

*Speech by*

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*Vaccine Development in the Developing World;  
past, present and future: SEAR Perspective*

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# **Vaccine Development in the Developing World; past, present and future: SEAR Perspective**

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According to cost-effectiveness studies in the 1980s and 1990s; immunization against childhood diseases is one of the most cost-effective public health interventions for prevention of child illness and death.

Although the cost of fully vaccinating a child has increased from US\$ 15 to US\$ 26 over the past 30 years, immunization remains one of the most cost-effective public health interventions. This cost increase has been mostly due to the introduction of additional antigens. There are several implications of introduction of new vaccines in developing countries, e.g., cost, affordability and sustainability, logistics, cold chain, adverse effects, safety, short-and long-term issues.

Prior to the introduction of routine immunization against the six traditional EPI diseases in the 1980s, countries in the South-East Asia Region (SEAR) reported a disease burden of more than 700,000 cases in a population of 1.05 billion. By 2008, as a result of routine immunization, the disease burden decreased by 81% to less than 140,000 cases in a population of 1.76 billion.

WHO estimates that immunization can be linked to a 25% reduction in the under-five child mortality. This is with the condition that a high coverage of 90% with traditional and new vaccines is achieved. There was global vaccine shortage during

the 1990s (1990-2000). Prior to this shortage, UNICEF procured a majority of the vaccines used in the Region. The vaccine shortage was due mainly to changes in the supply and demand for traditional EPI vaccines. These changes affected vaccine supply to a number of countries in the Region.

Some of these “market changes” are as follows: the merger of major pharmaceutical companies with large multinational conglomerates; the change in industry market strategy to stop production of traditional vaccines in favour of more sophisticated technology and more lucrative products, such as combination vaccines, i.e., Hib-pentavalent vaccine, which uses Diphtheria, Tetanus, and Pertussis (DTP) as its base.

In order to meet demand for the production of combination vaccines, manufacturers procured a major proportion of the available DTP in the market, particularly from vaccine manufacturers in developing countries.

With a greater variety in the availability of vaccines in the global market, developed and developing countries started using different vaccines. e.g., vaccines produced by the use of more sophisticated technology; more advanced developed countries started using DTP vaccine containing acellular pertussis, which is more expensive; while developing countries continued using DTP containing whole cell pertussis which has less sophisticated technology and is cheaper.

This situation jeopardized the global supply of the affordable vaccines; supply policy, funding policy, the EPI programme in developing countries due to lack of funds to buy vaccines. Due to the demand for different vaccines, developing

countries emerged as a distinct and important market for vaccines influenced by large multinational conglomerates; expensive vs cheap vaccines. From 2000 to 2010, 10 of the 14 vaccine manufacturers with long-term agreements with UNICEF, either partially or totally stopped production of the traditional EPI vaccines. At the same time, by 2010, the global market for vaccines had grown annually by 15% in financial terms, reaching US\$ 21 billion.

The vaccine demand in developed countries represented 82% of industry revenue, but, this demand is only 12% of its volume. Profitability has risen significantly. This profitability has been driven by proprietary products and technology, targeting the high-income market. Consequently, the investment in R&D rose significantly, comparable with the pharmaceutical industry.

In developing countries which also include some countries in the South-East Asia Region, the vaccines used in national immunization programmes were non-patented products produced in the private sector (of developing countries). In order to meet the demand, these private companies tried to focus on increasing their capacity for large volume production. There was lack of investment in R&D.

At the same time, they were trying to establish quality assurance systems in compliance with WHO criteria. In 2000, to ensure a consistent supply of affordable quality vaccines, manufacturers in developing countries formed a non-profit public health alliance called the “Developing Country Vaccine Manufacturers’ Network” (DCVMN). SEAR with its large population and three vaccine manufacturing countries has become an important focus for global vaccine supply and demand.

SEAR represents a large market; it produces a significant quantity of vaccine; and it provides a centre for clinical trials. Two out of every three children born in the world get immunized with at least one vaccine coming from country members of the DCVMN. This demonstrates the critical role played by vaccine manufacturers in developing countries in ensuring global supply of essential vaccines.

