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Gavi Secretariat Management Response to the Outcomes and Impact Evaluation of the Pilot Advance Market Commitment for Pneumococcal Vaccines

The pilot Advance Market Commitment (AMC) for pneumococcal disease aimed to encourage the development and production of affordable vaccines tailored to the needs of developing countries. The pilot AMC was officially launched in 2007 to "reduce morbidity and mortality from pneumococcal disease by accelerating the development, availability and uptake of pneumococcal conjugate vaccines (PCVs)". The Governments of Italy, the United Kingdom, Canada, the Russian Federation, Norway and the Bill & Melinda Gates Foundation collectively pledged a total of US$ 1.5 billion to fund the pilot.

In 2015, and as per the AMC monitoring and evaluation framework and following a competitive tendering process, the Gavi Secretariat commissioned the Boston Consulting Group for an outcomes and impact evaluation, in order to assess the extent to which the pilot AMC has achieved its stated objectives and the overarching goal of reducing morbidity and mortality from pneumococcal disease. The evaluation also captures lessons learned in the pilot and recommendations for future impact evaluations of the AMC. This paper provides the Gavi Secretariat's response to the recommendations outlined in the evaluation.

Key summary findings

This evaluation has validated that the pilot pneumococcal AMC contributed towards accelerating vaccine supply availability and uptake in Gavi countries, as well as supporting reduction in morbidity and mortality from pneumococcal disease.

Objective 1: Accelerating the development of vaccines that meet developing country needs. The Gavi Secretariat acknowledges the limitations of the pull mechanism of the pilot AMC and some of its timing and design elements in accelerating research and development (R&D) timelines for PCVs and in being able to secure the market entry of additional manufacturers to date. This is due to the technical complexity of developing a conjugate vaccine with such a high number of serotypes, which has led to challenges with product composition, clinical development and production processes. Nonetheless, Gavi agrees that the two manufacturers have met the minimum requirements of the AMC Target Product Profile and have continued to develop PCV presentations more suited to Gavi countries, such as the four-dose vials that are estimated to be pre-qualified in the next 12-24 months. The rich PCV R&D pipeline also demonstrates that the AMC-associated demand was able to incentivise manufacturers to continue to pursue product development.

Objective 2: Bringing forward the availability of vaccines. The Gavi Secretariat agrees that the pilot AMC provided the appropriate incentives for manufacturers to make investment decisions to further expand capacity to meet Gavi market demand. Demand was unprecedented, and Gavi acknowledges that the manufacturers did not increase supply quickly enough and this led to delays in country introductions in the initial years of AMC

2 Chemin des Mines
1202 Geneva. Switzerland
Tel. + 41 22 909 65 00
Fax + 41 22 909 65 50
www.gavi.org
info@gavi.org

implementation. As highlighted in the report, these delays were rectified more quickly than if the AMC did not exist. The unprecedented demand for PCV is now being fully met and both manufacturers have demonstrated willingness to accommodate further demand, including the large birth cohort Gavi countries that are not yet accessing the vaccine through the AMC. We agree with the evaluation's finding that transparency with manufacturers in the assumptions and degree of confidence behind demand forecasting may support matching of supply and demand, and note that Gavi shares its latest long-term forecast regularly and convenes discussions with manufacturers to review these in detail.

Objective 3: Accelerating vaccine uptake. The Gavi Secretariat agrees that PCV uptake in Gavi countries over the first five years of programme implementation (December 2010 – December 2015) has been unprecedented in terms of the number of introductions and immunisation coverage and concurs that the AMC was a significant contributor in ensuring that this objective was achieved. Securing supply at sustainable pricing is critical to achieving this objective. The Secretariat notes that the tail price ceiling was set at a level to allow more than one manufacturer to participate in the AMC, based on available understanding of their cost structures at the time. While the Alliance has achieved reductions to the tail price in the most recent negotiation of AMC supply agreements with both suppliers, a priority objective within Gavi's supply and procurement roadmap remains to reduce the tail price short- to medium-term. Gavi will seek to optimise market outcomes in future AMC tenders drawing from some of the lessons learned from experiences to date.

Overarching goal: reducing morbidity and mortality from pneumococcal disease. The Gavi Secretariat is in agreement that the pneumococcal AMC has played an important role in the overall goal reducing morbidity and mortality from pneumococcal disease in Gavi countries, with 3 million under-five deaths estimated to be averted by 2030.

While the Gavi Secretariat understands that the successful achievement of the AMC goals and objectives also needs to be attributed to a number of other factors, such as Gavi financial support towards pneumococcal programmes, a strong WHO recommendation on pneumococcal vaccine introduction in settings with high infant mortality, or initiatives such as the PneumoADIP and the Accelerated Vaccine Introduction, it is clear that such achievements in supply availability, country demand, and PCV implementation and coverage, would not have been possible without the pilot AMC and the funding from the six donors.

Lessons for future AMCs

The evaluation also provides valuable insights into the design of future AMCs. We note in particular the finding that to accelerate R&D outcomes for vaccines in early stages of development, especially those that are technically complex, a portfolio of incentive mechanisms beyond a pull mechanism such as an AMC may be required. Indeed, individual Alliance partners (e.g., BMGF and PATH) are continually evaluating opportunities to engage with manufacturers to help bring additional pneumococcal conjugate vaccines to market and are currently working directly with some manufacturers.

In addition, we echo the study's findings on the importance of aligning across stakeholders on a clear prioritisation of objectives and on engaging closely with vaccine manufacturers. Both elements are critical to achieving successful outcomes for an AMC, and any market shaping intervention. Indeed, in the update of the Alliance's Supply and Procurement Strategy for the

2016-2020 period which is currently underway, we will be enhancing our focus on these activities.

Considerations for future evaluations

Gavi acknowledges the limitations of this evaluation to assess the AMC impact on mortality and morbidity. The evaluators however suggest 4 actions that could strengthen the capacity to measure AMC impact in the planned evaluation in 4 years:

Recommendation 1: Continue investment in empirical studies and population surveillance. Gavi will continue investing in vaccine effectiveness studies as well as the Full Country Evaluations project which includes evaluation components related to outcomes and impact of PCV. In addition, in December 2015 the Gavi Board approved the Data Strategic Focus Area (SFA) as part of the Partner's Engagement Framework for the new Gavi Strategy 2016-20. The Data SFA defines three areas of focus including where the first one, immunisation delivery, coverage and equity focuses on investments in population data and coverage estimates.

Recommendation 2: Build uncertainty ranges and sensitivity analyses to academic models. Gavi and the modelling teams for LiST (Lives Saved Tool) and TRIVAC (model which includes 3 vaccines) are already working on putting in place uncertainty ranges for their respective models, which is expected to be available in the coming months.

Recommendation 3: Validate academic models using sub-national data. We agree that one important remaining gap in the use of the academic impact models is the lack of validation of output with empirical data. It is expected that the first area of the Gavi Data SFA will include investments in immunisation delivery, coverage and equity at all levels from global to sub-national during the next years. The second area will focus on vaccine-preventable disease surveillance investing in strengthening country surveillance systems and developing regional networks of surveillance sites.

Recommendation 4: Delineate drivers of differences across mortality revisions. The Secretariat is committed to continuing to share findings and results from the pilot pneumococcal vaccine AMC to aid potential designers of future AMCs.