

Immunization Financing in
Developing Countries and the
International Vaccine Market

TRENDS AND ISSUES

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Preface

The Asian Development Bank, in its Policy for the Health Sector, emphasizes the importance of primary health care and its provision to everyone in Asia. The policy favors immunization because of its cost-effectiveness, its significant impact on the burden of disease, and its considerable public health advantages particularly for the poor, children, and women.

But, despite these benefits, immunization programs in the region continue to face many challenges. Among these are the high rate of vaccine-preventable disease; stagnating, declining, or unequal coverage; the slow introduction of new vaccines; and diminishing internal and external resources.

ADB launched the Asian Vaccination Initiative (AVI) in answer to these challenges and in line with its commitment to reduce poverty. The initiative, a regional approach to vaccine financing, is intended to assist developing member countries in strengthening their immunization programs. Under AVI, ADB has helped developing member countries determine the resources they need to carry out such programs.

This report is the first in a series of reports to be published under AVI. It gives an overview of critical issues in immunization financing in developing countries and the international vaccine markets, and it documents financing and procurement mechanisms that have succeeded. With the help of its findings, policymakers in our developing member countries should be able to strengthen their immunization programs and extend their reach to more of the poor and the disadvantaged.



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Abbreviations

ADB	Asian Development Bank
AVI	Asian Vaccination Initiative
BCG	Bacille-Calmette-Guerin Vaccine (antituberculosis vaccine)
CAR	Central Asian Republics
CDC	Centers for Disease Control and Prevention
CIDEF	International Center for Childhood and the Family
CVI	Children's Vaccine Initiative
DtaP	DTP vaccine with acellular pertussis
DTP	diphtheria and tetanus and pertussis vaccine
DT	diphtheria and tetanus vaccine
EPI	Expanded Program on Immunization
EU	European Union
GATT	General Agreement on Tariffs and Trade
GAVI	Global Alliance for Vaccines and Immunization
GNP	gross national product
HBV	Hepatitis B vaccine
Hib	Haemophilus influenzae type B
IPR	intellectual property rights
IPV	injectable polio vaccine
JICA	Japan International Cooperation Agency
KGCC	Korean Green Cross Corporation
NIDs	National Immunization Days
NIH	National Institutes of Health (US)
OPV	oral polio vaccine
PAHO	Pan American Health Organization
PATH	Program for Appropriate Technology in Health
PMC	Pasteur-Merieux-Connaught
PMSV	Pasteur-Merieux Serums et Vaccins
R&D	research and development
SKB	SmithKline Beecham
TAG	Technical Advisory Group
TT	tetanus toxoid

UCI	Universal Child Immunization
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
VII	Vaccine Independence Initiative
WHO	World Health Organization

Introduction

Dramatic and constant change has occurred over the last 20 years in immunization financing for developing countries and in the international vaccine market.

In 1977, the World Health Assembly declared that, by 1990, all children in the world would be immunized. Five years later, UNICEF set the Universal Child Immunization (UCI) target of 80 percent for the six standard childhood vaccines, also by 1990.

Donor funding then increased substantially, and international procurement mechanisms were put in place to help ensure that quality vaccines were provided on time and at affordable prices. The subsequent rapid expansion of the international vaccine market led to economies of scale (for manufacturers and bulk purchasers) and improved production processes. Vaccine prices fell initially, until the cost of expanding production infrastructure reversed the trend.

Donor funding dropped after the UCI goal was achieved, and shifted its focus from general program support to vaccine procurement. New technology and new, albeit often expensive, patented vaccines, as well as growth in the number of vaccine manufacturers, have contributed to further change.

Over this time, manufacturers and purchasers defined the characteristics of the international vaccine market and exploited its possibilities. These two groups have recently started to work on a more collaborative basis.

By 1999, the decline in donor funding, slow progress in introducing new vaccines into countries that needed them, and the danger of reversing gains made in coverage and disease control through UCI had led to a new global initiative—the Global Alliance for Vaccine and Immunization (GAVI). This high-profile alliance of public- and private-sector partners has rapidly mobilized large amounts of funding, both to procure new vaccines for qualified (poor) countries and to improve their immunization programs overall. The alliance is again changing the immunization landscape, through its financial size and force.

The start of a potentially new era in immunization would seem an opportune time to examine the trends and issues in vaccine and immunization financing in developing countries over the last 20 years. The following will be discussed in this paper:

- Recent and projected future trends in grant financing for vaccines and immunization programs

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In 1977, the World Health Assembly declared that, by 1990, all children in the world would be immunized

- International vaccine procurement and financing mechanisms, among them, the Revolving Fund of the Pan American Health Organization (PAHO) and the Vaccine Independence Initiative (VII) of UNICEF
- Major issues in the international vaccine market, including vaccine pricing and strategies to make vaccines more accessible in developing countries

- The price history of Hepatitis B vaccine, as a case study

Lessons learned and conclusions drawn from a discussion of these issues may help guide future investments in immunization.

This paper gives background information for the Asian Vaccination Initiative (AVI), the Asian Development Bank's response to the continuing challenges faced by developing countries in sustaining and strengthening their immunization programs.

Trends in Grant Financing for Vaccines and Immunization Programs

Declining Donor Funding

The UCI goal of 80 percent global coverage for basic EPI vaccines mobilized significant financial support for developing-country immunization programs. However, once the goal was reached in 1990, donor contributions for immunization in general, and vaccines in particular, began to decline. This is shown in Figure 1 by the decrease in funding for immunization programs from UNICEF, traditionally the largest global contributor.

UNICEF grant financing data represent all contributions to the general fund and bilateral donor funds that support country programs through UNICEF. The data show that overall support declined by 67 percent between 1990 and 1998, from \$182 million to about \$60 million. At the same time, immunization assistance declined from 57 percent of total UNICEF health spending to less than 30 percent.

Shifting Donor Focus

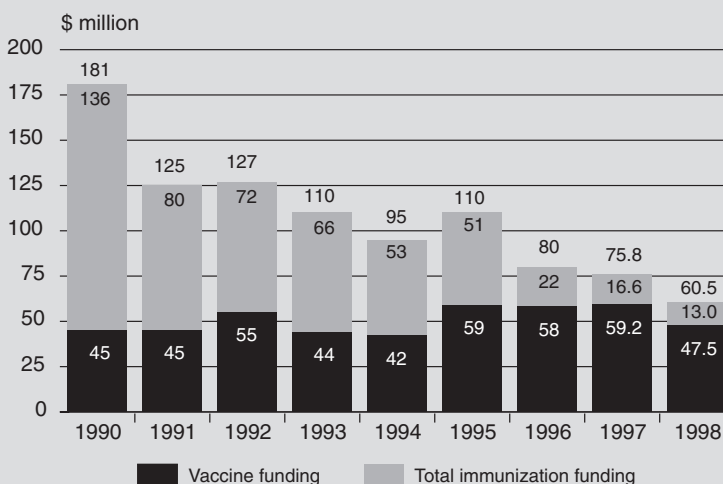
Figure 1 also shows that a growing percentage of immunization funding is moving away from general program support and focusing specifically on vaccines. In 1990, vaccines took up only 25 percent

of total immunization financing; by 1998, they accounted for 78 percent. In real terms, vaccine funding through UNICEF rose from \$45 million in the early 1990s to a peak of \$59 million in 1995–1996 before dropping again in 1998 to \$48 million. Therefore, UNICEF was increasingly funding vaccines (a recurrent cost) at the expense of capital investment in the cold chain, infrastructure, or other program-strengthening areas such as training.

The focus on polio eradication drew funds away from general program support. Data on USAID spending from 1987

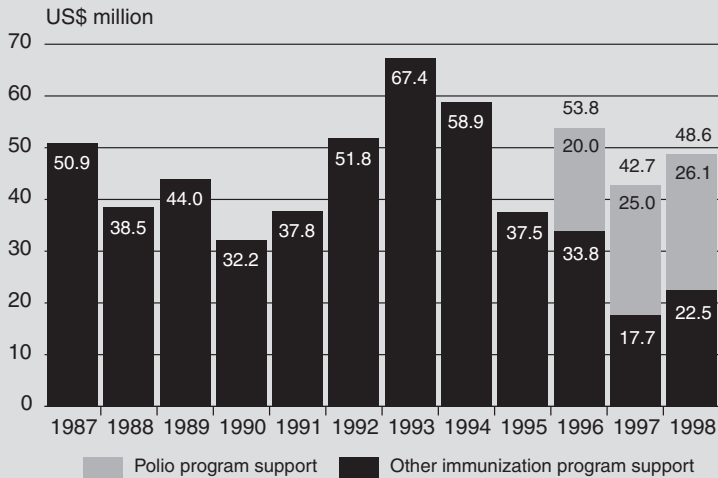
The focus on polio eradication drew funds away from general program support

FIGURE 1
Estimated Contributions for Immunization and Vaccines through UNICEF, 1990–1998



Source: UNICEF (New York)

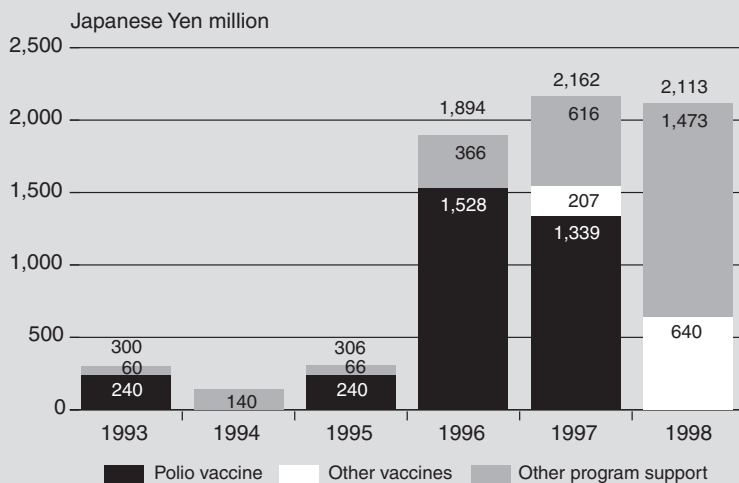
FIGURE 2
USAID Support for Polio and Other Immunization Programs^a



^a Includes funding for technical assistance, cold-chain equipment, training, VII vaccination, some vaccines

to 1998 (Figure 2) clearly show this trend. Funding levels stayed about the same between 1992 and 1998, but since 1996 more than 35 percent of total funds (54 percent in 1998) have been redirected to polio eradication. Meanwhile, USAID support for routine immunization programs has declined markedly, from a high of \$67 million in 1993 to just over \$22 million in 1998.

FIGURE 3
JICA Grant Funding for Worldwide Immunization, 1993–1998



Contrary to the general trend of supporting vaccine procurement, however, USAID support, including assistance for polio programs, has been directed to information, education, and communication (IEC) materials, training, technical assistance, disease surveillance, research, and other key program components. Therefore, despite its specific focus on polio eradication, USAID support is likely to have contributed as well to strengthening immunization and disease control programs overall, especially the development of national surveillance systems and national and regional control laboratories.

Grant financing from the Japan International Cooperation Agency (JICA) rose sharply over the six years to 1998 (Figure 3) but, like UNICEF assistance, went mostly to the procurement of vaccines, particularly polio vaccine (OPV), rather than program strengthening. Vaccines accounted for 81 percent of total immunization support from JICA in 1996 and 72 percent in 1997. JICA spending priorities, however, underwent a reversal in 1998, when 70 percent of its total immunization finance supported program inputs other than vaccines.

Global Alliance for Vaccines and Immunization

With global immunization rates at a standstill, donor funds declining, and disparities in vaccine access widening between industrialized and developing countries, the Global Alliance for Vaccines and Immunization (GAVI) was formed in 1999 to “re-energize the world’s commit-

ment to vaccines and immunization.” GAVI is a coalition of public- and private-sector partners including national governments, organizations associated with the Children’s Vaccine Initiative (WHO, UNICEF, the World Bank Group), the International Federation of Pharmaceutical Manufacturers Associations (IFPMA), and the Bill and Melinda Gates Foundation.

GAVI has had dramatic success in mobilizing resources. Its financing arm, the Global Fund for Children’s Vaccines, was created in 1999 with an initial grant of \$750 million (to be used over five years) from the Bill and Melinda Gates Foundation. The Fund has since leveraged additional funding support from governments and other donors.

The Fund provides financial support directly to low-income countries (per capita GDP of less than \$1,000) to strengthen their immunization services

and to purchase new and underused vaccines. In the future, resources may also be used to speed up the development of vaccines for diseases such as HIV/AIDS, tuberculosis, malaria, and acute respiratory diseases, which cause significant mortality in developing countries.

GAVI has committed more than \$250 million for the five-year period 2001–2006 after two funding rounds, and should commit an even greater amount as further rounds are completed. UNICEF, for its part, contributed \$60 million to immunization programs in 1998.

In summary, donor funding for immunization programs declined overall in the eight years up to 1999 yet gave increasing support to the procurement of vaccines in general, and OPV in particular. However, GAVI, which has mobilized significant global resources within a year of its establishment, is proving to be a powerful force in reversing this trend.

In the future, resources may also be used to speed up the development of vaccines for diseases such as HIV/AIDS, tuberculosis, malaria, and acute respiratory diseases

International Vaccine Procurement and Financing Mechanisms

The decline in donor financing for vaccines and immunization programs has forced countries to finance and procure their vaccine supply independently. However, many countries lack the necessary management and technical capacity, purchasing power, access to hard currency, and international credit to do this effectively. International vaccine procurement mechanisms have accordingly been established to provide assistance and ensure access to high-quality vaccines at reasonable prices. The two most widely used mechanisms—the PAHO Revolving Fund and UNICEF’s Vaccine Independence Initiative (VII)—will be discussed in this section. Their main features are summarized in Table 1.

The PAHO Revolving Fund

The PAHO Revolving Fund is a common fund for the purchase of vaccines and immunization supplies for Latin American and Caribbean countries. Established in 1979, it was the first multi-country mechanism that gave countries access to low-cost, high-quality vaccines (using regional economies of scale), in the process, making the countries more self-sufficient.

The Fund offers the option of paying in local currency and on delivery, thus eliminating two major procurement obstacles developing countries face in the international open market.

