

## A look back on a year of announcements by vaccine companies

12 January, 2018

In the past year, vaccine companies have made 18 separate announcements that could impact immunisation coverage. These include a series of promising developments, with the majority (13) being related to vaccine R&D. The Foundation completed this review to track how vaccine companies continue to address access to vaccines. It follows on from the publication of the first Access to Vaccines Index by the Foundation in March 2017.

The 2017 Access to Vaccines Index mapped how the world's largest vaccine companies are improving access to vaccines in low- and middle-income countries. It revealed a high level of diversity in how vaccine companies are improving access to vaccines for people living in low- and middle-income countries. This diversity is generally linked to the size of their portfolios and pipelines. The Index evaluated eight companies' actions in relation to 107 countries and 69 infectious diseases.

### In brief

The Foundation looked at publicly available information released by the eight companies evaluated in the 2017 Access to Vaccines Index between 1 April, 2017 and 3 January, 2018.

- Vaccine companies report more activity in R&D than in other areas, making nine announcements relating to clinical trials and four about R&D partnerships that aim to advance the effectiveness of products or to make products more accessible to resource-limited communities.
- An announcement regarding a technology transfer supports the view that licensing is a feasible and effective way of increasing access to vaccines. More companies can take advantage of licensing as a way of introducing their vaccines in new markets.
- Three companies announced developments that can help make vaccine supply more reliable, including of pneumonia, influenza and polio vaccines.

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**ACCESS TO MEDICINE FOUNDATION**

The Access to Medicine Foundation is a non-profit organisation. It aims to advance access to medicine in low- and middle-income countries by stimulating and guiding the pharmaceutical industry to play a greater role in improving access to medicine and vaccines. For ten years, the Foundation has been building consensus on the role for the pharmaceutical industry in improving access to medicine and vaccines. It published its first benchmark of industry activity in this area in 2008, in the first Access to Medicine Index. In 2017, it published the first Access to Vaccines Index and is developing the first Antimicrobial Resistance Benchmark.

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# About this Update

Vaccines are one of the most powerful and cost-effective health interventions available. Yet WHO states that an estimated 19.5 million infants worldwide are still missing out on basic vaccines. The global community shares the responsibility of ensuring everyone can benefit from immunisation. The companies that develop and manufacture vaccines have a clear role to play here: in developing new and improved vaccines; in addressing the affordability of vaccines; and in aligning supply and demand.

On 6 March, 2017, the [Access to Medicine Foundation](#) published the first [Access to Vaccines Index](#), the first data-driven tool that maps vaccine companies' policies and behaviours on making vaccines more accessible to communities with limited resources. It revealed a high level of diversity in how vaccine companies are improving access to vaccines for people living in low- and middle-income countries. This diversity is generally linked to the size of company portfolios and pipelines.

This Update analyses publicly available information released between 1 April, 2017 and 3 January, 2018, as a supplement to the Index, and to gauge the momentum within the industry toward global targets for improving immunisation coverage. It provides a commentary on companies' most recent announcements regarding access to vaccines and their implications in low- and middle-income countries.



An infant receives Sanofi's inactivated polio vaccine. The multi-dose vial lasts 28 days after opening, helping to reduce wastage.



Nepal has recently introduced the injectable vaccine with the virus either killed or deactivated (instead of the live attenuated oral vaccine).

“We published the first Access to Vaccines Index in 2017 – this was the first time we had a complete picture of how the biggest players in the vaccine market were addressing access to vaccines. Since then, we have continued to track their actions as they have made them public. Such insight shows where further energies can be invested.”

- **Jayasree K. Iyer**, Executive Director, Access to Medicine Foundation

INTRODUCTION

# Why we need to continue accelerating immunisation coverage

The [2017 Assessment Report of the Global Vaccine Action Plan \(GVAP\)](#) notes that in 2016, some progress was made toward the goals set out in the GVAP. The GVAP was signed by 194 Member States of the World Health Assembly in May 2012, with targets such as polio elimination by 2015 and introduction of one or more new or under-utilised vaccines in at least 90 low- and middle-income countries (LMICs). The GVAP assessment report states that 2016 had the fewest cases of wild poliovirus ever reported, and that three more

countries were certified as having achieved maternal and neonatal tetanus elimination. It also noted that 108 LMICs had introduced one or two new or under-utilised vaccines in their routine immunisation programmes.

The report however also states that the current rate of progress is unfortunately too slow for most GVAP goals to be reached by the end of 2020. The World Health Organization (WHO) estimates that in 2016, 19.5 million infants worldwide missed out on basic vaccines, a number that is slightly above

that of 2015 (19.4 million). Vaccination coverage for some diseases was as low as 28% in LMICs (see Figure 1). The GVAP assessment report notes that the [2017 monitoring indicators data](#) confirm the slow rate of change seen in previous years. Despite some progress, coverage levels are in general not increasing as rapidly as might have been hoped. While immunisation is primarily the responsibility of national governments, vaccine companies will continue to have a critical role to play at least until the GVAP targets are met.

