Fact sheet: pneumococcal disease, pneumococcal conjugate vaccines, and Pneumosil®

About pneumonia and other pneumococcal diseases

- Pneumonia is an infection of the lungs that kills more children before their fifth birthday worldwide than any other infectious disease each year, accounting for 15% of all-cause deaths among these children.[i]
- The pneumococcus bacterium (Streptococcus pneumoniae) is the primary cause of deadly childhood pneumonia. Other deadly and disabling complications include invasive pneumococcal diseases (IPD) like meningitis and sepsis (blood infection), as well as more common infections such as otitis media (middle ear infection) and sinusitis.
- The pneumococcus is a complex bacterium with more than 90 varieties (serotypes) that vary by region and kills nearly 300,000 children under five years old globally each year, mostly in Africa and Asia.[ii]
- Roughly 50% of the world's annual pneumococcal child deaths occur in 4 African and Asian countries: India (~68,700 deaths); Nigeria (~49,000); Democratic Republic of Congo (~14,500); and Pakistan (~14,400).[ii]
- The pneumococcus spreads through contact with people who are ill or carry the bacteria in their nose and throat.
- Transmission occurs from respiratory droplets from the nose or mouth of an infected person. People, especially children, can be carriers without being sick and spread the bacterium to others.
- Vaccines are the best way to prevent pneumococcal disease. Antibiotics (e.g., amoxicillin) are first-line treatments, while oxygen therapy can help treat pneumonia but is often a scarce resource for children in low-resource settings. Exclusive breastfeeding,[iii] good nutrition, hand washing,[iv] and abating indoor air pollution are other preventive measures.[v]

Pneumococcal conjugate vaccines (PCVs): a history

- The pneumococcal vaccines available for children are called PCVs, which cover some, but not all, serotypes.
- PCVs are used in many countries worldwide; have a long, safe, and effective track record against the serotypes they cover; and have led to dramatic reductions in pneumonia and other pneumococcal diseases where introduced.
- For infants, the World Health Organization (WHO)-recommended schedules for PCVs are 3 + 0 or 2 + 1.
- The first PCV, Prevenar®, was produced by Wyeth (now Pfizer, Inc.) and introduced in high-income countries starting in 2000. It included 7 serotypes.
- Second-generation PCVs by Pfizer (Prevenar13®) and GlaxoSmithKline (Synflorix®) expanded serotype coverage to 13 and 10 serotypes, respectively, which added coverage against serotypes relevant to low-income countries (LICs).
- PCVs are one of the most complicated and expensive vaccines to manufacture, which translates to inherently high prices (e.g., roughly US$180 per dose in the United States).[vi]
- Both second-generation PCVs are WHO-prequalified, meaning they can be procured by United Nations agencies and Gavi, the Vaccine Alliance for use in LICs.
- Donor financial support and innovative financing mechanisms such as the Advance Market Commitment have enabled PCV to be available for Gavi-eligible LICs at around $3 per dose, co-paid by countries and Gavi. PCV rollouts in LICs began in 2009.
- Paying for PCVs takes up a disproportionate amount of donor resource compared to other vaccines—including nearly half of Gavi's forecasted vaccine expenditures for 2016-2020.[vii]

About Pneumosil

- The newest WHO prequalified PCV is Serum Institute of India Pvt., Ltd.'s Pneumosil, which protects against the 10 most relevant serotypes most likely to cause serious disease in the world's highest-burden regions—Africa and Asia including many LATAM countries.
- Pneumosil's more efficient innovative manufacturing process lowers costs but preserves quality. It will be available to Gavi-eligible LICs and middle-income countries at around US$2 per dose—roughly 30% less than the current Gavi-supported PCV price.

