World Health Organization

MI4A
MARKET INFORMATION FOR ACCESS TO VACCINES

GLOBAL MARKET STUDY
PNEUMOCOCCAL CONJUGATE (PCV) AND POLYSACCHARIDE (PPV) VACCINES

Key Takeaways

- National introduction of PCV in infant routine immunization in 42 countries – including large ones like India, China and Indonesia – will trigger an increase of demand in excess of 60 million doses over the next ten years.
- Supply of PCV will increase by 60%, with at least two new manufacturers with prequalified vaccines entering the market in the next five years.
- The supply/demand balance for PCV is currently sufficient, with limited buffer, and is expected to improve with additional manufacturers' entrance. However, over the medium-term, strong country preferences for specific vaccine subtypes may cause imbalances and require specific action. The evolution of demand for older populations also requires monitoring, particularly in the context of potential increased demand due to COVID-19 and potential policy changes.
- PCV introduction has been particularly slow in non-Gavi, non-PAHO middle-income countries (MICs), which have the lowest percentage of countries introduced (58%) and infants immunized; PCV demand in non-Gavi, non-PAHO MICs could more than double by 2030. Where introduced, PCV represents a substantial strain on immunization budgets. Lower prices for MICs are expected from new entrants.
- PPV demand and supply, concentrated in MICs and high-income countries (HICs), is unstable and should be carefully monitored, particularly in the context of potential increased demand due to COVID-19.

QUICK STATS

NUMBER OF VACCINE TYPES
2

NUMBER OF VACCINE SUBTYPES
3

2019 ESTIMATED GLOBAL DEMAND
PCV ~245 million doses
PPV ~20 million doses

2019 NUMBER OF MANUFACTURERS
6

2019 DEMAND/SUPPLY RATIO
PCV
PPV

2018 REPORTED PER DOSE PRICE
PCV ~US$ 3–132
PPV ~US$ 8–52

Context and Rationale

Pneumococcal vaccines comprise two types – pneumococcal conjugate (PCV) and pneumococcal polysaccharide (PPV) – each providing protection against a subset of the >90 known serotypes of *Streptococcus pneumoniae*.

WHO recommends the inclusion of a three-dose schedule of PCV (10 or 13 valent subtypes) in childhood immunization programmes worldwide for children as young as 6 weeks old.[1] Whenever possible, catch-up vaccination at the time of PCV introduction should be used to accelerate the vaccines' impact on disease in children aged 1-5 years. The choice of vaccine subtype should be based on programmatic and local factors.

WHO does not currently recommend routine immunization of high-risk populations over 5 years of age or elderly people with PCV or 23-valent pneumococcal polysaccharide vaccine (PPV23), but this option is under consideration by WHO Strategic Advisory Group of Experts (SAGE).

Some HICs and MICs currently recommend immunization with one to two doses of pneumococcal vaccine in older age groups. The target age is primarily above 60 years (ranging from 50+ years to 65+ years) and overwhelmingly relies on PPV23 (nearly 90% of adult pneumococcal vaccination uses PPV23).

Supply of PCV for low-income countries (LICs) has primarily benefited from support provided by the Advance Market Commitment (AMC), an innovative financing mechanism that supports availability and affordable pricing of PCV to poorer countries.[2]

Demand

PCV drives 91% of global pneumococcal vaccine demand; the remaining 9% of demand is for PPV.

More than 95% of PCV demand comes from infant vaccination programmes with more limited PCV demand arising from adult use, primarily in 12 HICs.[3]

1 WHO Pneumococcal Conjugate Vaccines Position Paper, Feb 2019: https://apps.who.int/iris/bitstream/handle/10665/310968/WER9408.pdf
2 For further information see: https://www.gavi.org/investing/innovative-financing/pneumococcal-amc/
3 Austria, Bahrain, Belgium, Czech Republic, Finland, Greece, Italy, Luxembourg, Malta, Poland, Slovakia and (with the largest share of adult demand) USA.