ABOUT THE ACCESS TO VACCINES INDEX

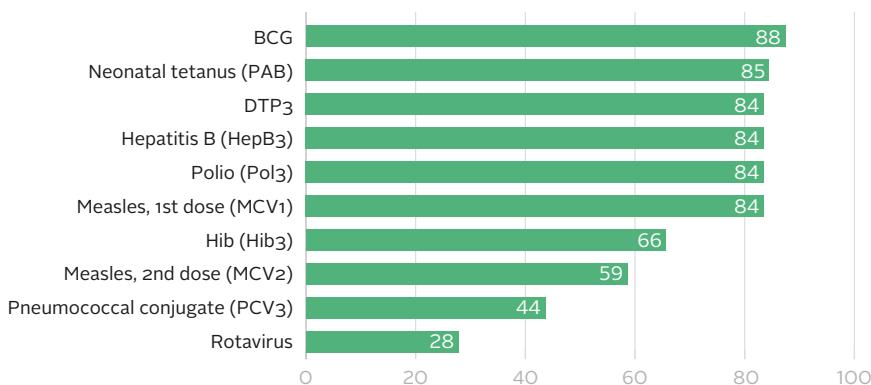
The 2017 Access to Vaccines Index was developed to stimulate vaccine companies to do more to improve vaccine coverage, and to increase accountability within the vaccine industry. Stakeholders engaged with the global vaccines market have confirmed that companies have become more engaged following the work of the Access to Medicine Foundation.

The 2017 Access to Vaccines Index measured eight vaccine companies: seven large research-based pharmaceutical companies based in mature markets and one vaccine manufacturer based in an emerging market. The disease scope of the 2017 Access to Vaccines Index consists of 69 diseases that are vaccine preventable, and have the highest priority when it

comes to improving access to immunisation. The Index covers countries with the highest perceived need for greater access to vaccines: 107 low- and middle-income countries, Least Developed Countries and countries with high levels of inequality. The full analytical scopes and methodology can be downloaded from [www.accesstovaccinesindex.org](http://www.accesstovaccinesindex.org).

Figure 1. Average immunisation coverage in LMICs in 2016 (%)

Immunisation coverage for a number of high burden diseases was 84-88% in 2016. GVAP indicators monitoring data for 2017 show that there will likely be very little change in 2017.



Source: WHO

## UPDATE RESULTS

# Vaccine industry activity, following Index publication

## FINDINGS IN BRIEF

This Update to the 2017 Access to Vaccines Index analyses publicly available information released between 1 April, 2017 and 3 January, 2018. In this review, the Access to Medicine Foundation identified a total of 18 announcements from all companies in the scope of the Index (see Table 1), including a range of promising positive developments. However, gaps in new information indicate where there is seemingly little action being taken. Two companies, Johnson & Johnson and Sanofi, accounted for almost half (8/18) of all announcements (each made four announcements), and all eight companies made at least one announcement each. This update also found that about two thirds (13/18) of announcements were related to R&D, and only two were related to pricing and registration of vaccines.

The key announcements are summarised here and discussed in the next pages. An overview of all 18 company announcements is provided in the next section.

### Positive developments

- Both Johnson & Johnson and Takeda announced vaccine R&D for priority diseases in collaboration with Biomedical Advanced Research and Development Authority (BARDA), a public organisation (increasing the likelihood that vaccines developed will be made more widely available).
- Takeda made a licensing agreement with a biopharmaceutical manufacturer that aims to increase affordability of five essential vaccines to LMICs.

- GSK received WHO prequalification for a key vaccine for pneumonia, which will allow international organisations such as the United Nations Children's Fund (UNICEF) to procure the vaccine for LMICs.

### Gaps in information

- Pneumonia, which had one of the lowest immunisation coverages in 2016, needs critical attention. There are opportunities for licensing agreements between companies that can ensure such critical vaccines can be affordably introduced to markets that need them most.
- The announcements did not indicate if the companies have strong processes to support ongoing global alignment of supply and demand.

Table 1: About two thirds of company announcements are related to R&D

Company	Category			Total
	Research & Development	Licensing & Procurement	Manufacturing & Supply	
Daiichi Sankyo	1	0	0	1
GSK	1	1	0	2
Johnson & Johnson	4	0	0	4
Merck & Co., Inc.	1	0	0	1
Pfizer	2	0	0	2
Sanofi	2	0	2	4
Serum Institute of India	0	0	1	1
Takeda	2	1	0	3
<b>Total</b>	<b>13</b>	<b>2</b>	<b>3</b>	<b>18</b>

## ANNOUNCEMENTS BY CATEGORY: R&amp;D

# New R&D partnerships for priority vaccines

- **13 announcements made; nine relate to vaccines in clinical trials and four relate to vaccine development partnerships.**
- **Johnson & Johnson announced a collaboration with Bavarian Nordic to develop vaccines against hepatitis B virus (HBV) and human immunodeficiency virus (HIV-1).**
- **Both Johnson & Johnson and Takeda announced vaccine R&D for priority diseases in collaboration with BARDA, a public organisation (increasing the likelihood that vaccines developed will be made more widely available).**

Johnson & Johnson announced a collaboration with Bavarian Nordic to develop vaccines against HBV and HIV-1. The two companies will combine Bavarian Nordic's MVA-BN® technology with Johnson & Johnson's AdVac® and DNA-based vaccine technologies in the development of these potential new

vaccine regimens. HIV is a major global public health issue that has claimed 35 million lives so far. WHO estimates that there were approximately 36.7 million people living with HIV/AIDS at the end of 2016, and 257 million living with HBV. Both HIV/AIDS and HBV require long-term treatment, placing a high financial burden on those affected. The objective of the collaboration between the two companies is to identify functional cures for HIV/AIDS and HBV to control the viruses and prevent potential disease progression without the need for life-long treatment.

#### Vaccines for recent epidemics

Johnson & Johnson announced that it would further advance its investigational Ebola vaccine regimen, and Takeda announced that its investigational Zika virus vaccine candidate will progress to Phase 1 clinical trials. Both companies have received funding from public partners such as BARDA for these projects, which increases the likelihood that

the vaccines may be made available for high-burden resource-limited settings.