Description

The Fund operates as follows (see Figure 4):

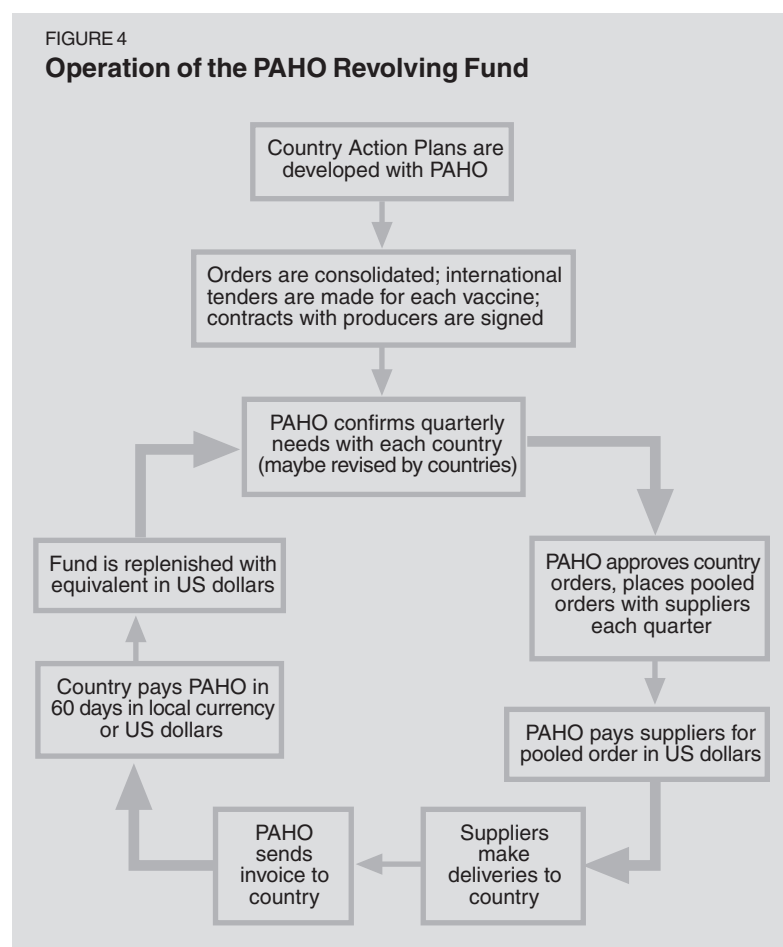


TABLE 1

Main Features of the PAHO Revolving Fund and the Vaccine Independence Initiative (VII)

Feature	PAHO Revolving Fund	VII
Procurement system	PAHO procurement system. International tenders are solicited for each vaccine yearly, on the basis of consolidated orders from countries. Two suppliers with the lowest bids are contracted for each vaccine/antigen	UNICEF procurement services are used for VII countries and many others. Biannual contracts with suppliers, following international tenders, are based on anticipated needs
Commodities purchased	Vaccines, syringes, needles, small cold-chain equipment (cold boxes, etc.)	Vaccines, supplies for some countries
Type of revolving fund	Common regional fund	Individual revolving fund for each country, with fixed ceilings on outstanding amount at any one time. No revolving fund for countries with "modified" VII agreements
Capitalization of revolving fund	Donor contributions plus 3% service charges in excess of amount that will keep the reserve fund at \$100,000 level. All funds are pooled into common fund (no earmarking for specific countries)	Donor contributions to revolving funds in individual countries or to general fund. Thirty percent of donor contributions are tied to specific countries, making it more difficult to shift funds to make up for temporary shortfalls
Budget line item required?	Yes	Vaccines must be in government budget but not necessarily as a separate line item although line-item budgeting for vaccines is encouraged
Payment terms for countries	Local currency accepted up to absorption capacity of the PAHO country office. Beyond this, hard currency is required. Currently, only around 20% of countries pay in local currency. Payment within 60 days of receipt of invoice (after delivery)	Local currency accepted in countries where UNICEF country program can absorb sufficient local currency. Hard currency required in countries where UNICEF program is small or nonexistent. Payment required after goods are received (45–60 days after receipt of invoice)
How countries pay for commodities	Government financing (budgetary allocations), with additional donor funding for poorer countries	Mixed government/donor funding in most countries. Progressive share of government financing over time specified in agreements with former Soviet states. EU structural adjustment funds used to pay for vaccines in the seven EU Initiative countries in west/central Africa
No. of participating countries, by WHO/UNICEF band (and % of total)	Band A: 2 (5.7%) Band B: 15 (43.0%) Band C: 16 (46.0%) Band D: 2 (5.7%)	Band A: 7 (27%) ^a Band B: 12 (46%) Band C: 7 (27%) Band D: 0

^aSix of the seven Band A countries receive structural adjustment financing for vaccine purchases as part of the EU Initiative. For an explanation of band categories, see page 32 of this paper.

- PAHO advisers work with national immunization program managers to determine Country Action Plans, including vaccine supply needs, for the coming year.
- PAHO consolidates the orders from the Country Plans at its headquarters in Washington, D.C., and then solic-

its international tenders from WHO-prequalified manufacturers.¹

¹ WHO certifies the quality of a manufacturer's vaccine using a strict regulatory code. Procuring countries can thus be assured of the quality of the vaccine from "qualified" manufacturers. This certification is especially important for countries without strong regulatory authorities.

- PAHO negotiates annual contracts to supply and deliver the vaccines to each country. It usually enters into contracts with two producers for each vaccine, to avoid supply problems arising from a production failure by either manufacturer.
- PAHO sets one price for each vaccine for the year (by “blending” the quotes from the two selected manufacturers) and makes the price known to all member countries.
- The PAHO procurement office then places the orders consolidated from all countries with the producers each quarter, paying them in advance out of the common fund, which is capitalized in US dollars.
- After the goods are delivered, PAHO invoices the participating government for the total cost of delivery (shipping, insurance, etc). A service fee of 3 percent covers foreign exchange losses, lost shipments, and other contingencies. The fee receipts are placed in a reserve fund, whose balance is kept at \$100,000. Excess funds are added to the capital of the common fund.
- Participating countries may pay PAHO within 60 days, in local currency or in US dollars, depending on their agreement with PAHO.²
- US dollars are deposited directly into the common fund. PAHO uses pay-

ments in local currency for its in-country operations and replenishes the Fund with the equivalent amount in US dollars.

- Countries cannot receive additional orders until they have repaid the Fund, to prevent depletion of working capital.

Benefits

The revolving fund mechanism, as PAHO points out, has the following benefits:

- Countries are forced to plan and budget their vaccine and supply needs yearly, allowing time for procurement and delivery. Disruptions in supply and therefore immunization services are minimized.
- More reliable demand forecasts allow manufacturers to schedule production for the entire year. They can thus increase efficiencies and reduce costs.
- Consolidating vaccine orders allows economies of scale to be maximized, leading to lower and more stable vaccine prices.
- Countries are assured of high-quality vaccines, as only manufacturers prequalified by WHO are used.
- Countries can pay in local currency when they receive the goods, saving limited foreign exchange.

Accomplishments

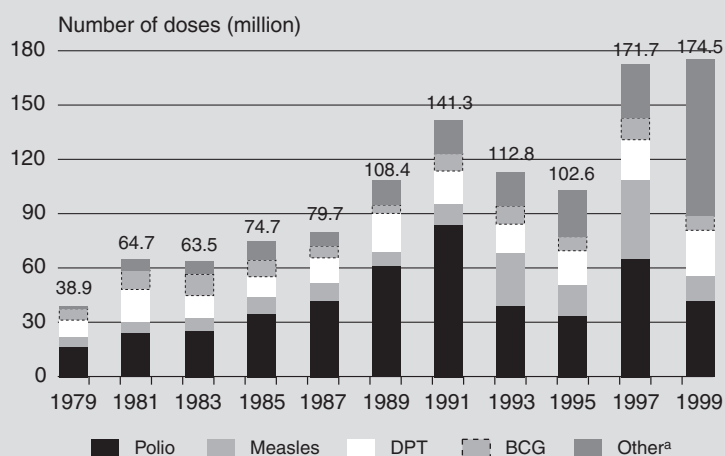
The operations of the Revolving Fund have grown significantly over the past 20 years, as reflected in the increased participation of member countries, the introduction of new vaccines onto the procurement list, and a substantial rise in the Fund’s capital.

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² If the local PAHO office cannot absorb all of the local currency given by the government as payment for the vaccines, the government pays in local currency up to the amount that can be absorbed and must pay the rest in US dollars.

FIGURE 5

Number of Vaccine Doses Procured through the PAHO Revolving Fund, 1979–1999



^a Includes TT, DT, MMR, and from 1998 on Hepatitis B, Hib and pentavalent.

By 1999, all the countries in the PAHO region, except for Chile and Venezuela, were using the Fund to procure some or all of their vaccines

Participation

The Revolving Fund had 19 participating countries when it began in 1979; today it has 32 to 34.³ Brazil's entry in 1997 increased the population represented by the Fund by 57 percent. By 1999, all the countries in the PAHO region,⁴ except for Chile and Venezuela, were using the Fund to procure some or all of their vaccines. Vaccines purchased through the Fund have also grown tremendously in volume and in value in the past 20 years, from 38.9 million doses amounting to \$2.6 million in 1979 to an estimated 174.5 million doses worth about \$85 million in 1999 (see Figure 5).

New vaccines

The Fund first procured Hepatitis B vaccine for individual countries in 1994; by 1999, it was purchasing 12.1 million

³ Some countries such as Chile, Argentina, and Mexico join and leave the Fund in any given year and may use it only to purchase certain vaccines.

⁴ The PAHO region consists of all countries in Latin America and the Caribbean.

doses for routine immunization or the vaccination of high-risk groups in 24 countries. The Hib vaccine had been introduced in 18 countries (including Brazil and Mexico) by 1999. That year, PAHO procured about 20.5 million Hib vaccine doses for 14 countries and the pentavalent vaccine HBV-DPT-Hib for Mexico, Peru, and Uruguay. The Fund purchases the measles-mumps-rubella (MMR) vaccine as well for several countries.

Capitalization

The Fund received an initial contribution of \$1 million from PAHO when it began in 1979. Since then, donors (including UNICEF, the Netherlands, and the US) and PAHO member countries have contributed an additional \$2.7 million to capitalize the Fund. In 1999, capitalization was more than \$12 million; of this amount, more than \$8 million (67 percent) was raised from the 3 percent service fee and short-term investments. Most of the growth in the Fund has occurred in the last few years and is due to the increase in the total value of vaccines purchased resulting from the higher volume of purchases (particularly since Brazil joined the Fund) and the inclusion of more expensive vaccines (Hepatitis B, Hib, and the pentavalent). But despite the total capitalized value, reserves fluctuate throughout the year because of the interval between the time suppliers are paid and the time the Fund is reimbursed by the countries.

Assessment

To date, there has been no formal independent evaluation of the PAHO Revolving Fund. Most of the information for this report came from PAHO headquarters,

making an objective assessment difficult. Nonetheless, in view of the growth in the number of participating countries and the volume of vaccine purchases, and the high degree to which participating countries finance their vaccine purchases themselves (discussed below), most observers consider the Revolving Fund to be a success. According to UNICEF, “[the Revolving Fund] has been instrumental in achieving the high coverage rates and the virtual eradication of poliomyelitis in the Western Hemisphere” (UNICEF 1992). The Fund’s success is ascribed to factors such as the following:

- Its link to the overall program of political, policy and technical assistance
- Compliance with strict criteria and rules
- Strong regional coordination
- A strong Technical Advisory Group
- Continuity of program staff

Links to overall technical assistance

Rather than being just a vaccine procurement mechanism, the Fund is one component within a broader program of political, policy, and technical assistance. PAHO works with member countries to determine their priorities, project their vaccine needs, assess and improve their immunization infrastructure (e.g., cold-chain system), and analyze the cost-effectiveness of introducing new vaccines. According to Freeman (1999, p. 1), “the Revolving Fund . . . serves as a lever for encouraging countries to evaluate their immunization strategies in terms of the epidemiology, cost-effectiveness and financial and logistical sustainability.” A subregional Technical Advisory Group (TAG) and the well-respected regional

TAG conduct technical and strategic reviews of each country’s immunization program. PAHO advisers can also help mobilize resources from bilateral donors for countries that need those resources.

PAHO has been instrumental as well in securing the passage of laws in several countries mandating government financing for vaccines. It drafted laws for the Latin American and regional parliaments, which were later used as models for similar legislation in Venezuela, Peru, Guatemala, Ecuador, and Brazil (Ciro de Quadros, personal communication).

This comprehensive package of assistance has been critical to improving country immunization programs. Indeed,

. . . using the prices and stability of the Fund’s procurement apparatus as leverage, PAHO was able to require participating countries to plan their immunization programs more comprehensively, to improve infrastructure, to share their data and program experiences in regional and subregional meetings and to help countries abide by the recommendations of the Technical Advisory Group The message PAHO has labored to send throughout Latin America is: “Do your homework, prepare to disclose your data and strategy for a critical review across the region, or buy your vaccines outside the Fund.” (Freeman 1999, p. 6)

Strict criteria and rules

The criteria that PAHO has set for member countries have shaped a “culture of discipline,” which has helped to keep the Fund solvent and ensured that program advice is taken seriously (Freeman 1999, p. 3). For example, countries joining the Fund must have:

The criteria that PAHO has set for member countries have shaped a “culture of discipline,” which has helped to keep the Fund solvent and ensured that program advice is taken seriously

Some countries from time to time have been late in paying, but their number has decreased and all countries have eventually reimbursed the Fund in full

- A specific line item in the national budget for vaccines and syringes
- A realistic and comprehensive national program plan
- Adequate infrastructure for vaccine storage and distribution
- A national program manager authorized to develop and implement the program⁵

Also, a new vaccine cannot be purchased through the Fund until PAHO finds the vaccine to be cost-effective and is assured that the country has adequate financing and infrastructure to introduce the vaccine without jeopardizing the rest of the immunization program.

The Fund stays solvent because countries that do not pay their invoices on time have their future orders suspended until they repay the Fund. Some countries from time to time have been late in paying, but their number has decreased and all countries have eventually reimbursed the Fund in full (Peter Carrasco, personal communication).

Regional coordination

PAHO periodically holds subregional and regional meetings, during which countries share data and experiences, in the process finding solutions to common problems. Collective feedback to PAHO has also helped improve the administration of the Revolving Fund.

A strong Technical Advisory Group and continuity of program staff

The regional TAG, well respected by countries and donors alike, provides critical advice to countries about their immu-

nization programs. The strong leadership and continuity of PAHO staff in charge of the Fund as well as the “superior market intelligence” they have built up over the years are considered factors in the program’s success (England 1999).

The impact of the Revolving Fund program on immunization program performance, government financing, and the financial sustainability of immunization programs is discussed in Impact of Vaccine Procurement Mechanisms below.

The Vaccine Independence Initiative

Encouraged by the success of the PAHO Revolving Fund, UNICEF established the Vaccine Independence Initiative (VII) in 1991. The VII was created primarily to help middle-income countries become self-reliant in vaccine financing and procurement, and thus to “ensure the availability of funding for the introduction of new vaccines...by freeing up donor funds for this purpose” (UNICEF 1999a, p. 3).

Description

VII operates on the same principles as the PAHO Fund, allowing participating countries to pay for low-cost vaccines in local currency (with some exceptions) after deliveries are made. It thus provides a reliable means (through UNICEF’s procurement system in Copenhagen) of procuring high-quality vaccines at sustainable prices. The VII also obliges countries to plan their vaccine needs annually, with technical assistance, and to include the cost of vaccines in the national budget. A specific vaccine line item is encouraged but not required.

