

# Role of vaccine manufacturers in developing countries towards global healthcare by providing quality vaccines at affordable prices

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## Abstract

Vaccines represent one of the greatest achievements of science and medicine in the fight against infectious diseases. Vaccination is one of the most cost-effective public health tools to prevent infectious diseases. Significant progress has been made in expanding the coverage of vaccines globally, resulting in the prevention of more than two million deaths annually. In 2010, nearly 200 countries endorsed a shared vision to extend the benefits of vaccines to every person by 2020, known as the Decade of Vaccine Initiative (DoV). Vaccine manufacturers in developing countries, as represented by the Developing Countries Vaccine Manufacturers Network (DCVMN), make a significant contribution to DoV by supplying quality vaccines at affordable prices to the people who need them most. About 70% of the global Expanded Program on Immunization (EPI) vaccine supplies are met by DCVMN. Besides EPI vaccine supplies, DCVMN is also targeting vaccines against rotavirus, Japanese encephalitis, pneumonia, human papillomavirus, meningitis and neglected tropical diseases. This article reviews the roles and contributions of DCVMN in making the vaccines accessible and affordable to all.

**Keywords:** Affordable healthcare, decade of vaccines, Developing Countries Vaccine Manufacturer Network, vaccines

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## Introduction

The last decade saw significant advances in developing, introducing and expanding the reach of vaccines globally. More people than ever before were vaccinated, resulting in significant achievements, including the near eradication of polio and significant reductions in deaths caused by vaccine-preventable diseases (diphtheria, measles, neonatal tetanus, pertussis). Around 2 million deaths among children under 5 years of age are prevented annually despite an increase in birth cohorts every year [1]. Further, increasingly sophisticated vaccines, including pneumococcal conjugate vaccine and rotavirus and human papillomavirus (HPV) vaccines, were rolled out globally [2]. The vaccine industry based in the developed world (as represented by the International Federation of Pharmaceutical Manufacturers Association) and developing countries (represented by the Developing Countries Vaccine Manufacturers Network, DCVMN) plays a significant role in the achievement of global immunization targets. The International Federation of

Pharmaceutical Manufacturers Association contributed with research and development of newer vaccines and DCVMN played a crucial role in supplying the required quantities of Expanded Program on Immunization (EPI) vaccines at affordable prices, which resulted in more vaccine coverage and universal accessibility of EPI vaccines [3]. In 2010, nearly 200 countries endorsed a shared global health vision known as the Decade of Vaccine Initiative (DoV) (2010–2020) with the overall aim of increasing vaccine coverage in developing countries to 90% to prevent the deaths of around 7.6 million children under 5 years of age [4]. The vaccine industry in developed and developing countries will play a significant role in these initiatives. This article provides an account of the roles and contributions of DCVMN in increasing access to basic childhood vaccines and of their contributions to the fight against pandemic and regional infectious diseases.

This review is a qualitative case study analysis based on published literature reports and the authors' experience in the domain. This article summarizes the trends observed in the

global market, especially after the manufacturers from the developing countries started supplying their vaccines to United Nations (UN) agencies after getting them prequalified by WHO. This had a tremendous impact, especially in the developing countries where these vaccines were introduced, through the availability both of cheaper vaccines and of newer vaccines at an early date after their introduction in the developed world. This especially includes the combination vaccines containing diphtheria/tetanus/pertussis (DTP), e.g. DTP-hepatitis B, DTP-*Haemophilus influenzae* type B (Hib), DTP-hepatitis B-Hib; and also vaccines containing measles, e.g. measles, measles-rubella, measles-mumps-rubella. The recent example of introduction of meningococcal A conjugate vaccine (MenAfriVac™) in the Sub-Saharan Africa meningitis belt is a classic example of this success story. In addition to this, the progress made by the developing countries vaccine manufacturers for developing vaccines against pandemic influenza and seasonal influenza is a great example, which not only made these vaccines available, but also increased global capacity for making influenza vaccine (both seasonal and pandemic) in the developing world, which could be harnessed in future pandemics.

### Global Vaccine Business: Growth in Developed, Emerging Markets and UN Agencies Procurements

The global vaccines market was estimated at around US\$ 32.05 billion in 2012. The market witnessed growth rates of above 8% and is expected to reach US\$ 84.44 billion by 2022 [5]. The increase in sales has been the result of new product introductions and rising usage, particularly in South America, Europe, India and China. North America leads the market with a share of >40%, followed by Europe with 32% and the developing world with a share of around 20%. The developed markets represent 15% of the total global population but contribute 82% of total sales in value, which is attributed to high vaccination rates and the launch of newer vaccines.