As of 2019, 152 countries have fully or partially introduced routine PCV immunization of infants,[4] while 42 countries have not yet introduced PCV (see Figure 1).[5]

Most Gavi-supported countries have introduced PCV for infants and all are forecast to introduce by 2026. Current routine PCV demand for Gavi-supported countries is estimated at ~130M doses and is expected to grow to >200M annually by 2030. Full country introductions in India and Indonesia are the major demand increase factors, contributing an additional ~55 million doses of annual base demand at peak.[6] Catch-up immunization at the time of introduction is forecasted for seven Gavi-supported countries and accounts for one-time demand totalling ~12 million doses between 2022 and 2026.[7]

Just over half of non-Gavi non-PAHO MICs have introduced PCV nationally (28 of 48 as of November 2019) and 2019 demand for this group is estimated at ~45M doses.[8] By 2030, demand from non-Gavi non-PAHO MICs could more than double (105M doses).[9] The 20 non-Gavi, non-PAHO MICs that have not introduced PCV have a total birth cohort of ~20M and demand of almost 60M doses (15% of global PCV demand for infants) by 2030 (see Figure 2). The largest countries are China, Egypt and Iran. National introduction in China of PCV as a government-purchased vaccine would increase demand by approximately 40 million doses and result in decreased private-sector use.

The majority of HICs have introduced PCV, and some use it for both children and adults (sometimes along with PPV23). HICs have variable schedules: the majority recommend three doses for infant immunization, one country has a two-dose schedule,[10] and 14 countries have four-dose schedules. The potential for more countries to adopt a two-dose schedule could decrease future demand, but this is not included in the forecast at this time.

PPV23 demand originates entirely from use in elderly adults and high-risk populations in ~30 upper-middle-income countries (UMICs) and HICs, including substantial demand from China and the USA. PPV23 demand is forecasted to be steady during the study period.

Nevertheless, the use of pneumococcal vaccines for people >50 years old could increase if SAGE and/or National Immunization Technical Advisory Groups recommend this use. Depending on the specific recommendations and product characteristics, demand for higher valency PCV could replace demand for PPV. While there is currently limited information on whether COVID-19 is associated with an increased risk of pneumococcal infection, the COVID-19 pandemic may also drive an increase in older age group demand for pneumococcal vaccination, which can prevent both primary and secondary bacterial infections and the unnecessary use of antibacterial medications (antibiotics).

FIGURE 1: INTRODUCTION STATUS AS OF NOVEMBER 2019

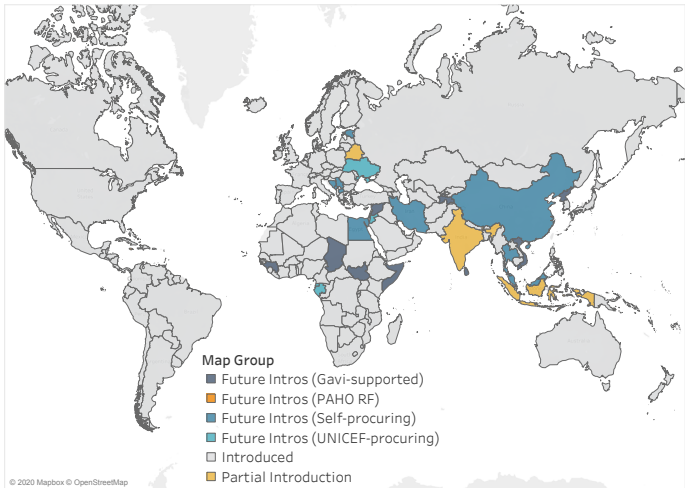
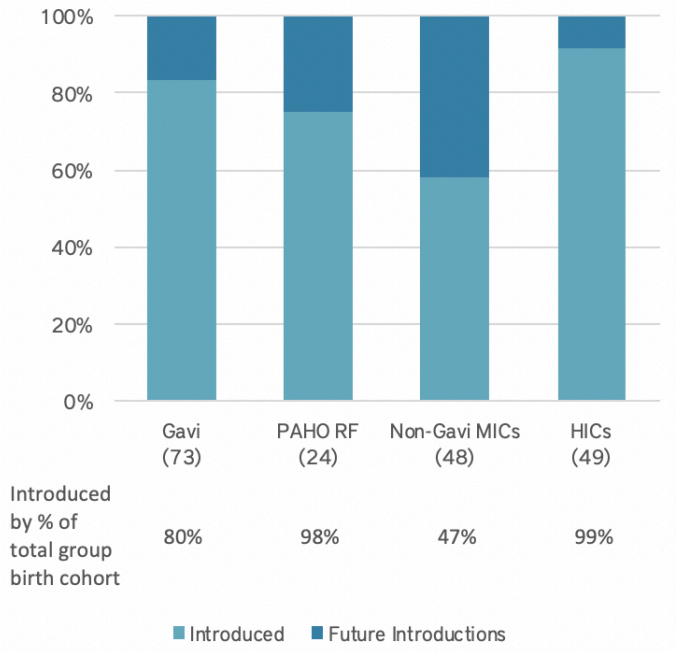