⁵ However, according to some informants, these requirements have not always been as strict in practice.

There are, however, some important differences between the operations of VII and those of the PAHO Revolving Fund. These are:

- Instead of a common fund for all countries, as in the PAHO mechanism, the VII establishes a revolving fund for each participating country.
- VII maintains a greater separation between procurement services and fund management; the PAHO uses service fees to capitalize its revolving fund.
- Unlike the PAHO, the VII enters into formal annual contracts with participating countries for their vaccine purchases.
- The VII is implemented in a greater variety of ways.

Individual revolving funds

The VII establishes a revolving fund for each participating country instead of a common fund for all countries. The country funds are managed by UNICEF (New York) and capitalized by donor contributions to targeted countries or to the VII general fund. UNICEF pays for vaccines from the funds (in dollars) and governments reimburse the funds in local or hard currency once they receive the vaccines. At no time can the outstanding orders or payments of a country exceed its capitalization (the country's "ceiling"). The revolving funds are designed to "turn over" twice a year. That is, the government should reimburse UNICEF within six months after placing an order. Each year a country can thus purchase vaccines worth up to twice the amount of its capitalization (i.e., a fund capitalized with \$500,000 which turns over twice a year can buy \$1,000,000 worth of vaccines).

Separation between fund management and procurement services

While the UNICEF headquarters in New York manages the VII and the individual revolving funds, the UNICEF Supply Division in Copenhagen procures vaccines for participating countries. The Supply Division keeps the 6 percent service fee charged by UNICEF (double what PAHO charges) to cover its operational costs. Therefore, the accumulated fees do not go back into the VII revolving funds, as they do in the PAHO program, where they constitute an important source of additional capital.

More formal agreements with participating countries

Unlike the PAHO program, the VII requires countries to sign annual contracts stating the government's budget for vaccine purchases for the year and its commitment to pay for the vaccines. The contract also stipulates the amount of vaccines to be procured through UNICEF, the estimated unit price for each vaccine for the year, and the total value of vaccines that can be purchased for the year.

More varied implementation

A number of countries have "modified VII agreements," under which they receive UNICEF assistance in planning and forecasting their vaccine needs, have access to UNICEF's procurement services, but pay for the vaccines in advance and do not use the revolving fund mechanism. To quote England (1999, p. 24), "the VII will accept any mechanism that results in Ministries of Health becoming self-reliant in the supply of quality vaccines."

The VII also

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their vaccine

needs annually,

with technical

assistance, and

to include the

cost of vaccines

in the national

budget

TABLE 2

Countries Participating in the Vaccine Independence Initiative

Category	Description	Countries
1	Countries using revolving funds and financing their own vaccines	Morocco, Bangladesh (for some vaccines only), 12 Pacific Island countries, Philippines (until 1998)
2	Countries with revolving funds and financing from EU structural adjustment grants	Senegal, Cape Verde, Burkina Faso, Niger, Chad, Mauritania, Gambia
3	Countries with modified VII (no revolving funds)	Kazakhstan, Turkmenistan, Uzbekistan, Mali, Uganda
4	Countries with special emergency fund	Ghana

Participation

Morocco and the Philippines were the first countries to join the VII in 1993.⁶ Now 27 countries, including 12 Pacific Island nations, have VII agreements with UNICEF. There are four categories of participation, as shown in Table 2.

Category 1: Self-financing

Morocco, the Pacific Island countries, and Bangladesh (which uses the VII to purchase only a portion of its vaccine supply),⁷ pay for the vaccines from government budget allocations and have individual revolving funds.⁸

Category 2: European Union Initiative

Since 1996, seven west and central African countries have participated in the VII through the European Union (EU) Initiative. Through this initiative, coun-

tries use structural adjustment funding provided by the EU to purchase vaccines. Each country makes use of a revolving fund, paying for the vaccines in the local currency once they are received.

Category 3: Modified agreements

Kazakhstan, Uzbekistan, Turkmenistan, Mali, and Uganda have modified agreements (i.e., no revolving fund), under which they pay in advance for the vaccines either in hard currency (in the case of the Central Asian countries) or in local currency (Mali and Uganda). The central Asian countries each have a VII agreement between the government, UNICEF, and the Japanese Government to co-finance vaccines procured through UNICEF. The government increases its share of financing each year until it reaches self-sufficiency, usually in five to nine years.

Category 4: Emergency fund

Ghana used the VII to set up a “vaccine stabilization fund,” capitalized by USAID, to purchase emergency supplies for disease outbreaks and shortfalls in routine vaccines.

⁶ The Philippines left the Initiative in 1998 and now purchases vaccines directly from suppliers (using loan funds from the World Bank) through an international tender and bid process.

⁷ VII vaccines in Bangladesh are financed by the Government (30 percent), a World Bank loan (43 percent), and donors (27 percent).

⁸ Morocco also uses loan funds from the World Bank to finance vaccines.

Capitalization

The VII was used to purchase \$11 million worth of vaccines in 1998 and over \$50 million since it began in 1993 (UNICEF 1999a). The revolving funds are currently capitalized at \$8.6 million, about 30 percent of which is earmarked for specific countries and 70 percent for the general fund. Three-fourths of the funding has come from three sources: USAID, (40 percent), UNICEF (23 percent), and the Netherlands (13 percent).

Assessment

As with the PAHO Revolving Fund, there has been no formal independent evaluation of the VII.⁹ The VII was originally designed to assist middle-income countries, many of which, including Pakistan, Egypt, Nepal, and Sri Lanka, chose not to join, opting instead to buy vaccines on the open market. The countries that have joined tend to be poorer than was originally anticipated, with three-fourths of them in the WHO/UNICEF Band A or B (see Figure 10), and only 27 percent in Band C, the originally targeted middle-income countries. Consequently, many of the countries in the VII still depend on donors to finance at least some of their vaccine, and in the case of the EU Initiative countries, all of their vaccine supply.

In any case, according to UNICEF, the VII has strengthened the commitment of participating governments to carry out their immunization programs and to secure funding for vaccines.

The negotiation and signing of the VII agreement with the Ministry of Health...

⁹ An assessment of the program was made in Morocco, early in the implementation period.

has proven one of the most useful and effective aspects of the VII process. The agreement formalizes the government's commitment to paying for vaccines, provides a signed document attesting that the budget for vaccines is assured, and provides for continuity of the budget commitment across changes in personnel. (UNICEF 1999a)

Administration

The system of separate revolving funds limits the ability of countries to place large single orders (e.g., for National Immunization Days) that temporarily exceed their ceilings. It also limits UNICEF's flexibility in managing funds, as it cannot move funds from one country to another as demand fluctuates. The separate funds were established largely in response to the way the VII was initially supported. Donors, especially USAID, tended to earmark funding for specific countries, instead of contributing to the general fund for all countries.¹⁰ Earmarking made it impossible to create a common fund or to shift funds from one country to another.

This inflexibility in country ceilings and the inability of UNICEF to shift funds from one country to another to accommodate changing needs have sometimes led to the inefficient use of funds, according to UNICEF. In response, UNICEF is moving toward a common fund model, encouraging donors to contribute only to the general fund (for use by any participating country) and allowing countries to exceed their ceilings "on an exceptional basis." These changes were made only in

¹⁰USAID contributions are often earmarked because the funds actually come from country missions, which are required to fund activities that benefit their country only.

1999 and it is still too soon to tell if they have made a difference.

Procurement administration has proven to be somewhat of a burden for both countries and UNICEF. Unlike the PAHO program, which requires countries to submit their vaccine needs once a year, with quarterly confirmation, countries participating in the VII must submit their orders every three months. Delays have occurred in deliveries, the receipt of invoices from UNICEF, and government repayment. As countries are limited by the ceiling of their individual revolving fund, any of these delays can deplete the balance of their fund and cause vaccine shortages. However, it is not known to what extent vaccine supply has actually been disrupted.

Countries have also complained of exchange-rate difficulties when rates change between the time orders are placed and the time the invoice is received. The program in Morocco solved some of these administrative problems by shifting the responsibility for billing from Copenhagen to the local UNICEF office, thus reducing the time from delivery to billing from months to days, and by stipulating fixed exchange rates for the entire year in the contract.

New vaccines

One of the main objectives of the VII was to free up donor funding to finance the introduction of new vaccines. Except for the Pacific Islands countries, which pay for the traditional EPI vaccines themselves but receive donor funding for Hepatitis B vaccine, this does not appear to have occurred. Some participating countries, such as Morocco, have begun to introduce Hepatitis B vaccine, but with government funds and World Bank loan funding. As

discussed in Impact of Vaccine Procurement Mechanisms below, before GAVI was established, donors were reluctant to pay for Hepatitis B and other new vaccines because of the higher cost and the potentially huge demand from developing countries.¹¹

Impact of Vaccine Procurement Mechanisms

As formal evaluations of the PAHO Revolving Fund program and the VII have yet to take place, it is difficult to assess the impact these mechanisms have had on country immunization programs. Available information, however, does allow us to draw some conclusions on the impact of the VII and the PAHO Revolving Fund on program performance, government financing, and sustainability of immunization programs.

Program performance

PAHO: Data from PAHO countries show that immunization coverage rates have, in general, increased since countries joined the Revolving Fund. How much this increase can be attributed to the Fund (or to other factors such as UCI) is not possible to determine. Countries reportedly experienced some disruptions in vaccine supply early in the program because of operational problems such as delays in placing orders as well as an inadequate level of

¹¹The Global Alliance for Vaccines and Immunization (GAVI), which began funding in 2000, has dramatically increased the demand for Hepatitis B vaccine. This initiative is discussed further in the previous main section of this report.

capitalization of the Fund (Carrasco et al. 1983). However, according to PAHO, these problems have diminished as PAHO and the countries have gained experience in managing the Fund. Supply disruptions are now at a minimum and if the Fund is low at any one time, countries must pay in advance for any further orders.

VII: Evidence of the impact of the VII on immunization programs is also largely anecdotal. An assessment of the VII in Morocco, as part of a country case study on immunization financing, showed:

- The Government was able to double the value of its vaccine purchases since joining the VII in 1994, leading to the successful implementation of a polio eradication program.
- Immunization coverage rates increased after the VII began, with DPT3 and OPV3 coverage rising 10 percent from 1992 to 1995.
- Disruptions in vaccine supply have been minor since the Government began financing all vaccine purchases through the VII¹² (Kaddar et al. 1999).

Again, the degree to which the VII is responsible for these improvements is difficult to determine.

Government financing and sustainability of immunization programs

Operational self-sufficiency is a key element in immunization sustainability. Of

¹²However, Morocco uses loan funds from the World Bank to pay for its vaccines. The country reportedly planned to increase its Government allocations in 2000 to cover vaccine purchases, including Hepatitis B vaccine, instead of using loan funds. This would be a truer test of its ability to become self-sufficient in vaccine financing and of the usefulness of the VII in assisting the Government to achieve this goal.

primary importance is vaccine self-sufficiency, which is achieved if a country purchases or produces all the routine EPI vaccines it requires.

PAHO: Data from PAHO show that most countries participating in the PAHO Revolving Fund finance their entire vaccine supply. Several poorer countries, with the exception of Haiti, Bolivia, and Guatemala, finance most of their vaccines and related recurrent costs. The increased share of financing over the past four years is shown in Table 3.

TABLE 3
Proportion of Recurrent Costs Financed by National Resources in Selected Countries in the Americas, 1995–1999^a (%)

Country (Band)	1995	1996	1997	1998
Bolivia (B)	49	72	68	44
Ecuador (B)	69	81	77	91
El Salvador (B)	100	100	100	100
Guatemala (B)	100	92	79	85
Haiti (A)	19	22	25	—
Honduras (B)	78	82	96	91
Nicaragua (B)	67	76	78	95
Peru (B)	97	99	100	100

Source: PAHO (1999) (slides)

— = not available

^aCovering vaccines, syringes, and small cold-chain equipment

This financing trend, in conjunction with the increase in number of PAHO countries that have introduced the more expensive Hepatitis B and Hib vaccines, suggests that government financing of vaccines is now sustainable in several countries. Although increases in governments' share of vaccine financing are also part of a global trend, possibly driven by decreases in donor funding, the support that

PAHO gives to ministries of health in promoting immunization programs has likely contributed to this increase.

Nonetheless, most countries in the Revolving Fund, even those financing their entire vaccine supply, continue to receive some donor support for critical inputs, most notably training, cold-chain equipment, disease surveillance, and social mobilization (DeRoeck and Levin 1999).

VII: Most countries participating in the VII finance much less of their vaccine supply than PAHO countries, although governments' share of vaccine financing has generally been increasing, as shown in Table 4. However, comparisons with PAHO countries should be made cautiously, as VII countries are generally much poorer. The VII agreements for the three central Asian countries call for the

government to pay an increasing share of vaccine costs until they become self-financing, according to predetermined schedules. So far, two of these countries have been meeting their payments on schedule, while one is behind on its payments (Simidjiski 1999).

The main exceptions to the increase in government financing of vaccines among the VII countries are the west and central African countries participating in the EU Initiative. On paper, financing for vaccines comes out of each government budget, but the funds actually come entirely from EU structural adjustment grants. Although the countries participating in the Initiative are meant to gradually assume a greater share of vaccine financing from their own internal resources, there is as yet no way of differentiating between financing from internal resources and structural adjustment funding. Countries therefore have little incentive to increase their share of vaccine financing—a major criticism of the EU Initiative.

Nonetheless, one important success of the VII has been in convincing governments of the importance of financing their immunization programs and in creating budgetary line items for vaccines and/or immunization programs. This is a critical first step.

Lessons learned

A number of lessons have been learned from the experiences of the PAHO Revolving Fund and the VII. These include:

- *The importance of providing procurement mechanisms within the framework of overall technical assistance.* Both PAHO and UNICEF stress that these mechanisms, by themselves,

TABLE 4

Proportion of Vaccine Financing by Governments in Selected Countries Participating in the VII, 1995–1997^a

Country	1995	1996	1997
Burkina Faso ^b	—	33.8	0.0
Band A			
Chad ^b	0	0.0	0.0
Gambia ^b	—	0.0	0.0
Niger ^b	0	0.0	0.0
Mauritania ^b	0	0.0	0.0
Uganda	0	35.0	49.0
Band B			
Bangladesh	84	74.0	53.0 ^c
Morocco	100	100.0	100.0
Senegal ^b	—	0.0	0.0
Cape Verde ^b	—	0.0	0.0
Band C			
Kazakhstan	—	20.0	38.5
Turkmenistan	—	9.3	11.5
Uzbekistan	—	16.0	30.0
Fiji	—	50.0	—

— = not available

^a Including loan funds from the World Bank used to purchase vaccines

^b Countries receiving EU structural adjustment funds for vaccines through the EU Initiative, which began in 1996

^c Levin et al. (1999)

Source: UNICEF (New York)

will not lead to better immunization programs or to increased government responsibility for financing programs. Critical to success has been the technical assistance that is provided to countries to help assess and strengthen their immunization programs, and to convince other government ministries (e.g., the ministry of finance) of the importance of immunization. For example, PAHO's well-respected and informed Technical Advisory Group has been considered a vital asset to the PAHO program.