The emerging markets in India, China, Brazil, Russian Federation, Republic of Korea, and Turkey recorded double digit growth rates in 2012 vaccine sales and are anticipated to become larger than the developed markets by 2020 [6]. For instance, the markets in India and China, with rapidly expanding pharmaceutical and biotechnology industries, are expected to reach US\$ 2.7 billion and US\$ 3.1 billion, respectively, in 2015. Similarly, the South America vaccine market is expected to rise by 10.0% per year to reach US\$ 2.7 billion in 2015. Key factors driving growth for human vaccines in emerging markets include significant unmet medical needs,

and the increased funding support from government and non-government international agencies for the development and introduction of new vaccines in the developing world. The UN Educational, Scientific and Cultural Organization (UNESCO) science report in 2010 shows that the emerging markets of China, India and Brazil are by many indications leading most of the world in the pace of scientific and technological developments [7].

Supplies through the UN Vaccine division cater to around 36% of the world's children as part of its commitment to improving child survival. In 2012, the UN Children's Fund (UNICEF) procured around 1.9 billion doses of vaccines, including polio, measles, tetanus, bacillus Calmette-Guérin and yellow fever, at a value of \$ 1053 million, which constitutes around 4–7% of the total vaccine market in value [8]. About 75% of vaccines currently procured by UN agencies are produced by manufacturers in developing countries, represented by DCVMN.

The last decade also saw significant growth in the capabilities of suppliers and vaccine manufacturers located in emerging markets. These manufacturers have historically been more focused on UN, Global Alliance for Vaccines and Immunization (GAVI) and WHO markets in the developing world, and are now increasing their product pipelines with newer innovative vaccines to target other markets. The recent acquisition of Bilthoven Biologicals in the Netherlands (sole supplier of inactivated polio vaccines) by one DCVMN member, the Serum Institute of India Ltd, Pune, has allowed the Serum Institute to target markets relevant to polio and combination vaccines with inactivated polio vaccine in both the developing and developed world. In another instance, Shantha Biotech (an ex-member of DCVMN) was acquired by Sanofi Aventis to tap the strengths of Shantha Biotech and manufacture quality affordable vaccines, which further demonstrates the attractiveness of emerging markets [9].

### DCVMN: a Public Health Driven Alliance to Develop Affordable Vaccines

DCVMN was established in 2000 with the vision and mission of increasing the availability and affordability of quality vaccines to protect against known and emerging infectious diseases. It largely supplies vaccines to UN agencies. Historically, vaccine manufacturers based in developed countries have supplied the majority of prequalified vaccines for all countries. During recent years, developed country manufacturers have shown declining interest in EPI supplies and have increasingly focused their production on vaccines that are primarily used in developed countries. As a result of this, the role of developing

country manufacturers in ensuring the global UN supplies of EPI vaccines has become important. Vaccines supplied to UN agencies must be prequalified for consideration in the tenders. The prequalification process is devised and determined by WHO. The manufacturers satisfying certain strict norms of quality, safety and efficacy are prequalified by WHO and listed on the WHO website [10]. The first products developed by developing countries were prequalified for supplies to UN agencies in 1994. Since then, the process has continued, with more products from DCMVN being prequalified every year. Such prequalified and other vaccine manufacturers in developing countries are represented by DCMVN (Tables 1 and 2). As of October 2013, DCMVN has 39 members in 15 countries in Latin America, the Middle East, Africa and the Asia Pacific Region [3, 11].