The Ebola outbreak in west Africa in 2014-2016 had a case fatality of 50%. An experimental Ebola vaccine was found to be highly protective in a major trial of 11,841 people conducted in Guinea in 2015. Of the 5,837 people who received the vaccine, no Ebola cases were recorded 10 days or more after vaccination. In comparison, 10 days or more after vaccination, there were 23 cases among those who did not receive the vaccine. The collaborative partnership between Johnson & Johnson and BARDA will support the company's ongoing commitment to develop a novel prime-boost vaccine regimen to help prevent the future spread of Ebola. However, the focus is on the West Africa Ebola outbreak, which belongs to the Zaire Ebola virus species, with less attention for other strains of the virus, such as the Sudan Ebola virus. It is common that when a disease is no longer receiving public attention (e.g., in the case of an outbreak) companies may also lose interest in the issue. This is a dangerous trend because it means that there is less preparation should the epidemic come back. The Zaire strain was first reported in 1976, and over the years multiple outbreaks across the globe have been reported with death rates as high as 89% (2002-2003). Pharmaceutical companies must be incentivised to keep developing vaccines and maintaining supply so as to mitigate future outbreaks. It is especially critical given the alarming rate at which antimicrobial resistance is rising for different infectious diseases.



Inspecting cholera vaccines at Sanofi's Hyderabad plant, India. Companies direct their capacity building efforts to a few middle-income countries, including India.

## ANNOUNCEMENTS BY CATEGORY: LICENSING &amp; PROCUREMENT

# Support for licensing as a feasible and effective way to increase access to key vaccines

- **Two announcements made, about licensing and WHO prequalification.**
- **Takeda made a licensing agreement that may increase affordability of five essential vaccines.**
- **GSK received WHO prequalification for a key vaccine for pneumonia, which will allow international organisations to procure the vaccine more efficiently.**

Takeda and Biological E. Limited announced a licensing agreement to transfer Takeda's measles and acellular pertussis vaccine technologies to Biological E. The transfer will allow the development of low-cost combination vaccines (including diphtheria, tetanus and acellular pertussis and measles-rubella) for LMICs. This is a critical movement by Takeda as it targets five key vaccines, two of which had low global coverage in 2016 (measles and pneumonia). The collaboration aims to ensure that these key vaccines will be affordable for LMICs. The vaccines represent four out of seven vaccines that Takeda reported as being marketed in the 2017 Access to Vaccines Index. The voluntary licensing agreement between the two companies is an important movement in the industry that other companies can emulate to ensure much needed vaccines for high burden diseases are made available in resource-limited settings. At the time of the 2017 Access to Vaccines Index publication, Takeda was researching ways to make its vaccines accessible for both Gavi and non-Gavi eligible countries. Even though the company

was not assessed in the research area of Pricing & Registration, the collaboration with Biological E. will undoubtedly have a major impact in this area.

## The case for pneumonia

Pneumonia, which has one of the lowest immunisation coverage rates in 2016, needs critical attention. Pneumonia is an infectious disease that can be caused by viruses, bacteria or fungi, and accounts for about 16% of all deaths of children under 5 years old. Preventing pneumonia in children is an essential component of a strategy to reduce child mortality, and immunisation is the most effective mode of prevention.

At the time of the Index publication, GSK reported that it was committed to seeking WHO prequalification as a method of expediting access to its vaccines for LMICs. WHO prequalification ensures that essential vaccines will be available for procurement by United Nations agencies such as UNICEF. On 18 October, 2017, the WHO awarded prequalification to GSK for its four-dose vial presentation of Synflorix™ pneumococcal vaccine, which is targeted mainly for countries that receive support from Gavi. The supply of Synflorix™ to Gavi-eligible countries started in 2010 under the Advance Market Commitment mechanism. As part of this ongoing commitment, GSK agreed to make 720 million doses of Synflorix™ available by the mid-2020s. The company has not disclosed plans to make the drug available for non-Gavi eligible countries.

Many middle-income countries (MICs) do not qualify for Gavi assistance, but still need assistance to procure drugs. It is especially critical as immunisation coverage was about 30% on average in 2016 for pneumonia in MICs. Nonetheless, getting pre-qualification from WHO is an important step forward.

In August, India's patent office granted Pfizer a patent for its pneumococcal vaccine Prevnar 13®. Opponents to this decision have argued that such a move not only prevents other companies from selling or manufacturing cheaper versions of the vaccine in India, but also that it means a 68% rise in the cost of this key vaccine for developing countries. The Indian patent authorities chose to uphold their decision despite these oppositions. Coverage for pneumonia in LMICs was only 44% in 2016 (see Figure 1). While Pfizer agreed to offer the vaccine at as low as USD 9.15 per course to Gavi through UNICEF, Serum Institute of India had agreed to offer USD 6 per course. Other companies, such as GSK, that have pneumonia vaccines have an opportunity here to engage and make partnerships with other manufacturers so as to make this critical vaccine available.