- *The benefits of a common revolving fund and flexible donor financing.* UNICEF has learned the limits of earmarked donor funding and the establishment of individual country revolving funds and is now moving toward a common fund model similar to PAHO's. Having a common fund into which all donor contributions are placed and which is used to purchase vaccines for all participating countries provides the flexibility for countries to buy larger quantities of vaccines than normal (e.g., for NIDs) and to purchase emergency supplies.
- *The advantages of keeping the management of the revolving fund and the procurement operations closely tied.* Keeping these two functions close together is one way to improve the management of the program overall. It also allows the program to put any service fees back into the fund. As mentioned above, accumulated fees account for nearly 70 percent of the capitalization of PAHO's Revolving Fund.
- *The lower-than-expected importance of easy credit terms to many countries.* Both the PAHO fund and the VII

allow countries to pay for vaccines in local currency, after deliveries are made. PAHO and UNICEF thought these credit terms to be an important advantage to countries and a major incentive for them to join these programs. Experience has shown, however, that these credit terms are less significant for many countries. Around 80 percent of countries in the PAHO Revolving Fund, for instance, pay in hard currency (although the ability to pay in local currency is critical for the remaining 20 percent). The VII countries are more likely to require the local-currency option, but many have found it easier to pay for the vaccines in advance, because of their government's budget processes. These countries do not need a revolving fund.

Many countries join these programs mainly for the low vaccine prices and easier procurement procedures (they do not have to deal directly with suppliers or issue international tenders), as well as the availability of technical assistance.

- *The benefits of a regional initiative.* Having a program within one region makes it easier for participating countries to share information and experiences. For PAHO, this occurs during the periodic meetings of countries participating in the Fund. The EU Initiative in west and central Africa also provides for periodic meetings and ways of sharing information. In addition, countries participating in the EU Initiative lend one another vaccines in emergencies until supplies arrive (UNICEF 1999b).

The International Vaccine Market: Major Issues

Main Characteristics

The international vaccine market differs in many ways from the general pharmaceutical market.

Its major features are:

- Dominance by a few manufacturers
- The limited number of worldwide buyers
- High degree of market segmentation and tiered pricing
- Scale sensitivity of vaccine development and production

Dominance by a few manufacturers

Until quite recently, the international vaccine market was dominated by a few manufacturers. These manufacturers can be divided into three main groups:

- Multinational private-sector manufacturers in industrialized countries, usually owned by large pharmaceutical companies
- Public-sector manufacturers in industrialized countries, which produce solely for their domestic use
- Manufacturers in developing countries, usually government-owned

About 20 manufacturers are currently certified by WHO to supply vaccines. However, the global vaccine market is dominated by four multinational firms,

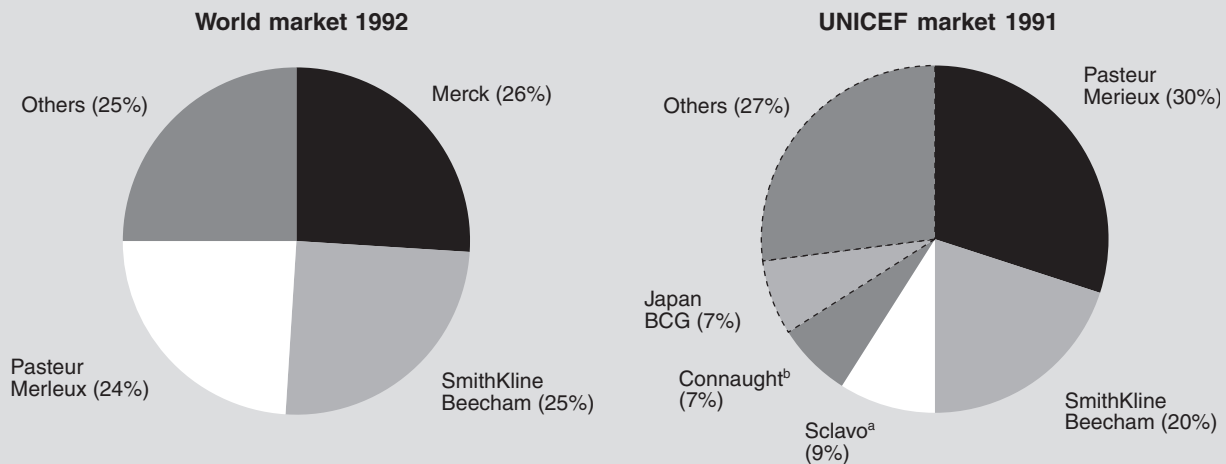
making it a “quasi-monopoly.” In the early 1990s, SmithKline Beecham (SKB), Pasteur Merieux (PMSV), Merck & Co. (MSD), and Lederle had an estimated 75 percent share of the global market for all vaccines (Poirot and Martin 1994). Figure 6 shows each producer’s share of the world and UNICEF markets in the early 1990s.

Despite the entry of new producers, especially from Asia, since the early 1990s, multinationals continue to dominate the international market. In fact, mergers and acquisitions among these firms in the 1980s and 1990s have concentrated the international market even further. PMSV, for example, acquired Connaught in 1994 and became Pasteur-Merieux-Connaught. Its parent company, Rhone Poulenc, merged with a German company in 1999, creating the new company Aventis, and the vaccine division is now called Aventis-Pasteur.

Limited worldwide buyers

The market is also distinguished by the limited number of worldwide buyers. In 1990, UNICEF, PAHO, and WHO purchased about 62 percent of the total volume of vaccines consumed globally and 69 percent of the classic EPI vaccines (EFPIA 1994; Guerin et al. 1993).

FIGURE 6

Producers' Shares of the World and UNICEF Vaccine Markets

Source: Schwabe (1993)
^a Since acquired by Chiron
^b Since merged with Pasteur Merieux

UNICEF procured vaccines for 88 countries in 1996, while PAHO currently procures vaccines for more than 30 countries in the Latin American and Caribbean region. Market dominance has given large bulk purchasers significant negotiating power, keeping prices low. Consequently, according to the International Center for Childhood and the Family (CIDEF), “vaccine prices can be seen as the outcome of more or less implicit negotiations between the few producers and institutional buyers, or certain states which can exert an influence in the market” (CIDEF 1998).

High degree of segmentation and tiered pricing

The vaccine market is highly segmented and has an associated high level of tiered pricing. Market segmentation for vaccines has two dimensions:

- Industrialized vs. developing countries
- Public vs. private sector, within a country

In industrialized countries, adult vaccines and the newer proprietary (or patented) vaccines such as Hepatitis A, Hepatitis B, and Hib dominate in terms of volume of vaccines consumed. The flu vaccine (administered largely to adults), for example, accounted for an estimated 35 percent of all vaccines used in industrialized countries in 1990, whereas traditional EPI vaccines accounted for 57 percent (CIDEF 1998).

This contrasts with the public-sector developing-country market, where, in 1990, 99 percent of vaccines procured by UNICEF and PAHO consisted of the traditional EPI vaccines. OPV alone accounted for nearly half of the total vaccine usage in these countries. However, a growing number of governments in developing countries have introduced Hepatitis B vaccine and MMR into their national immunization programs, and plan to introduce Hib, potentially breaking down product segmentation by income level of the country.

The government sector and the private sector also represent quite different segments of the vaccine market, especially in developing countries. Most government programs in developing countries provide the traditional EPI vaccines only. However, the private sector offers (to people who can afford it), Hepatitis A, Hepatitis B, Hib, yellow fever, and other vaccines not available through government services in their countries.

Vaccine prices are highly tiered according to these segments, as is true for pharmaceuticals in general. As shown in Table 5, the catalog (list) price that the US private health sector pays for vaccines is, on average, three times the price the US Government pays for vaccines to supply public-sector providers. These prices are anywhere from 2 to 17 times the prices charged to UNICEF and PAHO for less developed countries, for the same vaccines and same presentations. Vaccine prices in the private sector in developing countries are also considerably higher than those

paid by the public sector. Tiered pricing is made possible by the cost structure of vaccine development and production.

Most vaccines are consumed in developing countries because of their large population and the tremendous growth in immunization coverage in the 1980s and 1990s. Developing and in-transition countries accounted for about 88 percent of the volume of vaccines purchased in 1990 (CIDEF 1998). However, as shown above, the vaccine industry generates its profit in industrialized countries. While only 12 percent of the total volume of vaccines purchased in 1990 went to industrialized countries, this represented 75 percent of the total value of sales. Similarly, UNICEF and PAHO purchased for developing-country use about 50 percent of EPI vaccines produced by major manufacturers in 1992, but this represented less than 5 percent of the total revenues from vaccine sales worldwide (UNICEF 1994a). Table 6 summarizes the characteristics of the public-sector vaccine market.

TABLE 5

Price of a Pediatric Dose of Vaccine in the US Domestic Market and PAHO, 1999

Vaccine	US Market			PAHO	
	Private-Sector (catalog) price per Dose ^a	Government CDC price per Dose ^a	Private Difference: Private vs Public Sector	Price per Dose	Price Difference: US Government vs PAHO
OPV	\$10.93 (1-dose vials)	\$2.9 (1-dose vials)	3.8x	\$0.087 (10-dose vials)	33.3x
MMR (1-dose vials)	\$27.46	\$14.69	1.9x	\$0.88	16.7x
Measles (1-dose vials)	\$10.40	\$6.51	1.6x	\$0.68	9.6x
Recombinant Hepatitis B (1-dose vials)	\$24.20	\$9.00	2.7x	\$0.92	9.8x
Hib (10-dose vials)	\$15.88	\$4.75	3.3x	\$2.18	2.2x

Sources: CDC website, PAHO price list
^aIncludes \$0.75 per dose excise tax

Clearly, industrialized countries are heavily subsidizing the developing-country vaccine market. But, as discussed below, this is changing, as is the huge discrepancy between volume and profit, as more and more middle-income countries finance their own vaccines and purchase newer, more costly vaccines such as Hib.

Scale sensitivity of vaccine development and production

The cost of production of vaccines depends greatly on the fixed cost and, as a result, is highly scale-sensitive. According to a study conducted by Mercer Management for UNICEF in 1994 (UNICEF 1994a), on average, 85 percent of the total costs of developing and producing a vaccine are fixed. About 50 percent of these are related to labor costs throughout the business, including research and development, quality control, and marketing and sales.

Vaccines are produced by batch (or lot) and a large portion of the fixed cost is linked to the production of each batch. Therefore, the more vaccine a producer manufactures, especially by increasing the size of each batch, the lower the cost per dose or vial. Unit costs also decrease over time as manufacturers learn to make the vaccine more efficiently, and this is referred to as the “learning effect.” Given the dominance of fixed costs and the influence of the learning effect, vaccine production is therefore highly scale-sensitive. A large manufacturer can produce the same vaccine for up to one-fifth of the cost per dose of a smaller producer, according to the Mercer study. Indeed, the pharmaceutical industry considers a vaccine market of less than 40 million people not profitable because of these “econo-

mies of scale” (CIDEF 1998). It is therefore in the interest of manufacturers to maximize production, as this will lower the cost per unit.

These economies of scale have enabled vaccine manufacturers with excess capacity to significantly (and easily) increase their output to meet the growth in demand resulting from EPI and UCI efforts, without a substantial rise in costs. Because of this, it has been possible for less developed countries, through UNICEF and PAHO, to be charged the marginal cost for a vaccine. This minimal price covers the direct cost in personnel and materials of producing an additional dose, plus a small share of overhead costs. According to Mahoney (1999b), the marginal cost of producing vaccine beyond 20 million doses is basically the cost of the diluent, vial, and stopper. The full value of fixed costs, including research and development, equipment depreciation, and profit, are charged to industrialized countries and to the private sector in developing countries.

The scale sensitivity of vaccine development and production has therefore made the system of tiered pricing between less developed and industrialized countries possible.

Factors Affecting Prices

The main factors that have affected, or continue to affect, the price of vaccines are listed in Table 7. Some of these factors, such as the system of tiered pricing and the power of a few bulk purchasers, were discussed above. Other factors and their likely effect on prices, particularly for newer vaccines, are discussed below.

TABLE 6

The Segmented Public-Sector Vaccine Market, 1990

Aspect	Industrialized Countries	Developing Countries
Number and types of vaccines in child immunization schedule	Can include DTaP, IPV, MMR, Varicella (chicken pox), Hepatitis B, Hib	Basic EPI vaccines (DPT, measles, BCG, OPV, TT), Hepatitis B (in a growing number), some Hib
Share of world vaccine market in volume	12%	88%
Share of vaccine market in value	75%	25%
Costs included in price	Full costs, including R&D, equipment depreciation, promotion/advertising, taxes, profit	Marginal costs (raw materials, direct labor, some overhead, very small profit margin)

Source: CIDEF (1998)

Development and production costs

The marginal cost of producing EPI vaccines in bulk is negligible, as discussed in Scale Sensitivity of Vaccine Development and Production above. However, the new vaccines, such as Hib and pneumococcal, require (advanced) conjugate technology, which is more costly than traditional vaccine production.

The newer vaccines also require a considerable investment in research and development, as they use genetic engineering techniques. Developing, getting approval for, and launching a new vaccine can cost as much as \$500 million (Rosegrant 1998a). SmithKline Beecham estimated that it cost \$230 million to bring recombinant Hepatitis B vaccine to the market, even though the basic technology was developed elsewhere (Poirot and Martin 1994).¹³ Manufacturers will try to recoup these investment costs before patents expire (see Intellectual Property Rights below), such that new vaccines remain relatively expensive.

¹³However, it had to pay royalties to the company that invented the technology and held the primary patent.

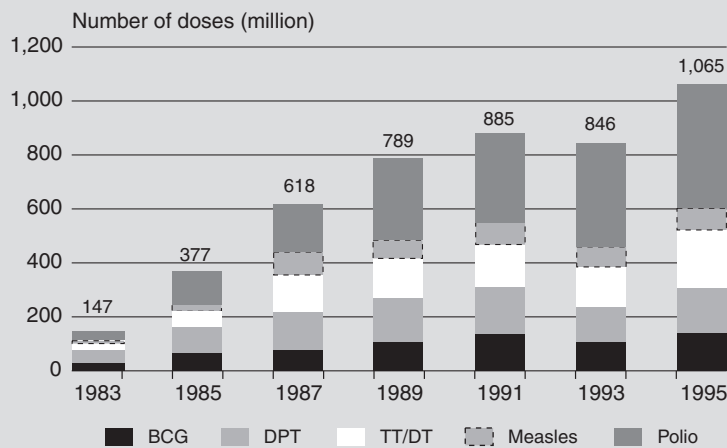
The increased upfront and ongoing costs of the new technology may prevent the price of these vaccines from ever coming down to the level of EPI vaccines, even as global competition and volume increase over time.