The DCMVN has consistently worked since its inception (in 2000) towards strengthening the capacity of manufacturers to supply high-quality vaccines. They have contributed >30 vaccine types in various presentations that have been prequalified by WHO for immunization programmes around the

**TABLE 1. List of Developing Countries Vaccine Manufacturers Network members by country. There are a total of 39 members spread over 15 different countries; 12 members are WHO prequalified, which are indicated in bold**

Country	Vaccine manufacturer
Argentina	National Administration of Laboratories and Institute of Health Anlis Dr Carlos G. Malbran
Bangladesh	Incepta Vaccine limited
Brazil	<b>BioManguinhos/Fiocruz</b> Instituto Butantan
China	Beijing Minhai Biotechnology Co., Ltd Changchun BCHO Biotechnology Co. <b>China National Biotech Corporation</b> Hualan Bio Liaoning ChengDa Biotechnology Co., Ltd Sinergium Biotech Sinovac TiantanBio Walvax Biotechnology Co., Ltd Xiamen Innovax Biotech Co., Ltd Finlay Institute <b>The Center for Genetic Engineering and Biotechnology</b>
Cuba	Vacsera
Egypt	Bharat Biotech International Limited
India	Cadilla Pharmaceuticals <b>Biological E Ltd</b> <b>Haffkine Bio-Pharmaceutical Corporation Ltd</b> Indian Immunologicals Ltd <b>Panacea Biotech Limited</b> <b>Serum Institute of India Ltd</b>
Indonesia	<b>Bio Farma</b>
Iran	Razi Vaccine & Serum Research Institute Pasteur Institute of Iran
Korea	<b>Greencross Corporation</b> EuBiologics Co., Ltd <b>LG Life Sciences</b> SK Chemicals
Mexico	Birmax
South Africa	Biovac
Taiwan	The National Institute of Infectious Diseases and Vaccinology
Thailand	BioNet-Asia Co., Ltd Queen Saovabha Memorial Institute <b>The Government Pharmaceutical Organization</b>
Vietnam	Institute of Vaccines and Medical Biologicals Vabiotech

**TABLE 2. WHO Prequalified Vaccines available from Developing Countries Vaccine Manufacturers Network (DCVMN). Source WHO website (accessed on 1 November 2013).**

Name of DCVMN member	WHO prequalified vaccines
1. Bio Farma/Indonesia	TT, DT, Td, DTwP, Hep B, DTwP-Hep B, Measles, mOPV, bOPV, tOPV
2. Biological-E/India	TT, DTwP-Hep B-Hib, JE
3. BioManguinhos/Fiocruz/Brazil	YF, Men. A + C
4. The Centre for Genetic Engineering and Biotechnology/Cuba	Hep B, Hib
5. Chengdu Institute/China	JE
6. Green Cross Corp./Korea	Seasonal and Influenza A (H1N1)— Pandemic Influenza vaccines
7. The Government Pharmaceutical Organization/Thailand	Measles
8. Haffkine Institute/Mumbai	mOPV, bOPV, tOPV
9. The Pasteur Institute, Dakar	YF
10. Serum Institute of India	TT, DT, Td, DTwP, Hep B, BCG, Hib, Measles, Rubella, MR, MMR, Meningococcal conjugate vaccine against serotype A, H1N1 Pandemic Influenza, bOPV, tOPV, DTwP-Hep B, DTwP-Hib, DTwP-Hep B-Hib
11. LG Life Sciences/South Korea	Hep-B, DTwP-Hep B-Hib
12. Panacea Biotech, India	DTwP-Hep B-Hib

*Abbreviations:* Upper-case letters denote full-strength doses of diphtheria (D) and tetanus (T) toxoids and pertussis (P) vaccine. Lower-case 'd' denotes reduced doses of diphtheria used in the adolescent/adult-formulations. Hep B, hepatitis B vaccine; Hib, *Haemophilus influenzae* type b vaccine; wP, whole cell pertussis vaccine; DTwP-HepB, DTwP-Hib or DTP-HepB-Hib, DTwP-based combination vaccines containing Hep B or Hib or both antigens; OPV, oral polio vaccine; mOPV, monovalent oral polio vaccines; bOPV, bivalent oral polio vaccine; tOPV, trivalent oral polio vaccine; IPV, inactivated polio vaccine; YF, yellow fever; JE, Japanese encephalitis vaccine; MMR, combination vaccine containing measles, mumps and rubella antigens.

world. DCMVN is now a major supplier to UN agencies and represents 75% of total procurement volume and around 50% of value in 2012. Additionally, DCMVN members were among the top ten suppliers of Pan American Health Organization (PAHO) supplies in 2012 [12]. DCMVN supplies also helped GAVI in its efforts to immunize an additional 370 million children since 2001, which is reported to have prevented >5.5 million future deaths from hepatitis B, Hib, measles, pertussis, polio, rotavirus diarrhoea and yellow fever. In 2012, 50% of GAVI vaccine suppliers were DCMVN members [13].