FIGURE 2: PORTION OF COUNTRIES WITH ROUTINE INFANT PCV IMMUNIZATION BY CATEGORY (2019) (INTRODUCED INCLUDES PARTIAL INTRODUCTIONS)



Supply

PCV supply includes three manufacturers (Pfizer, GSK and Serum Institute of India) of two prequalified vaccine subtypes (PCV10 and PCV13), seven vaccine products, and three affiliations with local manufacturers.[11] TThe prequalified vaccine products are available in preserved and unpreserved multi-dose vials and single-dose vials;

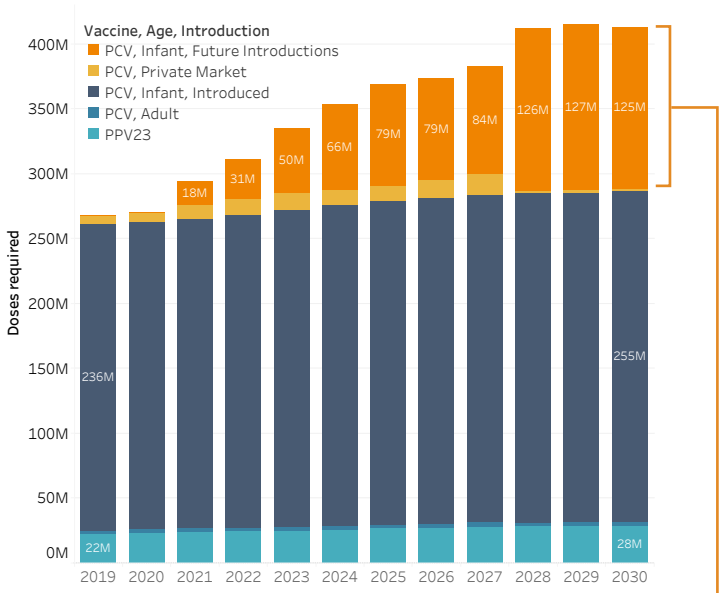
4 The demand forecast (see Figure 3) assumes all countries will introduce PCV for infants by 2030. Timing of introductions for countries without specific plans is based on intelligence from WHO Regional Offices and assumptions based on country income group and competing new vaccine introductions.
5 WHO IVB Introduction Status of Select Vaccines, November 2019 (under 6.6, slides): https://www.who.int/immunization/monitoring_surveillance/data/en/
6 All coverage estimates are per the 2019 Gavi base Strategic Demand Scenario (SDS).
7 Gavi PCV SDS, Aug 2019
8 Forecasted demand for all non-Gavi countries is calculated based on DTP1 coverage.
9 Introduction plans are not available for 23 countries, but all are assumed to introduce by 2030 based on income level and other future vaccine introductions (e.g. Rota, HPV)
10 The United Kingdom
11 Affiliations can take the form of a technology transfer that is pprogressive – starting with fill/finish and leading to also include bulk manufacturing or a simpler distribution agreement – but always represent a dependent relationship with another manufacturer and not one that will increase the total ASC.

pre-filled syringes are available and not prequalified. Between 2020 and 2025, at least five additional manufacturers are expected to license PCVs and at least two are anticipated to seek prequalification and concentrate on providing vaccine to LICs and MICs, including their local markets. Over the same period, multiple vaccine PCV subtypes, from 7-valent through 20-valent, may become available. After 2025, a number of other producers and a second generation of pneumococcal vaccine designed to protect against a wider range of serotypes could be available.

The diversity of manufacturers and available supply for commercialization (ASC) for PCV will grow by 30% over the short-term, by 60% over the medium-term and by 75% over the long-term to reach a higher level of market health. By 2030, a minimum of four new manufacturers are forecast to contribute more than 50% of global ASC, representing a significant diversification of manufacturers – contributing to lower risk of shortages. Nevertheless, this diversification will also fragment ASC into numerous vaccine subtypes (from two to seven), creating potential mismatches between specific country preferences and supply availability as well as vaccine security issues if products are not interchangeable. Careful information and coordination on the demand side will be required.