ANNOUNCEMENTS BY CATEGORY: MANUFACTURING & SUPPLY

# Companies are making investments to increase the supply of vaccines

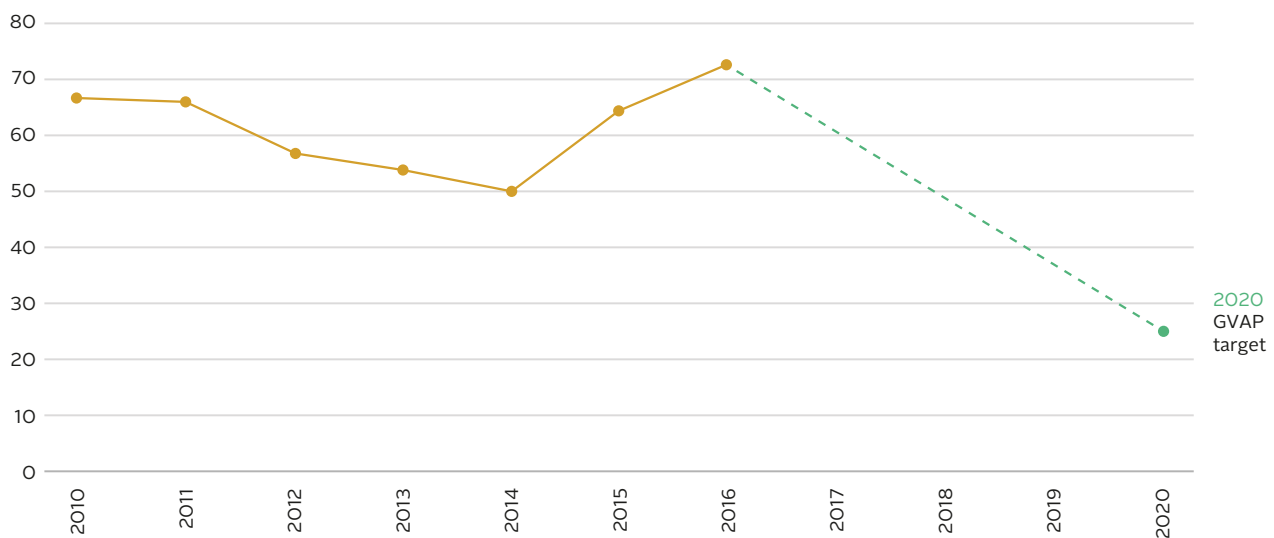
- Three announcements were made that could impact on manufacturing and supply.
- GSK’s new pneumonia vaccine formulation extends shelf life to address a major barrier to access in the supply chain.
- Serum Institute of India made an acquisition that could potentially increase the supply of its polio vaccine fourfold.

- Sanofi made a financial commitment to ensure long-term supply of its influenza vaccine.

GSK’s Synflorix™ is a four-dose vial pneumococcal conjugate vaccine whose formulation is designed to address cold-chain challenges and significantly reduce storage requirements in developing countries. It allows storage across a longer period of time after opening; 28 days, compared to six hours for the two-dose vial. This is a positive step forward that addresses major barriers in the supply chain for a high burden disease.

Serum Institute of India acquired the Czech arm of US-based firm Nanotherapeutics, and believes the deal will help increase production capacity of polio vaccines by fourfold to more than 200 million doses by 2020, making it the largest injectable polio vaccine maker in the world. Polio immunisation coverage is currently only 84% in LMICs. The GVAP goal of zero new cases of polio by 2015 is yet to be realised as 37 new cases were reported in 2016. Serum Institute of India commits to staying in vaccine markets in which there are few other suppliers. However, it is unclear whether the

Figure 2. The number of countries reporting stock-outs for essential vaccines continues to rise



The number of countries reporting a national stockout rose again in 2016, continuing a recent trend of increasing disruptions in vaccine supply. Some 73 countries reported 131 national-level stockout events for at least one vaccine for an average duration of 51 days in 2016. These 73 countries account for 38% of WHO Member States and represent 34% of the world’s birth cohort. The vaccine supplies most commonly affected were DTP-containing vaccines and poliovirus vaccines.

Source: 2017 GVAP Assessment Report





Following the approval of Sanofi's Dengvaxia® in 2015, the Philippines began the first public immunisation programme against dengue in 2016.

company has strong processes to support ongoing alignment of supply and demand with global targets. Nonetheless, its acquisition will support the global goal of complete eradication and containment of all polioviruses by increasing supply of its polio vaccine.

Sanofi announced that it is investing EUR 170 million to expand a vaccine manufacturing site in Val de Reuil, France. The expansion strengthens

Sanofi's position as one of the world's leading seasonal flu vaccine providers. The new facility will expand supply of VaxigripTetra® (which was approved in the UK in July 2016) to up to 70 countries in six continents. The new quadrivalent influenza vaccine contains two A strains and two B strains of influenza virus. The WHO recommends annual vaccination for high-risk groups (children between 6 months and 5 years old, pregnant women, and those over 65), which

means that it is essential for companies to ensure continuous long-term supply for this vaccine. Sanofi therefore continues to show strength in consideration of vaccine supply needs.

Overall, there remains a great need to align demand and supply within the industry, as many vaccines with low immunisation coverage have not been targeted. Furthermore, the GVAP assessment report notes that the number of countries reporting a national stockout rose again in 2016; 73 countries reported 131 national-level stockout events for at least one vaccine for an average duration of 51 days in 2016 (see Figure 2). These 73 countries account for 38% of WHO Member States and are home to 34% of the world's birth cohort. The vaccine supplies most commonly affected were of DTP-containing vaccines and poliovirus vaccine. Serum Institute of India's acquisition is bound to help fill this gap in supply for polio. But what of the other gaps? There is an opportunity for companies to align their manufacturing and supply to global burdens and demands.

## CONCLUDING REMARKS

# Many opportunities for pharmaceutical companies to improve immunisation coverage remain

- Companies doing their part to make vaccines accessible must be recognised, and those that are lagging behind must be encouraged and incentivised to act.
- Governments from both mature and emerging markets have a critical role to play in ensuring vaccines reach target populations, especially in low-resource settings.
- Both big pharma and generics companies can win through proactive licensing.

The Index metrics are a [reflection of stakeholders' views](#) on how vaccine companies can contribute to global immunisation targets. There has been some positive movement in the industry as illustrated above, which shows that companies are, in general, willing to do their part in addressing global public health concerns. Nonetheless, many challenges still remain. Some activities from both governments and industry may hinder the promotion of public health. The Vaccines World Summit 2018 team created a [survey](#) directed at vaccine manufacturers, which revealed that manufacturers in, e.g., India, rate R&D, regulation and funding as their three top challenges.