Considering research and development capabilities, DCMVN members have >45 products in the pipeline. Also, the first prequalified Japanese encephalitis vaccine was made available by DCMVN for global procurement in 2013. DCMVN work on other vaccines, e.g. rotavirus, pneumococcal and HPV vaccines, is ongoing and the DCMVN members are likely to launch them at affordable prices (Table 3) [14].

The emergence of DCMVN is an excellent example of a partnership model wherein organizations such as WHO, UNICEF, the Bill & Melinda Gates Foundation, donor governments, the Program for Appropriate Technology in Health (PATH), national regulatory agencies and national governments have played a significant role in building the capacity of the vaccine industry in developing countries.

**TABLE 3. Developing Countries Vaccine Manufacturers Network (DCVMN) and future pipeline of vaccines. This list is based on details given in ref. [27]**

Vaccines	DCVMN manufacturer	Country	Comments
Pneumococcal conjugate	BioManguinhos/GSK	Brazil	Under development
	Chengdu Institute/PATH	China	
Rotavirus	SII, India/PATH	India	Phase-3
	Finlay Institute	Cuba	
	Serum Institute of India	India	Phase-2
	Instituto Butantan	Brazil	
Meningococcal vaccines (Includes polysaccharide and conjugate vaccines)	China National Biotech Group	China	Under development
	Biological Evans	India	Under development
	China National Biotech Group	India	Under development
	Finlay	China	Under development
	Serum Institute of India Ltd	Cuba	Under development
	Panacea Biotech	India	Under development
	BioManguinhos	Brazil	Under development
Japanese encephalitis vaccine	Vabiotech	Vietnam	Under development
	Bharat Biotech	India	Phase 3
	Indian Immunologicals	India	Under development
	Panacea Biotech	India	Under development
Seasonal and Pandemic influenza vaccines (also includes vaccines with oil in water adjuvants)	Vabiotech	Vietnam	Under development
	GPO	Thailand	Phase III
	IVAC	Vietnam	Under development
	Butantan	Brazil	Phase I/II (new adjuvant)
	Chinese National Biotech Grp	China	Under development
Malaria vaccine	Birmax	Mexico	Under development
	BioManguinhos	Brazil	Under development
Typhoid vaccine	Bharat Biotech	India	Under development
Dengue vaccine	Finlay Institute	Cuba	Under development
	Biological Evans	India	Under development
Yellow fever	BioManguinhos/Bionet	Brazil	Under development
Yellow fever	ANLIS	Argentina	Phase III
Hepatitis A	BioManguinhos	Brazil	Under development
Leishmaniasis	BioManguinhos	Brazil	Under development
Leptospirosis	BioManguinhos	Brazil	Under development
Human papillomavirus vaccine	Serum Institute	India	Under development
	CCGEB	Cuba	Under development
	Innovax	China	Under development
	Indian Immunologicals	India	Under development
Chikungunya	Indian Immunologicals	India	Under development
Anthrax vaccine	Panacea Biotech	India	Phase III

The case studies that follow highlight the achievements of DCVMN in facilitating important milestones of global health.

## Case Studies

### DCVMN and the Measles & Rubella Initiative

The Measles & Rubella (MR) Initiative is a global partnership committed to eliminate measles, rubella and other associated syndromes such as congenital rubella syndrome (CRS) from the globe. Founded originally as the Measles Initiative in 2001, it is led by the American Red Cross, the UN Foundation, UNICEF, the US CDC (Atlanta, GA, USA) and WHO. Since

2001 the initiative has facilitated the delivery of more than 1 billion doses of measles vaccine in more than 60 developing countries leading to 85% measles vaccination coverage and 74% reduction of measles deaths globally [15]. These efforts have contributed significantly to a reduction in overall child mortality, as per Millennium Development Goal 4.

Members of DCVMN played an important role in supplying vaccines to the MR Initiative. It is worth noting that the bulk of the measles vaccine supplies to the MR Initiative was by a sole DCVMN supplier, Serum Institute of India Ltd (70% of supplies), which is now the world's largest manufacturer of MMR group vaccines.

