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 like meningitis and sepsis (blood infection), as well as more common infections such as otitis media (middle ear infection).
- The pneumococcus is a complex bacterium with more than 90 varieties (serotypes) that vary by region and kills nearly 400,000 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).[iii]
- The pneumococcus spreads through contact with people who 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 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,[iv] good nutrition, hand washing,[v] and abating indoor air pollution are other preventive measures.[vi]

Pneumococcal conjugate vaccines (PCVs): a history

- The pneumococcal vaccines available for children are PCVs, which cover a limited number of serotypes.
- PCVs are used in many countries worldwide; have a long, safe, and effective track record; and have led to dramatic reductions in pneumonia and other pneumococcal diseases where introduced.
- For infants, the World Health Organization (WHO)-recommended PCV schedules are 3+0 or 2+1 depending on programmatic factors (e.g., vaccination timeliness and expected coverage). The 2+1 may have added benefits because the last vaccination occurs after an interval of at least several months, providing a better boost to protective antibodies and contributing to herd immunity.[vii]
- 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 coverage to 13 and 10 serotypes, respectively—adding serotypes relevant to low- and middle-income countries.
- PCVs are one of the most complicated and expensive vaccines to manufacture—translating to inherently high prices (e.g., US$12.85-$14.50/dose in non-Gavi, middle-income Pan American Health Organization countries depending on the PCV).[viii]
- 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 Pneumococcal Advance Market Commitment (AMC) 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.[ix]

About PNEUMOSIL

- The newest prequalified PCV is Serum Institute of India Pvt., Ltd.'s PNEUMOSIL®, which protects against 10 serotypes (1, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F, and 23F) most likely to cause serious disease in the world's highest-burden regions—Africa and Asia.
- The manufacturing process for PNEUMOSIL® has been optimized to make it more efficient, which lowers costs while preserving quality. The target Gavi price is around US$2 per dose—roughly 30% less than the current Gavi-supported PCV price.
- Serum Institute and PATH advanced PNEUMOSIL® 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, PATH, WHO, and other partners to develop the meningococcal serogroup A (meningitis A) vaccine, MenAfriVac®, which has since helped eliminate meningitis A epidemics where introduced in Africa.
- 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.
- Serum Institute is sponsoring ongoing clinical studies in India for marketing authorization nationally.

About the pivotal PNEUMOSIL® Phase 3 clinical study in The Gambia

- The Phase 3 study provided the pivotal results for the data package required for PNEUMOSIL®'s 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.
- The study was sponsored by PATH and conducted by a team of experienced researchers from MRC Unit The Gambia—part of the London School of Hygiene and Tropical Medicine.
- Other study partners included FHI Clinical; the WHO Reference Laboratory for Pneumococcal Serology at the Great Ormond Street Institute of Child Health, University College London; and other laboratories.
- 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 that PNEUMOSIL® elicited immune responses on par with (i.e., non-inferior to) the WHO-prequalified PCV. Per WHO guidelines,[x] non-inferiority to a licensed PCV is considered predictive of a PCV's ability to prevent invasive pneumococcal disease.
- 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 given in the study elicited equivalent immune responses—indicating consistent manufacturing performance.
- A summary of the Phase 3 results was presented at the 2019 European Symposium on Pediatric Infectious Diseases and a study manuscript is pending peer-review publication.

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[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] GBD 2017 Causes of Death Collaborators. Global, regional, and national age-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2019;392:1736-1788.

[iii] Wahl B, O'Brien KL, Greenbaum A, 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*. 2018;6:e744-57.

[iv] 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.

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

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

[vii] WHO. Pneumococcal conjugate vaccines in infants and children under 5 years of age: WHO position paper – February 2019." *Weekly Epidemiological Record*. 2019;8(94):85-104.

[viii] PAHO. "Expanded Program of Immunization Vaccine Prices for Year 2019." June 26, 2019. Accessed at: https://www.paho.org/hq/index.php?option=com_docman&view=download&category_slug=vaccines-9979&alias=49243-vaccine-prices-2019&Itemid=270&lang=en

[ix] 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/

[x] 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.