PPV23 supply is unstable with a recent market exit and only a few vaccines in development. Currently, the supply is limited to one global manufacturer with several affiliates and three manufacturers based in China with two additional vaccines in development. All manufacturers of PPV23 except one are also engaged in manufacturing or development of a PCV and share manufacturing steps across the two vaccine types.

FIGURE 3: 2019–2030 PNEUMOCOCCAL VACCINES GLOBAL DEMAND FORECAST[12]

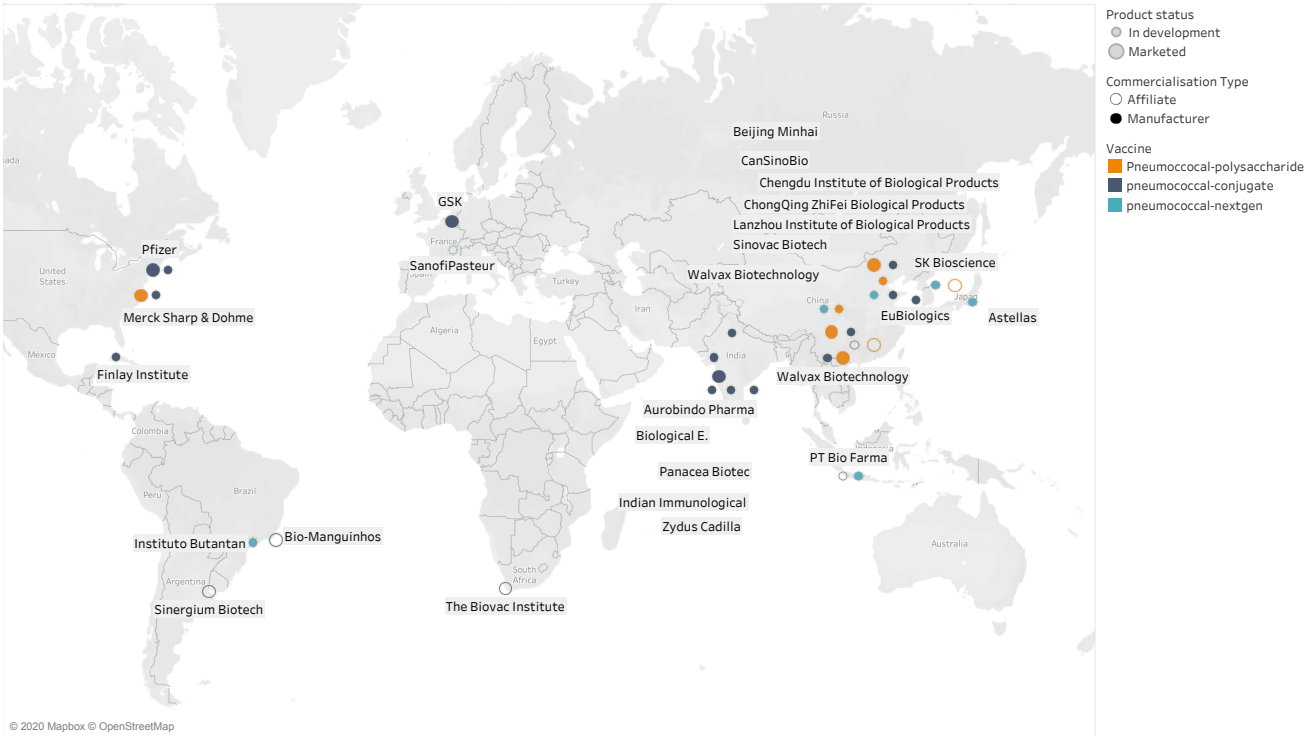


12 Assumes no change to country immunization schedules (i.e. number of doses).

2030 Demand from Future Introductions:

India (states not introduced before 2020): 35%	China: 34%	Non-Gavi, Non-PAHO MICs: 13%	Gavi: 10%	Indonesia: 8%

FIGURE 4: PNEUMOCOCCAL VACCINE MANUFACTURERS (MARKETED & IN DEVELOPMENT)



The number of manufacturers providing PPV23 is not expected to grow, given the relatively low level of demand and market trend toward higher valency PCV that could eventually decrease demand for PPV23. ASC is expected to decrease as manufacturer resources are directed to PCV instead of PPV or if manufacturers choose to exit this smaller market.