### DCVMN and eradication of rubella and CRS in the WHO region of the Americas

PAHO adopted a resolution in 1993 calling for the elimination of rubella and CRS in the Americas by 2010. Elimination was defined as the interruption of endemic rubella virus transmission in all countries of North America, Central America, South America and the Caribbean for >12 months and no occurrence of CRS cases attributed to endemic transmission. To accomplish this goal, PAHO developed a strategy of introducing rubella-containing vaccine into the routine vaccination programmes of all countries for children aged 12 months and reaching  $\geq 95\%$  coverage in all municipalities. It was decided to use MR vaccine in this campaign based on benefit, and risks versus price. From 1998 to 2005, vaccination campaigns were carried out in Chile, Brazil, Costa Rica, Honduras, Ecuador and El Salvador; another 18 countries were added in subsequent years. The campaigns had a huge impact on measles as well as preventing the re-establishment of endemic measles virus transmission in the region [16].

A consistent supply of vaccine was ensured by the DCVMN member, the Serum Institute of India, to whom PAHO later extended a special award. This vaccination effort led to eradication of rubella in the Americas, with the last endemic case observed in February 2009, which was 10 months before the target. It is reported that beginning in 2001, over a 15-year period the rubella and CRS initiative will have saved an estimated US\$ 3 billion by preventing >112 500 CRS cases in Latin America and the Caribbean. The eradication of rubella in the Americas is also an excellent example of pull mechanisms for accelerated immunizations. With the notable success of the MR initiative and rubella elimination in the WHO region of the Americas, the MR Initiative launched a new Global Measles and Rubella Strategic Plan in 2012 that includes goals for reduction of global measles deaths by at least 95% compared with 2000 levels, and for achieving regional MR/CRS elimination. Manufacturing capacities of DCVMN will be important for Global Measles and Rubella and the Strategic Plan [17].

### DCVMN and supply of pentavalent vaccines

The development and uptake of pentavalent vaccines against five diseases—diphtheria, tetanus, pertussis, Hib and hepatitis B—represents the most important cornerstone of this decade. DCVMN is a major partner to this initiative, which was launched by the GAVI alliance and aims to achieve maximum coverage of pentavalent vaccines. GAVI pentavalent demand from 2013 to 2016 is c.750 million doses, representing c.84% of the global pentavalent volume, 81% of the global pentavalent value, and 63% of the global DTP value [18]. Over 70% of current GAVI/UNICEF pentavalent supplies are met by DCVMN members based in India. This has also resulted in pricing innovation wherein the price of the pentavalent vaccine has dropped by 66% in the last 6 years, moving from US\$ 3.60 in 2006 to US\$ 1.19 (ten-dose presentation quoted by one DCVMN member) in 2013.

### Global Polio Eradication Initiative and DCVMN

In the last decade, the Global Polio Eradication Initiative achieved great progress. The best indicator for this achievement is the eradication of polio from India, which was at one time termed a world epicentre of polio cases [19,20]. This achievement would not have been possible without the consistent and timely supplies of oral polio vaccines (OPV) by DCVMN members. In this initiative the DCVMN member Panacea Biotech, India, contributed 9.2 billion doses of OPV over two decades (1990–2011). Other members of the network, Bharat Biotech and Haffkine, based in India also each contributed about 1.5 billion doses since 2006. The world is now looking towards the introduction of IPV vaccines as a measure to interrupt polio virus transmission and an increase in global production capacities for IPV is envisaged. DCVMN members are already taking steps to increase production capacities. The development of IPV vaccines will also involve dose-sparing approaches, such as the use of adjuvants or process innovations to further increase production capacities or reduce vaccine costs [21,22].

### DCVMN and fight against regional epidemics

Vaccine manufacturers in DCVMN have also accelerated their efforts in undertaking development and production of innovative vaccines. The DCVMN research and development product pipeline currently houses 100 projects, of which 15 target new antigens in the area of regional diseases. One of the major highlights is the recent development of a polysaccharide conjugate vaccine against group A meningitis, which has been responsible for causing recurring epidemics in the meningitis belt of Sub-Saharan Africa with a population of 300 million. In 2001, it became apparent that no developed country manufacturer was ready to develop or supply this vaccine at an

affordable price of <50 cents/dose. The Serum Institute of India Ltd, a DCVMN member, was approached for development of this vaccine through partnerships with the Meningitis Vaccine project, PATH, WHO and the Center for Biologics Evaluation and Research, USA (CBER) [23,24]. The vaccine was licensed and prequalified in 2010 and within 6 months of vaccine introduction in Burkina Faso, Mali and Niger, only four cases of meningitis A were reported, compared with 250 000 cases and 25 000 deaths in the worst ever epidemic in the year 1996–1997 [25,26]. By the end of 2012, more than 100 million people were vaccinated in ten countries in Africa and it has been reported that vaccination resulted in a 94% drop in rate of incidence during the meningitis season. Furthermore, no cases of serogroup A meningococcal meningitis were detected in the three vaccinated regions. This is reported as one of most significant outcomes from public health interventions.

