meet to be eligible for AMC funding.
2. **Increase availability** of effective PCVs for developing countries by guaranteeing the initial purchase price, for a limited quantity of the new vaccines, representing value for money and incentivizing manufacturers to invest in scaling up production capacity to meet developing-country vaccine demand.
3. **Accelerate vaccine uptake** by ensuring predictable vaccine pricing for countries and manufacturers, such as through binding commitments by participating companies to supply vaccines at low, long-term sustainable prices after the AMC finances are depleted.
4. Test the effectiveness of the AMC mechanism as an **incentive for supplying** needed vaccines, and to learn lessons for possible future AMCs for other vaccines.

After more than a decade of implementation, the AMC demonstrated success in increasing supply capacity of vaccine manufacturers, and PCV availability in developing countries. However, the AMC failed in fulfilling all of its objectives. Two Gavi AMC Secretariat-commissioned evaluations, one on the AMC's Process and Design,[3] and a second on Outcomes and Impact,[4] highlighted major weaknesses in the AMC design limiting its success in implementation:

- **R&D not accelerated**: The AMC was flawed from the outset in its selection of pneumococcal disease, which already had a vaccine on the market, since 2000.[7] PCV was virtually inaccessible to developing countries due to its high price, not because of a lack of R&D. The selection of a disease

with an existing vaccine provided little, if any, incentive for accelerating R&D timelines of other manufacturers who had already begun development prior to the AMC inception.

- **Competition low among manufacturers**: In 2007, US$1.5 billion was pledged from six donors – Canada, Italy, Norway, Russia, UK, and the Bill & Melinda Gates Foundation – for the launch of the AMC.[6] While the funding was intended to help encourage competition to reduce the overall price of PCV, in reality the bulk of the money essentially served as a subsidy for Pfizer and GlaxoSmithKline (GSK), which until December 2019 were the only two manufacturers of PCV. Of the $1.5 billion, $1.238 billion (82%) was disbursed to Pfizer and GSK. In 2020, a third PCV manufacturer, and the first in a developing country, the Serum Institute of India, was finally awarded a portion of the funding at $75 million (5%).[8]
- **Lack of transparency and expertise for affordable pricing**: A lack of transparency on costs, capacity, and pricing decisions fed criticism that the AMC acted as a vehicle for private companies to make unnecessarily high profits at the expense of broader vaccine access. The AMC design team lacked critical information and sufficient expertise to appropriately negotiate the original price per dose. If more data from the manufacturers on the costs of production and capacity scale-up had been forthcoming, and if more experts with economic or vaccine-industry experience had been involved, the initial price ceiling of $3.50 per dose might have been lower but still sufficient to incentivize manufacturers to participate in the AMC. The final subsidy of $3.50 for the first 21% of supplied doses under each contract *on top of* the $3.50 tail price (total of $7.00 per dose) is still high; developing countries may not be able to afford this base price as they lose Gavi support. Additionally, over the past decade of AMC implementation, Pfizer and GSK have provided minimal price decreases (~15%).[9] PCV remains one of the most expensive among the 12 vaccines supported by Gavi.[10]
- **Supply capacity of existing manufacturers did not meet full PCV demand**: During AMC implementation, demand at times exceeded supply despite the large subsidies given to the manufacturers to scale up production capacity. Pfizer and GSK were conservative in expanding their production capacity to only fulfill the number of doses stipulated in supply agreements, but these agreements were based on initial forecasts that were lower than the actual demand. This resulted in supply shortages of up to 29 million doses from 2012 to 2014, delaying 23 country introductions, and leading to an estimated 26 million children born without access to PCV.
- **Lack of improvement in technological capacity for developing countries to produce and supply PCV to their own populations**: No incentive or plan for PCV technology transfer to developing-country manufacturers was included in the design of the AMC. The AMC has yet to prove that it can serve as a model for encouraging long-term, sustainable vaccine production.

Gavi management acknowledged the findings of the two Gavi AMC Secretariat-commissioned evaluations in published responses, though they steered clear of offering serious critique.[11,12]

In total, five sets of supply agreements[8] for the PCV AMC were signed between Gavi (and UNICEF, as Gavi's procurement agency) and manufacturers: four with Pfizer and GSK (2010, 2011, 2013, 2018) and one with the Serum Institute of India (2020).

Overall, the evaluations' findings lend support to the criticism that the AMC mechanism in effect increased profits of multinational pharmaceutical corporations at rates higher than necessary to incentivize their involvement to achieve vaccine access in developing countries, while doing nothing meaningful to stimulate competition from developing-country vaccine manufacturers. As recently stated by the Executive Director of the Serum Institute of India, "I attended almost each and every meeting of the AMC since the beginning and therefore I feel extremely depressed with the final outcome when even the small amount could not be available for the developing country vaccine manufacturers. Many years ago, someone asked

me what I thought would be the fate of the AMC. They asked if I thought Serum would end up getting any money out of it. I said that I was 99 per cent sure that most of the money would go to big pharma with maybe a few crumbs left for us."[13]

Looking forward, as Gavi's AMC model is replicated for other vaccines, such as future COVID-19 vaccines, this critical analysis of the PCV AMC experience provides an opportunity to learn and avoid having the same flaws in future AMCs, in order to improve and sustain vaccine access to benefit as many people as possible. The following **recommendations** are proposed:

- **Pricing and affordability**: Renegotiate agreements with Pfizer and GSK to bring down the price of their PCVs, which are now at least 36% more than the new lowest global price recently set with the entry of a developing-country manufacturer.
- **Fair profit margin**: Require cost information from vaccine producers to make informed decisions on fair pricing.
- **Country accessibility**: Create a strategy with clear measurable objectives for addressing countries that have transitioned out of Gavi funding eligibility, as well as never-eligible countries.
- **Competition**: Develop a strategy to remove intellectual property (IP) and technological barriers to enable a diverse group of manufacturers, especially within the Developing Countries Vaccine Manufacturers Network (DCVMN), to accelerate development and stimulate real competition.
- **Technology transfer**: Negotiate agreements with requirements for vaccine technology transfer to other potential producers.
- **Clear investment criteria:** Use WHO-based objective criteria to guide AMC financial investments that allocate funding to products anticipated to facilitate optimal access.

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