Demand

The demand for vaccines surged during the 1980s and early 1990s as a result of the EPI and UCI programs and the subsequent increase in coverage rates from 5 percent in the mid-1970s to 80 percent in 1990. The substantial and steady expansion in the volume of vaccines supplied by UNICEF between 1982 and 1995 (Figure 7) reflected this increase in demand.

Economic theory suggests that rising demand will lead to higher prices. However, for EPI vaccines the increase in demand has been largely in developing countries, which need a low-cost product provided through the public sector. When the tremendous growth in demand occurred, these vaccines were being purchased through a procurement mechanism (a few large purchasers, such as UNICEF, PAHO,

FIGURE 7

Volume of Vaccines Procured by UNICEF, 1983–1995

Source: CIDEF (1998)

and WHO) with enough negotiating power to keep prices low. Therefore, although demand has increased, the nature of the market has effectively kept prices low.

Demand for vaccines in less developed countries also depends, to a large extent, on donor funding. For example, a sudden increase in donor funds available for newer vaccines may create significant changes in the market, particularly if procurement is centralized in one agency. For example, the expected dramatic growth in demand for Hepatitis B vaccine generated by GAVI (see discussion under Trends in Grant Financing for Vaccines and Immunization Programs above) and supplied through UNICEF will heavily influence the price of the vaccine.

Predictability of demand

Vaccine producers say they need credible forecasts and predictable demand to manage production costs efficiently. UNICEF and PAHO have been able to negotiate low prices for developing countries, in part by providing producers with accurate requirements of need and a guaranteed volume.

Production capacity

As mentioned above, if manufacturers have excess capacity they can reduce their cost per dose by increasing production, especially by increasing the size of a batch, but only up to full capacity. According to Batson (1998a, p. 488), “given the impact of scale and learning, a large volume ‘global’ manufacturer can benefit from a rapid decline in costs per dose and can attain a more competitive position than smaller manufacturers.”

Once the maximum production capacity is reached, a manufacturer would have to expand the plant facilities, and make a large capital investment in the process, to achieve any further increase. In the early 1990s, the Universal Child Immunization initiative drove demand beyond production capacity worldwide. Manufacturers therefore invested in larger production infrastructure—the main reason given by industry for the 22 percent average increase in EPI vaccine prices charged to UNICEF and PAHO between 1991 and 1992.¹⁴ Higher prices allowed manufacturers to recoup their investment costs, but then increased competition from new international producers caused prices to plateau or even fall again in 1994 and 1995, as a result of increased production capacity.

The cost savings from maximizing the production of the newer vaccines that use conjugate technology may be somewhat less than for the traditional EPI vaccines. According to Hausdorff (1996, p. 1180), increasing the batch size of these vaccines may be “disproportionately more complex and costly than for the current vac-

¹⁴Although a drop in competition as producers consolidated and increased research and development costs were likely factors as well.

cines.” If this is true, the price difference between what less developed countries are charged and what industrialized countries pay may narrow.

Competition

Probably the greatest factor determining vaccine prices is competition. As price is the biggest determinant of vaccine profitability (see page 35), private-sector manufacturers will seek to maximize profits by charging the highest price a market will bear. For example, vaccine prices in some industrialized countries can be as much as 250 times the price charged to developing-country governments (UNICEF 1994a).

The entry of several Asian manufacturers into the market in the 1980s and 1990s had a significant impact on vaccine prices during those years. For example, the price per dose of plasma-derived Hepatitis B vaccine dropped suddenly from \$15–\$30 to less than \$1 when two Korean manufacturers new to the market tendered an international bid for Indonesia. PAHO also attributes the decline in most EPI vaccine prices in 1995 to the entry of other new Asian manufacturers into the international market.

While increased competition has helped maintain or lower the price of EPI vaccines and Hepatitis B vaccine, the situation for newer and upcoming vaccines,

TABLE 7

Main Factors Affecting Vaccine Prices

Cost	Research and development costs: Significant portion of new vaccine costs; these grow as new technologies are developed Production costs: Low variable costs (e.g., materials, additional labor). New technologies (e.g., conjugate) and more stringent quality control requirements are raising costs
Production capacity	Maximized use of existing capacity reduces cost per dose
Price tiering	Prices for industrialized countries and private sector in developing countries cover return on investment, including R&D and profit. This allows low prices to be charged to developing countries, covering only marginal costs
Patents/IPRs	An issue only for new vaccines, for both basic technology (e.g., recombinant DNA) and specific vaccines. Creates monopolies, limits competition, and keeps prices high. Can be extended by licensing to other producers, tiered royalties, or other arrangements
Demand/Volume	Demand in developing countries has grown tremendously but is mainly for low-cost vaccines. Excess capacity, sharply tiered pricing, and donor funding allowed producers to meet growing demand in 1980s and 1990s
Number of buyers/Bulk purchasing	The fewer the buyers, the greater their influence in negotiating prices with producers. Bulk purchasing by UNICEF and PAHO has kept prices for basic vaccines low
Predictability of need	Predictability of need and planning are conducive to more cost-efficient manufacturing. Guaranteed volume by UNICEF and others should help keep costs low
Competition	Has increased for classic EPI vaccines with new developing-country producers. Consolidation among large international producers and the high cost of new technologies and patents for new vaccines are limiting competition for new vaccines
Existence of local producers	Can prevent lower-cost competitors from other countries from entering the local market

including Hib and combinations such as DPT-Hepatitis B-Hib vaccines, is quite different. These vaccines are or will be produced exclusively by European and American manufacturers. This will likely be the case for sometime for two main reasons:

- New vaccines are more costly to produce than the traditional EPI vaccines, as they depend on conjugate and other new technologies.¹⁵ Perhaps more importantly, the investment costs, particularly for production facilities, are high. Smaller manufacturers, especially those from developing countries, often cannot afford these investment and production costs.
- Some of these vaccines, such as pneumococcal conjugate vaccine, are protected by patents (see Intellectual Property Rights), which are currently held only by European or American producers.

Competition in the new vaccine market may be further limited by the strong likelihood that European and North American vaccine producers will continue to consolidate, reducing the number of major global producers to a handful. For instance, before 1985, there were three separate companies producing vaccines: Institut Pasteur and Institut Merieux (both French), as well as Connaught Labs (Canadian). By 1994, they were all one company—Pasteur-Merieux-Connaught (PMC)—owned by the large pharmaceutical firm Rhone-Poulenc. PMC has since formed a joint venture (Pasteur Merieux MSD) with the US company Merck to

¹⁵Others dispute this claim; how the production process affects price is still an unanswered question, they say.

supply the European vaccine market. Furthermore, Rhone-Poulenc merged in 1999 with another company, creating Aventis; the vaccine division is now called Aventis-Pasteur. Similarly, RIT (Belgium), SmithKline of the US, and Beecham (UK) consolidated into SmithKline Beecham (SKB), which was recently acquired by Glaxo Wellcome and is now known as Glaxo-SmithKline.

Local producers

More and more developing countries are producing EPI vaccines for domestic consumption through state-owned companies. Several manufacturers in developing countries in Asia, including the People's Republic of China, India, and Viet Nam, also produce Hepatitis B vaccine. The existence of local state-owned producers can limit competition within a country and discourage the government from inviting bids through international tenders, thus keeping prices artificially high.

Intellectual property rights

Patents are a form of intellectual property rights (IPR), which allow manufacturers to have a monopoly on their invention for 20 years. Patents can be filed for vaccines, their components (such as a bacterial or viral strain), or the manufacturing process. Patents encourage companies to invest in research and development for new vaccines or new vaccine technology by allowing them to recoup costs (over the period of the patent) through high prices, which can be maintained because of a lack of competition. Patent holders can also grant licenses for the use of their invention to other companies in exchange for royalty payments.

TABLE 8

Status of New Vaccines: Producers, Patents, Technology

Vaccine Presentation	Technology Type and Complexity	Producers in International Market	Brand Name	Status of Patent
Hepatitis B (recombinant)	DNA recombinant, using yeast cells; relatively inexpensive	Aventis Pasteur, SmithKline Beecham, Korean Green Cross, Lucky Goldstar (Korea), Boryung Biopharma Co. (Indonesia), Merck	GenHevac B Pasteur, Engerix-B	Biogen DNA technology patent still considered valid only in US and Canada
Hib (liquid or lyophilized)	Conjugate technology; more complex and costly than recombinant	Aventis Pasteur, SmithKline Beecham, Wyeth Lederle, Chiron (Italy)	AHIB, PHIB, ActHib; HibTITER	Conjugate technology is in public domain, as is PMC vaccine
DPT-Hepatitis B (quadrivalent)	Easier	SmithKline Beecham		Same as for recombinant Hepatitis B
DPT-Hepatitis B–Hib (pentavalent)	Complex and costly	SmithKline Beecham, (Aventis Pasteur planning to produce)		Same as for recombinant Hepatitis B
DPT-Hib	Complex and costly	Aventis Pasteur, SmithKline Beecham, Wyeth/Lederle	ProHIBit-DPT; DPT-ActHIB, TriHIBit; Trivax-Hib; Tetramune	
Rotavirus	Conjugate technology	Wyeth/Lederle withdrew from market in 1999	Rotashield	Vaccine developed by NIH (US); license granted solely to Wyeth so far
Pneumococcal	7- to 11-valent conjugate vaccine; more complex and costly than monovalent vaccines	Wyeth/Lederle; PMC and SmithKline gearing up		Some process patents

As patents for EPI vaccines have long expired, these “public domain” vaccines can be produced by anyone with access to the technology. However, the newer vaccines—DNA recombinant Hepatitis B vaccine being the first—are usually covered by patents.

The monopolies or limited competition that patents create and, to a lesser extent, the royalties paid to the original patent holder by the licensed companies tend to keep vaccine prices high. For instance, Biogen’s broad patent for all recombinant methods of making Hepatitis B virus antigens limited the competition for recombinant Hepatitis B vaccine for many years

to two firms that Biogen licensed (Cook 1996). According to James Maynard of the Program for Appropriate Technology in Health (PATH) (personal communication), this broadly defined patent, which was later found by a British court to be invalid, prevented competition from driving down the price of recombinant Hepatitis B vaccine for 10 years. After the patent expired a few years ago in most parts of the world, other manufacturers, particularly in Asia, began making the vaccine, and the price came down considerably.

Conjugate technology used to make the Hib vaccine and other vaccines such as pneumococcal is in the public domain and

thus not controlled by patents. However, what will likely limit competition for these vaccines is, as mentioned above, the more complex production process and the higher capital investment costs involved. This is especially the case with the new pneumococcal vaccine, which are polyvalent (7-, 9-, or 11-valent) to provide protection against different serotypes, as opposed to the monovalent Hib vaccine.

Effects of These Factors on Vaccine Price Trends

PAHO data for DPT and OPV from 1979 to 1999 show how the above market forces have affected prices over the past 20 years. The price pattern for DPT is similar to that for BCG, TT, and DT.

DPT

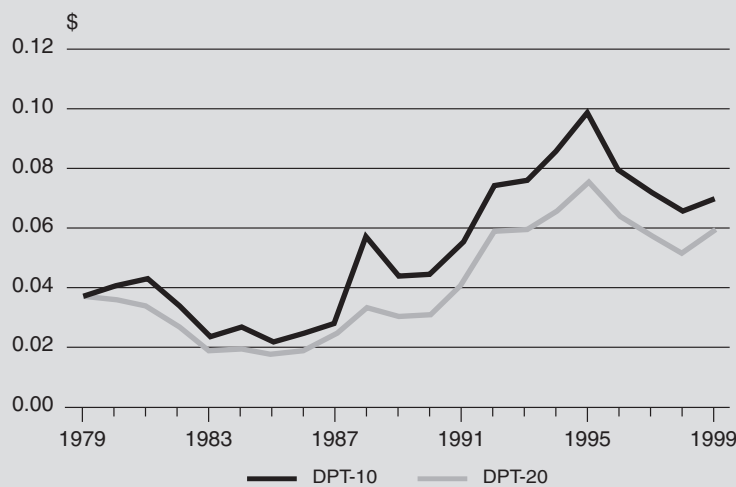
The pattern for DPT, as shown in Figure 8, reflects consistently low prices (less than \$0.10 per dose) over the past 20 years. The price from 1979 to the mid-

1980s remained stable; according to PAHO, this was due to low demand and excess production capacity (Peter Carrasco, personal communication). The increase in demand under the UCI, which started in 1987, led to an initial sharp rise, a decline, and then steady increases over the next three years. The price jumped, however, from 1991 to 1993 (as it did for nearly all EPI vaccines) and manufacturers attribute this to the upgrading and expansion of facilities necessary to meet the increased demand. Consolidation of companies during this time, increased research and development costs, and the expenses incurred to maintain WHO quality control standards may also have played a role in these price increases (Schwabe 1993). The price decreased again after 1995; PAHO ascribed the drop to the entry of a new Asian supplier into the international market and the increased competitiveness of other established producers with newly increased capacity.

OPV

The picture for OPV, shown in Figure 9, is somewhat different, particularly after 1993. Similar to DPT, the expansion of production facilities (among other factors) drove up the price per dose of the 10-dose vial to nearly double between 1989 and 1993 (from \$0.0425 to \$0.08). However, the price did not decrease to the same extent as DPT after this, and the 1999 price was the highest in 20 years. Since 1999, the price has again jumped by 33 percent. One explanation for this is that the complexities involved in manufacturing OPV have kept lower-cost manufacturers out of the international market and held competition to a minimum, while

FIGURE 8
Price per Dose of DPT Vaccines Obtained through the PAHO Revolving Fund, 1979–1999



Source: PAHO

demand has increased dramatically with the worldwide Polio Eradication Program.

Recent Developments Formalizing and Expanding Tiered Pricing

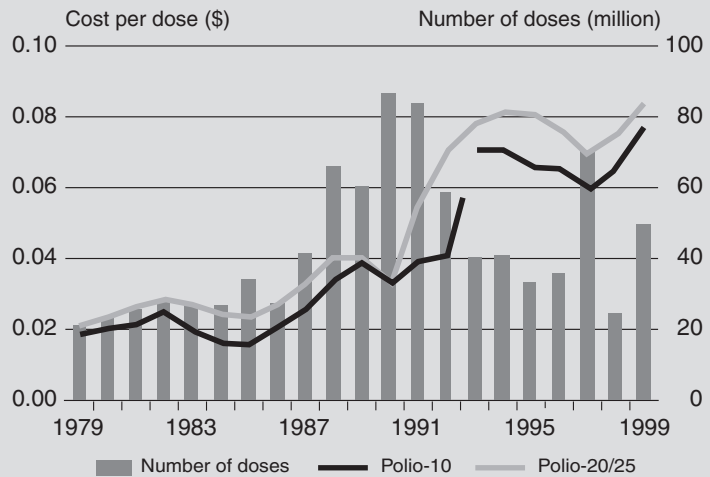
Vaccine manufacturers and consumers have been using tiered pricing for many years. Developing countries have greatly benefited from industrialized countries (and to a lesser extent, private-sector markets in developing countries) subsidizing their public-sector vaccines. By accessing high-quality vaccines at extremely low (marginal) prices, often through UNICEF or PAHO, countries have been able to increase their immunization coverage rates significantly over the past 15 years.