Other innovation highlights from DCVMN in the fight against regional threats are the development and recent approval of the world's first hepatitis E vaccine, which was jointly developed by Xiamen Innovax Biotech and the China National Institute of Diagnostics and Vaccine Development in Infectious Diseases. As per WHO estimates, over three million cases of hepatitis E are reported every year. Xiamen Innovax, a member of DCVMN, is also developing HPV vaccines using virus-like-particle-based approaches [27].

Another achievement of DCVMN in the fight against regional threats has been the development, licensing and WHO prequalification of Japanese encephalitis vaccine by DCVMN members Biological Evans, India and Chengdow, China in 2013. It is expected that the availability of WHO prequalified vaccines from DCVMN members will increase global access to this vaccine. In yet another significant development, the launch of rotavirus and typhoid vaccines by Bharat Biotech, India further supports the DCVMN potential to undertake development and licensing of sophisticated vaccines.

### DCVMN and the fight against pandemic threats of global importance

An effort to ensure global access to pandemic influenza vaccine and to increase the global vaccine production capacity of influenza vaccines was launched by WHO in 2006–2009 [28]. DCVMN responded to this initiative positively and member manufacturers developed pilot capacities to develop seasonal influenza vaccines until 2008 [29]. In 2009, the influenza A (H1N1) virus pandemic threat was detected and issues related to access, supply and affordability were highlighted and a call was issued globally to produce the vaccine. It is noteworthy that three DCVMN members from India readied the vaccine for global use in a record time of 9 months [30]. The vaccine was used globally in the fight against pandemic influenza. This



constitutes an interesting example wherein DCVMN members showed maturity and capacity to undertake vaccine development in the case of future pandemics [31]. One of the DCVMN members also obtained WHO prequalification for its intranasal and injectable inactivated influenza vaccine in 2013.

## Discussions and Perspectives for the Future

Members of DCVMN have played a major role in supplying quality vaccines at affordable prices to UN agencies. The previous sections provide an overview of the contributions of DCVMN towards reliable and consistent vaccine supplies. Clearly, vaccines against diseases such as polio, measles, rubella, diphtheria, tetanus and pertussis have a significant impact on reduction of deaths in children under 5 years of age. DCVMN members have taken demonstrable steps towards developing production capacities for basic EPI vaccines, which is also evident from the fact that WHO prequalified vaccine manufacturers in DCVMN have nearly doubled in the last decade. The manufacturers followed approaches of build or buy (fill or finish), or partner-based approaches to meet these supplies, e.g. availability of OPV bulk from PT BioFarma (Bandung, Indonesia) to other DCVMN members resulted in not only meeting demand for OPV in countries' immunization programmes but also WHO Pulse polio programmes towards the eradication of polio. The case studies of measles, rubella and polio are the best examples of DCVMN achievements in meeting global EPI supplies. The production capacities of DCVMN for EPI vaccines are expected to play a significant role in DoV objectives of further increasing the coverage of measles, polio, rubella and DTP vaccines in resource-poor countries. These achievements of DCVMN are also attributed to the support partner organizations such as WHO, Netherlands Vaccine Institute, UNICEF, PAHO, Bill & Melinda Gates Foundation, PATH, National Institute for Biological Standards and Control (NIBSC), CDC Atlanta, Sabin Vaccine Institute and CBER, which led to capacity building of member manufacturers [32,33]. The network itself has strengthened the capacity of manufacturers by facilitating information sharing, encouraging technology transfer activities and representing the manufacturers at various international forums.