Many MICs do not qualify for Gavi assistance, but still face challenges procuring vaccines at affordable prices. Coverage for some key vaccines is very low in these countries (for example, cover-age is about 30% on average for pneu-monia in MICs). Governments of these countries could form coalitions that can allow them to purchase these vaccines in bulk, and so have additional leverage and negotiate better prices from companies.

Since they reduce the need for antibiotics, vaccines can also support the fight against antimicrobial drug resistance (AMR). [Kyaw and colleagues \(2006\)](#) found that the introduction of a pneumococcal conjugate vaccine for infants in the United States in 2000 brought about a 57% decline in invasive disease caused by penicillin-resistant strains and a 59% decline in strains resistant to multiple antibiotics. AMR is currently one of the major global public health issues that requires multiple stakeholders in order to be addressed effectively. The Foundation recently published the [Antimicrobial Resistance Benchmark Methodology](#) that sets baseline metrics on how to assess industry activity in AMR, and plans to launch the Antimicrobial Resistance Benchmark in mid-January 2018.

There are opportunities for solidarity between R&D-based vaccine companies, other vaccine manufacturers, public organisations and governments to stimulate, foster and respond to pull and push incentives to ensure vaccines reach resource-limited communities. Non-R&D-based vaccine companies can proactively seek licensing opportunities from patent-holders for key vaccines, as they are often able to manufacture them at lower costs. In turn, R&D-based companies must be open to working with non-R&D-based vaccine manufacturers that can reach certain emerging and frontier markets which are not target markets for them. This is an opportunity for R&D-based companies to make additional profits from their vaccines, and for communities in need to receive much-needed vaccinations. Governments in high-income countries can also create incentives that reward R&D-based companies that work successfully with other vaccine manufacturers to make priority vaccines available in resource-limited settings through mechanisms such as voluntary licensing.

# Appendices

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## Appendix I

Overview of all vaccine company announcements released by companies in the scope of the 2017 Access to Vaccines Index

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## Appendix II

2017 Access to Vaccines Index 2017 — How the industry performs

### Key findings

- Adaptations to existing vaccines account for half of vaccine R&D projects
- When setting prices, all companies consider countries' Gavi status — most also consider GNI per capita
- Companies take diverse approaches to aligning supply with demand

## APPENDIX I

# Overview of all vaccine company announcements released by companies in the scope of the 2017 Access to Vaccines Index

The Access to Medicine Foundation found a total of 18 relevant company press releases regarding vaccines from the 8 companies evaluated in the Vaccines Index between 1 April, 2017 and 3 January, 2018. In general, a press release by any entity is done with the intention of either announcing good news, or doing damage control. Therefore, the Update may have a bias toward positive developments due to this focus on company press releases as the major database. Our evaluation found that all but one company press release was announcing good news.

**Data-collection period: 1 April, 2017 and 3 January, 2018 (data included announcements from company websites only)**

## Daiichi Sankyo

**12 October, 2017** – Daiichi Sankyo announced the commencement of an industry-government-academia R&D collaboration for the development of a genetic vaccine platform utilising in-house developed new nucleic acid delivery technology.

## GlaxoSmithKline

**27 June, 2017** – The Committee for Medicinal Products for Human Use (CHMP) of the EMA issued a positive opinion for a new four-dose vial presentation of GSK's Synflorix™ pneumococcal vaccine.

**18 October, 2017** – GSK today announced that WHO awarded the company pre-qualification for the new four-dose vial presentation of Synflorix™ pneumococcal vaccine targeted mainly for countries that receive support from Gavi.

## Johnson & Johnson

**14 March, 2017** – Johnson & Johnson reported that investigational “prime-boost” Ebola vaccine regimen induced a durable immune response that persisted in 100 percent of healthy volunteers one year following vaccination.

**24 July 2017** – Johnson & Johnson announced encouraging first-in-human clinical data for a Phase 1/2a study for investigational HIV preventive vaccine.

**26 July, 2017** – Janssen announced a collaboration with Bavarian Nordic to develop vaccines against hepatitis B virus and HIV-1.

**29 September, 2017**– Johnson & Johnson announced that it will further advance its investigational Ebola vaccine regimen with a new award from the BARDA.

## Merck & Co., Inc.

**10 October, 2017** – Merck & Co., Inc. announced results from final analyses of Phase III efficacy, immunogenicity, and safety clinical trial for Gardasil® 9 (Human Papillomavirus 9-valent Vaccine, Recombinant) for prevention of cervical, vulvar, vaginal, and anal cancers.

## Pfizer

**19 June, 2017** – Pfizer announced the start of a phase 1 clinical trial to evaluate group B Streptococcus vaccine.

**13 December, 2017** – the New England Journal of Medicine published results from two pivotal Phase 3 studies of Pfizer's Trumenba® (meningococcal group B vaccine). Data from both studies demonstrated that Trumenba®, as a three-dose series, elicits a protective immune response against diverse meningococcal group B strains representative of prevalent strains causing invasive disease in the United States and Europe.

## Sanofi

**28 August, 2017** – Sanofi announced that it completed the acquisition of Protein Sciences, a vaccines biotechnology company, which adds a promising product to its influenza vaccine portfolio: Flublok® (influenza vaccine).

**12 October, 2017** – Sanofi announced that it is investing €170 million to expand a vaccine manufacturing site in Val de Reuil, France, which will expand supply of VaxigripTetra® to up to 70 countries in six continents.

**29 November, 2017** – Sanofi asked health authorities to update information provided to physicians and patients on its dengue vaccine Dengvaxia® in countries where it is approved. The request is based on a new analysis of

long-term clinical trial data, which found differences in vaccine performance based on prior dengue infection.