By the early 1990s, however, this simple two-tiered price system was beginning to appear unsustainable both to donor and multilateral agencies and to the vaccine industry. The emergence of a number of factors has contributed to this. These factors include:

- Increases in the price of traditional EPI vaccines in the early 1990s
- The likelihood that new vaccine prices would remain high for some time, largely because of the limited competition (the result of patents and high production costs) and the need to maintain high profit margins to recoup heavy research and development investments
- The decline in immunization coverage rates after 1990 in a number of countries, especially in sub-Saharan Africa (Taylor 1996)

FIGURE 9

OPV Purchased through the PAHO Revolving Fund, 1979–1999



Source: PAHO

- Decreases in donor support for immunization programs once UCI ended in 1990, and the reluctance of donors to finance the new, more expensive vaccines
- The slow introduction of the new vaccines, such as Hepatitis B, into developing countries, where they are most needed
- The growing reluctance of the vaccine industry to continue selling vaccines at marginal cost through UNICEF and PAHO to countries which they believed were wealthy enough to buy them, and represented “legitimate,” higher-priced markets. According to Batson (1998b) of the World Bank, industry has insisted to UNICEF that it would sell the new proprietary vaccines at the lowest-tiered price only to the poorest countries and not to all developing countries, as was done in the past.

Given these challenges, UNICEF and WHO concluded that without changes in

the current procurement system and vaccine price structure:

- New vaccines would not be accessible to the countries that needed them most (and were often the poorest).
- The current coverage rates for the EPI vaccines would become increasingly difficult to sustain.

The Mercer study

The first step in developing a new, more sustainable vaccine procurement and financing strategy was taken by UNICEF when it commissioned Mercer Management Consulting, Inc., in late 1993 to carry out a study of the global vaccine industry. The intent was to gain a better understanding of the global market, the economics of the industry, and UNICEF's impact on the world market.

The study demonstrated that through economies of scale, large producers have been able to sell vaccines (produced by using their excess capacity) to UNICEF and PAHO at low prices without losing money. In addition, the study concluded that:

- Marginal profits generated from the large bulk sales to developing countries through UNICEF were not enough to drive research and development programs.
- Producers could sell new vaccines to developing countries and still recoup their research and development costs if they maximized economies of scale from the beginning. This would effectively shorten the typical product life cycle,¹⁶

¹⁶A new product is first introduced into industrialized countries and private sectors in developing countries at high prices and does not "mature" for 10 to 20 years until the patent expires and other manufacturers begin to compete, driving down the price.

which usually meant a 10- to 20-year delay in introducing a new vaccine into developing countries. However, a shortened life cycle would be acceptable to the industry only if different price tiers within the developing-country market were created, based on the countries' ability to pay.

The natural tensions between the large vaccine purchasers and the vaccine industry (buyer and seller) must be minimized if vaccines are going to reach developing countries quickly. As such,

UNICEF and the global community must recognize the inherent tradeoffs between gaining the lowest price for existing vaccines and the option of accessing new vaccines. Early access to new vaccines will require a procurement strategy emphasizing greater collaboration and partnership with vaccine manufacturers... (UNICEF 1994a, p. 12)

The "banding" strategy

The Mercer study, decreases in donor funding, and industry's insistence on having access to more developing-country markets led to the development in 1994 of a new "targeting strategy" by UNICEF, WHO, and industry representatives. This strategy grouped developing countries into four bands (A–D) on the basis of their relative wealth (per capita GNP), total market size (based on overall GNP), and population size (a measure of market influence).

The resulting grid, shown in Figure 10, provided a framework for UNICEF and other donors to target vaccine assistance.

- Bands A and B are the poorest and smallest countries, which cannot procure or produce vaccines without assistance.

- Bands C and D are considered “self-sufficient” and thus no longer eligible for donor assistance.
- Band C countries could still use UNICEF to procure EPI vaccines but are encouraged to procure new vaccines through direct negotiation with manufacturers.

Band D countries would no longer have access to UNICEF’s procurement services and marginally priced vaccines. According to Batson (1998b), “market forces in these countries [Bands C and D] will result in a realistic but affordable price for vaccines.”

The strategy would effectively reduce UNICEF’s market intervention (through the procurement of low-cost vaccines) on behalf of about 80 percent of the world’s population to 25 percent (Band A and B countries only). It also created at least one new price tier because Band C and D and even many B countries would now negotiate prices for new vaccines directly with producers. These prices would fall somewhere between the marginal-price tier offered to the poorest, smallest countries and the high-price tier paid by industrialized countries and private-sector markets. This strategy has been referred to as “planned tiered pricing” or “differential pricing.”

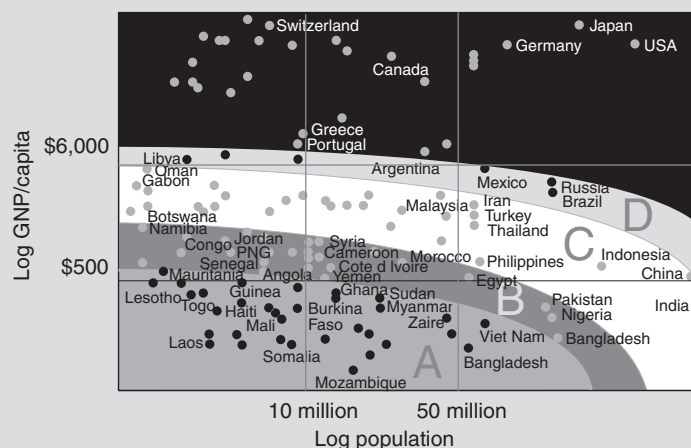
Objectives

Apart from providing industry with increased access to “legitimate” markets, the strategy was also meant to improve self-financing for vaccines and to speed up the introduction of new vaccines into developing countries.

To encourage self-financing, the following targets were set for each band:

FIGURE 10

WHO/UNICEF Global Banding Strategy



A = Financial support, B = Gradual hand-off, C = Self-sufficient, D = Rapid independence

- Band A countries: 10 percent to 25 percent, within four years
- Band B countries: 80 percent to 100 percent, within four years
- Band C and D countries: 100 percent self-financing, as quickly as possible

The VII (see page 12), established in 1991, was available as a mechanism to help countries (especially those in Bands B and C) achieve financing self-sufficiency. Countries that produced their own vaccines were also able to access WHO technical assistance to assess and strengthen their production capacity.

The second objective was to introduce new vaccines, especially Hepatitis B, more quickly into the poorest (Band A and B) countries, where the need for the vaccine was often the greatest. Donor assistance would be targeted to these countries and UNICEF would negotiate with producers to obtain an affordable low-tiered price. To finance this scheme, a Global Vaccine Fund was to be established, and donors would pool their resources to finance new and existing vaccines for the

targeted countries, strengthening their vaccine supply overall (UNICEF 1994c).

Support

Industry readily accepted the targeting strategy, as it would increase the number of “legitimate markets” where new vaccines could be sold directly. This would, in turn, increase the opportunity to recoup research and development costs as well as profit margins. Industry viewed UNICEF’s efforts to introduce new vaccines into developing countries “not as a potential pricing threat, but as a kind of pre-marketing service” (Rosegrant 1998b, p. 3).

Donors also generally favored the strategy, as it focused their assistance and decreasing resources on the neediest countries. The possibility that countries most in need of Hepatitis B vaccine and other proprietary vaccines could obtain the vaccines much sooner than if they had to wait for these vaccines to reach “maturity” made the strategy attractive.

Results

The targeting strategy has had mixed results. According to UNICEF, the goals established for this strategy have been met. By 1999, over 75 percent of donor support for vaccines was going to Band A countries and about 78 percent of vaccines purchased for routine programs in developing countries were self-financed (Sakai 1999).¹⁷

Self-financing. Whether increased self-financing is attributable to the targeting

strategy, or general decreases in donor funding, or both, is difficult to determine.

New vaccines: The strategy has not facilitated the introduction of Hepatitis B and other newer vaccines into the national programs of poorer countries. Manufacturers responded to a UNICEF tender in 1995 “with creative bids” (Rosegrant 1998b, p. 4), but funding from donors did not materialize. UNICEF therefore purchased Hepatitis B vaccine only on behalf of the 10 countries participating in the Pacific Island Hepatitis B Control Project, and for periodic orders from individual countries (e.g., the Philippines).

Increased “legitimate” markets. There has been only a limited opening up of new markets to major manufacturers for new vaccines since the strategy was developed in 1994. Although some countries, including Iraq, Zimbabwe, Egypt, and Philippines, now buy Hepatitis B vaccine directly from the original manufacturers in the West, the growth in the number of manufacturers (and the consequent decrease in price) has led to many countries purchasing from non-Western manufacturers. Indeed, Hepatitis B vaccine is fast becoming a generic vaccine like the classic EPI antigens (see The Price History of Hepatitis B Vaccine: A Case Study below) making its sale to developing countries less attractive to the traditional major manufacturers. Aventis Pasteur, for example, now distributes the Korean Lucky Goldstar Hepatitis B vaccine instead of its own product.

The relatively high price of Hib has kept it out of the immunization programs of most developing countries. The greatest inroads in introducing it have been made in Latin America but most coun-

¹⁷As noted earlier, a number of countries reported to be self-financing are using alternative funding sources such as the EU Initiative (using structural adjustment grants) and World Bank loans.

tries are buying it through the PAHO Revolving Fund, at a single low price, preventing manufacturers from dealing directly with the “legitimate” markets.

In addition, not all the organizations concerned have adopted the targeting strategy. PAHO never agreed to the concept and, in fact, has encouraged more countries, including Brazil (Band D), to join the Revolving Fund since the banding strategy was introduced. Instead of having wealthier or large countries negotiate prices independently, PAHO prefers to increase its purchasing power to be able to negotiate a single, low price for each vaccine. Therefore, all but two Band C and D countries in the Latin American and Caribbean region (Chile and Argentina) currently take advantage of PAHO’s Revolving Fund for all or some of their vaccine purchases.

GAVI

Efforts to speed up the introduction of new vaccines into the poorest countries using the multi-tiered pricing concept received a considerable boost with the creation of the GAVI (see page 4). GAVI will provide funds for new vaccines only to the poorest countries (those with a per capita GNP of less than \$1,000). These countries will procure the vaccines entirely through UNICEF, negotiating a specific low-tiered price. For countries not eligible for the fund, UNICEF will issue separate tenders for new vaccines on their behalf, but prices will generally be higher than those obtained for GAVI countries.

GAVI operations will effectively implement “planned tiered pricing” while increasing the use of new vaccines—both objectives of the targeting strategy.

The tiered pricing vs. bulk purchasing approaches to vaccine pricing are discussed further below.

Different Approaches to Pricing

There are two schools of thought regarding how pricing can be structured to best facilitate and speed up the introduction of vaccines, particularly new ones, into the countries that need them most.

The first model, promoted by WHO, UNICEF, the World Bank, and GAVI, and supported by the industry, is planned or formalized tiered pricing or “differential pricing,” discussed above. Under this model, developing countries are divided into tiers, depending on the viability of their commercial market for new vaccines. Those too poor or too small to have a viable market receive a low price for the new vaccines, through a procurement system such as UNICEF’s. Countries considered to have commercial markets must, in most cases, negotiate directly with manufacturers (or through UNICEF) and pay a higher price.

The second model, championed by PAHO, among others, promotes bulk purchasing with pooled funding from many countries as the most effective, efficient, and equitable means of introducing new proprietary vaccines into less developed countries. This is called the bulk purchasing or uniform pricing strategy.

Both models assume that industrialized countries will continue to pay a higher price than developing countries for the same vaccines (the high-priced tier), as

shown in Figure 11. The main arguments for and against each approach are described below, and summarized in Table 9 and Table 10.

Planned tiered pricing

This approach responds to manufacturers' arguments that they cannot afford to provide the new (patented) vaccines at marginal prices for the entire developing-country market. However, it is maintained that low prices can be offered to the poorest countries, and the introduction of vaccines accelerated in those countries, if higher, more commercially viable prices are negotiated for wealthier or larger developing countries. Such an approach shortens the normal product life cycle by creating a large demand for the vaccines from the beginning.

Arguments for

Producers can afford to offer a low price to a limited number of countries because:

- The increase in volume to supply these countries can achieve economies of scale and learning effects.

- Higher prices charged to other developing countries will improve the producers' overall profit margin.

The nontargeted countries in the middle tier will still be charged prices that “are ‘affordable’ given their economy” (Batson 1998a, p. 489). Without this approach, it is argued, the introduction of new vaccines will continue to be delayed. Only the wealthier countries, such as Thailand, Indonesia, and a number of Latin American countries, will be able to add new vaccines to their national immunization programs.

At the same time, low prices for a limited number of poor countries will also encourage donors to contribute to the procurement of the new vaccines. Until now, donors have been reluctant to finance Hepatitis B and other newer vaccines because of the high costs involved and the potentially huge demand from developing countries.

One of the strongest price-tiering arguments is that limiting low prices and allowing manufacturers to increase profits in the rest of the developing world will encourage producers to invest in research and development for other vaccines, such as those for malaria and schistosomiasis. Vaccines for malaria and other “developing-country diseases” “for which no significant commercial market exists” have received very little attention mostly because of the lack of profitable markets. Under the price-tiering strategy, however, research and development costs could be recouped from all but the poorest developing countries, serving as an incentive to manufacturers to invest more in these needed vaccines.