The profit margins for these non-patented vaccines is much less than for patented vaccines; thereby reducing the capacity of DCVMN members to invest in vaccine R&D. Out of 28 members of the DCVMN, 10 are in SEAR, including India, Indonesia and Thailand. India has become a major vaccine producing country, accounting for more than 80% of the DTP group of vaccines produced by DCVMN members.

Since 2000, substantial financial support made by various “international initiatives” has resulted in a focus on clinical trials in developing countries and on technology transfer. Point for consideration – clinical trial vs technology transfer or on importing vaccine in bulk to develop production capacity in developing countries of non-patented vaccines. For example in SEAR, Biofarma – Indonesia, Serum Institute of India, and Biological Evans Limited, India.

These benefited from technology transfer from the National Vaccine Institute (NVI) in the Netherlands in the production of conjugate Haemophilus influenza b vaccine. In 2009, these manufacturers in India and Indonesia produced around 53 million doses of Hib containing vaccine. SEAR has increasingly become a centre for clinical trials.

For example, in India, there are vaccines in clinical trial for oral cholera, rotavirus, anthrax, pneumococcal, meningococcal, measles aerosol, and H1N1. In Indonesia, pre-clinical trials have been initiated for H1N1 vaccine. In Thailand, H1N1, dengue, H5N1 vaccines are being tested; as well as phase 3 clinical trials for HIV vaccine.

In this process, there is an issue of interest of governments' technology transfer, (to invest). SEAR has a large community of well qualified scientists, particularly in the three vaccine producing countries. These countries have rather sophisticated laboratory facilities. The Region with its recognized vaccine producing countries will become an important player in the field of vaccine development and production if the issue of interest and investment by governments can be overcome. (Link to the appreciation of disease prevention).

Vaccines produced in the Region have the potential for global use because of their affordable cost (and assured quality). This potential will provide for regional vaccine security. With this perspective in view, there are challenges that must be overcome for the Region to realize its full potential in achieving self-reliance in the production of affordable vaccines of assured quality.

The lack of interest, incentive and support from governments for R&D, government, institutes, industry – private. Lack of investment by governments and the lack of full compliance with regulatory requirements. Issues relating to IPR. The lack of coordination and cooperation among stakeholders, universities, research institutes, manufacturers, national regulatory authorities (NRAs) and the national

immunization programmes, the lack of fully operational NRAs to provide oversight in all aspects of vaccine development and production.

This is particularly important in considering the number of new vaccines entering the market. Lack of public-private partnerships in the area of vaccine regulation. With WHO support, countries in SEAR have made substantial progress in building the capacity of their NRAs. This is particularly through the process of producing WHO pre-qualification vaccines.

WHO will continue working with governments to strengthen NRA in all 11 Member States. In the three vaccine producing countries, WHO will continue supporting and assisting in improvements in market authorization and licensing; clinical trial authorization and monitoring; on-site regulatory inspections; establishing and monitoring quality management systems within NRAs; and responding to adverse events following immunization (AEFI).

While in the process of review and revisiting its Regional Policy on Vaccine Development, WHO is actively encouraging each Member State to develop a national vaccine policy with goals for the next five to 10 years. As a way forward in fostering regional solidarity, WHO will continue promoting cooperation and coordination among vaccine manufacturers and the regulatory network within the Region. Cooperation – Public/Private, Private/Public, NRAs and Lab Capacity.

This is to ensure a fully functioning vaccine regulatory authority in every country. An important part of this endeavour is for WHO to provide mechanisms for sharing information among countries, guidance to harmonize practice procedures

across the countries and facilitate agreements on regulatory procedures that could be accepted by countries with limited vaccine regulatory expertise.

With these measures, countries with limited regulatory resources would have better access to high quality vaccines at affordable cost. Experience from India, vested interests behind discussion on patent, does push expensive vaccines, make a healthy profit.

### **DCVMN**

India

Indonesia

Mexico

China

Cuba

Brazil

Iran

Senegal

Tunisia

Yugoslavia

Thailand

South Korea

Vietnam

Egypt

South Africa

International Initiatives – Financial Support to Clinical Trials in Developing Countries

The International Finance Facility for Immunization (IFF Imm)

The International Vaccine Initiative (IVI)

Product development partnerships, i.e.

The Malaria Vaccine Initiative

The Advance Market Commitment.