Supply and Demand balance

For PCV, the current base ASC is sufficient. Medium-term, the base ASC is likely to meet or exceed demand, subject to the timing of availability from pipeline manufacturers and of increased MIC demand stemming from the pace of national expansion in India and Indonesia and new introductions in MICs. The largest uncertainty, and one that is contained to China, on medium- to long-term supply and demand balance is the timing of China's introduction of PCV as a government-purchased vaccine. Over the long term, stabilized demand will be met with sufficient supply in the **base** supply scenario. In a **low** supply scenario that includes the medium-term market exit of a large manufacturer, ASC could be reduced by 30% with supply deficits limiting new introductions and creating shortages for countries that have already introduced PCV. This would require careful dialogue by immunization partners with the manufacturer. In a **high** supply scenario, there could be significantly more ASC than demand.

PPV supply is vulnerable to a single large manufacturer that accounts for the largest volume of ASC outside of China. Advanced information on supply changes from manufacturers to public and private health entities at global and local levels will be required to avoid supply shortages.

FIGURE 5: PCV SUPPLY/DEMAND BALANCE[13]

ASC / demand ratios	Current	Short term (current year +2)	Medium term (current year +5)	Long term (current year +10)
Base supply / base demand	●	●	●	●
High supply / base demand	●	●	●	●
Low supply / base demand	●	●	●	●
Ratio of ASC / demand	< 1.1	1.1 - 1.4	1.5 - 1.7	> 1.7

FIGURE 6: PPV SUPPLY/DEMAND BALANCE[14]

ASC / demand ratios	Current	Short term (current year +2)	Medium term (current year +5)	Long term (current year +10)
Base supply / base demand	●	●	●	●
High supply / base demand	●	●	●	●
Low supply / base demand	●	●	●	●
Ratio of ASC / demand	< 1.1	1.1 - 1.4	> 1.5	

13 Red represents insufficient ASC compared to demand; yellow represents low supply risk; green represents sufficient ASC compared to demand and dark green represents more than sufficient ASC compared to demand.

14 Where red represents insufficient ASC compared to demand; yellow represents low supply risk, green sufficient ASC compared to demand and dark green represents more than sufficient ASC compared to demand.

Pricing

PCV public market prices per dose range from US$ 3 for Gavi countries through UNICEF (and the AMC) to US$ 132 in the USA. For self-procuring countries, the country-reported prices from 2018 are tiered by income, but with a wide range and overlap in prices in MICs and HICs (see Figure 7).

MICs have voiced affordability of PCV as an important concern. WHO conducted an analysis to identify countries that are likely to be constrained due to vaccine affordability; countries were compared to their peers on factors including other introduced vaccines, vaccine choices, vaccine procurement strength, and the percentage of government expenditure spent on health. The PCV affordability analysis was conducted on 32 non-Gavi, non-PAHO MICs (16 introduced and 16 not introduced) where data were available to support the analysis. For six countries in the analysis, adding PCV to their immunization schedule appears to be an affordability challenge. For these countries, an estimated 53–87% of the immunization budget would need to be spent on PCV.

For PPV23, countries reported prices between US$ 5 and 35. Self-procuring countries who reported PPV23 prices suggested a trend of increasing price per dose from 2015 to 2018 (see Figure 8). This is also evident for USA prices, which increased 60% over the same time period. The PAHO RF price remained relatively stable.

FIGURE 7: SELF-PROCURING, COUNTRY-REPORTED PCV PRICES (2018)