Proponents also argue that planned tiered pricing would increase competition

FIGURE 11

Two Models of Vaccine Pricing

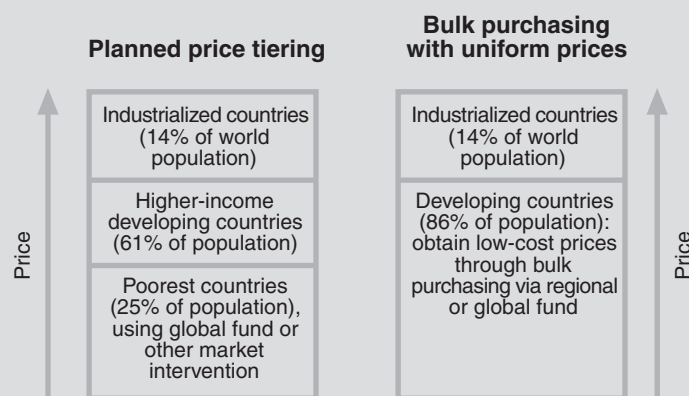


TABLE 9

Planned Tiered Pricing: Arguments For and Against

Issue	For	Against
Access to and availability of new vaccines	<p>The slow introduction of Hepatitis B and other new vaccines in poorer countries shows the limits of the existing two-tiered price system (industrialized vs. developing countries) and the need for a new price structure.</p> <p>A guaranteed low price from the beginning for the neediest countries will shorten the normal product life cycle, accelerating access to newer vaccines for the countries that need them the most.</p>	<p>Price is not the only reason some important vaccines have not been incorporated into immunization programs. For example, MMR and yellow fever vaccine are reasonably priced but underused. Other factors (e.g., governments' insufficient appreciation of the value of vaccines) are also in play.</p> <p>The life cycle of new vaccines can be shortened, and low prices obtained, as effectively through bulk purchasing.</p>
Competition	<p>Strategy should encourage manufacturers to respond to UNICEF bids for lowest-tiered countries, in return for free entry into more lucrative developing-country markets. This will increase competition among producers and keep lowest-tiered prices down.</p>	<p>Planned tiered pricing decreases competition by preventing middle-tiered countries from obtaining the lowest price.</p> <p>Natural "friendly adversarial" relationship between purchasers (e.g., UNICEF) and producers helps maintain competition and should not be eliminated.</p>
Price	<p>Will result in affordable (low-tiered) price of new vaccines for poorest countries. Prices gained, through international tenders, for better-off developing countries will be higher but still affordable for their economy."</p>	<p>Strategy constitutes a form of "price fixing." This interferes with the ability of economies of scale to lower prices, as wealthier or larger developing countries (representing around 60% of the world's population) will not have access to the best prices. The strategy therefore keeps prices of new vaccines relatively high for the majority of the world's population.</p>
Research and development	<p>Profits from industrialized countries currently drive research and development. Therefore focus has been on developing vaccines for these markets. This is one reason for the slow development of malaria vaccines.</p> <p>Reducing the number of countries benefiting from marginal prices, and thereby increasing revenues for manufacturers, will allow a quicker return on research and development investments. This will encourage research and development investment for vaccines against diseases predominant mainly in developing countries.</p>	<p>A substantial portion of research and development funding for vaccines comes from the public sector. Public-sector funding will always be a driving force in developing vaccines of interest mainly in developing countries. What is needed is increased public-sector funding for vaccine development (e.g., for malaria).</p>
Equity	<p>Providing new vaccines to the neediest countries by lowering prices and targeting external aid is an equitable approach. It enables countries to pay according to their means.</p>	<p>Strategy discriminates against countries with larger commercial markets. The majority of the population in developing countries will not obtain the lowest-tiered price; hence, this approach is inequitable.</p>
Availability of donor funding for new vaccines	<p>It is the only viable way for donors to fund the introduction of new vaccines since new vaccines cannot be added for the whole world. Limited donor funds will be used to fill critical gaps.</p>	<p>Establishing a special fund for the poorest countries, as part of a bulk purchasing system, can achieve the same results. Fund sources can include donor contributions, contributions from member countries, and accumulated capital from fees.</p>
Sustainability/ Viability of strategy	<p>Directing donor financing for new vaccines to a limited number of countries makes this approach more sustainable than the existing two-tiered pricing system.</p>	<p>The introduction of new vaccines in the neediest countries under this strategy depends totally on donor funding. What will happen when the funds run out?</p>

TABLE 10

Bulk Purchasing Model with Uniform Prices: Arguments For and Against

Issue	For	Against
Access to and availability of new vaccines	All but one of the developing countries that have introduced both Hepatitis B and Hib belong to a bulk-purchasing system (the PAHO Revolving Fund or the GCC in the Middle East). This shows the effectiveness of the system in getting developing countries to introduce new vaccines by driving down prices. The neediest countries can obtain the vaccines, at the same low price, with donor funding.	The neediest countries will not have access to the new vaccines for a long time, since prices will still be unaffordable to them.
Competition	Instead of the price fixing of the tiered pricing approach, this strategy increases competition by encouraging producers to compete for very large orders through international tenders. It thus allows normal market forces to drive down prices.	The large difference between the one, low price for each vaccine for all developing countries and the price paid by industrialized countries has discouraged US manufacturers from supplying UNICEF/PAHO and has laid them open to accusations from US politicians of price discrimination against the US market.
Price	The promise of large-volume purchases, coupled with international competition, results in very low prices, which benefit all developing countries, not just the poorest or smallest.	The resulting prices for new vaccines will still be too high for many of the neediest countries to afford. This strategy can work only if mainly wealthier countries are involved, as is the case in Latin America with the PAHO Revolving Fund.
Equity	Since this approach does not discriminate between very poor or smallest countries and larger, wealthier developing countries, it is much more equitable than planned tiered pricing.	Since the poorest countries still will not be able to afford the newer vaccines, the tiered approach is actually more equitable. Also, it is not fair for industrialized countries to continue subsidizing marginal prices for middle-income countries.
Sustainability/ Viability of strategy	This is the only sustainable approach since it uses classic market forces to drive down prices and does not depend on any deal with producers or time-limited funding from donors.	For the foreseeable future, many of the poorest countries will be relying on donors to support their programs independently of the mechanism used for procurement.

by encouraging more manufacturers to respond to UNICEF bids. For example, two US manufacturers were believed to be reconsidering entering the UNICEF market after the targeting strategy became official policy by UNICEF and WHO (Rosegrant 1998b). Competition would also be increased for the vaccine market in the “middle tier” of countries, where manufacturers can make greater profits.

Arguments against

Critics of this strategy contend that it constitutes a form of “price fixing,” which

limits the free-market forces of competition and economies of scale from driving down prices as much as possible. This results in larger, middle-income countries not having access to the lowest tiered price. As such the policy discriminates against poor people in these larger or slightly wealthier countries, where most of the people in the world live. Not only will these countries have to pay more for the same vaccines than their smaller or poorer neighbors, the higher prices offered to them may continue to delay the introduction of these vaccines.

It is also argued that research and development for vaccines against malaria and other diseases affecting mainly developing countries have been, and will continue to be, heavily supported by the public sector in industrialized countries and not entirely by industry. For example, the National Institutes of Health in the US developed both the new rotavirus vaccine and the original plasma-derived Hepatitis B vaccine. Also, the slow development of vaccines is often due to the scientific complexity of the process. There is no malaria vaccine yet, for example, because it is extremely difficult to develop one that must act against a parasite (as opposed to much smaller viruses or bacteria). Indeed, critics of planned tiered pricing are not convinced that procurement initiatives developed by multilateral agencies will influence the research and development decisions of manufacturers.

Bulk purchasing/Uniform pricing

This approach centralizes vaccine orders from various countries in one mechanism (such as the PAHO Revolving Fund) and involves international tenders and bids for bulk purchases of each vaccine. The promise of bulk orders to producers helps ensure very competitive prices—a feasible prospect due to the associated economies of scale. Therefore, the more countries participating in a regional or even global fund, the greater the volume to be purchased, and the lower the prices obtained from manufacturers through large annual or multi-year contracts. Competition also drives down prices, as evidenced by the decrease in prices for Hepatitis B, DPT, and other vaccines offered to the PAHO

Revolving Fund in recent years after new Asian producers entered the picture.

Arguments for

This strategy takes advantage of the effects of demand, economy of scale, and competition to drive prices down to the level where, according to its proponents, most developing countries can afford them. It is argued that these market forces apply not only to EPI vaccines but also to new vaccines. “In the future, as in the past, volume will make production costs low and competition will be the factor in keeping vaccines affordable” (PAHO 1999, p. 3). According to this argument, the way to shorten the natural product life cycle is, therefore, to intensify or enhance the effects of volume and competition in bringing down prices and not to create artificial price tiers or otherwise interfere with natural market forces.

PAHO points to the fact that price quotes for DNA-recombinant Hepatitis B vaccine purchased through its Revolving Fund decreased from \$11 per dose in 1994 to \$0.69 per dose in 1999 as evidence of the forces of bulk purchasing and increased competition driving down prices. During this period, the number of countries purchasing Hepatitis B vaccine through the Revolving Fund increased from one or two (through spot buys) to twenty.

Rather than limiting access to new vaccines, proponents of this strategy argue that bulk purchasing systems enhance it. In 1998, for example, of the seven developing countries that had introduced both Hib and Hepatitis B vaccines, all but one were part of a bulk purchasing program (either the PAHO Revolving Fund or the Gulf CC in the Middle East). Also,

several countries in Latin America now purchase the pentavalent DPT-HBV-Hib (at \$3.50 per dose) through the Revolving Fund.

The bulk purchasing approach may also be considered more equitable. The planned tiered pricing approach will lower prices only for countries where a minority of the people in the world live. This is especially true if the WHO/UNICEF bands are used to determine price tiers, since large C and D countries with poor populations, such as India, will not have access to the lowest-tier price and this could delay the introduction of the newer vaccines into these countries. Bulk purchasing, on the other hand, allows all developing countries to benefit from competitive prices.

Finally, one of the primary arguments for this approach is its long-term sustainability. It does not depend on any special arrangement between manufacturers and large procurers like UNICEF, and it depends less on donor funding to provide needier countries with access to the newer vaccines than the price-tiering approach. Indeed, it may be possible to develop a sustainable fund that grows in capitalization from an accumulation of service fees and that could be used to finance or subsidize the procurement of vaccines for the neediest member countries.

Arguments against

Critics of the bulk purchasing/uniform pricing approach say the history of prices for classic EPI vaccines does not serve as a good model for the new proprietary vaccines. The prices of the newer vaccines will not decline to the level of the traditional EPI vaccines for many years, if ever. For example, although the price of Hepatitis B vaccine has decreased markedly in recent years, it is still higher than the price of all other EPI vaccines combined. Very poor or smaller countries will not be able to afford the new vaccines for many years if they have to wait for patents to expire, new producers to enter the market, and economies of scale to drive down the price. In addition, many of the newer vaccines are costly to produce and economies of scale and competition can only bring the price down so far, probably never to the level of the traditional EPI vaccines. Therefore, this approach can work only in a region or area that has mostly larger, better-off countries (such as Latin America). It will not work in sub-Saharan Africa, for instance, or on a global scale.

Critics of this strategy also argue that it will not encourage producers to invest in research and development for vaccines against diseases that affect mainly developing countries.

The Price History of Hepatitis B Vaccine: A Case Study

This section will analyze the price changes that Hepatitis B vaccine has undergone since its development in the 1980s and discuss the major factors contributing to these price changes.

Introduction

In 1992 the World Health Assembly recommended that all countries incorporate Hepatitis B vaccine into their EPI by 1997. This was the first proprietary vaccine to be added to the EPI since the program began in the mid-1970s. By 1999, more than 90 countries had incorporated the vaccine into their national programs.

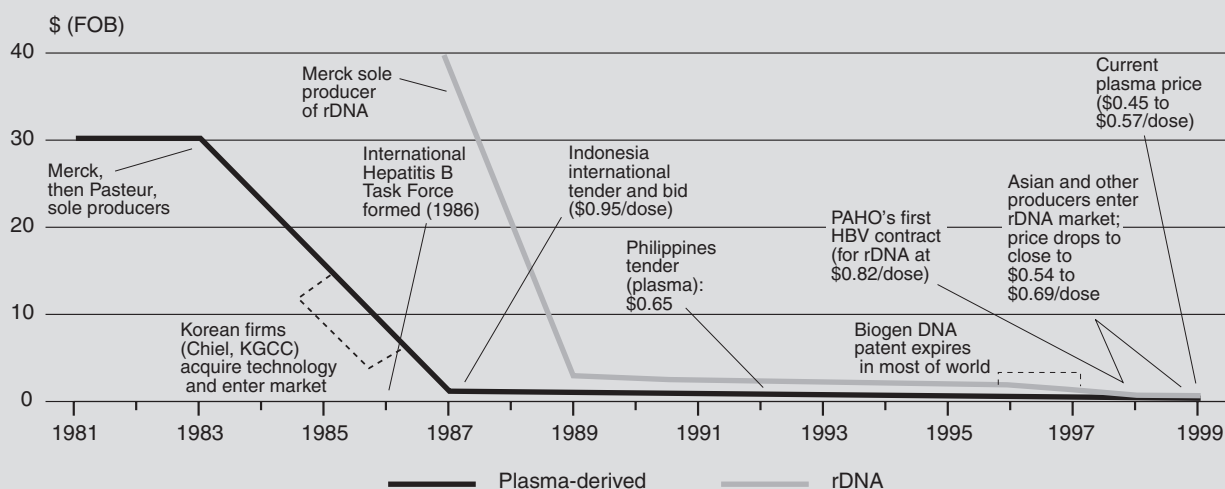
There are two types of Hepatitis B vaccine:

- Plasma-derived vaccine
- Recombinant DNA vaccine

Developing countries now obtain prices as low as \$0.40–\$0.50 per dose for the plasma-derived vaccine, and as low as \$0.54–\$0.69 per dose for the recombinant DNA vaccine. An examination of the price changes in the vaccine over the past 18 years and the main factors involved could be relevant to the future price patterns of other new and upcoming vaccines. The history of the changes in the price of Hepatitis B vaccine for developing countries is shown in Figure 12.

FIGURE 12

Changes in Hepatitis B Vaccine Prices for Developing Countries (lowest prices obtained)



Plasma-derived vaccine

This is made from the blood of infected people, and was developed by the US National Institutes of Health in the 1960s. The technology was first acquired by Merck and Co. (US), which put it on the market in 1981, at a price of about \$30 per dose, or nearly \$100 for the complete series of three shots. Because of its high cost, the vaccine was first used mainly to immunize health workers and others at high risk in industrialized countries.

Recombinant DNA vaccine

The Hepatitis B surface antigen is produced in yeast or mammalian cells using bioengineering technology. When Merck and SmithKline Beecham brought the recombinant DNA vaccine to the market in the mid-1980s, it also carried a high price of between \$30 and \$40 per dose.

Plasma-Derived Vaccine

When Merck's plasma-derived vaccine first appeared on the market at \$30 per dose, it was labeled by some in the international public health community as "a rich man's vaccine and a poor man's disease" (Muraskin 1995, p. 21). The vaccine used a technology involving chemical purification, which some experts found to be too elaborate and expensive to be appropriate and affordable for most developing countries. According to Muraskin,

the plasma-derived Hepatitis B vaccines had all been originally developed for the limited purpose of servicing the small market in the developed world. The developers desired a perfect vaccine, one that would receive quick approval by their regulatory authorities. To achieve this goal they chose to utilize

high technology and expensive methods to guarantee the highest level of safety. Only after the companies were successful at producing such a Hepatitis B vaccine did they realize that the real need was not in the West but in the countries of Asia and Africa. (1995, p. 44)

Within 10 years however, simplified technology, a proliferation of manufacturers, the integration of the vaccine into national immunization programs in a number of developing countries (especially in Asia), and a sharp decline in the price paid by the public sector in developing countries changed the above picture. The main developments accounting for these changes are the following.