**1 December, 2017** – Sanofi announced that it would end the development of *Clostridium difficile* vaccine because the clinical trial program concluded that the probability that the study will meet its primary objective is low.

#### **Serum Institute of India**

**26 April, 2017** – Serum Institute of India acquired the Czech arm of US based firm Nanotherapeutics, and believes the deal will help increase production capacity of polio vaccines four-fold to more than 200 million doses by 2020,

making it the largest injectable polio vaccine maker in the world.

#### **Takeda**

**5 April, 2017** – Takeda announced the completion of the enrolment of 20,100 children and adolescents ages 4 through 16 in its phase 3 Tetravalent Immunisation against Dengue Efficacy Study (TIDES) trial. The study is designed to evaluate the efficacy, safety and immunogenicity of its live-attenuated tetravalent dengue vaccine candidate TAK-003.

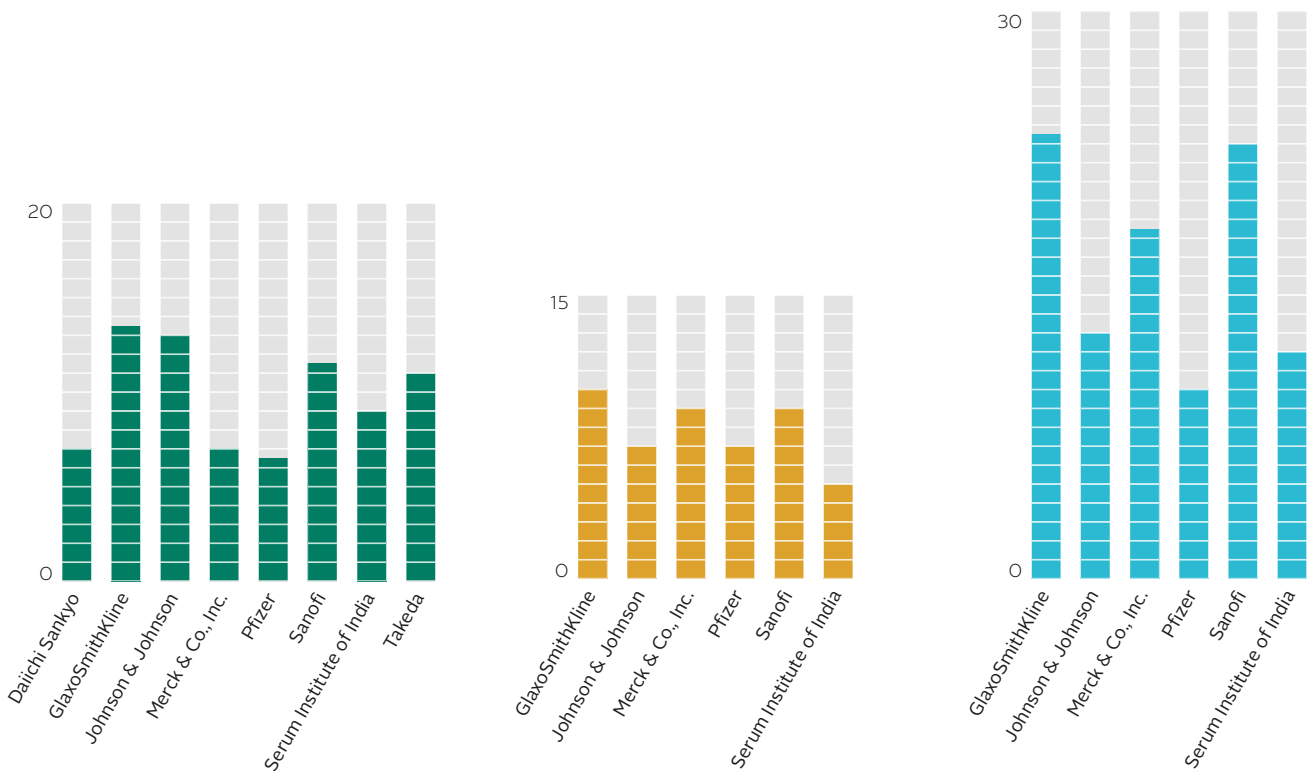
**26 June, 2017** – Takeda and Biological E. Limited (BE) announced a partnership to transfer Takeda's

measles and acellular pertussis vaccine technologies to BE. The transfer will allow the development of low-cost combination vaccines (including diphtheria, tetanus and acellular pertussis and measles-rubella) for low- and middle-income countries.

**28 November, 2017** – Takeda announced that its investigational Zika virus vaccine candidate (TAK-426) progressed into Phase 1 clinical trial. The clinical trial intends to evaluate safety and immunogenicity of TAK-426 in 240 subjects between the ages of 18 and 49 across the continental US and US territories.

APPENDIX II

# Access to Vaccines Index 2017 — How the industry performs



**RESEARCH & DEVELOPMENT**

In Research & Development, GSK and Johnson & Johnson lead, with strong yet differing approaches. GSK has the largest pipeline, while Johnson & Johnson makes the largest R&D investments as a proportion of vaccine revenue. Both companies aim to address high-need vaccine gaps, and both have access plans in place for over half their late-stage vaccine candidates.

**PRICING & REGISTRATION**

In Pricing & Registration, GSK leads, followed by Merck & Co., Inc. and Sanofi with equal total scores. GSK’s pricing strategy for vaccines is the most sensitive to each country’s ability to pay, relative to peers’ strategies. GSK and Merck & Co., Inc. lead in transparency, publishing their complete pricing strategies and reporting that they do not prohibit governments from publishing manufacturer prices. Sanofi is the leader in registration, filing to register most of its relevant vaccines in 30-50% of both low- and lower middle-income countries in scope.