Technology transfer is the process of sharing skills, knowledge, technologies, methods of manufacturing and facilities among companies, governments and other institutions to ensure that the scientific and technological developments are accessible to a wide range of users. Technology transfers played an important role in capacity building of developing country manufacturers towards the supply of Hib, influenza and meningococcal conjugate vaccines [34,35]. It is important to

note that not every emerging manufacturer is a candidate for such technology transfers. The recipient should have the scientific capacity to facilitate the transfer process, stringent manufacturing and regulatory standards to ensure that the transferred product is safe and effective and is scalable [36]. International agencies such as WHO, PATH, GAVI, Netherlands Vaccine Institute, Bill & Melinda Gates Foundation, CBER, CDC Atlanta and national regulatory agencies played a significant role as partners for these technology transfers. The case studies of pentavalent supplies, development of meningococcal conjugate A vaccine at <50 cents/dose and development of pandemic influenza vaccines highlight the importance of technology transfers and the capacity of DCVMN to undertake such successful technology transfers. These technology transfers and partnerships further helped in building the capacity of developing country manufacturers in undertaking the development of sophisticated vaccines [37]. Table 3 highlights the products in development, suggesting that in the next 5 years DCVMN will see the launch of innovative vaccines such as those against rotavirus, pneumococci, HPV and cholera, and vaccines against neglected diseases including dengue fever and *Leishmania* diseases. The products in the pipelines also reflect the merits of innovative access models based on push and/or pull mechanisms, such as advanced market commitment for pneumococcal conjugate vaccines. These vaccines will be important for DoV initiatives as rotavirus and pneumonia kill around 500 000 and 800 000 children, respectively, in developing countries each year. The rotavirus and pneumonia vaccines from DCVMN members are expected to bring down the prices of these vaccines globally. The future offers new opportunities for building vaccine capacities in developing countries, product development partnerships, joint ventures and best practices for quality control and guarantee of vaccines, leading to greater coverage. To seize these opportunities the vaccine industry in developing countries will also need to demonstrate continued success in addressing the challenges affecting regulatory approval, manufacturing, intellectual property regimens, financing and, most importantly demand predictability [38].

Newer vaccines in DoV offer opportunities to improve public health. However, to realize their benefits in developing countries, DCVMN expects support from international agencies in terms of funding, advocacy, strengthening national agencies in making evidence-based decisions on introduction of vaccines and enhancing the operational components of vaccine supplies including storage and supply chains [39]. The DoV also poses an important question of whether the existing financing mechanisms will suffice to maintain coverage at current levels for existing vaccines while supporting the introduction of newer vaccines. It is estimated that by 2030 there may be as

many as 20 vaccines in routine use whose applications will cost the world as much as US\$ 20 billion a year, which is far in excess of the US\$ 1–2 billion a year that is currently available [4]. There are similar questions on DCVMN business models to deliver affordable vaccines on a sustainable basis. In a recent study on emerging vaccine manufacturers performed for GAVI, it was suggested that emerging vaccine manufacturers who are prepared to develop innovative products and license these products for global markets will have better chances of sustaining the future markets [9]. Many manufacturers in DCVMN are taking significant steps in investing or upgrading their manufacturing capacities, improving their quality systems and most importantly becoming partners in international initiatives for the development of sophisticated vaccines [10]. DCVMN expects that international models of partnerships, synergies, political will, efficient policies that support the latest manufacturing capabilities, supplies, access and support to research and development innovations will maximize the benefits of immunization. In summary, DCVMN offers the right blend of public and private companies to deliver affordable vaccines and will have an important role to play in meeting the future immunization targets of global healthcare.

## Conclusion

The review showcases the growth, potential and achievements of DCVMN in the global vaccination landscape. The review further highlights the aspirations of DCVMN to undertake the development of innovative vaccines. DCVMN expects new approaches, policies to enhance capabilities, better and innovative business models, collaborations with international firms, improved intellectual property protection regimens, etc. It is important to realize that success in biopharmaceutical innovation is about the potential to adapt, scientifically, globally and nationally in relation to the broader global pipeline of vaccines. DCVMN is observing technological upgrading of existing manufacturers leading to more competitive vaccines for the generic market and at the same time is improving capabilities when it comes to development of newer vaccines at lower development costs. In this respect, DCVMN, in terms of greater economies of scale and scope of capabilities, appears to be in an advantageous position to undertake the DoV initiatives and goals.

## Transparency Declaration

The authors SJ, MG and SG are affiliated to the Serum Institute of India Ltd, which is a DCVMN member. The views expressed

in the article are solely based on authors' studies and analysis and do not necessarily represents the opinions of either the Serum Institute of India or DCVMN.

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