- Serum Institute and PATH advanced Pneumosil a tailored PCV with relevant serotypes causing majority of pneumococcal diseases in developing countries from preclinical development to prequalification through a collaboration originating in 2008 and with funding contributed by the Bill & Melinda Gates Foundation.
- The Pneumosil project was a natural evolution from a previous conjugate vaccine collaboration that included Serum Institute and PATH among other partners to develop the meningitis A vaccine, MenAfriVac®, which has since helped eliminate meningitis A epidemics where introduced in Africa's meningitis belt countries.
- On the pathway to prequalification, PATH has been responsible for sponsoring Phase 1/2 and 3 clinical studies in The Gambia—a representative setting where the vaccine could be a valuable tool for protecting children.
- On a separate track, Serum Institute is sponsoring clinical studies in India for marketing authorization nationally.

About the pivotal Pneumosil Phase 3 clinical study in The Gambia

- The Phase 3 infant study provided the pivotal results for the data package required for Pneumosil to receive an Indian export license and subsequent WHO prequalification.
- The study examined Pneumosil's safety and tolerability, how it affects infants' immune responses compared to a licensed PCV, what happens when it is given at the same time as other routine vaccines, and lot-to-lot manufacturing consistency.
- Study partners included PATH; MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine; Serum Institute; contract research organization FHI360; and the WHO Reference Laboratory for Pneumococcal Serology at University College London and other laboratories. Funding came from the Gates Foundation.
- The study included 2,250 infants with parental informed consent, who received either Pneumosil or a WHO prequalified PCV comparator (Synflorix®) in a 3 + 0 schedule along with other routine childhood immunizations. A subset of infants received a booster dose at 9 months of age.
- Results showed Pneumosil to elicit immune responses on par with (i.e., non-inferior to) the WHO prequalified PCV. Per WHO PCV guidelines,[viii] non-inferiority to a licensed PCV is considered predictive of a PCV's ability to prevent IPD.
- Pneumosil elicited functional antibodies (immune responses that correlate with a PCV's ability to prevent disease), which were more often higher among Pneumosil recipients than comparator vaccine recipients.
- No Pneumosil-related safety concerns arose during the study—adding to the vaccine's good safety record from previous clinical studies in The Gambia and India.
- Relative to the licensed PCV comparator, Pneumosil was shown not to interfere with the performance of other routine childhood immunizations when given at the same time.
- Pneumosil met requirements for lot-to-lot manufacturing consistency, meaning that the three vaccine lots administered during the study elicited equivalent immune responses—an indication of consistent manufacturing performance.
- A summary of the Phase 3 results was presented at the 2019 European Symposium on Pediatric and Infectious Diseases and a study manuscript is pending peer-review publication.

I UNICEF, WHO, World Bank Group, United Nations. "Levels & Trends in Child Mortality: Report 2019." UNICEF. 2019. Accessed at: https://data.unicef.org/resources/levels-and-trends-in-child-mortality/.

ii Wahl B, et al. Burden of Streptococcus pneumoniae and Haemophilus influenzae type b disease in children in the era of conjugate vaccines: global, regional, and national estimates for 2000-15. Lancet Global Health. 2018;6(7):e744–57.

iii Roth DE, et al. Acute lower respiratory tract infections in childhood: opportunities for reducing the global burden through nutritional interventions. Bull World Health Organ. 2008;86:356-364.

iv O'Dempsey TJ, et al. Pneumococcal disease among children in a rural area of west Africa. Pediatr Infect Dis J. 1996;15: 431-37.

v Niessen LW, et al. Comparative impact assessment of child pneumonia interventions. Bull World Health Organ. 2009; 87(6):472-480.

vi US Centers for Disease Control and Prevention. "CDC Vaccine Price List." September 1, 2019. Accessed at: https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html

vii Gavi, the Vaccine Alliance. The 2016-2020 Investment Opportunity. Gavi. Accessed at: https://www.gavi.org/library/publications/replenishment/the-2016-2020-gavi-alliance-investment-opportunity/

viii WHO. Recommendations to assure the quality, safety and efficacy of pneumococcal conjugate vaccines, Annex 3, Technical Report Series 977, 2009. Replacement of WHO Technical Report Series, 927, Annex 2." 2009. Accessed at: https://www.who.int/biologicals/vaccines/TRS_977_Annex_3.pdf?ua=1.