- More accessible technology and an increased number of manufacturers
- The work of the International Task Force on Hepatitis B Immunization
- The pilot Hepatitis B vaccination program and international tender in Indonesia
- Increased competition, production capacity, and interest in recombinant DNA vaccine

More accessible technology and increased number of manufacturers

With the aim of developing a Hepatitis B vaccine more appropriate for use in developing countries, Alfred Prince of the New York Blood Center invented a vaccine using a flash heat purification method, a much simpler and cheaper process than the chemical process used for the existing Hepatitis B vaccines. Also, much smaller doses of the vaccine were required for it to be effective. Prince transferred this technology to Cheil Sugar Company of Korea, a subsidiary of

Samsung Corporation, which brought the vaccine into production by 1982. Within a short time, other companies had acquired the technology, including another Korean manufacturer (Korean Green Cross Corporation, or KGCC), three Japanese manufacturers, and a Taiwanese company. The Japan Kitasato Institute transferred its technology to the People's Republic of China, which was producing the vaccine in five production centers by the late 1980s. By 1987 there were nine producers of Hepatitis B vaccine on the international market and by 1989, there were twelve (Muraskin 1995; Maynard and Hadler 1989).

Creation of the Hepatitis B Task Force

In 1986, several Hepatitis B experts formed the International Task Force on Hepatitis B Immunization. The overall goal of the Task Force was to improve the control of Hepatitis B worldwide by:

- Forcing down the high price of the vaccines through international tenders and through efforts (ultimately successful) to facilitate the technology transfer of the Prince vaccine from Chiel to local producers in developing countries. The Task Force also assisted countries in undertaking international tenders to maximize competition.
- Convincing developing countries and the international health community to make Hepatitis B control and mass immunization of infants a top priority. As mentioned above, in 1992 the World Health Assembly recommended worldwide routine immunization of infants with Hepatitis B vaccine.

- Proving that developing countries could successfully integrate Hepatitis B vaccination into their immunization programs, without overtaxing their existing programs. To do this, the Task Force helped design and manage pilot or model projects in several countries. Even in countries such as Thailand, where interest within the Government for mass infant Hepatitis B immunization was already high, the Task Force provided a critical “outside push” to “help break bureaucratic logjams and conflicts that had immobilized [the Thais]” (Muraskin 1995, pp. 152–153).

The model Hepatitis B program and international tender

In 1987, a pilot Hepatitis B vaccination program was conducted in Lombok, Indonesia, with assistance from the Task Force and political commitment from the Indonesian President. The Task Force solicited international tenders for the supply of the vaccine, which generated responses from all suppliers registered in the country. An important condition of the tender was a commitment by the bidders to offer Indonesia the same price once it introduced the vaccine nationwide, to prevent them from offering promotional prices at the start and then increasing prices substantially later on. Bidders also committed to offering the same low price to other developing countries. The winning bid, by Korean Green Cross at \$0.95 per dose, was a “price-shattering achievement,” which instantly drove down the current world price of \$15–\$30 per dose to less than \$1. According to Muraskin, “the sealed bid and tender, followed by

the public announcement of the winning offer, broke the price of the vaccine and removed the chief obstacle to an effective war against Hepatitis B.” The low price obtained also “demonstrated that if a mass market was created, an affordable price could be achieved” (Muraskin 1995, p. 97).

The Lombok project proved that Hepatitis B vaccine could be successfully integrated into an immunization program without overburdening it, and, in fact, could result in dramatically higher immunization coverage rates for all childhood vaccines. Buoyed by this success, the Indonesian Government adopted universal Hepatitis B immunization of infants nationwide in 1991. Model programs developed with the Task Force’s assistance followed from 1988 to 1991 in Thailand, the People’s Republic of China, Kenya, and Cameroon. The Task Force also helped countries to develop international tenders in several countries, including the Philippines. By 1992, a number of Asian countries, including the People’s Republic of China, Thailand, Indonesia, the Philippines, and Mongolia, had introduced Hepatitis B into their immunization programs. The price decreased further, to as low as \$0.65 per dose offered to the Philippines in 1991.

Increased competition, production capacity, and interest in recombinant DNA vaccine

In the late 1990s increased demand for plasma-derived vaccine (at least in Asia) led to excess production capacity and drove down prices. This was followed by a shift in demand from plasma-derived to the recombinant DNA vaccine, further contrib-

uting to overcapacity as well as to a decline in prices. Responding to an ADB survey, countries in Asia reported paying around \$0.50 per dose in a 10-dose vial FOB¹⁸ for the plasma-derived vaccine. A recent price quote from Korea was \$0.24 per dose (PMC, personal communication). The plasma-derived vaccine is therefore becoming a “generic” vaccine, with prices approaching those of some EPI vaccines. However, it took 18 years for this to occur.

Recombinant DNA Vaccine

The price history of the recombinant DNA vaccine parallels, to some extent, that of the plasma-derived vaccine, as shown in Figure 12 above. However, patents on the basic vaccine production process played a much larger role for this vaccine than for the plasma-derived vaccine. The existence of the patent, along with the considerable capital investment costs involved, limited the number of manufacturers for a number of years. Consequently, the price remained high and took twice as long to get below \$1 than the price of the plasma-derived vaccine (12 years vs. 6 years). The main factors and events that affected the price of the recombinant vaccine were as follows:

- Limited number of licensees for the Biogen patent
- Competition with the plasma-derived vaccine
- Increased international competition
- Increased demand

¹⁸Free on board, i.e., before insurance, shipping, and handling charges are added to the price.

Limited number of licensees for the Biogen patent

The first successful technology using recombinant DNA to make Hepatitis B vaccine was developed by the American firm Biogen in the late 1970s. Biogen was granted a broad patent covering all methods of making Hepatitis B vaccine antigens using recombinant technology, including methods not used by Biogen.¹⁹ For several years, Biogen granted a license to scale up production of the vaccine to only two companies—Merck and Co. and SmithKline Beecham—both of which charged prices as high as \$40 per dose at first. Merck offered prices to the US public sector (Centers for Disease Control and Prevention) of around \$7–\$8 beginning in 1990, but charged private-sector providers in the US nearly double. Nonetheless the price, kept high by the lack of competition, stayed out of the developing world's reach.

Competition with the plasma-derived vaccine

A major factor that drove down the price of the recombinant DNA vaccine was competition with the plasma-derived vaccine. Hepatitis B vaccine manufacturers tend to make either the recombinant or the plasma-derived vaccine, but not both. The recombinant vaccine could dominate the Hepatitis B vaccine market if the price were only marginally higher than that of the plasma-derived vaccine. As such, by 1993, prices as low as \$1.25 to \$2.00 per dose (for 10-dose vials) for developing countries were quoted (Kane 1993).

¹⁹This broad patent was found to be invalid by a British court in 1996.

These prices, however, were still many times the cost of the traditional EPI vaccines.

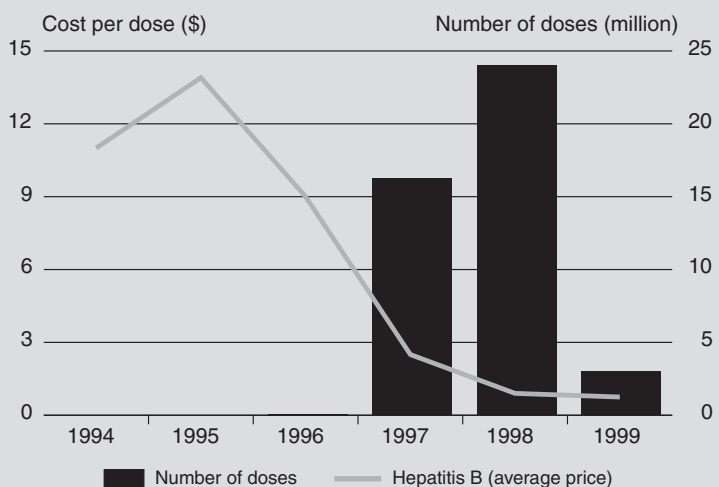
Increased competition

By the mid-1990s the Biogen patent had expired in many parts of the world, especially once the General Agreement on Tariffs and Trade (GATT) went into effect in 1995. Now able to acquire the technology, a number of new manufacturers entered the market. These included two Korean manufacturers, KGCC and Lucky Goldstar. At least ten producers now sell the DNA recombinant vaccine on the international market. These include three Indian firms with the capacity to supply both the domestic Indian market (once Hepatitis B is added to the national immunization schedule) and the export market (PMC, personal communication).

Increased demand

As shown in Figure 13 below, when PAHO purchased recombinant DNA vaccine on

FIGURE 13
Price of Recombinant Hepatitis B Vaccine and Amount Purchased through the PAHO Revolving Fund, 1994–1999



Source: PAHO

behalf of individual countries in 1994–96, it paid a very high price per dose (\$9–\$14). However, by the time it entered into its first Revolving Fund supply contract in 1998 (24 million doses), the price had fallen to \$0.82 per dose FOB (for 10-dose vials). In 1999, after KGCC and Lucky Goldstar began producing the vaccine, the price had fallen again to \$0.69 per dose, illustrating the power of increased demand and the impact of new competition on prices. Indeed, FOB prices as low as \$0.54 per dose for the recombinant vaccine were quoted in 1999. The price has been forecasted to continue declining to \$0.30–\$0.40 per dose in the near future (PMC, personal communication), approaching the price of the plasma-derived vaccine.

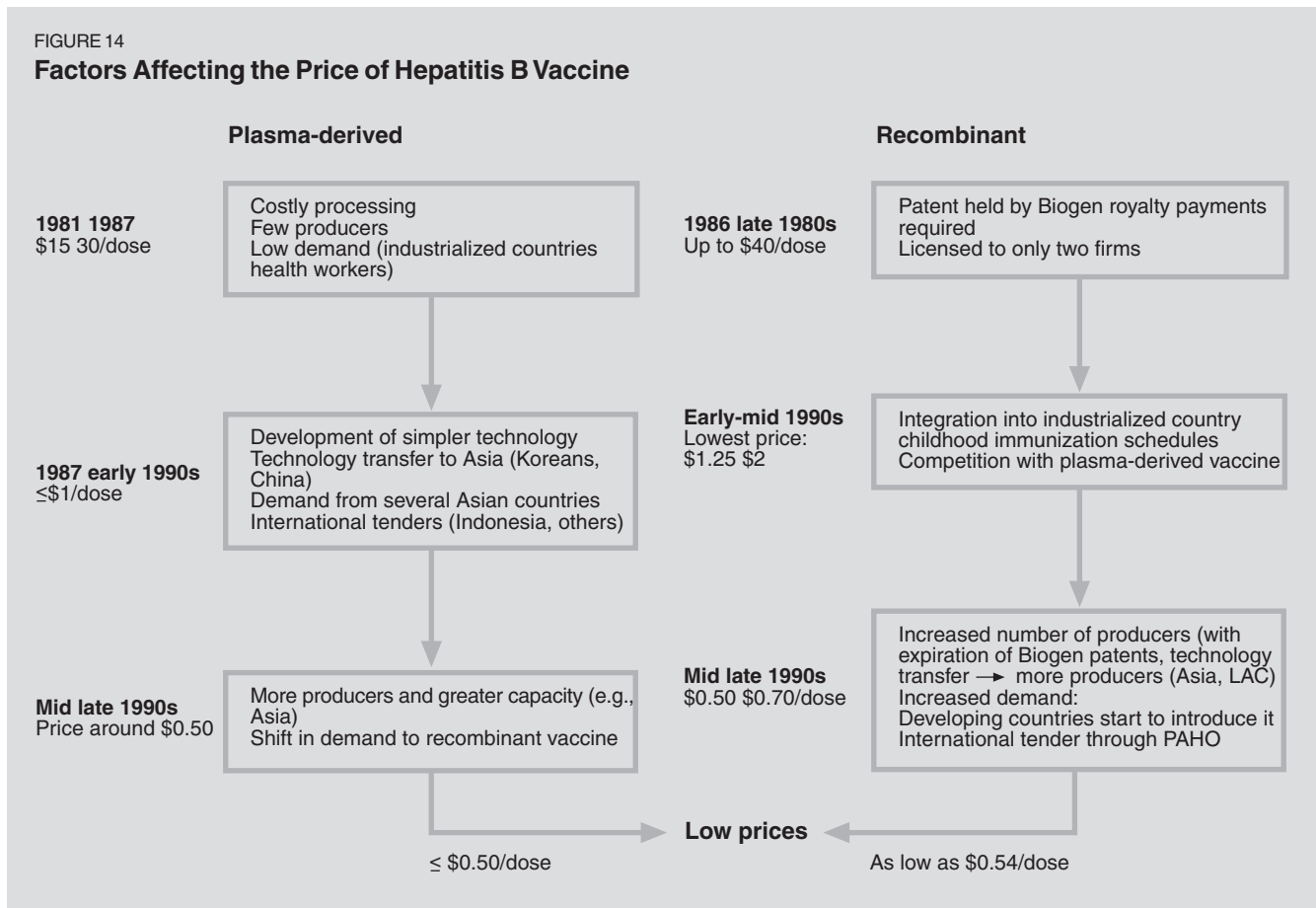
Summary

In summary, the price pattern for both plasma-derived and recombinant DNA Hepatitis B vaccine shows a sudden drop in price in the late 1980s, followed by a more gradual decrease over the next 10 years. The drop in price of the plasma-derived vaccine was due to a simultaneous increase in competition (and therefore capacity) from new manufacturers outside Europe and the US and an increase in demand, specifically from several Asian countries that held international tenders. The International Hepatitis B Task Force served as the catalyst for both demand- and supply-side forces.

While it took six years (1981–1987) for the price of plasma-derived vaccine to

FIGURE 14

Factors Affecting the Price of Hepatitis B Vaccine



dip below \$1, it took twice as long (1986–1998) for the price of the recombinant vaccine to drop to this level. The delay was due to high capital investment costs, limited competition (partly a result of the broad patent), and limited demand. The price of recombinant DNA vaccine is now declining fast, and approaching that of the plasma-derived vaccine.

The main factors affecting the price of the Hepatitis B are summarized in Figure 14.

Lessons learned

Some of the main lessons learned from Hepatitis B vaccine price trends over the years are:

- Simple and inexpensive production processes for effective vaccines must be developed. For example, the Prince plasma-derived vaccine using flash heat technology is as effective

as the vaccines using chemical processes, but much easier and cheaper to produce.

- Technology transfer to producers outside Europe and the US is critical to increasing competition and thus access to vaccines by developing countries.
- International tenders and bids have been effective in driving down prices, as long as there is enough competition.
- The patent on the technology used to make the recombinant DNA vaccine limited competitors from producing this vaccine for 10 years or so, keeping the price high. Innovative approaches, such as tiered royalties, need to be found to reduce the negative impact of intellectual property rights, including patents, on competition.

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