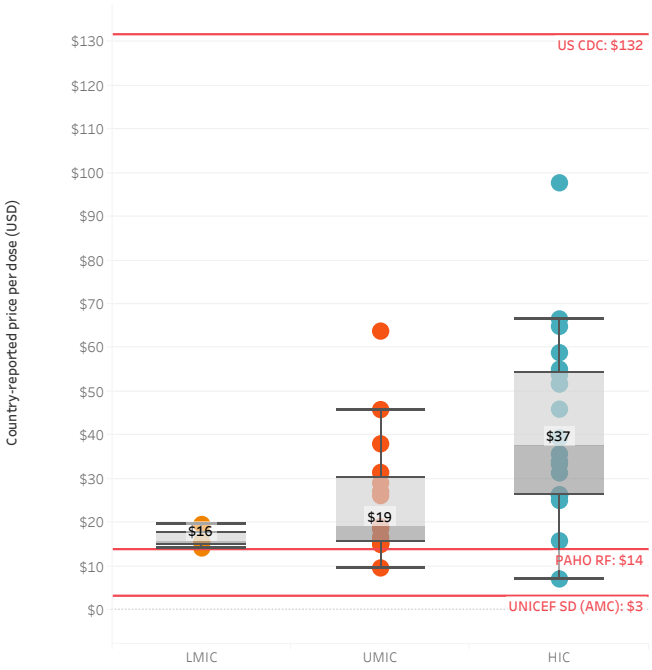
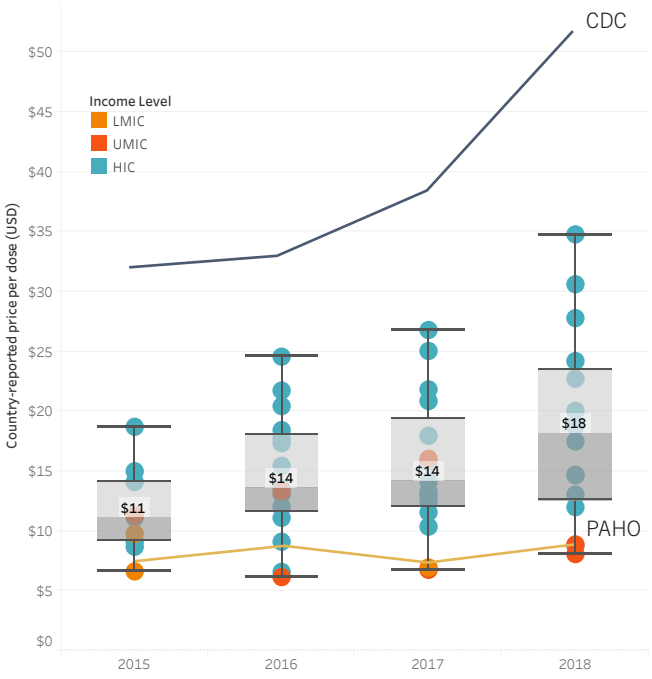


FIGURE 8: PPV23 SELF-PROCURED, COUNTRY-REPORTED PRICES (2015-2018)



Areas for Action

To enhance sustainable access to supply of PCV and PPV in coordination with immunization partners, WHO will:

- Issue early guidance to countries to inform careful consideration of the future choices among PCV subtypes to help prevent supply constraints for specific vaccine subtypes.
- Develop all required evidence and guidance to ensure clarity on product interchangeability opportunities and challenges to inform countries in case of specific vaccine subtype shortages.
- Lead the policy process for developing WHO's position on adult use of pneumococcal vaccines with consideration to market and supply availability risks and opportunities.
- Continue to give high priority to prequalification of PCV from new manufacturers, specifically those who are most likely to significantly improve access.
- Maintain close and high-level dialogue with key manufacturers to mitigate the risk of access issues resulting from market exits for both PCV and PPV.
- Continue working with partners to assist MICs in accessing PCV supply.

In the context of the COVID-19 pandemic, evolution of pneumococcal vaccine demand should be carefully monitored.

For more information, contact:
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Other Resources

WHO Immunization in the time of COVID-19: FAQ:
https://apps.who.int/iris/handle/10665/331818

WHO February 2019 position paper on pneumococcal conjugate vaccines in infants and children under 5:
https://apps.who.int/iris/bitstream/handle/10665/310968/WER9408.pdf?ua=1

WHO position paper 2008 on 23-valent pneumococcal polysaccharide vaccine:
https://www.who.int/wer/2008/wer8342.pdf?ua=1

UNICEF December 2018 Pneumococcal Conjugate Vaccine: Supply and Demand Update:
https://www.unicef.org/supply/files/PCV_5_Supply_Update.pdf

Advanced Market Commitment for Pneumococcal Vaccines, Annual Report: 1 January – 31 December 2018; available from:
https://www.gavi.org/investing/innovative-financing/pneumococcal-amc/