**MANUFACTURING & SUPPLY**

In Manufacturing & Supply, GSK and Sanofi score highest. Both demonstrate strong processes and commitments to help ensure vaccine production meets demand. They further support global vaccine supply through capacity building in manufacturing. The two companies have also implemented vaccine presentations and packaging that help to overcome local access barriers (e.g., vaccines that are easier for health workers to administer).

**Figure 4. Access to Vaccines Index - Overall performance**

The number of cells represents the maximum possible score. Coloured cells represent points attained.

**KEY FINDING: R&D FOR VACCINE ADAPTATIONS**

# Adaptations to existing vaccines account for half of vaccine R&D projects

The characteristics of a vaccine – such as its thermostability, number of doses required, or the serotypes it targets – have a substantial impact on how immunisation programmes can be effectively implemented, particularly in low-resource settings. Often, the best combination of characteristics becomes apparent once a vaccine has been rolled out in real-world settings. Once this happens, further R&D is required to improve the vaccine.

The Access to Vaccines Index has evaluated the pipelines of eight vaccine companies: Daiichi Sankyo, GSK, Johnson & Johnson, Merck & Co., Inc., Pfizer, Sanofi, Serum Institute of India and Takeda (see figure 8). The industry is responding to cases where existing vaccines need to be adapted: such projects account for 48% of projects in the pipeline (43/89), with one project aiming for multiple adaptations (see figure 9).

Some 30% of adaptive R&D projects involve multivalent vaccines. For example, Serum Institute of India is developing a 10-valent pneumococcal conjugate vaccine (PCV). It targets the serotypes prevalent in 70% of the population affected by pneumococcal disease in Africa, Asia and Latin America. Meanwhile, 28% of adaptive R&D projects focus on either characterising or improving the temperature stability of a vaccine, and 44% target a range of other improvements, including in efficacy, immunisation schedules, yield of production, or formulations to allow for easier administration.

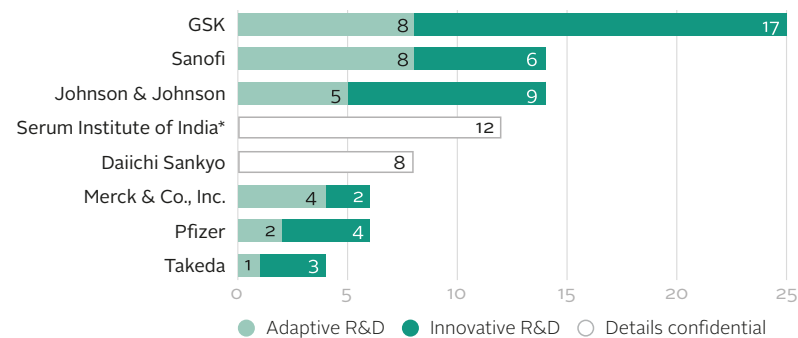
Taken as a group, the 43 adaptive R&D projects are diverse, with companies

working toward a wide variety of adaptations. For example, GSK is characterising the thermostability of its PCV Synflorix®; Sanofi is doing the same for its cholera vaccine Shanchol®; and in 2015, Merck & Co., Inc. received Controlled Temperature Chain approval for its HPV vaccine Gardasil®. Five pro-

jects focus on approving vaccines for use in lower age groups: including GSK for influenza vaccines and Sanofi for a meningococcal vaccine. Serum Institute of India received approval in late 2014 for children under one year to receive a 5 µg dose of its meningococcal A vaccine (MenAfriVac®).

**Figure 8. Vaccine adaptations account for half of R&D projects; individual company pipelines vary.**

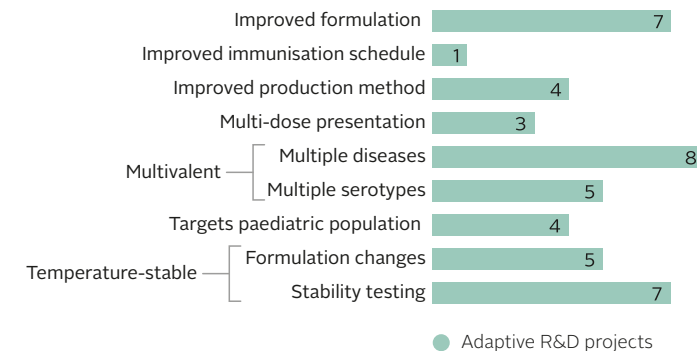
GSK and Sanofi are undertaking the most projects to adapt existing vaccines.



\* Serum Institute of India's pipeline is based on publicly available sources. It has additional projects for which the data are confidential.

**Figure 9. Companies are working toward a wide variety of vaccine adaptations.**

Companies have 43 adaptive vaccine R&D projects for diseases in scope. Adaptive R&D projects for multivalent vaccines are the most common, followed by temperature-stability projects.



One project is counted twice: it falls into two categories of adaptation.

**KEY FINDING: VACCINE PRICING**

# When setting prices, all companies consider countries’ Gavi status – most also consider GNI per capita

Vaccines are among the most cost-effective ways of protecting people against disease, not least children, who can be safeguarded from the often debilitating impact of many childhood illnesses. Nevertheless, immunisation programmes involve considerable costs, with vaccine prices accounting for a significant proportion. Understanding how vaccine prices are determined can help shape expectations for procurers, donors, market-shapers and other companies when entering negotiations. A better understanding here can lead to more affordable vaccines, in turn enabling greater immunisation coverage and greater market sustainability. The Access to Vaccines Index asked six companies which factors they consider when setting vaccine prices: GSK, Johnson & Johnson, Merck & Co., Inc., Pfizer, Sanofi and Serum Institute of India.

Collectively, the six companies consider 18 diverse factors when setting vaccine prices, with the most attention being paid to the conditions (not least economic conditions) in a given country. Indeed, the only factor considered by all six companies is a country’s eligibility for Gavi support; four companies also consider Gross National Income (GNI) per capita. Cost plays a role in vaccine pricing, including investments companies make in clinical development or in manufacturing facilities. The public health value of a vaccine to healthcare systems is also used to inform vaccine prices.

All six companies offer discounts to Gavi-eligible countries. Most also publicly commit to offer discounts for some vaccines for a set time period to the 16 countries classified in 2016 as Gavi-transitioning. Companies generally offer their lowest prices to Gavi-eligible countries. However, many middle-income countries (MICs) are not eligible for Gavi support (or PAHO’s Revolving Fund).

Many also face healthcare budget constraints. The Index does not find clear evidence that companies systematically consider countries’ ability to pay when setting vaccine prices in MICs. This raises concerns that many MICs may not be able to afford vaccines, thus limiting immunisation coverage, particularly of newer, more expensive vaccines.

**Figure 10. Companies report considering 18 factors when setting vaccine prices.**

The 18 factors can be divided into five different groups. The largest focuses on conditions in a given country, such as its Gavi status. Others look at aspects of government commitment, or the value of or need for the vaccine in question, including related costs.

Type of factor	Factor	GSK	Johnson & Johnson	Merck & Co., Inc.	Pfizer	Sanofi	Serum Institute of India
Country feature	Gavi status (eligible, transitioning)	●	●	●	●	●	●
	GNI per capita, for at least some countries	●	●		●	●	
	Humanitarian emergency discount	●			●		
	Fiscal capacity and health spending			●			
	Mechanisms & policies for procuring vaccines			●			
	Competitive environment					●	
	Existence of distinct distribution networks (e.g. public/private)					●	
Extent of government’s commitment	Target population coverage	●		●			
	Covering entire birth cohort				●		
	Vaccinating catch-up cohorts	●					
	Volume to be purchased	●					
	Duration of contract	●					
Value of vaccine	Public health value to healthcare system			●	●		
	Scientific innovation vaccine represents				●		
Need for vaccine	Public health need			●			
	Disease burden & which population segments are affected by the disease					●	
Required investment	In clinical development programmes				●		
	In manufacturing facilities & workforce				●		



**KEY FINDING: ALIGNING SUPPLY AND DEMAND**

# Companies take diverse approaches to aligning supply with demand

Vaccine demand can outstrip supply for a range of reasons, including unexpected outbreaks, inaccurate demand forecasting and manufacturing interruptions. In recent years, many countries have reported vaccine shortages. These can disrupt immunisation programmes, putting herd immunity at risk and increasing the chance of outbreaks. While coordination between stakeholders is needed to address shortages, vaccine companies can take specific actions to help prevent them (see figure 11). The Access to Vaccines Index has evaluated the approaches taken in this area by six companies: GSK, Johnson & Johnson, Merck & Co., Inc., Pfizer, Sanofi and Serum Institute of India.

Four of the companies take comparatively strong approaches to aligning vaccine supply with global demand: GSK, Johnson & Johnson, Merck & Co., Inc. and Sanofi. Their approaches are deemed strong because their internal processes for aligning supply and

demand include four or more of the eight elements the Index has identified as key to improving supply, and because they commit to staying in vaccine markets where there are few or no other suppliers and/or to communicating when they plan to reduce or cease supply of a vaccine (see figure 11).

All six companies implement a combination of the elements assessed. No particular combination is identified as best practice, but implementing more elements is expected to better prevent shortages. Each company's approach is likely to be linked to its portfolio, structure and business model. Five companies regularly review levels of supply and demand, and four have processes for scaling up production when shortages are forecast. Five also commit to continuing to supply needed vaccines, and/or to notifying stakeholders when planning to reduce supply. As vaccines for specific diseases may have few suppliers, such commitments help

to increase accountability and provide confidence around supply. Where companies do exit markets, providing stakeholders with early notice can allow other suppliers' production and distribution plans to be adjusted to minimise negative impacts on public health.

All six companies are taking action to align supply with demand, which suggests that vaccine shortages are, in some cases, being detected, mitigated and/or prevented. The existence of ongoing vaccine shortages, however, shows that more needs to be done. The industry needs to continuously monitor and improve its approaches to preventing shortages, for instance by considering how they can implement the key actions shown in figure 11. Other stakeholders also need to play their part, with clear, accurate and timely demand forecasting supported by sustainable purchasing commitments where possible.

**Figure 11. Companies take diverse approaches to aligning supply with demand**

Most companies implement elements and supply commitments. GSK, Johnson & Johnson, Merck & Co., Inc. and Sanofi take stronger approaches.

	GSK	Johnson & Johnson	Merck & Co., Inc.	Pfizer	Sanofi	Serum Institute of India
<b>Key elements for preventing/responding to shortages</b>						
Commitment to ensure access in case of shortages	●	●	●			
Regular and timely supply-and-demand review process	●	●	●	●	●	
Clear process for escalating and acting on identified issues	●				●	
Reserve stocks (not including externally managed stockpiles)		●	●	●		
Processes for scaling up production		●		●	●	●
Processes for re-allocating stocks	●				●	
Donations or affordability measures in emergency situations	●					
Consideration of other suppliers in a market when making decisions	●					
<b>Commitments to continuing supply of vaccines</b>						
Commitment to stay in vaccine markets where needed		●	●			●
Commitment to communicate plans to reduce supply externally	●		●		●	

● Company has a clear commitment/process



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